Proceedings Book

1st ECOP (European Conference of Oncology Pharmacy)

27–29 September 2012, Budapest, Hungary

Published as Supplement 1 to
European Journal of Oncology Pharmacy, Volume 6, 2012

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Proceedings Book

1st ECOP (European Conference of Oncology Pharmacy), 27-29 September 2012, Budapest, Hungary

European Journal of Oncology Pharmacy (EJOP) is the official Journal of the European Society of Oncology Pharmacy (ESOP).

SCOPE

The *European Journal of Oncology Pharmacy* (EJOP), published quarterly, sets out to offer a professional communication platform to European oncology pharmacy practitioners. As the official journal of ESOP, the scope of EJOP is to satisfy ESOP members' needs in terms of improvement on professional standard, setting guidelines, further education and sharing practice experience. EJOP offers ESOP members an insight into the differences and commonalities of oncology pharmacy standards and training, as well as the opportunities to learn the unique benefits and advantages from the different oncology pharmacy practitioners.

EJOP carries an editorial focus for providing information on current development in oncology treatment, sharing practice-related experiences as well as offering an educational platform via conference/meeting reports. The editorial content includes papers in the area of scientific, clinical, therapeutic, economic and social aspects. Prominent experts and eminent professionals support EJOP by sharing their original and qualitative knowledge and insight via high quality review papers covering drug break-throughs, developments in oncology treatment along with practice guidelines and educational topics which fall within the scope of oncology pharmacy practice.

EJOP is published quarterly and distributed to more than 3,000 oncology pharmacists, pharmacy technicians, subscribers and key opinion leaders in 33 countries and at major international and national conferences. EJOP is available online (www.ejop.eu).

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Letter of Welcome

On behalf of the European Society of Oncology Pharmacy (ESOP) and the Organising Committee, we warmly welcome you to the first European Conference of Oncology Pharmacy (ECOP), in the time-honoured city of Budapest, Hungary, 27–29 September 2012.

Close cooperation between oncology physicians and oncology pharmacists is essential for optimal patient care. ECOP 2012 offers a tremendous opportunity for exchange and debate between its 2,625 members, colleagues and partners worldwide.

The primary focus of this unique European Conference is to promote the highest standards of pharmaceutical care in the management and support of patients with tumours. The latest advances in research, patient management and practice are being showcased in keynote lectures, scientific symposia and poster sessions in two distinct tracks, clinical and practical.

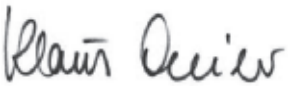
We know that a multi-professional, multidisciplinary approach in oncology will not only ensure economic use of resources but also significantly improve patient safety. For this reason, we are delighted that Professor Martine Piccart, President of the European Society for Medical Oncology, will participate in the Opening Lecture.

We would like to take this opportunity to invite you to the Opening Event held in the exhibition area of the Conference venue on Thursday 27 September 2012 from 18:15, providing you with the opportunity to meet colleagues from around the world, to network in a convivial setting and forge new links for future collaboration.

Lastly, but by no means least, our host city will match the exciting promise of the Conference itself. Speakers, participants, guests and friends should make time to discover the wonderful city that is Budapest with its wealth of historical buildings on both sides of the river Danube.

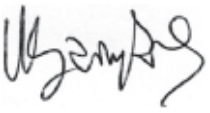
We trust that you will return from the Conference inspired by colleagues from around the world and that you will have made new friends and scientific contacts that will support you in your essential work.

We are delighted to be welcoming you to what promises to be a highly educational, collaborative and successful Conference.



Klaus Meier

ECOP Conference Chair



Mikael Daouphars

ECOP Scientific Chair

Conference Committees

Organising Committee

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Mikael Daouphars (France), Scientific Chair
Andreja Eberl (Slovenia), Organising Committee Co-Chair
Monika Kis Szölgyémi (Hungary), Organising Committee Co-Chair
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Camille Groos (Luxembourg)
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Adrián Munilla (Spain)	Marta Trojniak (Italy)

Acknowledgements and Accreditation Information

The European Society of Oncology Pharmacy wishes to thank the following companies and organisations for their support of the Conference by taking part in the exhibition.

Company	Booth number
Baxter Deutschland GmbH	A4-A5
BD Medical	A6
European Society of Oncology Pharmacy (ESOP)	A7
European CanCer Organisation (ECCO)	
Eurospital SpA	A2-A3
ICU Medical Europe	B1
Medac GmbH	A1
Mediware	A8
Nova Laboratories	B2
Sandoz	A9
Teva Pharmaceuticals	B3

Special thanks to GlaxoSmithKline for providing a Satellite Symposium.

Official Media Partner

On behalf of the ECOP Conference Committees, we would like to acknowledge the collaboration and support of our official media partner:

EJOP
European Journal of Oncology Pharmacy
Official Journal of the European Society of Oncology Pharmacy (ESOP)
www.ejop.eu

ECOP 2012 has been accredited by ACOE and the UEMS/EACCME

What does it mean for you?

The Accreditation Council of Oncology in Europe (ACOE) accreditation label provides delegates with a guarantee of a high quality and unbiased educational activity. ACOE accredited events are awarded an agreed number of CME credit points (1 CME credit per educational hour, 3 CME credits for a half-day, with a maximum of 6 credits per day).

ECOP 2012 has been granted European endorsement by the UEMS (European Union of Medical Specialists) and awarded a maximum of 12 hours of European Continuing Medical Education Credits (ECMEC). The Conference operates an honour system implying that each participant is expected to claim only those hours of credit that he/she actually spent at the Conference (with a maximum of 6 credits per day, 3 CME credits for a half-day).

ACOE works in conjunction with the European Accreditation Council for Continuing Medical Education (EACCME) operating under the umbrella of the UEMS. EACCME acts as a clearing house, facilitating the accreditation endorsement by the national CME regulatory bodies.

CME credits gained through participation at ECOP 2012 are recognised by most national CME authorities in Europe, which have agreed to cooperate in this European system. Through a mutual agreement between the UEMS and the American Medical Association (AMA), European CME credits are also recognised towards the Physician's Recognition Award (PRA). To convert European CME credits to AMA PRA Category 1 Credits please contact AMA at: www.ama-assn.org

www.acoe.be

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The first European Conference of Oncology Pharmacy (ECOP) is organised by ECCO, the European CanCer Organisation, on behalf of the European Society of Oncology Pharmacy (ESOP).

Conference Secretariat

c/o ECCO - the European CanCer Organisation
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E-mail: ecop2012@ecco-org.eu

Conference Venue

Novotel Budapest Conference
1-3 Jagelló út
HU-1123 Budapest
Hungary
www.bcc.hu

During the Conference, the Secretariat can be reached by:

Tel: +36 (0)361 372 5436 from outside the Novotel Budapest Conference. Tel: 7179 from within the Novotel Budapest Conference

Transportation from Budapest Ferihegy Airport to the Novotel Budapest Conference

Upon arrival at the airport a shuttle company 'Airport Shuttle-Minibusz' can be found in the arrivals terminal. A one-way shuttle to the Novotel Budapest Conference and nearby hotels costs approximately HUF 3,200 (€12). Taxis are also available, however, in order to avoid unpleasant surprises please verify the approximate costs with the driver before taking the taxi.

Public Transport

Budapest has a fairly extensive and efficient public transport system. It is cheaper than in most Western European cities. A wide variety of trams, buses, trolleys and metro trains run in the city. Tickets can be purchased at metro stations.

You may also want to consider purchasing a Budapest Card for the duration of your stay, allowing you to use all the lines of the BKV transport which include trams, trolley-buses, the Millennium Underground, metro lines, buses and the suburban railway (within the administrative boundaries). For further information, please ask at your hotel's front desk, tourism office or search for the Budapest Card online.

Badge

For security reasons, participants are requested to wear their badge at all times during the Conference.

Participants who lose their badge can obtain a replacement badge at the registration desk. A replacement fee of Euros 100 will be charged.

Catering

Lunch

Friday 28 September 2012 from 12:00 to 13:30: A complimentary lunch will be served in the exhibition area - Aula Hall

Coffee Breaks

Complimentary coffee breaks are served in the exhibition area – Aula Hall:

Thursday 27 September 2012 from 15:45 to 16:15

Friday 28 September 2012 from 10:00 to 10:30 and 15:00 to 15:30

Saturday 29 September 2012 from 10:00 to 10:30

Certificate of Attendance

Following accreditation approval by ACOE, ECOP 2012 has been granted European endorsement by the UEMS and awarded 12 European Continuing Medical Education Credits (ECMEC).

Certificates of attendance will be available at the registration area as of Friday 28 September 2012 from 15:00 onwards. Participants will be requested to complete a Conference evaluation form in exchange for their certificate.

The Conference Secretariat will not mail Certificates of Attendance to participants after the Conference. For information on CME accreditation see page 9.

Cloakroom

A cloakroom is available in the exhibition area – Aula Hall – and will be open:

Thursday 27 September 2012 from 10:00 to 20:00

Friday 28 September 2012 from 08:00 to 17:30

Saturday 29 September 2012 from 08:00 to 14:00

A charge of HUF 200 is applicable per item stored in the cloakroom.

Currency

The official currency in Hungary is the Hungarian Forint (HUF). Currencies can be exchanged in banks, hotels or exchange offices. International credit cards are accepted in most hotels, restaurants and shops.

Exhibition

The exhibition is held in the Aula Hall.

Exhibition opening hours:

Thursday 27 September 2012 from 15:00 to 19:30

Friday 28 September 2012 from 10:00 to 17:00

Saturday 29 September 2012 from 08:30 to 12:00

For a list of exhibitors, see page 14–15.

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www.ejop.eu

First Aid

A first aid room is located behind the Patria Hall stage.

Insurance

The organisers of ECOP 2012 do not accept liability for individual medical, travel or personal insurance. Participants are strongly recommended to obtain their own personal insurance coverage. The organisers disclaim all responsibility for loss due to theft or negligence.

WiFi Access

Free WiFi is available throughout the Conference venue.

Username: ECOP

Password: Budapest

Language

The official language of the Conference is English. No simultaneous translation is offered during the Conference.

Lost and found

All enquiries should be directed to the reception desk of the Novotel Budapest Conference centre.

Participants are advised to mark their Conference bag and materials with their name. The organisers disclaim all responsibility for loss due to theft or negligence.

Non-smoking

There will be a strict non-smoking policy within all areas of the facilities used by the Conference.

Opening Lecture

The Opening Lecture access is free for all registered participants. Please refer to the Scientific Programme for further details.

Poster Sessions

Posters are displayed in the Mirror Corridor and Bartok Corridor.

Posters will be on display in the dedicated poster area for the entire duration of the conference and during all poster sessions.

On Thursday 27 September 2012 starting at 12:00, poster presenters will be allowed access to the poster area to mount their poster on the poster board displaying their assigned poster number. For assistance, please check with the ECOP staff onsite.

Posters must be removed on Saturday 29 September 2012 by 13:30. Please note that any posters remaining after this time will be removed by the organisers and cannot be reclaimed.

Presenting authors are kindly requested to be present at their poster for poster defense during assigned poster viewing and coffee breaks.

Best Poster Award

The Best Poster Award recognises outstanding posters presented at ECOP 2012. All posters will be evaluated by a committee and the winner will be notified during the conference. The award will be presented in the Closing Session. The winner must reconfirm his/her presence at the conference and at the ceremony.

Registration

The Conference is open to all registered participants. For security reasons, participants are requested to wear their badges at all times.

Registration opening hours:

Thursday 27 September 2012 from 09:30 to 19:30
Friday 28 September 2012 from 08:00 to 17:00
Saturday 29 September 2012 from 08:00 to 13:30

The registration package includes:

- Entry to all scientific sessions and exhibition
- Entry to all Satellite Symposia organised during the conference
- Proceedings book
- Official Lunch and coffee breaks during the Conference
- Conference bag
- Attendance at the Opening Event on Thursday 27 September 2012 at 18:15 in the exhibition area

Speaker Preview Room

The Speaker Preview Room is located in the Brahms room.

Speakers are requested to bring their PowerPoint presentations to the Speaker Preview Room at least four hours before their session starts or one day in advance if the session starts early in the morning. To ensure the smooth running of the sessions and avoid lengthy breaks in between speakers, the use of laptops in the session rooms is actively discouraged.

Opening Hours:

Thursday 27 September 2012 from 09:30 to 19:30
Friday 28 September 2012 from 08:00 to 16:30
Saturday 29 September 2012 from 08:00 to 13:00

Satellite Symposia

Satellite Symposia are taking place during ECOP 2012. For schedules and more information, see the section 'Satellite Symposia' on page 16.

Social Media

Twitter is available during the conference – tweet, network, and follow updates at #ECOP2012.

Networking Events

Opening Event

All delegates are invited to join the Organising Committee and ESOP Board at the Opening Event in the exhibition area of the Conference venue on Thursday 27 September 2012 from 18:15 to 19:30. This is your chance to meet colleagues from around the world, to network in a convivial setting and forge new links for future collaboration.

European Society of Oncology Pharmacy (ESOP)

The European Society of Oncology Pharmacy, founded in 2000 in Prague, Czech Republic, is the largest organisation of oncology pharmacists in the world with 2,625 members from 43 countries.

Aim and Objectives

ESOP supports optimal treatment for cancer patients with objectives to develop and promote clinical and oncology pharmacy practice through:

1. Education and training;
2. Safe handling and administration of drugs;
3. Quality management;
4. Research and development;
5. Pharmaceutical care.

The Oncology Team – Cooperation

The pharmacy as coordinator of Centre of Cytotoxic Therapy implements quality management of oncology pharmacy services and takes responsibility in patient care and personnel protection regarding all areas of cytotoxic therapy. The pharmacy collects and processes all medical and toxicological data relevant to cytotoxics, as well as supportive measures. Focusing on cytotoxic treatment alone is not enough. We also need to focus on appropriate diet, adequate analgesic medication and correct anti-emetic scheme, and we cannot ignore the social and psychological needs of the patient.

Financial resources have become limited, and it is necessary to intensify our services to increase cost-effectiveness, to ensure adequate treatment and to prevent quality loss.

Ljubljana Declaration 2006

'The close cooperation between oncology physicians and oncology pharmacists is vital for optimal patient care. The multi-professional approach will deliver best practice to patients within a clinical governance framework. Professional, close and timely collaboration will ensure economic use of resources and improve patient safety.'

Our Goals: Quality Standards, Continuous Education and Certification

The fourth edition of *Quality Standards for the Oncology Pharmacy Service* (QuapoS) – translated into 24 languages – presents changes with respect to the position of our service. They are used for standardisation of national principles and to speak with one voice in Europe. The beneficiary of these efforts will always be the patient.

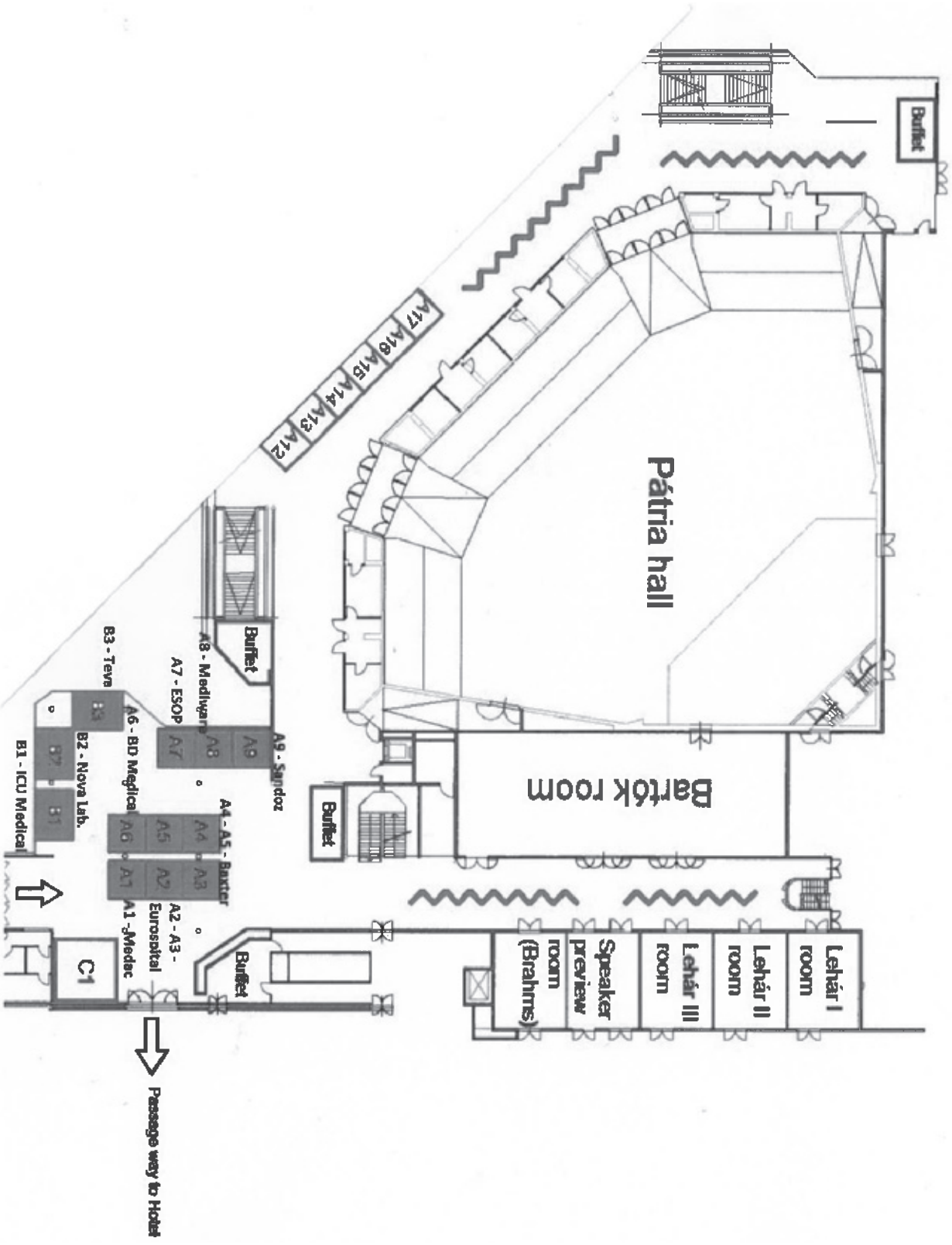
Specific Activities

The ESOP Masterclass in oncology pharmacy practice is an event providing continuing education in oncology for hospital pharmacists, whose duties require expertise on cytotoxic drug preparation, handling and administration including risk management. It is also for clinical pharmacists, so they can give patients the best possible care and support. The *European Journal of Oncology Pharmacy* (EJOP), published by Pharma Publishing and Media Europe, was launched in 2007 to satisfy these needs.

www.esop.eu

Floor Plan

Venue and Exhibition Floor Plan



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List of Exhibitors and Exhibitor Profiles

Exhibitor Name	Booth Number
Baxter Deutschland GmbH	A4-A5
BD Medical	A6
European Society of Oncology Pharmacy (ESOP)	A7
European CanCer Organisation (ECCO)	
Eurospital SpA	A2-A3
ICU Medical Europe	B1
Medac GmbH	A1
Mediware	A8
Nova Laboratories	B2
Sandoz	A9
Teva Pharmaceuticals	B3

Baxter Deutschland GmbH — A4-A5

Baxter International Inc., through its subsidiaries, develops, manufactures and markets products that save and sustain the lives of people with haemophilia, immune disorders, infectious diseases, kidney disease, trauma, and other chronic and acute medical conditions. As a global, diversified healthcare company, Baxter applies a unique combination of expertise in medical devices, pharmaceuticals and biotechnology to create products that advance patient care worldwide.
www.baxter.com

BD Medical — A6

BD is a leading global medical technology company that develops, manufactures and sells medical devices, instrument systems and reagents. The Company is dedicated to improving people's health throughout the world. BD is focused on improving drug delivery, enhancing the quality and speed of diagnosing infectious diseases and cancers, and advancing research, discovery and production of new drugs and vaccines. BD's capabilities are instrumental in combating many of the world's most pressing diseases. Founded in 1897 and headquartered in Franklin Lakes, New Jersey, BD employs approximately 29,000 associates in approximately 50 countries throughout the world. The Company serves healthcare institutions, life science researchers, clinical laboratories, the pharmaceutical industry and the general public. For more information, please visit www.bd.com/uk

ECCO – the European CanCer Organisation

The European CanCer Organisation (ECCO) represents the interests of over 50,000 oncology professionals. It drives multidisciplinarity in the field and connects the European cancer community by leveraging knowledge, promoting education and building awareness. ECCO also proactively engages with policymakers to promote the interests of cancer research, cancer patients and all other oncocommunity members.
www.ecco-org.eu

Eurospital SpA — A2-A3

Eurospital, active since 1948, is an industrial and commercial reality leader in its reference markets with pharmaceutical products, medical devices and *in vitro* diagnostic systems.

The Hospital Division is active in the sector of prevention of chemical hazards in the hospital environment and develops solutions to improve the safety level for patients and healthcare workers thus contributing to limit the total operating costs in hospitals.

We are proud to introduce our new Integra system designed for the automation and tracking of the compounding of antineoplastic agents.

GSK

GSK Oncology is dedicated to the patients, physicians and communities pursuing the fight against cancer. At GSK Oncology, what defines us is our pledge to engage and work in concert with our communities. At GSK Oncology, our portfolio of medicines represents a heritage spanning more than five decades. Whether you are a physician, researcher, or patient, we aspire to know how GSK Oncology might engage with you in fighting the global pandemic known as cancer.

ICU Medical Europe — B1

ICU Medical Inc (headquartered in San Clemente, California, USA) develops, manufactures and sells innovative medical technologies used in vascular therapy, oncology and critical care applications.

We connect patients and caregivers through safe, life-saving, life-enhancing medical devices and provide clinicians around the world with innovative and cost-effective patient care solutions for unmet clinical needs.

Our products help clinicians improve patient outcomes by helping prevent bloodstream infections and help protect healthcare workers from exposure to infectious diseases or hazardous drugs.

ICU Medical's diverse product line includes needlefree vascular access devices, custom infusion sets, closed system hazardous drug handling devices and systems, advanced sensor catheters, needlefree closed blood sampling systems and innovative hemodynamic monitoring systems.

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These clinically-proven innovations are the result of a unique company culture, supported by visionary leaders and resourceful minds, united by the common desire to redefine the limits of patient and healthcare worker safety.

In the field of oncology, ICU Medical provide trusted solutions for the safe handling of hazardous drugs.

ICU Medical have set a new standard in accuracy, safety and efficiency for the safe preparation, reconstitution and delivery of hazardous drugs with their User-controlled Automated Compounding System—Diana™.

Like all of ICU Medical's oncology products – the Diana system is needlefree, easy to use, generates less biohazardous waste and costs significantly less than other automated compounding systems. Diana™ also reduces the risk to pharmacists and technicians of repetitive strain injuries.

To learn more visit ICU Medical on Stand B1 at ECOP.
www.icumed.com

Medac GmbH **A1**

Medac has specialised in the treatment of malignant diseases since its foundation in 1970. Now, Medac is one of the leading manufacturers of oncology products not only in Germany, but in many international markets. Medac offers both, innovative and well proven, therapeutic options in the fields of oncology, haematology, urology, autoimmune diseases and fibrinolysis and is one of a handful of companies which is also specialised in the field of diagnostics.

Mediware **A8**

Mediware is a leading provider of specialised healthcare solutions with over four decades of experience in developing and delivering innovative software designed to ensure the highest level of safety and efficiency.

We take complex—and often inefficient—clinical processes and automate them. Our software solutions are designed to make things easier and more cost effective for you while eliminating the opportunities for errors so your patients are safer too.

Mediware is building on a strong history of leadership in Blood, Biologics and Medicines Management by expanding into Chemotherapy and Cellular Therapy Solutions. Developed by experienced clinicians, our software fully integrates complex components of therapy in safe and specialised systems.

Chemotherapy Management System (CMS) software supports all professionals within hospitals to prescribe, plan, produce and administer chemotherapy drugs. Our mission is to improve the quality of chemotherapy with reliable information technology using a dynamic process to support and enable an efficient workflow.

CMS is accessible through a web portal which means that prescribing and the administration are integrated seamlessly with other systems such as the Electronic Patient File. The work flow process is automated in CMS which enables the doctor, pharmacist and nurse to monitor the whole procedure of care including, prescribing, preparation and administration of cytostatic drugs.

Today, more than 1,500 prestigious healthcare organisations across the US, Canada, the UK and Europe use our innovative, best-of-breed technologies and services. They include organisations of every size and complexity.

Sandoz **A9**

Sandoz, a Division of the Novartis group, is a global leader in the field of generic pharmaceuticals, offering a wide array of high quality, affordable products that are no longer protected by valid and enforceable third-party patents. Sandoz has a portfolio of approximately 1,000 compounds and sells its products in about 130 countries. Sandoz develops, produces and markets these medicines along with pharmaceutical and biotechnological active substances. In 2011, Sandoz employed more than 24,000 people worldwide and posted sales of US$9.5 billion.

Teva Pharmaceuticals **B3**

Teva is a global generic pharmaceutical leader and one of the top fifteen pharmaceutical companies in the world. Teva specialises in the development, production and marketing of a wide range of generic and branded products, as well as active pharmaceutical ingredients (API).

Headquartered in Israel, Teva operates in 60 countries, distributes its products in over 100 markets and has more than 47,000 employees worldwide. Established in 1901, Teva takes great pride in its long tradition of leadership and dedication to excellence.

At the very heart of Teva's mission is the commitment to develop and manufacture high quality, safe products that promote global good health and well-being.

With 60 billion tablets manufactured yearly, a portfolio of 1,250 molecules and 2,500 prescriptions per minute, we are able to link the healthy growth of our company to better patient care and enhancement of patient well-being.

Friday 28 September 2012

Satellite Symposium: *GlaxoSmithKline*

The Pharmacist's Role in Managing mRCC Patients on Votrient®

12:30 – 13:30 Room Lehár

Workshop overview

The workshop is part of a dedicated programme aimed at supporting oncology pharmacists through the metastatic renal cell carcinoma (mRCC) patient journey. The session will be focused on reviewing a patient case study in an interactive manner using voting pad technology. Attendees will have the opportunity to discuss practical side effect management tips during the Q&A session.

Workshop objectives

1. Identify the key decision points undertaken by pharmacists across the patient journey
2. Provide practical advice on the role of the clinical pharmacist in the management of mRCC patients on Votrient®, including monitoring and management of diarrhoea, hypertension and liver enzyme elevation
3. Share practical tips with colleagues from other hospitals and countries

Faculty

Chairman – ***Professor Klaus Meier***

Co–Chair – ***Navin Joshi (GlaxoSmithKline)***

Speakers Panel – ***Professor Alain Astier, Maria Jose Tames, Franca Goffredo***

Agenda

TIME	TOPIC	Faculty role
12:30	Welcome note	*Klaus Meier*
12:40	Join the patient journey – What do you need to know about Mr. D.C.? – What is the rationale behind his treatment selection? – How would you manage his cardiovascular & gastrointestinal adverse events? – How would you manage his liver enzyme elevation?	*Alain Astier*
13:05	Challenge the Panel – Q&A to the faculty and open discussion with the audience	*Panel*
13:15	Multidisciplinary care in practice	*Maria Jose Tames*
13:25	Key learnings	*Klaus Meier*
13:30	End of session	

Programme Overview: ECOP 2012

Please note that this Programme Overview is provisional and therefore subject to change. For all the latest updates please visit: www.ecco-org.eu

Thursday, 27 September 2012

Room "Bartók"	Room "Lehár "
Opening 14.00 - 15.00	
Keynote lecture 15.00 - 15.45	
Coffee break 15:45 - 16:15	
New Horizons Practical 16:15 - 17:15	Clinical interactive session 16:15 - 17:15
New Horizons Clinical 17:15 - 18:15	Practical interactive session 17:15 - 18:15
OPENING EVENT 18:15 - 19:30	

Poster Viewing 15:00 - 19:30

Exhibition 15:00 - 19:30

Friday, 28 September 2012

Room "Bartók"	Room "Lehár "
Symposium - Clinical 08:30 - 10:00	Proffered papers - Practical 08:30 - 10:00
Coffee break 10:00 - 10:30	
Symposium - Practical 10:30 - 12:00	Proffered papers - Clinical 10:30 - 12:00
Lunch / Poster viewing 12:00 - 13:30	
Poster Discussion - Basic Research 12:00 - 13:30	GlaxoSmithKline - Satellite Symposium 12:30 - 13:30
Debate Clinical / Practical 13:30 - 15:00	
Coffee break 15:00 - 15:30	
Interactive - Practical 15:30 - 17:00	Interactive - Clinical 15:30 - 17:00

Poster Viewing 10:00 - 17:00

Exhibition 10:00 - 17:00

Saturday, 29 September 2012

Room "Bartók"	Room "Lehár "
Meet the Expert: Practical Cases 08:30 - 10:00	Poster discussion - Clinical 08:30 - 10:00
Coffee break 10:00 - 10:30	
Meet the Expert: Clinical Cases 10:30 - 12:00	Poster discussion - Practical 10:30 - 12:00
Closing Session / Patient Advocates Message / Plenary Lecture 12:00 - 13:30	

Poster Viewing 08:30 - 12:00

Exhibition 08:30 - 12:00

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Thursday 27 September 2012

Opening Session

14:00 - 15:00 Room Bartók

Abstract Nr

14:00 **Welcome Message from the President of ESOP**
Speaker: K Meier (Germany)

14:15 **Personalized Anticancer Therapy: Dream or Reality?**
Speaker: MJ Piccart-Gebhart (Belgium) 1

Keynote Lecture

15:00 - 15:45 Room Bartók

Abstract Nr

Chair: K Meier (Germany)

15:00 **Medical Oncology - Past, Present, Future - A Personal Experience**
Speaker: DK Hossfeld (Germany) 2

Practical Session: New Horizons - Which Stability Data can we Rely on and how are They Done?

16:15 - 17:15 Room Bartók

Abstract Nr

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Thursday 27 September 2012

Opening Session

1 Personalised Anticancer Therapy: Dream or Reality?

MJ Piccart-Gebhart[1]

[1]*Institut Jules Bordet, Brussels, Belgium*

Over the past decade, the complete sequencing of the human genome and the advent of high-throughput processing methods have produced landmark advances in our ability to characterise molecular alterations in individual cancers and unravel the key biological drivers of human malignancy. Previously, researchers could only investigate a single biomarker in isolation, using techniques that were cumbersome, time-consuming, and of limited statistical power to detect association with disease outcome.

This rapid pace of technological and biological discovery, however, has not been matched by commensurate gains in cancer treatment. Current drug testing is inefficient, with too many drugs failing late in the development.

There is also a great concern, particularly in early breast cancer, that many women are prescribed adjuvant chemotherapy while they would be cured by loco-regional therapy with or without endocrine therapy.

TRANSBIG, the translational research network of the Breast International Group (BIG), launched a research programme in 2004 that initially focused mainly on improving tools to evaluate breast cancer prognosis. Within this programme it was initially demonstrated that different gene expression prognostic signatures had similar prognostic performance, outperforming the currently used risk assessment tools such as Adjuvant! Online or algorithms for treatment decision making, such as those provide by the St Gallen consensus expert panel. As a next step, the MINDACT trial was designed and has recruited more than 6,600 women in order to provide level I evidence for the utility of the 70-gene classifier (MammaPrint by Agendia) in routine clinical practice.

In patients who need therapy in view of a high risk of relapse, choosing the best treatment at an individual level remains very challenging.

The traditional model of establishing initial activity in unselected patients with advanced refractory disease with subsequent retrospective biomarker discovery and validation in the adjuvant setting has failed to establish targeted drugs that can be optimally used in the clinic. As a result, efforts are underway to move the discovery and validation of predictive biomarkers into earlier phases of drug development in the neoadjuvant setting. The NeoBIG programme is being developed by the Breast International Group (BIG) to accelerate biomarker discovery and drug development in early breast cancer. Under this platform, a series of neoadjuvant randomised phase II clinical trials (each with 300–600 patients) will be concomitantly launched to evaluate promising novel targeted therapies in different molecular breast cancer subtypes. These studies will integrate emerging technologies, such as genomics, proteomics, metabolomics, pharmacogenetics and functional imaging, to develop predictive markers of efficacy that can be validated in a subsequent adjuvant registration trial.

Keynote Lecture

2 Medical Oncology - Past, Present, Future - A Personal Experience

No abstract submitted.

Practical Session: New Horizons - Which Stability Data can we Rely on and how are They Done?

3 Practical Stability Studies - A Powerful Approach to Decrease the Cost of Monoclonal Antibodies

A Astier[1], M Paul[1], V Vieillard[1]

[1]*Henri Mondor Hospital Group APHP, Pharmacy Department, Creteil, France*

Introduction: Stability studies performed by the pharmaceutical industry are only designed to fulfil licensing requirements. Thus, post-dilution or -reconstitution stability data are frequently limited to 24 hours only for bacteriological reasons regardless of the true chemical stability which could, in many cases, be longer. In practice, the pharmacy-based centralised preparation may require infusions to be made several days in advance to provide, for example, the filling of ambulatory devices for continuous infusions or batch preparations for dose banding. Furthermore, a non-justified limited stability for expensive products is obviously very costly. Thus, there is a compelling need for additional stability data covering practical uses of anticancer drugs. A European consensus conference was held in France, May 2010, under the auspices of the French Society of Oncology Pharmacy (SFPO) to propose adapted rules on stability in practical situations and guidelines to perform corresponding stability studies (Bardin C, Astier A, Vulto A, et al. Ann Pharm Fr. 2011;69:221-31).

For therapeutic proteins, especially for monoclonal antibodies (mAbs), practical stability studies are fundamental considering their very high cost. Therefore, any lost due to inappropriate stability data will induce unacceptable waste of resources.

Material and methods: Since several years we have performed studies on the stability of mAbs in practical situations: influence of storage temperature, dilution and exposure to mechanical stresses. The influence of temperature was estimated on bevacizumab, cetuximab, trastuzumab and rituximab. The influence of the use of pneumatic network has been evaluated on trastuzumab The physical and chemical stability of these complex molecules was fully investigated using validated several complementary method: size-exclusion and ionic chromatography, peptide mapping, turbidimetry, second-derivative UV and IR spectroscopy, turbidimetry, diffusion-laser spectroscopy, thermal-induced aggregation curves. In some case, the biological activity was estimated.

Results and discussion: We have demonstrated that cetuximab and bevacizumab are stable after dilution stored in their final bags (polypropylene) at 4°C for more than 3 months and more than 1 month at 37°C. Similarly, we have demonstrated that rituximab (600 mg/500 mL propylene bag in NaCl) is stable for more than 6 months at 4°C. Trastuzumab is not modified until 3 entire cycles in the pneumatic network.

Conclusion: These results permitted us to propose dose banding and in advance batch preparation for rituximab which have optimised workload at the pharmacy level and induced important money saving (up to Euros 100,000/years). These results justify also the safe use of bags accidentally exposed to room temperature in case of rupture of the cold chain, i.e. dysfunction of fridge during a week. Finally, our results indicate that mAbs exhibit an acceptable stability in most of the practical situations they encounter.

4 Obtaining Valid Stability Data for Cytotoxics - An International Matter

I Larsson[1]

[1]*Amgros, The Danish Research Unit for Hospital Pharmacy, Copenhagen Ø, Denmark*

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Traditionally the compounding of cytostatics was done just before the patient was given the drug. Today cytostatic compounding is undertaken by hospital pharmacies and here increasing workload has urged the needs of technology in forms of robots and semi-automated solutions and batch production with corresponding requirements for extended stability data.

Taking the compounded cytostatics into this new cycle of lifetime stresses the need for extended stability data. In Denmark and other European countries, this challenge often is solved by using a mix of information consisting of: information provided by the companies; information from literature and websites; and information given in the Summary of Product Characteristics (SPC).

We have examined these sources of prolonged stability data. We have evaluated 150 SPCs for 13 cytostatics regarding available information of how to handle the compounded product. Dialogue with 14 suppliers of cytostatics was conducted to identify their views on expanding the SPC information on shelf lives to include extended shelf lives of compounded products and a literature review for stability data on 4 of the 13 cytostatics has been performed.

Our analysis showed that often information on shelf life stated in the SPC is very short and sparse in basic information regarding the compounded product. The dialogues with the companies revealed that longer shelf lives will probably not be stated in the SPCs, and the literature review revealed very different stability data. The conclusion is that none of this kind of information can be applied as documentation for extended shelf lives and it is crucial to document the extended stability oneself. To prevent all countries from spending lots of resources on performing identical stability studies a better solution would be to coordinate the generation of reliable stability data of cytotoxics based on common guidelines.

Clinical Interactive Session: The age of Oral Chemotherapy - A Time of Opportunities and Responsibilities for Oncology Pharmacists

5 Oral Chemotherapy - Confronting Theory to Reality

No abstract submitted.

6 Enhancing Adherence to Oral Chemotherapy

U Jaehde[1], L Krolop[1], S Simons[1], S Ringsdorf[1]

[1]*Institute of Pharmacy, Clinical Pharmacy, University of Bonn, Germany*

Introduction: Efficacy of orally administered chemotherapy depends on a high level of patient adherence. In our group we have developed a multidisciplinary pharmaceutical care programme to enhance the adherence of cancer patients treated with capecitabine, a prodrug of fluorouracil, used in the treatment of colorectal and breast cancer patients.

Patients and methods: Adherence to capecitabine chemotherapy was measured in two prospective observational cohort studies using an electronic medication event monitoring system (MEMS®). In the first study, 48 patients participated: 24 patients received standard care (control group), whereas the other received multidisciplinary pharmaceutical care consisting of written and spoken information (intervention group). To utilise the limited resources in health care most efficiently we designed a second study dividing the patients into two groups based on measured adherence during the first cycle. Initially non-adherent patients (adherence < 90%) received the specific intervention, whereas initially adherent patients (adherence ≥ 90%) were only monitored to reveal whether they remained adherent during the entire course of their chemotherapy.

Results and discussion: In the first study, patients in the intervention group exhibited an enhanced but not significantly different mean overall adherence compared to the control group (97.9% vs 90.5%, p = 0.069). Mean daily adherence was significantly higher in the intervention group (96.8% vs 87.2%, p = 0.029). Variability of both adherence parameters was considerably reduced when pharmaceutical care was provided. At the end of the observation period of 126 days, the probability of still being treated with capecitabine was found to be 48% in the control group and 83% in the intervention group (p = 0.019, log-rank test). Patient recruitment for the second study has recently been finished, data analysis is still ongoing.

Conclusion: The development of an adherence monitoring and enhancing infrastructure is a necessary prerequisite to exploit the full potential of oral chemotherapy. The provision of multidisciplinary pharmaceutical care can enhance adherence to capecitabine. However, not every patient is in need of an adherence-enhancing intervention. Screening systems detecting potential non-adherers would support the rational utilisation of the required resources.

This work was published in part in Support Care Cancer. 2011;19(7):1009-18.

Clinical Session: New Horizons in Cancer Treatment

7 What is the Right Timing for Antineoplastic Therapy

K Geissler[1]

[1]*Krankenhaus Hietzing, Onkologie, Vienna, Austria*

An enormous number of clinical studies are demonstrating the efficacy and toxicity of antineoplastic therapy in cancer patients, however, the number of studies investigating the right timing of chemotherapy is limited. Therefore the question with regard to the right moment to start and to stop cytotoxic treatment remains an important issue for the scientific discussion. There is solid evidence from randomised trials in breast and bladder cancer, that neoadjuvant chemotherapy is feasible, that it is not associated with increased operative morbidity and that the outcome in patients having received pre-operative chemotherapy is not inferior as compared to patients who were treated post-operatively with the same regimen. In colon cancer patients who are candidates for adjuvant antineoplastic therapy delay of chemotherapy for more than 3 months is consistently associated with worse outcome in retrospective analyses. In breast cancer patients, delay of adjuvant chemotherapy was generally not associated with worse outcome in the majority of studies. Early adjuvant chemotherapy (within 3 weeks), however, may be of benefit in premenopausal ER-patients, and delay for > 4.8 months may have a negative effect on the outcome. There are data in colorectal cancer patients showing that there is no benefit in continuing adjuvant chemotherapy for more than 6 months. In the palliative setting of various cancer entities there is little if any evidence from randomised trials and meta-analyses that early treatment in asymptomatic patients may improve overall survival (OS). Stopping chemotherapy after 12 weeks and restarting treatment on progress has been demonstrated to decrease toxicity without compromising OS in patients with metastatic colorectal cancer without increased platelet counts. Also in breast cancer patients maintenance chemotherapy following induction chemotherapy does not improve OS but increases toxicity in the palliative setting.

8 Therapeutic Drug Monitoring (TDM) in Clinical Oncology - The Pros and Cons

H-P Lipp[1]

[1]*University of Tübingen, Clinical Pharmacy, Tübingen, Germany*

Therapeutic Drug Monitoring (TDM) has been established as an essential tool during the use of defined drugs such as several anticonvulsant,

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antimicrobial, antifungal or psychoactive agents. Based on defined therapeutic windows, the risk for either sub- or supra-therapeutic, highly toxic drug levels can be clearly minimised by TDM.

Pros: Most cytotoxic anticancer drugs have revealed to present a narrow therapeutic index in clinical oncology, however, besides high-dose methotrexate, no other agents undergo routine TDM in clinical practice, although the potential advantages appear to be obvious: (1) reduction of acute, subchronic or even chronic drug-related adverse effects; (2) optimisation of clinical response by avoidance of subtherapeutic drug levels in time; (3) feasibility to get more precise insights regarding (I) potential drug distribution into tumour-infiltrated deeper compartments, or (II) clinical pharmacokinetic drug behaviour in selected conditions (e.g. extreme obesity, dialysis, severe hepatic dysfunction); or (4) improved engraftment after reinfusion of peripheral blood stem cells when persistent cytotoxic drug levels could be excluded in individual patients; and (5) in addition, physicians might get more insight by TDM in respect to patient`s non-adherence or unsuspected drug interactions, e.g. sunitinib and green tea or irinotecan and smoking.

Cons: The reasons why TDM plays still a neglectable role in routine clinical oncology practice are multifactorial and primarily based on the following reasons: (1) the absence of commercially available test kits which allow rapid measuring of drug levels at an acceptable cost level; (2) the difficulty to clearly define substance-specific therapeutic windows which may vary from tumour type to tumour type; (3) the difficulty to define the target agents which have to be measured, e.g. if prodrugs are used; (4) limited message for overall tumour response when the probability of response may be reflected in more detail by intratumoural circumstances, e.g. drug resistance phenotype, rather than plasma levels; (5) the lack of prospective clinical trials highlighting the significant advantages to TDM; and (6) the ongoing availability of new drugs in clinical oncology which may favour the use of novel mechanisms of action rather than TDM-guided older treatment protocols.

Perspectives: There are increasing scientific interests to bring TDM or related strategies, e.g. genotyping or phenotyping of individual drug metabolism profiles, more forward in the near future. Current examples include challenges: (1) to maintain 5-FU drug levels between 2–3 mg/mL in order to improve the probability of response and tolerability; (2) to focus on imatinib levels of at least 1 mg/mL; or (3) to implement TDM for several TKI to learn more about intra- and inter-individual variability, e.g. in case of concomitant food intake.

In conclusion, pharmacists should be familiar with pro and contra arguments in respect to TDM in clinical oncology. In addition, there is increasing evidence that TDM-guided cytotoxic and targeted tumour therapy appears to be beneficial for the patient when substance-related therapeutic windows have been defined in more detail.

Practical Interactive Session: Extended Stability of Anticancer Drugs - The Dream Become a Reality?

9 Extended Stability of Rituximab, Bortezomib and Azacitidine - Application in the Daily Practice in Haematology

J Vigneron[1]

[1]*CHU Nancy - Hôpital de Bradois, Pharmacy Department, Vandoeuvre les Nancy, France*

Introduction: Rituximab (Mabthera®), bortezomib (Velcade®) and azacitidine (Vidaza®) are used for the treatment of haematologic diseases and mainly administered to outpatients. The timely provision of chemotherapy is a constant challenge for hospital pharmacy aseptic units. Our objective was to diminish or eliminate the waiting time of the patient by preparing chemotherapy in advance. This objective needs long-term stability data of the 3 drugs.

Material and method: For rituximab we used the results of a stability study performed by Astier et al. with a 6-month stability for the infusions. For bortezomib and azacitidine we carried out two long-term stability studies.

Results and discussion: By using validated stability indicating High Performance Liquid Chromatography methods, we demonstrated a 35 days stability for the 1 mg/mL bortezomib solution in polypropylene syringes stored at 4°C and a 8-day stability for the 25 mg/mL azacitidine suspensions in polypropylene syringes stored at –20°C.

For the three drugs we obtain the prescriptions in advance. With the agreement of the prescribers, the doses are standardised: 600, 660, 720, 780 and 840 mg for rituximab, 1.6, 1.8, 2.0, 2.2, 2.4 and 2.6 mg for bortezomib and 55, 60, 65, 70 and 75 mg for azacitidine. Doses outside these scales or products for clinical trials (around 20%) are not prepared in advance but on the day of the administration and according to the body surface area calculations.

Azacitidine syringes are thawed for 45 minutes at room temperature every morning at 09:00 and sent to the ward at 10:00 in a refrigerated container with an expiry time at 17:00. This standardisation allows the reuse of the preparation if the dose is cancelled or postponed. This re-labelling is done according to a written procedure in accordance with the ISOPP standard of practice (Chapter 20). However, the thawed azacitidine syringes cannot be reused.

Conclusion: These long-term stabilities allow the preparation in advance with many advantages:

- waiting time of the patient diminished or eliminated
- preparation during the afternoon
- decrease the stress on the pharmacy staff
- enhance the organisation of the nursing staff
- save money.

10 Benefits of Extended Drug Stability and Compatibility Data in Clinical Practice

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Introduction: For preparing cytostatic drugs, stability data are required. Beside the SPC, extended stability and compatibility data are available in the scientific literature. If a microbiological validation and matching stability data are available, longer shelf life can result in a more economic preparation. This can be a benefit for the hospital pharmacies, the patients, the authorities, the health insurance funds, the scientists, the manufacturers and the environment.

At the University Medical Center Freiburg more than 1,000 cytostatic preparations/week were produced. The extended stability data play an important role for economic preparation. We also perform stability and compatibility studies in our laboratory and publish them in the scientific literature and the stabilis database. Respectively, it was interesting to know how other pharmacies are dealing with stability data in their clinical practice.

Material and methods: To explore the view of the German hospital pharmacies on extended stability studies a systematic survey was conducted. For this purpose a questionnaire with demands about the clinical practice with extended stability data was sent by email to 407 hospital pharmacies in Germany. About 10 days later we phoned the pharmacies as a reminder to answer the questionnaire.

Results and discussions: We obtained finally the answers of 105 (= 25.8%) hospital pharmacies. More than 90% of them are working with extended stability data, only 8.3% use only the SPC. These pharmacies have a very small production and longer shelf life would not result in an economic benefit. All others use extended stability data

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and the limit of stability often is the period of the microbiological validation. As the SPC provides the highest level of legal security, it is important not to lower it by using extended stability data. For this purpose, besides extended stability data sheets of the manufacturers, guidelines for the practical stability studies of anticancer drugs can be helpful.

Other unexpected benefits for the hospital pharmacy are worth noting: extended stability studies can give information about the quality of a drug. Our compatibility studies show that visually compatible admixtures can comprise totally different main components than the starting drugs.

Conclusion: Our survey shows that extended stability studies play an important role in clinical practice of German hospitals. The benefits for the hospital pharmacy can be minimising costs and waste. The analytical methods can otherwise be useful for the quality control of its own products or comparing different manufacturers for purchasing. Compatibility studies can avoid adverse effects or contribute to find new active substances.

Friday 28 September 2012

Symposium: Clinical Session - Innovative Roles of Pharmacists in the Healthcare Team

11 Pharmacist Prescribers in Cancer Care: Innovate, Challenge and Inspire

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Introduction: In the UK, the Health and Social Care Act 2001 allowed for the introduction of supplementary prescribing for non-medical professionals, including pharmacists, followed by independent prescribing in 2006. Independent prescribing is defined as '*prescribing by a practitioner responsible and accountable for the assessment of patients with undiagnosed or diagnosed conditions and for decisions about the clinical management required, including prescribing.*' All licensed medicines, including controlled drugs, can be prescribed within the independent prescribers' competence with no need for endorsement by a medical prescriber.

In 2003, the first cohort of UK pharmacists undertook training to become non-medical prescribers (NMPs) and started prescribing in 2004. Over 1,600 pharmacists in Great Britain are registered prescribers.

Prescribing in cancer care: Pharmacist prescribing in the UK is well established and many pharmacists are independent prescribers running their own clinics. Cancer care pharmacists might typically start with prescribing non-complex adjuvant systemic anticancer therapy (SACT), then as experience and confidence grows, expand into metastatic regimens. However, it was the emergence of oral SACT that offered new opportunities for pharmacist prescribers. Chemotherapy activity increases year on year and capacity, skill mix and workforce planning needed to be addressed. New care pathways were developed and many hospitals redesigned their cancer services to exploit the extended role of their cancer care pharmacists.

In 2009 the British Oncology Pharmacy Association and the Faculty of Cancer Pharmacy produced *Guidance for the development of pharmacist non-medical prescribing and review of patients receiving anti-cancer medicines*. This guidance is an excellent resource for pharmacist prescribers.

Conclusion: Pharmacists are experts in medicines and ideally placed to monitor and review patients undergoing SACT. UK cancer care pharmacists have embraced the opportunity to become NMPs and their clinical practice has become enriched by this role extension.

12 Community Pharmacists - Are They the Missing Link?

No abstract submitted.

13 The Pharmacovigilance Pharmacist - In the Service of the Patient

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Introduction: Pharmacovigilance is an activity contributing to the protection of patients and public health. Good Pharmacovigilance Practice (GVP) is necessary to prevent, detect and assess adverse reactions to medicinal products for human use placed on the European Union market.

Although all medications go through clinical trials; rare side effects, long-term effects, effects on special patient populations and even Adverse Drug Reactions (ADRs) are sometimes not yet known by the time of marketing authorisation.

Material and method: European Union Efforts are regulated by the European Medicines Agency (EMA). For medicinal products authorised through the centralised procedure the European Commission is the competent authority. The European Commission is responsible for the adoption of decisions on the basis of the Committee for Medicinal Products for Human Use (CHMP) opinions relating to medicinal products authorised through the centralised procedure and those products. The European Commission also has responsibilities for the overall community system of pharmacovigilance and for the legal framework. By July 2012 all Member States have to implement the regulation that was published in the *Official Journal of the European Union* in December 2010 at national level. The pharmacovigilance reorganization in seven modules was done to tighten, empower and harmonise pharmacovigilance in the European Union. It was clearly stated that in future duplication of work by the national authorities should be avoided, burden on pharmaceutical industry should be reduced and therefore the level of safety augmented, also by involvement of the patients.

Results and discussion: Oncology pharmacists prepare cytostatics, provide training on safe administration and handling of drugs, do research and provide pharmaceutical care. All of them generate potentially useful information that is discussed within the healthcare team. This input is of general interest and therefore reported to national authorities and quality management departments of hospitals.

Tools in this field for a pharmacovigilance pharmacist are collecting, monitoring, researching, assessing and evaluating information from the health care team and also patients on the adverse effects of medication.

Besides the legal obligation to report at national level, intensive, focused programmes concentrating on new drugs, or on controversial drugs, or on the prescribing habits of groups of physicians, or involving pharmacists in reporting are innovative approaches towards patient safety. In future such intensive schemas, which tend to be the exception now, will replace simple ADR reporting.

The contribution of pharmacists to pharmacovigilance will greatly enhance the understanding of ADR, but also purpose-designed educational interventions.

Conclusion: Being in the service of the patient means taking over responsibility to prevent harm to patients and having profound knowledge both on drugs and GVP.

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Proffered Papers: Practical

14 Lean Thinking Applied to a Chemotherapy Centralised Preparation Unit

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Introduction: Most of cancer patients are treated by intravenous chemotherapy and receive their treatment in the Chemotherapy Day Unit (CDU). Due to an increasing demand in our cancer centre, the CDU and the Chemotherapy Centralized Preparation Unit (CCPU) face difficulties with waiting times for patients and work pressure on staff. To improve the efficiency of the CCPU and its planned renewal, we have introduced a business approach based on lean thinking that aims at eliminating 'muda' or waste, in workplace processes.

Material and method: A multidisciplinary workgroup was created including pharmacy staff and quality department. Lean thinking was implemented step by step: 5S principles (Sort, Set-in-order, Shine, Standardize, Sustain), time-and-motion study ('Spaghetti diagram'), Value-Stream Mapping (VSM) to map out essential tasks within the CCPU and in relation with the Pharmacy Department and the CDUs (Haematology and Oncology). Lead-times in healthcare operations were determined during a 5-day study. All relevant stakeholders were identified.

Results and discussion: 5S was used to organise the different areas in the CCPU and to improve staff working conditions. On the basis of the current VSM and through discussions with the different stakeholders, waste processes are being identified, and a redesigned future state process map is underway. Brainstorming meetings are used to propose solutions to the wasteful processes related the 7 'classical' muda (i.e. transportation, inventory, motion, waiting, over-processing, over-production, defects). A DMAIC (Define, Measure, Analyse, Improve, Control) approach to evaluate these proposed solutions is utilised, and current lead-times will serve as a basis, along with quality indicators and patients satisfaction questionnaires.

Conclusion: Lean thinking is still under implementation in the chemotherapy preparation unit. Effective completion of the identified improvements should free up resources on the ward, which can be redirected towards providing better direct care to patients. If successful in the Pharmacy Department this business approach could be extended on clinical wards.

15 Carry-over of Cytostatics in Dutch Hospital Pharmacies

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Introduction: In 2004, a Dutch national guideline was issued describing mandatory safety measures for compounding of cytostatics. The guideline was aimed at preventing occupational exposure of staff. For the pharmacy, safety measures included:

- compounding of cytostatics in a separate, dedicated room with entry through a lock
- zero % air recirculation from the compounding room
- compounding in a safety cabinet or isolator with negative air pressure
- use of full cover protective clothing including footwear which should be changed at least daily
- unpacking of cytostatic vials in a dedicated area with hand protection
- double packaging of compounded cytostatics before transport
- daily cleaning protocol with a dedicated set of cleaning equipment.

All hospital pharmacies implemented these guidelines in the following years. In 2011, we investigated the phenomenon of carry-over of cytostatics through contact with surfaces, because this could be a potential source of exposure.

Materials and methods: A dataset of wipe tests (n = 2,647) from nine hospitals (year 2001–2011) was reviewed. Measured cytostatics were iphosphamide, cyclophosphamide, 5-fluorouracil, methotrexate and platinum-derivatives. Samples were taken from a wide variety of locations, both inside the compounding areas as well as in adjacent rooms and locks. With reference to carry-over, the investigators only considered locations outside safety cabinets or isolators, attempting to paint a picture of how a contamination migrates through the preparation and distribution areas.

Results and conclusion: The analysis showed that 18 out of 275 test results from adjacent rooms were contaminated (6%). These positive results were found in two hospitals, one of which was responsible for 15 results. Moreover, they were all found in the same place on a table in the preparatory room. Prompted by these results, this hospital has meanwhile taken precautions. In another hospital, three positive samples were found: two on a pair of tweezers, and one on the exterior of a vial.

Furthermore, contaminations in the compounding room located at further distance from the safety workbench were studied. A positive percentage of 13% was found (39 out of 297). Samples from the exterior of vials were not included because we do not regard these as carry-over or dragging of cytostatic traces, but as attributable to the manufacturer. Because contaminations were found in the background of compounding rooms, the conclusion is justified that traces of cytostatics may end up outside the safety cabinet in the process of preparation. This is not supposed to happen. However, as the persons working in the compounding room are equipped with strict personal protection gear, these contaminations will not lead to internal exposure.

The fact that hardly any contaminations were found in adjacent rooms is indicative of the way in which the Dutch hospital pharmacists have modelled the procedures, so as to prevent any further spreading of such contaminations.

The data were also analysed in terms of years. Contaminations outside the preparation room no longer occurred after 2007.

Discussion: The carry-over of cytostatics to adjacent rooms did occur in the past, but is no longer detectable since 2008 in the sample survey of 2,647 test results. This gives rise to the conclusion that, provided that the present strict working procedures are maintained, carry-over outside the preparation/compounding room is no longer relevant.

16 Cleaning Effectiveness of Workplace Surface Exposed to Cytotoxic Agents - Influence of the Cleaning Protocol

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Introduction: To limit the environmental cytotoxic contamination and the occupational exposure of healthcare workers potentially exposed to contaminated surfaces, suitable cleaning protocols are required. The

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detergent efficiency depends not only on the cleaning solution but also on the cleaning protocol used during the chemical decontamination.

The aim of the study was to evaluate the influence of the volume, the mode of application and the contact time of the cleaning agent during the cleaning protocol of workplace surfaces exposed to carboplatin contamination.

Material and method: The central surface of a 1,500 cm^2 stainless steel plate (30 cm x 50 cm) was exposed to a calibrated contamination of carboplatin corresponding to 105,000 ng of platinum element. After cleaning according standardised protocol, the plate was partially sampled by 10 cm x 10 cm surface (8 samples per plate corresponding to more than 96% of the total residual contamination) with swabs. Samples were then analysed after cloud point pre-concentration by graphite furnace atomic absorption. Results were expressed in ng of platinum per 800 cm^2.

Five cleaning protocols have been evaluated for one detergent and one disinfectant solution frequently used in chemotherapy units: 4 mL or 8 mL soaked on gauzes by wiping, 4 mL or 8 mL spraying directly on the plate without contact time and 8 mL spraying with 5 min of contact time.

Results and discussion: For both disinfectant and detergent, the influence of the volume and the mode of application were similar even if quantities of residual platinum were different. The cleaning efficiency was higher with 8 mL than 4 mL both by wiping (for disinfectant: 5 658 ng*vs* 11,849 ng; for detergent: 2,533 ng*vs* 14,503 ng) and spraying without contact time (for disinfectant: 3,972 ng*vs* 9,321 ng; for detergent: 1,446 ng*vs* 5,116 ng). However, 5 minutes of contact time after spraying 8 mL on the plate decrease the cleaning efficiency of the detergent solution (12,344 ng) but not considerably changing the efficiency of disinfectant (4,518 ng).

The cleaning protocol using 8 mL of solution directly sprayed on the plate corresponds to the best cleaning efficiency according to all protocols tested with better efficiency for the detergent than the disinfectant.

Conclusion: Major factors influence the decontamination efficiency as surface materials, cleaning solutions and cleaning protocols. Thus, this study illustrates the necessity to evaluate, standardise, and validate the cleaning protocol used to optimal chemical decontamination.

17 Crew Resource Management Training is a Suitable Method to Further Improve Risk Sensibility of a Team Preparing Cytostatics

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Introduction: To improve risk sensibility of a specifically trained and experienced team of pharmacists and pharmaceutical technical assistants in preparing cytostatics by using the Crew Resource Management Training (CRMT) method on top of an established risk management system (Failure Mode and Effects Analysis).

Material and method: CRMT has been developed several years ago in aviation on the basis of intensive research on accidents and almost accidents. Non-professional reasons rather than insufficient professional skills were identified as cause for the majority of incidents. Meanwhile it is common sense that human mistakes can happen anywhere at any time and are ultimately unavoidable. Based on this experience the CRMT method has been transferred to other domains including medicine. Using this method, we defined the following key aspects of training: communications, teamwork, risk situation awareness, culture of a learning organisation. A questionnaire with 15 questions was used to evaluate anonymously and independently the personal assessment of risk-sensibility on a scale from 0 (never applies) to 10 (always applies) before and after use of the CRMT method.

Results and discussion: All team members, 3 pharmacists and 4 technicians, participated in the evaluation of the method. Risk sensibility increased by use of the method from 66,76 to 74,10, i.e. by 11,0 % (mean). The median value increased from 68,67 to 78,67, i.e. 14,5 %.

Conclusion: Use of the CRMT method had a positive impact on the teams risksensibility. The training led to an intensive exchange of personal experience,strengthened trust within the team and made risk situations transparent. CRMTwill continue to be used in our institution.

18 Innovative Strategy for Antibiotics Administration Using Elastomeric Pump - Stability Studies and Preliminary Pharmacokinetics Evaluation

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Neutropenia after cytostatic therapy, lasting for more than seven days and generally with fever, is caused by infectious origin. The occurrence of infectious complications can affect the quality of patients life, producing toxicities associated with anti-infective therapy, need of hospitalisation and furthermore, impact on healthcare costs. The therapeutic approach able to reduce hospitalisation is an important objective. Therefore, the continuous infusion of drugs through the elastomeric pump can be appreciated. Based on this premise, this study addresses the intravenous antibiotics administration by continuous infusion using elastomeric pump, in immunosuppressed cancer patients with sepsis. In the work the stability of 3 widely used antibiotics, i.e. vancomycin (Hospira® 500 mg), teicoplanin (Targosid® 200 mg/3 mL) and meropenem (Merrem® 1 g), was evaluated. The storage temperature and the compatibility between drugs and materials were investigated. The quantitative determination of the 3 antibiotics was carried out using the high performance liquid chromatographic analysis (HPLC). Elastomeric pumps Diafuser® having a volume of 250 mL, with a flow rate of 250 mL/h and with a medical grade silicon reservoir were used. Samples of antibiotics were analysed every 24 hr for a total period of 8 days stored at 4, 25 and 37°C. In the second part of the work a preliminary pharmacokinetic study was carried out. Meropenem (1 g every 8 hr) was administrated in elastomeric pump to 3 patients (2 with acute myeloid leukaemia and 1 non-Hodgkin's lymphoma) hospitalised. The study evidenced that the temperature is the main parameter affecting the stability, either for samples stored in vials or in elastomeric pump; formulation stored at 4°C, have proved to be more stable than those stored at 25 and 37°C. The plasma concentrations of meropenem from samples withdrawn 1.5, 4.5, and 8 hours after administration are completely superimposed with the data reported in the literature after continuous intravenous infusion. The present study achieved the objective to investigate and to validate innovative method for antibiotics infusion, which in future could allow to ensure the immuno-compromised septic patient proper intravenous antibiotics therapy without being hospitalised. Home-based therapies and then, decreased hospitalisations may also greatly reduce the cost and, therefore, give the possibility to more critical patients to receive the appropriate treatment at the hospital.

19 Chemical Contamination? When Quinine is On …

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In controlled atmosphere zone, cytotoxics reconstitution made in biological safety cabinet requires specialised technicians to ensure a safe product. And what about chemical contamination? The aim of this study is to

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manipulate with a non-cytotoxic marker. The goal is to analyse contamination location during operators' manipulations. Improvements will be implemented, if necessary, to preserve the environment and staff safety.

The chosen chemical contamination marker is quinine. That's a colourless compound in contrast to fluorescein. Quinine fluorescence is revealed under a UV lamp. A protocol to perform a test simulating cytotoxics reconstitution with quinine was written.

Non-sterile vials containing a quinine acidified solution were prepared to replace the cytotoxic vials (50 mg of quinine hydrochloride and 25 mg of citric acid per vial). 10 successive preparations were realised by each preparation technician: pockets prepared with spikes and needles, empty pockets and syringes. Manipulations related to our daily practices were performed on a bench in a controlled atmosphere zone. Three operators have run the test. Analysis of finished preparations and necessary equipments revealed contamination traces. Technician gloves present projections. The luer lock of connected Z was also contaminated. At the opening of the syringes stopper, quinine droplets were present on the internal and the external thread of the luer lock counterpart and on the stopper. The location and the kind of contamination allowed us to understand the risky production steps. Our practices were reviewed: the importance of the connect Z rinsing; the adjustment of the syringe volume to flush the luer (preparation technicians used to let a droplet over the luer to avoid bubbles in the syringes during the stopper's closing); increasing of gloves change frequency. This study shows that despite of the training of technicians, there are critical contamination points. The limitation of our study is the lack of contamination quantification. However, test results are sufficient to modify our manipulation process. The handlers were aware of the importance of the quality of their actions. Manipulations have been revised with the manipulators in order to limit contamination of the equipment and of the environment by cytotoxic products.

The quinine test will be early replicated as it will be integrated into the annual handlers validation in addition of the media fill test.

Symposium: Practical Session: Medication Errors - How Patient Safety can be Improved

20 Clinical Pharmacy Interventions in the Oncology Setting

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Introduction: Oncology patients receive multiple drugs that predispose them to many drug-drug interactions and adverse drug events. Even though clinical pharmacists are actively involved in patient care, many of their efforts remain undocumented, resulting in an underestimation of the importance of their services and missed opportunities for improvements and new directions. The objective of the study was to describe, evaluate and document the prevention of medication errors by clinical pharmacy interventions in oncology patients. Clinical pharmacists participate on ward rounds at the Bank of Cyprus Oncology Center and they are members of the multi-professional team for supportive care of the hospital.

Materials and methods: A documentation template was designed to collect patient data, supportive care issues, drug-specific interventions, and written prescriptions. Data collected from January 2012 to April 2012 and were analysed.

Results and discussion: During patient visits, supportive care issues were addressed including anaemia, pain management, constipation/diarrhoea, and nausea/vomiting. Major drug-specific interventions included drug addition/discontinuation, and dose adjustment. Pharmacy interventions included: detecting medication errors in the outpatient dispensary, detecting chemotherapy errors during the verifying of the prescribed chemotherapy regimen, detecting inpatient errors during clinical pharmacist's visits on the ward. On the ward, clinical pharmacists reviewed the patient's treatment charts and performed patient interviews in order to obtain medication history. Identified drug-related problems were discussed with doctors and the appropriate interventions were made. Patient outcomes were evaluated by patient interviews on the following clinic visit or by follow-up phone calls. All interventions were documented in pharmacy documentation forms. The majority of interventions were not related to chemotherapy. The most frequent activity was patient counselling followed by therapeutic recommendations after discussion and acceptance by the doctor. Most frequent interventions included drug choice, drug additions or discontinuation, dosage modification and prescribing issues. Other interventions included drug interactions, route and frequency of administration, therapeutic drug monitoring, extravasation, antiemetic treatment and drug information.

Conclusions: The clinical pharmacy interventions among oncology patients can reduce the number of medication errors. Clinical pharmacists have a significant role in the management of oncology patients and should be members of multi-professional teams of each hospital. Pharmacy input can lead to a decrease in healthcare costs and to an improvement of the quality of patient care. Interacting with the healthcare team in patient rounds, identifying drug-related problems and providing information to the patients and physicians can result in an improved outcome both for the patient and the hospital.

21 Radio-frequency Identification (RFID) - A Useful Tool in Preparation and Administration of Cytostatics

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Introduction: Wrong dose of cytostatics can endanger the patient very easily and these drugs are perilous also for the personnel handling them. Therefoire, in the pharmacy of Masaryk Memorial Cancer Institute (MMCI/MOU) we intended to implement a system that would be able to improve the quality and safety of cytostatic preparation and add some safety value on the side of the patient as well as the personnel. Prior to the introduction of Radio-frequency Identification (RFID) technology, there were several critical points in the process, where an error could have occurred, both in the preparation and administration phase. For example, in some cases, it was not possible to backtrack the batch number of drug used, which is important in the case of side effects. In the course of the project, it was decided to include the outpatient clinic so that the administration of cytostatics could be recorded and supported, too. There are several ways to monitor such a process and the possibilities of information technology can offer numerous solutions. In the end, RFID was chosen because it is more advantageous in some aspects than other systems.

Technical solution: RFID technology is based on the communication between a unique carrier of information, i.e. a RFID tag, and a suitable reader. This technology has recently found its use in health care [1, 2, 5]. Technical report prepared by RAND [3] for the European Commission describes seven cases within the European Union. In one case, the project failed completely, in two cases, the RFID technology was replaced by another technology for economic reasons. It was these two cases, where RFID technology was used in hospital pharmacies to control the preparation and administration of drugs. One of these cases was the University hospital in Geneva [4]. The RAND report praises the technology as it can lead to increase in quality of health care; on the other hand,

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the report warns against its high costs when compared with other technologies, e.g. barcode or its derivatives. RFID technology was used in hospital pharmacy also in Akita University Hospital in Japan. In the Czech Republic, RFID technology is used in three hospitals, in one case for equipment, in one case for laundry and in our case for the control of preparation and administration of cytostatics. Another hospital announced its plan to introduce RFID identification in its management of blood and blood products.

In MMCI, the system is based on three independent information systems: hospital, pharmacy, outpatient clinic. This three information systems exchange and store information allowing its backtracking or control. The system works with standard hardware, only some additional items were necessary, for instance, readers, printers. Passive RFID tags, ISO standard 15693, working frequency 13.56 MHz are used. Basically, these tags are used in three different forms: adhesive labels for the vials, adhesive labels for the infusion bags, on which RFID printer prints further information, and identification cards (pharmacists, nurses, patients).

The system produces various data, as almost any operation is to some extent recorded. This enables retrospective control and traceability of who, when and how a particular step is performed. These data can be further processed and analysed and the results can be used to improve the process.

Conclusion: The project was implemented in full run in October 2009. Neither erroneous preparation nor administration has been recorded. Within the Czech Republic, the RFID technology in preparation and administration of cytostatics is used solely at MMCI. It is an example of a multidisciplinary solution which was tailored to the needs of the MMCI. However, the general principle is robust enough to allow for implementation in other hospitals, too. The goal, i.e. the reduction of the human factor in the whole process, was fulfilled.

In 2006–2009, the system was co-financed by Czech Ministry of Education, Youth and Sports (grant 2C06024), nowadays, the costs are standard part of the hospital budget.

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22 Proffered Papers - Recommendation for Error Prevention in Anticancer Drug Therapy

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Introduction: Due to high toxicity of anticancer drugs and their low therapeutic index, the errors in cancer therapy can determine serious damages, event at approved doses. The Ministry of Health, under the Programme for Patient Safety, has developed a spcific Recommendation for the proper management of treatment with anticancer drugs.

Material and methods: A working group consisting of pharmacists, oncologists, nurses, psychologist and patient representatives was set up. The same format of other Recommendation made by Ministry of Health for patient safety was followed.

Results and discussion: The Recommendation is directed to Regions, Autonomous Provinces, health facilities, clinical risk managers, health workers; it finds application inside the Medical Oncology and Haematology Units of private and public hospitals, inside hospital pharmacies and at patients' homes. The Reccomendation is to protect patients needing anticancer drugs treatments. Highlights: hospitals should provide working instruments and develop a procedure including all the instructions for proper anticancer drugs management. Also, they should define the training plan, undertake initiatives to promote communication and integration between health workers, adopt a procedure collecting the informed consent in cancer chemotherapy documentation, implement interventions for the overall care, information needs and psycological and social support for the patient.

Conclusion: The Recommendation is a reference for health professionals involved in anticancer drugs handling, providing information about the patient's health objectives and expected benefits from treatment. Correct and complete information is the key tool of the therapeutic alliance in order to ensure the quality and safety of care. The document provides guidance aimed at preventing errors that can occur during anticancer drugs treatment and includes solutions encouraging clinical governance promotion. Soon a verification of the Recommendation implementation will be expected.

http://www.salute.gov.it/qualita/qualita.jsp

Proffered Papers: Clinical

23 Proton Pump Inhibitors as Adjunct Therapy for Triple-negative Breast Cancers

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Introduction: Triple-negative breast cancers (TNBC), lacking overexpression of all three important mammary epithelium receptors (for oestrogen, progesterone and human epidermal growth factor receptor 2, HER2) represent ~15% of all breast cancers. TNBC is particularly difficult to treat and it is a very aggressive disease with limited chemotherapy options. Clinical use of one of the most commonly used agent doxorubicin is complicated by its serious adverse effects. Improving effectiveness of doxorubicin therapy by allowing for lower dose is therefore of great importance. Hypoxia and increased intracellular acidity in tumours have been shown to have a role in resistance to chemotherapy and proliferation and metastatic capacity. Activity of variety of trans-membrane proton pumps allows tumour cells to free themselves from dangerous pro-apoptotic H^+ ions. The main proton pump, responsible for the maintenance of the pH in tumours, is the vacuolar H^+-ATPase. Proton pump inhibitors (PPIs) such as omeprazole are normally used in the treatment of gastritis and Zollinger-Ellison syndrome and have been shown to be highly effective at inhibiting V-ATPases both *in vitro* and *in vivo*.

Material and method: Model system used in this study included normal breast epithelial cells and breast cancer cell line MDA-MB-468, a good model for triple-negative breast cancer considering their ER/PgR/HER2 phenotype and ability to form aggressive xenografts in nude mice. Cultured cells were treated with doxorubicin (0–10 mM) and/or omeprazole (0*100 mM); cell viability and proliferation were assessed with automated cell counter; intracellular pH changes in omeprazole

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treated cells were evaluated by fluorescence microscopy using pH-sensitive fluorescent probe BCECF-AM; expression of V-ATPase subunit A was assessed by immunofluorescence; accumulation of autophagic vacuoles in omeprazole treated cells was determined by microscopy and cell migration potential (a measure of metastatic ability) was performed using our originally developed matrigel droplet assay.

Results and discussion: Compared to normal breast epithelium, MDA-MB-468 cells have shown an increase in V-ATPase subunit A expression and sensitivity to esomeprazole. In MDA-MB-468 cells esomeprazole caused increase in intracellular pH and accumulation of autophagic vacuoles whereas proliferation and ability to migrate was significantly decreased. Furthermore, MDA-MB-468 cells were more sensitive to doxorubicin when exposed simultaneously to esomeprazole.

Conclusion: It was found that doxorubicin sensitivity in breast tumour cells was greatly increased and cancer-related processes suppressed in presence of esomeprazole, suggesting that PPIs could successfully be used as an addition to the current breast cancer chemotherapy protocols.

24 Peptide-mediated Drug Delivery Systems for Breast Cancer Therapy and Imaging in Animal Models

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Anticancer drugs lack selective toxicity leads to their dose-limiting side effects which compromise clinical outcome. Targeting liposomes that bind to surface receptors of cancer cells is a recognised strategy for improving the therapeutic effectiveness of conventional chemotherapeutics. In this study, we isolated several ligands from a phage-displayed peptide library that bind to breast cancer cells. We found a new phage-displayed peptide, PC90, which would bind to breast cancer cells but not to normal cells. In severe combined immunodeficiency (SCID) mice bearing breast cancer xenografts, the targeting phage PC90 bound specifically to tumour masses. Its tumour homing ability was inhibited by competition with the cognate synthetic peptide SP90. The targeting peptide-linked liposomes were capable of translocating across the plasma membrane into endosomes through receptor-mediated endocytosis. More importantly, PC90 recognised the tumour tissue in surgical specimens of breast cancer patients, with a positive rate of 90%. The tumour site fluorescent intensity in the mice treated with targeting peptide-linked quantum dots (QD) was around 28-fold of that in the mice treated with QD. When the SP90 was coupled to liposomes carrying doxorubicin, the therapeutic index against breast cancer xenografts was enhanced. Furthermore, 12.0 times more drug accumulated in the tumour tissues of mice treated with the targeting liposomes than in those treated with free drugs. We conclude that the targeting peptide SP90 show great promise for their applications in tumour-targeted drug delivery and imaging.

25 The Pharmacist of the Department for Errors Prevention in Clinical Oncology

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Introduction: The literature highlights the advantages related to the establishment of the department Pharmacist indicating adverse events reduction with significant savings in healthcare costs and shortening of hospital stays. The Ministry of Health launched several activities with the aim to improving the quality of healthcare and the management of drugs therapies.

Material and methods: In March 2010 started this project in order to give a reference model for the implementation of the pharmacist at the department level. The model was tested in 5 hospitals with strong safety culture by young scholar pharmacists. For the realisation of the project the Ministry enlisted regional health experts, Italian Society of Hospital Pharmacy, Federation of Association of Italian Pharmacists, European Association of Hospital Pharmacists and Italian Association of Medical Oncology.

Results and discussion: The trial produced a policy document providing all the necessary information to test this professional and it shows the real contribution that the department pharmacist can offer in medication errors preventing and in improving quality of care. Field experience involved detailed reports about changes between before and after the department pharmacist experience, through process and outcome indicators such as: signalling to the AIFA Oncology Registry, monitoring of off-label prescriptions, money value reduction of medicines stocks on the wards, decrease of hospitalisation for adverse drug events, recording of near misses, customer satisfaction by patients and health professionals.

Conclusion: On the basis of this experience a handbook was produced and published addressed to all Italian Hospitals, and it is available on the website of the Italian Ministry of Health. This handbook is useful in clinical risk management training and it will be implemented in our Country next months.

26 Clinical Rule on Safe Methotrexate Prescribing and Dispensing in The Netherlands

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Introduction: To ensure proper handling of methotrexate in the Dutch pharmacies a national clinical rule has been developed and implemented in 2010. The reason for this was some (fatal) incidents. In this poster we shall provide you with information on how this was done and what results were achieved. We shall also share the daily practice in our Division of Clinical Pharmacy, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands; and in the St Elisabeth Ziekenhuis Tilburg, The Netherlands. In the field of oncology pharmacy prevention of medication errors is especially relevant. Pharmacists should conduct their efforts to reduce medication errors within the pharmacy by implementing SOPs and records. Reporting and prevention of errors will improve quality. Medication errors related with chemotherapy are among the most deleterious. So, pharmacist as member of the oncological team should actively participate in quality management outside the pharmacy.

Rationale: Methotrexate is a drug with different indications and various dosages. In oncology administration is often on daily basis depending on the chemotherapy scheme, whereas in rheumatology the drug is given in weekly regimens. There were some fatal incidents in The Netherlands when methotrexate was taken daily instead of weekly by rheumatological patients. These incidents were recorded in the national database CMR. The CMR is a national web-based institute for reporting medication related incidents. The majority of Dutch hospitals report to the CMR. Analysis of the incidents prompted Dutch pharmacists to draw up national clinical rules for prescribing and dispensing methotrexate to ensure proper handling of this drug.

Results: Daily Practice in our hospitals Rheumatology ward after implementation of the clinical rule:

- No storage of this drug on the wards
- Dosage control in the pharmacy for all prescriptions

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- 100% alert in the computerised provider order entry (CPOE) system
- Dispensing only after authorisation by a pharmacist
- Performing a medicine review for each patient with emphasis on drug-drug interactions and renal function
- Administration of folic acid orally as an antidote
- Interview with the patient with regards to the exact use of methotrexate, e.g. indication, dosage, day of administration
- Only usage of tablet strengths of 2.5 mg

Conclusion: With our practice we contribute to increased patient safety. The interventions can be implemented in a short period of time and do not ask a lot of time of the pharmacy technicians and pharmacists in our hospitals. This kind of practice could be an important challenge for the pharmaceutical patient care on the wards in Europe.

However, it can also be carried out in general practice outside the hospitals.

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27 Observational Study Regarding Toxicity Associated with Colorectal and Breast Cancer Treatments in Four Piedmontese Centres

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Introduction: Oncology patients are expected to meet toxicity while they receive oncological treatments. In fact toxicity is not always reported completely in daily practice. The Piedmont Region funded this multi-centre study inside a bigger pharmacovigilance project.

The aim of the study was to observe toxicity in common practice, the measures adopted in order to control it and related consequences, in five day ward centres in Piedmont.

Material and method: From April 2007 to December 2010, 340 patients admitted to day wards and receiving drugs included in regimens for colorectal and breast cancer treatments were monitored for toxicity and the consequences related to it. Patients receiving radiotherapy were excluded. WHO criteria were adopted. Patients were followed from the first cycle to the end of programmed treatment or interrupted for some reason. The different treatments used in the various centres for neoadjuvant, adjuvant and first-line regimens were also observed. In this presentation we report preliminary data.

Results: The median age of our sample varied from 45 to 64 years; the majority of the patients 323 showed an ECOG Performance Status equal to zero with at least one additional disease, co-morbidity (more than 50%), the most common of which was a grade 3 CIRS scale hypertension (it was found in 44 patients, at the time of enrollment). The majority of them, 182 patients had breast cancer; 154 patients received adjuvant therapy; 23 patients received neoadjuvant therapy; 158 patients of our sample had colorectal cancer among which 106 received adjuvant therapy, 51 first-line therapy. 125 patients had a dose reduction due to toxicity, 116 patients interrupted the treatment: 11 patients definitely, 43 temporarily because of toxicity, 38 patients because of disease progression and 23 for other reasons. A fifth centre did not obtain authorisation by local Ethics Committee, so it was not included.

Conclusion: The results we found seem to be very interesting and we think it is worthwhile developing this topic. Pharmacists, as responsible for pharmacovigilance in many centres in Italy, have developed good expertise and can be of great help in monitoring toxicity of oncological treatments. Despite this, we found some resistance by the various Ethics Committees in authorising the project, in different centres, which resulted in delay in starting. Sometimes this is a problem.

Now pharmacists in Italy are being more and more involved in monitoring oncological patients. The Italian Oncological Register is an example of this.

28 Retrospective Analysis of Cisplatin-based Radiochemotherapy for Locally Advanced Head and Neck Squamous Cell Carcinoma - Toxicity-dependent Dose Reduction

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Introduction: Concomitant cisplatin-based radiochemotherapy (RCT) is a standard treatment for locally advanced head and neck squamous cell carcinoma (HNSCC). However, to date, there is no consensus regarding the optimal concomitant cisplatin-based regimen. A recent meta-analysis by Ghi et al. (2011 ASCO Annual Meeting Proceedings. J Clin Oncol. 2011;29: (Suppl; Abstr 5534), indicated that the best overall survival characterised by a Hazard Ratio (HR) = 0.59 [0.46–0.74] is achieved with the cisplatine total dose of 300 mg/sqm (cycled every three-weekly) and this HR is significantly reduced when the cisplatine total dose is lower the 150 mg/sqm (HR = 1.04 [0.85–1.27]. The main objective of our study was to determine the exact cisplatine total dose (300 mg/sqm or lower) used in RCT for HNSCC in our Institute and to identify the main events leading to a total dose reduction which is associated with a lower survival rate according to the previous meta-analysis.

Material and methods: The medical records of all patients with HNSCC treated by concomitant cisplatin-based RCT in the Paul Strauss Cancer Center in Strasbourg, France, between January and June 2011 were reviewed retrospectively.

Results and discussions: 29 patients with HNSCC were included in our study with a common regimen corresponding to cisplatin 100 mg/sqm on day 1, 22 and 43 of radiotherapy (65 to 70 Gy for 6 to 7 weeks). Only 17% of patients received the intended total dose of cisplatine (300 mg/sqm) theoretically associated with the best survival rate and 52% of patients received a total dose higher than 200 mg/sqm which is still associated with an improved survival. Second and/or third administrations of cisplatine were cancelled for 2 (7%) and 13 (45%) patients, respectively. Moreover, a dose reduction (lower than 100 mg/sqm) was applied for 68% of the patients. Both cure cancellation and dose reduction were mainly related to RCT-induced toxicity with 40% because of neutropenia, 27% because of mucosis and 13% related to nephrotoxicity. Finally, nutritional status analysis revealed that 50% of patient required nutritional support and almost 80% lost weight during their treatment.

Conclusion: Half of patients treated by concomitant cisplatin-based RCT for HNSCC did not receive an optimal total dose of cisplatin associated with an improved survival rate which is consistent with previous studies as well as the causes of dose reduction. Thus, another optimal regimen is still mandatory.

Poster Discussion: Basic Research

Abstracts of Poster Discussions are presented in the Poster Sessions.

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Practical Interactive Session: Can new Technologies Help in Preparation Processes?

29 CytoCare Robot - An Experience in Belgium

No abstract submitted.

30 The PharmaHelp Robot

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Introduction: The handling of cytotoxic drugs is associated with an increased risk of contamination for personnel working in this field. Additionally it needs a lot of resources especially in terms of labour.

The PharmaHelp robot (PHR) by Medical Dispensing Systems was developed for the automated production of individualised preparations.

Material and method: The PHR is a small scale pharma robot tailored to the needs of pharmacists. It features high safety through gravimetric controlled dispensing an integrated vision system combined with the usage of RFID tagged adapters for vials and IV bags. Its compact size and low weight makes it easy to install in every pharmacy, making cleanroom changes unnecessary. It is able t fill IV bags, syringes and pumps. The automated production is done in combination with a specially developed anti-aerosol PharmaNeedle (APN).

It can be interfaced with prescription software systems.

Results and discussion: The automated production hands-off- production in combination with the specially developed APN reduces bio burden and contamination to enhance product shelf life. It is adaptable to an isolator or a laminar airflow hood. It avoids leakage of cytotoxic agents during the automated production. The gravimetric controlled dispensing, integrated vision system and the RFID tagged adapters help to eliminate medication errors.

The PHR enhances pharmacy output and preparation. It reduces the necessary number of technicians and it is capable to produce 25 to 35 individual preparations per hour.

Conclusion: The PHR is an innovative solution in comparison to other robots which are available. Its simplicity together with high flexibility makes it a robust solution to set staff free from preparation to use these technicians for other work.

31 Robot Validation and new Legal Opportunities in Cytotoxic Preparation

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Introduction: Most pharmacies across the world have experienced increasing demand to the quality and quantity of reconstitution of cytotoxic drugs. As reconstitution of these drugs until recently only has been done manually it often create problem for the staff engaged in this repeated stressful operation and therefore created a demand for automation in the field.

Several attempts to develop automation have been done and a few machines are now on the market in form of robots for the use in hospital pharmacies. Among these are the Cytocare robot being validated through an EU founded project SafeChemo. The validation and its results will be presented.

A survey of the quality of magistrel preparation in Europe has been published in Pharmeuropa. 2010;22(4):405 and a suggestion for uniform quality of these products have been accepted as a Resolution from the Council of Europe (CE) January 2011.

The resolution gives new inspiration to national legislators on how regulation of reconstitution can be carried out, and thereby new possibilities for our profession. The presentation will include these new possibilities.

Material and method: The robot validation was structured in: Safety outcome measures, Efficiency outcome measures and Human aspects outcome measures. The presentation will focus on the first 2 areas showing data on accuracy, operator exposure and microbiology. Methods used are conventional methods normally accessible for the hospital pharmacist.

Experiences sampled from Conference exhibitions and personal contact shows that new generations of robots are been developed.

Result and discussion: The validations shows that safety issues for relevant parameters on sterility, accuracy, staff exposure to cytotoxics and cross contamination could be carried out within the frames of manual preparation or even better, Pit falls in the process was observed in the implementation of the equipment leading to low performance and even the fact that equipment was not accepted as production tool for the pharmacy. New generations of robots seem to have overcome some of the problems.

New opportunities in the CE Resolution for applied optics reconstitution of cytotoxics will enable the hospital pharmacist in some cases to simplify the daily work and thereby remove the pressure for more quality and load of work from the system being used today.

Conclusion: A programme for the validation of robots used for the reconstitution of robots has been developed and tested on a first generation CytoCare robot. The results show major variations when used as a tool in an implementation process carried out at a hospital pharmacy, questioning the use of the robot in pharmacy practice.

Data on new generations of robots seems to indicate that the problems mentioned can be solved. In a way that stressful manual work for the hospital pharmacy can be automated.

Other sources to changes can be new legal regulations for reconstitution introduced by the CE Resolution.

Clinical Interactive Session: Access to new High Cost Cancer Drugs - The Role of the Cancer Pharmacist

32 An Overview of Issues to Access to High Cost Cancer Drugs Across Europe

No abstract submitted.

33 The Role of the Cancer Pharmacist in Decision Making - Patient Access Schemes

No abstract submitted.

34 The Role of the Cancer Pharmacist in Decision Making - Health Technology Assessment

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Introduction: Health Technology Assessment (HTA) forms an essential part of the managed entry of any new medicine into clinical practice. NHS funding of medicines which have received a positive Technology Appraisal from the National Institute for Health and Clinical Excellence (NICE) is mandatory, but funding streams for medicines which have either not been appraised by NICE or have been negatively appraised are varied across the 10 Strategic Health Authorities (SHAs) in England. In October 2010 the government introduced

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an Interim Cancers Drugs Fund (ICDF) of GBP 50 million to improve access to cancer medicines in England and from April 2011, the Cancer Drugs Fund (CDF), GBP 200 million per year for 3 years, was introduced to act as a bridge until the introduction of Value Based Pricing in 2014. Each SHA was tasked with implementation of the CDF for their population.

Method: In London, the approach to the implementation of the CDF has built on the process of prioritsation of cancer medicines, which has been in place for five years. The process and implementation has been overseen by the London Cancer New Drugs Group (LCNDG), coordination and implementation being the responsibility of the Cancer Network Pharmacists. The LCNDG is constituted of oncologists, haematologists, pharmacists, commissioners, with lay representation. Clinical reviews for consideration by LCNDG are prepared by the Regional Medicines Information Centre, based at Guy's and St Thomas' NHS Foundation Trust.

A scoring tool was developed by a clinical panel composed of oncologists, haematologists and pharmacists, where, for each drug and indication considered, a numerical value was assigned for clinical benefit (from the overall survival, progression or disease free survival demonstrated in clinical trials) demonstrated above the previous standard of care for that particular indication. Additional points were assigned relating to the degree of unmet need, quality of life and toxicity. In addition a letter was assigned, to record the strength of evidence which demonstrated the clinical benefit, for example, A = 2 x randomised Controlled trials, U = unpublished data. Oncologists were invited to submit the drugs and indications they wanted to be considered for prioritisation. Multidisciplinary assessment panels were convened to assess the clinical data for all applications and a final seminar was held to validate the scores, to which all applicants were invited.

Results and discussion: The result was a ranked list of medicines, which was used to inform the workplan of the LCNDG. Drugs and indications would then be recommended for funding via the London CDF, once a positive recommendation had been made by the LCNDG. In 2011, the prioritsation process for 2012–13, reviewed 45 drugs and indications, five were already on the London CDF list, seven drugs have been added to the CDF list and a further seven remain on the LCNDG work plan. The ranked list also highlighted 10 drugs and indications, where the data were not yet published. It was therefore possible to highlight that as data matures, that the ranking of these medicines may change, if for instance the results of ongoing studies become published.

Conclusion: The London CDF has been implemented using a prioritisation process which informs the workplan of the LCNDG. By April 2012, there were 45 drugs and indications on the London CDF list and the number of patients who had received approval to access cancer medicines from the CDF, to this date was 1,768.

Saturday 29 September 2012

Meet the Expert: Practical Cases

35 Lessons Learned From Safe Handling

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Introduction: Progress made in the last decade has led to new standards in the handling of cytotoxic agents. These improvements were triggered by a deeper understanding of critical steps in the workflow of the whole handling procedure as well as technical developments. In parallel, several monitoring studies helped to identify weak points in our system stressing the relevance of ongoing research in this field.

Results and discussion: In combination with training and the raised awareness, we have now a situation, which offers a very high, but not absolute safety level.

- These lessons learned—among several others—include:
- Organisation of cytotoxics preparation in specialised units
- Adequate room design and air ventilation systems
- Correct personal protective equipment
- Specified safety workbenches
- Correct aseptic techniques, handling procedures and supporting techniques
- Differences between hospital pharmacies and oncologic wards
- Waste disposal
- Documentation
- The essential role of training and permanent education.

This substantial progress should not obscure the fact that there are still some open issues for the future such as workplace contamination and individual exposure to cytotoxics, monitoring strategies, exposure in different workspaces and different occupational categories, and a comprehensive risk analysis. The most difficult task probably is the assessment of exposure and the resulting effect on an individual base. All these issues require research efforts that have been neglected in the last years for a variety of reasons such as lack of funding, but also lack of initiative from pharmacists to engage in these crucial questions.

Conclusion: In comparison with the historical situation, the current status is characterised by beneficial safety improvements, which have been continuously implemented over the last years. To maintain this safety level, periodic training, acute awareness of the problems and permanent education is of the same importance as the ongoing technical progress.

36 Technical Equipment

No abstract submitted.

37 How can we Improve the Safe Handling of Antineoplastic Agents? Can Devices Be Helpful?

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The risk of exposure to hazardous drugs during the preparation and administration of antineoplastic drugs have been discussed many times. The awareness about the occupational exposure to antineoplastic drugs among the hospital personnel handling these hazardous pharmaceutical seems to be well known. However, numerous studies confirmed that despite developing the standard safety precaution contamination still occurs in practically all facilities where the antineoplastic drugs are handled.

At present pharmaceutical companies promote various special devices designed to reconstitution and administration of antineoplastic drugs. The main purpose is to support safe handling of the hazardous agents by preventing or minimising any possible contamination through containing the hazard inside. Considering the safe handling of antineoplastic agents all stages of chemotherapy production from **delivery** of drug to the preparation areas, **reconstitution** themselves, through **delivery to oncology departments**, **administration** to patients and to final **disposal** after application must be taken into account as an inseparable chain. In different way, there is a risk that the toxic substance can be released into the environment leading to exposure of workers.

With todays rapidly extension of chemotherapy services, every additional factor suitable to reduce or minimise any potential risk of exposure to antineoplastic drugs is indispensable. This goal requires a continuous effort in investigations and research to introduce new approaches such as evaluation of different self-contained systems,

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assessment and validation of specific and general procedures, their implementation in the daily routine of hospital departments as well as proper education and training of involved staff members.

Poster Discussion: Clinical

Abstract of Poster Discussions are presented in the Poster Sessions

Meet the Expert: Clinical Cases

38 Experience with Erlotinib in the Treatment of Lung Cancer

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Erlotinib (trade name Tarceva) is per-oral drug from a pool of anticancer-targeted therapies. It is a reversible tyrosin kinase inhibitor, which inhibits the tyrosine kinase activity of the human epidermal growth factor receptor (HER1) signalling pathway inside the cell. Erlotinib is a small molecule designed to target the HER1 pathway, which is one of the factors critical to cell growth in non-small cell lung cancer (NSCLC) and pancreatic cancer. HER1 is also known as EGFR.

Erlotinib is indicated for maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy and for treatment of locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen. Erlotinib is also indicated for first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine. Erlotinib is administered until a disease progression or a strong intolerance. Actually, in lung cancer, erlotinib extends life by an average of 3.3 months at a cost of CDN$95,000.

Treatment of lung cancer with erlotinib has been shown to be effective in patients with or without EGFR mutations, but appears to be more effective in the group of patients with EGFR mutations. The response rate among EGFR mutation positive patients is approximately 60%. Mutations can occur in all types of patients.

As with other ATP competitive small molecule tyrosine kinase inhibitors, patients rapidly develop resistance. In the case of erlotinib this typically occurs 8–12 months from the start of treatment. Over 50% of resistance is caused by a mutation in the ATP binding pocket of the EGFR kinase domain.

The standard dose of erlotinib for NSCLC is 150 mg/day. Erlotinib should be taken on an empty stomach at least one hour before or two hours after food.

From serious side effects we can see interstitial lung disease (ILD)-like events, acute renal failure and renal insufficiency. We have to interrupt erlotinib administration in the event of dehydration and monitor renal function and electrolytes in patients at risk of dehydration. Cases of hepatic failure and hepatorenal syndrome have been reported. We have to monitor periodic liver function testing and interrupt or discontinue erlotinib administration, if liver function changes are severe.

We can rary also see gastrointestinal perforations, bullous and exfoliative skin disorders, myocardial infarction/ischaemia and corneal perforation and ulceration. International

Normalized Ratio (INR) elevations and bleeding events (including fatalities), associated with concomitant warfarin administration have been reported.

The most common adverse reactions (> 20%) are rash, diarrhoea, anorexia, fatigue, dyspnea, cough, nausea, infection and vomiting.

For everyday practice drug interactions with erlotinib are very important. CYP3A4 inhibitors (azol antifungal drugs, protease inhibitors and macrolide antibiotics) may increase erlotinib plasma concentrations. CYP3A4 inducers (rifampicine, phenytoine, carbamazepine, barbiturates, St John's Wort) may decrease erlotinib plasma concentrations. CYP1A2 inducers may decrease erlotinib plasma concentrations, for example, cigarette smoking decreases erlotinib plasma concentrations.

Erlotinib solubility is pH dependent. Drugs that alter the pH of the upper GI tract may alter the solubility of erlotinib and hence its absorption.

In clinical cases we can see how to work with this molecule in clinical practice, how is current situation in the Czech Republic and with which difficulties patients typically suffer.

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39 Metastatic Breast Cancer in Real Life Practice

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Introduction: Metastatic breast cancer (MBC) remains essentially incurable, and the main treatment goal is palliation, with the aim of prolongation of overall survival time without negatively impacting quality of life. Due to advances both in early detection and in treatment options, mortality rates from breast cancer have been decreasing, however, it is still the leading cause of cancer mortality in women worldwide.

Material and methods: There are few proven standards of care in MBC management; therefore, well-designed, independent, prospective trials should be prioritised. In addition, it may be crucial to assess the real clinical impact of different therapeutic regimens taking into consideration specific sequences. Web-based drugs national registries with mandatory surveillance, such as Italian Onco-AIFA registry (Italian Agency on Drugs), may result of great support for these purposes.

Results and discussion: Treatment options for metastatic breast cancer range from chemotherapy, endocrine therapy, psychosocial interventions and supportive care. Women with advanced breast cancer have an average survival of about two years, although some of them may live for many years beyond this. Therefore, it is important to investigate different systemic treatment options that can improve survival outcomes but also can cause toxic side effects. Decisions regarding the timing and aggressiveness of therapy are influenced by the site of the metastases. There are many chemotherapeutic agents that have reasonable activity against breast cancer. There is no evidence, however, that

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any specific sequence of chemotherapy is superior and that use of combination chemotherapy rather than single cytotoxic drugs improves overall survival. Anthracycline and taxane-based therapies have traditionally shown the highest degree of activity in MBC. Hormonal therapy is preferred systemic treatment for patients with ER/PR-positive MBC with an indolent course or with asymptomatic visceral disease allowing for delayed cytotoxic therapy. As for chemotherapy, optimal sequencing of various endocrine agents and their role in combination regimens have not yet been resolved.

The advent of targeted therapies, anti-HER2 and anti-angiogenic therapies, gives more strategic options in MBC management. These agents are not necessarily less toxic than traditional cytotoxics since potentially they are associated with serious adverse events. Actual research focuses on the development of biologic markers of disease; consequently targeted strategies will continue to become more individualised.

The requirement for every new drug approval is a demonstration of net clinical benefit, but even RCT could fail to show relevance in modifying the natural history of a disease in clinical practice. As demonstrated for Bevacizumab in MBC, after accelerated approval intended to get novel treatments to patients sooner, follow-up trials indicated no improvement in overall survival, according to FDA. Generally, little is known about the clinical outcomes of innovative drugs in real life practice when they reach the market.

Conclusion: While providing life-extending treatments with chemotherapy, hormonal therapy, and targeted therapies, the supportive care is also very important in order to optimise fatigue and pain management. Patients' preferences should always be taken into account regarding both treatment options and methods of treatment administration. The post-marketing studies are essential in order to verify both effectiveness and safety in general population testing external validity of the randomised trials. This kind of assessment lacks in the approval RCTs, further emphasising the importance of multicentre observational investigations of clinical practice.

40 Clinical Cases - One Step Further Towards Oncology Pharmacy Practice

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'Simple interventions such as medication calendars, individualised counselling, and carefully selected educational materials are routinely offered and keep many problems from occurring at our institution' [1].

Cancer patients require our attention and our professional knowledge in many respects.

On the one hand, there is the centralised aseptic preparation of chemotherapy drugs and delivery of oncology medication with respect to individual requirements. On the other hand, there is the monitoring of therapy including supportive medication, the reduction of the risk of medication errors and drug-related problems, safe drug handling, pharmacoeconomics. All of these require our professional involvement. In order to provide care for cancer patients, it is necessary to establish a structural procedure.

For oncology pharmacists and technicians who decide to work in a more patient-oriented and clinical way working with clinical cases can be an effective strategy. The first step towards Pharmaceutical Care through problem-based learning is to create patient documentation and use the SOAP procedure according to the Case Reports User Manual of ESOP. (www.esop.eu)

Working with case reports by using documentation often starts with evaluating prescriptions, counselling patients, studying medication profiles or analysing drug-related problems. The documentation of case reports using the SOAP scheme as a standard is a very helpful tool for assessment and planning.

This system of approach includes:

S = Subjective Data
Info about symptoms and problems (case history).

O = Objective Data
Blood parameters, diagnosis, drug treatment etc.

A = Analysis/ Assessment
Pharmaceutical Assessment of subjective and objective data. The focus is on the drug therapy.

P = Plan
For example, action planning to optimise and monitor current therapy to avoid or prevent drug-related problems.

With this method, pharmacists learn more about patients and their treatment plans and are able to select patients with potential problems. In addition, they learn to work in a multidisciplinary team and to take part in conferences about the treatment of individual patients.

The collection of clinically relevant information about patients and their treatment puts the patient at the centre of our attention. This work approach builds up experience at the pharmacy and leads to more acceptance by doctors, nurses and patients.

The assessment of clincal cases also makes it possible to implement instruments such as patient questionnaires, standard procedures and intruments for cost controlling. For junior pharmacists it is very helpful to learn using existing clinical cases and helps them develop case reports of their own which are then discussed with senior pharmacists. This access to knowledge makes fruitful discussion possible because well-known or common problems are documented and can, at any time, serve as a basis for problem-based learning.

Developing a constructive, relevant relationship between patient and pharmacist has to be cultivated and begins with the issue of the first prescription.

Reference

1. Parker PE, Finkbiner KL. The expanding role of the oncology pharmacist. Oncology. 2002;17(6):34-6.

Poster Discussion: Practical

Abstracts of Poster Discussions are presented in the Poster Sessions

Closing Session

41 Message From a Patient Advocate

No abstract submitted.

42 Patient Expectations from Oncology Pharmacy

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Our high expectations to improve the patients' quality of life and support optimal treatment in cancer care by ESOP as expressed in the pre-word of the English publication of Quapos 4 have been met with resounding success. Launched on the existing science and research in laboratory and clinical pharmacology it is now an integrated, indispensable ring in the strong chain of multi-professional care for the cancer patient.

Joining forces with the other healthcare professionals resulted in the very specific handling of oncology drugs and radiopharmacy on all levels of health care with quality management as a driving force.

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Frankly we could and can not envisage any lesser performance of a science where chemistry, in all its forms and specific requirements, is the baseline for performance.

We, as patients, have witnessed the fantastic progress in drug design, in the handling of cytostatic drugs and in fighting cancer shoulder to shoulder with your medical and nursing colleagues. We are grateful for your performance in establishing and providing optimal medical treatment for the cancer patient.

Forgive us to expect the same dedication and enthusiasm to provide holistic individual patient care. These expensive words mean that you share your expertise with clinical and community pharmacist, the collaborative professional specialists, general practitioners and your patient partners.

It is recommendable but not enough to reduce the myriad of medication errors, to prevent drug interactions, assure quality control of prescription drugs and provide needed drugs in the service delivery. We would like you to feel responsible for the information, education and counselling of cancer patients as we expect from the medical and nursing community. The interest and empathy of the pharmacist can complement the many gaps in providing the needed medication to each and every patient and increase his/hers quality of life. As a patient group we hope that ESOP surveys the access and pricing of innovations for all patients. We all have different perspectives of our responsibility and we require better understanding, communication and collaboration among all health providers. It remains a challenge to be met but we have great trust in ESOP to reach this goal.

Poster Presentations

Poster Session: Basic Research

43 TMPO and OLFM4 Were Potentially Prognostic Markers for Taiwanese Colorectal Cancer Patients

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Introduction: Colorectal cancer (CRC) is a significant public health problem worldwide. Each year, nearly 1,000,000 new cases of CRC are diagnosed, and there are 500,000 deaths from CRC. Approximately 25–40% of patients who undergo curative resection subsequently develop metastatic disease. One of the major causes of relapse is the presence of disseminated tumour cells shed from the primary carcinoma into the circulation before, during, or after surgery. Several reports have described the detection of circulating tumour cells (CTCs) in the peripheral blood of CRC patients, having important prognostic and therapeutic implications The commonly used techniques for the detection of nucleic acid material of disseminated tumour cells in the last decade were polymerase chain reaction, reverse-transcriptase PCR (RT-PCR), or real-time quantitative PCR (Q-PCR) assays. Due to the heterogeneity of gene marker expression in blood, a multi-marker assay would be more reliable and sensitive than a single-marker assay. The development of biotechnology has made biochips an important tool in clinical diagnosis or drug efficacy evaluation.

Material and method: This study explored the overexpression of liver metastasis associated mRNAs in human CRC by using a well-established weighted enzymatic chip array (WEnCA) platform. Analysis of 8 CRC cancer tissue specimens and their normal adjacent tissues revealed that 25 genes including PSG2, TMPO, CD55, ATP2A2, CK20, etc. genes were up-regulated in CRC cancer tissue by microarray and bioinformatics analysis. A gene chip including 25 candidate genes was constructed to investigate the circulating tumour cells in blood specimens of 150 CRC patients and further validated by RT-PCR.

Results and discussion: Liver metastasis was significantly correlated with overexpression of TMPO and OLFM4. The OLFM4 overexpression may affect metastatic behaviour of tumour cells in CRC patients. Results from this study demonstrated that overexpression of PSG2 and TMPO genes were correlated with tumour stage, and OLFM4 gene was significantly associated with liver metastasis in Taiwanese CRC patients.

Conclusion: These genes may be suitable new markers pre-operatively for CRC prognosis and liver metastasis. Suitable biomarkers can predict disease prognosis, and also aid in making appropriate treatment strategy decisions.

44 Vesicular Stomatitis Virus - A Candidate Tumour Therapeutic Prostate Cancer Cells Response to Oncolytic Viral Strains

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Introduction: Oncolytic viruses that are able to infect and kill cancerous cells offer a promising alternative approach compared to conventional cancer therapies. Oncolytic viruses are able to exploit tumour specific genetic defects recently have been trailed clinically for their antitumour capabilities. Variety of tumour cells acquired defective cellular and anti-viral response, so oncolytic viruses selectively can replicate and kill tumour cells due to this diminished cellular response. Genetically engineered oncolytic viruses are being developed to combat cellular innate immune response.

VSV could be a potential oncolytic candidate due to its property to specifically target tumour cells defective in IFN signalling. VSV could be engineered to express gene product that could blunt the IFN response. Engineered VSV like M51R is unable to resist anti-viral response, thus cannot replicate in normal cells harbouring intact immune response. However it could retain its ability to grow in cancer cells with defective antiviral signalling.

In most of tumour pathogenesis IFN response genes are involved. It has been shown previously VSV M protein mutant enhanced VSV selectively for malignant cells compared to normal cells. This VSV M51R also sufficiently up regulates the IFN response to infected normal cells, render its more susceptible to host innate immune response and causes the virus to be safely cleared from normal cells. VSV-M51R specifically kills the malignant cells compared to wild type VSV which inhibit host innate immune response.

Materials and methods: In this study we used five different strains of VSV to infect prostrate cancer cells and adopted system biology approach to quantify gene expression by RNA microarray assay, qRealtime-PCR, quantitative immunoblotting and multi-analyte ELISA.

Results and discussion: Our experimental data showed that VSV-N3 (where N gene translocated from position one to three) similarly like M protein mutant M51R could activate host antiviral IFN response compared to inhibitory effect of wild typet-VSV. Our system biology approach (global gene expression study by RNA microarray assay) demonstrated that VSV-N3 similarly like VSV-M51R up-regulated several genes involved in cellular immune response and cancer cell biology signaling pathway.

Conclusion: The goal of any viral therapy for cancer treatment is to efficiently kill primary and metastatic cancer cells while sparing normal cells. VSV (N1, N3 and M51R) infected PC3 (intact immune response) were used to quantify gene expression involved in apoptosis. The results showed that N3 and M51R up-regulated several pro-apoptotic genes product compared to wt-VSV-N1.

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45 Paclitaxel Resistance is Associated with Drug Accumulation in Intracellular Compartments in Human Lung Cancer Cell Lines

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Introduction: Several mechanisms have been suggested for paclitaxel resistance in cancer cells, including overexpression of the multidrug transporter gene, ATP-binding cassette, sub-family B, member 1 (ABCB1), and the presence of a point mutation in the β-tubulin gene at the paclitaxel-binding site. However, the mechanisms underlying resistance to this agent have not yet been completely elucidated.

Material and methods: Three human lung cancer cell lines, II18, A549, and RERF-LC-KJ, were analysed; their 50% inhibitory concentrations of paclitaxel were -8.33, -7.69, and -4.51 logM, respectively. The cell lines did not have any β-tubulin mutation. We evaluated the expression levels of ABCB1, intracellular accumulation of paclitaxel, paclitaxel-induced stabilisation of microtubules, and intracellular localisation of Oregon Green® 488-conjugated paclitaxel in these cell lines.

Results and discussions: The ABCB1 expression level was strongly correlated to intracellular [3H]-paclitaxel accumulation (r^2 = -0.804) but was not related with paclitaxel resistance. The changes in the quantities of polymerized tubulin after paclitaxel exposure were not related to paclitaxel resistance. Differences were observed between the intracellular localisation of paclitaxel in RERF-LC-KJ, the most resistant cell line, and in the other 2 cell lines. The use of Oregon Green® 488-conjugated paclitaxel enabled visualization of not only the normal microtubule formation in the partial cells but also the aggregated vesicle formation in RERF-LC-KJ cells; aggregated vesicle formation was not remarkable in the other cell lines.

Conclusion: The intracellular compartments in which paclitaxel accumulates could play an important role in the development of paclitaxel resistance, in addition to the mechanisms already proven to be involved in drug resistance.

46 Dose Calculation Based on Four Dimensional Computed Tomography for Liver Cancer Patients Using Three Dimensional Dosimery Verification System

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Introduction: To investigate the difference between the static dose of three dimensional conformal radiation therapy (CRT) or intensity-modulated radiation therapy (IMRT) plan and the reconstuction dose on the free-breathing motion for liver tumours using COMPASS system.

Material and methods: Twenty-three free-breathing liver tumours radiotherapy patients, planned on three dimensional computed tomography (3DCT) were selected. The CRT or IMRT plans were delivered to the linear accelarator by treatment plan system (TPS). The high-resolution 3D dose distribution was measured using Matrix measurements and reconstructed on each breathing phase of the four dimensional computed tomography (4DCT). Accumulation dose were calculated on one of the ten phases using deformable registration according to the time-weighting factors for each breathing phase.

Results and discussions: Relative to static plans, mean dose change (range) after deformable dose accumulation (as % of prescription dose) was 3 (-2 to 6) to mean liver, -5 (-10 to 3) to maximum bowel, -4(-15 to 1) to maximum stomach, and -2 (-6 to 9) and -1 (-6 to 1) to mean left and right kidneys. Compared to static plan there were no significance for reconstruction accumulation dose for all above dose parameters.

Conclusion: Dose calculation based on 4DCT could accurately evaluate the actual dose of the normal tissue for liver tumours radiotherapy. Potentially significant dose changes were observed in the majority of patients to either a tumour or normal tissue, compared to static plans.

47 The Standardised Uptake Value Change for Small Cell Lung Cancer after Chemoradiotherapy Using Functional Image

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Introduction: The purpose of this study was to detect small cell lung cancer after chemoradiotherapy using standardised uptake value (SUV) change by fluorodeoxyglucose positron emission tomography (FDG-PET) scanning.

Material and methods: A total of 21 stage – small-cell lung cancer lesions accepting chemoradiotherapy were examined. The therapeutic effects were evaluated by pre-treatment SUV, post-treatment SUV and % change in SUV.

Results and discussions: All patients after therapy were observed, the volume of gross targets (GTV) became smaller than pre-treatment ($p < 0.05$). A significant difference was found at the post-treatment SUV and the % change in SUV. Taking the post-treatment SUV of 3 and the % change of 60 as a cut-off value, a significant difference was found in all cases. Therefore, it is useful to predict the therapeutic effects after chemoradiotherapy by a combined analysis of the post-treatment SUV and the % change in SUV ($p < 0.05$).

Conclusion: The results suggest that it may be possible to predict stage – small-cell lung cancer therapeutic effects using SUV and % change in SUV. Therefore, the use of analysis of FDG-PET between the pre-treatment and post-treatment findings is considered to be helpful in choosing the optimal therapy.

49 BPR000K, a Novel Aurora Kinase Inhibitor

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Aurora kinases A, B, and C, members of sereine/threonine kinase, are key mitotic regulators involved in maintaining the genomic integrity of daughter cells. Because over-expression of Aurora A and Aurora B is frequently associated with tumour genesis, these molecules have been targeted for cancer therapy. Here we describe the profile of BPRoooK, a specific and potent small molecule inhibitor discovered by the Institutes of Biotechnology and Pharmaceutical Research, National Health Research Institutes, targeting the Aurora kinase.

BPRoooK showed potent *in vitro* Aurora kinase A inhibition (IC_{50}: 41 nM) and caused 4N-DNA accumulation at low concentration

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(26 nM). Moreover, BPR000K exhibited anticancer activity against a broad spectrum of cancer cells (IC_{50}: 10~500 nM against Colo205, TW039, HCT-116, MOLM-13 and MIA Paca-2). In HCT-116 xenograft model, BPR000K suppressed tumour growth up to 90% at 20 mg/kg twice-a-day for 10-day treatment by IV administration, and showed better antitumoural activity than the reference agent (VX-680 at 50 mg/kg). The body weight loss is less than 10% during the dosing period. BPR000K also exhibited significant tumour regression *in vivo* by IV administration at 50 mg/kg once a day for 10-day treatment in Colo205 and MIA Paca-2 xenograft models. BPR000K suppressed tumour growth up to 90% at 50 mg/kg twice a day for 10-day treatment by IV administration in pancreatic cancer xenograft models.

50 Isolation, Proliferation, and Phenotyping of Cancer Stem Cells From Primary Breast Cancers - A Model for Evaluating the Response to Antitumour Drugs

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Background: Recent years have witnessed an increasing interest in the role of cancer stem cells (CSCs) in carcinogenesis and tumour progression due to their unique characteristics that allow them of selfrenewal, promoting metastasis, and resisting radio- and chemotherapies. In addition, the high levels of CSCs in tumour mass were linked to a poor prognosis, relapse and metastasis, which had led to recognising CSCs as promising therapeutic targets. Based on that, the need for establishing *in vitro* cellular models that maintain the original characteristics of CSCs, including their ability to self-renew and differentiate into heterogeneous cellular populations inside the tumour mass, and to resist chemotherapy, is currently a main focus of cancer research.

Objective: This study aims at establishing a CSC cellular model, which might enable the testing of new chemotherapeutics and/or combinatorial therapies for currently used agents.

Material and methods: We culture tumour cells obtained from primary breast of a number of Syrian patients. This was followed by isolating stem cell population existing in the primary tumour by means of serial dilution of cells, and the characterisation of these cells by flow cytometry based on their morphology, surface antigen profile (CD44+/high/CD24-/low), and their growth and enrichment in suitable culturing media in both adherent and non-adherent conditions. Finally, the viability of CSCs was tested after freezing cells in liquid nitrogen.

Results and discussion: In this study, we were able to isolate CSCs from primary breast tumour with high purity exceeding 90% and we showed their CSC characteristics, which included: i) CD44+high/CD24-/low profile; ii) their ability to form tumourspheres in non-adherent/suspension conditions; and iii) their ability of resisting chemotherapeutic agents in comparison with non-purified/non-stem breast tumour cells.

Conclusions: Our results confirm the establishment of a cellular model representing the characteristics of cancer stem cell population. This breast CSC model could be useful in conducting future research enabling the identification of responsible mechanisms behind breast cancer resistance to chemotherapeutics and/or involvement in metastasis. In addition, this model might enable the examining of new combinatorial therapeutics and/or improving the currently used therapeutic strategies by evaluating the effects of drug combinations targeting the different and heterogeneous cell populations inside breast tumours, both tumour non-stem as well as tumour stem cells, thus, achieving the desirable therapy outcomes.

52 Intake of Aloe Vera Extract Withstands Against Enhancement of the Tumour Marker CEA

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Introduction: Various studies indicate that several factors including stress can influence serum level of tumour markers. In this study, we evaluated the effects of immobilization stress and *Aloe vera* extract on serum level of CEA in male rats.

Materials and methods: Male Wistar rats were used in our study. Animals were randomly devided into control, *Aloe vera* extract receiving, acutely or chronically immobilized, and acutely or chronically immobilized *Aloe vera* extract receiving of 5 each. The subjects were exposed to chronic or acute immobilization stress for 2 hr/day or 8 hr/day for a period of 3 weeks or one week, respectively. *Aloe vera* extract (300 mg/kg/day) was fed by gavage feeding orally. Blood samples were collected using cardiac puncture technique. Following serum collection, CEA level was determined by radioimmunoassay method. Data were compared statistically between groups (ANOVA).

Results: Serum CEA level was significantly increased in acutely or chronically immobilised rats compared with control rats ($p < 0.001$). However, there were no significant differences in serum CEA levels of *Aloe vera* extract receiving or acutely or chroniallyc immobilised *Aloe vera* extract receiving groups compared with control animals.

Conclusion: Conclusively, our findings indicate that immobilisation stress enhances serum CEA level, however, intake of *Aloe vera* extract withstands against increasing effect of immobilisation stress on serum level of CEA.

53 Comparative Analysis of Estrogen Receptor Beta Expression in Non-small Cell Lung Cancer by Using Different Antibodies

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Introduction: Estrogen receptors beta (ERbeta) are prognostic markers in non-small cell lung cancer (NSCLC) and potential target for anti-estrogen therapy. In NSCLC evaluation of ERbeta is performed by using different antibodies – against ERbeta or their wild type (ERbeta1). Could it be the reason of erroneous estimation of ERbeta status? To answer this question we have analyzed parallel ERbeta and ERbeta-1 expression in the same samples of NSCLC with methodology developed by us.

Material and method: 32 NSCLC surgical specimens were analyzed by immunofluorescence methodology by flowcytometry. Single-cell suspensions obtained from the tumours were incubated with primary antibodies (anti-ERbeta 14C8, IgG1, IgG2a, Abcam; anti-ERbeta-1 EMR02, Novocastra) overnight and with secondary FITC-conjugated antibody (F2772, Sigma) for 1.5 hr. Mean cell fluorescence and number of stained cells were analyzed with WinMDI software and Kolmogorov-Smirnov statistical approach. Three indexes of ER expression level were used for the comparison: high – ER was revealed more than in 50% of the cells; moderate – in 30-49%; low – less than in 30%. For ER expression intensity we used two indexes: high – intensity of specific cell fluorescence is higher 2.0 times and more than intensity of isotypic control; low – less than 2.0 times higher.

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Results and discussion. ERbeta and ERbeta-1 was revealed in all the patients. Mean level of ERbeta and ERbeta-1 was the same (?=0.102) but it was often individual differences in concrete sample. However differences between intensity of ERbeta and ERbeta-1 was significant (1.9±0.8 ? 3.2±2.1, ?=0.009). Low intensity of ERbeta was shown in 59% of samples, high – in 41% of tumour. Antipodal trend was achieved for ERbeta-1 – 61 and 39%, respectively. Low level of ERbeta in tissue of NSCLC was found in 44% of patients, moderate – in 38% and high – in 18% of patients. For ERbeta-1 the similar indexes were 35, 26 and 39%, respectively. But no significant difference between described distributions was revealed (? > 0.05).

Conclusion: For prognosis of NSCLC disease progress in clinical practice it is necessary to use antibody for ERbeta because of existence individual differences between ERbeta and ERbeta-1 expression indexes in concrete patient. But these differences do not affect on mean expression indexes in the groups of patients. That is why for correlation of ERbeta status with clinicopathologic features of disease it is possible to use both antibodies. Supported by RFBR (Grants N10-04-00551-a, N12-04-00028-a).

54 An Anti-angiogenic Marine Compound, Austrasulfone, for Suppression of Metastatic Melanoma

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Introduction: Metastatic melanoma is one of the most lethal types of cancer, underscoring the need for development of novel therapeutic agents. Austrasulfone is an anti-angiogenic marine compound derived from Taiwan soft coral and well tolerated in the pre-clinical animal studies. The present study evaluated the therapeutic potential of Austrasulfone for treatment of lung-metastatic B16-F10 melanoma model.

Material and method: The influence of Austrasulfone on proliferation, apoptosis and anchorage-independent growth of B16-F10 cells was evaluated using MTT assay, flow cytometry analysis and colonies formation assay, respectively. The *in vitro* effect of Austrasulfone on the motility and invasion of B16-F10 cells was evaluated using scratch wound assay and trans-well assay, respectively. B16-F10 cells engineered to express firefly luciferase (luc-B16-F10) were employed for *in vivo* bioluminescence analysis of lung metastatic events in C57Bl/6 mice. After intravenous injection of luc-B16-F10 cells for 1 day, the mice were treated with intraperitoneal injection of Austrasulfone (100 and 300 mg/kg/day; n = 8 per group) for 14 days. The extent of lung metastasis was monitored by bioluminescence analysis on day 7 and day 14, and by histological analysis after sacrificing the animals on day 15.

Results and discussion: Despite of little influence of proliferation and apoptosis, application of Austrasulfone potently inhibited anchorage-independent growth of B16-F10 cells with a half-maximal inhibitory concentration (IC_{50}) of 2.5 mM. Besides, Austrasulfone significantly attenuated the motility and invasiveness of B16-F10 cells. Bioluminescence analysis revealed that Austrasulfone treatment perturbed the lung metastasis in a dose-dependent manner on day 7 and day 14. Histological analysis showed that Austrasulfone therapy reduced the lung colonies by up to 70% of control group. Moreover, Austrasulfone induced apoptosis and neovascularization blockade of metastatic melanoma.

Conclusion: The anti-angiogenic Austrasulfone therapy may hold potential for control of metastatic melanoma.

55 A Novel Histone Deacetylase Inhibitor, MPT0B291, Exerts Potent Anticancer Activity in Human Prostate Cancers

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Introduction: Pathogenesis of prostate cancer is paralleled by aberrant transcriptional regulation which involves gene silencing by histone deacetylase (HDAC). Therefore, HDAC inhibitors have been developed as promising anticancer agents for treating prostate cancer. We recently designed and synthesized a series of novel nitrogen-containing [6, 5]-fused heterocycles as HDAC-targeted agents. Among them, MPT0B291 was identified as a potential lead based on cytotoxic and HDAC inhibitory properties. The present study aimed to investigate the therapeutic efficacy of MPT0B291 toward human prostate cancer *in vitro* and in pre-clinical animal model.

Materials and methods: The *in vitro* and *in vivo* anticancer effect of MPT0B291 was examined by the two dimensional (2D) cell culture, three dimensional (3D) cellular spheres, and human xenograft model. HDAC enzymatic assay, flow cytometry, and Western blotting were used to reveal molecular events in this study.

Results and discussions: MPT0B291 possesses potent anti-proliferative activity in all test prostate cancer cells, including PC3, DU145, LNCaP-104S, LNCaP-104R1, and LNCaP-104R2. In addition, it also disrupted the spheroid structure of prostate tumours in concentration-dependent manner. This result revealed that the cytotoxic effect of MPT0B291 was equally potent between 3D spheroid culture and 2D culture. Furthermore, we analysed its inhibitory activity against HDACs in hormone-independent PC3 cells. The result demonstrated the MPT0B291 significantly inhibited a variety of HDAC isoforms, including HDAC1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 in time- and concentration-dependent manners. Consistent with the HDAC inhibition, MPT0B291 increased histone H3, H4, and tubulin acetylation, up-regulated p21 protein, and promoted cell-cycle arrest, inducing G_1- and G_2/M-phase accumulation in PC3 cells. MPT0B291 also increased sub-G_1 population, activated caspase-3, -8 and -9, and induced PARP cleavage in PC3 cells. These results indicate that MPT0B291 induces apoptosis. Moreover, MPT0B291 treatment of nude mice bearing PC3 xenografts suppressed tumour growth and induced tumour cell apoptosis of tumour-bearing mice.

Conclusion: Our findings demonstrate that MPT0B291 is a novel pan-HDAC inhibitor with potential chemotherapeutic value in prostate cancer therapy and warrants further investigation in this regard. (**Grant support:** DOH101-TD-C-111-004)

56 Differential Modulation of Cell Cycle and Apoptosis in Hepatoma Cells by HBx Protein

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Introduction: Hepatitis B virus (HBV) is one of the major risk factors for hepatocellular carcinoma (HCC) and HCC-associated diseases, including liver cirrhosis, acute hepatitis B, and chronic hepatitis B. The *X* gene is essential for early steps in infection during the viral

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life cycle, viral genome replication, HBV-associated diseases, and development of HCC. The HBx protein promotes cell cycle progression via down-regulation of cell cycle suppressive proteins, such as p21 and p27, and up-regulation of cell cycle progressive factors, such as Cyclins D and E, and PCNA in Huh7, Chang, and HepG2 cell lines [6-8]. However, HBx down-regulates the expression of Cyclins D1, E, A, and B1, CDKs 2 and 4, and PCNA, and it induces G1 phase arrest and repressed cell growth via the GSK-3β/B-Catenin cascade in Chang-X cells.

The HBx protein is believed to influence apoptosis, cell cycle progression, and cell growth. However, the exact role of HBx is still not fully understood. In the present study, we examined its effects on regulation of cell cycle and apoptosis in normal liver and hepatoma cell lines, in an effort to gain more understanding of some of these controversial HBx activities.

Material and methods: We established the Huh7-X and Chang-X cell lines that constitutively express HBx. The cell cycle was examined by flowcytometry, western blotting and RT-PCR.

Results and discussions: There were differences between the two cell lines in terms of cell cycle regulation and expression of p27 and transforming growth factor-β. Expression of HBx proteins dramatically increases expression of Bcl-2 and reduces levels of cleaved PARP protein in Chang-X cells, and it inhibits apoptosis under unfavourable conditions such as serum starvation, in Chang-X and Huh7-X cells.

Conclusion: Our findings provide clues about the intracellular roles of HBx and demonstrate that expression of this protein is important for multiple cellular processes, i.e. cell cycle progression and apoptosis, in hepatoma cells and normal liver cell lines.

59 New Hydantoin Derivatives - Promising Candidates for Anticancer Therapy

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Introduction: Hydantoin derivatives have various biochemical and pharmacological properties such as anticonvulsant, fungicidal, herbicidal, antitumour, anti-inflammatory, anti-HIV, hypolipidemic, antiarrhythmic and anti-hypertensive activities. Although hydantoin compounds are studied extensively there are not many studies that investigate their multidrug resistance reversing effect, such as bacterial efflux pump modulating activity and anticancer properties. The aim of this study was to investigate the efflux pump modulating and apoptosis inducing activity of new hydantoin derivatives on mouse T-lymphoma cells overexpressing the P-glycoprotein (ABCB1) and the apoptosis inducing activity of these derivatives on colon carcinoma model using Colo 205/S sensitive and Colo 320/R resistant colon carcinoma cells having an over-expressed ABCB1 system.

Material and methods: The hydantoin derivatives were evaluated for their efflux modulating effects in cancer cells using fluorescence activated cell sorting measuring the accumulation of rhodamine 123 and their apoptosis inducing effect using Annexin V-FITC labelling in fluorescence activated cell sorting.

Results and discussions: In cancer cells, the compounds investigated were not cytotoxic and some of them significantly increased the retention of the P-glycoprotein substrate rhodamine 123 in L5178Y mouse T-lymphoma cells, furthermore, eight compounds showed synergistic effect with the anticancer drug doxorubicin. The hydantoin derivatives could increase the intracellular accumulation of rhodamine 123 in multidrug resistant Colo 320 cells, however they could not induce the apoptosis of Colo 320 cells.

Conclusion: In cancer cells, some derivatives can be promising candidates to treat the P-glycoprotein-related resistance. The most active structures contained aromatic substituents as well as some tertiary amine fragments. Surprisingly, the derivatives did not induce apoptosis on Colo 320/R resistant colon carcinoma cells, indicating that these hydantoin compounds are potent efflux pump inhibitors (EPI) without affecting the signalling pathways that regulate apoptosis.

60 Obesity as a Risk Factor in Colorectal Cancer and Correlated Toxicity in Patients in Antiblastic-Chemotherapy Treatment

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Introduction: In Europe, obesity is associated with an increased risk factor for colorectal cancer equivalent to 15% in men and 17% in women. The conditions of overweight and obesity are more prevalent among men than among women: 45.2% of men are overweight and 11, 3% are obese compared to 27.7% and 9.3% of women. In Italy at the local level is observed that the condition of overweight and obesity is more prevalent in the South with an obesity rate of 12%. The study aims to evaluate, the correlation between BMI (body mass index) and colorectal cancer in a population treated with antiblastic chemotherapy, than the normal population and the possible increase of toxicity in obese patients.

Materials and methods: A retrospective analysis was conducted on patients with metastatic colorectal cancer treated in 2011 in two cancer hospitals centres in Sicily. It was compared to the percentage of obese subjects (BMI > 30) between the normal population derived from literature and the study population. In addition, we evaluated the potential increase of toxic effects of antiblastic chemotherapy in obese patients with metastatic colorectal cancer in the study population.

Results and discussion: Among patients with colorectal cancer in the study, there is a condition of obesity in 17.8%, with 16.7% in males and 19.6% in women. In clinical practice a dose reduction is found for the 16.7% in obese patients, for the 44.4% in overweight patients, and 38.9% in patients of normal weight. The 72.2% of the regimens in which practice of reducing doses containing oxaliplatin and the 25% irinotecan; comparing the toxicity of oxaliplatin addition to BMI, it is observed that this drug represents 100% of the treatments reduced among the obese, 75% of treatment reduced in overweight and 57% reduced in the treatment of normal weight.

Conclusion: Among patients in the study highlights a condition of obesity is more widespread than the normal Italian population, which in women is doubled to confirm an increased risk factor. The reductions plan of antiblastic chemotherapy dose occur for approximately 61% in obese or overweight also the toxicity of oxaliplatin is steadily increasing, rising from normal weight to overweight to represent the totality of dose reductions in the obese. We reserve to conduct further studies on larger population samples to confirm these results and to detect any differences between obese males and females in colorectal cancer.

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61 Regulation of Slug/Snail 2 Phosphorylation Through GSK-3ß

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The Snail family proteins, such as Snail, Slug/Snail2, EF1(ZEB-1), SIP1(ZEB-2), and TWIST, contain four tandem C2-H2 zinc finger motifs at the COOH-terminus and a highly conserved SNAG repression domain (1-9 amino acids) that is important for co-repressor interaction at the NH2-terminus. The zinc finger binds to a DNA target sequence called the E-box motif (CANNTG), which is usually found in tandem in Snail target genes, including E-cadherin. Another Snail family member, Slug/Snail2, is also upregulated in breast cancer and in malignant mesothelioma, is a mediator of EMT and metastasis, and is shown to be induced by fibroblast growth factor and hepatocyte growth factor. Based on putative GSK-3β phosphorylation sites within the Slug/Snail2, we explored the significance of GSK-3β-mediated phosphorylation in Slug/Snail2 expression during EMT. To understand the role of GSK-3β phosphorylation sites in the function of Slug/Snail2, we mutated the serine residues to alanines (S87A, S92/96A, or S100/104A), because reasoned that mutations in this region might disrupt the phosphorylation of Slug/Snail2 and stabilise the protein. Mutation of the putative GSK-3β phosphorylation sites (S92/96A or S100/104A) enhanced the Slug/Snail2-mediated EMT properties of E-cadherin repression and vimentin induction, compared to wild-type Slug/Snail2. S92/96A mutation inhibited degradation of Slug/Snail2 and S100/104A mutation extended nuclear stabilisation. Inhibition of GSK-3β activity caused similar effects as did the phosphorylation mutations. This study provides evidence that GSK-3β-mediated phosphorylation of Slug/Snail2 results in localisation and degradation in the cytosol, leading to efficient E-cadherin suppression and inhibition of EMT. Taken together, our study suggests that GSK-3β-mediated phosphorylation can regulate the function of Slug/Snail2 in controlling EMT. Our study not only reveals a molecular mechanism underlying Snail2-induced EMT, but also has valuable implications in the development of effective treatment strategies for metastatic cancer progression.

Poster Session: Cytotoxic Drug Preparation

62 Evaluation of a Standard Training on Cytotoxic Drugs Reconstitution by a LC-MS/MS Method

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Introduction: Fudan University Shanghai Cancer Center (FUSCC) is one of the most famous cancer centres in China. During 2011, the number of patients received chemotherapy exceeded 100 thousand. These overwhelming forces drive our pharmacists executing their clinical practices mandatorily and mightily. To standardisation the compounding and reconstitution process, to evaluate the outcome of the standard training programme, as well as to monitor the spill or extravasation of cytotoxic agent.

Material and methods: A tuition video was produced and a liquid chromatography-tandem mass spectrometry method was developed. 12 pharmacists were divided into two groups randomly. Group 1 (n = 6) receiving empirical training by pharmacist A who had being working in this field for more than 3 years. Group 2 (n = 6) receiving standard training by using the tuition video under the supervision by another pharmacist B who had the same experience as pharmacist A. These two groups were trained for 4 weeks. Each of the 12 pharmacists was required to reconstitute irinotecan, paclitaxel and docetaxel in a biocabnet with a brand new sterile chemo-prep pad. When completing reconstitution, the pad was collected and 10 pieces of 1 cm x 1 cm samples were cut and vortexed vigorously with ethyl acetate and evaporated under N2 atmosphere. After reconstitution, all the samples were analysed by injecting to Acquity™ Waters UPLC system which was connected with AB 4000 Q Trap.

Results and discussions: According to Table 1, the concentrations of irinotecan, docetaxel and paclitaxel were found significantly lower in samples from Group 2 comparing to Group 1. Given that the total area sampled from a single chemo-prep pad was 10 cm^2 which was 1/160 of the total area, the maximum concentrations of irinotecan, docetaxel and paclitaxel spilled by pharamacists from Group 1 can reach 22.4, 5.4, and 15.3 μg.

Table 1: Concentrations detected in the chemo-prep pad samples

	Concentrations found (ng/mL)		
Sample	**Irinotecan**	**Docetaxel**	**Paclitaxel**
Group 1 Mean ± SD	59 ± 47	16 ± 14	41 ± 37
Group 2 Mean ± SD	1.2 ± 1.2	0.2 ± 0.2	1.4 ± 0.8
p values between Groups 1 and 2	0.0303	0.0366	0.0444

Conclusion: From these results, we can draw the conclusion that the standard tuition video is effective and reliable in training reconstitution skills. And all of our pharmacists should receive this standardisation instead of the empirical training.

63 Safety Assessment and Revision of a Central Cytostatic Unit According to ESOP Guidelines

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Introduction: The safety status of a central cytostatic unit in a regional hospital with 1,600 beds was reviewed. The cytostatic unit produces 80–100 infusions daily with a staff of 1 pharmacist and 2 pharmacy technicians. Staff education, standard operating procedures (SOPs), workplace environment, environmental concerns and personal protective measures were assessed, based on the guidelines of ESOP's QuapoS 4.

Methods and discussion: The manual method used for cytotoxic drug preparation poses some inherent risks of both human and environmental exposure, as well as potential medication errors and repetitive strain injuries. It was found that a comprehensive revision of the above mentioned areas was required. This revision consisted of the following stages:

- As a fundament, a revised operating protocol was created containing specific and detailed SOPs for every aspect of the unit's work.
- A training programme was developed including ESOP's 'Clean Working' in-house course, which the staff is required to participate in on a semi-annual basis.
- The personal protective equipment set was also revised, introducing new syringes, injection spikes, closed-system drug transfer devices, gloves, protective clothing and respiration masks.
- To assess the workplace contamination, a series of surface wipe sampling tests were performed. Based on the results, a new

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laminar air flow safety cabinet was installed and the cleaning SOPs were also thoroughly revised. New cleaning materials, safety mats and waste disposal systems were introduced and the cleaning staff was also enlisted in the semi-annual in-house training seminars.
- To prevent accidental environmental exposure, ESOP's standard spill kits were put in use. The decontamination SOPs were also updated accordingly.
- A greatly enhanced level of medication safety could be achieved by introducing a computer-aided therapeutic and drug preparation system. The installation of one such software solution is currently under authorization.

Conclusion: The purpose of this work was to adopt safe-handling practices and precisely regulated SOPs together with continuous staff education, thus minimizing the risk of human and environmental exposure while maintaining the highest level of medication safety. In the case presented above, the systematic revision of the central cytostatic unit provided a substantial leap forward in all of the areas stated above.

64 Procedures Handling Cytotoxic Drugs in Two Units From Two Countries of the European Community

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Introduction: The centralised manipulation of cytotoxic drugs within pharmaceutical services is the result of legal requirements with regard to technical competence of these services, as well as the need for rigorous control in terms of quality assurance.

This methodology and determination have also the purpose of reducing costs with this therapy to allow the reuse of medical products, owing to the use of strict aseptic technique and the follow-up of the studies on physical and chemical stability of drugs used.

In Europe and specifically in the European Community, we can find handling procedures in order to ensure the quality of the final preparations, as well as the protection of handlers and the environment.

The lack of standards and procedures with legal imperatives, has meant that each unit prepares its procedures in order to adapt to their reality the different recommendations, in particular those emanating from specific country legislation, European Medicines Agency European Society of Oncology Pharmacy, American Society of Health System Pharmacists, British Oncology Pharmacy Association.

Study Objective: The main objective of this study is to make a description of the procedures followed in two centralised units handling cytotoxic drugs incorporated in two hospitals in different countries, which have in common the fact that they are located in Europe and are integrated into the European Community.

Material and method: The study was done in 'General Teaching Hospital' located in Prague (Czech Republic) and in 'Hospital de Faro, EPE', located in Faro (Portugal).

It is based on a detailed description of all standards and procedures followed in each of those units.

Results and discussion: Handling medication is made in a Clean room class C in both Hospitals, but while General Teaching Hospital located in Prague uses 3 isolators, Faro Hospital uses a Biosafety cabinet class II Laminar Flux Chamber.

In continuation we described individually the physical structure of each unit centralised handling cytotoxic in the hospitals. We described also, in detail the procedures arising from the activity inherent focus on: Protective aids; Medical order; Processing of orders; Cleaning and disinfection; Preparation; Checking and dispensing; Transport; Working hours.

Finally a comparison is made between the premises and the working procedures of the two units trying to identify the aspects in common, the main differences and what improvements could be implemented.

Conclusion: After the overall evaluation we can verify hospitals with different dimensions and different realities in terms of working methodologies have as objective the maintenance of quality of preparations made.

This work enabled the exchange of knowledge and the ability to work together for the achievement of standards and procedures that can be validated by local bodies and at European level and which may serve as a reference for other units included in the European Community.

65 Cancer Morbidity Among Population Chemotherapy and New Agents Anticancer Medicines in Mongolia

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Introduction: Mongolia is a country located in the centre of Asian continent and has 1.6 million square kilometres area. Its population is 2.6 million and comparably young. Approximately 30% of population are people under 16 years, 4% are people aged over 65 years. Cardiovascular diseases, oncologic diseases, trauma and injuries are the three main causes of mortality among population and their cases are increasing year by year. As reported in the National Cancer Centre annual reports in 2011 in total more than 85 thousand people were served by outpatient ambulatory service and from them 6250 people were hospitalized. From last five years data cancer diseases of liver, stomach, lung, oesophagus, cervical and breast cancer were in the leading positions among morbidity. 70% of newly registered cancer cases are diagnosed in the late stages or in the third or fourth stages. In 2011 were done chemo therapy for 4200 cases and in most cases chemo therapy was combined with radiation therapy or with surgical treatment.

We conducted this study to analyse cancer morbidity, to evaluate chemo therapeutic preparations, their utilisation, and to study problems in cancer chemo therapy.

Material and methods: In the study was used data from National Cancer Centre of Mongolia, its statistical registration for 2011. Statistical analysis was made in chemo therapy data comparing statistical analysis in groups, graphically analysing results.

Results and discussion: In Mongolia cancer chemotherapy has been conducted since 1960s and from 1960s to 1998 there were only 4-6 types of chemo drugs used in cancer treatment alone or in combination with radiation and surgical treatment. During 2000 to 2006 number of cancer chemo drugs have been increased to 8-10 types.

In Mongolia, during 2008–2011 new chemo drugs in additional amount have been registered and in Mongolian pharmaceutical registration now 26 cancer chemo drugs are registered. It is almost 2 times increase comparing with 10 years before. In our country there are no cancer chemo drug manufacturer and cancer chemo drugs are 100% imported. In National Cancer Centres clinical practice since 2010 chemotherapy drugs such as **Paclitaxol, Oxaliplatine, Gemsitabine, Etoposite, Carboplatine, Irinotecane** and some other new preparations, drugs were used and patients have now more choices. We evaluated new chemotherapy preparations, outcomes of their clinical course of treatment. In comparison with old chemo preparations new drugs and their clinical course of treatment had lower rate of side effects, less complications for patients, patients life expectancy has prolonged and almost 90% of patients were living more than 1.6 years more after chemo therapy. We suggest that we use cancer chemo drugs safely and effectively

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establishing and developing better equipped clinical pharmaceutical environment. Financial capacity and support is now problem in pharmaceutical services. Our centre is an only institution in our country to provide cancer chemo therapy and its standards for chemotherapy has been changing for last years in order to develop clinical pharmaceutical basis for chemo therapy, establish safe high technology for cytostatic drug preparation, technology for safe mixing techniques.

Conclusion: Our study has clinical significance. Study results of various combinations of chemo preparations are useful in clinical chemo therapeutic practice. New registered cancer preparations and their clinical treatment courses have comparable results with international published studies. New registered preparations have better clinical outcome lowering side effects, extending patients life expectancy.

Improving clinical pharmaceutical service, improving facilities and equipment, providing better working environment for staff and using closed technology for preparing cytostatic preparations using international standards are now in our objectives.

66 Centralised Cytotoxic Drug Preparation Organised Considering Contamination

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Introduction: In the University Medical Centre Ljubljana, chemotherapy is prepared centrally in the pharmacy. The preparation is organized in order to meet GMP and QuapoS standards and to implement the results of articles concerning cross-contamination and FDA directive.

Objectives: Our preparation of cytotoxic drugs is manual and covers approximately 50 preparations per day, 7 days a week. Cytotoxics and monoclonal antibodies are prepared in the same biological safety cabinet (BSC). The preparation is supervised and optically controlled by a pharmacist and organized to assure the following criteria:

- microbiological quality
- reduction of cross-contamination to minimum
- rationalisation of time of preparation and application
- rationalisation of used materials and drugs, and
- reduction of waste.

Materials and methods: The preparation sequence is drug based. Between each group of preparations we leave laminar air flow to circle in an empty BSC for 3–5 mins, the upper gloves are changed and all the vials with active substance are removed from the BSC.

Test samples for testing microbiological quality are prepared with either 0.9% NaCl or 5% glucose at the beginning and at the end of working procedure.

To determine the degree of cross-contamination, we dissolve 20 vials of testing substance. To the same BSC we place 20 vials of water for injection with an inserted needle that is left unprotected. After different exposure times, we measure the amount of the testing substance in the water for injection vials.

Results and discussion: Microbiological quality was checked in accordance to the guidelines of Ph Eur on 520 test samples and all results were negative. We can conclude that our working procedure assures microbiological quality of preparation.

To assess the degree of cross-contamination, test samples are not yet analysed due to economical reasons. The results published in various articles show that cross-contamination is a serious risk. We can hypothetically state that the working procedure organized on drug basis (preparing all therapies with the same selected drug for the selected day), assures a lower degree of cross-contamination than the patient-based preparation (preparing all therapies for the selected patient successively).

Conclusions: Our working procedure assures microbiological safety and also confirms the assumption that cross-contamination in the case of drug-based preparation is reduced to minimum.

67 Automation of Compounding Cytostatics - Drivers and Pitfalls to Be Avoided

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Introduction: Danish hospital pharmacies have experienced an increase in the demand for compounded cytostatics from 213.000 units in 2005 to 274.000 units in 2011 and this development is expected to continue. This expected need for increased compounding capacity combined with a demographic development predicting shortage of staff and a wish to improve working conditions within the compounding departments, formed the background for looking into automated compounding and subsequent stockholding of cytostatics. The aim of this study was to describe and evaluate a national centralised compounding unit using robotic solutions to meet the 2020 needs for compounded cytostatics.

Material and method: A national dialog based survey was conducted in order to estimate the overall need for Danish compounding capacity by 2020.

A centralised solution was developed and described theoretically through the elaboration of a business case. This scenario was evaluated against a decentralised solution involving necessary expansion and automation of existing compounding facilities.

The identification of risk factors when implementing robotic solution was studied during an 8 months implementation project at the Capital Region Pharmacy.

Results and discussion: The need for compounded cytostatics by year 2020 is estimated to 400.000 units. This reflects an increase of about 50 % compared to the 2011-capacity.

Experiences from the elaboration of the business case show that the initial drivers for automation has been overtaken by an economic approach as focus on costs, investments and compounding fees when the point of final decisions was approached.

The business case showed that the establishment of a new compounding unit serving all Danish Hospital Pharmacies with a capacity for compounding 80,000 doses of cytostatics annually including a 'ready to use' antibiotics production line using robot technology would cost approximately Euros 13.3 million. Of this approximately one third was necessary investments in setting up a new company. The fee per bag would be approximately Euros 38. The costs of a decentralised expansion and rebuilding at 4 existing hospital pharmacies was estimated to approximately Euros 10.4 million. The fee per bag was 27 € – 71€.

From the study on implementing robot solutions five main pitfalls were identified:

- Pharmacy will become very dependant on the supplier of the chosen technology.
- The technical maturity of the robot and practical experiences are determining.
- The pharmacy must adapt to automation and special skills need to be developed.
- The extent of automation increases the complexity in the interplay between software, machine and GMP.
- Production flow and large-scale operation is essential to get low prices.

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Conclusion: Be aware of what is driving the wish for automation and what will be crucial for decisions. The drivers may change throughout the process, but to get to automation you probably need to fulfill all drivers.

68 Comparative Analysis of Environmental Contamination in the Central Cytostatics Department

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Introduction: The potential for contamination associated with handling cytostatic drugs exists in the workplace despite compliance with the protective measures for the safe handling of cytostatics. Given the lack of any national data on cytostatic surface contamination in Hungary, it was decided to carry out the first wipe sample testing in the Pharmacy of Bajcsy-Zsilinszky Hospital, Budapest, Hungary.

Material and methods: The goal of this study was to evaluate cytostatic environmental contamination in our hospital pharmacy by using surface wipe testing (Cytostatic wipe sample set by PharmaMonitor). The first wipe test took place in March, 2011. Five defined areas were tested: laminar airflow (LAF) cabinet, workbench, floor in front of the LAF cabinet, transport box and the handle of the refrigerator located in the make-ready room. The samples were analysed for 8 cytotoxic drugs: 5-fluorouracil (5-FU), cyclophosphamide (CP), ifosfamide (Ifos), gemcitabine (Gem), etoposide (Eto), methotrexate (MTX), pacli-taxel (Pac), docetaxel (Doc) in the Institute of Energy and Environmental Technology, Duisburg, Germany. Following the first test, the use of 0,1 m NaOH decontamination solution and a closed system drug transfer device (PhaSeal®) was introduced.

In December 2011, the wipe test was repeated on the same surfaces (except the refrigerator handle).

Results and discussion: The results of the first sampling showed that the level of substances detected on the refrigerator handle were under the detection limit. The LAF cabinet was the most contaminated area, where the level of 5-FU, Gem, MTX, CP were above the German reference value (0.1 ng/cm^2) and also the Ifos and Doc contamination levels were high. The detected levels on the other three surfaces, ranked in descending order were as follows: workbench, floor and transport box. 5-FU, Gem, CP were present on every surface in large quantities.

After seven months the levels of surface contamination showed significant improvement on every surface. MTX, CP, Ifos, Doc were not detectable in the LAF cabinet and the levels of 5-FU and Gem reduced dramatically.

Conclusion: The results suggest that implementing appropriate decontamination method and preparing with closed system drug transfer device can minimise cytostatic environmental contamination.

69 New Technologies Applied to Anticancer Drugs Preparation

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Introduction: An automatic system for anticancer drugs compounding (APOTECAchemo) has been recently installed at the Oncologic Pharmacy of the European Institute of Oncology (IEO, Milan). The introduction of the automatic system improves the quality of preparations, ensures safer conditions for both patients and operators, and guarantees the data integrity and traceability of all preparation steps.

The automation of hazardous manual activities and the introduction of additional measuring and monitoring steps assure the exact correlation between the prepared and the prescribed dosage, minimizing the risk of human error. The purpose of this work is to analyse the production rate and the workflow re-engineering straight after the robot installation.

Material and methods: The APOTECAchemo activity has been analysed over a seven-month period to detect the temporal production trend and its correlation to the operator. The analysis involves six technicians, from 20 to 45-years old. All the technicians took part in a two-week training course carried out by a Loccioni technician (the manufacturer Company).

Drugs compounded in the automatic system are mainly liquid solution and represent 60% of all the molecules used in our pharmacy.

Results and discussions: The preparations compounded in 32 weeks of work are 6,276, 4,024 prepared in the last 16 weeks, showing an increase of 64% with respect to the previous ones. In the first four months of clinical activity (from March to June), therapies compounded increases of 126%.

Moreover, the production rate (preparations versus hour) doubled from March to September, mainly thanks to process reorganisation: introduction of multidose vials; downtime reduction; therapy schedule by drug rather than by patient.

Conclusion: APOTECAchemo results to be very user-friendly as shown by the high learning rate. The machine performance does not depend on the operator. Conversely, the re-engineering of the pharmacy workflow plays a central role.

To conclude, APOTECAchemo ensures the highest standards of quality of care and safety for operator and patient in oncology pharmacy.

70 Occupational Risk of Handling Monoclonal Antibodies

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Introduction: Little is still known about the occupational risk of monoclonal antibodies (mAbs). As stated by NIOSH a hazardous drug is genotoxic, carcinogen, teratogen or can cause severe organ impairment. IARC does not classify the level risk of mAbs and according to ICH it is not mandatory to test genotoxicity or carcinogenicity. In Parma Hospital, cytotoxic therapies are admixed in a pharmacy compounding facility (UMaCA) under a vertical laminar flow cabinet according to GMP. UMaCA staff wear personal protective equipment. A great concern is related to undefined potential risks from long-term exposures to mAbs. The aim of this work was to produce a risk management procedure for mAbs compounding based on current knowledge.

Materials and methods: Summaries of product characteristics (SPC), safety datasheets (SDS) and published toxicity warnings were collected and a literature review was undertaken for all mAbs used in Parma Hospital. A working group composed of UMaCA pharmacists and chemical safety consultants of the Health and Safety Department got together to evaluate the risk of anticancer mAbs handling and establish safety procedures. A software for the traceability has been used to define molecules, amounts and times of exposure for each worker. An economic evaluation about the use of closed circuit handling devices was conducted comparing it to the use of needles and open circuit devices.

Results and discussion: Tables were built for every anticancer mAb handled in UMaCA. No mAbs showed carcinogen or mutagen

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properties. Rituximab, bevacizumab, trastuzumab displayed developmental toxicity in pre-clinical studies with a potential fetal risk. NIOSH did not include anticancer mAbs in 2012 hazardous drugs list. However, it recommends that the substances be categorized as dangerous if the mechanism of action suggests toxic effects. No Occupational Exposure Limits were defined. Since UMaCA start up in 2008, mAbs therapies have increased by 130% for a total amount of almost 3,300 grams. An additional effect should be considered since healthcare staff handle more than one mAb type during work sessions. Software handling reports are useful to plan a medical surveillance programme. In 2011, the use of closed-circuit devices would have represented an increase in costs of Euros 22,660.

Conclusion: In accordance with the 'As Low As Reasonably Achievable' (ALARA) concept, mAbs therapies should be compounded applying procedures to preclude exposition and cross-contamination with cytotoxic agents. The use of personal protective equipment is recommended. Needleless closed-circuit devices significantly increase costs but could prevent exposition. ALARA principle can sustain working procedures but, to avoid overestimation of the occupational risk, further data including specific studies on humans and warning in SDS are necessary and strongly advisable to develop guidelines on mAbs occupational hazard.

71 The Management of Onco-haematology Infusional Chemotherapy not Administered to Patients

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Introduction: An unexpected economic resource should come from a correct management of infusional chemotherapies that are not administered to patients if preparation of cytotoxic drugs takes place in centralised unit of the Hospital Pharmacy. In this work we analysed the activity of the 'Management of Returned Chemotherapy'.

Materials and methods: The study was carried out from January 2010 to December 2011. In this period patients we have dispensed infusional chemotherapies were 3,118. Over 52,701 therapies, 794 (1.51%) were returned to pharmacy because not used. In these cases, department staff have followed a dedicated procedure in order to alert the pharmacist. For all therapies returned, a 'Delivery form' has to be provided. The pharmacist records in a 'Returned Chemotherapy Registry' data from the therapy (date, department, patient, motivation, drug, dosage) and deletes the scheduled therapy in an electronic database. The pharmacist examines the therapy in order to check the correct conservation modalities and degradation's index of the active compound. The reconstitution or post-dilution chemical and physical stability data were carried out on specific tables for each drug. These data are provided by the manufacturers, but in addition practical stability data are taken from literature and databases. In the eligible cases in which the therapy can be used for another patient, the pharmacist approved the reused dose in the Registry. Then, the pharmacist puts the data of the reused preparation in a worksheet in order to send the information to the technician. In case of negative outcome of the previous steps, the preparation will be eliminated.

Results and discussion: The cost of drugs not administered between 2010 and 2011 is Euros 269,396. The 56.7% of returned therapies were fully or partially recovered for an estimated budget of Euros 205,822. Incidence of returned therapy was calculated for each department in our Hospital. For Oncology Division data show this distribution: Day Hospital (DH) of Penne 3.12%, DH of Pescara 1.86%, DH of Popoli 0.93% and Oncology ward 0.97%. For Haematology Division of Pescara: DH 1.46%, Women's and Children's ward 0.66%, Men's ward 0.56%, Haematopoietic Stem Cell Transplantation Unit 0.49%. The most reused monoclonal antibodies were: rituximab (94%), bevacizumab (76%), cetuximab (64%) and trastuzumab (58%). Some drugs were never reused, such as azacitidine and pentostatin.

Conclusion: The role of the pharmacist is crucial to establish if a chemotherapy will be reused or not but may be important collaboration with the staff of Oncology and Haematology. This multidisciplinary team increases the efficiency of economic resources. The institution of 'day-drug therapy' involves a reduction of production waste, but also a greater chance of recovery made. Obviously, the result would be more relevant in terms of efficient working in 'dose-banding' with extended infusion stability.

72 Cleaning Effectiveness of Workplace Surface Exposed to Cytotoxic Agents - Influence of Cleaning Solutions

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Introduction: Cytotoxic drugs provide therapeutic benefits to patient but also represent a risk of occupational exposure for health care workers who handled these drugs by direct contact or by transfer of the cytotoxic contamination from contaminated surfaces. To minimise this exposure risk, the residual contamination on workplace surface must be eliminated or at least limited. Thus, efficiency of cleaning protocols has to be evaluated.

The aim of this study was to compare the detergent effectiveness of different cleaning solutions frequently used in chemotherapy preparation units to ensure workplace decontamination.

Material and method: The central surface of a stainless steel plate 30 cm x 50 cm was exposed to a calibrated contamination of carboplatin corresponding to 105,000 ng of platinum. After cleaning according a standardised protocol, the plate was sampled by 10 cm x 10 cm surface (15 samples per plate) with swabs. The residual contamination was then quantified by graphite furnace atomic absorption after pre-concentration.

Seven cleaning solutions were tested: 2 hydro-alcoholic solutions, 3 disinfectants and 2 detergents according a standardised cleaning protocol: 4 mL soaked on a first gauze to horizontally clean then 4 mL soaked on a second gauze to vertically clean the plate.

Results and discussion: With more than 20 000 ng of residual platinum on the plate, hydro-alcoholic solutions were the less efficient tested solutions used to remove contamination from work surface. On contrast, the use of detergents resulted in the lowest residual contamination with 2 793 and 4 780 ng/plate. Disinfectants have intermediary efficiency with 5 891 ng and 6 122 ng/plate for ready to use solutions and 15 360 ng/plate for pre-soaked gauzes. Thus, cleaning solutions have different detergent efficiencies. Detergent and disinfectant solutions are at least 6 and 3.3 times respectively more efficient than hydro-alcoholic solutions to remove the contamination on the deposit surface.

Conclusion: The choice of the solution depends on the surface and the objective of the cleaning (disinfection or detergence). If microbiological decontamination is required, the use of disinfectant with surfactant must to be preferred to ensure both protection of the preparation and better chemical decontamination than hydro-alcoholic solutions. On the other hand, detergent has the best chemical decontamination efficiency and can be combined to a compatible disinfectant.

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74 Central Unit of Cytotoxic Preparation's Activity

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Introduction: Exposure to cytotoxic agents is one of the most important risk factors in hospital pharmacy. This way the necessity of controlling the activity of manipulation units arises to prevent these risks. The present study describes in a qualitative and quantitative manner the manipulation in the central unit of cytotoxic preparation in Hospital Faro EPE.

Material and method: It was implemented by the healthcare professionals working in the Central Unit of Cytotoxic Preparation a daily registration of the activity in the unit. In a twelve month period relative to 2011, the healthcare professionals registered data relative to their exposure, namely hazardous drug, dosage (in mg) and exposure time (in hours). During the same period, the number of patients and preparations that were dispensed for the different hospital's services was also registered.

Results and discussion: The most handled cytotoxic agent during the period of the study was 5-Fluouroracil (^{3} 8871.5g), and consequently that was the drug to which the healthcare professionals presented a higher exposure time. Regarding the manipulation time of hazardous drugs was verified a medium of 110 hours/month and the month with higher manipulation time and consequently higher exposure time for the health care professionals was July with 138.5 hours. However the month with more preparations was August with 1,201 preparations, there were less 191 preparations in July. The service to which a greater number of preparations were dispensed was the Oncology Day Hospital.

Conclusion: It could be inferred that 5-fluouroracil is the most handled drug since the neoplasias of colon and rectum are one of most treated pathologies in the studied hospital. It was found that the number of preparations was not directly proportional to the time dispended in their manipulation, which may be due to the specificities of manipulation, dosage or final presentation of each drug. As expected, the hospital service to which are dispensed a higher number of preparations is the Oncology Day Hospital because it is the service responsible for the treatment of the different existing neoplasias. The other services have fewer annual preparations for the reason that they present different specificities, which include a specific age or pathology.

75 Potent Antitumour DNA Bifunctional Alkylating Agent Indolizino[6,7-b]indole Derivatives Against Various Human Solid Tumour Xenografts

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Introduction: We have previously reported that bis(hydroxymethyl)pyrroline derivatives, including bis(hydroxymethyl)cyclopenta[a]indenes, bis(hydroxymethyl)pyrrolo[1,2-b]- isoquinoline and bis(hydroxymethyl) benzo[d]pyrrolo[2,1-b]thiazole derivatives, are able to induce DNA interstrand cross-linking and exhibited potent antitumour activity in inhibiting various human tumour xenografts. To further explore new bis(hydroxymethyl)pyrroline analogues for antitumour studies, we have recently synthesized a series of bis(hydroxylmethyl)indolizino[6,7-b] indole derivatives for antitumour evaluation.

Material and method: Bis(hydroxylmethyl)indolizino[6,7-b]indole derivatives were easily prepared starting from L-tryptophane (1), which was reacted with formaldehyde to give 1,2,3,4-tetrahydro-1H-pyrido [3,4-b]indole-3-carboxylic acid (2). The reaction of 2 with dimethyl acetylenedicarboxylate (DMAD) in acetic anhydride yielded diester 3, which was converted into the 1,2-bis(hydroxymethyl) derivatives (4) via N-alkylation and reduction (lithium aluminium hydride). Carbamoylation of 4 with various alkylisocyantes gave the corresponding 1,2-bis(alkylcarbamates) derivtives (5).

Results and discussion: The *in vitro* cytotoxicity studies revealed that these agents exhibited significant cytotoxicity in inhibiting a variety of human solid tumour cell growth in culture. The structure-activity relationships of these derivatives were studied. Among these derivatives, 1,2-bis(hydroxymethyl)-3,6-dimethylindolizino[6,7-b]indole (BO-1922) was selected for further antitumour studies. It was shown that this compound displayed potent therapeutic efficacy against human colon cancer HT-29, lung adenocarcinomalung A549, and primary pancreatic adenocarcinoma BX-PC3 xenografts. We also showed that this derivative is more potent than Irinotecan (CPT-11) against human colon cancer HT-29 xenograft and is as potent as CPT-11 against lung cancer A549 and pancreatic cancer BX-PC3 in xenograft model. The alkaline agarose gel shifting assay showed that this agent is able to induce DNA interstrand cross-linking. Flow cytometric assay revealed that BO-1922 induced cell cycle arrest at G1/S phase in non-small cell lung carcinomas CL141T.

Conclusion: The above studies suggest that BO-1922 may be a promising candidate for pre-clinical studies.

Poster Session: Automation/Robotics

76 Cytotoxic Surface Contamination in a Robotic System in Comparison to Manual Compounding

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Introduction: The preparation of cytotoxic drugs involves the occupational risk of contamination by aerosolized drug product or contact contamination. Some of these drugs are known to be carcinogenic, mutagenic or teratogenic in humans, therefore, the operator exposure should be kept as low as possible. To work with a robot could be an option to reduce the operator's risk, however, some previous works showed that the contamination with cytotoxic drugs during automated preparation could be similar or higher that during the manual preparation. The main goal of this study was to compare the surface contamination with cytotoxic drug substances during automated preparation and during the manual preparation process.

Material and method: The contamination level of 5 predetermined areas with a possible high risk of contamination inside the Apoteca™ cabinet was investigated with swab tests, according to a known method [1]. In the first series, 15 bags of 5-FU and 15 bags of platinum containing cytotoxic drugs were prepared during two consecutive days. All surfaces were swabbed before and after the preparation process and in addition the outer surface of each bag was swabbed. A second identical series was prepared. In parallel, the surface contamination during the manual preparation was studied. 15 bags of 5-FU and 15 bags of platinum containing cytotoxic drugs were prepared during two consecutive days. 4 pretermined areas of the laminar air flow, the gloves of the technician and all bags prepared were swabbed by the same method. 5-FU suspect samples were analysed by gas chromatography-mass spectrometry and platinum suspect samples were analysed by inverse voltammetry after UV-digestion.

Results and discussion: Cytotoxic contamination was observed in the working area of the Apoteca™ and on the outer surface of several

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products automatically compounded but the contamination levels were comparable or lower during robotic preparation than during manual preparation.

Conclusion: The key parameters to reduce a cytotoxic surface contamination with an automated robotic system for chemotherapy compounding are the adjustments of the robotic arm. In addition, a good and reliable cleaning method needs to be regularly performed in order to remove thoroughly the potential surface contamination.

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77 Accuracy of Preparations Compounded by a Robotic System in Comparison to Manual Compounding

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Introduction: In chemotherapy compounding, the accuracy of preparation is related to patient safety. Accuracy of manually compounded preparations depends on the skills of the operator and the precision of the devices used as the operator adjusts the dose by volumetric measures. A robotic system, performing gravimetric controls, could improve accuracy and consequently patient safety, in assuming that the accuracy of the preparations automatically compounded is better than those compounded manually. The main goal of this study was to compare the accuracy of preparations compounded by an automated robotic system (ApotecaTM) with preparations compounded manually.

Material and method: For automated compounding with ApotecaTM, 3 types of syringes with different sizes (3 mL, 10 mL and 50 mL) are stipulated. To 250 mL bags prefilled with 0.9%NaCl solution, 8 different doses (1.0 mL, 1.5 mL, 2.0 mL, 2.5 mL, 3.0 mL, 10.0 mL, 10.5 mL and 50.0 mL) of sterile water were added. For each dose, 10 bags were compounded. All bags were weighed before and after compounding on an external balance. In parallel, bags with the same nominal doses were prepared following standard manual procedures. In the first series, the same types of syringes like in the robot were used (3 mL, 10 mL and 50 mL). In the second series, syringes were used in accordance with the standard operating procedures of manual compounding in our facility (1 mL, 2 mL, 3 mL, 10 mL, 20 mL and 50 mL).

Results and discussion: The preliminary results show that the accuracy of the products compounded by the robotic system is similar to the accuracy obtained by the manual compounding process. There were small differences in the weight of the products compounded manually and the products compounded with the robot, and also between the products compounded manually with different sizes of syringes, but all the doses remained in an acceptance failure level of 5%.

Conclusion: Accuracy of robotic preparation with Apoteca™ is highly acceptable. Differences between the actual dose and the nominal dose are in general less than 5%.

78 Will Robots Solve the Problems with Increasing Demand for Compounded Cytostatic?

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Introduction: Increasing demand for compounded cytostatic has forced Danish hospital pharmacies to look for automation solutions that support a more effective workflow, otherwise future delivery of cytostatics may be compromised.

Automation of cytostatic compounding is a relatively new field with only a few suppliers that have announced robotics and automated solution suitable for hospital pharmacies.

The aim of the study was to explore the maturity of the technologies as well as analysing throughput, investment levels and production economy of three robotic solutions and a semi-automated compounding set-up.

Material and methods: Based on experience from several automation projects at Danish Hospital Pharmacies, the team developed a data collection form, and an investment and production cost budget model. In addition to material received from the vendors, the team carried out on-site visits to hospital pharmacies in Germany, Italy, and USA, to gather user experience on the technologies. In order to evaluate the fit and effectiveness of the semi-automated compounding solution, a LEAN based value-stream-mapping of the compounding process was carried out at the Hospital Pharmacy in Århus, Denmark.

Results and discussions: The production speed of the robotic solutions is comparable and in some cases slightly faster than the manual production speed. The semi-automated solution is more than 50% faster than the manual production, but is designed for compounding dose-banded cytostatic.

The number of technicians needed in each set-up varies only slightly and is (almost) comparable to the manual production flow. However, when compared to a manual production set-up, the stress levels and RSI sources are lower, resulting in an improved working environment.

Robotics solutions results in both higher investment levels and higher total production cost levels than a semi-automated or a manual production set-up.

Conclusion: Based on the present analysis it is expected that a semi-automated production set-up will be more investment and cost-effective when compared to the three robots. Furthermore, semi-automated solutions are more efficient than manual production.

Next generation robotic solutions must address this efficiency gab in order to become the solution of choice from an investment and efficiency perspective.

80 The First Totally Robotised Laboratory for Oncology Drugs Production

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Introduction: The Oncology Pharmacy of the University Hospital of Ancona, Italy, began the process of robotisation of its laboratory five years ago thanks to an agreement with Loccioni Humancare which manufactures APOTECAchemo (the automated system for compounding cytotoxic drugs). Before that, our laboratory was working with two laminar air flow cabinets that usually produced about 20,000 oncology drug preparations every year. After the introduction of the first system, the work was gradually transferred to the robot, leading to one laminar air flow cabinet becoming disused.

The robot substantially increased productivity, while the arrival, at the end of 2009, of a new generation prompted us into a rethink of the activity of the pharmacy, thereby putting in place the first totally robotised laboratory for the preparation of oncology drugs. The new objectives we established were: 1) to ensure that more than 85% of total production was carried out by robots; 2) to maintain delivery times to the administration units. This work shows the impact of robotised pharmacy on the oncology workflow.

Material and method: Data were obtained from the robot database. One other advantage of automation is related to data mining. Every step

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is measured and traced, providing a huge amount of information which is helpful for both performance statistics and process re-organisation.

Results and discussion: The amount of preparations compounded by the robots were 16,200 in 2010 and 19,300 in 2011. In reality, in the first three months of 2012, we produced 4,980 bags of therapies, and we expect to exceed 20,000 delivered preparations by the end of 2012. Our yearly workload was exactly 20,220 preparations in 2010 and 20,680 in 2011, therefore, robots were responsible for 80% and 93% respectively of the whole activity. Occasionally, robotic production was greater than 96% of the workload. The delivery time has not increased.

Conclusion: The automated production of the cancer therapies represents a big leap forward for the safety of the patient and operator, thanks to the verification and traceability of each preparation, and to the confinement of the hazardous activities. We are confident this technology is going to represent the standard for oncology pharmacy in the near future.

81 Assessing Surface and Cross-contamination After an Intense Use of a Robotic System for Chemotherapy Compounding

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Introduction: The verification of chemical contamination is a fundamental requirement to ensure the safety of operators and patients. Robotic systems are designed to minimise the risk of chemical and microbial contamination. The main source of chemical contamination occurs during the handling of cytotoxic drugs and depends mainly on the working procedures applied. In this work, we wanted to evaluate the level of environmental contamination and cross-contamination generated during a thorough use of the robotic system.

Material and methods: Fluorescein was chosen as a marker for chemical contamination verification due to its high fluorescence, which, when analysed by means of chromatography (HPLC with fluorimetric detector), allows the detection of minimal traces (LOD = 1ppb). The protocol provided for the simulation of hospital pharmacy daily activity, including worst case conditions. Fluorescein vials of 1 mg/mL concentration in NaCl 0.9% solution were used in different vial formulations: single-dose and multi-dose liquid solutions and powder. Wipe tests were carried out at the end of the activity, without performing any cleaning procedures, and involved the surfaces of the inner chambers of APOTECAchemo, the external surface of the compounded bags, the touch-screen monitor and the handle of the bar code scanner. Cross-contamination is verified by detecting the marker inside test preparations compounded simultaneously with those having the tracer, but compounding only NaCl 0.9%.

Finally, the data were analysed using the Sessink's threshold [1].

Results: None of the surfaces sampled outside the robot showed contamination (values < LOD), including the external surfaces of the bags that were compounded. As expected, low levels of contamination (between 0.02 and 0.06 ng/cm^2) were recorded in some internal surfaces of the compounding room. These positive samples are well below the safety limit identified by Sessink [1]. With regard to cross-contamination, no detectable traces of fluorescein were recorded inside the bags.

Conclusion: A systematic protocol to assess drug contamination was designed and carried out. No relevant contamination was recorded after a massive amount of drug was reconstituted. This work represents the first step towards pointing out that robotic compounding can be considered to operate at a safe level for environmental and cross-contamination. The next steps provide for extending this approach to cytostatic drugs, such as fluorouracil and cyclophosphamide.

Reference

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Poster Session: Quality Assurance/Microbiology/Analytics/Stability

83 Stability of the Ready-to-use Solutions of Eribulin for Intravenous Infusion

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Eribulin mesilate is a non-taxane inhibitor of microtubule dynamics marketed under the trade name Halaven(R). Eribulin received approval by the US Food and Drug Administration in November 2010, and by the European Medicines Agency in March 2011 for the treatment of advanced breast cancer patients who have received at least two prior chemotherapeutic regimens for late-stage disease, including both anthracycline-and taxane-based chemotherapies. Eribulin is also being investigated for use in a variety of other solid tumours, including non-small cell lung cancer, prostate cancer and sarcoma. To our knowledge, no other data are available in the literature concerning the stability of this compound. Thus, we undertook to study the effects of temperature and room light on the stability of eribulin over a period of 14 days. The aim of our study was to reproduce the different conditions of use and storage encountered at the hospital. A simple HPLC-UV method was developed to determine the stability of ready-to-use eribulin solutions under different storage conditions. The developed method was validated with respect to linearity, accuracy, precision and ruggedness. The following admixtures were prepared: vials pierced with a stoppered 18 gauge needle, 3-mL polypropylene syringes at concentration of 440 µg/mL, and multilayer laminate polypropylene containers containing 0.9% sodium chloride (50 mL) at concentrations of 15.4 and 43.3 µg/mL. The following storage conditions were tested: 4°C in the refrigerator; and 20°C under room light exposure and light protection. The drug was also subjected to stress conditions of hydrolysis, oxidation, photolysis and thermal degradation. The solutions were assayed immediately after preparation (day 0) and after 1, 3, 7, 10 and 14 days. The drug concentration never fell below 97% of the initial concentration over the 14 days study period. Therefore, eribulin in vials for intravenous injection, in polypropylene syringes or in multi-layer laminate polypropylene containers was stable for 14 days when stored at 4°C in the refrigerator or at room temperature with and without any protection against light. For all samples, there was no visible evidence of precipitation, gas formation, or colour change throughout the observation period. The pH values measured over the 14-day period remained stable. When eribulin was exposed to heat no decomposition was observed. Likewise, the drug was stable against the effect of photolysis and in acidic or alkaline conditions (pH 2.1-9.4). But the drug gradually underwent greater degradation by increasing permanganate concentration. Admixtures of eribulin solutions in open-vials, syringes or polypropylene bags at clinically relevant concentrations were physically compatible and chemically stable for at least 14 days at 4°C in the refrigerator and 20°C with or without any protection against light. Stress studies were performed on eribulin and it was found that no degradation was observed under acidic, basic conditions, photolytic and upon heat treatment, while the drug was found to be unstable to oxidative stress.

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84 Analysis and Management of Non-conformities in a Quality Laboratory for Chemotherapeutic Control

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Introduction: Since 2004, pharmacists of the European Georges Pompidou Hospital (Paris, France) have developed an online control of chemotherapeutics via an analytical high performance liquid chromatography platform. This measure avoids administration of defective preparations, contributes to guarantee high quality products and secure the preparation process with on-line conformity specification. Some non-conformities (NC) are detected during the quality control: production or control failures are responsible for delayed liberation.

The aim of this study was to minimise the time from prescription to administration and to improve the quality assurance system by applying an original critical scoring method to analyse the statement and manage the laboratory NC. This scoring method allowed the detection of critical points and the identification of primary causes in order to target the corrective actions.

Material and methods: First, a multidisciplinary team was formed to list 14 relevant NC systematically registered by technicians from January 2011 to March 2012. For each type of NC, a criticality index (CI) was calculated by the multiplication of 3 scores: the NC frequency, the severity for the production (production delay) and the severity for the laboratory (control delay). Then, NC were classified and prioritised. For major NC, an Ishikawa diagram was established to identify its causes and the forthcoming corrective actions.

Results and discussion: Over 15 months, 25,246 controlled preparations were performed, 224 NC (0.88 %) were reported and among them, 70 preparations were destructed (0.27%). Our team described 14 types of NC. 50.0 % of NC were due to a lack of mixing (CI 14) and were quickly resolved after remixing. The 3 most critical causes were: 1) errors of dose (CI 60); 2) drug errors (CI 36); and 3) absence of drugs (CI 24). Material inventory and procedure revision were the first actions to set up. Thus, communication was the keyword to explain the need of formation, to aware and motivate all the actors and to create and anchor a real security culture.

Conclusion: This study revealed that quality control permitted to improve the product quality and moreover to avoid severe errors which could lead to acute adverse effects for patients like dose or molecule errors. This study is also relevant to focus on priorities when time and human resources are limited.

Keywords: Chemotherapeutics quality control, non-conformities, quality management

85 Pneumatic Conveying Systems and Physical Stability of Monoclonal Antibodies - Example of Rituximab

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Background: Proteins such as monoclonal antibodies (mAb) are sensitive products which could undergo complex degradation pathways during the various manipulation steps also during transport. Aggregation can be induced by mechanical stresses which can occur during manipulations and transport and could induce loss of efficacy and/or toxic effects such as immunogenicity. Currently pneumatic conveying systems are in place in some hospitals but are not currently used for transport of proteins since no stability data under this specific stress is available. Manufacturer's drug information is not useful giving only sentences such as 'avoid shaking'. The objective of this study was to verify if the pneumatic conveying systems could be used to send bags containing the mAb rituximab to the clinical services.

Material and method: Various protein characterisation methods: size exclusion chromatography (SEC), dynamic light scattering (DLS) describing submicronic populations and corresponding mean diameters, turbidity (350 nm) and infra-red spectroscopy (FTIR) were used to determine changes in physical properties of Rituximab aggregation mechanically induced. Several conditions were tested: presence of residual air in bags, travel time, number of travel cycles (1 to 8). One concentration was tested (1 mg/mL). All experiments were performed on the same day.

Results and discussion: Up to 8 travel cycles and without head space or bubbles into the bags, no modification was noticed in comparison with the control (no run). Indeed, we observed only one peak by SEC, a monodisperse population (polydispersity index < to 0.1) of 11.34 ± 0.03 nm by DLS, a slightly increased of optical densities (OD) at 350 nm (0.0019 up to 0.004) and no modification of the FT-IR spectra (similarity coefficients were close to one). In the opposite, in presence of air, significant modifications were found after 4 cycles since OD reached to 0.007 and 2 populations were found by DLS with a polydispersity index of about 0.24. Moreover, modifications of FTIR spectra were also observed (similarity coefficient < 1) suggested alteration of the secondary structure. These results demonstrate that aggregation during the pneumatic is strongly dependant on the presence of air/liquid interfaces.

Conclusion: In practice, a pneumatic system can be safely used for the transport of diluted rituximab (and probably other mAbs), but the presence of air into the bags must be avoided.

86 Stability of Bendamustine Reconstituted With Water for Injection at 2.5 mg/mL and Diluted with 0.9% or 1.5% Sodium Chloride

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Introduction: Bendamustine (Levact®) is a nitrogen mustard used for the treatment of chronic lymphocytic leukaemia (CLL), non-Hodgkin's lymphoma and myeloma. Bendamustine must be reconstituted with water for injection to obtain a 2.5 mg/mL solution. There is no data on the stability of this solution. The drug must be further diluted with 0.9% sodium chloride to be administered intravenously by infusion. There is only one publication on the stability of this drug in 0.9% sodium chloride (Krämer et al. Pharmazie. 1994;49(10): 775-7.) which gives a stability of 9 hours at room temperature and 4 days in the refrigerator (stability defined as > 90% of the initial concentration).

The objectives of this work were to study the stability of the reconstituted solution and then, the influence of the concentration of sodium chloride (0.9% vs 1.5%) on the stability of diluted solutions at 0.25 and 0.6 mg/mL in glass vials.

Material and method: We used the High Performance Liquid Chromatography method published by Krämer et al. Column C18 5µ 200 x 4.6 mm. Mobile phase (sodium sulphate buffer/methanol 40/60), flow rate: 0.8 mL/mn, wavelength: 331 nm, injection volume: 10µL, column temperature: 20°C. The HPLC method was validated according to ICH guidelines (linearity, repeatability, stability indicating capability).

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Results and discussion: Stability was defined according to ICH guideline Q1A: above 95% of the initial concentration. The reconstituted solution at 2.5 mg/mL was stable for 8 hours at 4°C (99.4%/T0) but only 2 hours at room temperature (95.9%). In 0.9% sodium chloride, both concentrations were stable for 4 hours at room temperature and 24 hours at 2°C–8°C. In 1.5% sodium chloride, both concentrations were stable for 3 hours at room temperature, the 0.25 mg/mL solution was stable for 24 hours at 2°C–8°C and the 0.60 mg/mL solution for 72 hours. This slightly increased stability, only at high concentrations, makes it difficult to apply in clinical practice.

Conclusion: The stability data were not significantly improved by increasing the concentration of sodium chloride. The stability was only better at 0.6 mg/mL in the refrigerator. The new stability data, interesting for the daily practice, consists of a 8 hours stability for the reconstituted solution at 2.5 mg/mL. This new data allows the reuse of the reconstituted vial for another infusion and allows saving money.

87 Quality Assurance and Quality Control of Intensity Modulated Radiotherapy Treatment Plans for Nasopharyngeal Carcinoma Using MatriXX and COMPASS System

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Instroduction: We evaluated the performance of the COMPASS system to reconstruct three dimensional dose distributions on computed tomography (CT) image of the nasopharyngeal carcinoma (NPC) patient anatomy based on measured fluences using the MatriXX two-dimensional (2D) array (offline).

Methods and materials: For benchmarking the COMPASS dose calculation, various dose-volume indices of plan target volume and organs at risk were compared against 10 NPC patients intensity modulated radiotherapy (IMRT) treatment plan dose distributions. Gamma index evaluation and absolute point dose measurements were also performed in an inhomogeneous brain phantom using extended dose range films and ion chamber for 10 additional treatment plans.

Results and discussion: MatriXX based dose reconstruction showed excellent agreement with the ion chamber (< 1.5%), film (95% pixels passing gamma criteria 3%/3 mm) and mean dose volume indices (< 5%). The dose-volume histogram of plan target volume (maximum < 3%)and organs at risk (maximum < 5%) based dose reconstruction showed good agreement with Treatment Planning System CT plans.

Conclusion: The COMPASS system qualifies for NPC IMRT pre-treatment verification with the MatriXX detector and has good agreement for verification of treatment delivery with the dose-volume histogram of CT plans.

88 Chemical Stability of Bortezomib Solutions in Original Manufacturer Vials

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Introduction: Bortezomib is a drug used in the treatment of myeloma multiple. The experiments carried out demonstrate that bortezomib is cytotoxic for different types of neoplastic cells and reduces the tumour-like growth *in vivo* in many pre-clinical models of tumour, including myeloma multiple.

As an alternative to intravenous delivery, subcutaneous administration of bortezomib could be a good option for patients, particularly those with poor venous access. Subcutaneous administration eliminates the need for repeated intravenous access or insertion of long-term central venous access devices, improving convenience for patients and physicians. Subcutaneous administration is used for several antineoplastic agents that are not directly toxic to tissues, such as alemtuzumab. Intravenous injection is the standard administration route of bortezomib; however, subcutaneous administration is an important alternative.

In a recent study, was evaluated the effectiveness and security of the subcutaneous administration of bortezomib as opposed to the conventional intravenous administration. It is necessary to emphasize that the concentration of the solution used for subcutaneous administration is 2.5 mg/mL, unlike the dissolution for intravenous injection is prepared to 1 mg/mL. The objective of this work is to evaluate the stability of the bortezomib dissolution reconstituted with NaCl 0.9% at 2.5 mg/mL concentration in original manufacturer vial refrigerated at 4ºC in the dark.

Material and method: On study day 0, two vials of bortezomib were each one reconstituted with 1.4 mL of 0.9% NaCl to prepare solutions of concentration 2.5 mg/mL. One of the vials was stored in the refrigerator at 4ºC for stability study and the other was stored in the freezer for daily preparation of standards; both vials were protected from light. Using a HPLC-UV method, the concentration of the reconstituted bortezomib is measured at 270 nm at different days following storage at 4ºC in the manufacturer vial. The bortezomib concentration was determined by interpolation from the calibration curve prepared daily.

Results and discussion: The reconstituted bortezomib solutions remained physically and chemically stable throughout the respective study periods, with no precipitation or colour change and little or no loss of bortezomib.

Conclusion: Bortezomib, supplied in 3.5 mg vial and reconstituted with 1.4 mL NaCl 0.9% (concentration of 2.5 mg/mL), is physically and chemically stable during the studied period. Such use of bortezomib may improve cost-effectiveness by reducing bortezomib waste.

89 Stability of Lyophilised Oxaliplatin Formulation in Polyolefin Infusion Bags Containing 5% Dextrose Injection

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Introduction: The in-use stability of lyophilised oxaliplatin and lactose formulation diluted in 5% dextrose injection was studied to assess the feasibility of preparing Oxaliplatin solutions in advance by hospital pharmacy settings. Available data regarding the in-use stability of oxaliplatin solutions are based on 5mg/mL aqueous concentrate formulation.

Materials and methods: Oxaliplatin solutions of 0.5 mg/mL (n = 6), 0.7 mg/mL (n = 6) and 5 mg/mL (n = 6) were prepared, using oxaliplatin 100 mg powder, and 100 mL of 5% dextrose injection in polyolefin infusion bags. The samples were stored at 2°C–8°C without light protection and analysed at 1, 2, 4, 7, 14, 21 and 60 days. All preparations were manipulated and tested according to the Ph. Eur. The in-use stability was studied using the HPLC stability indicating method for detection of oxaliplatin concentration and degradation products. The solutions were checked for colour, particulate matter and pH.

Results and discussion: The mean concentrations of 0.5 mg/mL and 0.7 mg/mL oxaliplatin solutions in 5% dextrose injection decreased, within 7 and 14 days respectively, to less than 90% compared with the initial drug concentration in the solutions. The concentrated solution of 5 mg/mL oxaliplatin in 5% dextrose injection in infusion bags was stable

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(over 90%) for at least 60 days. The colour, clarity and pH remained unchanged throughout the storage period. Sterility and apirogenicity standards were met as defined in the Ph. Eur. Lactose monohydrate is present as an inactive ingredient at 900 mg in 100 mg oxaliplatin dosage strength. The addition of reducing sugars, such as lactose monohydrate, at a concentration of 5% w/v into aqueous solutions of 5 mg/mL oxaliplatin, result in the formation of new Pt (DACH) complexes at significant levels, which may be a cause of instability of diluted ready-to-use oxaliplatin solutions.

Conclusion: Lyophilised infusion solutions of Oxaliplatin 100 mg, 0.5 mg/mL and 0.7 mg/mL stored in polyolefin infusion bags, were chemically unstable within 7 days and 14 days respectively, at 2°C–8°C without light protection. 5 mg/mL oxaliplatin in infusion bags containing 5% dextrose injection was stable for at least 60 days in the same conditions. The poor stability of diluted solutions does not allow oxaliplatin to be prepared in advance and stored in pharmacy departments.

90 Development and Validation of a Wipe Sampling Procedure Coupled to LC-MS Analysis for Simultaneous Determination of 5-Fluorouracil, Doxorubicin and Cyclophosphamide on Contamination Surface

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Introduction: A wipe sampling procedure followed by a simple liquid chromatography-mass spectrometry method was developed and validated for simultaneous quantification of three cytotoxic drugs (5-fluorouracil, doxorubicin and cyclophosphamide) for the surface contamination determination.

Material and method: After a solid-phase extraction procedure on wiping filter paper, the separation was performed within 30 minutes using a gradient mobile phase consisting of 0.1% acetic acid/acetonitrile applied on a C18 analytical column. The cytotoxic molecules were detected by mass spectrometry in the single-ion monitoring mode. The method was validated according to the recommendations of the US Food and Drug Administration. Wiping was performed using Whatman© filter paper on different surfaces such as stainless steel, polypropylene and glass.

Results and discussion: The method was linear ($r^2 > 0.99$) between 10 and 500 ng per wiping sample (i.e. 0.1 to 5 ng cm^{-2}) and between 1 to 100 ng per wiping sample (i.e. 0.01 to 1 ng cm^{-2}) for 5-FU and doxorubicin and for cyclophosphamide, respectively. The lower limits of detection and quantification were 5 and 10 ng per wiping sample for 5-FU and doxorubicin, and 0.5 and 1 ng per wiping sample for cyclophosphamide. Within-day and between-day imprecisions were less than 5.6, 8.9, 6.5%, and inaccuracy did not exceed 5.4, 6.0 and 13.0%, respectively, for 5-FU, doxorubicin and cyclophosphamide. The method also provided satisfactory results in terms of time stability and specificity. Cyclophosphamide concentrations on the outside of glass commercial drug vials ranged between 0 and 34.7 ng per vial. The contamination rate was also measured in different places including cytotoxic production unit and room patients. Cyclophosphamide was the most commonly detected molecule.

Conclusion: This new sensitive methodology for surface contamination studies was successfully applied on commercial vials and different places in a cancer research hospital. This approach is particularly suitable to assess occupational exposure risk to cytotoxic drugs and optimise cleaning process, especially for the most toxic studied molecule, cyclophosphamide.

91 Physicochemical Stability of Diluted Trastuzumab Solutions Stored 6 Months at 4°C

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Background: Trastuzumab is a monoclonal antibody commercialised since 2000. It is used in women bearing breast cancer with an overexpression of the receptor *HER2*. Following the manufacturer's recommendations, the stability of Trastuzumab reconstituted by bacteriostatic water is up to one month. However, the same product reconstituted with water for injection is considered as stable only for 48 hours suggesting that stability limits are only based on the possible risk of bacterial contamination and not on real psychochemical stability. Very limited independent studies concerning the stability of reconstituted Trastuzumab are currently available except a Canadian monography that gives a one-month stability after storage at 4°C and Craemer very recently. In these studies, the physical stability was poorly evaluated. Therefore, the objective of this study was to fully assess the physical and chemical stability of diluted Trastuzumab (0.8 and 2.4 mg/mL) after storage up to six months at 4°C.

Material and method: Various protein characterisation methods were used to determine changes in physicochemical properties of Trastuzumab including size exclusion HPLC (SEC), dynamic light scattering (DLS) and turbidity, cation exchange HPLC (CEX), UV spectrometry and peptide mapping. Under aseptic conditions, 2 batches were prepared in normal saline for each concentration in Freeflex® polyethylene bags and stored at 4°C during 6 months. Samples were withdrawn and analysed at days D0, D14, D30, D90 and D180. Samples were centrifuged at 4,000 rpm – 5 min before SEC, CEX and turbidimetry at 350 nm. Results obtained at different times of storage were compared to those at day 0.

Results and discussion: No modification of Trastuzumab characteristics was observed until 6 months of storage whatever the methods used. By CEX, SEC and peptide mapping, no significant change in chromatogram profiles was detected. The size population stayed monodispersed with an unmodified mean hydrodynamic diameter (11.36 ± 0.04 nm). The melting temperature remained around 77.3°C indicating no structural destabilisation of the protein. No increase in absorbance at 350 nm was observed indicating the absence of sub-visible aggregation, as strongly suggested by the DLS analysis.

Conclusion: In the opposite of the manufacturer recommendations, diluted Trastuzumab is strongly physicochemically stable up to 6 months at 4°C. This excellent stability could authorise the safe anticipated preparation by pharmacy centralised units.

92 Determination of Cyclophosphamide in Urine of Hospital Personnel Occupationally Exposed to Antineoplastic Drugs

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Introduction: Several studies have shown evidence on adverse health effects associated with exposure to antineoplastic drugs. Hospital personnel involved in preparation and administration of antineoplastic drugs may be at risk if exposed to these hazardous pharmaceuticals. The purpose of the study was to assess exposure to antineoplastic drugs

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by determination of cyclophosphamide (CP) in urine of hospital personnel handling these drugs.

Material and methods: Urine samples were collected from 8 hospital workers: 2 pharmacists, 2 physicians and 4 nurses. One pharmacist prepared antineoplastic drugs while the other pharmacist assisted. All four nurses in the Oncology Department were engaged in the administration of the drugs. The two physicians did not handle the drugs but they had only contact with treated patients. Total 24 hr urine was collected in fractions and from each fraction the volume was registered and used to calculate the total amount of CP excreted over the 24 hr period. Samples were collected with Cyto Urine Kits from Exposure Control Sweden AB. Samples were stored frozen until analysis with GC-MSMS.

Results and discussions: Over the 24 hr periods, 62 urine samples from 8 hospital workers were collected. CP was detected in 31 urine samples (50%) concerning all pharmacists, all physicians and 3 nurses. The total amount of CP excreted per worker ranged from 106 to 500 ng/24 hr. The mean amount of CP excreted per worker on group basis was 234 ng/24 hr (physicians: 343 ng/24 hr, pharmacists: 239 ng/24 hr, nurses: 177 ng/24 hr). The highest amount of CP excreted was found for one physician (500 ng/24 hr) and for one nurse (492 ng/24 hr). The amount of CP excreted in urine from the pharmacist who assisted in preparation (358 ng/24 hr) was higher than from the pharmacist who prepared the chemotherapy infusions (120 ng/24 hr). CP was not detected in the urine samples of one nurse indicating no measurable exposure to CP.

Conclusion: The results show that almost all hospital workers were exposed to CP. Moreover, the study demonstrates the highest exposure of personnel not directly involved in the preparation and administration of antineoplastic drugs. Measures have to be taken to reduce the high exposure of the hospital personnel.

Poster Session: Computer and Software

94 Integral Oncology Patient Information System Implementation (ONCOBASS®) - Report From Five Years of Implementation

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Introduction: Computerised drug ordering software can prevent medical errors and provide benefits to ensure patients receive the safest and most efficient cancer care available.

The main objective of the ONCOBASS® (OBss®) project was to develop, maintain and implement an Integral Oncology Patient Information System (IOPIS), to integrate all the information related to a cancer patient, from diagnosis to the end of the process.

In this study we analyse results from five years of implementation of OBss® in a General Hospital.

Material and methods: Working in conjunction, physicians, pharmacists, nurses, technicians and computer programmers developed and implemented OBss® as an IOPIS, to assist clinicians in:

- Registering complete information for diagnosis, stage, surgery and biological markers.
- Drug ordering software: treatment strategies definition and validation, computerised physician order entry system, treatment plans follow-up and alert system for drug allergies, drug-drug and drug-disease interactions, special clinical conditions (renal, hepatic or blood disorders).
- Chemotherapy order validation: alerts for allergies, interactions, doses according to clinical condition, alerts for stability in solution, storage conditions.
- Conditioning: cytotoxic compounding procedures according to Good Manufacturing Practices, quality control of preparations (gravimetric control), traceability for all products used.
- Assisting nurses for safe administration.
- Register toxicities according to National Cancer Institute Common Toxicity Criteria.
- Assesment of tumour response according to Response Evaluation Criteria In Solid Tumors (RECIST).
- Statistical analysis.

This IOPIS was implemented in January 2007, and has been continuously developed during the last five years, with 100% physician adoption rate in January 2012.

A multidisciplinary team was created to follow-up the implementation of OBss® project.

Results and discussion: After five years of implementation, OBss® has been:

- Used by over 180 healthcare providers (23 oncologists, 20 haematologists, 16 pharmacists, 18 technicians, 103 nurses)
- Used for approximately 98% of all chemotherapy treatments for over 3,599 patients, with 20,501 preparations delivered.
- 100% of diagnosis and clinical data are registered in the system, including essential data required for prescribing specific drugs, e.g. HER2 status
- Complete integration with other health information technologies: laboratory, radiology, pharmacy.
- 100% biochemical data necessary to prescribe new chemotherapy cycle are integrated on line at the moment of prescription.

Conclusion: The OBss® project has achieved a 100% physician adoption rate and has become a safe, fully-automated, integrated tool. It is thought to continue been developed to support the delivery of best practices, improve quality of care, patient safety, and utilise data to improve accountability and enable better system planning and policy-making.

95 Helping Tool for Pharmacies to Become a Coordination Center in Cytostatic Therapy

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Introduction: The prescription and preparation of cytostatic drugs for parenteral application requires particular care. Owing to the toxicity of the treatment, quality management has always been a very important feature of oncology. Quality improvements are, therefore, an ongoing requirement in the interest of the patient. The evolution of the oncology pharmacy speciality and its growing responsibility in the last few years has been evident across Europe. With the centralising of cytotoxic drug preparation, pharmacists have incorporated Good Manufacturing Practices and improved safety for healthcare workers not only in pharmacies but also on the wards and in clinics. The pharmacist's role is changing from being purely supportive to becoming an active participant in the patient care decision process.

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Method: The pharmacists need a tool to achieve this goal. In addition to intensified efforts in continuing education, in several European countries as well as through the ESOP Masterclass, the installation of a computer programme that combines all healthcare stakeholders in the oncology patient service gives finally the pharmacist the opportunity to be his aspiration. A computer programme in our hospitals allows direct access to patient data and prescriptions both by the pharmacis and by the prescribing healthcare professional, thus supporting interdisciplinary collaboration and enabling the therapeutic team to access all treatment-related data at any time. The use of standard formats, including treatment regimens, schedules and supportive medication, allows documenting for the standard treatment programme of the hospital or medical practice site. The individual dose of the various substances can be calculated on the basis of body surface area or body weight. In addition, the target AUC can be obtained. The required dose is then calculated by taking into account the estimated glomerular filtration rate. All data which are automatically recorded in the Patient History section the enables pharmacists to review the prescription before the preparation starts. In the centralised preparation service the use of the IT implementation ensures consistency and high quality in the preparation of cytostatics – even with staff rotations. The quality management guarantees a uniform method of working process.

Conclusion: The contribution of the pharmacist as part of the team can be considered as significant element in the quality assurance measures of the oncological services. In the future, defining the idea of pharmaceutical patient care will be the first priority, this service will be understood as great support for the patient and will become increasingly important in the hospital.

Poster Session: Clinical Pharmacy/Pharmaceutical Care

97 Chemotherapy - Between Patient Satisfaction and Production Duration, Discussion is the Key

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After a patient complaint about the dispensation delay of chemotherapy preparation, patients of the Haematology Department received information about the chemotherapy production process. The aim of this study is to inform patients about chemotherapy preparations: actors, description and timing of each stage of production. We have evaluated their satisfaction about this information and identified their expectation about other chemotherapy subjects.

A booklet describing all stages of the chemotherapy circuit and advices on chemotherapy excretion has been written. During discussion in patient's hospital rooms, pharmacists have given the booklet to patients. At the end of the patient interview, a quiz has been delivered in order to evaluate their satisfaction and expectation about chemotherapy information.

During 1 month, pharmacists interviewed 52 patients in the Haematology Department. All of them accepted the interview of 20 minutes 42% (21) have fulfilled the quiz. 62% (13/21) have been totally satisfied about delivered information and 38% (8/21) quite satisfied. 52% have been totally satisfied about the booklet and 38% quite satisfied (10% non-respondents). The waiting time of the chemotherapy felt from the patient point of view (after physician prescription) is approximately 1 hour. 48% (10/21) of patients know that an incompressible production time exists. 100% find waiting time affordable. After the information, 57% (12/21) fell comfortable regarding preparation's quality and 38% (8/21) quite reassured (5% non-respondents). 62% (13/21) would like more explanations about: side effects (69%, 9/13), cytotoxic mechanism (46%, 6/13), associated treatments (31%, 6/13) and treatments monitoring (23%, 3/13). It is the first time that the pharmacy is implicated in Haematology Department business. The results show that patients are generally satisfied on information about the treatment. An exchange was often installed between pharmacy interns and patients. During the interview, lots of patients were looking for more information (associated treatment, antiemetics and side effects). Information enables less anxiety, less impatience, more understanding about the chemotherapy preparations' latency from the patients. The information provided was appreciated by patients. So, we have expanded this process to 73 patients of the Oncology Department. Regarding the patient's answers, we will start a therapeutic information project to inform them better about their treatments.

98 Why is Complementary and Alternative Medicine (CAM) Sometimes Taken by Cancer Patients Receiving Chemotherapy and What are the Risks?

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Introduction: Complementary and alternative medicines and therapies (CAM) cover a broad and diverse group of treatments and products that do not tend to be widely used by conventional healthcare professions. CAM that is systemically absorbed is the most likely to interfere with concurrent chemotherapy and potentially cause harm to cancer patients. A literature review was undertaken to investigate CAM usage by patients undergoing cancer chemotherapy, to determine what was being used, why it had been adopted and any associated risks.

Method: The literature search was undertaken between November 2010 and January 2012 using Medline, Embase and PsychInfo using a combination of subject heading and keyword searches. The citation database Google Scholar was used to find related material as was manual checking of selected article reference lists.

Results and discussion: Patients receiving chemotherapy may be consuming CAM to treat cancer, to lessen chemotherapy side effects, for symptom management, or to treat conditions unrelated to their cancer. A small proportion of cancer patients decide to use CAM alone to treat cancer and delay conventional treatment, which may worsen patient outcome.

Cancer patients may be influenced in their CAM decision making by others: practitioners, family, friends, spouse and even casual acquaintances met in waiting rooms and support groups. This influence may range from encouraging and supporting the patient's decision through to making the decisions for the patient.

When tested in rigorous clinical trials, no CAM cancer treatments alone have shown benefit beyond placebo. With the exception of ginger to treat chemotherapy induced nausea and vomiting, there is no compelling evidence to take complementary medicine for supportive care during chemotherapy treatment. There is however established evidence to use mind-body complementary therapies such as relaxation, meditation, hypnosis, self expression, mild exercise such as yoga, massage or acupuncture for supportive care during chemotherapy treatment.

Conclusion: Most complementary medicines ingested by cancer patients do not have compelling therapeutic evidence to risk taking whilst receiving chemotherapy and there are significant gaps in the literature on safety and interaction potential when used with chemotherapy.

As CAM may sometimes interact with chemotherapy leading to adverse effects and potential treatment failure, and many cancer patients consider CAM harmless and do not necessarily volunteer use even when specifically asked, conventional providers require skilled interview techniques to promote open disclosure and provide appropriate guidance.

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99 Identifying the Need of Community Pharmacists for a Specialised Educational Programme to Support Patients Receiving Oral Chemotherapy in Estonia

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Introduction: Administration of chemotherapy has been changed in last decades; the number of patients who receive oral chemotherapy instead of intravenous is increasing. This paradigm change means challenges both for patients and medical professionals including pharmacists. As oral chemotherapy is dispensed mostly in community pharmacies, pharmacists should provide adequate and appropriate pharmaceutical care for supporting cancer patients. The aim of our study was to identify the need of community pharmacists for a specialised educational programme to support patients receiving oral chemotherapy.

Materials and methods: A mail survey was conducted among community pharmacists in Estonia who have supplied oral chemotherapy at least once during last year. Pharmacists were asked to assess their knowledge about providing information and pharmaceutical care for cancer patients. The questions included drug indications, general administrating principles, drug interactions, adverse effects, and special handling precautions of oral chemotherapy medicine. Responses were analysed using a Likert-type scale where 1 indicated 'No knowledge' and 5 indicated 'Comprehensive knowledge'.

Results and discussions: 86 pharmacists responded to our survey. Average assessment by community pharmacists to their knowledge about oral chemotherapy was low (2.8, mean score). Pharmacists found themselves most knowledgeable about special handling of oral chemotherapy (3.5) and drugs indications (2.9) but least knowledgeable about general dosing principles (2.6) and interactions (2.6). Overall, 48% of pharmacists indicated that they are not confident about oral chemotherapy knowledge to provide service for patients; 44% of responders felt themselves somewhat confident and just 8% were strongly confident about their knowledge. Pharmacists were asked whether they would need a special training programme about oncology and oral chemotherapy. All responding pharmacists expressed their interest in participating in specialised educational programme on oral chemotherapy: 83% of responders answered 'Yes, certainly' and 17% of pharmacists answered 'Maybe'. None of the responders expressed reluctance to special training programme for pharmacists.

Conclusion: Data on pharmacists' self-confidence about providing pharmaceutical care and pharmacists' willingness to update their knowledge indicates evidential need for a special training programme about oncology and oral chemotherapy.

100 Building the First ELearning Paediatric Oncology Clinical Pharmacy Programme for Developing Countries

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Introduction: In the past few years the roles and responsibilities of clinical pharmacists have expanded dramatically. The need for a professional development programme became compelling, especially with the growing demands of qualified pharmacists.

The demand is even more pressing in Africa and the developing world. High turnover rate of the trainees in our centre, higher mobility costs and shortage of experts that can conduct training in Africa renders face-to-face courses not cost-effective.

At Children's Cancer Hospital Egypt 57357 (CCHE), the clinical pharmacy practice is one of the pillars of success of patient care where its integration in the multidisciplinary treatment team has helped in improving the patients outcome and minimising medication error in addition to offering better management and prevention of adverse events. Realising the global vision and mission of CCHE as a learning organisation and a leader in the clinical pharmacy in the Middle East we decided to develop online courses that deliver the tutorial part and act as continuously updated reference.

Material and methods: Planning for this course was initiated by the oncology pharmacists at the Research Department in collaboration with the Department of Pharmaceutical Services (DPS) at CCHE. The curriculum was designed based on the domains that were delineated by US Board of Pharmacy Specialties Council on Oncology Pharmacy and the recommendations of the ESMO/ASCO Task Force on Global Curriculum in Medical Oncology. Modifications were done on the programme to conform with Paediatric Oncology needs. The team consisted of a programme leader, qualified oncology pharmacists and e-learning experts. The course team decided to initiate the programme in a blended learning approach with face to face lectures and supplementary online discussions, tutorials, links, and quizzes. Each lecture was recorded and made available online to complete the full online modules. Later offerings were conducted totally online. Open source delivery portal was used to reduce the costs.

Pre- and Post-course assessments were conducted to evaluate the trainees performance and satisfaction.

Results and discussions: Initially, we had enrolled 20 clinical pharmacists and 10 research pharmacists for 6 months. Our programme helped the staff to become more confident and competent practitioners equipped with the knowledge and skills to meet current and future challenges facing Oncology Pharmacy practice.We invited pharmacy practitioners from other centres in Alexandria (far north) and Assiut (far south) in Egypt in addition to our colleagues from other African countries like Sierra Leone, Kenya, Tanzania and Morocco to join the programme.

Conclusion: Due to the low number of practitioners in the field of paediatric oncology clinical pharmacy, training programmes can be conducted online to connect practitioners and provide training for underprivileged countries.

101 Assessing the Quality of Patient Education Counselling at Outpatient Department of Children's Cancer Hospital Egypt (CCHE) 57357

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Introduction: This study was develop to assess the quality of the patient education counselling presented by trained clinical pharmacist at the Outpatient Department and Ambulatory Care in Children's Cancer Hospital Egypt (CCHE) 57357 by a well designed questionnaire.

Material and method: The study was carried out on 200 patients and their families during their scheduled visit at the Outpatient and Ambulatory Care in (CCHE) 57357. It was conducted during February 2012; they were interviewed directly through a well designed questionnaire

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about their knowledge of medications, effectiveness and satisfaction of counselling service presented by the Department of Pharmaceutical Service [DPS] at (CCHE).

Results and discussion: There was a good feedback from the patient and their families. Out of 200 patients involved in the study 116 (58%) were males and 84 (42%) were females.

The age range for patients was (1 to 16 years). Only 10% of patients do not know the diagnosis of their diseases. About 21.5% of patients were taking 5 or more drugs and only 46% recall the names of their medications. About 82% of patients were aware of the exact strengths and dose of their medications, 30% of patients did not know the side effects of their medications. It was found that the percentage of patients who recognised their medications by means of name was 68.5%, shape 21.5% and colour 10%. About 91% of patients were informed about special drug instructions, of these17% were provided by doctor, 41% by pharmacist and 42% by both (pharmacist and doctor). About 23% of the patients prefer instructions to be given verbally, 35% as written while 42% of patients preferred it to be both verbal and written. The evaluation of the parents to the health of their children after being treated in the hospital were 41% are excellent, 42% are good and 8% are needing to be better. There are only 9.5% of patients who stop their treatment by themselves without consulting their physician when they are feeling better. About 68% of the parents were totally satisfied about the medical performance. About 96% of the patients were totally satisfied on the answers of their questions. The evaluation of the pharmacist performance was 68% excellent performance, 24% good and 8% need to be better. The pharmacist care about the patient medical problems was 72%.

Based on these results, we put an action plan to improve the patient counselling service by implementing this service to the Inpatient Department by training of the inpatient clinical pharmacists in addition to making an Arabic patient education material for each disease and each medication**.**

Conclusion: The quality of the patient education counselling service regarding knowledge of patients about their medications, effectiveness and satisfaction of the counselling service at the Department of Pharmaceutical Service in Children's Cancer Hospital Egypt (CCHE), 57,357 was good as reflected by the feedback of the patients' parents. This study will help us to put an action plan to advance this service throughout the hospital.

102 EBM of Rituximab Anti-CD20 Monoclonal Antibody Therapy in Patients with Non-Hodgkin's Lymphoma - Efficacy of Treatment of First Line

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Objectives: To study the response in first-line treatment with rituximab, the chimeric monoclonal antibody anti-CD20 antibody, combined with chemotherapy in patients with indolent non-Hodgkin's lymphoma and aggressive

Materials and methods: We conducted a retrospective observational study including 36 patients with NHL with an average age of 70 years (26 to 84), resulted eligible from January 2008 to March 2012, according to the Registry Monitoring AIFA for oncology drugs used in Italy. The patients received 375 mg/m^2 of Rituximab plus chemotherapy every 3 weeks for 8 cycles.

Results and discussion: The overall response rate in the first line in 32 patients was 53.15% (28.125% complete response and 25% partial response), 28.1% had stable disease, 12.5% progression, 6.26% other. The overall response rate of patients with stage II was 30%, with stage III was 80%, with stage IV was 60% and the 40% of patients with stage II presented a disease stabilisation. The response rate in low-grade disease was 58.36 % (41.66% complete responses and 16.7% partial response), stable disease was 33.3 %, progression was 8.33%. The response rate of patients with low-grade malignancy was 100% in stage III, 57.2% in stage IV. The response rate in aggressive disease was 50% (20% complete response and 30% partial response), stable disease was 25%, progression was 15%. The response rate to the second stage was 30%, 85.67% in stage III and 66.6% in stage IV.

Conclusion: The overall response data were comparable to the data of published studies in the literature; for indolent NHL was observed a complete response greater than the literature at the expense of a lower partial response. We observe a correlation between staging and response that increases with the progress stages and at the third stage gives an answer greater than those of stage IV in both high and low-grade malignancy.

103 Oral Chemotherapy - a National Pilot Programme in Germany for Better Adherence in Europe

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Introduction: Antineoplastic chemotherapy describes a group of hazardous drugs commonly used in the treatment of cancer. Potential risks are not only recognised for patients, but extend to pharmacists and other healthcare workers. Guidelines for safe handling are well established in the traditional settings of hospitals and ambulatory clinics for the IV chemotherapy.

In tumour therapy, documentation, quality management and standardisation of interdisciplinary processes are increasingly gaining importance in form of therapy protocols and guidelines for clinical treatment.

Method: Non-adherence, application errors and interactions due to insufficient education of the patient can compromise therapeutic success. An adequate, quality assured, multi-professional care is therefore urgently required for oncology patients receiving oral chemotherapy. A programme is set up in Germany to teach 20,000 community and hospital pharmacist in the next year in supporting patients the best in taking oral cytotoxic drugs.

This initiative aims to reach the following goals for oncology patients:

1. On-site optimisation of oral chemotherapy and improvement of pharmaceutical care for oncology patients.
2. Cost-effective and reliable care for cancer patients due to professional collaboration of local physicians, pharmacists and other healthcare professionals at the right time.
3. Recognising and solving drug-related problems related to oral chemotherapy.
4. Enhancing the quality of life of oncology patients through a coordinated management of side effects and interactions during and after therapy.
5. Providing new insight as a contribution to health services research and to encourage drug safety.

Results: The necessary steps in order to reach the status and to start with the campaign will be shown. Not only the way to win the societies of doctors and community pharmacists but also to engage the industry

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to jump over their own marketing shadow. Finally the demand of ethic committees and also the agency for data privacy protection will give all other interested party a chance not to loose time.

Conclusion: The increasing role of oral cytotoxic drugs and the growing demand of its good use can finally only insured by well trained pharmacists. The campaign which is starting in Germany by 250 teaching meetings is followed in Austria, Estonia and Slovenia in order to demonstrate the good outcome in a few years.

104 An Evidence-Based Study on Non-AIDS Associated Kaposi's Sarcoma Patients: Focus on the Pegylated Liposomal Doxorubicin Use in Non-AIDS Associated Kaposi's Sarcoma Patients

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Background: Kaposi's Sarcoma (KS) is an angioproliferative disease of multifactorial origin. The disease arises in different clinic-epidemiologic forms. The fundamental condition for the development for this tumour is: infection with the Human Herpes Virus 8 (HHV8) and an immune-dysregulated state. Several local therapies are used to eradicate early and confined skin lesions. Systemic treatment is affirmed in patients with advanced or rapid progressive disease. There is no standard therapy for KS and treatment must be tailored to the individual patient.

Objectives: To evaluate the activity and toxicity of a treatment with Pegylated Liposomal Doxorubicin (PLD = Caelyx®) in first- or second-line for non-Acquired Immune Deficiency Syndrome (AIDS) associated KS patients in Bichât – Claude Bernard Hospital in Paris, France, in UZ Leuven and in UZ Antwerpen in Belgium.

Methodology: Analysis of the medical files of non-AIDS associated KS patients regarding the efficacy, side effects and tolerance of PLD as first- or second-line treatment and other treatments.

Results: Good results were observed on the patients treated with PLD in first- or second-line. This treatment leaded to a complete response for most of the patients.

Discussion: No statistical analysis was possible, because of the low number of non-AIDS associated KS patients who are treated in Hospital Bichât, France; and in Flanders, Belgium; and because of the problems in dispensing and safety of Caelyx® on this moment (from begin August 2011 until ...?). Expensive treatments are not systematically reimbursed in non-AIDS associated KS patients; such as PLD which has just a Market Authorisation Application (MAA) for AIDS-associated KS (AKS) patients.

Conclusion: The study documents the efficacy and tolerability of PLD in the treatment of non-AIDS associated KS patients, but this regimen needs to be further evaluated in future controlled randomised trials.

105 Competence Pharmacy - A German Approach to Quality in Oncology Pharmacy

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Introduction: Preparation of cytotoxic agents is a high-risk process. Staff working in oncology pharmacy needs continuing education about handling drugs, adverse drug events (ADR) and dosage regimens. But nowadays also oral chemotherapy takes more place in treatment of cancer patients. This demands a lot of additional knowledge regarding safe handling of oral chemotherapy agents. Community pharmacies need special education in order to counsel these patients, improve adherence and soothe ADRs. A large expert knowledge is also essential for communication with other healthcare professionals. It must be sure every patient gets the same high quality expert advice, regardless of which pharmacy staff member he is talking to. Therefore, every staff member needs the same level of high education. In order to make this sure we developed the project Competence Pharmacy DGOP. Material and method German society of oncology pharmacy (DGOP) developed in cooperation with medac the concept of Competence Pharmacy DGOP (CP DGOP) based on an online tool for continuing education in oncology pharmacy. Pharmacies who want to become CP DGOP need to verify their special knowledge of cytotoxic drugs. Therefore, every staff member gets an individual access to this e-learning platform by Alcedis® and passes through different trainings. The first level contains the topics 'safe handling of chemotherapy' and 'oral chemotherapy'. These are provided as online presentations. In the end of each topic everyone needs to pass through a multiple choice test. The first level finishes with the emblem CP DGOP—if all requirements are conformed. Later on competence pharmacies get easier access to the quality management system by DGOP.

Results and discussion: The online tool enables every member of the pharmaceutical team to study whenever it is possible for the individual. It is not needed, that the whole team studies together. Therefore, the daily flow of work is not impaired and everyone may take the time he needs to gain qualifications in certain fields of oncology pharmacy. Topics in step with actual practice please the students. The main target to ensure that every staff member has the same level of education is locked by a multiple choice test. So only if all staff members pass the test the next topic will be opened.

Conclusion: The concept of CP DGOP improves the quality in oncology pharmacy and helps oncology patients to find a specialised pharmacy. Pharmacy staff enjoys continuing education.

106 Safety and Efficacy of First-line Treatment with MFOLFOX-4 in Unresectable Advanced/Recurrent Gastric Cancer

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Introduction: The dismal outcome highlights the need for effective systemic chemotherapy to improve clinical results in patients with unresectable advanced/recurrent gastric cancer. An increase of adverse events with systemic chemotherapy is concerned in elderly patients, but it remains controversial whether they should receive the same chemotherapy as younger patients. We retrospectively studies of 73 patients with unresectable advanced/recurrent gastric cancer, including 48 non-elderly patients (< 65 years old) and 25 elderly patients (≥ 65 years old) who received modified FOLFOX-4 (mFOLFOX-4) therapy.

Materials and methods: From January 2006 to June 2011, a total of 73 patients with histologically confirmed unresectable advanced/recurrent gastric cancer were enrolled into this study. All patients were treated with mFOLFOX-4 regimen of oxaliplatin at 85 mg/m² plus leucovorin 200 mg/m² on the first day of treatment, followed by 5-fluorouracil (5-FU) via a 24-hour continuous infusion of 1,000 mg/ m² 5-FU on day 1–2 at intervals of 2 weeks. Treatment was continued until disease progression or intolerable adverse events.

Results and discussions: Clinical efficacy showed an overall response rate of 41.1% (30/73), and 26.0% (19/73) of patients exhibited stable disease as well as 32.9% (24/73) who had progressive disease. The response rate was 36.0% in the elderly group and 43.8% in the non-elderly group,

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respectively (p = 0.891). Likewise, the grade and frequency of adverse events were similar in the elderly and non-elderly groups (all p > 0.05). Median time to progress (TTP) was 8 months (95% CI: 7.5–8.5 months) and overall survival (OS) was 11 months (95% CI: 8.9–13.1 months). Major toxicities reaching NCI-CTC grade 3/4 included nausea/vomiting (16.4%), anorexia/fatigue (15.1%), neutropenia (11.0%), and stomatitis (9.6%).

Conclusion: mFOLFOX-4 as the first-line treatment appears to have favourable efficacy and safety in unresectable advanced/recurrent gastric cancer patients. Additionally, mFOLFOX4 therapy was well-tolerated and effective in both non-elderly and elderly patients.

107 Improving the Chemotherapy and Monoclonal Antibodies Safety by the Hospital Pharmacist: Retrospective Analysis of the Incidents and 'Near Misses'

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Introduction: Patient safety being a priority, a sensitizing programme to the medication error reporting has been developed by the Belgian health authorities. As a drug expert, the pharmacist plays a key role in the detection of preventable adverse drug events. How the reporting and analysis of medication errors by the pharmacist can improve patient safety? This study is aimed to analyse the reported errors in order to identify the inadequate processes and problems met during the treatments with chemotherapy and monoclonal antibodies.

Method: In collaboration with the patient safety team and the pharmacist, a medication error reporting system has been created in the hospital. According to WHO recommended taxonomy, the medication errors were reported by the pharmacists, physicians and nurses. The retrospective data analysis of the treatment prepared and delivered by the pharmacy, during 12 months (January 2011 to December 2011), concerned the chemotherapy, the monoclonal antibodies and concomitant/supportive therapies.

Results: Among the 6,454 prescriptions and 11,871 preparations, 283 events were identified. 97.9% of the events were detected by the pharmacist. The most frequent errors concerned the prescription process and more particularly errors related to dosage (n = 84), treatment schema (n = 85) and patient parameters (n = 68). Among the incidents reported, 12 had a repercussion on the patient or on the drug.

Conclusion: This study has enabled the pharmacy to identify the type of errors, their frequency and their severity. The 'cartography' obtained reveal an important proportion of prescription incidents and illustrate the central role of the pharmacist in their detection. WHO recommended taxonomy application offers the benefits of sharing the reports at a national level and dissemination of recommendation for improving medication patient safety.

108 Drug-drug Interactions in Chemotherapy Patients Treated at the Pulmonology Ward

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Introduction: The pharmacovigilance in cancer patients is currently open to improvement: (i) public pharmacists are insufficiently informed about chemotherapy regimens, and (ii) physicians are inadequately informed about the patient's current medications or drug–drug interactions with chemotherapy regimens. Omission of information could cause inadequate treatment, and subsequently toxic or sub-therapeutic doses of medicines.

St Elisabeth Hospital (Tilburg, The Netherlands) does not work with a Computerised Physician Order Entry (CPOE) system for intravenous administered chemotherapy. This forms a bottleneck in the current pharmacovigilance in cancer patients and is therefore not adequately secured at this moment. However, our hospital is keen to further improve medication safety. Therefore, a project was initiated to review drug-drug interactions between chemotherapy and patient's current medications during the first cycle of chemotherapy on the pulmonology ward.

Material and methods: During the project, a pharmacy technician carried out the medication reconciliation process (i.e. verification of the current medication) at hospital admission. Thereafter, the pharmacist reviewed the combination of the patient's current medication and chemotherapy for relevant drug-drug interactions. The pharmacist reviewed the current medication, as pharmacists are trained to check for drug–drug interactions. The pharmacist contacted the physician or public pharmacist in case of relevant drug-drug interactions. The mentioned drug-drug interactions are described in the G standard, a national guideline from the Royal Dutch Pharmacists Association (KNMP). According to this guideline there are 38 relevant drug-drug interactions with chemotherapy that need intervention [1].

Results and discussion: The medication of eight hospitalised patients on the pulmonology ward has been verified monthly. The majority of the drug-drug interactions did not require intervention. All the pharmacists' interventions were discussed with the physicians. During the study period, acceptance was > 90%.

Conclusion: It is important to check the current medication of patients by a pharmacist before chemotherapy starts, in order to avoid drug-drug interactions because possible drug-drug interactions in chemotherapy could have serious consequences for the patient. Furthermore, this check improves medication safety and secures pharmacovigilance in cancer patients. This project will be continued until a CPOE system for prescribing intravenous chemotherapy is implemented, and medication safety is secured electronically.

Reference

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109 Evaluation of Drug Prescriptions in Elderly Patients in a French Comprehensive Cancer Centre

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Introduction: Elderly patients present an increased risk of drug-related problems (DRP). Few studies have investigated these DRPs in elderly cancer patients. We evaluated the appropriateness of prescribing medicines for patients according to French national and international guidelines.

Material and method: This prospective study over 14 months, enrolled patients over 65 years hospitalised in oncology. Prescriptions were analysed according to Laroche criteria, a French equivalent of Beers Criteria, and drug-drug interactions (DDI) were identified with an official drug database, Banque Claude Bernard (BCB). Dose adaptation regarding age and renal function for all prescribed drugs, including chemotherapy, was evaluated according to BCB and International Society of Geriatric Oncology guidelines.

Results and discussion: One hundred and twenty-nine patients were enrolled: mean age 75 years (65–90), 67% females. 41% had no

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chemotherapy and 25% had oral chemotherapy. In average, patients had 7 medicines at the entrance and left the hospital with 9. Most common medications (21%) were gastrointestinal drugs, 16% were analgesics and 15% were related to cancer care (hormone therapy, rasburicase, ondansetron). Analgesics and antipsychotics prescriptions increased in 42% and 48% of patients respectively. At least one DDI was identified for 95% of patients. From 916 medications 228 DDI were observed (> 2 per patient). Only 3 DDI were contraindicated for bleeding risk, hyperkaliemia or sedation. According to BCB database, 25% of elderly patients received inappropriate medications, with 98% receiving at least a drug requiring cautions (monitoring or dose adjustment). According to Laroche criteria half of patients were prescribed inappropriate drugs. 70% of patients had a renal dysfunction and drug-disease interactions showed 65% of prescriptions contained a drug with cautions in renal failure. 17 patients (13.8%) had appropriate chemotherapy adaptation whereas 2 had no adaptation. 15.5% of patients (20 patients) did not necessitate dose adaptation and 26 patients had oral chemotherapy.

Conclusion: There is a lack of prescription re-evaluation in elderly cancer patients. An increase in medications is identified, in relation with pain relief, leading to possible CNS depression. Physicians faced difficulties to adapt doses regarding age or renal dysfunction as specific data are lacking in drug database or guidelines. A special training would also be required.

110 Use of Erythropoiesis-stimulating Agents (darbepoetina) in Patients with Chemotherapy-induced Anaemia - Results of a Retrospective Study in a General Hospital, 2008–2011

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Introduction: Chemotherapy-induced anaemia is a common side effect associated with cancer treatment which can be treated with erythropoiesis stimulating agents (ESA). Many publications have focused on risks associated with ESA use, mainly thromboembolic events and risk of tumour progression. In our centre ESAs prescription has been changing according to an accurate selection of candidates based on the recommendations of international clinical guidelines.

Objective: Evaluate changes in the use of darbopoetin in patients with solid tumours treated with chemotherapy from January 2008 to December 2011, as a result of the new recommendations.

Methodology: We reviewed the patients attended by the oncology unit who received darbopoetin during chemotherapy treatment from 2008 to 2011. The collected data is, age, sex, diagnosis, haemoglobin (Hb) levels at the moment of prescription.

Results: Of 753 reviewed patients, 69 received ESA, 41 men (59.4%) with mean age of 64.9 ± 9.5 years. Type of neoplasm: colorectal 22 (31.9%), lung 28 (40.6%), breast 9 (13.0%) and others, bladder, prostate, gastric, pancreas 10 (14.5%). The lowest initial levels of Hb were associated with bladder (mean 8.3 g/dL), gastric and pancreas (mean 8.6 g/dL) and lung (mean 9.5 g/dL) cancer. Duration of ESA treatment ranged from 1 to 24 weeks, mean 7.7 weeks. The percentage of darbopoetin administrations to patients with Hb levels below 10 g/dL was: 54.5% of all administrations in 2008, 61% in 2009, 60% in 2010 and finally, 75% in 2011. Only 3 patients were given ESA with Hb ≥ 12 g/dL (2 in 2008 and 1 in 2009) because of severe anaemia symptoms in previous chemotherapy cycles. The percentage of patients with ESA treatment according to neoplasm type was: 16.5% lung, 7.7% colorectal, 4.5% breast and 10.4% other.

Conclusion: Only 9.2% of patients with solid tumours treated with chemotherapy received darbopoetin. Because of the adherence to the new guidelines published, the selection of candidates to receive ESA has improved. Patients initiating ESA treatment with Hb < 10 g/dL ranges from 54% in 2008 to 75% in 2011. Hb values are lower in patients with stomach, pancreas and lung cancer and the difference was statistically significant (p <0.004). Globally, the accuracy of the selection of candidates improves safety of ESA treatment in patients treated with chemotherapy.

111 The Effect of Dimenhydrinate on Lower Oesophageal Sphincter Function

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Introduction: Dimenhydrinate (DIM) used frequently to treat vertigo and dizziness in patients with different malignant conditions during therapy with anticancer drugs. Due to its inhibition effect on vestibular stimulation of chemoreceptor trigger zone and inhibiting stimulation of vomiting centre in the brain it is used also to prevent nausea and vomiting. Its effect on lower oesophageal sphincter pressure (LESP) and function is not exactly determined. Aim of this work was to measure both LESP and relaxation in response to swallowing in patients who took this medication to evaluate the role of this drug on the function of lower oesophageal sphincter (LES).

Material and method: 40 volunteers took 50 mg DIM (Dramamine R) orally three times daily for 2 days due to different indications were included in this study. The age ranged from 40 to 49 years; 22 were males and 18 were females. LESP and relaxation were measured by solid state catheter by standard technique procedure. The procedure was done before and after 4 hours from DIM last dose intake. Those who suffer from angle-closure glaucoma, seizure disorders, prostatic hypertrophy are not included in the study. All of them were not suffered from disease of LES. The data was analysed using SPSS version 15 and t student table for statistical significance analysis.

Results and discussion: The standard motility measurements used were LESP and the lower oesophageal sphincter relaxation percentage (LESRP), before the intake of the drug mean LESP was 14.25 ± 1.498 mm Hg (range 12–16) after the drug intake LESP mean was 11.015 ± 0.754 mmHg (range 9.5–12). The difference is significant at 5% level ($p < 0.05$). Before the intake of the drug mean LESRP was 93.175 ± 4.41 mmHg (range 85–100%), after the intake of the drug LESRP mean was 83.43 ± 2.238 mm Hg (range 80.5–90%). The difference is significant at 5% level ($p < 0.05$). The intake of DIM leads to significant low values both in the pressure and in the relaxation of the sphincter in response to swallowing. This showed that DIM intake reduce the function of LES.

Conclusion: From the data of this work it is advised that when using these drugs in the treatment, the effect on LESP must be clear in mind. This is to avoid side effects.

112 Appropriateness and Use of Drugs Off Label in 2010 - Monitoring Outcomes and Results

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Introduction: Drugs must be administrated according to authorised indications (in-label use). Italian law allows prescription of off-label drugs in only few cases, such as in rare disease or if there is not any alternative

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effective treatment. In this case effectiveness of drug used 'off label' must be demonstrated by, at least, published phase II clinical trials.

Material and methods: In Liguria off-label use is regulated by regional law (DGR 271/08) which indicates a specific authorisation pathway and a regional database to register and to monitor off-label treatments. Last year we conducted our project with the aim not only to monitor off-label prescriptions but also to analyse treatment outcomes and to establish effectiveness by surrogate endpoints such as compliance to approved scheme and mortality. Surrogate endpoints make our project innovative: we do not find any study like ours in literature. All data had been collected by off-label regional database and by management information system of Oncology Pharmacy of our Hospital.

Results and discussions: In 2010, 2,950 oncology patients were treated, about which 80 (2.8%) received off label treatment. Off-label group was made up of 48 women and 32 men, 50% aged 50–70 years. We classified off label treatments according to disease and to treatment line. The first case includes 17 treatments for autoimmune diseases, 41 for haematological and 22 for oncological diseases. In the second 87.5% of off-label group was treated after at least a first-line standard therapy. In 77% of cases off-label use of drugs is due to other indications than those authorised, meanwhile in remaining cases it is due to different chemotherapy associations. 37.5% (30 patients) of off label group is adherent to approved scheme instead 62.5% (50 patients) is not adherent to it. Non-adherence reasons were: dose (20%) and deviation from off-label scheme (80%). To evaluate efficacy and appropriateness we calculate if and when patients died after treatment: 66% (53 patients) are alive, while 34% (27 patients) died; it is interesting to focus that deceased patients died within 1 month after off-label therapy. Results were discussed and a specific commission to evaluate off-label treatment was established.

Conclusion: It is necessary to develop specific culture to promote appropriate use of drug; our experience focuses attention of clinicians and pharmacists on this issue and make physicians more sensitive and aware of this topic**.**

114 The Role of Chemotherapy After Erlotinib Treatment in Patients with Advanced NSCLC: Post-progression Survival Analysis

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Introduction: Erlotinib is a potent inhibitor of epidermal growth factor receptor tyrosin-kinase activity and its efficacy has been demonstrated for the treatment of advanced non small-cell lung cancer (NSCLC) in large randomised trials.

Materials and methods: A prospective observational study was run, using institutional data collected through web-based National Oncology registry, from December 2006 to May 2011. The patients with non-small cell lung cancer, unselected for EGFR mutation/amplification and after at least one line chemotherapy, were treated with erlotinib (150 mg/day orally) until disease progression. Every patient was checked prospectively for toxicity, clinical outcomes, previous line treatments, length of treatment and for treatments following erlotinb using hospital databases.

Results and discussion: In overall study population (130 patients), the median Time to Progression (TTP) and Overall Survival (OS) were 2.4 and 4.4 months, respectively and 1-year survival rate was 25%. 4 patients achieved partial response and 23 patients achieved stable disease, making the disease control rate 21%. Grade 1–2 rash and diarrhoea were the most frequent adverse events.

The subgroups analysis showed significantly improved OS for patients with chemotherapy post-erlotinib (pemetrexed, docetaxel) compared to those with no chemotherapy post-erlotinib, 12.7 months and 3.0 months ($p < 0.0001$), respectively. The main prognostic factors, such as age, sex, histology, ECOG performance status, smoking status, treatment line and the median time to relapse of previous line treatments were equally distributed between these two subgroups. The data of EGFR mutation and EGFR FISH positive status were available for 21% of the patients, however, we did not find a significant association between EGRF expression and treatment response in both groups.

Conclusion: This evaluation has revealed significantly better survival with chemotherapy post-erlotinib regardless of the EGFR expression, giving evidence of other existing mechanisms.

The post-marketing studies in real life practice are needed in order to verify both effectiveness and safety in general population, testing for external validity of the randomised trials. Moreover, the post-progression survival assessment may be crucial to determine real clinical impact of investigational drug in combination with other treatments as it usually lacks in the approval RCTs.

115 The Stability of Epirubicin Hydrochloride Solutions Prepared for Injection - A Comparison of Three Formulations

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Introduction: Compared with concentrated solutions and dry powders, diluted solutions usually have shorter expiration dates for reason of chemical stability in solution. If longer storage of solutions were possible and the stability could be maintained, there would be operational benefits and cost reduction. In this study we measured the stability of three epirubicin hydrochloride solutions for injection use – one diluted from a concentrated solution and two created by dissolving of powders.

Material and methods: Three formulations of epirubicin hydrochloride were dissolved or diluted to 0.9% sodium chloride respectively for preparing the test solutions with a concentration of 0.4 mg/mL. These solutions were stored at two temperature conditions (room temperature 2°C–8°C) with or without shading. Samples were collected periodically at predetermined intervals (24th hour, 7th and 40th days). Average content was used to evaluate the stability of the three kinds of test solutions. Chromatograms were integrated for detecting the content of epirubincin and impurities.

Results and discussions: Three epirubicin hydrochloride solutions were stable when stored at 2°C–8°C under dark condition during at least 40 days and the average content of epirubicin could achieve 93.76%. The three solutions were also stable when stored at room temperature during at least 24 hours (the average content > 90%). When protected from light, the test solution diluted from the concentrated solution was more stable (the average content of epirubicin > 92.57% on the 40th day) than the two test solutions dissolved from dry powders (the average content < 90% after the 7th day).

Conclusion: The epirubicin solutions prepared from three different formulations were stable when stored either at 2°C–8°C under dark condition for at least 40 days or at room temperature for at least 24 hours. The test solution prepared from the concentrated solution was more stable than the solutions prepared from powders when stored at room temperature for a comparatively long period.

116 Effectiveness of Erlotinib in the Advanced Non-Small Cell Lung Cancer Cases After the Failure of NP Therapy

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Introduction: Reports had shown that the use of erlotinib, which is an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-KTI),

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will prolongs survival in non-small cell lung cancer (NSCLC) patients after the failure of N(vinorelbine)/P(cisplantin) treatment as first-line chemotherapy. Because there are no clinical trials on erlotinib as a second-line treatment for NSCLC patients previously treated by NP therapy until now, the only method for observing the effectiveness of erlotinib as a second-line therapy is clinical follow-up. In this study, we are investigating the performance of erlotinib as second-line therapy treated NSCLC patients and the risk factors influenced the effectiveness of applying erlotinib on NSCLC patients.

Material and methods: Forty-three patients who had previously failed on NP chemotherapy (vinorelbine 25–30 mg/m² days 1 and 8 plus cisplatin 75 mg/m², intravenously, day 1; 2–3 cycles) were recruited in this study. For the second-line treatment, all patients had orally received erlotinib 150 mg/d. The primary endpoint of the study was response rate. Characterisation of toxicity profiles was also used for measurements as secondary objectives. For comparing the risk factors influencing the effectiveness, histology and gender were considered. Chi-square test was used for categorical data.

Results and discussion: Among the 43 cases with erlotinib as second-line therapy, 38 cases were followed up whereas 5 cases were lost. The response rate was 50.0% (19/38) overall. The response rate of adenocarcinoma cases was better than that of non-adenocarcinoma cases (68.4% vs 31.6%, $p < 0.05$). The response rate in female cases was better than that in male cases (65.2% vs 26.7%, $p < 0.05$). However, between smokers and non-smokers no statistical significance was observed on response rate ($p > 0.05$). The main toxicities within the first week after assigned erlotinib were rash (81.6%) and diarrhoea (50%), which disappeared automatically. The response rates in patients between with rash and without rash was 61.3% and 0% ($p = 0.012$).

Conclusion: Subsequent erlotinib therapy is one of the therapeutic options in the treatment of NP failure cases. Female cases and adenocarcinoma cases might have better response rates compared with male cases and non-adenocarcinoma cases respectively. The patients with rash may have better progression-free survival.

117 The Use of High-dose Methotrexate With Calcium Leucovorin Rescue (MTX-LCV) Therapy in Osteosarcoma - Clinical Effect and Toxicity in Relation to MTHFR 677 Polymorphisms

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Introduction: It has been suggested that adolescents have high incidence of osteosarcoma, which is usually a highly aggressive tumour with invasive potential. High-dose methotrexate (MTX) is one of common chemotherapy strategies for the disease. Calcium folinate usually serves as an antidote to reduce the adverse reactions of high dose MTX therapy. MTHFR is one of the key enzymes in the folate metabolism, which may be related to the treatment effect of MTX. It has been confirmed that the MTHFR 677 C>T mutation decreases the activity of MTHFR and affect the response of MTX in clinical use. The purpose of this research is to examine the prevalence of the MTHFR C677T mutation in osteosarcoma patients in order to investigate the association between MTHFR 677 polymorphism and clinical efficacy and adverse drug reactions of high-dose MTX with calcium leucovorin (LCV) treatment in osteosarcoma patients.

Material and method: 210 blood samples of which the patients were treated by high-dose MTX with LCV trerapy were collected and MTHFR 677 genotypes were determined by RT-PCR. The clinical efficacy and adverse drug reactions were compared among various groups with different MTHFR677 genotypes.

Results and discussion: We found that the frequencies of MTHFR 677 CC, CT and TT genotypes were 54.8%, 30% and 15.2% respectively. There was no statistically significant difference of tumour cell necrosis rate among various genotype groups ($p > 0.05$). The incidence rate of haematuria was significantly higher in CT and TT groups than in CC group ($p < 0.05$). The frequency that renal adverse reaction occurred was significantly different among different genotype groups.

Conclusion: The role of MTHFR 677 polymorphism on the clinical effect of MTX with LCV and chemotherapy-induced toxicity should be highly considered in osteosarcoma patients receiving high-dose MTX with LCV.

118 Hospitalisation During First Cycle of a Lenalidomide Containing Treatment

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Introduction: The objective of this study is to evaluate the number and characteristic of hospitalisations during the first cycle of lenalidomide containing treatments outside clinical trials.

Material and method: Retrospective medical records review of patients treated with lenalidomide for any haematological malignancy.

Results: From 2006 to October 2011, 115 patients have been treated with lenalidomide containing regimes as part of their treatment for diverse haematologic diseases.

Eighteen (16%) required hospitalisation during the first cycle (first 21 days). Patients required hospitalisation due to fever (10), bleeding (4) and pain (4). Only 2 patients received support with filgastrim during this first cycle and 6 received also rh-EPO. Even presenting fever, neutropenia grade II to IV was detected in 3 patients but thrombopenia (grade II to IV) in 11 patients.

Conclusion: Even with correct control measures, first cycle with lenalidomide containing regimens is a treatment with a high risk of hospitalisation due to haematologic toxicity. A close monitoring is mandatory.

119 Information Expectations and Needs of Cancer Patients Treated by Oral Chemotherapy in a French Comprehensive Cancer Centre

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Introduction: Therapeutic Patient Education (TPE) has recently entered the field of cancer care, as has grown the awareness of non-adherence and side effects management issues with oral drugs in cancer patients. To better fit the ongoing TPE programme to our patients treated by oral chemotherapy, we have explored patients' expectations and needs regarding information related to their disease and its management.

Material and methods: A qualitative approach was adopted using a semi-structured interview guide to collect data, so as to ask the same major questions but also to be able to alter the sequence and to probe additional information, depending on participants responses. Questions were elaborated from international literature and reviewed by physicians, pharmacists and nurses. The study enrolled consecutive patients consulting at Oncology Day Hospitals (Cancer Centre and University Hospital) and treated by oral chemotherapy. Individual face-to-face interviews were conducted in January 2012.

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Results and discussion: Twenty-four cancer patients gave their consent to answer the questionnaire. The interviews lasted 45 minutes to one hour. Patients' age ranged from 36 to 83 years (mean: 63 years). Patients are mainly women, in couple and retired. Main patients' concerns in their everyday life were problems related to their emotional and social life, the disease and its psychological impact, especially self-esteem and body image. They mostly qualified received information on their disease and their treatment as satisfying. However 37.5% have turned to other sources as media to fill their knowledge needs and feel reassured. At the diagnosis announcement, 79% were in a state of shock. At the time of the interview, all are in a fighting spirit even half still remains anxious. Specific expectations in relation with the treatment are the daily management of medications and their side effects, e.g. fatigue, hand–foot syndrome, and hot flushes, which affect their quality of life. Half of our patients have used alternative and complementary medicines to relax and relieve cancer pain.

Conclusion: Repercussions of the disease and the oral chemotherapy on the patients' quality of life justify that the answers to their expectations and needs are included in the structured therapeutic educational programme.

120 Estimation of the Eligible Population for a Bevacizumab (BV) Treatment Combined With Platinum-based Chemotherapy in Advanced Non-small Cell Lung Cancer (NSCLC)

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Introduction: BV, in addition to platinum-based chemotherapy, is indicated for first-line treatment of patients with stage IIIb/IV NSCLC other than predominantly squamous cell histology. Although BV has been shown to improve survival, its use is limited by serious adverse events in daily practice. The aim of the present study was to describe the patient rate able to receive BV.

Methods: This is a prospective monocentric and systematic analysis on all patients with stage IIIB/IV NSCLC treated with first-line platinum + pemetrexed chemotherapy from November 2010 to April 2012. Co-prescription of BV was reviewed. Demographic patients and NSCLC characteristics, and reasons of no treatment with BV were also reported.

Results: Fifty-two patients were registered but only 16 patients (31%) received BV. All BV prescriptions were the subject of a pluri-disciplinary decision. Main characteristics at baseline in patients who received BV and others were respectively: 9 (56%) vs 30 (83%) males, 61 [38; 74] vs 61 [34; 82] years of median age, 15 (94%) vs 33 (92%) smokers or former smokers, 11 (69%) vs 20 (56%) with an ECOG performance status < 2, 13 (81%) vs 32 (89%) adenocarcinomas, 10 (63%) vs 27 (75%) with distant metastasis. The (single or cumulative) reasons of no use of BV were: prior thromboembolic events (12), unirradiated cerebral metastasis (symptomatic or not) (9), haemoptysis (6), radiotherapy delivered with chemotherapy (3), inflammatory bowel disease (3), tumour close to a large vessel (2) and unhealed wound (2). All other reasons were recorded in only one patient: uncontrolled severe hypertension; surgery provided, cutaneous metastasis, haematuria and prior BV administration for another cancer. Four patients treated with BV had previously irradiated cerebral metastasis. In the BV group, 4 patients missed at least one cycle of BV because of the implantable port insertion.

Conclusion: In our cohort, only 30% of patients with stage IIIb/IV NSCLC were eligible for concomitant administration of BV. Despite a modest effect of BV in pivotal studies, chemotherapy combining platinum + pemetrexed and BV is now used as standard arm in phase III of clinical trials. However, in clinical practice the actual contraindications/precautions of BV restrict its use. Assessment of its use in patients with prior thromboembolic events and cerebral metastasis could allow more patients to benefit of BV.

121 5-Fluorouracil Safety in Patients with Dihydropyrimidine Dehydrogenase Deficiency

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5-fluorouracil (5-FU) is the cornerstone of the treatment of digestive cancers. Its catabolism and deactivation mostly depend on dihydropyrimidine dehydrogenase (DPD). Patients with DPD deficiency are at high risk of 5-FU early related side effects. Our objective was to assess the safety of 5-FU in patients with DPD deficiency considering a pharmacokinetic approach by the Oncopharmacogenetics Laboratory.

We retrospectively analysed the files of patients who had DPD deficiency between 2004 and 2011. DPD deficiency was diagnosed by the Oncopharmacogenetics Laboratory considering a genotypic and a phenotypic analyse. 5-FU dosage adjusments were also suggested by this laboratory by calculating 5-FU plasma clearance after the first 5-FU infusion. 5-FU dosage suggested by the laboratory and the 5-FU dosage really prescribed were compared for each patient and each chemotherapy cycle. A standardised collection data sheet compiling demographics, clinical, biological and pharmaceutical data were perfomed.

Seventeen patients had DPD deficiency over the considered period**.** We were able to analyse the files of 11 patients (10 men, 1 woman). Three patients did not receive 5-FU and three others were not treated in our hospital. The average age was 58 years (32–82). Patients were mostly treated for gastrointestinal cancers. Six patients had an adjuvant treatment, two had neoadjuvant treatment and three were treated for a metastatic disease. Clinicians followed 5-FU dosage adjustments suggested by laboratory for seven patients. 5-FU dosage bolus and continuous infusion were consistent with laboratory suggestions in, respectively, 83% and 53% of cases. That meant clinical judgement was also important in determining 5-FU dosage. Two patients experienced an haematological toxicity, respectively grade 3 and grade 4. For those two patients DPD deficiency had not been searched prior to prescribing 5-FU. This study showed that 5-FU was well tolerated in patients DPD deficiency provided clinicians adjusted 5-FU dosage. Sample size and retrospective methodology are main limits of this study.

Our results showed that a pharmacokinetics approach was useful for preventing 5-FU side effects in patients with DPD deficiency. Further studies, in particular medico-economic studies would be interesting to confirm those results and assess economic impact of such tests in clinical daily practice.

122 Ambulatory Infusion of Trabectedin in Treatment of Sarcoma

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Introduction: Trabectedin is indicated for the treatment of patients with advanced soft tissue sarcoma, at the dose of 1.5 mg/m² as an intravenous infusion over 24 hr q3w. The 24 hr infusion classically requires an

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inpatient hospitalisation (IPH), while disposable pumps use might allow outpatient hospitalisation (OPH). We report the feasibility and the interest of an ambulatory infusion of trabectedin for the organization of hospital care.

Method: This is a retrospective monocentric and systematic analysis on all patients (pts) with soft tissue sarcoma treated with trabectedin from January 2009 to April 2012. Patient, sarcoma and treatment characteristics were reviewed. Disposable pumps [flow 4 mL/h-48h] from Silvert® were used for outpatient infusion. Silvert® has previously performed the concentration stability.

Results: 10 pts received trabectedin with classical infusions in IPH and 10 pts with a disposable pump OPH. The prior treatments were similar in the 2 groups: surgery (9 vs 7), radiotherapy (5 vs 4), anthracycline (10 vs 9) and ifosfamide (10 vs 8). Main characteristics at the baseline between outpatients and inpatients were respectively: a median age of 55 (31–79) vs 62 (31–88) years, metastasis (10 vs 7). Laboratory values and co-morbidities were also similar. The total number of cycles analysed were 52 for the IPH group vs 57 for the OPH group. The median intercycle times were not different between the 2 strategies: 22 (20–33) vs 21 (20–25) days. We noted that a median of 2 (1;6) days of hospitalisation were necessary to administer a cycle of trabectedin with the IPH strategy versus 1.0 day with the OPH strategy. The type of hospitalisation defines its average cost: an IPH cost Euros 2,350/cycle versus Euros 385 for daily stay (OPH). (Drug cost not included in both arms). Otherwise, with disposable pump, 2 technical hitches were reported and had no vitale or requiring hospitalisation consequences. The efficacy and safety of trabectedin have not appeared to be affected by ambulatory infusion but must still have been closely monitored.

Conclusion: The use of disposable pump for trabectedin administration could improve the quality of life of the pre-treated patients but also generate cost savings and place of hospitalisation for more appropriate patients. Patient information about infusion duration is important to be performed: less than 20 or more than 28 should be reported.

123 Pharmaceutical Care for Patients with Lung Cancer in National Cancer Institute

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Introduction: The lung cancer is one of the most frequent tumours and the Non-Small Cell Lung Cancer (NSCLC) is the most common. Erlotinib hydrochloride is a tyrosine kinase inhibitor used in the treatment of NSCLC patients with locally advanced or metastatic after failure one chemotherapy regimen, and as maintenance therapy for patients with advanced-stage NSCLC whose cancer has not spread or grown after pre-treatment of platinum-based chemotherapy, and also as first-line treatment in patients with advanced NSCLC, or recurrent with metastatic and active mutation in epidermal growth factor receptor. The Pharmaceutical Care is of utmost importance in this treatment because by monitoring the individual patient it is possible to identify and solve problems related to the drug.

Objective: To describe the results of the practice of pharmaceutical care of patients with NSCLC treated with erlotinib at the Cancer Hospital I (HCI) / National Cancer Institute (INCA).

Method: We used the Dáder Method for pharmacotherapy monitoring of 14 patients with NSCLC treated with erlotinib at the HCI/INCA between August and December 2011 and to measure the adhesion was used the Morisky-Green test.

Results: Patients had a median age of 61 years and 79% of patients were female. Except erlotinib, patients used a total of 60 drugs and the most widely used was ranitidine (57%). Except for NSCLC, a total of 41 types of health problems have been reported and the rash was more frequent among patients (93%), followed by hypertension (57%). Of the 41 types of health problems, 34% were suspected of adverse drug reaction (ADR), with a predominance of skin rash. During the pharmacotherapeutic monitoring a total of 41 interventions were performed, 34 pharmacotherapeutics. Of these, 21 (62%) were accepted and the negative outcomes associated with medications resolved or prevented. Drug interaction was responsible for 32% interventions and non-adherence accounted for 41%. The non-pharmacotherapeutic interventions, with 71% acceptance, consisted of guidelines regarding the use of moisturizer and sunscreen, which help control the dryness of the skin and skin rash and refer obese patients for nutritional assessment. Regarding a adherence to treatment, was identified noncompliance to treatment with erlotinib in 21% of patients, with anti-hypertensive, 50% of patients who were hypertensive had non-adherence; with codeine 75% of patients using this drug had no adherence; with anxiolytics, 57% of patients using anxiolytics had non-adherence. After the provision of pharmaceutical care service, adherence in relation to the use of erlotinib and codeine was 100% in treatment with anti-hypertensive drugs was 75% and as for anxiolytics, adherence remained.

Conclusion: The practice of pharmaceutical care favoured adherence and optimised treatment, whereas the occurrence of ADR, drug interactions and non-adherence can result in reduced efficacy and safety of cancer treatment.

124 Medication Verification at Hospitalisation

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In 2005, the Dutch Ministry of Health, Welfare and Sport initiated to compose a guideline for medication verification in multidisciplinary care settings. This guideline was presented in 2008 and implemented from January 2011 to decrease medication errors [1]. A project for implementation started in St Elisabeth Hospital, Tilburg, The Netherlands (27,496 admissions in 2010). Several Dutch studies show most effective medication verification if patients are interviewed by pharmacy technicians [2, 3]. High-risk patients (≥ 70 years or ≥ 7 drugs) and high-risk settings (Surgical Departments, ED) were defined.

Material and method:

Admission

Prior to hospitalisation an overview of dispensed medication during the past six months was retrieved from the local pharmacy*, for patients meeting the requirements. For patients admitted at the ED a medication overview was obtained through OZIS* and became directly visible in the computerised provider order entry (CPOE) system. The pharmacy technician screens the medication overview and interviews the patient. The interview includes, current medication use (dose, frequency, OTC), medication allergy, ADE and trial participation. The collected information is entered into the CPOE system and the Personal Health Record (PHR).

Discharge

A pharmacy technician draws up an overview of the current medication of the patient in the CPOE system, the clinician checks, corrects and verifies this overview. After verification the overview is communicated to the patient and the local pharmacy.

Results and discussion: In September 2011 pharmacy technicians started interviewing patients at admission and preparing discharge and in December 2011 this was enrolled on all the Surgical Departments and the ED. In 2012, weeks 13 and 14, 112 respectively; 124 patients were

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interviewed at hospitalisation, plus 19 and 28 patients interviewed at the ED. Medication errors due to incomplete medication verification at admission were reduced with approximately 30% on surgical departments and 50% on the ED. The correctness of the medication overview at discharge was defined for Orthopaedic/Urology/Gynaecology Department. Before the start of the project 10 of 40 (25%) overviews were correct and 28 (70%) incorrect. After 1 month 95% (19/20) and after 3 months 90% (18/20) overviews were correct. The pharmacy technician does not intervene with patients admitted for a short duration; these were the incorrect overviews.

Conclusion: Medication errors were reduced by 30–50% and time was saved by clinicians and nurses. Majority (70%) of hospital discharges before intervention were incorrect mostly incomplete discharge overviews and medication discrepancies. After 3 months of intervention at discharge this dropped to 10%.

**A medication overview is retrieved either by fax or OZIS. OZIS is a computerised coupling between the hospitals CPOE system and the local pharmacies, medication dispensed in the last six months can be obtained.*

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125 Off-label Use in a University Hospital - Management, Surveillance and Results

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Introduction: The Italian Law 94/1998 on the therapeutic use of a medicinal product outside authorised indications/posology/route of administration/combinations represents the legislative frame defining the Off-Label Use (OLU). In clinical practice, when authorised therapeutic alternatives are lacking and available efficacy data are supportive, OLU can be granted to a named patient, under the physician declaration of responsibility and signed informed consent. Additionally, the National Competent Authority AIFA by the 648/1996 legislation provides a list of drugs, periodically updated, which can be prescribed on the basis of consolidated evidence. It encompasses medicines already on the market in Italy with evidence of efficacy for new indication, or for different population (e.g. paediatric). Medicines in the 648 list are reimbursed by NHS, while OLUs are paid by the Hospital.

The aim of this surveillance is to achieve a picture of the OLU, to check for inappropriate use and quantify the impact of costs at Hospital level.

Material and methods: An internal Standard Operating Procedure (SOP) has been set up: it consists of a double evaluation on the appropriateness by Pharmacists and Medical Direction. A number of templates for application, follow-up and reporting of adverse events are also included. We analysed data on the OLUs in our local database in the timeframe between January 2011 and April 2012. The following main parameters were considered: active substance, number of involved patients, therapeutic indication, treatment schedule and duration, costs.

Results and discussions: We assessed 83 off-label applications accounting for 83 patients that received a positive opinion. About 45% of OLUs were approved in oncology/ haematology setting (26% oncology, 18% haematology), 7.5% for autoimmune diseases. The most representative substances were Bevacizumab (13), Triptorelin (6), Everolimus (5), Rituximab (4). Results confirm breast and colon cancers, followed by brain tumours as the most representative conditions for OLU in oncology, while lymphomas in haematology.

Conclusion: OLU may be useful therapeutic option in settings with unmet medical needs, like oncology. A case by case evaluation on the benefit/risk balance, followed by a careful monitoring of the safety aspects are always required. Just considering Bevacizumab use in the reported period (16 months), it accounts for a non-reimbursable cost of Euros 224,340. Overall, consideration should be given to reach a reduction of OLUs.

126 Adherence of Imatinib Therapy and the Impact on Response in Chronic Myeloid Leukaemia Patients

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Introduction: Progress in development of molecular target therapy leads to many oral drugs availability. Oral therapy allows the patient to treat at home and could also save resources from the hospital. However, the patient should have the pivotal role in this issue. The expected success of the therapy depends on patient adherence of the treatment. Imatinib mesylate has changed the course of chronic myeloid leukaemia (CML). Recent studies of patients with CML treated with imatinib suggest that non-adherence to treatment is the predominant reason for the inability to obtain adequate molecular response. This study shows the impact of adherence to the clinical response related to imatinib therapy.

Material and methods: Sixty patients with chronic myeloid leukaemia (CML) were prospectively included in the study. They were accompanied by pharmacists on the Pharmaceutical Care Programme at Brazilian National Cancer Institute. At least 18 months of continuous imatinib therapy was necessary to evaluate complete response. The haematologic, cytogenetic and molecular responses were correlated with adherence to treatment. Other factors that could influence the response were also analysed. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 13.0. Associations between variables were analysed by chi-square test or Fisher's exact test when appropriate, and all associations was considered significant when $p < 0.05$. The study was conducted according to guidelines of the Helsinki Declaration.

Results and discussions: Patients had a median age of 52 years, ranging from 22 to 76 years, and 67% were male. Regarding the staging of the disease at diagnosis, 87% of patients were in chronic phase and 13% in accelerated phase. Non-adherence to treatment with imatinib was observed in 33% of patients. In 40 patients with adherence to imatinib, 88% achieved optimal response to treatment, 10% sub-optimal response and 3% have failed. In contrast, the group of patients without adherence 55% achieved optimal response to treatment, 25% sub-optimal response and 20% have failed. These data indicates a strong correlation between adherence to treatment with imatinib and the response obtained ($p = 0.01$). No significant differences were observed between staging of disease at diagnosis and sex on response to treatment ($p = 0.42$ and $p = 0.80$, respectively).

Conclusion: This study suggests that adherence to treatment with imatinib is crucial to obtaining the best therapeutic response. The practice of pharmaceutical care leads to identify patients without adherence and provides interventions to ensure the correct management of oral therapy.

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127 Use of Complementary and Alternative Medicine in Cancer Patients in a University Hospital

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Introduction: A literature review suggested that the use of complementary and alterantive medicine (CAM) among cancer patients is common with a prevalence rate across studies of 31,4%. The aim of this study was to explore the use of CAM in cancer patients treated with oral chemotherapy.

Material and method: A descriptive, prospective study was developed from October 2011 to April 2012. We evaluated the use of CAM in all cancer patients who came to the hospital pharmacy for the first time, to collect the oral chemotherapy. We did a questionnaire that included: name, age, medical record, current standard treatment, eating habits and questions about CAM use (types of CAM and use before the diagnosis of cancer, since the diagnosis of cancer or currently).

Results and discussion: A total of 164 patients participated in the study, 34 of them (20,7%) used CAM: 14 (8,5%) female and 20 (12,2%) male. The CAM used were homeopathy (11), biologically-based therapies: herbs (13), vitamins/minerals (4), and dietary supplements (10). Patients were treated with: capecitabina (n = 71), everolimus (n = 5), sunitinib (n = 31), sorafenib (n = 8), gefitinib (n = 5), erlotinib (n = 7), lenalidomida (n = 1), temozolomida (n = 12), abiraterona (n = 3), lapatinib (n = 7), dasatinib (n = 2), imatinib (n = 9), nilotinib (n = 3), others (n = 5).

Conclusion: The use of CAM among cancer patients is a reality. Patients often do not inform their doctor the use of these therapies, and the heathcare professionals do not enquire but it is essential that health professionals are aware of the use of CAM with their patients, educate them about the potential benefits and the possible drug interactions.

130 Adherence to Appropriate Use of Perioperative Prophylactic Antibiotics - Results from a Two-round Intervention Study

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Introduction: Surgical infections are often associated with high morbidity, mortality and treatment costs. Despite this situation, perioperative antibiotics are abused or misused in many local Chinese hospitals. The aim of the study was to tentatively establish standards for perioperative antibiotic prophylaxis and to evaluate the intervention effects on perioperative antibiotic use from a local hospital's perspective.

Material and methods: A prospective intervention study was conducted in Anhui Medical University Anhui Provincial Hospital. Patients who received at least one of predetermined 11 clean surgical procedures were considered as eligible cases and enrolled in our study. Based on literature review and panel discussion, we initiated a model of interventions activities including establishing a management group on antibiotic use, developing a management system, and improving knowledge of proper antibiotic use among clinical pharmacists. According to the model, we conducted two rounds of intervention on antibiotic use among physicians and nurses and collected outcome data of the intervention at three time points (in March, June and September 2010) as phase 0 (before intervention), phase I (after the 1st round of intervention) and phase II (after the 2nd round of intervention) respectively. Outcome measures were antibiotic application rate, appropriateness of prophylactic antibiotic indication, comprehensive rate of appropriate administration, and overall antibiotic cost.

Results: We recruited 210, 203 and 207 cases at phase 0, phase I and phase II respectively. A positive impact of intervention was observed in terms of increasing rates of 'not indicated and not administered' (12.38%, 27.09% and 30.43% for phases 0, I and II respectively). No 'indicated but not administered' cases appeared in all three phases. Prolonged antibiotic use was more obvious after the intervention (19.05%, 42.86% and 63.29% for phases 0, I and II respectively), while rational use of antibiotic dose increased after intervention (45.17%, 53.57% and 74.30% for phase 0, phase I and phase II respectively). Comprehensive rate of appropriate medication improved from 12.38% in phase 0 to 33.99% and 51.21% in the two post-intervention phases. The average cost of antibiotic use initially increased from 1189.31RMB (phase 0) before intervention to 1548.20RMB in phase I, and subsequently decreased to 801.53RMB in phase II.

Conclusion: Although this intervention study achieved improvements in antibiotic application rate, appropriateness of prophylactic antibiotic indication, comprehensive rate of appropriate administration, it failed to reduce duration and dose of antibiotic use. Based on our practice, the intervention model established in this study proved to be feasible and effective in local Chinese hospitals.

Poster Session: Organisation and Management

133 Considerations to Improve the Availability of Biologic Medicines in a Cancer Centre

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Introduction: Oncology pharmacists play a key role in formulary decisions at cancer centres. As adequate drug availability is a growing concern with many generic injectables, reliable supply is an increasingly important consideration for pharmacists. With drug shortages, physicians and pharmacists may have to consider less desirable options, e.g. rationing, delaying critical treatments, and using less efficacious drugs. Although regulatory agencies are developing processes, e.g. rapid notifications, for early communication of drug shortages, these processes may not ensure the maintenance of continuous supply to patients.

Materials and methods: Using leading biologics manufacturers as an example, this report highlights critical supply chain parameters that pharmacists should consider when evaluating manufacturers' ability to maintain and deliver a continuous supply of cancer drugs.

Results and discussion: Inventory turns (replacements per year) for 7 major US manufacturers were evaluated (2006–2010). Biotech manufacturers (n = 2) had 1–1.5 turns, large pharmaceutical manufacturers (n = 2) had 1.5–2.0 turns, and generic manufacturers (n = 3) had 2–4 turns. In 2011, the biotech firms had no drug shortages; the 2 pharmaceutical firms had shortages of 1 drug and 2 drugs, respectively; and the 3 generic firms had shortages of 5, 25, and 46 drugs, respectively. Key factors to ensure a continuous supply of biologics include: 1) maintenance of strategic safety stock supplies to minimise the impact of any manufacturing delays or interruptions; 2) qualification of suppliers and dual sourcing of raw materials; 3) capabilities for multi-site manufacturing and strategic capacity management; 4) active management of robust, secure networks for cold chain distribution; and 5) integration of global manufacturing and distribution information systems linking patient demand to production scheduling. These factors require significant financial and human resources to ensure that approved products are available during normal operations and shortages. A checklist was developed from these critical supply chain parameters. Search criteria were identified to help pharmacists obtain manufacturer information from public sources.

Conclusion: Understanding and considering how manufacturers should manage drug supply is a key aspect of evaluating their ability to reliably deliver drugs. A checklist developed for pharmacists from critical supply chain parameters aids this evaluation process.

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134 Analysis of the Therapies in Paediatric Oncohaematology - the Role of the Hospital Pharmacist

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Introduction: Patient safety and the decrease of errors in pharmacological therapy are a priority of Healthcare Assistance. In accordance with this aim the Padua Hospital Centre has started up 'the Patient's Safety Project 2010–2012'.

Errors take place during the three main steps of the therapeutic process: prescription, preparation and administration.

The frequency of errors occurs mainly with oncology medicines because of their narrow therapeutic index, for their difficulty of management and for the complexity of the patients to whom they are dedicated.

According to this Pediatric Oncohematology is one of the main departments involved for the amount of clinical-assistance work and the variety of patients, in which the precision of oncology medicines preparation and the personalization of the therapy become an essential requisite.

Material and methods: Survey of the activity of both of the departments of Hospitalisation (DEG) and Day Hospital (DH) of the Padua Pediatric Oncohematology , and of the medicines in use, with indicators from administrative software. Completion of a questionnaire about medical records of two weeks index (from 9 to 22 January 2012) and analysis of the data acquired. Physiopathological arrangement of the main neoplasm treated, and of the therapeutic protocols in use.

Results and discussions: From the data analysis, the number of patients surveyed has been 180 in DH and 27 in DEG ranging from 6 to 14 years old. From analysis of pathologies, prevalent are Leukaemia (52% in DH and 40% in DEG) and Lymphomas (15% in DH and DEG), followed by Sarcomas (15% in DH and 9% in DEG). From the comparision between protocols and data of medicines used, the more prescribed medicines have been found to the methotrexate, ifosfamide and cyclophosphamide. From the analysis of the medical records it was evident that in 33 up to 154 prescriptions there had not been indicated the way of administration.

Conclusion: This study demonstrated that rationalisation and decrease of clinical risk outline important roles for the hospital pharmacists in a multidisciplinary team, which is where the therapeutic decisions are made, that is the department. They will take part in all the phases that characterise the course of a single medicine in the hospital: prescription, preparation, distribution, administration and monitoring. So it will be pharmacists' responsibility that all the medicines prepared in Centralised Pharmacy are conformed to protocols in a calm and stable manner. As a consequence the hospital pharmacist will guarantee a constant revision of the procedures and updating of the information, in order to improve quality of preparation and assure the highest patient safety.

135 Rare Cancer Treatment in Poland - The Legal Perspective

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A rare disease affects no more than 5 patients in a population of 10,000 people. Rare cancers include all the childhood cancers and many cancers in adults. Rare diseases constitute a serious problem for the public health, mostly related to ensuring unlimited access to treatment to all patients. The drugs used in the treatment of rare diseases, i.e. orphan medicinal products, are very expensive. The treatment of rare diseases has been acknowledged as a priority in the activities of the European Community. However, the reimbursement of the drugs used is not uniform in the EU and each Member State should have their national health policy in this respect. In Poland, the decision-making bodies with regard to what drugs and what procedures are subject to the reimbursement of health services from public funds are: the Minister of Health, the National Health Fund and the Medical Technology Evaluation Agency.

The current Polish legal solutions concerning rare cancer treatment are based on the Reimbursement Law of 2011. The public financing provides patients with standard chemotherapy which must, however, be based on the compliance of the procedure with registration data which very rarely include indications for rare cancer treatment. Rare cancer treatment is based on off-patent therapy, among others. In Polish law there are unfortunately no specific regulations on such a procedure, which gives rise to much controversy about the issue. Ambiguities about the availability of treatment according to the off-label procedure undoubtedly form a barrier to rare cancer treatment. Polish patients are offered drug programmes that in 2012 are undergoing a reform related to the introduction of price negotiations for particular drugs within separate drug programmes, on the 'per drug' basis (one disorder, many molecules). Drugs used under the same indication are combined in a therapeutic group subject to the same price limit. Unfortunately, the problem is that establishing such programmes takes a long time. A hospital pharmacy is in charge of the provision of drugs covered by drug programmes to patients.

The problem of access to rare cancer treatment also manifests itself in the relatively small number of clinical studies conducted in Poland (with few non-commercial studies). The little dynamics of clinical research development is primarily connected with the imprecise and unclear Pharmaceutical Law.

The regulations of Polish law govern the financing of the services related to rare cancer treatment from public funds, focusing on making the use of a special drug programme available.

136 Check of Computerised Prescription of Injectable Antineoplastic Drugs - Analysis of Prescribing Medication Errors

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Introduction: Centralisation in the process of compounding antineoplastic drugs is an important tool which has the purpose of reducing the use of drugs and enhancing security in compounding itself, and it allows to strengthen cooperation between physician and pharmacist. Computerised physician order entry can limit the risk of prescribing medication errors, and subsequent check of prescription done by pharmacist can limit furthermore this risk.

Materials and methods: From August 2011, we have started a collection of errors concerning chemotherapies, intercepted by the pharmacist while checking prescriptions: drug-drug or solvent incompatibility, way and time of administration, dose prescribed, other. These prescribing medication errors are 'near-miss', as each error was reported by the pharmacist to the physician, and corrected before compounding. This analysis considers only prescriptions from one oncologic ward of our hospital, selected based on the fact that 100% of prescriptions are computerised.

Results: During the first eight months of analysis, 16,227 doses of parenteral antineoplastic drugs were prepared for the whole hospital. In the oncologic ward analysed, considering 8,394 parental antineoplastic

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drugs prepared we have found 249 prescribing medication errors (2.9%). Errors were mainly distributed as follows: incorrect dose (0.4%), incorrect treatment duration (0.2%), unsigned prescription/incorrect date treatment/no evidence for clinical trial (1.1%), incorrect volume and/or inadequate solvent (1.2%), double prescription (2 errors), drug not necessary (1 error). According to potential clinical impact, 1.1% of errors were not significant, 1.8% significant or very significant, only one error was vital.

Conclusion: The frequency of prescribing medication errors in the ward considered for this analysis proved to be higher compared to published data from a similar survey (2.9 vs 1.5%) (Nerich et al, 2010). The major part of errors concerns incorrect volume of solvent. An explanation for such errors is that the software in use in our hospital modifies the drug dosage based on patient's clinical data, e.g. BSA, serum creatinine, but does not modify the solvent volume, which may result in a final drug concentration outside of the limits of stability. Overall, this analysis confirms the importance of an accurate check of prescriptions by the pharmacist in order to improve quality and security of antineoplastic treatments.

Poster Session: Palliative Care

138 Last Treatments for Cancer Patients in Palliative Stage

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Palliative care improves the quality of life of patients and families who face life-threatening illness, by providing pain and symptom relief, spiritual and psychosocial support to from diagnosis to the end of life and bereavement. They are active, continuous, evolutionary, coordinated and practised by a pluri-disciplinary team. Medications and treatments have a palliative effect if they relieve symptoms without having a curative effect on the underlying disease or cause.

Patients deceased in a palliative care unit were evaluated about the used drugs, the influence of a Mobile Palliative Care Unit (MPCU) on treatments and about the drugs costs the day of death.

Twenty-seven computerised prescriptions (with drugs administrations) were analysed until death.

All patients had a metastatic cancer. Gastric was the leading site of cancer (30%) followed by lung (22%), gynaecologic (19%), head and neck (11%), haematologic (7%). They mostly received midazolam (70%), opioids (89%), glucocorticoids (63%) and hydroxyzin (44%). 26% had a parenteral nutrition and 15% had an enteral one. Nineteen patients received antibiotics and seven had them until death. The mean cost of administrated drugs in the last 24 hours before death was Euros 21.45. MPCU gave pieces of advice or prescribed treatments for 9 patients (33%). No difference between patients was found either about the number and the type of treatments or about the cost of the death day ($p = 0.38$) after MPCU visit. Administration of intravenous or oral chemotherapy close to death was found in 20 patients (gemcitabine, capecitabine, cetuximab, erlotinib). Targeted therapies were questionable in some studies because possible side effects compared to few results in terms of overall survival. The medical and economic impact of using such drugs and their interest in the implementation of supportive care or use of conventional chemotherapy must be assessed (gain of life span, quality of life).

Continuation of treatments or clinical investigations would likely require a reassessment. Moreover, physicians are inaccurate in their prognoses for terminally ill patients, and the error is systematically optimistic.

139 Drugs in the Last Six Days of Life and Their Costs

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Introduction: Palliative care provides many advantages to the dying patient. In the last days of life five most common symptoms may occur: pain, nausea and vomiting, restlessness, dyspnoea and respiratory tract secretions. Essential medicines should be prescribed in advance to alleviate these symptoms.

Material and methods: The purpose of this retrospective study was to compare which drugs patients received in their last six days of life in case they were managed within our palliative team (25 patients) or not (25 patients). Both groups were comparable by the primary tumour site and patients' age.

Results and discussions: We found that the majority of patients in both groups received strong opioids, while other drugs to relieve symptoms such as haloperidol, midazolam, dexamethasone, butylscopolamine and metoclopramide were administered more likely to patients in palliative care group. Polypharmacy is also widespread in the last days of life. Patients treated in the palliative care group received on average 10 different drugs while those treated outside 14 different drugs. The costs for drugs were 2.7-fold lower in the group of patients treated in the palliative care group and account for Euros 15 per patient per day compared to Euros 42 in the control group. The difference in costs was mainly due to unnecessary prescribing of low molecular weight heparins, systemic antibiotics, antifungal drugs, and parenteral nutrition.

Conclusion: The biggest advantage of palliative medicine is improving the quality of life of patients with advanced incurable chronic disease. Better quality of last days of life will be achieved if we alleviate symptoms that usually occur in the phase of dying, and thus essential drugs become analgesics, antiemetics, sedatives, anxiolytics and anticholinergics. All unnecessary medicines should be omitted.

Poster Session: Pharmacotherapy

140 Evaluation of Bevacizumab Fluorouracil and Vinorelbine Combination in Women with Metastatic Breast Cancer and Pretreated with Taxanes

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Background: Bevacizumab (Beva) is indicated in combination with taxanes in first-line treatment of metastatic breast cancer (MBC). Subgroup analyses in two pivotal studies have suggested a maximum efficacy in women pretreated with taxane. In our hospital, the FUN regimen (fluorouracile [5-FU] 750 mg/m²/d from D1 to D5 and vinorelbine [VNB] 25 mg/m² at D1 and D5 q 3 weeks) is an alternative to taxane for patients with MBC and pretreated with paclitaxel or docetaxel. The aim of this study was to evaluate the efficacy and the safety of bevacizumab in association to FUN.

Patients and methods: From 05/2006 to 02/2011 we retrospectively identified in our databases all patients with MBC treated by FUN regimen ± beva in our breast care unit. All the patients must have been previously treated with anthracyclins and taxanes in metastatic or adjuvant setting and with trastuzumab if HER2 was overexpressed. The primary endpoint was the progression-free survival. We also recorded safety data for the FUN-Beva group.

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Results: 81 women (FUN alone n = 40, FUN-Beva, n = 41) were analysed. Patients characteristics were well balanced between the two groups except for HER2 overexpression more frequent in the FUN group (5 vs 1) and a higher median follow up in the FUN group (4.63 years (1.63–8.36) vs 2.4 years (0.45–4.21) with FUN-Beva). Median age was 51.3 years (30.5–76.1) in FUN group vs 49.0 (28.9–69.9) in FUN-Beva group; 17 women (42.5%) vs 18 (43.9%) had triple negative tumours; the time without metastasis was < 24 months in 19 (47.5%) vs 13 (31.7%); 13 (32.5%) vs 15 (36.6%) had 2 metastatic sites or more; 29 (72.5%) vs 30 (73.2%) had a visceral localisation. The treatment was a 1st-line chemotherapy in more patients in the FUN-Beva arm than in the FUN arm (21 first-line therapy vs 31, p = 0.028). The patients received a median of 8.8 (1–32) vs 7.1 (1-23) cycles of 5-FU and 10.8 (1–32) vs 10.4 (1–24) cycles of VNB in the FUN and FUN-Beva groups respectively (p = NS), with dose reductions in 40.5% vs 56.1% women (NS) for the 5-FU and 24.3% vs 19.5% (NS) for the VNB. In FUN-Beva, the number of antibody injections was 11.6 (1–34). Median PFS was 298 days [221–375] in FUN vs 321 days [294–348] (p = 0.21) in FUN-Beva arm (HR 0.71 [0.42–0.20]). The subgroup analysis of 1st-line metastatic gave very similar results. FUN-Beva was well tolerated. Disruption of treatment due to toxicity occurred in 3 women (7.3%). The most frequently grade 3/4 observed AEs were the febrile neutropenia in 29 (70.7%) and the mucositis in 12 patients (29.3%).

Conclusion: Our data do not suggest any benefit of the addition of bevacizumab to a FUN regimen in MBC, but might be limited by the design of our study. However, a trend to a longer PFS in the FUN-Beva group, though not significant, may warrant further investigations. With the widespread use of taxanes in aduvant setting for breast cancer, and the recently restricted role of bevacizumab in the MBC by the European health authorities, the combination of bevacizumab to taxane-free protocols should be evaluated in prospective studies, in particular in women pretreated with paclitaxel or docetaxel.

141 Off-label and Unlicensed Use of Cytotoxic Substances in Rare Cancers

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Introduction: Orphan drugs are medicinal products intended for the prevention, diagnosis and treatment of a life-threatening condition with a very low prevalence/incidence. Today only 62 orphan drugs are authorised in the 27 Member States of the European Union for 44 rare diseases, mainly rare cancers. Reimbursement is different in every EU Member State but strictly for on-label use.

Results: Off-label use is the use of pharmaceutical products 'as is' but in another indication, another dose or another patient group (mainly children) than is described in the package insert, EPAR or SFC. Unfortunately, very few information about the side-effects and the clinical added value of off-label use is collected. The pharmaceutical company is not allowed to mention this ('illegal') use such as clofarabine in AML, cladribine in non-Hodgkin's lymphoma and bevacuzimab in glioma. The prescribing physician is the responsible person.

Unlicensed use is the use of pure chemicals or medicines after being compounded in a different dosage form. At our Pharmacy Department we refused the use of dichloroacetate but developed a standard compounding procedure for carmustine ointment (lymphoma)–compounded with the injectable product (BICNU, CARMUBRIS)–for mitomycine eyedrops, and for capsules with arsenic trioxide and busulfan. Also a patient oriented information leaflet was created.

Conclusion: For most of the rare oncologic conditions there is no designated treatment. Therefore, therapy sometimes consists in the off-label or unlicensed use of medication with potentially toxic substances.

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142 Gefitinib as First-line Treatment for Non-small Cell Lung Metastasic Cancer-patients Presenting EFGR Mutations

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Introduction: Gefitinib has been established as first-line treatment for non-small cell lung cancer (NSCLC) if a patient presents an activating mutation of EGFR Tirosin Kinase. We study the incidence of EFGR mutations in our population and the results of this therapy.

Material and methods: Retrospective review between 16/04/2010 and 16/04/2012 of medical records of patients with NSCLC who underwent a test of the EGFR mutation and records from Pharmacy Service´s Oncology Unit.

Results: During the study period, 330 patients were tested for the presence of EGFR gene mutations. Of these, 52 (15%) presented mutations whose distribution was as follows: exon 19 deletion, 32 patients (61%), exon 20, 9 (17%), exon 21, 5 patients (9.6%) and exon 18, 4 patients (7.6%). Of the 52 patients with mutations, 30 of them received the Tyrosine Kinase Inhibitor gefitinib, 15 patients as first line and 15 during other lines of treatment. Among the15 patients who started first-line treatment with gefitinib, 9 were treated with a second-line chemotherapy after a median of 3 months (2–11 months). After 6 months from the start of treatment, overall survival was 64% (9/14) remaining on gefitinib 35% (5/14). Overall survival at 1 year is 36% (4/11). Patients were treated with gefitinib for a median of 5 months (1–19).

Conclusion: Although patients were selected acording to current knowledge, results are poor and it is necessary to continue evaluating the effectiveness of these therapies in the context of palliative care.

143 Antiepileptic and Antitumoural Effects of Levetiracetam in Patients with Malignant Tumours

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Introduction: Antiepileptic drugs (AEDs) are usually administered to the epileptic patients, including brain tumour-related epilepsy. However, interaction with chemotherapeutic agents remains a continuous matter because both the AEDs and these agents are usually metabolised through the P450 hepatic cytochrome system. Levetiracetam (LEV) is a unique AED, which is not disposed via P450, and does not influence with concomitant chemotherapy. Besides, LEV enhances P53-mediated O6-methylguanine-DNA methyltransferase (MGMT) inhibition and may improve clinical effect of temozolomide (TMZ), because MGMT down-regulate the antitumoural effect of alkylating agents, including TMZ which is commonly used to the patients with malignant brain astrocytoma.

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Material and method: We retrospectively reviewed consecutive 32 epileptic patients with brain tumours treated with LEV and examined efficacy and safety of LEV on the epilepsy treatment. Next, to evaluate antitumoural effect of LEV via MGMT inhibition, we reviewed 46 patients with recurrent malignant astrocytoma: 9 treated with TMZ and LEV (Group A), 37 with TMZ alone (Group B) as historical control. Overall survival (OS) and progression-free survival (PFS) of Group A were compared with those of Group B.

Results and discussion: Eighteen astrocytic tumours, three oligodendroglial tumours, seven metastatic brain tumours, and four other tumours were enrolled. A median dose of LEV was 1,000 mg/day (Standard deviation: 368). In the epileptic effect, 91% of patients treated with LEV showed the decrement of seizure frequency and 75% of them became seizure free. A major side effect was somnolence and fatigue (28%) but these symptoms were well tolerated. Severe sleepiness required the switch of AED in only one patient. No hepatic disorder was observed. In the antitumoural effect, no significant difference of characteristics (sex, age, KPS, tumour grade, methylation status of the MGMT promoter at diagnosis, recurrent period and tumour volume) was observed between Group A and B. Concurrent use of LEV with TMZ did not prolong the PFS and OS of the patients with malignant astrocytoma (6-month survival rate: 62.5% and 65.0% respectively). Chemotherapeutic toxicity of grade 3 or more (CTCAE version 4.0) occurred in the same rate between two groups. LEV well controlled the epilepsy but, unfortunately, we could not find the clinical effect of MGMT inhibition. Recent studies reported that methylation status of the MGMT promoter not at recurrence but at primary surgery well expected good prognosis of patients. Therefore, TMZ with LEV might be effective for primary cases rather than recurrent ones.

Conclusion: About LEV, the control rate for brain tumour-related epilepsy was very high and the side effect was mild and well tolerable, although antitumoural effect was still unknown.

144 Weekly Paclitaxel-carboplatin Plus Bevacizumab as First-line Chemotherapy in Advanced Ovarian Cancer - A Case Report

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Introduction: Paclitaxel and carboplatin every 3 weeks is the standard treatment for metastatic ovarian cancer (mOC). As an alternative regimen, we tried a weekly schedule with bevacizumab achieving complete clinical response without significant toxicity.

Material and method: We present the case of a patient treated with paclitaxel (80 mg/m2), carboplatin AUC 2 mg/mL per min given on days 1, 8, and 15, and bevacizumab (10 mg/kg every two weeks). Medical records were reviewed and clinical data on stage, surgical treatment, radiologic studies, pathologic assessments, laboratory test (complete blood count, chemistry profile with CA-125, renal and liver function tests), toxicity and response were collected. Tumour responses were evaluated according to RECIST criteria.

Results and discussion: A 70 year-old patient with ovarian papillary cystadenocarcinoma which surgical procedure involved bilateral oophorectomy with residual disease (> 1 cm), received four courses of chemotherapy. The initial CA 125 117.8 UI/mL decreased to 3.6 UI/mL (normal range: 0.0–35.0).

Complete response was assessed by computed tomography (CT). During the treatment there was no toxicity-related delay, but a prophylactic 5 ug/kg/d filgrastim dose was used 48 hours after chemo. Also the renal and liver function remained in normal ranges. The TC and CA 125 values revealed a complete response after four courses of chemotherapy and allowed our patient to became candidate for second look surgery.

Conclusion: This weekly schedule with bevacizumab represents an alternative treatment which conjugates the benefits of both dose dense chemo and anti-angiogenic therapy. This regimen was well tolerated without significant toxicity.

145 Trabectedin for Metastasic Soft Tissue Sarcoma - A Retrospective Analysis

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Introduction: Soft tissue sarcoma (STS) consists of a large variety of rare malignant tumours. Trabectedin was approved in 2007 for patients with advanced STS after failure of anthracyclines and ifosfamide, or for patients unsuited to receive these agents. This retrospective study analysed 24 patients who had been treated with trabectedin at our institution between 2009 and 2012 with the aim to obtain basic epidemiological information on patients with soft tissue sarcomas, standard treatment procedures, and results of trabectedin therapy in clinical practice.

Material and methods: 24 patients diagnosed with soft tissue sarcoma were retrospectively included in the database. Median age at the initiation of trabectedin therapy was 52 years (18–75 years). Leiomyosarcoma was the most frequent tumour (25%), liposarcoma occurred 20.8%, synovial and histiocytoma sarcoma occurred in 12.5% of patients, fibrosarcoma, schwannoma, angiosarcoma, rhabdomyosarcoma and unspecified sarcomas contributed 4.2% each. Trabectedin was administered in a dose of 1.5 mg/m2 once in 3 weeks. The majority (84%) had been heavily pre-treated with ≥ 2 previous lines of chemotherapy.

Results: Median number of administered cycles was 6 (1–15 cycles). Neutropenia (33.3% of patients) and elevation of liver transaminases/liver function tests (79.2% of patients) were the most frequent adverse effects. Only one patient achieving a partial remission (PR) and 9 stable disease (SD). Median overall survival (95% CI) was 6.7 months (4.3; 9.8), median progression-free survival (PFS) (95% CI) was 3 months (2.1; 3.2). PFS for all patients was 45% at three months and 28% at six months.

Conclusion: We conclude that trabectedin is an effective and generally well-tolerated treatment for STS particularly in liposarcomas and leiomyosarcomas, and good safety profile.

Poster Session: Pharmacokinetics/Pharmacodynamics

146 Use of Carboxypeptidase for Methotrexate (MTX) Overdosage Management - Pharmacological and Analytical Aspects

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Introduction: Methotrexate (MTX) is one of the most widely used anticancer agents and can be safely administered to patients with normal renal function by the use of alkalinisation, hydratation and pharmacokinetically guided leucovorin rescue. High doses of MTX cause acute renal dysfunction. This leads to delayed MTX elimination and life-threatening toxicity. MTX drug monitoring consists in determining MTX blood level by immunoassay. In case of acute intoxication associated with nephrotoxicity, use of the enzyme carboxypeptidase G2 (CPDG2) allows hydrolysis of MTX and main metabolite 7-OH-MTX to non-toxic metabolites: DAMPA, 7-OH-DAMPA and glutamate.

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We report 3 cases of overexposure to MTX and who underwent rescue therapy with CPDG2.

Material and methods: MTX blood levels of MTX were determined by two methods: immunoassay for conventional drug monitoring (Roche) and specific analysis using High Performance Liquid Chromatography (HPLC) associated with UV detection after CPDG2 was administered. Liquid-Solid extraction of MTX and DAMPA were performed. Lower limit of quantification of MTX was 0.08 µmol/L. Patients were respectively 62, 38 and 72 years old and received 3g/m². Renal function was normal before MTX administration.

Results and discussions: 24 hours after MTX infusion, blood levels were 43, 33 and 31 µmol/L respectively for the 3 patients and associated with a dramatically elevation of creatinine (220, 410 and 180 µmol/L). CPDG2 was administered at day 2. All patients had a rapid and prominent decrease in plasma MTX concentration measured by HPLC, within the first hours post-injection, which leads to non-toxic MTX levels in the following days. A second and more slowly decreased in MTX blood levels was observed with a significative rebound of MTX at 96 hours for one of the patients. Decrease in creatinine was associated to MTX elimination with a slow recovery of renal function. Immunoassays are unreliable after CPDG2 administration owing to a cross reaction between MTX and DAMPA. Only specific method as HPLC can be recommended. Given the rarity of the situation, centralisation of the samples in specialised laboratories could be justified. There is also a need for more rapid methods as UPLC for rapid monitoring. Also, samples for the determination of MTX concentrations need an inactivation of the CPDG2 with acid treatment for optimal stability before analysis.

Conclusion: In the three cases, we confirmed that CPDG2 is essential for rescue after severe acute intoxication by MTX. Good practices of pharmacological monitoring must be done.

147 Compassionate use - Pharmacovigilance

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Introduction: The use of compassionate drugs in Italy is a clinical practice employing drugs available in foreign countries but not in Italy: they have the authorisation for the same therapeutic purpose but are not available on the market, however they are or under clinical trials (CT) or have been tested in phase III or – when the patient is in critical clinical conditions – have achieved CT in phase II. As far as evaluating the efficacy of the treatment, a basic aspect of the CT is the valuation of the security of the used drugs. Great attention on this theme is focused in case of sponsored CT; in fact in the Decree Law (211/2003) the liable subjects for pharmacovigilance are expressly listed and a stress is put upon the course for the report of adverse drug reactions (ADR).

Materials and methods: About the use of compassionate drugs, there is no Decree Law that regulates the pointing out of ADR. The aim of this work is underlining how – in the common clinical practice – the reports of possible ADR emerging from compassionate studies are managed. For this purpose the database in use in our organisation was essential: the whole CT of our centre are listed there. The number of CT divided into typology (profit, no profit, compassionate) has been extracted, focusing on the third ones in particular. Then the number of treated patients has been drawn as well as the pathologies and the ADR pointed out during the meetings with the physicians.

Results and discussion: From this analysis it comes out that in our centre 197 studies (st) are active: 147 are profit, 27 no profit and 23 compassionate. Among these last ones, 8 are active by the Sarcoma Department, 5 by Haematology, 3 by Paediatrics, 6 by Medical Oncology and 1 by Urology. The examined pathologies are: GIST 4 active st, 6 patients (pt), Hodgkin's lymphoma 1 st (2 pt), T-cell lymphoma 1 st (1 pt), myeloma 2 st (1 and 15 pt), thyroid carcinoma 1 st (1pt), bone metastases 1 st (4 pt), melanoma 2 st (1 and 30 pt), villonodular tenosynovitis 1 st (4 pt), prostatic adenocarcinoma 1 st (4 pt), breast cancer 2 st (3 and 2 pt), leiomyosarcoma 1 st (2 pt), myxoid liposarcoma 1 st (6 pt), brainstem glioma 1 st (8 pt), NET 1 st (17 pt), acoustic neuroma 1 st (1 pt), idiopathic myelofibrosis 1 st (1 pt), LLC 1 st (1 pt).

Even if the CT for a compassionate use are fewer than other kinds of trials and require a very low number of treated pt – also because it is a matter of a nominal use and in particular conditions- this does not justify the lack of ADR signalling. As it is about drugs used for critical patients and often for not approved uses, it seems useful to focus on this aspect, as it allows to more and better investigations on the side of the safety of the drugs.

Conclusion: The results obtained underline the necessity of a better sensibility about the problem. As far as our centre is concerned, the results led to organise meetings with the physicians and to plan interventions in order to make sensitive about the problem and in order to start a process of pharmacovigilance over compassionate drugs.

148 Use of Pharmacovigilance to Evaluate Capecitabine-induced Drug Adverse Reactions in Patients Under the Capox Regimen at the National Cancer Institute of Brazil

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Introduction: The inclusion of pharmacovigilance in the hospital routine can help to raise the level of safety of pharmacotherapy in exercising its function of promoting the rational use of drugs, raising the quality of life of patients through the systematic monitoring. In oral cancer therapy, patients make use of anticancer drugs at home, so pharmacovigilance becomes an essential strategy because it provides useful information by examining the medical records and patient reports.

Material and method: This study aimed to assess the potential risks of adverse reactions and drug interactions in patients taking capecitabine under the CAPOX regimen (combination with oxaliplatin) at the Cancer Hospital I through interviews and analysis of medical records. We used the active search to collect data for evaluation of 13 patients with colorectal cancer (CCR) treated with capecitabine in the period from August to December 2011.

Results and discussion: Patients had a median age of 53 years and 69.2% were female. With respect to the CCR 30.8% of patients had liver metastases as an additional risk factor to the disease. All patients received treatment with capecitabine in concurrent use of other drugs with antiemetic ondansetron and dexamethasone as the more common (53.8%), placing second omeprazole (38.5%). There were 25 symptoms indicative of Adverse Drug Reaction (ADR), with a predominance of gastric and intestinal disorders in 61.5% of patients. During the interviews were developed eight ADR analysis processes, which had as the main parameter for evaluating the Naranjo algorithm. Most reactions recorded were classified according to causality as likely (50%), according to the severity as moderate (62.5%) and originated in the mechanism of action of drugs belonging to the treatment. Special attention was directed to the only reaction assessed as defined, the hand–foot syndrome with evolution and recurrence in perfect accordance with the provisions in the literature for the use of capecitabine. An intervention was made to develop a keratolytic agent for topical use of urea by pharmacotechnics, but structural limitations prevented the conclusion of the process.

Conclusion: The results confirmed the importance of monitoring patients on capecitabine through the resources of pharmacovigilance, which contributed to increase the safety of chemoterapy regimen.

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