The Canadian Association of Pharmacy in Oncology presents the
National Oncology Pharmacy Symposium 2011
Let’s Get Personal
Onsite Program

L’Association canadienne de pharmacie en oncologie présente le
Symposium National de Pharmacie en Oncologie 2011
Let’s Get Personal
Programme
Membership for Pharmacists, Technicians, Pharmacy Assistants, and Other Health Care Professionals Interested in the Practice of Oncology Pharmacy in Canada

CONNECT
- Online Member Forum
- Professional Network
- Awards and Grants

LEARN
- CAPhO’s Accredited Online Education
- Continuing Education Listing
- Resource Library

ENGAGE
- Annual National Oncology Pharmacy Symposium
- Standards of Practice

www.capho.org
The National Oncology Pharmacy Symposium, organised by the Canadian Association of Pharmacy in Oncology, is a major meeting for all pharmacists and other healthcare workers. It is an opportunity to brush up on the most innovative practices and recent developments that help improve the quality of pharmaceutical services and care available to cancer patients.

Through its broad range of activities, the Association provides pharmacists and other oncology professionals with an opportunity to hone their skills and network with others in the field from across Canada. It serves as an extremely rich forum for discussion and sharing experiences that benefit all members of the network.

To all those who will be attending the Canadian Association of Pharmacy in Oncology’s National Oncology Pharmacy Symposium, I would like to cordially welcome you to the wonderful City of Québec!

Yves Bolduc, Minister / ministre
Québec Health / Santé Québec
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Welcome Message from the CAPhO President / Mot de bienvenue du président de l’ACPhO

On behalf of the Executive Committee of the Canadian Association of Pharmacy in Oncology (CAPhO), I would like to welcome you to Quebec City for NOPS 2011.

Please join me in thanking the NOPS 2011 Organizing Committee members who have planned an outstanding program centred on the theme of "Let’s Get Personal". In addition to the plenary, breakout and oral sessions, we hope you take advantage of the 10 satellite symposia offered by our sponsors, and of the social / networking sessions placed throughout the program so that you can meet up with old colleagues and make new acquaintances.

Many of the CAPhO Executives are at NOPS 2011, and will be pleased to discuss the upcoming CAPhO initiatives. I encourage you to participate in the CAPhO Annual General Meeting that is being held on Saturday from 12:00 to 13:00, the Town Hall meeting on Sunday from 8:30-9:45 or visit us at the CAPhO booth.

On behalf of the CAPhO Executive, we hope that you enjoy this educational event!

Carlo DeAngelis
CAPhO President / Président de l’ACPhO
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Welcome Message from NOPS 2011 Chair

On behalf of the Planning Committee, it is with great pleasure that we welcome you to the historic and charming city of Québec for the 2011 National Oncology Pharmacy Symposium (NOPS): Let’s Get Personal.

NOPS has become the premier annual symposium for pharmacy personnel involved in the oncology field. NOPS, along with its associated satellite symposia, provides the opportunity for pharmacy personnel to keep on top of all the latest developments. Oncology pharmacists and technicians from across the country have volunteered their time and expertise to help develop a conference program that we hope you will find both educational and practical. As in previous years, part of the program allows for concurrent sessions to take place focusing professional development in the areas of clinical, administrative as well as technical roles.

The NOPS 2011 Planning Committee is proud to announce two major innovations for this year: the first is making the program available on a USB stick and therefore taking a “greener” route; the second is having NOPS 2011 recognized and accredited by CCCEP and offering CAPhO members educational credits they deserve.

NOPS would not be possible without the generous support of our pharmaceutical sponsors, the dedication of the Planning Committee and support from the CAPhO Executive Committee. NOPS provides attendees with three days of quality education at an affordable registration price. This affordability is made possible as a result of generous sponsorship in partnership with the pharmaceutical industry. Pharmaceutical industry sponsors along with other key stakeholders will have booths within the exhibit hall. We encourage attendees to visit the sponsors’ booths to become familiar with their products as well as to learn about the educational material they may have to benefit your patients.

NOPS offers attendees an excellent opportunity for networking with colleagues from all around the country. It is a time for learning something new, for exchanging experiences with colleagues and discovering a beautiful Canadian city. We hope you enjoy your time in the city of Québec and at NOPS.

Cheers,

Gabriel Gazze

NOPS 2011 Chair
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Learn more at XGEVA.ca
C’ est avec grand plaisir que le comité organisateur vous accueille à la charmante et historique ville de Québec pour le Symposium National de Pharmacie en Oncologie (NOPS) 2011 : « Let’s get personal ».

Le NOPS est devenu la conférence annuelle principale pour le personnel impliqué dans le domaine de l’oncologie. Le NOPS et ses symposiums satellites permettent au personnel de pharmacie d’être à l’affût des nouveaux développements. Des pharmaciens et techniciens de tout le pays ont investi de leur temps et de leur expertise afin de bâtir un programme scientifique des plus éducatifs et pratiques. Ainsi que par le passé, une partie du programme se déroulera en sessions parallèles afin de mieux se concentrer sur le développement professionnel à un niveau clinique, administratif ou technique.

Le comité organisateur du NOPS 2011 est fier d’annoncer deux innovations majeures pour cette année : la première est de rendre disponible le programme du congrès sur une clé USB permettant de prendre un virage plutôt « vert »; le deuxième est l’accréditation du NOPS 2011 par le CCCEP et ainsi d’offrir aux membres de CAPhO les crédits de formation continue tant mérités.

Le NOPS ne serait pas ce qu’il est sans la précieuse et généreuse collaboration de nos commanditaires pharmaceutiques, le dévouement des membres du comité organisateur et du support du Comité Exécutif de CAPhO. Le NOPS donne aux participants trois journées d’éducation de haut calibre à un prix abordable. Ceci est possible grâce à la précieuse et généreuse collaboration de nos partenaires de l’industrie pharmaceutique. Les commanditaires de l’industrie pharmaceutique et autres organismes clés auront des kiosques d’exposition dans le hall d’exposition. Nous vous encourageons de visiter les kiosques de nos commanditaires, de devenir familier avec leurs produits et de prendre connaissance de leur matériel éducatif dont bénéficieront indirectement vos patients.

Le NOPS est une excellente opportunité pour rencontrer des collègues de tous les coins du pays. C’est un moment pour apprendre quelque chose de nouveau, d’échanger des expériences avec des collègues et de découvrir une très belle ville canadienne. Nous espérons que vous vous plairiez au NOPS dans la ville de Québec.

Santé!

Gabriel Gazze
Président du NOPS 2011
Patient Safety as it Relates to Cancer Patients
Carole R Chambers,
B.Sc.(Pharm) MBA AHS Pharmacy
Director, Cancer Services
Tom Baker Cancer Clinic Pharmacy
Calgary, Alberta

Anti-Cancer Effects of Low Molecular Weight Heparins
Dr Jacob Easaw,
MD, PhD, FRCP(C)
Clinical Associate Professor
Head, NeuroOncology
GI Oncology
Tom Baker Cancer Center
Calgary, Alberta

Please RSVP with your name, title and organization to: Tiffany Cameron-Lavoie via email to tiffany.lavoie@leo-pharma.com

Agenda & Learning Objectives:
9:15 am: Carole Chambers:
Understand the impact of venous thrombosis in the life of a cancer patient
Q&A

9:45 am: Dr Jacob Easaw
Understand the importance of venous thrombosis, and the key guidelines and clinical evidence related to the management of venous thrombosis in patients with cancer
Understand the link between thrombosis and cancer, and how anticoagulant therapy may impact angiogenesis and metastasis of tumours.
Q&A

Symposium Chair
Carlo De Angelis,
RPh, ACPR, Pharm.D
Clinical Pharmacy Coordinator
(Oncology)
Department of Pharmacy
Sunnybrook Health Sciences Centre
Sunnybrook Odette Cancer Centre

Supported by an unrestricted educational grant by LEO Pharma Inc.
The Canadian Association of Pharmacy in Oncology (CAPhO) is the national forum for oncology pharmacy practitioners and other health care professionals interested in oncology pharmacy.

CAPhO, a voluntary organization, promotes the practice of oncology pharmacy in Canada by conducting educational events, maintaining appropriate professional practice standards, facilitating communication between oncology pharmacists, technicians, pharmacy assistants and other interested health professionals, and developing oncology pharmacy as an area of specialty practice.

CAPhO Membership / Devenir membre de CAPhO

We invite you to join CAPhO as a member. Visit www.capho.org/members to learn more and to apply.

Why join? Besides being a member of an association that represents your professional interests, benefits from belonging to CAPhO include:

- The online Member Forum (a discussion page where you can participate in issue discussions, pose questions and provide answers)
- Continuing education opportunities
- A network of professionals to support you and advocate on your behalf
- Executive, Committee and Task Force positions
- An invitation to the National Oncology Pharmacy Symposium (NOPS) at a substantially discounted registration rate ($100 off if paid six months prior to the NOPS start date)
- The opportunity to participate in the CAPhO Awards and Grants Program.

Nous vous invitons à devenir membre de l’ACPhO. Visitez le site www.capho.org/members pour obtenir plus d’information sur les modalités d’adhésion.

Pourquoi devriez-vous vous joindre à notre association? L’ACPhO défend vos intérêts professionnels et vous offre :

- un forum des membres en ligne (une page où vous pouvez participer à des discussions, poser des questions et donner des réponses);
- des possibilités de formation professionnelle continue;
- un réseau de professionnels vous représentant et défendant vos droits;
- des postes au sein de l’équipe de direction, des comités et des équipes de travail;
- une invitation au Symposium National de Pharmacie en Oncologie (NOPS) à un tarif préférentiel (réduction de 100 $ si vous payez six mois avant la date de l’événement);
- la possibilité de participer au Programme de bourses et subventions de l’ACPhO
Roche Canada is a proud sponsor of the National Oncology Pharmacy Symposium 2011.

Roche Canada est fière de commanditer le Symposium national sur la pharmaco-oncologie 2011.
CAPhO Awards / Prix de l’ACPhO

Merit Award / Prix d’excellence

This award consists of a certificate and a cash award of $1,000 given to a practicing oncology pharmacist(s), pharmacy technician(s) and/or pharmacy assistant(s) and member(s) of CAPhO in recognition of a project/innovation in oncology pharmacy aimed at improving patient care and outcomes. Up to two awards may be granted. Many pharmacy departments have initiated exciting programs in their centres, and this award is aimed at recognizing them.

Ce prix, qui comprend un certificat d’excellence et une bourse de 1000 $, sera remis à un ou plusieurs praticiens et/ou techniciens de la pharmacie en oncologie membres de l’ACPhO en reconnaissance de leurs projets ou innovations visant à améliorer les soins aux patients et les résultats qui en ont dégénéré dans leur sphère d’activité. Deux prix pourront être attribués au besoin. De nombreuses équipes pharmaceutiques ont instauré des programmes intéressants dans leur établissement, et ce prix a pour but de les récompenser pour leurs initiatives.

Poster Awards / Prix pour les affiches

Three poster awards will be awarded in the categories of Research, Pharmacy Practice and Administration.

Trois prix seront décernés pour récompenser les concepteurs des affiches les plus réussies dans les catégories suivantes : recherche, pratique de la pharmacie et administration.
Thank you / Merci

To our CAPhO Executive / Aux membres de la direction de l’ACPhO

Carlo DeAngelis, President / Président
Jennifer Jupp, President-Elect / Présidente désignée
Dana Cole, Past President / Présidente sortante
Lori Emond, Treasurer / Trésorier

Carlo DeAngelis, Advocacy Committee Chair / Président du comité d’intervention
Victoria Kletas, Awards Committee Chair / Présidente du comité des prix

Christopher Ralph, Communications Committee Chair / Président du comité des communications
Rhonda Kayln, Education Co-Chair CEC / Coprésidente du comité de la formation
Biljana Spirovski, Education Co-Chair NOPS/Research / Coprésidente du comité de la formation, NOPS/recherche
Betty Riddell, Membership Committee Chair / Présidente du comité d’adhésion
Yvonne Dresen, Technician Committee Chair / Présidente du comité technique

To the NOPS Planning Committee Members / Aux membres du comité de planification du NOPS

Flay Charbonneau
Odette Cancer Centre, Toronto, ON

Melanie Fortin
Hôpital Saint-François d’Assise (CHUQ), Quebec, QC

Gabriel Gazze
Royal Victoria Hospital, Montreal, QC

Kathy Gesy
Saskatchewan Cancer Agency, Saskatoon, SK

Michelle Koberinski
Cancer Centre for the Southern Interior, Kelowna, BC

Coleen Schroeder
McGill University Health Center, Montreal, QC

Biljana Spirovski
Humber River Regional Hospital, Toronto, ON

Pat Trozzo
CancerCare Manitoba and University of Manitoba, Winnipeg, MB

Thanh Vu
Health Canada, Burnaby, BC

Julie Zwicker
Alberta Health Services, Edmonton, AB

Volunteers / Bénévoles

We would like to thank those who have volunteered their time to assist NOPS 2011 attendees and organizers. We really appreciate the assistance you provide to ensure attendees have everything they need to participate effectively in NOPS 2011.
This session will provide a review of clinical data for Lapatinib (Tykerb™) including the mechanism of action, efficacy, role in the treatment of HER-2 positive cancer patients, and adverse events. Strategies to prevent and treat common adverse events will be illustrated through case presentations, along with recommendations to optimize patient compliance.

Objectives:
To encourage increased counselling and support of patients during their treatment with Lapatinib through:
• Patient education for the prevention and management of adverse events
• Partnership with the patient while focusing on compliance.

Speaker:
Lucie Surprenant, B.Pharm., M.Sc., BCOP
Oncology Pharmacy Coordinator
Oncology Department
St. Mary’s Hospital Center
Montreal, Quebec

How to register:
Contact Cheryl Vandenbroucke at cvandenbroucke@scimedcan.com or 905.762.0772, ext 254.

Plan to Attend!
Helping Patients During Treatment With Lapatinib (Tykerb™)

À inscrire à votre agenda!
Aider les patients pendant le traitement par le Lapatinib (TykerbMC)
### Program at a Glance / Survol du programme

#### THURSDAY, NOVEMBER 3

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<td>SATellite Symposium</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>13:00 – 14:00</td>
<td>CAPHO ANNUAL GENERAL MEETING</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>14:00 – 14:40</td>
<td>BREAKOUT#1: TECHNICAL STREAM</td>
<td>(Place D'Armes, Ground Floor, North Wing)</td>
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<tr>
<td>14:40 – 15:20</td>
<td>BREAKOUT#2: PART 1 – CLINICAL STREAM</td>
<td>(Laval, Third Floor, North Wing)</td>
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<td>15:20 – 15:50</td>
<td>BREAKOUT#3: PART 2 – CLINICAL STREAM</td>
<td>(Laval, Third Floor, North Wing)</td>
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<tr>
<td>15:50 – 16:35</td>
<td>BREAKOUT#4</td>
<td>(Place D'Armes, Ground Floor, North Wing)</td>
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<tr>
<td>16:35 – 18:30</td>
<td>BREAKOUT#6</td>
<td>(Laval, Third Floor, North Wing)</td>
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<tr>
<td>19:00 – 22:30</td>
<td>DINNER &amp; ENTERTAINMENT</td>
<td>(Museum of Civilization)</td>
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#### FRIDAY, NOVEMBER 4

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<th>Time</th>
<th>Event</th>
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<tr>
<td>07:30 – 09:00</td>
<td>SATellite Symposium: Hoffmann – La Roche</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>09:15 – 10:45</td>
<td>SATellite Symposium: Leo-Pharma</td>
<td>(Jacques Cartier, Ground Floor, North Wing)</td>
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<tr>
<td>11:00 – 12:30</td>
<td>SATellite Symposium: Carmel Pharma</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>12:45 – 14:15</td>
<td>SATellite Symposium: Amgen Canada</td>
<td>(Jacques Cartier, Ground Floor, North Wing)</td>
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<tr>
<td>14:30 – 16:00</td>
<td>SATellite Symposium: Hospira</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>16:15 – 17:45</td>
<td>SATellite Symposium: Janssen</td>
<td>(Jacques Cartier, Ground Floor, North Wing)</td>
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<tr>
<td>18:00 – 19:30</td>
<td>SATellite Symposium: Celgene</td>
<td>(Frontenac, Second Floor)</td>
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#### SATURDAY, NOVEMBER 5

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<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>06:30 – 08:00</td>
<td>SATellite Symposium: Eli-Lilly</td>
<td>(Jacques Cartier, Ground Floor, North Wing)</td>
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<tr>
<td>07:30 – 08:15</td>
<td>CONTINENTAL BREAKFAST</td>
<td>(Exhibit Hall, Sal de Bal, Second Floor)</td>
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<tr>
<td>08:15 – 10:00</td>
<td>WELCOME AND PLENARY</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>10:00 – 10:30</td>
<td>COFFEE BREAK</td>
<td>(Exhibit Hall, Sal de Bal, Second Floor)</td>
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<tr>
<td>10:30 – 12:00</td>
<td>PLENARY</td>
<td>(Frontenac, Second Floor)</td>
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#### SUNDAY, NOVEMBER 6

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<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
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<tbody>
<tr>
<td>07:00 – 08:30</td>
<td>SATellite Symposium: BAXTER</td>
<td>(Place D'Armes, Ground Floor, North Wing)</td>
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<tr>
<td>08:00 – 08:30</td>
<td>CONTINENTAL BREAKFAST</td>
<td>(Exhibit Hall, Sal de Bal, Second Floor)</td>
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<tr>
<td>08:30 – 09:45</td>
<td>CAPHO TOWN HALL MEETING</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>09:45 – 10:15</td>
<td>ORAL SESSIONS – AWARD WINNING POSTERS</td>
<td>(Frontenac, Second Floor)</td>
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<tr>
<td>10:15 – 10:30</td>
<td>COFFEE BREAK</td>
<td>(Exhibit Hall, Sal de Bal, Second Floor)</td>
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<tr>
<td>10:30 – 12:30</td>
<td>PLENARY</td>
<td>(Frontenac, Second Floor)</td>
</tr>
<tr>
<td>12:30 – 12:40</td>
<td>CLOSING REMARKS</td>
<td>(Frontenac, Second Floor)</td>
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### Registration Hours / Horaire d’inscription

- **Thursday, November 3:** 17:00 to 19:00
- **Friday, November 4:** 07:00 to 18:00
- **Saturday, November 5:** 06:00 to 16:30
- **Sunday, November 6:** 07:00 to 12:30

### Exhibit & Poster Hall Hours / Heures d'ouverture de la salle d'affichage

- **Saturday, November 5:** 07:30 to 18:30
- **Sunday, November 6:** 07:30 to 10:30

### Presentations / Séances

Recorded presentations (voice and slides) are available at www.capho.org.

**Board the bus between 18:30 - 19:15 at Fairmont entrance and present your Dinner Event ticket as you board. Buses return between 21:30-22:45.**
We share your commitment to improving the lives of cancer patients and are proud to be a sponsor of the 2011 National Oncology Pharmacy Symposium.

Nous partageons votre engagement à améliorer la vie des patients et nous sommes fiers de commanditer le Symposium national de pharmaco-oncologie 2011.
NOPS 2011 is being held at the Fairmont Le Château Frontenac.
A: 1 rue des Carrières, Québec, Quebec, G1R 4P5
T: 1-418-692-3861
www.fairmont.com/frontenac

Hotel Floor Plan / Plan de l’hôtel

Ground Floor
North Wing

Second Floor

Third Floor
North Wing
Lilly Oncology is a proud sponsor of the National Oncology Pharmacy Symposium 2011

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NOPS 2011 Program / Programme du NOPS 2011

Thursday, November 3 / Le jeudi 3 novembre

18:30 – 20:00
Satellite Symposium (Frontenac, Second Floor)
HELPING PATIENTS DURING TREATMENT WITH LAPATINIB
Lucie Surprenant, Oncology Pharmacy Coordinator, St. Mary’s Hospital Centre, Montreal, QC

Friday, November 4 / Le vendredi 4 novembre

07:30 – 09:00
Satellite Symposium: HOFFMANN-LA ROCHE (Frontenac, Second Floor)
TARGETED THERAPIES AND PERSONALIZED HEALTHCARE IN ONCOLOGY:
IMPROVING OUR ABILITY TO TAILOR TREATMENTS FOR PATIENTS
Presenters:
Kathy Gesy, Provincial Leader, Oncology Pharmacy Services, Saskatchewan Cancer Centre
Teresa Petrella, Medical Oncologist, Odette Cancer Centre
Robert Delage, Hematologist, Head of the Centre Universitaire d’Hématologie et d’Oncologie de Québec CHA, Hôpital de l’Enfant-Jésu
Robert El-Maraghi, Simcoe Muskoka Regional Cancer Program

09:15 – 10:45
Satellite Symposium: LEO-PHARMA (Jacques Cartier, Ground Floor, North Wing)
Chair: Carlos de Angelis, Clinical Pharmacy Coordinator, Sunnybrook Odette Cancer Centre, Toronto, ON
PATIENT SAFETY AS IT RELATES TO CANCER PATIENTS
Presenter: Carole R Chambers, Director, Cancer Services, Tom Baker Cancer Clinic Pharmacy, Calgary, AB

11:00 – 12:30
Satellite Symposium: CARMEL PHARMA (Frontenac, Second Floor)
SAFETY AND COST: ARE THEY MUTUALLY EXCLUSIVE WITH CLOSED SYSTEM DRUG TRANSFER TECHNOLOGY?
Moderator: Flay Charbonneau, Manager, Pharmacy, Sunnybrook Odette Cancer Centre, Toronto, ON
Presenter: James A. Jorgenson, Vice President & Chief Pharmacy Officer, Indiana University Health, Indianapolis, IN

12:45 – 14:15
Satellite Symposium: AMGEN CANADA (Jacques Cartier, Ground Floor, North Wing)
ADVANCED CANCER: BONE-TARGETED THERAPY
Chair: Annick Dufour, Hopital Charles-LeMoyne, Greenfield Park, QC
Presenters:
Jean Dufresne, CHUS - Hopital Fleurimont, Sherbrooke, QC
Tom McFarlane, Cambridge Memorial Hospital, Cambridge, ON
14:30 – 16:00
Satellite Symposium: HOSPIRA (Frontenac, Second Floor)
UNDERSTANDING ONCOLOGY DRUG SUPPLY
Presenters:
Grace Breen, Vice-President Commercial Quality
Beryl Chan, Director, Scientific Affairs
Tina Dematos, Director, Operations

16:15 – 17:45
Satellite Symposium: JANSSEN (Jacques Cartier, Ground Floor, North Wing)
Chair: Rick Abbott, Regional Pharmacy Manager, Dr. H. Bliss Murphy Cancer Center, St. John’s, NL
OPTIMIZING TREATMENT AND OUTCOMES FOR MULTIPLE MYELOMA PATIENTS
Presenter: Dominique Duquette, Pharmacist, CHA-Hopital Enfant-Jesus, Quebec, QC
CASTRATION RESISTANT PROSTATE CANCER: CHANGING PARADIGMS
Presenter: Roanne Segal, Medical Oncologist, The Ottawa Hospital, Ottawa, ON

18:00 – 19:30
Satellite Symposium: CELGENE (Frontenac, Second Floor)
ALTERNATE CLINICAL ENDPOINTS IN A POST-BLOCKBUSTER ERA
Chair: Gabriel Gazze, Montreal, QC
Presenters:
George Dranitsaris, Toronto, ON
Francois Tardif, Regional Medical Liaison, Celgene

Saturday, November 5 / Le samedi 5 novembre

06:30 – 08:00
Satellite Symposium: ELI LILLY (Jacques Cartier, Ground Floor, North Wing)
ADVANCES IN THE MANAGEMENT OF NSCLC: THE CLINICAL REALITY FROM 3 PERSPECTIVES
Moderator: Biljana Spirovski, Clinical Pharmacist, Humber River Regional Hospital, Toronto, ON
Presenters:
Sunil Verma, Medical Oncologist, Sunnybrook Odette Cancer Center, Toronto, ON
Tom McFarlane, Clinical Pharmacist, Waterloo Wellington Regional Cancer Program, Waterloo, ON
Vikas Aggarwal, Drug Access Facilitator, William Osler Health System, Brampton, ON

07:30 – 08:15
Continental Breakfast (Exhibit Hall, Sal de Bal, Second Floor)

08:15 – 08:25
Plenary (Frontenac, Second Floor)
WELCOME AND INTRODUCTION
Presenter: Gabriel Gazze, NOPS 2011 Chair

08:30 – 09:15
Plenary (Frontenac, Second Floor)
HOPE FOR REIMBURSEMENT, REIMBURSEMENT FOR HOPE AND THE RELEVANCE OF THE ELEPHANTS
Presenter: Dr. Jeffrey S. Hoch
09:15 – 10:00
Plenary (Frontenac, Second Floor)
**ADOLESCENT AND YOUNG ADULT ONCOLOGY: THE CHALLENGE IN SERVING A UNIQUE, UNDERSERVED POPULATION**
Presenter: Dr. Petr Kavan, MUHC - Royal Victoria Hospital, Montreal, QC

10:00 – 10:30
Coffee Break (Exhibit Hall, Sal de Bal, Second Floor)

10:30 – 11:15
Plenary (Frontenac, Second Floor)
**BIOSIMILARS OF BIOLOGICAL DRUG THERAPIES: CURRENT STATUS AND FUTURE DIRECTIONS**
Presenter: George Dranitsaris, Consultant in Health Economics and Biostatistics, Toronto, ON

11:15 – 12:00
Plenary (Frontenac, Second Floor)
**MALIGNANT MELANOMA: RECENT DEVELOPMENTS AND CLINICAL IMPLICATIONS**
Presenter: Dr. Michael Smylie, Cross Cancer Institute, Edmonton, AB

12:00 – 13:00
CAPhO Annual General Meeting (Frontenac, Second Floor)

13:00 – 14:00
Lunch (Petit Frontenac/Bellevue & Rose, Second Floor)
Dessert (Exhibit Hall, Sal de Bal, Second Floor)

14:00 – 15:20 Breakout #1: Technical Stream (Place D’Armes, Ground Floor, North Wing)
14:00 – 14:40
PART 1: MEASURING SURFACE CHEMICAL CONTAMINATION – A SASKATCHEWAN CANCER AGENCY EXPERIENCE
Presenter: Colleen Thurber, Saskatoon Cancer Centre, Saskatoon, SK

14:40 – 15:20
PART 2: INVESTIGATIONAL PRODUCTS AND THE PHARMACY TECHNICIAN
Presenter: Katrina Alexandropoulos, University of Alberta Hospital Pharmacy Department, Edmonton, AB

14:00 – 15:20, Breakout #2: Clinical Stream (Frontenac, Second Floor)
14:00 – 14:40
PART 1: HAEMATOPOIETIC STEM CELL TRANSPLANTATION
Presenter: Yves Rousseau, MUHC - Royal Victoria Hospital, Montreal, QC

14:40 – 15:20
PART 2: AN UPDATE ON PROSTATE CANCER
Presenter: Victoria Kletas, BC Cancer Agency, Vancouver, BC
**NOPS 2011 Program / Programme du NOPS 2011**

14:00 – 15:20, Breakout #3: Administrative Stream *(Laval, Third Floor, North Wing)*

**14:00 – 14:40**  
**PART 1: UPDATE ON THE PAN-CANADIAN ONCOLOGY DRUG REVIEW**  
Presenter: Mona Sabharwal, pan-Canadian Oncology Drug Review, Toronto, ON

**14:40 – 15:20**  
**PART 2: HOW DO YOU MEASURE UP? NEW ACCREDITATION STANDARDS FOR AMBULATORY SYSTEMIC CANCER THERAPY CARE SERVICES**  
Presenters:  
Roxanne Dobish, Alberta Health Services, Edmonton, AB  
Stephanie Carpenter, Accreditation Canada

15:20 – 15:50  
Coffee Break *(Exhibit Hall, Sal de Bal, Second Floor)*

15:50 – 16:35  
**Breakout #4: HIGH GRADE GLIOMA - COMPLEXITIES AND OPPORTUNITIES** *(Place D'Armes, Ground Floor, North Wing)*  
Danica Lister, CancerCare Manitoba, Winnipeg, MB

15:35 – 16:35  
**Breakout #5: A PICTURE IS WORTH A THOUSAND WORDS: THE DEVELOPMENT OF AN ONCOLOGY PATIENT COMPLIANCE TOOL** *(Frontenac, Second Floor)*  
Presenter: Kelly Smith, London Health Sciences Centre, London, ON

15:50 – 16:35  
**Breakout #6: CANCER, CLOTS AND KIDS** *(Laval, Third Floor, North Wing)*  
Presenter: John Wiernikowski, McMaster Children’s Hospital, Hamilton, ON

16:35 – 18:30  
Exhibits and Posters Viewing Reception *(Exhibit Hall, Sal de Bal, Second Floor)*

19:00 – 22:30  
Dinner & Entertainment *(Musée de la civilisation)*
NOPS 2011 Program / Programme du NOPS 2011

Social Events / Événements sociaux

This year’s Saturday afternoon and evening events will provide great opportunities to network with old and new friends while enjoying the “Joie de vivre” of Quebec City.

16:35 – 18:30
Exhibits and Posters Viewing Reception (Sal de Bal, Fairmont Le Château Frontenac)
The Exhibits and Posters Viewing Reception will take place amongst the exhibits in Sal de Bal Ballroom, located on the second floor, starting at 4:35pm. Participation is included in your registration fee.

19:00 – 22:30
Dinner & Entertainment (Musée de la civilization)
The Dinner Event at the Musée de la civilization will delight the senses with a Quebec inspired evening highlighting Quebecois hospitality through culture, food and entertainment.

Upon arrival at the Musée de la civilization, you will have the opportunity to explore two exhibitions and then enjoy the culinary delights of a Québécois three course meal and authentic entertainment by the enchanting Painchaud Family Musical Quartet. Be prepared for an evening full of networking, entertainment and fun!

Board the bus between 18:30 - 19:15 at Fairmont entrance and present your Dinner Event ticket as you board. Buses return between 21:30-22:45.
NOPS 2011 Program / Programme du NOPS 2011

Sunday, November 6 / Le dimanche 6 novembre

07:00 – 08:30
Satellite Symposium: BAXTER (Place D'Armes, Ground Floor, North Wing)
A DEBATE OF DISCOVERY
Presenters:
Rick Abbott, Eastern Health Pharmacy Services, St. John’s NL
Carol R. Chambers, Alberta Health Services, Edmonton, AB
Flay Charbonneau, Odette Cancer Centre, Toronto, ON

08:00 – 08:30
Continental Breakfast (Exhibit Hall, Sal de Bal, Second Floor)

08:30 – 09:45
CAPHO Town Hall meeting (Frontenac, Second Floor)
YOU HAVE A VOICE – JOIN THE CAPHO EXECUTIVE FOR AN OPEN DISCUSSION ABOUT THE ASSOCIATION

09:45 – 10:15
Oral Sessions - Award Winning Posters (Frontenac, Second Floor)
CAPHO AWARD WINNING POSTERS IN THE THREE CATEGORIES: RESEARCH, PHARMACY PRACTICE AND ADMINISTRATION
Presenter: Victoria Kletas, Awards Committee Chair

10:15 – 10:30
Coffee Break (Exhibit Hall, Sal de Bal, Second Floor)

10:30 – 11:15
Plenary (Frontenac, Second Floor)
BIOMARKERS IN CANCER: SHOULD WE GET INVOLVED?
Presenter: Lucie Surprenant, St. Mary's Hospital Center, Montreal, QC

11:15 – 12:00
Plenary (Frontenac, Second Floor)
THERAPEUTIC DRUG MONITORING FOR TARGETED AGENTS IN ONCOLOGY PRACTICE: BACK TO THE FUTURE IN CLINICAL ONCOLOGY PHARMACY PRACTICE
Presenter: Carlo De Angelis, Sunnybrook Health Sciences Centre, Toronto, ON

12:00 – 12:30
Plenary (Frontenac, Second Floor)
PHARMACY RESEARCH BY "NON-RESEARCH" PHARMACISTS
Presenter: Mario de Lemos, BC Cancer Agency, Vancouver, BC

12:30 – 12:40
Plenary (Frontenac, Second Floor)
CLOSING REMARKS
Presenters:
Gabriel Gazzé, NOPS 2011 Chair
Kathy Gesy, NOPS 2012 Chair
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

**DR. JEFFREY S. HOCH**

Director, Pharmacoeconomics Research Unit, Cancer Care Ontario, Toronto

**BIOGRAPHY**

Jeffrey Hoch received his PhD in health economics from the Johns Hopkins School of Public Health. He also holds a Masters in Economics from Johns Hopkins University, and a Bachelor of Arts degree in Quantitative Economics and Decision Sciences from the University of California at San Diego. An award winning teacher, Dr Hoch has taught Health Economics and Economic Evaluation classes in Canada, the United States and internationally. In 2007, he was asked to develop and direct the Pharmacoeconomics Research Unit at Cancer Care Ontario. As Director of the unit, Dr Hoch has pursued research making health economics more useful to decision makers. Special interests include health services research related to cancer, mental health, and other health issues affecting poor and vulnerable populations.

**SYNOPSIS**

**HOPE FOR REIMBURSEMENT, REIMBURSEMENT FOR HOPE AND THE RELEVANCE OF THE ELEPHANTS**

*Saturday, November 5th, 08:30 – 09:15 • Frontenac, Second Floor*

**Learning Objectives**

1. Recognize the implications of scarcity and define the concept of opportunity cost;
2. Explain the mathematics behind why cancer drugs are becoming less cost-effective;
3. Describe why Canada’s drug funding arrangements facilitate heterogeneous drug funding decisions.

In their article, “Access to Cancer Drugs in Canada: Looking Beyond Coverage Decisions” Chafe and colleagues note that given the high cost of many cancer drugs, patients in Canada often are forced to rely on publicly funded drug programs in order to obtain care. These programs are independently run by the provinces, with each provincial government determining the structure and eligibility requirements for its own programs. These programs also independently decide which drugs will be eligible for public coverage in each province. This situation can result in cancer patients in different provinces having differential access to care. Previous studies examining variation in access to cancer drugs have found considerable variation in public coverage both for specific drugs and within the categories of drugs covered for various populations. This talk will introduce health economics concepts like scarcity, opportunity cost and cost-effectiveness to provide an additional perspective yielding new insights about cancer drug funding in Canada.
Please join us at the Baxter Corporation Symposium for an interactive debate with a panel of delegates from across the country to discuss topics relating to LEAN process options for efficiency, as well as the impact of IV and Oral Chemotherapy treatments on Pharmacy practices.

**SPEAKERS**

<table>
<thead>
<tr>
<th>RICK ABBOTT</th>
<th>CAROLE R. CHAMBERS</th>
<th>FLAY CHARBONNEAU</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.Sc (Pharm)</td>
<td>B.Sc (PHARM), MBA</td>
<td>B.Sc (PHARM), MBA</td>
</tr>
<tr>
<td>Eastern Health Pharmacy Services</td>
<td>Alberta Health Services</td>
<td>Odette Cancer Centre</td>
</tr>
</tbody>
</table>
**DR. PETR KAVAN**

Medical Oncologist, MUHC - Royal Victoria Hospital, Montreal

**BIOGRAPHY**

Dr. Kavan did his medical and oncology training at Charles University in Prague, Czech Republic, before doing his fellowship at the Texas Children's Cancer Center, Baylor College of Medicine, Houston, USA, and St. Jude's Children's Hospital, Memphis, USA. His clinical specialties include medical and paediatric oncology with bone marrow transplant, and neuro-oncology. New therapeutics introduction and treatment algorithms are the main area of his research interest as well as Brain, Colorectal and Gastro-Intestinal Cancers.

He is currently the director of the Adolescent and Young Adult Oncology program at McGill University in Montreal, Quebec. The AYA team received the Hope Award for having made a significant difference to young adults living with cancer, and the groups’ contributions to the community to inspire hope. He represents McGill at the NCIC and he is author of over 90 publications and over 100 invited lectures.

**SYNOPSIS**

**ADOLESCENT AND YOUNG ADULT ONCOLOGY: THE CHALLENGE IN SERVING A UNIQUE, UNDERSERVED POPULATION**

*Saturday, November 5th, 09:15 – 10:00 • Frontenac, Second Floor*

Progress in paediatric oncology has been among the most dramatic advances in the history of medicine. In contrast, survival rates for adolescents and young adults (AYA) with cancer have plateaued since the late seventies. Reasons for this are not fully understood and include lack of understanding of age specific tumour biology and host/tumour physiology, lack of specific clinical trials with overall poor enrolment into clinical trials, frequent loss to follow-up and insufficient registration data. In 2003, McGill University created an AYA oncology program, with a corresponding patient registry, to address these issues, and after five years in existence we report increased enrolment into clinical trials (including AYA specific trials) along with reduced loss to follow-up. The program has also facilitated tumour banking and the implementation of crucial psychosocial services required by this population. Ongoing challenges that likely affect similar programs being established, and to which we propose possible solutions, are the need to increase awareness about the unique therapeutic and psychosocial needs of this population as well as increase the number of available clinical trials and finally increase the number of referrals. As was done for pediatric oncology, improved outcomes in the AYA population will likely require a centralization of AYA oncology programs with national and international cooperation.
GEORGE DRANITSARIS
Consultant in Health Economics and Biostatistics, Toronto, ON

BIOGRAPHY
George Dranitsaris is an oncology pharmacist with graduate training in biostatistics, pharmaco economics, decision analysis and clinical epidemiology and is currently doing a PhD in health economics. His current areas of interest include the measurement of cost effective drug use in the oncology setting, cancer supportive care research and the application of statistical modeling techniques for evaluating drug performance outside of the trial setting. He has over 90 publications in the national and international literature, is past president of the Canadian Association of Pharmacy in Oncology, a statistical reviewer for the Journal of Clinical Oncology and a member of the editorial board of the Journal of Oncology Pharmacy Practice, Oncology Exchange and the European Journal of Hospital Pharmacy Science.

SYNOPSIS
BIOSIMILARS OF BIOLOGICAL DRUG THERAPIES: CURRENT STATUS AND FUTURE DIRECTIONS
Saturday, November 5th, 10:30 – 11:15 • Frontenac, Second Floor

Biologics are distinct from small molecule drugs in that they are larger, more structurally complex agents. While the overall risk is modest, the active protein structure characteristic of biologics makes them more prone to induce an acute and/or chronic immune response. Biosimilars are a new class of drugs intended to offer comparable safety and efficacy to the reference, off-patent biological. They are not generic alternatives per se and are generally not interchangeable. Given their structural complexity, multifaceted manufacturing process and risk for immunogenicity, unique regulatory pathways are required for biosimilars. In this presentation, the clinical, safety and submission requirements for biosimilars in several major markets will be reviewed. I will also highlight issues of ongoing debate amongst key stakeholders and examine some of the commercial challenges faced by developers of biosimilars. As the leader of biosimilars drug approval and product uptake, the European Union will be highlighted.

Learning Objectives:
• To understand the manufacturing, pharmacodynamic and pharmacological differences between small molecules and biological therapies.
• To introduce biosimilars in the context of oncology pharmacy practices.
• To review the preclinical and clinical requirements for biosimilars drug approval.
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BIOSIMILARS OF PROTEIN BASED DRUGS: CURRENT STATUS AND FUTURE DIRECTIONS

George Dranitsaris B.Pharm. PhD
Oncology Product Consultant

OVERVIEW OF PRESENTATION

- Present working definitions of biosimilars
- Discuss the manufacturing process of protein based drugs
- Review the current regulatory status of biosimilars in Canada and around the world
- Discuss clinical trial design issues related to biosimilars
- Address health policy issues and clinical considerations related to biosimilars

DISCLAIMER

No Conflicts of Interest

What is a Biosimilar?

- Protein based drugs are made by living organisms.
- Recombinant technology has allowed the commercialization of protein-based or biological drug therapies.
- So a biosimilar is a protein based therapy that is biologically and clinically comparable to an innovator product.
- However, they are NOT generic copies of the original product.
- In Canada and the U.S., biosimilars are called “Subsequent Entry Biologics (SEB)” and “Follow on Biologics” respectively.

R&D Efforts are Shifting Towards Biologics

Products Receiving FDA Approval: 1993 to 2004

Source: IMS Data, Dec 2009

The Share of the Pharma Pipeline due to Biologics

Source: IMD Data, Dec 2009
Why have Biosimilars generated so much interest?

- In 2009, global sales of biologicals were approximately $130 billion (Kueppers, 2010).
- The patent expiration of the first generation biologicals has led to the development of alternative versions of these original products.
- By 2014, the global biosimilars market is expected to reach $19.4 billion.

The biosimilars market has huge growth potential

- By 2016, another $25 billion worth of biologicals will be going off patent.
- Therefore, several large generic and brand companies have gone into the biosimilars arena.
- These include Teva, Sandoz, Hospira, Mylan, Merck and Pfizer.

Making a Protein Based Drug is Complex

Adopted from Gottlieb, 2008

Why are Biosimilars NOT Generics of Existing Biologicals

- Traditional generic drugs are exact copies of existing drugs.
- However, biosimilars are much bigger than a typical generic copy of a small molecule.
- Biologicals are also made up of amino acids, which form unique folds and glycosylation patterns may also vary.
- Therefore, they are much more complex.
- Combined with the complicated manufacturing process, an exact copy of a biological cannot be made.
Biosimilars: The Goal is Clinical Interchangeability

Chemistry, manufacturing and quality control
- Chemical, biological characteristics and purity must be compared to the reference product.
- Experience from brand companies is that glycosylation patterns are also affected by the manufacturing process.
- Since biosimilar companies do not have access to proprietary data from the brand company, how will they be able to measure the product quality attributes?
- Hence, biosimilar companies will need to establish a quality control strategy with data generated from their own product.

Red Cell Aplasia (RCA): The Epoetin Alfa Story

- In the 1990s, RCA were reported patients who were receiving treatment with SQ epoetin alfa.
- After an intensive investigation, the most likely cause of the RCA was a formulation change, which led to antibody formation against all circulating erythropoietin.
- IRCA cases increased dramatically after the removal of human serum albumin from the formulation and its replacement with polysorbate 80 as a stabilizer.
- In the end, it was found that organic compounds leached from uncoated rubber stoppers in prefilled syringes for SC injection if the formulation contained polysorbate 80.

Biosimilars: Non-Clinical Studies

- Non-clinical pharmacology studies and in vitro potency relative to the reference product must be demonstrated.
- Pharmacokinetics: Equivalence in PK parameters in a relevant animal model must be demonstrated.
- Lack of meaningful differences in toxicology studies need to be demonstrated in animal models relative to the reference product.

Biosimilars: Clinical Considerations

- What types and how many studies should be conducted?
- What should the primary endpoint be in such trials; a surrogate endpoint, a drug activity signal or patient benefit?
- In the case of oncology, should it be RR, PFS or OS?
- Can the results from one disease site be extrapolated to another?
- As an illustration, Remicade and Enbrel are both anti-TNF biologicals approved for use in RA. However, Enbrel is not active in Crohn’s disease.

Equivalence Margins: How similar is similar enough?

- Clinical equivalence (not non-inferiority) trials must be undertaken for a biosimilar relative to the brand product.
- The European Medicines Agency (EMA) is the most advanced in providing guidance on clinical trials but they stop short at providing precise equivalence margins.
- Equivalence margins vary by product class and depend on what difference in outcome is considered clinically meaningful.
- This is called the MCID or “Minimally Clinically Important Difference”.
- E.G. For the biosimilar interferon alfa, the MCID for response was ±15%.
- For the biosimilar of filgrastim, the MCID was ± 1 day of severe neutropenia following chemotherapy.

Immunogenicity Concerns

- This is the ability of a substance to induce an immune response.
- Many factors can cause such reactions, but the tendency to form aggregates is one of the most common, since these may structurally simulate a viral particle.
- Given these risks and the small patient safety and efficacy database, the EMA requires a rigorous pharmacovigilance program post-approval.
Patent and Data Protection Issues

- The intent of a patent is to allow the innovator to recoup their investment and make a profit.
- In addition to the actual molecular structure, the manufacturing process of a biological is also patented.
- Hence, the brand company is under no obligation to disclose their manufacturing process to regulatory authorities who are evaluating a biosimilar drug submission.
- It is also possible that the therapeutic quality of the product may be linked to the manufacturing process.
- So how can comparability in manufacturing and quality control be determined?

The Biosimilar Approval Process in Europe

Biosimilars Approved in Europe

<table>
<thead>
<tr>
<th>Biologic</th>
<th>Indications Tested</th>
<th>Total Num Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPO</td>
<td>3</td>
<td>1,978</td>
</tr>
<tr>
<td>Binocrit (Sandoz)</td>
<td>2</td>
<td>826</td>
</tr>
<tr>
<td>hGH</td>
<td>2</td>
<td>871</td>
</tr>
<tr>
<td>Nutropin (Genentech)</td>
<td>1</td>
<td>242</td>
</tr>
<tr>
<td>Valtropin (Biopartners)</td>
<td>1</td>
<td>164</td>
</tr>
<tr>
<td>G-CSF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retacrit (Hospira)</td>
<td>1</td>
<td>371</td>
</tr>
<tr>
<td>Zarzio (Sandoz)</td>
<td>1</td>
<td>316</td>
</tr>
<tr>
<td>Ralaglastim (Ratiopharm)</td>
<td>3</td>
<td>877</td>
</tr>
</tbody>
</table>

Ref: EU public assessment reports

Randomized Trial of Biosimilar G-CSF (Zarzio) in Breast Cancer (Gascon, 2009)
What risks are biosimilar developers facing?

- A large investment is required: a biosimilar G-CSF = $150 million; a monoclonal antibody = $500 million.
- Therefore, how much of a discount could be offered relative to the brand product?
- A large well trained sales force would also be needed. For an oncology product in the U.S., the estimate is 250 reps (Malecki, 2010).

Biosimilars Drug Development is Costly and High Risk

- A well designed pharmacovigilance program post launch is required.
- Market prospects are also uncertain. What will be the rate of biosimilar uptake? Need to build physician comfort with biosimilars.
- Brand companies will also fight hard to protect market share: Brand loyalties, 2nd generation products (e.g. T-DM1) and lobby regulatory agencies to set high hurdles.

What kind of data do physicians want to see?

Physicians were asked to indicate the level of clinical trial data they require to begin prescribing biosimilars.

- Efficacy relative to reference drug
- Head-to-head studies
- Immunogenicity
- Pre-marketing safety

Market Penetration in Europe

In Europe, biosimilars cost up to 30% less than the branded products

Substitution Practices in Europe

- UK: Substitution of biosimilars for reference product not permitted.
- Germany: Branded biologicals cannot be automatically substituted.
- Spain: Has created an official list of non-substitutable drugs; biologicals are included.
- Italy: Automatic substitution of injectable biologicals not permitted.
- France: Automatic substitution of biologicals prohibited.

Global Biosimilar Regulation

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Europe</th>
<th>US</th>
<th>Canada</th>
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<tbody>
<tr>
<td>Reference product</td>
<td>Local</td>
<td>Local</td>
<td>Local preferred</td>
</tr>
<tr>
<td>Full quality dossier</td>
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<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>PK &amp; PD data</td>
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<td>yes</td>
<td>yes</td>
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<tr>
<td>Efficacy in one indication only</td>
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<td>Possibly</td>
<td>Possibly</td>
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<tr>
<td>Comparable safety</td>
<td>yes</td>
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<tr>
<td>Extrapolation</td>
<td>Acceptable</td>
<td>Possibly</td>
<td>Possibly</td>
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<tr>
<td>Pharmacovigilance program</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>
The Current Situation in Canada

- In 2008, Health Canada (HC) issued draft guidelines for stakeholder comment.
- The main stakeholder concerns were related to IP protection, the reference product used and interchangeability.
- This was followed by the 2010 release of a final guidance document.
- Unlike generic drugs, biosimilars or SEBs are approved using the “New Drug Submission” pathway.
- Unlike generic drugs, a SEB is not declared bioequivalent to the reference drug.
- An SEB cannot be automatically substituted for its reference drug and will always require a clinical trial prior to HC approval.

Biosimilars in Canada: Future Possibilities

- HC may continue to use the “New Drug Submission (NDS)” pathway.
- HC may allow biosimilars to file via the “Abbreviated New Drug Submission” pathway, just like generics are.
- Allow filing a full NDS submission where a direct comparison to the innovator drug has not been made, but sufficient safety and efficacy data has been provided.
- HC may develop stand along regulations for biosimilars.

Where are the provinces with respect to Biosimilars?

- There is no standardized approach to assess biosimilars in the provinces.
- In the short term, it is unlikely that interchangeability will be permitted.
- The provinces are also seeking guidance from HC and CADTH.
- Educational programs around biosimilars will be critical to shape future thinking/policy.

Omnitrope: A Canadian Example

- Omnitrope is a biosimilar to Genotropin, a branded biological human growth hormone.
- The efficacy of Omnitrope was compared to Genotropin in a 4 arm trial involving 89 children.
- No clinical data was provided for the adult indication.
- 57% and 2% of Omnitrope and Genotropin patients developed antibodies against the growth hormone.
- In addition, hypothyroidism was almost 4 times more common with Omnitrope.

CEDAC Advice for Omnitrope

CEDAC Final Advice – Subsequent Entry Biologic

SOMATROPIN
(Omenitrope – Sandzor Canada Inc.)
Indication: Growth Hormone Deficiency in Adults and Children

Advice:
The Canadian Expert Drug Advisory Committee’s (CEDAC) advice on Omnitrope is that the drug plan consider a similar reimbursement policy for Omnitrope as for other growth hormone products.
Conclusions

- Biosimilars represent a high risk undertaking, but given the market size, companies will continue to develop these products.
- Eventually, the regulatory pathways will be streamlined and development costs will become lower, which will reduce the risk of biosimilar drug development.
- Cost constraints will also make biosimilars attractive to drug formulary committees.
- Hence, oncology pharmacists will need to have a good understanding of biosimilars in order to safely incorporate them into our practice.

Thank you
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

**DR. MICHAEL SMYLIE**  
Medical Oncologist, Cross Cancer Institute, Edmonton, AB

**BIOGRAPHY**

Dr. Michael Smylie is a Medical Oncologist at the Cross Cancer Institute in Edmonton, Alberta. He holds an academic appointment as a Professor in the Department of Oncology at the University of Alberta. He is the past Site Leader for the Clinical Trials Committee and the past site Leader of the National Canada Institute of Cancer (NCIC). He is very active in designing and participating in clinical trials in malignant melanoma. His other interest includes lung cancer. His major research is targeted therapy and new drug development in metastasis melanoma. He has chaired several National Melanoma meetings and is the current chair of the Canadian National Melanoma Meeting in Canada.

**SYNOPSIS**

**MALIGNANT MELANOMA: RECENT DEVELOPMENTS AND CLINICAL IMPLICATIONS**  
Saturday, November 5th, 11:15 – 12:00 • Frontencac, Second Floor

The incidence of malignant melanoma has been increasing faster than any other cancer, except for lung cancer in women. If the current trends continue, it is now estimated that by 2015, roughly 1 in 50 Caucasians born in the United States will develop melanoma in their lifetime. Although the vast majority of patients present with early stage disease that is often cured by surgery, for those who either present with advanced disease, or develop recurrent disease, the prognosis remains poor. Although malignant melanoma was first described as a disease entity by Rene Laennec in 1804, it was not until 1975 that the FDA approved Dacarbazine for the treatment of metastatic melanoma. Dacarbazine was approved after Phase II showed response rates of 15-20%, however when Dacarbazine was used as the control arm in larger studies in the 1990's, the response rates consistently fell and now are closer to 7-10%. In fact, if Dacarbazine was submitted to either the FDA or Health Canada today, it would likely not be approved for the treatment of metastatic melanoma. Despite the poor response rates, it wasn't until 2011 that any drug was shown to be superior to single agent Dacarbazine in randomized controlled studies. In 2010, the first positive study in metastatic melanoma, looking at a novel immune agent called Ipilimumab was shown to be superior when compared to a control arm of GP100 vaccine in both survival and response rates. In 2011, a follow-up first line Ipilimumab registration trial that looked at Dacarbazine plus Ipilimumab versus Dacarbazine plus placebo showed a statistically improved benefit in overall survival, and an improvement in one, two and three year survivals in the Ipilimumab arms. This study led to the approval of Ipilimumab by the FDA and approval by Health Canada is pending.

The molecular changes involved in the transformation of a benign melanocyte to a malignant melanoma cell are being elucidated. Work out of Boris Bastian's laboratory led to a landmark paper by Leslie Fecher et al, showing that melanoma could be classified into 4 molecular subtypes. Each subtype had specific mutations that were key to the development of melanoma. In particular in about 50% of all melanoma patients, there is a specific mutation in the MAPKinase pathway affecting the Braf gene. This is typically a V600E mutation. A selective inhibitor of the mutated V600E Braf gene called vemurafenib was superior in both overall survival and time to tumor progression when compared in a randomized study to single agent Dacarbazine. The median duration of response was approximately 6 months and resistance is largely due to up regulation of other receptor kinases or through activation of Craf. Several Phase I and II studies are currently looking at dual

continued...
pathway blockade in BRAF resistant patients. Acral lentiginous melanoma, mucosal melanoma, and melanoma associated with chronic sun damage have a high incidence of C-Kit mutations. Trials are currently ongoing to test C-kit inhibitors in patients with C-Kit mutations.

In summary the molecular pathways to melanoma development are being elucidated and targeted therapies are showing promise with high response rates, and improved overall survival and progression free survival. Likewise greater understanding of the immune system has lead to the approval of the CTLA-4 antibody called Ipilimumab. Other monoclonal antibodies such as PD-1 are also being evaluated in the treatment of metastatic melanoma. These new treatments are associated with unique toxicities and health care professionals involved in the treatment of metastatic melanoma will encounter a unique set of novel toxicities. This will also require a good understanding of the treatment algorithms to manage these toxicities.
**Malignant Melanoma: Recent Developments and Clinical Indications**

Michael Smylie
Quebec City November 2011

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**Disclosures**

- ASCO support BMS 2010
- International Advisory Panel for Ipilimumab development
- Honoraria BMS
- Honoraria Roche

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**Lifetime Risk of Developing Melanoma**

![Graph showing lifetime risk of melanoma](image)

*US statistics

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**Sunbathing 1890**

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**What does this woman have to do with Malignant Melanoma?**

---

**And this Man?**

---
Metastatic Melanoma: 2009

- Rapidly rising global incidence
- Young age at onset
- Poor prognosis, limited therapeutic options
  - 1-year survival ~25%; 2-year survival ~10%
- No approved therapies for pretreated pts
- No randomized clinical trial has ever demonstrated survival benefit


Landmark Meta-analysis: Overall Survival (OS) in Metastatic Stage IV Melanoma

- Median OS 6.2 months (95% CI, 5.9-6.5 months)
- 25.5% alive at 1 year (95% CI, 23.8%-27.4%)
- Only 10% alive at 24 months

Survival data from 42 Phase II trials with over 2,100 stage IV patients

Options for the Management of Metastatic Melanoma

**Available Options**
- Surgery
- Immunotherapy
- Chemotherapy
- Supportive care

There has been little improvement in treatment options in the past 30 years.

**There is Currently No Standard of Care for Unresectable Metastatic Melanoma**

NCCN recommends entering a clinical trial as the only standard of care for patients with metastatic melanoma. NCCN Clinical Practice Guidelines in Oncology. Melanoma version 2. 2011.

**Evolution of Therapies Over the Past Decades**

<table>
<thead>
<tr>
<th>Canadian Approvals</th>
<th>FDA Approvals</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTIC</td>
<td>Ipilimumab</td>
</tr>
<tr>
<td>1975</td>
<td>2011</td>
</tr>
<tr>
<td>IL-2</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td></td>
</tr>
<tr>
<td>IFN-a</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
</tr>
<tr>
<td>Temozolamide</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel plus Carboplatin Immunotherapy</td>
<td></td>
</tr>
<tr>
<td>Interleukin-2 (IL-2) – high dose</td>
<td></td>
</tr>
<tr>
<td>Chemo-immunotherapy (Biochemotherapy)</td>
<td></td>
</tr>
</tbody>
</table>

Current Therapies for Metastatic Melanoma

- Cytotoxic chemotherapy
  - Dacarbazine (DTIC)
  - Temozolamide
  - Paclitaxel plus Carboplatin Immunotherapy
  - Interleukin-2 (IL-2) – high dose
  - Chemo-immunotherapy (Biochemotherapy)

Melanoma is inherently resistant to standard chemotherapeutic approaches.

Neither immunotherapy with cytokines, nor chemo-immunotherapy have demonstrated consistent overall survival in clinical trials.

Current Therapies for Metastatic Melanoma

- Cytotoxic chemotherapy
- Immunotherapy
- Supportive care
- Surgery
- Chemotherapy

There is Currently No Standard of Care for Unresectable Metastatic Melanoma

NCCN recommends entering a clinical trial as the only standard of care for patients with metastatic melanoma. NCCN Clinical Practice Guidelines in Oncology. Melanoma version 2. 2011.

**Summary of Shortcomings of Current Therapies for Metastatic Melanoma**

- Low response rates
  - 7.5-15%
- Low grade of response
  - <5% complete response
- Low survival rates
  - <2% at six years
- Poor tolerability
- Hematologic and non-hematologic toxicities are common

**Novel Immune Therapy for Unresectable and Metastatic Melanoma**

- CTLA-4
- PD-1

Ipilimumab is approved for adjuvant therapy in the U.S. & Canada. It is however not commonly used in clinical practice.
Ipilimumab: Mechanism of Action

- **Mechanism of Action of CTLA-4:**
  - The Brake on T-cell Activation

  **Ipilimumab is a fully human monoclonal antibody that blocks the CTLA-4 receptor on activated T cells.**

  - Blocks CTLA-4 signaling:
    - Prolongs T-cell activation,
    - Restores T-cell proliferation,
    - Amplifies T-cell-mediated immunity, and
    - Enhances the patient’s capacity to mount an anti-tumour immune response.

  **Mechanism-based side effects**
  - Immune-related Adverse Events (irAEs)
  - Onset predominantly in first 12 weeks
  - Management with vigilant follow-up and early steroids required

  **Ipilimumab in Treatment of Cancer**
  - Down-regulates T-cell activation

  **Ipilimumab**
  - Fully human monoclonal antibody
  - Blocks CTLA-4 receptor
  - Potentiates T cell activation

**Ipilimumab in Treatment of Cancer**

**Ipilimumab: Phase II Experience**

- Ipilimumab monotherapy
  - 20–30% durable disease control and 2-year survival

- Mechanism-based side effects
  - Immune-related Adverse Events (irAEs)
  - Onset predominantly in first 12 weeks
  - Management with vigilant follow-up and early steroids required

**Ipilimumab: Phase II Experience**

**Ipilimumab in Treatment of Cancer**

**Ipilimumab: Phase II Experience**

**Ipilimumab in Treatment of Cancer**

**Ipilimumab: Phase II Experience**

**Ipilimumab in Treatment of Cancer**
**MDX010-20: Study Design Details**

- **Accrual:** September 2004 – July, 2008
- **125 Centers in 13 Countries**
- **Randomized (3:1:1), Double-Blind**
- **Stratified for M Stage and prior IL-2**
- **Induction**
  - Ipilimumab: 3 mg/kg q 3 weeks X 4 doses
  - gp100: 1mg q 3 weeks X 4 doses
- **Re-induction (same regimen) in eligible patients**

**Statistical Considerations**

- **Primary Endpoint**
  - Original: BORR (N=750)
  - Changed to OS (Jan. 2009) before unblinding
- **Primary Comparison**
  - Ipilimumab + gp100 vs gp100 (3:1)
  - 385 events required
  - 90% power to detect: 10.8 vs 8.6 months OS
- **Secondary Comparison**
  - Ipilimumab vs gp100 (1:1)
  - 219 observed events
  - 80% power

**Kaplan-Meier Analysis of Survival**

"FIRST TIME EVER"

<table>
<thead>
<tr>
<th>Comparison</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arms A vs. C</td>
<td>0.68</td>
<td>0.004</td>
</tr>
<tr>
<td>Arms B vs. C</td>
<td>0.66</td>
<td>0.026</td>
</tr>
</tbody>
</table>

**Ipilimumab Improves Best Objective Response Rate**

<table>
<thead>
<tr>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
</tr>
</thead>
<tbody>
<tr>
<td>ipi + gp100</td>
<td>ipi + pbo</td>
<td>gp100 + pbo</td>
</tr>
<tr>
<td>N=403</td>
<td>N=137</td>
<td>N=136</td>
</tr>
<tr>
<td><strong>BORR, %</strong></td>
<td><strong>P-value: A vs C</strong></td>
<td><strong>P-value: B vs C</strong></td>
</tr>
<tr>
<td>5.7</td>
<td>0.043</td>
<td>10.9</td>
</tr>
<tr>
<td>1.5</td>
<td></td>
<td>0.0012</td>
</tr>
<tr>
<td><strong>DOR, %</strong></td>
<td><strong>P-value: A vs C</strong></td>
<td><strong>P-value: B vs C</strong></td>
</tr>
<tr>
<td>20.1</td>
<td>0.0079</td>
<td>28.5</td>
</tr>
<tr>
<td>11.8</td>
<td></td>
<td>11.0</td>
</tr>
</tbody>
</table>

*Across entire study duration

**Most Common Immune-Related Adverse Events* (irAEs; All Grades)**

<table>
<thead>
<tr>
<th>irAE</th>
<th>ipi + gp100 N=403</th>
<th>ipi + pbo N=137</th>
<th>gp100 + pbo N=136</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All grades</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>58.2</td>
<td>61.1</td>
<td>31.8</td>
</tr>
<tr>
<td><strong>Dermatologic</strong></td>
<td>40.0</td>
<td>43.5</td>
<td>16.7</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td>32.1</td>
<td>29.0</td>
<td>14.4</td>
</tr>
<tr>
<td><strong>Endocrine</strong></td>
<td>3.9</td>
<td>7.6</td>
<td>1.5</td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td>2.1</td>
<td>3.8</td>
<td>4.5</td>
</tr>
</tbody>
</table>

*Across entire study duration

---

**Dr. Michael Smylie | Presentation Handouts pg5**
Most Common Immune-Related Adverse Events* (Grades 3, 4 and 5)

<table>
<thead>
<tr>
<th>% of Patients</th>
<th>Any</th>
<th>Dermatologic</th>
<th>GI</th>
<th>Endocrine</th>
<th>Hepatic</th>
<th>Death due to irAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=380</td>
<td>9.2</td>
<td>0.3</td>
<td>0</td>
<td>1.1</td>
<td>0</td>
<td>1.5</td>
</tr>
<tr>
<td>N=131</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>N=132</td>
<td>1.5</td>
<td>0.6</td>
<td>0</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Summary of MDX010-20 Data

- First randomized phase III trial to show survival improvement in metastatic melanoma (HR=0.66, 0.68)
- Superior OS in two independent comparisons of ipilimumab vs gp100
- Survival rates in the ipilimumab arms
  - 1 year: 44%, 46%
  - 2 years: 22%, 24%
- Consistent superiority of ipilimumab for all secondary efficacy endpoints
  - PFS, BORR, DCR

New Patterns of Response

- Conventional responses
  - Response in baseline lesions
  - “Stable disease” with slow, steady decline in total tumor burden
- New patterns of responses:
  - Response after initial increase in total tumor burden
  - Response in index and new lesions after the appearance of new lesions

Example of Evolution of Response to CTLA-4 Inhibitor

Near Complete Resolution of Innumerable Liver Metastasis with Ipilimumab

- Response to ipilimumab therapy in patient with melanoma metastases to the liver, kidney, and mesenteric lymph nodes
- Treatment with ipilimumab resulted in a gradual, near complete resolution of all measurable liver metastases
- Lymphocyte recovery was consistent with immune reconstitution reflective of decreasing tumor burden with ipilimumab treatment

Pivotal Phase 3 Study of First-line Ipilimumab in Unresectable and Metastatic Melanoma

- MDX-024
* naive patients with metastatic melanoma (N=502)

** Placebo

| Q3W: every 3 weeks, Q12W: every 12 weeks, R: randomized |

---

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo + Dacarbazine</th>
<th>Ipilimumab + Dacarbazine (n=250)</th>
<th>Ipilimumab + Dacarbazine (n=252)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SURVIVAL, MONTHS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median overall survival, months</td>
<td>9.1</td>
<td>11.2</td>
<td>9.1</td>
</tr>
<tr>
<td>1 year survival, %</td>
<td>47.3</td>
<td>52.0</td>
<td>43.7</td>
</tr>
<tr>
<td>2 year survival, %</td>
<td>27.5</td>
<td>31.0</td>
<td>22.9</td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease progression, number of events</td>
<td>223</td>
<td>203</td>
<td>52.0</td>
</tr>
<tr>
<td>HR for progression:</td>
<td>0.76; P=0.006</td>
<td>0.72; P&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Duration of response, months</td>
<td>8.1</td>
<td>19.3</td>
<td>8.1</td>
</tr>
<tr>
<td>P value</td>
<td>0.03</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Best overall response rate, %</td>
<td>10.3</td>
<td>15.2</td>
<td>10.3</td>
</tr>
<tr>
<td>Disease control rate, %</td>
<td>30.2</td>
<td>33.2</td>
<td>30.2</td>
</tr>
<tr>
<td>Complete response, %</td>
<td>0.8</td>
<td>1.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Partial response, %</td>
<td>9.5</td>
<td>13.6</td>
<td>9.5</td>
</tr>
<tr>
<td>Stable disease, %</td>
<td>19.8</td>
<td>18.0</td>
<td>19.8</td>
</tr>
<tr>
<td>Progressive disease, %</td>
<td>52.0</td>
<td>44.4</td>
<td>52.0</td>
</tr>
</tbody>
</table>

---

**MDX-024: Overall Survival**

**MDX-024: Immune-related Adverse Events**

- **Any adverse events, regardless of cause** | 94.0 | 98.8 | 40.1 | 16.2 | 17.9 | 9.6 |
- **Any immune-related adverse event** | 38.2 | 77.7 | 15.9 | 31.6 | 3.2 | 2.8 |

---

**MDX-024: Duration of Response**

Data shown for patients with a confirmed complete response (CR) or partial response (PR)

**MDX-024: Conclusions**

- Second randomized phase III trial to show significant survival in metastatic melanoma with ipilimumab
  - Adding ipilimumab to dacarbazine in previously untreated patients with metastatic melanoma:
    - Reduced risk of progression by 24%
    - Significantly prolonged OS
    - Provided significantly longer duration of response
  - Ipilimumab-associated adverse events were consistent with prior reports
  - Most common adverse events involved the gastrointestinal tract, skin, liver, and endocrine system
  - Apparent shift in the ratios of adverse events associated with ipilimumab possibly due to dacarbazine, a known hepatotoxic agent

---

**MDX-024: Primary and Secondary Endpoints**

---

**Inclusion criteria**

- **Age**
  - 18 years; Stage IIIc or stage IV melanoma
- **ECOG PS**
  - 0-1; No prior therapy for advanced disease
- Regardless of BRAF mutation status or HLA type
Summary of Phase III Ipilimumab Clinical Trials

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Phase III (n=137)</th>
<th>Phase II (n=250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median overall survival, mo</td>
<td>10.1</td>
<td>11.2</td>
</tr>
<tr>
<td>12-mo survival, % (95% CI)</td>
<td>45.6</td>
<td>47.3</td>
</tr>
<tr>
<td>24-mo survival, % (95% CI)</td>
<td>23.5</td>
<td>28.5</td>
</tr>
<tr>
<td>Best overall response rate, %</td>
<td>10.9</td>
<td>15.2</td>
</tr>
<tr>
<td>Disease control rate, %</td>
<td>28.5</td>
<td>33.2</td>
</tr>
<tr>
<td>Complete response, %</td>
<td>1.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Partial response, %</td>
<td>11.3</td>
<td>11.4</td>
</tr>
<tr>
<td>Stable disease, %</td>
<td>17.5</td>
<td>18.0</td>
</tr>
<tr>
<td>Progressive disease, %</td>
<td>51.1</td>
<td>44.4</td>
</tr>
</tbody>
</table>

In both studies, overall survival was significantly longer in ipilimumab-treated groups.

Ipiilimumab: Dosing

The recommended induction dose is 3 mg/kg administered IV over a 90-minute period every 3 weeks for a total of 4 doses as tolerated.

No dose reductions are required.

Targeted Therapies

“We now have Hope”

Most attractive targets are those on which cancer cell is dependant upon for its survival

- Concept of “oncogene addiction”
- Enzymes such as kinases, proteases, and phosphatases are good therapeutic targets
- Examples include Braf, Nras, MEK, mTor
- FTIs were some of the first targeted agents to be used in melanoma

Molecular Classification Of Melanoma

- Malignant melanoma without CSD
  - Braf mutations – 59%, Nras – 22%
  - strong link between MCH-I and Braf
- Malignant melanoma with CSD
- Acral lentiginous melanoma
  - CDKN2A deletions, CDK4 amplifications
- Mucosal melanoma
  - CDKN2A deletions, CDK4 amplifications

What about Gleevec?

Phase III Trial of Nilotinib

Fecher et al jco vol 26 Apr.2007
New Agents in Clinical Trials

- Abraxane
- ABT-888
- PLX4032 (RO7204)
- Sorafenib
- Tasisufam
- Nilotinib
- Gleevec

- Ipilimumab
- Tremelimumab
- Aliswefin
- Oncovex
- IL-21

BRAF V600E Mutation

- Oncogenic mutation of BRAF
- ~8% of all solid tumors
- ~50% of malignant melanomas
- shRNA knock down experiments support its role in neoplastic behavior
- BRAF mutation knock-in mice develop melanoma-like malignancies
- RO7204 arrests abnormal cell growth in melanoma models

The Target: BRaf Kinase

An important mediator of cellular proliferation

- RTK
- Raf
- B-Raf V600E
- Ras
- MEK
- ERK

RO7204: co-Structure with kinase domain of B-RAFV600E (Bollag et al., Nature 2010)

An Open-Label, Multicenter Phase II Study of Continuous Oral Dosing of RO7204 (PLX4032) in Previously Treated Patients with BRAF V600E Mutation-Positive Metastatic Melanoma

Endpoints:
- Primary: BORR (IRC)
- Secondary: duration of response, PFS, OS, and safety

Statistical Considerations
- Target BORR is 30%
- 10% patients considered unevaluable
- Total of 90 patients required to demonstrate the lower boundary of the exact 95% CI is at least 20%

Eligibility Criteria
- PD after prior IL-2 or standard chemotherapy (DTIC, TMZ, C/T, fotemustine)
- PS=0 or 1
- Brain metastases allowed if treatment with stereotactic RT or surgery, and stable for >3 mo

BRIM-2 Study Design

Endpoints:
- Primary: BORR (IRC)
- Secondary: duration of response, PFS, OS, and safety
Tumor Responses Assessed by IRC

BORR 52% by IRC
BORR 55% by investigator assessments (INV)
RR, including unconfirmed, 68% (INV)
6 patients were unevaluable

Adverse Event All Grades, % Grade 3, %
Arthralgia 57.6 6.1
Rash 51.5 6.8
Photo-sensitivity 49.2 3.0
Fatigue 38.6 1.5
Mucitis 13.3 0
Cutaneous SCC 24.2 24.2
Pruritis 27.3 2.3
Skin papilloma (verruca) 27.3 0

Most Commonly Reported Drug-Related AEs (≥25% of Patients)

Characteristics of KA subtype
- Raised button-like, central crater
- Well-differentiated neoplasm with low probability of invasion/metastasis
- Can grow rapidly; may involute and regress
- Typically treated by excision

KA in the Phase I RG7204 Trial
- Occurred on sun-exposed skin
- Did not result in treatment discontinuation

BRIM-2 Summary & Conclusions

Safety
- Common AEs include skin-related toxicities (including cutaneous SCC), arthralgia, fatigue, LFT abnormalities

Efficacy
- BORR=52%; median response duration of nearly 7 months
- Median PFS=6.2 mo
- Median OS has not been reached
- AEs are generally reversible with dose modification or interruption

Conclusion
- BRIM-2 has met its primary endpoint.
- RG7204 is an effective agent in BRAF mutation-positive melanoma patients.
Phase III BRIM3 Study design

**Screening**
- BRAFV600E mutation

**Randomization**
- N=675

**Vemurafenib**
- 960 mg po bid (N=337)

**Dacarbazine**
- 1000 mg/m² iv q3w (N=338)

Overall survival (Dec 30, 2010 cutoff)

- Hazard ratio 0.37 (95% CI; 0.26 - 0.55)
- Log-rank P<0.0001

Objective response rates (RECIST 1.1)

- CR: Vemurafenib 8.9% vs Dacarbazine 0%
- PR: Vemurafenib 47.5% vs Dacarbazine 5.5%
- Overall response rate: Vemurafenib 54.4% vs Dacarbazine 5.5%

Maximal tumor shrinkage by individual patient

- Vemurafenib
- Dacarbazine

Selected adverse events (% of patients)

- Vemurafenib vs Dacarbazine
- Adverse events All Grade 3 Grade 4
- Arthralgia 49 3 - 3 <1 -
- Rash 36 8 - 1 -
- Fatigue 33 2 - 31 2 -
- Phototoxicity 30 3 - 4 -
- Thrombosis 13 7 <1 5 1 -
- Cutaneous SCC 12 12 - <1 <1 -
- Keratoacanthoma 8 6 - - -
- Skin papilloma 18 <1 - - -
- Nausea 30 1 - 41 2 -
- Neutropenia <1 - <1 11 5 3
Conclusions

- Vemurafenib associated with 63% decrease in hazard of death (p<.0001)
- 74% decrease in hazard of tumor progression (p<.0001)
- Benefit seen in all subgroups, including M1c and LDH
- Manageable safety profile with few drug related discontinuations
- First single drug for melanoma to improve response rate, PFS, and OS compared to standard chemotherapy
- Vemurafenib is a promising new therapy for patients with metastatic BRAFV600E-mutated melanoma and a foundation upon which to build combination therapies

Potential Mechanisms of Drug Resistance


The Future of Targeted Therapy for Melanoma

XL281

We have made our first critical gains in the targeted therapy of melanoma, with many other avenues to explore.

Modified from K Flaherty

RG7204

GSK 21184338

Nilotinib Clinical Trial / DTIC

Ipilimumab

C-kit

Braf

Vemurafenib

Ipilimumab

Yes

No

Yes

No

Progression

Clinical Trial / DTIC

Nilotinib

Braf

Vemurafenib

Ipilimumab

Metastatic Melanoma Patient Canada 2011

Treatment Pathway 2011

Conclusions

- Biology of melanoma is being understood
- Multiple targets and pathways have been elucidated
- Inhibitors to these targets are in clinical use or development
- Combinations of targeted agents need to be tried – who will pay for this?
- Vemurafenib $9,500.00 per month in U.S.A.
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

COLLEEN THURBER
Senior Pharmacy Technician, Saskatoon Cancer Centre, Saskatoon, SK

BIOGRAPHY

Colleen is a Senior Oncology Pharmacy Technician at the Saskatoon Cancer Centre and has been employed there for the past 7 years. Previous to joining the Saskatchewan Cancer Agency, Colleen was employed at Royal University Hospital in Saskatoon. She is a 1998 graduate of the SIAST Pharmacy Technician Program.

SYNOPSIS

BREAKOUT #1 - PART 1: MEASURING SURFACE CHEMICAL CONTAMINATION – A SASKATCHEWAN CANCER AGENCY EXPERIENCE

Saturday, November 5th, 14:00 – 14:40 • Place D’Armes, Ground Floor, North Wing

Practices relating to safe-handling within oncology pharmacies began to change in 1990 when the American Society of Hospital Pharmacists (ASHP) introduced the term “hazardous drugs”. A hazardous drug is defined as a drug that due to its inherent toxicity presents a danger to health care personnel. Since the early 1990’s, various comprehensive guidelines were developed and adopted in an effort to protect workers from exposure to hazardous drugs. Studies have shown that reported surface contamination continues to exist in areas where hazardous drugs are prepared, including facilities thought to be following recommended handling guidelines. The NIOSH alert in 2004 further highlighted the need to protect health care workers from exposure to hazardous drugs. More recently, use of closed system drug transfer devices throughout the preparation and administration of hazardous drugs and efforts by pharmaceutical companies to deliver products free from exterior surface contamination have supported the efforts to maintain a clean work environment.

A relatively sensitive sampling and analysis for surface contamination has been developed to test for some of the more common hazardous drugs, such as cyclophosphamide, 5-fluorouracil, methotrexate, and paclitaxel, commonly used in oncology pharmacies across Canada. For this reason and possible health concerns associated with hazardous drug exposure, The International Society of Oncology Pharmacy Practitioners (ISOPP) recommends surface sampling to establish the level and extent of workplace contamination. Once workplace contamination is measured, steps can be taken to reduce contamination to an acceptable level.

Learning Objectives:
• Review NIOSH alert in 2004 and risks to health care personnel
• Explore routes of exposure (dermal, inhalation, hand-to-mouth ingestion)
• Measures to reduce introduction/spread of surface contamination (ventilation tools, training, PPE, regular decontamination, closed-system transfer devices)
• Identify workplace monitoring recommendations (NIOSH, ISOPP)
• Share Saskatchewan Cancer Agency response to surface contamination analysis at our sites
• Identify companies which have services available for surface sampling and analysis
• Describe methods of sampling
• Share Saskatchewan Cancer Agency experience with monitoring
New Packaging
In Oncology
Nouvel emballage en oncologie

Leader in injectables
Chef de file des injectables

Safety and Protection from Production to Disposal

The new Onco Blok™ was designed to provide maximum safety and protection from the manufacturing site to the pharmacy, including all key steps in the distribution and handling of cytotoxic medications, up to disposal.

The Onco Blok™ is made of polypropylene, which is free of solvents, dyes or pigments.

The Onco Blok™ is disposed of together with the vial it contains. Incineration provides safe disposal as polypropylene breaks down into CO₂ and H₂O.

www.sandoz.ca

Sécurité et protection de la production à la destruction

Le nouveau contenant Onco Blok™ a été conçu pour offrir un maximum de sécurité et de protection du site de production à la pharmacie, y compris toutes les étapes importantes touchant la distribution et la manutention de produits cytotoxiques, et ce, jusqu’à la destruction.

Fait de polypropylène, Onco Blok™ est exempt de solvant, de colorant et de pigment.

Il suffit de jeter le contenant Onco Blok™ en même temps que la fiole qu’il contient.

L’incinération assure une destruction sûre du contenant, puisque le polypropylène se décompose en CO₂ et en H₂O.

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Measuring Surface Contamination of Hazardous Drugs

Presented by: Colleen Thurber
Senior Oncology Pharmacy Technician
Saskatoon Cancer Centre

Disclaimer
No conflicts of interest

A Glimpse of Saskatchewan

Objectives
- Discuss risks to healthcare personnel
- Identify routes of exposure
- Explore methods to reduce surface contamination & recommendations for workplace monitoring
- Methods to measure surface contamination of hazardous drugs
- Share SCA experience

Timeline

NIOSH ALERT (2004)

“Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possible leukemia or other cancers.”

National Institute of Occupational Safety and Health (NIOSH)
Did You Know?

- Most anti-neoplastic drugs are non-selective in their mechanism of action, affecting cancerous cells along with non-cancerous cells.
- Only two thirds of approximately 140 hazardous drugs are anti-neoplastics.

Hazardous Drug Characteristics

- **Carcinogenicity**: produce invasive cancer cells from normal cells.
- **Teratogenicity**: cause malformations in an embryo or fetus.
- **Reproductive Toxicity**: interfere with normal reproduction (adverse effects on sexual function and male / female fertility).

Routes of Exposure

**Inhalation**
- Droplets, particulates
- Vapors when they create aerosols
- Dust from crushing tablets
- Spills

**Dermal**
- Touch contaminated surfaces during preparation, administration, disposal & receipt
- Drug residue on the outside of vials

**Oral**
- Hand-to-mouth contact
- Food & drinks stored, prepared, or consumed in work areas (airborne)
- Direct skin contact from cleaning spills
- Cosmetics, chewing gum

**Accidental Injection** is rare!
Reducing the Introduction and Spread of Contamination

Workers may be exposed to a drug throughout its lifecycle:
- Manufacture
- Transport/delivery
- Preparation/distribution
- Administration
- Waste/disposal

Adherence to recommended work practices and use of engineering controls and personal protective equipment (PPE) has been shown to substantially reduce worker exposure.

Preventing Occupational Exposures to Antineoplastic Drugs in Health Care Settings by Thomas H. Connor & Melissa A. McDermid

Factors which adversely affect safe handling practices of hazardous drugs include:
- Increased workload
- Understaffing
- Improper training
- Budgetary constraints
- More complex regimens
- Use in non-oncology settings

NIOSH Recommendations

1. Handle drugs safely
2. Use and maintain equipment properly
3. Assess the hazards in the workplace

Handle Drugs Safely

- Wear suitable PPE
- Properly label all hazardous drugs
- Store and transport drugs in proper containers

Preparation and Administration of Drugs

- Evaluate preparation & administration policies
- Wear suitable PPE
- Limit access
- Wash hands with soap and water before donning and after removing gloves

- Properly maintain engineering controls as required by the manufacturer
- Work in facility with a ventilated cabinet designed to reduce worker exposure

Spill Control

- Manage spills according to written policy & procedure
- Locate spill kit where exposures may occur
- Dispose of spill material in hazardous chemical bin

Medical Surveillance

- Participate in medical surveillance program at work or see your doctor if a program does not exist
- Include: CBC, urinalysis, physical exam, reproductive/gen. health questions
Handle Drugs Safely

Also consider:
- Closed system drug transfer devices (CSDTD)
- Whenever possible, use cytotoxic drug products supplied in specially designed molded plastic containers meant to contain possible contamination and protect against shock during transport

Assess the hazards in the workplace

Studies from several countries have shown contamination of surfaces of BSC’s, countertops, floors, equipment, and most surfaces in areas patients are treated.
- In all studies, at least one of the drugs was detected.
- In many studies, all drugs were detected, indicating that other drugs for which analyses were not performed were most likely present.

USP 797 Recommendations for Environmental Sampling

- Suggest routine environmental sampling to detect uncontained hazardous drugs
- Initial benchmark and every 6 months or more as needed
- Surface wipe sampling of BSC and adjacent areas including the floor directly under the work area, counter tops, and patient care areas
- Common marker drugs include cyclophosphamide, ifosfamide, methotrexate, and fluorouracil

Use and maintain equipment properly

Staff education
- Cleaning routines
- Aseptic technique
- Handling spills or waste
- Use of PPE
- Use of specialized equipment

Assess the hazards in the workplace

“Some Pharmaceutical Manufacturers have developed occupational exposure limits (OEL’s). The situation within a hospital is totally different and this makes the use of OEL’s inappropriate.

For genotoxic products, there is no such thing as a safe maximal exposure limit and zero contamination should be the target.”

USP 797 Recommendation for Environmental Sampling

- If any measurable contamination is found, practitioners shall make the decision to identify, document and contain the cause
- Action may include retraining, thorough cleaning, and improving engineering controls
- USP notes that cyclophosphamide levels greater than 1.0 ng/cm² has been found to cause human uptake
ISOPP Recommendations for Environmental Sampling

- If contract laboratories are used to analyze surface wipe samples, methods of collection, storage, & shipping must be carefully documented and controlled.
- Both negative (blanks) and positive (spiked samples) controls should be coded so they are analyzed blindly.

Surface Wipe Kits

A typical wipe kit may include:
- Tissues (or collection matrix)
- Solvent to aid recovery of drug
- Containers with labels & plastic mini bags
- Gloves
- Registration form
- Instructions of use

Results from Analysis at the Saskatoon Cancer Centre Pharmacy

Not a Surprise…
Found significant contamination of our working environment in pharmacy areas.

Sessink Risk Level Model

- Dr. Paul J. M. Sessink, PHD medical science and author of “Monitoring Occupational Exposure to Antineoplastics”
- Based on predictive model for additional cancer cases per million workers based on cyclophosphamide urine levels.
- Stride risk level is 1 extra cancer case a year per million workers.
- Prohibitory risk level is 100 extra cancer cases a year per million workers.

<table>
<thead>
<tr>
<th>Stride Risk Level</th>
<th>Prohibitory Risk Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine CP (ug/24 hr)</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>Contamination CP (ng/cm²)</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Action</td>
<td>None</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Periodic</td>
</tr>
</tbody>
</table>

Actions taken…

- June 2007 – surface samples
- December 2007 – surface samples
- December 2007 – implement CSDTD
- May 2008 - thorough decontamination of pharmacy and nursing unit
- June 2008 – surface sample
- May 2009 - thorough decontamination of pharmacy and nursing unit
- June 2009 – surface sample
Measurement of surface contamination at the Saskatoon Cancer Centre 2007 - 2009

<table>
<thead>
<tr>
<th>Sample Code</th>
<th>Department</th>
<th>Description</th>
<th>CP (ng/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>December 2007</td>
</tr>
<tr>
<td>1</td>
<td>Pharmacy</td>
<td>BSC surface</td>
<td>22.00</td>
</tr>
<tr>
<td>2</td>
<td>Pharmacy</td>
<td>BSC floor</td>
<td>4.70</td>
</tr>
<tr>
<td>3</td>
<td>Pharmacy</td>
<td>Checking table</td>
<td>3.65</td>
</tr>
</tbody>
</table>

Available testing labs:
- 3 Laboratories
  - Exposure Control (Netherlands)
  - Laboratoire de Toxicologie (INSPQ) (Quebec)
  - Pharmalytics (Saskatoon)

In April 2011, we tested the same 6 surface locations using the sampling kits from each of the above laboratories.

Surface Sample Locations
- pharmacy sterile room
  - BSC #1
  - BSC #2
    - floor adjacent to BSC #1
    - checking counter
- pharmacy anteroom
  - checking counter
- treatment area
  - soiled room

Surface Sample Locations
- 1
- 2
- 3
- 4
Testing Procedures

- Determine sample sites
- Read instructions thoroughly
- Calculate required surface area to be wiped and mark
- One person to wipe surface sites (uniform technique)
- Use new gloves for each site to prevent cross contamination
- Adjacent sites for each of the 3 companies
- Label all samples and complete forms
- Package kit for transport and analysis

Highlights of Testing Methods

- Comparative discussion of three testing methods available

Where surface contamination measurement has taken us ….

- Implementation of a CSOTD
- Deep decontamination of environment
- Many changes to safe handling practices
- Development of policies addressing routine cleaning, decontamination and disinfection of surfaces in the pharmacy
- Regular monitoring of surface contamination
- Recruitment enhancement
- Staff appreciation of workplace safety initiatives
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

KATRINA ALEXANDROPOULOS
Research Pharmacy Technician, University of Alberta Hospital Pharmacy Department, Edmonton, AB

BIOGRAPHY
Katrina is a pharmacy technician at the University of Alberta hospital with experience in the management of investigational drug studies as well as the procurement of Special Access Products for hospital inpatients. Katrina graduated with a Pharmacy Technician certificate from Red Deer College in 2005. After graduation, Katrina worked with a local college as the program lead for a Pharmacy Technician – Retail program. Later, in 2008, Katrina moved into a challenging role with the Pharmacy Research Office, where she began her involvement with clinical trials and special access products.

SYNOPSIS
BREAKOUT #1 - PART 2: INVESTIGATIONAL PRODUCTS AND THE PHARMACY TECHNICIAN
Saturday, November 5th, 14:40 – 15:20 • Place D’Armes, Ground Floor, North Wing
As Canadian Pharmacy Technicians pursue regulation, roles and responsibilities for Pharmacy Technicians are increasing. This includes involvement in new areas including clinical research trials and the procurement of Special Access Programme products. How can Pharmacy Technicians, with their knowledge and expertise, support Pharmacists in this specialized area? What processes can be implemented when dealing with oncology products in the investigational area?
At Sanofi, we are committed to improving lives by bringing hope to the seven billion people around the world. Our medicines, vaccines and services offer health, protection and peace of mind. We work tirelessly, investing in R&D for new products, supporting local communities and developing immunization programs around the globe. Our 2,000 employees in Canada and 100,000 employees worldwide are proud to make a difference by providing hope for a better tomorrow.

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How do you define “sustainability”? At Teva Canada, “sustainability” is a multi-faceted concept that stretches into our corporate responsibilities as a global leader. We continue to support the Canadian Medicine Aid Programme, which in the past three years has donated over $20,000,000 worth of our products to people in developing areas around the world. Here at home, we’ve made a multi-year financial commitment to our primary corporate charity, the Childhood Cancer Canada Foundation, which helps children with cancer and members of their families.

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Investigational Products and The Pharmacy Technician

Objectives
- What is the Special Access Programme (SAP)?
- Oncology products and SAP
- Clinical Trials…What’s Involved?
- Pharmacy Technician’s role in clinical trials
- Oncology clinical trials….special considerations

DISCLOSURE
- I have nothing to disclose.

The Health Canada document "Special Access Programme (SAP) Instructions for Making a Special Access Request" states the following:
- The Special Access Programme (SAP) provides access to non-marketed drugs for practitioners treating patients with serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable.
- The SAP authorizes a manufacturer to sell a drug that cannot otherwise be sold or distributed in Canada.
- Drugs considered for release by the SAP include pharmaceutical, biologic, and radio-pharmaceutical products not approved for sale in Canada.

What drugs are available?
- There is a list naming all drugs eligible which can be accessed through an internal system called “The Special Access Management System” (SAMS).
- Since this list changes continuously those interested in the status of a particular drug may contact the manufacturer or the SAP.

The SAP operates 24-7
- Regular business hours are 830-1630, EST
- On call service is available after 1630 and throughout the weekend

What drugs are available?
- There is a list naming all drugs eligible which can be accessed through an internal system called “The Special Access Management System” (SAMS).
- Since this list changes continuously those interested in the status of a particular drug may contact the manufacturer or the SAP.

Katrina Alexandropoulos | Presentation Handouts pg1
The scope of the SAP has gradually expanded to address requests for a broader range of unauthorized drugs.

**Drugs in shortage/backorder:**
These are drugs authorized by Health Canada that are sold in Canada but are temporarily unavailable for release (recent examples include Cytarabine). The SAP will consider authorizing access to an alternative source of an otherwise marketed drug for the duration of the shortage/backorder.

**Discontinued and Withdrawn Drugs:**
Discontinued drugs are those that have been approved for marketing and have been available for sale but are currently not offered for sale on the Canadian Market, typically for economic reasons. Withdrawn drugs are similar but were withdrawn from the market either voluntarily by the manufacturer or on order from Health Canada.

**Safety of SAP products**
- The SAP authorization given to a patient does not constitute an opinion or statement that a drug is safe.
- It is the physician’s responsibility to obtain patient consent and present the risks/benefits.

**Future Use Supply**
- There are circumstances where hospitals may require certain SAP drugs to be available on-site in anticipation of an emergency. These are considered “Future Use.”
- In such cases, the practitioner must provide justification as to why such products cannot be requested on a patient-by-patient basis.
- For example, UAH has large burn centre which has future use approval for Mafenide Cream in order to not delay treatment.

**Manufacturer’s Role**
- In all cases, the manufacturer has the final word on whether the drug will be supplied.
- The manufacturer has the right to impose certain restrictions or conditions on the release of the drug to ensure that it is used in accordance with the latest information available.
- They may restrict the amount of product released, request further patient information, determine payment requirements and place conditions on shipping arrangements.

**Quantity**
- A maximum quantity equivalent to a six month duration may be authorized for chronic treatments.
- Repeats must be re-ordered through the usual SAP request procedure.
Request Process
- Requests are processed within 24 hours of receipt however requests for life-threatening conditions take precedence over other less urgent matters
- A permanent record of SAP drugs received and dispensed (including prescription details) MUST be maintained by the Pharmacy Services provider

Step by Step Process
1. Prior to prescribing the SAP drug the Physician should consult the clinical Pharmacist/Pharmacy Provider and the Facility Site Leader Medical to see if the drug can be supplied.

Step by Step Process
2. With a Physician’s order for an SAP drug, the clinical Pharmacist or nurse contacts the prescriber to discuss viable alternative formulary and/or marketed in Canada drug therapy. Whenever possible, a formulary drug is chosen.

Step by Step Process
3. Should the Pharmacy Provider/Clinical Pharmacist and prescriber agree that there is no viable formulary or marketed in Canada drug alternative and that a reasonable case to justify the use of an SAP drug can be made, then the prescriber seeks informed consent for the use of the drug from the patient and/or family.

Step by Step Process
4. After informed consent has been obtained and documented on the patient's Health Record a Special Access Request Form is completed and faxed. (Pharmacy may be required to create a purchase order)

Patient Supply
- If a patient receives authorization for a drug at one hospital but is then transferred to another hospital, new SAP forms must be completed
- The stock can be sold to the new site once authorization is granted from Health Canada
- The forms should indicate that no supply is needed and that supply is being purchased from a different site
Patient Supply

- If a patient is authorized to receive a SAP drug but is discharged or discontinued without using the complete supply it can remain on site.
- If the patient is restarted on therapy or re-admitted within a reasonable period of time at the same site they can continue on therapy if supply has not been transferred to a new patient.

Patient Supply

- If a patient does not use all supply that is authorized the supply can be transferred to another individual.
- The forms would then indicate this prior to submitting to Health Canada and the pharmacy would state: “No Supply Needed.”

Where to find information?

Health Canada Website
www.hc-sc.gc.ca

Example: CYTARABINE

- Manufacturers were unable to create product due to lack of supply of one ingredient and quality control.
- Health Canada stepped in to regulate who would be able to access the product to ensure supply would last until ingredient was available.
- Physicians were required to be very specific in order to receive authorization.
- Health Canada would only approve vials to cover the total cycle dose. This resulted in a change in process for UAH pharmacy.
- SAP provided a main contact in order to streamline requests.

Suggestions

- Segregate: place in a separate area labeled as Cytotoxic/Hazardous to ensure proper dispensing procedures are followed.
- Create a specific binder for that product containing instructions for staff and SAP forms for each patient needing drug.
- Create a log specific to the item to document incoming and outgoing stock.
- Create a specific log to ensure only amount approved is used.
- Ensure same lot number and expiry is used for each dose as well as the same brand for entire course.
- Create workcards for each brand being used to ensure preparation is done correctly.

PEG-Asparginase

- Used as first line therapy in the treatment of ALL (Acute Lymphoblastic Leukemia).
- PEG-Asparginase is pegylated therefore a longer acting medication in comparison to other asparginase products.
- Product is not available in Canada thus requires SAP approval.
- Ordered in on a patient specific basis.
- Short expiry date.
The Standards of Practice for Oncology Pharmacy in Canada Version 2 November 2009 states:

- “Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with Good Clinical Practice and the applicable regulatory requirements.”

- “Specific requirements for pharmacists involved with clinical trials at their practice site include: Following the standard pharmacy department policies and procedures for management of clinical trials. Oncology trials often are of study drugs in earlier phases of development and include more toxic drugs than found in clinical trials in other medical disciplines.”

Clinical trial professionals should be mindful of the need to maintain a high level of quality in a study and to build quality control measures into the study.

Quality control continues to receive attention because many oncology trials are stopped early, with approval given to oncology treatments based on positive results of tumor response.

Good quality control practice begins with prospective study planning.

How do Oncology Clinical Trials affect Pharmacy Research?

- Clinical Trials are a significant component of oncology pharmacy practice at many cancer treatment centres.

- It is advantageous to have a formalized process to handle and review clinical trials involving oncology pharmacy services as well as education and training needs for support staff.

- “It is important to involve the oncology pharmacist in the cognitive review of each oncology clinical trial, but technical issues may be incorporated into general pharmacy operations or may be managed by a pharmacy technician.”

Pharmacy Research Services

Include:
- Expert consultation to investigators on medication-related issues
- Creation of procedures for pharmacy dispensing of investigational drugs
- Preparation of pharmacy budgets
- Excellent resource for investigational drug-related questions
- Maintenance of drug inventory

How can Pharmacy Technicians Help?

- Receive in-depth training regarding the preparation of chemotherapy admixture
- Pharmacists receive general overview of aseptic technique; more theory based
- Review protocols for clinical investigational drug studies and assess it for technical aspects
- Collaborate with investigators and clinical study coordinators to establish pharmacy’s role
- Assist in the set-up and preparation of study medication
- Communicate and train other technical staff

It is advantageous to have a formalized process to handle and review clinical trials involving oncology pharmacy services as well as education and training needs for support staff.

- “It is important to involve the oncology pharmacist in the cognitive review of each oncology clinical trial, but technical issues may be incorporated into general pharmacy operations or may be managed by a pharmacy technician.”
Storage and receipt
- Normally a task assigned to Pharmacy Technicians
- Ensure OHSW & NIOSH procedures are followed
- Documentation
  - Site may require specific information recorded on patient workcards in addition to protocol

QUESTIONS

RIVA ensures every chemotherapeutic admixture prepared is safe and effective.

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888-778-7482 • www.intelligenthospitals.com
YVES ROUSSEAU  
MUHC - Royal Victoria Hospital, Montreal, QC

**BIOGRAPHY**

Yves Rousseau is a clinical hemato-oncology pharmacist at the McGill University Health Centre (MUHC) in Montreal and is a clinical associate at the Faculty of Pharmacy of the University of Montreal. He received his Bachelor degree in Pharmacy in 1984 and his Master degree in Pharmacy Practice the following year both from the University of Montreal. In 1989 he implemented the pharmaceutical care services on the hemato-oncology unit of the Royal Victoria Hospital where he has since been working. The care of haematopoietic stem cell transplant patients represents an important part of his daily activities. He is a Board Certified Oncology Pharmacist (BCOP) since 2000.

**SYNOPSIS**

**BREAKOUT #2 - PART 1: HAEMATOPOIETIC STEM CELL TRANSPLANTATION**

*Saturday, November 5th, 14:00 – 14:40 • Frontenac, Second Floor*

Haematopoietic stem cell transplantation is used primarily for the treatment of advanced haematological diseases and in some circumstances can be considered a curative option. After this presentation the attendee should be able to:

- Understand the role of haematopoietic stem cell transplantation in the treatment of diseases for which it is indicated
- Know which kind of transplant is indicated depending on the type of disease and patient
- Be able to list the most common conditioning regimens and their complications
- Recognize the role of the pharmacist in supporting the transplant patients
Haematopoietic stem cell transplantation

Yves Rousseau, pharmacist BCOP
McGill University Health Centre
November 5

Disclosure
I have no conflict of interest to declare

Learning objectives
• To understand the role of haematopoietic stem cell transplantation in the treatment of diseases for which it is indicated
• To know which kind of transplant is indicated depending on the type of disease and patient
• To be able to list the most common conditioning regimens and their complications
• To recognize the role of the pharmacist in supporting the transplant patients

Plan of presentation
• Principles of transplantation
  • Autologous transplantation
  • Indication
  • Procedure
  • Conditioning regimens
  • Monitoring
  • Allogeneic transplantation
  • Indication
  • Procedure
  • Conditioning regimens
  • Monitoring
  • Question period

Principles of transplantation
• Autologous Transplants
  • No evidence of disease in the blood or bone marrow
  • Transplant related mortality (TRM) lowest with autol (<5%)
  • Relapse rates are higher depending on the disease
  • Absence of graft versus tumor effects
  • Chemo-sensitive tumor
  • Ideally should obtain Minimal Residual Disease (MRD)
  • Dose-intensity chemo
  • Rescue marrow from high dose chemo
  • Other organ toxicities = dose-limiting

Principles of transplantation

Allogeneic Transplants
- High TRM (30-50%) (?)
- Lower relapse rates due to graft versus host effects
- Availability of donor
- Age
- Performance status


Principles of transplantation

- Eligibility
  - Age < 65
  - Autologous, reduced intensity (RIC)
  - Myeloablative allogeneic
- Exclusions
  - CHF, uncontrolled diabetes mellitus, active infections, renal insufficiency

Principles of transplantation

- Sources of Haematopoietic stem cell (HSC)
  - Bone marrow
  - Peripheral blood
  - Umbilical cord blood
  - Immunologic source of HSC
    - Allogeneic
    - Match related (MRD)
    - Match unrelated donor (MUD)
    - Syngenic (identical twin)
    - Autologous

Principles of transplantation

- Allogeneic Transplants
  - RIC:
  - Patients not candidates for myeloablative transplants
  - T-cell mediated = graft versus tumor (tumor) effect
  - Low-dose chemo with high immunosuppression
  - Preferred source of cells = peripheral (more T-cells)
  - Less chemo-induced toxicity but more GVHD (late complications)


Principles of transplantation

- Eligibility
  - Age < 65
  - Autologous, reduced intensity (RIC)
  - Age < 55
  - Myeloablative allogeneic
- Exclusions
  - CHF, uncontrolled diabetes mellitus, active infections, renal insufficiency

Principles of transplantation

- RIC:
  - Patients not candidates for myeloablative transplants
  - T-cell mediated = graft versus tumor (tumor) effect
  - Low-dose chemo with high immunosuppression
  - Preferred source of cells = peripheral (more T-cells)
  - Less chemo-induced toxicity but more GVHD (late complications)


Principles of transplantation

- Eligibility
  - Age < 65
  - Autologous, reduced intensity (RIC)
  - Age < 55
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- Exclusions
  - CHF, uncontrolled diabetes mellitus, active infections, renal insufficiency

Principles of transplantation

- Sources of Haematopoietic stem cell (HSC)
  - Bone marrow
  - Peripheral blood
  - Umbilical cord blood
  - Immunologic source of HSC
    - Allogeneic
    - Match related (MRD)
    - Match unrelated donor (MUD)
    - Syngenic (identical twin)
    - Autologous
Autologous transplantation - PBSC vs Bone Marrow

- PBSC better than marrow
- Faster engraftment
- Decreased supportive care
- Better quality of life
- Decreased cost
- No difference in disease-free survival

Allogeneic transplantation - PBSC vs Bone Marrow

- Best source of stem cells controversial
- Normally Bone Marrow contains 18X more CD34+ cells vs Peripheral Blood
  - This can be improved by the use of G-CSF
- PBSC:
  - Faster engraftment
  - More T cells? more acute and chronic GVHD?
  - Increased GVHD = increased graft-versus-host effect = better long term survival?
  - For advanced diseases: PBSC better vs BM re transplant related mortality

Principles of transplantation

- Collection of stem cells
  - Autologous
    - Filgrastim (G-CSF) 10 mcg/kg + chemo
    - Cyclophosphamide + Filgrastim (G-CSF)
    - For failures: Plen Al + Anastrozole + Filgrastim (G-CSF)
  - Target = 5 X 10^6/kg CD 34+ cells
  - Allogeneic
    - Bone marrow = OR
    - Peripheral = Filgrastim 5-10 mcg/kg X 5 days

- Time for collection
  - Time to Mobilization CD34+ Cells > 20/ul
Autologous transplantation

• Indications
  - Multiple myeloma
  - High dose Melphalan
  - NHL
  - BEAM
  - Hodgkin’s disease
  - BEAM
  - Amyloidosis
  - High dose Melphalan
  - Neuroblastoma
  - Ovarian cancer
  - Germ-cell tumors
  - Autoimmune disorders
  - AML

Autologous transplantation – High dose Melphalan

- Carmustine (BCNU) 300 mg/m² IV
- Etoposide (Vp-16) 200–400 mg/m² IV
- Cytarabine (Ara-C) 200–400 mg/m² IV
- Melphalan 140 mg/m² IV

Autologous transplantation – Complications

- Infections
- Mucositis
- N/V/D
- Malnutrition
- Fluid overload
- Electrolytes imbalance
- Fatigue

Autologous transplantation – Hematologic toxicity

Autologous transplantation – Mucositis
Autologous transplantation – mucositis

Allogeneic transplantation

- Indications
  - AML
  - ALL
  - CML
  - MDS
  - MPD
  - NHL
  - Hodgkin’s Disease
  - CLL
  - Multiple myeloma
  - Juvenile CML

- Aplastic anemia
- PNH
- Fanconi’s anemia
- Blackfan-Diamond
- Thalassemia major
- Sickle cell anemia
- SCID
- Wiskott-Aldrich
- Inborn errors of metabolism

Indications
- Choice to go transplant vs conventional chemo
- Risks factors
- Cytogenetics
- Age
- Co morbidity
- Availability of donor

Conditioning regimens
- Myeloablative
  - TBI – Cyclo
  - BuCy2
- Non myeloablative or reduced intensity (RIC)
  - TBI – Flu
  - Flu – Bu
  - Flu – Mel
  - Bu – Mel

Probability of Survival after HLA-matched Sibling Donor Transplants for ALL, Age ≥20 Years, 1998–2007
- By Disease Status

- By Disease Status
Allogeneic transplantation – Complications - cGVHD

Epidermal cGVHD
- Lichen planus-like
- Papulosquamous
- Lichenoid lesions
- Psoriasiform
- Keratosis pilaris-like
- Acral erythema

Dermal cGVHD
- Lichen-sclerosus-like
- Dermal sclerosis

Subcutaneous cGVHD
- Subcutaneous sclerosis
- Fascitis

Allogeneic transplantation – Complications – SOS (VOD)

- Within the first three weeks after transplant (typically < Day 35)
- Hyperbilirubinemia (> 34 \( \mu \text{mol/L} \)) with 2-3 of the following:
  - Weight gain
  - Ascites
  - Hepatomegaly (painful) or right upper quadrant pain

- Mortality rate in severe VOD approx 90%

Prevention
- Ursodiol

Treatment
- Defibrotide

Copelan EA. NEJM 2006;354:1813-1826.

Autologous transplantation for NHL – Parma study

Table 1: Outcomes of Hematopoietic Stem Cell Transplantation in Hematologic Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Main Cause of Failure</th>
<th>100 Day Mortality Rate</th>
<th>1 Year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogeneic transplantation</td>
<td>Graft-versus-host disease</td>
<td>1-5</td>
<td>60-80</td>
</tr>
<tr>
<td>Acute graft-versus-host disease</td>
<td>Autologous</td>
<td>5.4</td>
<td>50-60</td>
</tr>
<tr>
<td>Selective</td>
<td>Autologous</td>
<td>5.6</td>
<td>50-60</td>
</tr>
<tr>
<td>Dose-refractory leukemia</td>
<td>Autologous</td>
<td>6.3</td>
<td>50-60</td>
</tr>
<tr>
<td>Bone marrow failure</td>
<td>Autologous</td>
<td>6.3</td>
<td>50-60</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Autologous</td>
<td>6.3</td>
<td>50-60</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>Autologous</td>
<td>6.3</td>
<td>50-60</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>Autologous</td>
<td>6.3</td>
<td>50-60</td>
</tr>
<tr>
<td>Acute leukemia</td>
<td>Autologous</td>
<td>6.3</td>
<td>50-60</td>
</tr>
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<td>Chronic lymphocytic leukemia</td>
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<td>6.3</td>
<td>50-60</td>
</tr>
</tbody>
</table>

The estimated rates of death are based on recent reports.
This table was updated with information from multiple centers and institutions.

Merci !

Yves Rousseau
Presentation Handouts pg7
**Speaker & Session Descriptions / Aperçu des séances et des présentateurs**

**VICTORIA KLETAS**  
Oncology Drug Information Specialist, BC Cancer Agency, Vancouver, BC

**BIOGRAPHY**

Victoria Kletas is a clinical pharmacist currently practicing at the BC Cancer Agency (BCCA) in Vancouver. Her various roles include being an Oncology Drug Information pharmacist providing drug information as part of the Provincial Drug Information team, as well as being the Genitourinary Tumour Group Pharmacist. Victoria has a longstanding involvement with CAPhO having served as a NOPS co-chair for several years, including being the current CAPhO Awards Committee Chair.

**SYNOPSIS**

**BREAKOUT #2 – PART 2: AN UPDATE ON PROSTATE CANCER**  
Saturday, November 5th, 14:40 – 15:20 • Frontenac, Second Floor

This presentation will focus on outlining prostate cancer as a disease, while focusing on hormone refractory prostate cancer. Presentation objectives include defining hormone refractory prostate cancer, highlighting drug therapy and providing an update on upcoming treatment options for prostate cancer patients.
Update on Prostate Cancer

Victoria Kletas BSc Pharm, MSc Pharm
Provincial Drug Information Specialist
BC Cancer Agency
Vancouver, BC

Disclosure

Nothing to declare

Outline

- Outline prostate cancer as a disease
- Define castrate resistance
- Highlight therapeutic options

Prostate Cancer

- Most common ca in men – 25,000 new cases in 2011
- Incidence: 1 in 7
- Mortality rate: 1 in 28 – 3rd most lethal ca
- Highest RSRs for prostate cancer: New Brunswick (99%), Ontario (98%), lowest are in Saskatchewan (91%), Manitoba (92%) and Alberta (92%).

Canadian Cancer Statistics 2011

Prostate Cancer

- Risk increases with age
- Survival is consistently high (>95%) in men aged 40-79 peaking at 99% for those diagnosed btw 60-69 yrs
- Survival is lowest for 80-99 yrs (83%).

Canadian Cancer Statistics 2011
Risk Factors
- Increasing age: Rarely occurs in men <40yr, incidence increases progressively thereafter
- Ethnic or geographical differences: Higher in African-Americans compared with other ethnic groups
- Genetic Factors: Mutations in BRCA1 and BRCA2
- Diet, hormone levels, obesity- some effect, but role is limited.

Screening
- Prostate specific antigen (PSA)
  - Elevation in prostate ca due to increased PSA production and more PSA released into serum
  - PSA elevation can precede clinical dx by 5-10 yrs
  - PSA can also be elevated in BPH or prostatitis
- PSA testing lead to dramatic increase in incidence of prostate ca
- PSA screening - controversial

Diagnosis
- Digital Rectal Exam (DRE): Annually for men 50-70 yrs
- Prostate biopsy indicated
  - Clinical Symptoms
  - Abnormal DRE
  - Elevated serum PSA
- Needle biopsy
- Gleason score

Treatment
- Early/low risk: Active surveillance
- Localized:
  - Prostatectomy
  - Radiation therapy

Adverse effects
- Reduced testosterone, loss of lean body mass, increased body fat and decreased muscle strength
- Observed association btw ADT and CVD
- Sexual dysfunction
- Hot flushes
- Osteoporosis and bone fractures
  - Bisphosphonates (pamidronate, zoledronic)
  - Denosumab
Denosumab

- Human monoclonal antibody against RANKL
- RANKL drives osteoclast
  - Formation
  - Function
  - Survival
- RANKL inhibition decreases sclerotic changes

Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study

Primary Endpoint: Non-Inferiority SRE
Secondary Endpoint: Superiority SRE, time to second SRE

Median time to SRE:
- Denosumab 20.7 months (D) vs. 17.1 months (Z)

Survival

CRPC, Bone Metastases
ECOG 0-2
N = 1904
Denosumab 120 mg SC 4 weekly
Zoledronic Acid 4 mg IV 4 weekly

Stratified by:
- previous SRE
- recent chemo
- PS level

12 months Follow-Up

SRE defined as:
- Pathological fracture
- Bone Radiation
- Bone Surgery
- Spinal Cord Compression


Castration resistant prostate cancer

Serial rise in PSA despite castrate levels of testosterone (<20-50 mg/dL)
- PSA ↑ 50% from post treatment nadir (if PSA response to initial therapy ↓ >50%) and minimum 2-5 ng/mL
- PSA ↑ 25% from post treatment nadir (if PSA response to initial therapy ↓ <50%)

PSAWG (Prostate-Specific Antigen Working Group)

Chemotherapy

- Docetaxel + Prednisone
- Mitoxandron + Prednisone
- Abiraterone + Prednisone
- Cabazitaxel + Prednisone

Mitoxantrone

Tannock 1996 (JCO)

<table>
<thead>
<tr>
<th>Hormone Refractory Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 161</td>
</tr>
</tbody>
</table>

Prednisone (10 mg daily)
N = 81

Prednisone (10 mg daily) + Mitoxantrone (12 mg/m² q 3/52)
N = 80

Primary: 12%
Secondary: Analgesic, 7/81; Duration 18 wks

Toxicity: Combination arm cardiotoxicity in 5/130 patients, grade 3/4 neutropenia (45%)

Randomized, Non-blinded, Phase III (TAX-327)

Primary Endpoint: Overall Survival
Secondary Endpoints: Reduced pain, PSA response, Treatment Duration: Maximum 10 cycles

Gift of Pharmacology

Victoria Kletas | Presentation Handouts pg3
Cabazitaxel

- Semi-synthetic taxane
- Potent tubulin-binding taxane
- Designed to overcome taxane resistance, including docetaxel-refractory mCRPC
- Similar potency to docetaxel in vitro

Adverse effects:
- Dose-limiting toxicity neutropenia
- Diarrhea
- Fatigue, asthenia
- Nausea, vomiting

Abiraterone

- Potent, irreversible inhibitor of CYP17A1
- Approved after progression on a docetaxel-based regimen
- Favorable side effect profile:
  - Toxicities of mineralocorticoid excess (hypertension, hypokalemia, edema)

Abiraterone and Increased Survival in Metastatic Prostate Cancer

- Phase III, Randomized, Double-Blind, Placebo Controlled
- Primary Endpoint: OS
  - Median follow up: 12.8 months
  - OS: 14.8 months (A) vs. 10.9 months (P)
  - Time to PSA progression: 10.2 months (A) vs. 6.6 months (P)
  - PFS: 5.6 months (A) vs. 3.8 months (P)
  - PSA response rate: 29% vs. 6%, P<0.001
  - Delayed incidence of skeletal related events
  - Improved pt reported pain outcomes

Lancet. 2010 Oct 2;376(9747):1147-54.
MONA SABHARWAL
Executive Director, pan-Canadian Oncology Drug Review, Toronto, ON

BIOGRAPHY

Mona Sabharwal is the inaugural executive director of the pan-Canadian Oncology Drug Review (pCODR).

Ms. Sabharwal has worked in drug technology assessment and formulary management, in both British Columbia and Ontario, for more than 15 years. Before joining pCODR, she was the Senior Manager for Drug Programs Management with the Ontario Ministry of Health and Long-Term Care. In this role, she had operational oversight of the drug submission and evaluation process for Ontario’s seven public drug programs.

Ms. Sabharwal is a registered pharmacist with experience in both community and hospital pharmacy practice. She has also conducted practice-based research focused on finding concrete ways to improve the delivery of pharmacist-based professional services. She obtained both her Bachelor of Science in Pharmacy and her Doctor of Pharmacy from the University of Toronto.

SYNOPSIS

BREAKOUT #3 – PART 1: UPDATE ON THE PAN-CANADIAN ONCOLOGY DRUG REVIEW
Saturday, November 5th, 14:00 – 14:40 • Laval, Third Floor, North Wing

The pan-Canadian Oncology Drug Review (pCODR) evolved from the interim Joint Oncology Drug Review (iJODR), which demonstrated the value that a national collaborative platform can provide to cancer care decision-making. Established by the provincial and territorial Ministries of Health, pCODR is designed to bring consistency and clarity to the assessment of new cancer drugs. The pCODR review process will reduce duplication of effort by individual provinces and territories. Clinical and cost effectiveness evaluations will be conducted in a timely manner by leading Canadian experts, and with the input of patient advocacy groups, pharmaceutical manufacturers and clinician-based tumour groups. Recommendations will help guide funding decisions of participating provinces and territories, although final coverage decisions will remain the responsibility of each jurisdiction. Along with the provinces and territories, with the exception of Quebec, pCODR partners are the provincial cancer agencies, the Canadian Partnership Against Cancer (CPAC) and the Canadian Agency for Drugs and Technology in Health (CADTH).

By the end of the presentation, participants will:
• Understand the rationale for this pan-Canadian initiative
• Become familiar with the guiding principles that ground pCODR’s work
• Understand the pCODR process for reviewing new drug submissions
• Learn about the pan-Canadian structures that support the pCODR review process, such as committees and advisory groups
• Describe how pharmacists, patients, physicians and economists from across Canada are all involved in the pCODR review process
Disclosure

- There are no real or apparent conflicts of interest associated with this presentation

Presentation Objectives

- Understand rationale for this pan-Canadian initiative
- Become familiar with guiding principles that ground pCODR’s work
- Understand pCODR process for reviewing drug submissions
- Learn about various pan-Canadian structures that support pCODR review process, such as committees and advisory groups
- Describe how pharmacists, patients, physicians and economists from across Canada are all involved

Why pCODR

- Historically, every province and cancer agency had its own way to evaluate cancer drugs before they would fund
- Some evaluation processes were more defined than others
- pCODR process enables all provinces and cancer agencies to:
  - take advantage of a single approach to cancer drug evaluation
  - reduce duplication of effort by individual jurisdictions
  - benefit from clinical and economic evaluations being conducted in a timely manner by leading Canadian experts

About pCODR

- pCODR assesses cancer drugs and makes recommendations to provinces and territories to guide their drug funding decisions
- Designed to bring consistency and clarity to assessment of cancer drugs by looking at clinical evidence, cost-effectiveness and patient perspectives
- Evolved from Interim Joint Oncology Drug Review (iJODR), which demonstrated value that a national collaborative platform can provide to cancer care decision-making
- Along with provinces and territories, with exception of Quebec, pCODR partners are provincial cancer agencies, Canadian Partnership Against Cancer (CPAC) and Canadian Agency for Drugs and Technology in Health (CADTH)

The Evolution from iJODR to pCODR

- Experts from across Canada will be involved with formulating recommendations
- The Provincial Advisory Group (PAG) was created to help ensure recommendations are useable
- Membership on Economic and Clinical Guidance Panels from across Canada
- Formal involvement of cancer agencies
- Broad outreach to solicit input during a drug review itself
- Committed to transparency and accountability to patients and public, and responsive to industry
- Posting all reports on a publicly-accessible website
**pCODR Guiding Principles**

**Health System Focus**
- Cancer drugs are evaluated within a review process and decision making framework that are consistent with those used for drugs for other diseases

**Evidence-based**
- A review process with capacity for rigorous and consistent evidence-based clinical and pharmacoeconomic reviews to support evidence-based decision-making

**Excellence**
- A review process that reflects an ongoing commitment to excellence through incorporation of best practices in a spirit of continuous quality improvement

**Ethical Framework**
- A review process that includes an ethical framework which balances the need for timely and quality cancer therapies with broader societal values

**pCODR Review Process**

1. Conduct Pre-Screening Planning activities including getting input from PAG and notifying Patient Advocacy Groups
2. Prepare & submit Request for Drug Review
3.1 Screen Submission and Initiate Review Process
4.1 Conduct Clinical Review
4.2 Conduct Economic Review
5. Summarize & Review with pERC
6. Prepare & Publicly Post Initial Recommendations
7. Get Feedback from PAG
7.1 Get Feedback from Submitter (and impacted manufacturer)
7.2 Get Feedback from PAG
7.3 Get Feedback from Patient Advocacy Group
7.4 Eligible for Early Conversion?
8. Summarize & Review with pERC
9. Prepare & Publicly Post Final Recommendations & Post Input

*Includes pCODR Secretariat, Clinical Guidance Panel, Economic Guidance Panel, pCODR Expert Review Committee (pERC) and Provincial Advisory Group (PAG)

Estimated 99–149 business days

Next steps could include Recommendation implementation, Procedural Review or Resubmission
pCODR Review Process (Video)

pCODR Structures

- pCODR Expert Review Committee (pERC): Dr. Charles Blanke & Olaf Koester
- pCODR Steering Committee:
  - Co-Chairs: Dr. Charles Blanke & Olaf Koester
  - pCODR Executive Director: Mona Sabharwal
- Provincial Advisory Group (PAG): Steve Long
- Clinical Guidance Panels
- pCODR Staff

Inputs into pERC Recommendations

Submission from Manufacturer or Tumour Group
- Clinical Guidance Report
  - Includes systematic review, summaries of patient advocacy group, AHRQ input
- Clinical Guidance Report
  - Includes critique of economic evaluation and BIA

Presentation of Data by pERC Members

Deliberation & Recommendation (based on pERC Deliberative Framework)

pERC Deliberative Framework

- Developed collaboratively by pCODR Clinical and Process working group and pCODR Steering Committee
- Outlines elements to be considered during pERC deliberations
- Reinforces that no single element overtakes another, rather it is sum of all elements that pERC must use
- Can be applied to all oncology drugs and situations, including rare cancers or end of life drug treatments
- Reinforces there is no threshold that must be met for any single element in the review
- It is the individual drug, disease and context that determine pERC’s information needs for each element of the framework

Detailed Description of Each Element of the pERC Deliberative Framework (1)

<table>
<thead>
<tr>
<th>Detailed Description of Each Element of the pERC Deliberative Framework (1)</th>
<th>Detailed Description of Each Element of the pERC Deliberative Framework (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Criteria</td>
<td>Sub-Criteria</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>Systematic review in the Clinical Guidance Report</td>
</tr>
<tr>
<td>Safety</td>
<td>Systematic review in the Clinical Guidance Report</td>
</tr>
<tr>
<td>Burden of Illness</td>
<td>Clinical Guidance Report, patient advocacy group input</td>
</tr>
<tr>
<td>Need</td>
<td>Clinical Guidance Report, patient advocacy group input</td>
</tr>
<tr>
<td></td>
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<tr>
<td>Alignment with Patient Values</td>
<td>Patient Values</td>
</tr>
<tr>
<td>Cost Effectiveness</td>
<td>Economic Evaluations</td>
</tr>
<tr>
<td></td>
<td>Organizational Feasibility (Provincial Advisory Group input)</td>
</tr>
</tbody>
</table>
Role of Guidance Panels and pERC

- pERC deliberates on the drug and makes a funding recommendation, using the full Deliberative Framework.
- Clinical Guidance Panel makes conclusions on the net overall clinical benefit of the drug for consideration by pERC.
- Economic Guidance Panel contribute by providing an evaluation in an Economic Guidance Report of:
  - cost-effectiveness - based on an economic model
  - feasibility of adoption - based on budget impact analysis

PAG – Roles & Responsibilities

- Provide input to pCODR to ensure clinical and economic reviews leading to pERC recommendations address local needs and issues.
- Provide input to pERC during its deliberations, regarding potential implementation issues related to recommendations.
- Review and provide feedback on pERC recommendations regarding any implementation issues before recommendations are finalized.
- Facilitate consultation and information exchange among participating jurisdictions, cancer agencies, relevant organizations and pCODR.
- Inform pCODR about important trends in development and utilization of cancer agents, and significant issues relevant to their assessment.

PAG Input

- Received early in review process.
- Provides important contextual information for a pERC recommendation.
- Informs of potential impact and feasibility of adopting new drug or a new indication for a drug into health system, broadly considering following questions:
  - In your jurisdiction, what factors would you consider might impact the ease with which the drug might be adopted into the health system?
  - What are potential enablers or barriers in the health system to implementing a funding recommendation for this drug? Generally, enablers/barriers could be operational, capital, human resources, legislative, or regulatory in nature.
  - Categories of input: comparators, patient population, accessibility, dosing issues, implementation costs/cost avoidance, other.

What does pCODR mean for oncology pharmacists?

- pCODR brings consistency and clarity to the cancer drug funding review process.
- pCODR is allowing for pre-NOC submissions for any new drug to encourage more timely decision making.
- Improved quality of decision making: involvement of physician, pharmacist and economist experts from across Canada, integration of patient input.
- Reduced duplication of effort by individual provinces and agencies.
- Provinces / agencies retain responsibility for final funding decisions.
Co-Chairs
- Dr. Anthony Fields, Oncologist
- Dr. Jeanneau Trudel, Oncologist

Members
- Dr. Chen B., Economist
- Dr. Scott B., Oncologist
- Bryson Brown, Patient
- Dr. N. de Lemos, Pharmacist
- Dr. S. Desai, Oncologist
- Dr. P. Devereux, Economist
- Dr. B. Evans, Oncologist

Vice-Chair
- Dr. Jeanneau Trudel, Oncologist

The pCODR Steering Committee is the leadership body of the pCODR, responsible for ensuring that the process for assessing the clinical evidence and cost effectiveness of new cancer drugs is carried out in an effective and timely manner. The Committee is comprised of six senior level P/T representatives, four senior level cancer agency representatives, one CADTH representative (observer), and one FRCPC representative (observer).
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

ROXANNE DOBISH
Manager, Patient Safety Monitoring, Alberta Health Services, Edmonton, AB

BIOGRAPHY
Roxanne Dobish graduated from the Faculty of Pharmacy at the University of Alberta with a BSc in Pharmacy. She worked at the Cross Cancer Institute in Edmonton as a staff pharmacist and in various pharmacy management positions for 22 years during which she developed a strong interest in medication and patient safety. In 2007 she accepted a position as Chemotherapy Safety Project Leader and in 2010 moved to a position with Alberta Health Services as the Manager, Patient Safety Monitoring.

STEPHANIE CARPENTER
Accreditation Product Development Specialist, Accreditation Canada

BIOGRAPHY
Stephanie Carpenter, MA, is an Accreditation Product Development Specialist at Accreditation Canada. She is the lead Product Development Specialist for the Ambulatory Systemic Cancer Therapy Services Standards that have been developed through a partnership with the Canadian Partnership Against Cancer (CPAC) and the Canadian Association of Provincial Cancer Agencies (CAPCA). In addition to her work on standards for systemic cancer therapy services, her projects include Cancer Care and Oncology Services, the upcoming standards on Spinal Cord Injury, and all standards for Aboriginal Health Services including the upcoming standards for Remote and Isolated Health Services. She holds a Master of Arts from the University of Western Ontario and a Bachelor of Arts from McMaster University.

SYNOPSIS

BREAKOUT #3 – PART 2: HOW DO YOU MEASURE UP? NEW ACCREDITATION STANDARDS FOR AMBULATORY SYSTEMIC CANCER THERAPY CARE SERVICES

Saturday, November 5th, 14:40 – 15:20 • Laval, Third Floor, North Wing

Accreditation Canada has developed Ambulatory Systemic Cancer Therapy (ASCT) standards in collaboration with the Canadian Partnership Against Cancer (CPAC) and the Canadian Association of Provincial Cancer Agencies (CAPCA). These standards were developed to address key quality and safety issues in the delivery of systemic cancer therapy services, the cancer care needs of an ageing population, the number of Canadians affected by cancer, and Accreditation Canada's commitment to continuous quality improvement.

continued...
The ASCT standards were developed under the guidance of an advisory committee composed of experts in the field of oncology. In addition, the standards have been evaluated through a web-based national consultation and pilot tested in four Canadian organizations. The standards are designed for application in a variety of settings where systemic cancer therapy is offered and includes content for the multi-disciplinary team in providing safe, evidence informed, client centered care to the oncology patients receiving systemic cancer therapy services.

Accreditation Canada’s ASCT standards not only address the safety needs of clients receiving systemic cancer therapy, but provide a tool for organizations to continuously improve their services through national standards of excellence.

Presentation Objectives:
- Provide an overview of Accreditation Canada and the Qmentum program.
- Provide an overview of the motivation to develop standards for Ambulatory Systemic Cancer Therapy Services.
- Provide an overview of the process to develop national standards for Ambulatory Systemic Cancer Therapy Services.
- Outline key content in the Standards relevant to pharmacy services.
HOW DO YOU MEASURE UP?
New Accreditation Standards for Ambulatory Systemic Cancer Therapy Services

Stephanie Carpenter, Accreditation Product Development Specialist, Accreditation Canada
Roxanne Dobish, Cancer Network Pharmacy Manager, Alberta Health Services

Disclosure
Speakers have no conflicts of interest to disclose

Overview
- What is accreditation?
  - Qmentum
- Ambulatory Systemic Cancer Therapy Services
  - Partnership
  - Standards development
  - Pilot testing and national consultation
  - Release

Accreditation Canada
- National accreditation body for organizations across all health sectors since 1958
  - Over 1000 client organizations
  - Over 600 surveyors
- Independent, non-governmental, non-profit organization
- Accredited by:

Accreditation Canada
- Our clients are regional, institution-specific, national, and market-specific
- Clients are from all sectors of the care continuum
- Both public and private organizations participate
- Surveyors are senior health care professionals
Standards Areas

- **POPULATIONS (used by regions)**
  - Cancer
  - Child/Youth
  - Chronic Conditions
  - Maternal/Child
  - Mental Health
  - Public Health

- **SECTORS and SERVICES**
  - Acquired Brain Injury
  - Ambulatory Care
  - Ambulatory Systemic Cancer Therapy
  - Assisted Reproductive Technology
  - Infection Prevention and Control
  - Laboratory and Blood
  - Long Term Care
  - Managing Medications

What is accreditation?
- Process that organizations use to evaluate and improve the quality of their services
- Involves examining everyday activities and services against standards of excellence
- Strong focus on quality improvement, capacity building, and sustainability

Qmentum
- Qmentum was introduced in 2008
- Flexible process, customized to the organization’s priorities
- Outcome-oriented
- Brings QI into daily work

Qmentum standards
- Enable an organization/team to ‘stretch’ to improve care, to reach and raise the bar
- Developed with the input and guidance of experts in the field
- Updated on a regular basis to ensure relevance and value

QUALITY DIMENSIONS

<table>
<thead>
<tr>
<th>DIMENSION</th>
<th>TAG LINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>POPULATION FOCUS</td>
<td>Working with communities to anticipate and meet needs</td>
</tr>
<tr>
<td>ACCESSIBILITY</td>
<td>Providing timely and available services</td>
</tr>
<tr>
<td>SAFETY</td>
<td>Keeping people safe</td>
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<tr>
<td>WORKLIFE</td>
<td>Supporting wellness in the work environment</td>
</tr>
<tr>
<td>CLIENT-CENTRED SERVICES</td>
<td>Putting clients and families first</td>
</tr>
<tr>
<td>CONTINUITY OF SERVICES</td>
<td>Experiencing coordinated and seamless services</td>
</tr>
<tr>
<td>EFFECTIVENESS</td>
<td>Doing the right thing to achieve the best possible results</td>
</tr>
<tr>
<td>EFFICIENCY</td>
<td>Making the best use of resources</td>
</tr>
</tbody>
</table>

On-site survey activities
- REVIEW client files and documents
- RECORD what is read, heard, and seen
- OBSERVE direct observation and tours
- TALK and LISTEN to individual interviews, discussions, and group sessions
**Benefits of accreditation**

- Enables ongoing self-analysis of performance in relation to standards
- Decreases variances in practice between healthcare providers
- Provides an impetus for change and its effective management

**Benefits of accreditation**

- Demonstrates commitment to quality and accountability, and increased credibility of healthcare organizations
- Strengthens organizational learning and capacity building
- Contributes to better patient outcomes

**New Standards**

Ambulatory Systemic Cancer Therapy (ASCT) Services

**Standards Development Process**

- Literature review
- Advisory Committee
  - Face-to-face meetings
  - Teleconferences
- Site visits
- National Consultation
- National Pilot Testing

**Ambulatory Systemic Cancer Therapy**

- Partnership
  - Accreditation Canada
  - Canadian Partnership Against Cancer
  - Canadian Association of Provincial Cancer Agencies

**Advisory Committee**

- A Pan-Canadian Advisory Committee has been involved in guiding the development of the Ambulatory Systemic Cancer Therapy Services standards every step of the way
- Membership selected to represent:
  - Service providers
  - Accreditation Canada surveyors
  - Experts in the field
  - Participants from across the country
  - Range of procedures performed
Evaluation of the standards
- National Consultation
- On-site Pilot Evaluation
- Evaluation Report
- Results presented to Advisory Committee

National Consultation
- April 2011
- 2-3 Weeks
- Clear?
- Important?
- Measurable?
- Comment

On-Site Pilot Evaluation
- May / June 2011
  - Worked through the standards
  - Completed the self assessment questionnaire
  - 2-2.5 day on-site survey with Accreditation Canada surveyors
  - Provided feedback through focus group and questionnaire

Evaluation Feedback
- Evaluation Report
  - Overall, very positive feedback about the standards
  - Support for the ASCT Standards
  - Rigor of standards appropriate
  - Quality and safety issues covered in the standards
  - Positive feedback from pilot sites
  - Feedback content was discussed with the Advisory Committee and minor changes were made for the September 2011 release

Key quality and risk areas identified
- Client Access to Services
- Staff Education and Safety
- Client Education
- Safe Handling - specific to systemic cancer therapy medications
- Safe Administration
- Transfer / Support
ASCT standards

- For use:
  - By any organizations who deliver systemic cancer therapies in an ambulatory setting
  - As the primary set of service excellence standards in facilities providing ambulatory systemic cancer therapies
  - In conjunction with other standards (e.g., Cancer Care and Oncology Services Standards) in organizations providing more comprehensive oncology services

- Subsections
  - Investing in ASCT services
  - Engaging prepared and proactive staff
  - Providing safe and appropriate ASCT services
  - Maintaining safe and effective equipment
  - Maintaining accessible and efficient clinical information systems
  - Monitoring quality and achieving positive outcomes

Investing in ASCT Services

- Team develops ASCT services to meet needs of clients
- Organization provides leadership and support to deliver ASCT services

Engaging prepared and proactive staff

- Team uses interdisciplinary approach to deliver ASCT services
- Team promotes well-being and worklife balance of each of its members

Engaging prepared and proactive staff (continued)

- Team members and service providers are educated, trained, qualified, competent
- Team has up-to-date information and training regarding systemic cancer therapies

Providing safe and appropriate services

- Team delivers services that are client-centred
- Team coordinates timely access to services for current & potential clients, families, service providers, and referring organizations
- Team provides effective services to clients and families
Providing safe and appropriate services
(continued)
- Team handles systemic cancer therapy medications in a safe and accurate manner
- Team safely manages ASCT medications
- Team has specific policies and procedures for preparing and dispensing ASCT medications

Medication Content
- Content in this section is associated with the Managing Medications standards and address pharmacy specific safe handling

Medication Content
- Standards related to medication error prevention for ASCT are included

Providing safe and appropriate services
(continued)
- Team provides clients with education regarding their treatment
- Team conducts an ongoing assessment of each client
- Team safely administers ASCT medications
- Team prepares clients and families for transition to another service team, setting or service provider

Maintaining safe and effective equipment
- Organization verifies safety of medical equipment related to delivery of ASCT services

Maintaining accessible and efficient clinical information systems
- Team keeps client records accurate, up-to-date and secure
- Team has access to information technology to deliver ASCT services
Monitoring quality and achieving positive outcomes

- Team uses best available research, evidence-informed guidelines and best practice information to improve quality of services
- Team promotes safety in service environment
- Team makes ongoing improvements to ASCT services

Full set of standards available to member organizations at: www.accreditation.ca

Thank you!
Questions?

The leader in raising the bar for health quality
Le leader qui hausse la barre en matière de qualité de santé
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

DANICA LISTER
Clinical Pharmacist, CancerCare Manitoba, Winnipeg

BIOGRAPHY

Danica Lister is a pharmacist at CancerCare Manitoba in Winnipeg where she works as a clinical pharmacist within the Provincial Oncology Drug Program. She has worked in oncology since 2002, with clinical experience with a variety of solid tumour/hematological malignancies. Since 2005, she has been a member of the multidisciplinary care team in the Brain Tumour Clinic at CancerCare Manitoba.

Danica graduated from the Faculty of Pharmacy at University of Manitoba and completed an Accredited Hospital Pharmacy Residency at The Ottawa Hospital. She is a Board Certified Oncology Pharmacist, a Clinical Lecturer at the Faculty of Pharmacy, University of Manitoba, a member of the CAPhO Education Committee, and a member of the newly established pCODR Expert Review Committee.

SYNOPSIS

BREAKOUT #4: HIGH GRADE GLIOMA – COMPLEXITIES AND OPPORTUNITIES
Saturday, November 5th, 15:50 – 16:35 • Place D’Armes, Ground Floor, North Wing

High grade gliomas (HGGs) are the most common type of primary brain tumour, with over half being the most aggressive subtype, glioblastoma multiforme. High grade gliomas are rare, but incurable, and have significant disease-related morbidity and mortality. This presentation will provide an overview of the current treatment of HGGs, as well as summarize emerging therapeutic approaches. The common supportive care issues of HGG patients will be discussed and the new Response Assessment in Neuro-Oncology (RANO) criteria will be reviewed. Lastly, the important opportunities for pharmacists in the care of patients with HGGs will be highlighted.

Learning Objectives:

Upon completion of the presentation, attendees will be able to:
• Discuss the current standard treatment of high grade gliomas.
• Discuss emerging therapies for high grade gliomas.
• Identify and describe common supportive care issues in neuro-oncology patients.
• Understand the monitoring parameters used the assessment of treatment response in neuro-oncology, as compared to other solid tumour malignancies.
• Understand the pharmacist’s role in the care of patients with high grade gliomas.
Speaker & Session Descriptions / Aperçu des séances et des présentateurs

KELLY SMITH

Oncology Pharmacist, London Regional Cancer Program - London Health Sciences Centre, London, ON

BIOGRAPHY

Kelly Smith graduated from the Faculty of Pharmacy at the University of Manitoba in 1998 and then completed the hospital pharmacy residency program in Winnipeg. Kelly began her career at the Royal Victoria Hospital in Barrie, Ontario. In 2001 she moved to London, Ontario to her current employer London Health Sciences Centre, where she started in the orthopedic/trauma program. In 2002, Kelly transferred to the London Regional Cancer Program, which provides care to adult oncology patients across Southwestern Ontario.

SYNOPSIS

BREAKOUT #5: A PICTURE IS WORTH A THOUSAND WORDS: THE DEVELOPMENT OF AN ONCOLOGY PATIENT COMPLIANCE TOOL

Saturday, November 5th, 15:50 – 16:35 • Frontenac, Second Floor

This presentation will focus on the development, implementation and evaluation of an oncology patient compliance tool. The medication regimens that patients take at home as part of their cancer treatment have become more complex. Errors in taking supportive care or oral chemotherapy medications can lead to serious consequences. With the goal of improving patient understanding of how to take medications appropriately, our cancer program developed a patient compliance tool.

The web based program was developed with a computer programming student to create a patient friendly compliance tool. The pharmacist can input data into the program, which can be saved or edited, and print off a paper “calendar” for the patient to take home. This “calendar” is an illustrated medication schedule which shows the patient when to take their medication in a visual format.

Every new patient receiving supportive care medications with their chemotherapy receives a paper copy of the calendar. Patients who are prescribed complex oral chemotherapy regimens also receive a calendar.

An evaluation of the compliance tool by patients and staff is being completed at our centre. Based on the results of those evaluations future directions of the program will be determined.

Learning Objectives:

• Recognize the complexity of medication regimens in oncology patients and the need to improve patient understanding of how to properly take those medications.
• Describe the development and implementation of an oncology patient compliance tool.
• Evaluation of the compliance tool and determination of future directions.
A Picture is Worth a Thousand Words: The Development of an Oncology Patient Compliance Tool

Kelly Smith
Oncology Pharmacist
London Regional Cancer Program
London Health Sciences Centre

Disclosure
None!

Objectives
- Recognize the complexity of medication regimens in oncology patients and the need to improve patient understanding of how to take those medications
- Describe the development and implementation of an oncology patient compliance tool
- Evaluation of the compliance tool and determination of future directions

Name that Medication?

Dexamethasone: Take two tablets every 12 hours for three days starting the day before chemotherapy.
Ondansetron: Take one tablet every 12 hours for three days starting the day of chemotherapy.
Prochlorperazine: Take one tablet every 4-6 hours as needed for nausea and vomiting.
Neulasta: Inject contents of syringe 24 hours after chemotherapy.

Name That Drug

Illustrated Medication Calendar
What is in a name?

- Dexamethasone
- Prochlorperazine
- Ondansetron
- Metoclopramide
- Lomustine
- Granisetron
- Aprepitant
- Aprepitant
- Temozolomide
- Etoposide
- Temozolomide

What is in a name?

- Osatandehemex
- Zapporhiercelorn
- Sadennortan
- Codammolitreep
- Seimtulon
- Omegtaum
- Nettapiap
- Parpatten
- Delmootizoom
- Peestodio
- Mesutoomied

What is in a name?

- Stop sign/star
- Back up pill
- Yellow Football
- Little White Pill
- Green Chemo pill
- Little Triangle
- Two Day pill
- First Day Pill
- Blue Chemo
- Orange Chemo pill
- Little Chemo

The Aha Moment

- Complex Medication Regimen
- Patient Language
- Medication Calendar

What is it?
Patient JC

- 67 year old retired teacher
- Early stage breast cancer
- Cardiac history, so wish to avoid anthracyclines
- Docetaxel/cyclophosphamide (TC)

Ondansetron: Take one tablet every 12 hours for three days starting the day of chemotherapy

Dexamethasone: Take two tablets every 12 hours for three days starting the day before chemotherapy

Prochlorperazine: Take one tablet every 4-6 hours as needed for nausea and vomiting

Patient DR

- 45 year old construction worker
- Glioblastoma
- Completed radiation phase of adjuvant treatment
- Temozolomide monthly

Temozolomide 100 mg: Take two tablets daily for 5 days

Temozolomide 5 mg: Take one tablet daily for 5 days

Granisetron: Take two tablets one hour before temozolomide

Temozolomide 140 mg: Take one tablet daily for 5 days
As Easy as ...

One

Two

Three
Oral Chemotherapy
Evaluation and Future Directions

- An evaluation of the compliance tool by patients and staff is being completed at our centre.
- Based on the results of those evaluations, future directions of the program will be determined.

Patient/Caregiver Survey
Evaluation Results - Patient

In Their Own Words

I really like the calendar, especially for older people, it’s easy to read and understand. It will all be confusing on someone at just one time but each day the calendar will be clear. It’s clear what my mother needs to take.

Diagrams of pills are very helpful. Will need to use. Sizes and colors good.

It is an additional reminder of what and when to take medication. Found it very helpful. I wasn’t from missing any.

Staff Survey

Evaluation Results - Staff

Future Directions
JOHN WIERNIKOWSKI
Clinical Pharmacist, Paediatrics, McMaster Children’s Hospital, Hamilton, ON

BIOGRAPHY
John obtained his pharmacy degree from the University of Toronto (1985) and PharmD from the State University of New York at Buffalo (1987). He started working in Paediatric Haematology/Oncology at McMaster University in 1987 and has over 24 years experience in the field. John’s interests are focused primarily on management of febrile neutropenia; musculoskeletal morbidity; and thrombotic complications of cancer treatment in children. John is a full member of the Children’s Oncology Group (COG) and is actively involved with the research initiatives of the Neuroblastoma and Cancer Control Committees.

SYNOPSIS

BREAKOUT #6: CANCER, CLOTS AND KIDS
Saturday, November 5th, 15:50 – 16:35 • Laval, Third Floor, North Wing

The association of thrombosis with cancer in adults is a well known clinical entity; with good deal of information on epidemiology and potential etiology/pathogenesis. There is an increasing awareness of thrombotic complications occurring in children with cancer; and increasing study of potential factors important in the etiology and pathogenesis of this complication in this patient population.

By the end of this presentation the participant will learn about:
1. The epidemiology of Thromboembolic Events (TE) in children with cancer and the impact of age and cancer diagnosis on risk of TE.
2. The Pathogenesis of TE in children with cancer and the roles played by the malignancy, chemotherapy, central lines and inherited pro-thrombotic defects on clot development.
3. Treatment of TE once they occur with respect to:
   a. Heparins (unfractionated vs. Low Molecular Weight Heparin(s))
   b. Oral anti-coagulants
   c. Newer anti-coagulants
   d. Primary vs. Secondary prophylaxis.
Kids, Cancer and Clots
John T. Wiernikowski, PharmD, FISOPP
McMaster Children’s Hospital
Hamilton, Ontario

Disclosure Statement
No Conflicts of Interest to Declare

What we know from the Adult context
- Strong association between presence of cancer & development of acute venous thrombembolism (VTE)
- Up to 20% of patients with VTE as a first event had underlying cancer.
- Newer imaging technology finding occult/asymptomatic clots.
- More recent data indicate differences between incidence of VTE among cancer diagnoses:
  - Pancreas, CNS, Stomach, Ovarian relatively higher risk as well as Leukemia/Lymphoma patients.
  - Prostate, Breast, Melanoma have lower rates of VTE.

What we know from the Adult context
- Risk of VTE also correlates with initial Stage of disease, with advanced stage having higher risk.
  - Biological aggressiveness of the cancer is a risk factor for VTE.
  - Risk is also highest early in diagnosis and falls off over time.
- Most importantly: presence of VTE is an independent predictor of mortality.
  - When compared to all cause mortality, VTE ranks 2nd after progressive/unresponsive disease as a predictor of mortality.
  - New therapies e.g. Lenalidomide add to the risk of VTE

What we know about VTE in kids with Cancer (so far...)
- In comparison to adults, VTE in children occurs much less frequently.
  - Neonates represent the highest risk group
  - Children with cancer represent the next highest group
  - Children with cardiac conditions (esp requiring cardiac surgery); those with trauma represent the next most common group
  - Presence of an inherited pro-thrombotic disorders (Protein C/S deficiency, AT-3 deficiency, Factor V Leiden, Lupus etc.)

What we know about VTE in kids with Cancer (so far...)
- High rates of Central Venous Line (CVL) use in these populations is a major factor predicting the development of VTE.
- Among Cancers highest rates reported for:
  - Acute Lymphoblastic Leukemia (ALL)
  - Non Hodgkins Lymphoma (NHL)
  - Bone Sarcomas (Osteo, Ewings)

Table 2: Characteristics of children with thromboembolic events

<table>
<thead>
<tr>
<th>Reference</th>
<th>Total</th>
<th>Did VTE</th>
<th>Age at onset of TE</th>
<th>Venous</th>
<th>Spontaneous</th>
<th>CT, related</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revel-Weik et al. [19]</td>
<td>42</td>
<td>No</td>
<td>0.5 (0.3)</td>
<td>0.56</td>
<td>0.19 (0.25)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Li et al. [17]</td>
<td>43</td>
<td>No</td>
<td>0.5 (0.3)</td>
<td>0.56</td>
<td>0.19 (0.25)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Salazar et al. [15]</td>
<td>44</td>
<td>No</td>
<td>0.5 (0.3)</td>
<td>0.56</td>
<td>0.19 (0.25)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Incidence of TE in Children with Cancer

Athale et al, Pediatr Blood Cancer 2008;51:792

- Retrospective Cohort analysis of 726 children with cancer.
- Children with VTE were identified; and factors impacting on risk of VTE were identified.
  - CVL (type, dysfunction, infection)
  - Disease type, and location (presence of intra-thoracic disease, pelvic disease)
  - Age (+/- 10 years)
  - Gender

Incidence of TE in Children with Cancer

Athale et al, Pediatr Blood Cancer 2008;51:792

<table>
<thead>
<tr>
<th>Factors</th>
<th>Patients without TE (n = 660)</th>
<th>Patients with TE (n = 57)</th>
<th>Overall (n = 716)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>7.77 (3.3)</td>
<td>9.70 (5.48)</td>
<td>7.94 (5.54)</td>
</tr>
<tr>
<td>Gender, female</td>
<td>399 (62.6%)</td>
<td>21 (56.1%)</td>
<td>320 (44.5%)</td>
</tr>
<tr>
<td>Cancer type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL</td>
<td>211</td>
<td>30</td>
<td>14.2 (9.8, 19.7)</td>
</tr>
<tr>
<td>CNS tumor</td>
<td>201</td>
<td>1</td>
<td>0.5 (0.01, 2.7)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>101</td>
<td>12</td>
<td>11.9 (6.3, 19.6)</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>68</td>
<td>9</td>
<td>13.2 (6.2, 25.6)</td>
</tr>
<tr>
<td>AML</td>
<td>51</td>
<td>3</td>
<td>5.88 (1.23, 12.34)</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>43</td>
<td>1</td>
<td>2.33 (0.03, 6.83)</td>
</tr>
<tr>
<td>Wilms' tumor</td>
<td>42</td>
<td>1</td>
<td>2.38 (0.06, 12.57)</td>
</tr>
</tbody>
</table>

Incidence of TE in Children with Cancer

Athale et al, Pediatr Blood Cancer 2008;51:792

Incidence of TE in Children with Cancer

Athale et al, Pediatr Blood Cancer 2008;51:792

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>n</th>
<th>Patients with TE</th>
<th>% with TE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>211</td>
<td>30</td>
<td>14.2 (9.8, 19.7)</td>
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Incidence of TE in Children with Cancer

Athale et al, Pediatr Blood Cancer 2008;51:792

Incidence of TE in Children with Cancer

Athale et al, Pediatr Blood Cancer 2008;51:792

| Table V. Multivariable Analysis Evaluating the Effect of Various Risk Factors on the Prevalence of TE in Children With Cancer (n = 525) |
|---------------------------------|-----------------|-----------------|-----------------|
| Factor | Reference value | Odds ratio | 95% CI | P-value |
| Age (≥10 years) | <10 years | 1.84 | (0.90, 3.74) | 0.094 |
| Diagnosis era (recent) | Past | 2.11 | (1.18, 3.77) | 0.012 |
| Cancer type (ALL) | Other | 4.25 | (1.6, 11.32) | 0.004 |
| Cancer type (lymphoma) | Other | 2.38 | (0.77, 3.73) | 0.174 |
| Cancer type (sarcoma) | Other | 2.99 | (0.9, 9.97) | 0.073 |
Incidence of TE in Children with Cancer

Ahale et al, Pediatr Blood Cancer 2008;51:792

**TABLE IV. Univariate Analyses Evaluating the Effect of Various Risk Factors on the Prevalence of TE in Children With Cancer (n = 525)**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Reference value</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (continuous)</td>
<td>1-year increase</td>
<td>1.06</td>
<td>1.0, 1.1</td>
<td>0.024</td>
</tr>
<tr>
<td>Age (≥ 10 years)</td>
<td>&lt;10 years</td>
<td>1.82</td>
<td>1.0, 3.2</td>
<td>0.036</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>Female</td>
<td>1.21</td>
<td>0.7, 2.1</td>
<td>0.518</td>
</tr>
<tr>
<td>Cancer type (ALL)</td>
<td>Other</td>
<td>4.64</td>
<td>1.8, 12.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Cancer type lymphoma (Other)</td>
<td>Other</td>
<td>3.78</td>
<td>1.3, 11.1</td>
<td>0.016</td>
</tr>
<tr>
<td>Cancer type sarcoma (Other)</td>
<td>Other</td>
<td>4.27</td>
<td>1.4, 13.3</td>
<td>0.012</td>
</tr>
<tr>
<td>CVL (internal)</td>
<td>External</td>
<td>0.95</td>
<td>0.5, 1.8</td>
<td>0.878</td>
</tr>
<tr>
<td>Diagnosis era (recent)</td>
<td>Past</td>
<td>2.38</td>
<td>1.4, 4.2</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Pathogenesis of VTE in Children with ALL

- Commonest malignancy in childhood (~30%)
- Universal use of CVLs
- Long duration of Therapy (2+ years)
- Clear evidence of excess Thrombin generation at time of diagnosis
- Therapy under-pinned by 2 important agents
  - L-asparaginase (E. coli; PEG-asparaginase, Erwinia)
  - Corticosteroids
  - Prednisone, Dexamethasone

L-asparaginase & VTE

- Bacterially derived enzyme utilized to deplete the circulating extra-cellular asparagine pool. Lymphoblasts lack asparagine synthase; are therefore dependent upon exogenous asparagine.
- Resulting inhibition of protein synthesis impacts on formation of pro-coagulant and anti-coagulant proteins.
  - Thrombotic and hemorrhagic complications have been reported, but thrombotic complications are more commonly observed.

L-asparaginase Induced Coagulopathy

Wiernikowski JT et al; Thrombosis Res 2006; 118:137-52

- Reduced Fibrinogen, Plasminogen and Anti-Thrombin 3 (AT)
- Protein C (PC) and Protein S (PS) levels are also consistently lowered with L-asparaginase therapy; role in pathogenesis of VTE is unclear.
- Induces a consistent qualitative defect in Von Willebrand Factor (vWF)
- Effects may be amplified when given with concomitant corticosteroid therapy.
- Data on Erwinia preparations indicated less of an effect on coagulation proteins; but also less asparagine depletion compared to E. Coli preparations.

Corticosteroid Coagulopathy in ALL

- Mostly extrapolated from adult data (often from use for non-malignant disorders)
- Only 3 studies of steroid effects on coagulation proteins/parameters in children.
- Therapy with Prednisone consistently leads to:
  - Elevations in Factor VIII levels
  - Elevations in vWF
  - Elevations on Prothrombin levels
  - Decreased levels of Fibrinogen
  - Decreased levels of Plasminogen
- Some evidence that Dexamethasone may not have as big an impact on coagulopathy as Prednisone.
VTE in children with ALL on BFM Protocols—

prednisone vs. dexamethasone administration

Table 1. Plasminogen activation and fibrinolytic factors

<table>
<thead>
<tr>
<th>Procoagulant factors</th>
<th>PRED group</th>
<th>DEXA group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIIIa, units/mL</td>
<td>43 (10-60)</td>
<td>101 (43-66)</td>
</tr>
<tr>
<td>Antithrombin activity, %</td>
<td>56 (41-98)</td>
<td>76 (55-111)</td>
</tr>
<tr>
<td>Protein C activity, %</td>
<td>68 (45-146)</td>
<td>72 (53-136)</td>
</tr>
<tr>
<td>Fibrinogen, mg/dL</td>
<td>53 (38-98)</td>
<td>64 (44-103)</td>
</tr>
<tr>
<td>Plasminogen activity, %</td>
<td>47 (29-79)</td>
<td>59 (29-101)</td>
</tr>
<tr>
<td>von Willebrand Factor antigen, %</td>
<td>108 (68-172)</td>
<td>214 (100-442)</td>
</tr>
</tbody>
</table>

Median (range) values of plasminogen activation and fibrinolytic factors during maximum CAP treatment on days 27 to 33 in children during induction therapy. BFM 90/95 protocol (PRED group) versus BFM 2000 protocol (DEXA group).

Validation of a Predictive Model for TE risk in Children with ALL. Mitchell et al, Blood 2010;115:4999

- Risk Factors incorporated into Predictive Model
  - Induction phase without Steroids.
  - Treatment with L-asparaginase and steroids.
  - Presence of a CVL.
  - Genetic Thrombophilic abnormality.
  - Family History (1).
  - Combined thrombophilic abnormalities (>1).
  - Deficiency states of AT, Protein C or S were not included.

Validation of a Predictive Model for TE risk in Children with ALL. Mitchell et al, Blood 2010;115:4999
Validation of a Predictive Model for VTE Risk in Children with ALL. Mitchell et al, Blood 2010;115:4999

<table>
<thead>
<tr>
<th>Parameter of Interest</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score greater than 2.5</td>
<td>6.22</td>
<td>1.85-20.59</td>
<td>.005</td>
</tr>
<tr>
<td>Age at treat. y</td>
<td>0.94</td>
<td>0.86-1.04</td>
<td>.33</td>
</tr>
<tr>
<td>No. of AIP</td>
<td>0.76</td>
<td>0.50-1.19</td>
<td>.30</td>
</tr>
<tr>
<td>Brovias versus Port</td>
<td>0.90</td>
<td>0.25-3.20</td>
<td>.88</td>
</tr>
<tr>
<td>Enoxaparin (yes)</td>
<td>2.58</td>
<td>0.80-15.90</td>
<td>.094</td>
</tr>
<tr>
<td>Transition y</td>
<td>1.40</td>
<td>0.18-10.90</td>
<td>.74</td>
</tr>
</tbody>
</table>

**Treatment of VTE in Children with Cancer**

- Rarity of VTE in children vs. adults.
- Evolution of the coagulation is a continuum from neonates through to puberty.
- Lack of child friendly doseage forms.
- Additional complexities in children with cancer.
  - Impact of Therapy on Nutritional status.
  - More frequent episodes of F/N ➔ Antibiotic induced changes in gut flora.
  - More marrow suppression ➔ Thrombocytopenia.
- Most data [initially] has been extrapolated from adult studies.

**Challenges in Defining Optimum Therapy for Children with VTE**

- Rarity of VTE in children vs. adults.
- Evolution of the coagulation is a continuum from neonates through to puberty.
- Lack of child friendly doseage forms.
- Additional complexities in children with cancer.
  - Impact of Therapy on Nutritional status.
  - More frequent episodes of F/N ➔ Antibiotic induced changes in gut flora.
  - More marrow suppression ➔ Thrombocytopenia.
- Most data [initially] has been extrapolated from adult studies.

**Guidelines for Antithrombotic Therapy for Children with Cancer**

- Initial Therapy (Idiopathic VTE)
  - Unfractionated Heparin to achieve anti-Xa activity of 0.35-0.7 Units/mL.
  - Low Molecular Weight Heparin (LMWH) to achieve anti-Xa activity of 0.5 – 1 Units/mL.
  - Initial treatment of 3-5 days and then transition to Warfarin (for children without cancer)
  - Transition to (or continue) LMWH in children with cancer.
  - Treat for a minimum of 3-6 months.

- Secondary VTE in children with Cancer.
  - Same dosing recommendations as for idiopathic VTE.
  - Continue for as long as putative risk factor(s) is/are in place or at least 3 months.
  - If CVL is functional...no need to remove.
  - Interrupt [if necessary] L-asparaginase therapy to re-establish blood flow in smaller blood vessels. L-asparaginase therapy can be completed.
  - After initial 3 months of therapy, transition to prophylaxis to maintain anti-Xa activity of ~ 0.5 Units/mL.
  - If re-thrombosis occurs, re-initiate therapy for a further 3 months, then continue prophylaxis.
**Guidelines for Antithrombotic Therapy for Children with Cancer**  
Monagle P et al, Chest 2008(133):8875-968S

- What about Primary Prophylaxis?
  - PARKAA Study  
    - Open Label study of Antithrombin supplementation in children with ALL.
  - Trend in favour of supplementation, but ultimately NS and not sufficiently powered to determine efficacy.
  - Warfarin prophylaxis for CVI related VTE  
  - Randomized trial of low dose warfarin.
  - Study terminated early due to lack of efficacy.
  - PROTEKT Trial  
  - LMWH (Reviparin) compared to standard care.
  - Low recruitment, terminated early.
  - No difference observed between groups.

**Newer Anticoagulants in Children with VTE**

**Direct Thrombin Inhibitors (DTIs)**

- Argatroban
  - Reversibly binds to catalytic site of Thrombin.
  - Inhibits Thrombin induced/catalyzed reactions.
  - May lead to false elevations in INR levels.
  - Experience limited to kids having cardiopulmonary by-pass, ECMO, or who have experienced HIT from UFH/LMWH.

- Bivalirudin
  - Direct binding to Thrombin (without co-factor).
  - Inhibits Thrombin mediated platelet activation.
  - Published data limited ot ECMO, CPB, and case reports of use in HIT.

- Dabigatran
  - Direct binding to Thrombin.
  - Marketed in Europe for prophylaxis post knee/hip surgery.
  - Phase II study in adolescents is currently on-going.

**Direct Thrombin Inhibitors (DTIs)**

- Lepirudin
  - Irreversibly binds to active and fibrinogen binding exosite of Thrombin.
  - Able to bind to both circulating and clot-bound Thrombin.
  - Due to potency, greater concern over bleeding complications.
  - Similar data as for other DTIs.

- Fondaparinux
  - Direct binding to Thrombin
  - Marketed in Europe for prophylaxis post knee/hip surgery.
Factor Xa Inhibitors  Chan VH et al, Blood Coag & Fibrinolysis 2010(21):144-51

Table 1  Factor Xa inhibitors

<table>
<thead>
<tr>
<th>Name of action</th>
<th>Tinzaparin Sodium (INN)</th>
<th>Fondaparinux</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of action</td>
<td>Activity of factor Xa activation inhibited</td>
<td>Activity of factor Xa activated</td>
</tr>
<tr>
<td>Habitat</td>
<td>Impaired in all tissues, including tissues in the leg</td>
<td>Impaired in all tissues, including tissues in the leg</td>
</tr>
<tr>
<td>Reactivity</td>
<td>Reactivity to factor Xa</td>
<td>Reactivity to factor Xa</td>
</tr>
<tr>
<td>Lumping time</td>
<td>Lumping time</td>
<td>Lumping time</td>
</tr>
<tr>
<td>Dose (mg)</td>
<td>Dose (mg)</td>
<td>Dose (mg)</td>
</tr>
<tr>
<td>PT, aPTT, INR</td>
<td>PT, aPTT, INR</td>
<td>PT, aPTT, INR</td>
</tr>
</tbody>
</table>

**Questions?**

Thank you for your attention
**Speaker & Session Descriptions / Aperçu des séances et des présentateurs**

**LUCIE SURPRENANT**

Oncology Pharmacy Coordinator, St. Mary’s Hospital Center, Montreal, QC

**BIOGRAPHY**

Lucie Surprenant graduated in 1978 from Université de Montréal as a pharmacist and works in oncology since 1992. She became a Board Certified Oncology Pharmacist (BCOP) in 2000. Lucie is a member of Comité d’évolution de la pratique en oncologie (CEPO), Direction québécoise du cancer. She chairs the groupe des pharmaciens du CEPO, responsible for the elaboration of Administration Guides and patient information pamphlets, available on the GEOQ website. She is the co-author of a few publications (e.g. OnTarget) and web-based programs and gave many presentations in the oncology community over the years.

**SYNOPSIS**

**BIOMARKERS IN CANCER: SHOULD WE GET INVOLVED?**

*Sunday, November 6th, 10:30 – 11:15 • Frontenac, Second Floor*

This presentation will give an overview of biomarkers in cancer, their importance in establishing a diagnosis, selecting the appropriate treatment, monitoring efficacy or progression. Clinical cases will illustrate their uses and limitations. Pharmacists’ understanding of this growing topic is crucial for dispensation of quality pharmaceutical care and will be discussed.

**Learning Objectives:** After this presentation, the participants will be able to

- Recognize clinically significant biomarkers
- Determine the appropriateness of selected therapy based on the biomarkers.
- Monitor the efficacy or suspect progression based on the biomarkers.
Biomarkers in Cancer: Should We Get Involved?

Lucie Surprenant, B.Pharm, MSc, BCOP
St. Mary's Hospital Center, Montreal

2011-11-05

Potential Conflicts of Interest

- Amgen
- Bristol Myers Squibb
- Celgene
- Glaxo Smith Kline
- Hoffman-La Roche
- Hospira
- Janssen
- Merck
- Novartis
- Ortho-Janssen
- Sanofi-Aventis

2011-11-05

Biomarkers:

- Her-2
- Ki-67
- CEA
- CD-20
- PSA
- BRCA1, BRCA2
- CA-125
- K-ras
- ER, PR
- β-2 microglobuline
- EGFR
- β-HCG
- TTF-1
- CA 19-9
- α-fetoprotein
- C-Kit
- CA 15-3
- BCR-ABL

2011-11-05

Ideal Tumor Marker

- Protein or protein fragment that can be easily detected
- in the patient’s blood or urine only when cancer is present
- in tissues by the pathologist using different methods
- IHC (Immunohistochemistry)
- Fish (Fluorescence in situ hybridization)
- ELISA (Enzyme-linked immunosorbent assay)
- Chip Technology

2011-11-05

Type of Tumor Markers

- Proteins
  - Cell-surface receptors (e.g. CD-20)
  - Tumoral antigen such as PSA,
  - Peptides found in serum, urine, sputum, body fluids
- RNA-based markers
- DNA-based markers
  - Single-nucleotide polymorphisms (SNPs)
  - Chromosomal Aberrations (e.g. BCR-ABL translocation)
  - Microsatellite instability (Changes in the number of copies of DNA)
  - Differential promoter-region methylation

2011-11-05

Clinical Use of Biomarkers

- Before diagnosis
  - Risk assessment (e.g. BRCA-1 or 2)
  - Screening (e.g. PSA)
- At diagnosis
  - Staging (sometimes included in a prognostic index such as LDH in FLIPI)
  - Identification in a pathologic sample (ex: TTF-1 or HER-2)

2011-11-05
Clinical Use of Biomarkers

- **After diagnosis**
  - Treatment selection (e.g., Her-2, CD-20, Bcr-Abl, c-KIT)
  - Response monitoring in conjunction with physical exam and medical imaging
  - Recurrence detection (CA-125, CEA, PSA)

- Several biomarkers are non-specific and may be elevated in benign conditions (CA-125, CEA)

Biomarkers throughout the clinical evolution of cancer

<table>
<thead>
<tr>
<th>Case #1: 50 y woman with breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date</strong></td>
</tr>
<tr>
<td>Initial diagnosis Jan 2001: ER+PR- Adj Tx: Doxo-Docetaxel (NSABP B-30 group 2 followed by TAM)</td>
</tr>
<tr>
<td>Recurrence April 2003 Her 2+ Tx: trastuzumab- vinorelbine</td>
</tr>
<tr>
<td>Sept 2006 progression vino replaced by capecitabine-trastuzumab continued</td>
</tr>
<tr>
<td>09-06-06</td>
</tr>
<tr>
<td>09-06-09</td>
</tr>
<tr>
<td>09-07-20</td>
</tr>
<tr>
<td>09-07-02</td>
</tr>
<tr>
<td>09-09-14</td>
</tr>
<tr>
<td>09-12-07</td>
</tr>
<tr>
<td>10-02-01</td>
</tr>
<tr>
<td>10-07-05</td>
</tr>
<tr>
<td>Next treatment: patient will refuse any treatment which will cause hair loss. EOCOG 1. Her decision: Palliative care. Patient died in November 2010</td>
</tr>
</tbody>
</table>

Breast Cancer

<table>
<thead>
<tr>
<th>Step</th>
<th>Biomarker</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>BRCA-1 or BRCA-2 mutation</td>
<td>Genetic counseling</td>
</tr>
<tr>
<td>Staging (prognosis)</td>
<td>ER, PR</td>
<td>Hormonal Treatment</td>
</tr>
<tr>
<td></td>
<td>Her-2</td>
<td>Trastuzumab</td>
</tr>
<tr>
<td></td>
<td>Ki-67</td>
<td>Chemotherapy or not</td>
</tr>
<tr>
<td></td>
<td>Oncotype DX</td>
<td>Treatment</td>
</tr>
<tr>
<td>During and after treatment</td>
<td>CA15-3, CEA, CA-125</td>
<td>Monitoring</td>
</tr>
</tbody>
</table>

Ovarian Cancer

<table>
<thead>
<tr>
<th>Step</th>
<th>Biomarker</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staging (prognosis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>During and after treatment</td>
<td>CA-125</td>
<td>Monitoring</td>
</tr>
</tbody>
</table>
CA-125 and Ovarian Cancer

- CA 125
  - Useless for screening because of its low selectivity and specificity
  - CA-125 is elevated in several benign conditions such as diverticulitis, normal periods, endometriosis and other cancers
  - Used for monitoring of disease
  - Role in early detection of a recurrence
  - Controversial since the presentation at ASCO 2009 of an abstract during the Plenary Session. (J Clin Oncol 27:18s, 2009 suppl; abstr 1)
  - No survival benefit when patients are treated based on a CA-125 elevation compared with starting treatment when the patient becomes symptomatic.

Case #2: 78 y woman with ovarian cancer

<table>
<thead>
<tr>
<th>DATE</th>
<th>CA-125</th>
<th>COMMENTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>05-12-06</td>
<td>227.9</td>
<td>Pre-op</td>
</tr>
<tr>
<td>06-01-12</td>
<td>100.1</td>
<td>Start paclitaxel-carbo</td>
</tr>
<tr>
<td>06-07-12</td>
<td>14.0</td>
<td>Last paclitaxel-carbo (total 8)</td>
</tr>
<tr>
<td>07-05-06</td>
<td>152.7</td>
<td>Cisplatin chemo</td>
</tr>
<tr>
<td>07-07-17</td>
<td>63.5</td>
<td>Cisplatin stopped(noneffective ++++))</td>
</tr>
<tr>
<td>07-08-14</td>
<td>51.8</td>
<td>Carboplatin-AUC 2 with variable intervals</td>
</tr>
<tr>
<td>07-11-28</td>
<td>98.7</td>
<td>Last carboplatin</td>
</tr>
<tr>
<td>07-12-12</td>
<td>108.0</td>
<td>Liposomal doxorubicin</td>
</tr>
<tr>
<td>08-07-03</td>
<td>159.8</td>
<td>Last Liposomal doxorubicin</td>
</tr>
<tr>
<td>09-07-08</td>
<td>323.4</td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>09-11-28</td>
<td>987.0</td>
<td>Last gemcitabine</td>
</tr>
<tr>
<td>10-01-06</td>
<td>1933.0</td>
<td>Topotecan</td>
</tr>
<tr>
<td>10-03-24</td>
<td>5322.0</td>
<td>3rd cycle topotecan – treatment discontinued</td>
</tr>
</tbody>
</table>

Colorectal Cancer

- CEA: Oncofetal protein expressed during embryonic development
- Increased with many gastro-intestinal tumors
- ASCO guidelines for the use of CEA
  - Should be obtained preop in patients with known CRC to aid for staging, surgical treatment planning, assessment of prognosis
  - Also increased in non-cancerous diseases
  - Pancreatitis, hepatitis, renal failure, smoking
  - CEA not a screening tool!!

Case #3: 75 y man with colon cancer

<table>
<thead>
<tr>
<th>DATE</th>
<th>CEA</th>
<th>COMMENTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-01-11</td>
<td>33.8</td>
<td>Pre-op</td>
</tr>
<tr>
<td>2010-02-10</td>
<td>85.0</td>
<td>Post-op, chemo delayed because of poor ECOG due to unrelated back problems</td>
</tr>
<tr>
<td>2010-02-17</td>
<td>38.1</td>
<td>S-FU, LV, irinotecan, irinotecan + CPT-1155</td>
</tr>
<tr>
<td>2010-03-17</td>
<td>59.9</td>
<td>Bevacizumab-POLFOX</td>
</tr>
<tr>
<td>2010-05-24</td>
<td>59.1</td>
<td></td>
</tr>
<tr>
<td>2010-08-04</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>2010-09-15</td>
<td>7.9</td>
<td>Scan confirms progression</td>
</tr>
<tr>
<td>2010-10-19</td>
<td>9.4</td>
<td>FOLFRI</td>
</tr>
<tr>
<td>2011-01-16</td>
<td>8.2</td>
<td></td>
</tr>
<tr>
<td>2011-04-27</td>
<td>40.0</td>
<td>Test for K-RAS mutation requested</td>
</tr>
<tr>
<td>2011-06-10</td>
<td>47.8</td>
<td>Cetuximab/EZN-38 started</td>
</tr>
<tr>
<td>2011-06-20</td>
<td>101.3</td>
<td>Scan requested, to continued</td>
</tr>
<tr>
<td>2011-09-03</td>
<td>149.7</td>
<td>Progression confirmed, transfer to PCU</td>
</tr>
</tbody>
</table>

Pancreatic Cancer

- CA 19-9 Monitoring

<table>
<thead>
<tr>
<th>Step</th>
<th>Biomarker</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staging (progress)</td>
<td>CA 19-9</td>
<td>Monitoring</td>
</tr>
<tr>
<td>During and after treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Case #3: 75 y man with colon cancer

- CEA: Oncofetal protein expressed during embryonic development
- Increased with many gastro-intestinal tumors
- ASCO guidelines for the use of CEA
  - Should be obtained preop in patients with known CRC to aid for staging, surgical treatment planning, assessment of prognosis
  - Also increased in non-cancerous diseases
  - Pancreatitis, hepatitis, renal failure, smoking
  - CEA not a screening tool!!
Prostate Cancer

- PSA (Prostate-Specific Antigen)
  - Specific to prostate but not specific to cancer
  - Screening tool but needs interpretation
    - Increased by prostatic manipulation, prostate biopsy, TURP, BPH, and prostatitis
    - Decreased by 50% by finasteride, dutasteride
  - Diagnosis requires a prostate biopsy
  - Monitoring of therapy

Non Small Cell Lung Cancer

Screening

<table>
<thead>
<tr>
<th>Step</th>
<th>Biomarker</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Diagnostic

- TTF-1

Choice of therapy

- EGFR mutation
  - Response to gefitinib

During and after treatment

- CEA Monitoring

Case #6: 41y man with an unknown primary cancer

<table>
<thead>
<tr>
<th>Date</th>
<th>CEA</th>
<th>CA-125</th>
<th>CA 19-9</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-06-23</td>
<td>4.7</td>
<td>103.4</td>
<td>324.7</td>
</tr>
<tr>
<td>10-07-14</td>
<td>7.6</td>
<td>3578</td>
<td></td>
</tr>
<tr>
<td>10-07-21</td>
<td>8.0</td>
<td>106.2</td>
<td>2635</td>
</tr>
<tr>
<td>10-08-12</td>
<td>3.5</td>
<td>67.6</td>
<td>1690.2</td>
</tr>
<tr>
<td>11-01-26</td>
<td>1.6</td>
<td>22.2</td>
<td>169.0</td>
</tr>
<tr>
<td>11-05-26</td>
<td>2.9</td>
<td>618.6</td>
<td>565.3</td>
</tr>
<tr>
<td>11-07-20</td>
<td>8.9</td>
<td>463.6</td>
<td>1413.4</td>
</tr>
</tbody>
</table>

Pathologic unable to identify the primary cancer/Abdominal symptoms, weight loss, ECOG 1: Treatment choice between ECF or unknown primary regimen (paclitaxel, carboplatine, gemcitabine)

- Treatment re-started
- Progression; Tx stopped
Case #7 Oncologist’s Dilemma...

What is the diagnosis based on the following tumor markers?

Answer came from the pathologist.

Examples of Other Tumor Markers

- p53 mutations
  - Associated with inferior survival rates in patients with NSCLC
- β2 microglobulin
  - Prognostic indicator in patients with multiple myeloma or lymphoma
- Microsatellite instability (MSI)
  - Not currently used at the moment. Could predict if chemo (5-Fu) will bring benefit to a patient

Biomarkers in the Future

- They will be used for screening, diagnosis, monitoring of treatment and prediction of recurrence.
- Help in the decision-making process regarding the treatment of a specific patient with cancer
  - Treatment or not
  - Selection of therapy
  - Surgery or not
  - Surgery and/or radiotherapy
    - Extent of surgery (e.g. Total mastectomy vs partial)
    - When to use systemic treatments

The Path to Personalized Medicine

- Success depends on accurate diagnostic tests to identify patients that can benefit from targeted therapies

- 5FU: 5-Fluorouracil
- Cisplatin: Cisplatin
- Carboplatin: Carboplatin
- Paclitaxel: Paclitaxel
- Gemcitabine: Gemcitabine
- Etoposide: Etoposide
- Bevacizumab: Bevacizumab

My Answer to the Question: Should We Get Involved?

- YES, absolutely!
- As pharmacists, we are responsible for
  - Make sure the patient receives the appropriate therapy
  - Monitoring of the therapy
  - Patient education and counselling

Understanding the increasing role of tumor markers will benefit our patients!

questions?
CARLO DE ANGELIS  
Clinical Pharmacy Coordinator - Oncology, Sunnybrook Health Sciences Centre, Toronto, ON

BIOGRAPHY

Carlo earned his Bachelor of Science in Pharmacy from the University of Toronto in 1981 and completed a Hospital Pharmacy Residency at Sunnybrook Health Sciences Centre in 1982. He graduated with a Doctor of Pharmacy from the State University of New York at Buffalo in 1984. From 1985 to the present, Carlo has been the Clinical Pharmacy Coordinator for Oncology at the Odette Cancer Centre, Sunnybrook Health Sciences Centre and has owned and managed a community pharmacy, Panacea Pharmacy since 1994. He is the current President of the Canadian Association of Pharmacy in Oncology.

SYNOPSIS

THERAPEUTIC DRUG MONITORING FOR TARGETED AGENTS IN ONCOLOGY PRACTICE: BACK TO THE FUTURE IN CLINICAL ONCOLOGY PHARMACY PRACTICE  
Sunday, November 6th, 11:15 – 12:00 • Frontenac, Second Floor

Therapeutic Drug Monitoring (TDM) for a broad range of medications has been used in the clinical care of patients with various medical conditions for over 50 years. Despite pharmacologic characteristics (narrow therapeutic range, large inter-/intra- patient pharmaco-kinetic/dynamic variability) which would make antineoplastic agents ideal candidates for TDM; with the exception of the monitoring of methotrexate levels to guide leucovorin rescue TDM is not used in day to day adult clinical oncology practice. Although there has been much research with the aim of individualizing anticancer therapy, the application of TDM principles in oncology has been hindered by several factors, including: the heterogeneity in tumour biology (even within the same tumor type), a poor understanding of the drug concentration–pharmacologic–effect (either efficacy or toxicity) relationship, the use of combination therapy, the difficulty in characterizing how the interaction of the various agents in the combination influence the drug- (either individually or collectively) concentration–pharmacologic–effect relationship, intermittent/pulsed dosing strategies, the delayed/cumulative effects of these agents and the difficulty in measuring drug concentrations in vivo. However the recent therapeutic advances in anticancer therapy involving targeted anticancer medications will soon change this.

Targeted anticancer agents have pharmacological characteristics very distinct from “traditional” antineoplastic agents. The molecules are designed to interact with specific extra/intra-cellular receptors which influence cell growth, replication and angiogenesis, are highly selective with respect to receptor binding; they are thought to be cytostatic rather than cytotoxic, are typically given on a continuous basis and are predominantly orally administered. Recently there is evidence that to achieve benefit from a targeted therapy there is a need for the patient to have an optimal systemic exposure to the drug as measured by either trough serum concentrations or area under the plasma-concentration-time curve. While the oral route of administration for many of these agents has clear advantages for the patient with respect to obviating the need for intravenous drug administration, it does put onus on the patient to be adherent to therapy. Despite the life threatening nature of cancer, the need for long term administration of these agents combined with their associated side effects has contributed to patient non-adherence to therapy. An additional challenge with the orally administered targeted therapies is the potential for drug-drug interactions which may influence systemic exposure contributing to either loss of efficacy or increased toxicity.

The above circumstances have led to a renewed discussion and consideration of the role of TDM in oncology practice. The presentation will review the current state of knowledge regarding the relationship between systemic exposure to such targeted agents as imatinib, sunitinib, gefitinib, erlotinib and sorafenib and therapeutic response. The use of TDM to assess not only therapeutic efficacy but also for adherence monitoring of targeted anticancer therapy will be discussed. An algorithm for interpreting drug concentration values, clinical decision making and dose adjustments for targeted therapies will also be proposed.
Therapeutic Drug Monitoring for Targeted Agents in Oncology Practice: Back to the Future in Clinical Oncology Pharmacy Practice

Carlo De Angelis, RPh, PharmD
Clinical Pharmacy Coordinator – Oncology
Clinical Pharmacology Rounds
2011-September-29

DISCLOSURE
No Conflicts of Interest

Objectives
At the end of this presentation you will be able to:
• Discuss the importance of dose individualization and the concept of therapeutic drug concentrations when using targeted anticancer therapies
• Discuss the various factors that may affect attainment of therapeutic concentrations of targeted anticancer therapies
• Describe the potential role of therapeutic drug monitoring of targeted therapy in oncology

Therapeutic Drug Monitoring in Oncology - The Past/Future
"If recent emphasis on dose and a critical factor in success of cancer chemotherapy is substantiated, then the need to apply therapeutic drug monitoring within oncology will become more pressing"
Moore MJ and Erlichman C 1987
"The expanded application of therapeutic drug monitoring to the clinical practice of oncology will require a better understanding of the relationship between drug levels, toxicity, and therapeutic benefit . . ."
Henner WD Clin Lab Med 1987

History of Systemic Cancer Therapy
Chabner BA et al. Nature Reviews Cancer 2005

What is Targeted Therapy?
"An agent directed against predetermined & well-defined extracellular, transmembrane, or intracellular molecules involved in pathways controlling cellular growth, differentiation, transcription, or angiogenesis"
Ideal Characteristics of a Targeted Therapy Agent

- High specificity & affinity for target
- Good oral absorption
- Metabolically stable - Long half-life
- No interaction with cytochrome P450
- Favourable toxicity profile

Goal of Targeted Therapy Development

Cytotoxic Drug Dose Response Curve  Targeted Drug Dose Response Curve

Challenges in Development of Targeted Agents

- Cytostatic instead of cytotoxic
- Traditional Phase I study design/endpoints irrelevant
  - Dosing based on body surface area
  - Wide therapeutic window
  - MTD dose strategy may not be applicable
- Not all patients or tumour types express target

Clinical Pharmacology Developments in Oncology

- Pharmacogenetic Determinants
  - Polymorphisms in drug ADME
  - Dihydropyrimidine dehydrogenase & Thiopurine methyltransferase, Methylenetetrahydrofolate reductase
  - Role of single nucleotide polymorphisms in drug metabolizing/Transporting genes
    - Cytochrome P450
    - UDP-glucuronosyltransferases
    - Transporter proteins
- Tumour regulatory genes
  - Methyguanine methyltransferase, Thymidylate synthase
  - Microarray technology
- Integrated modeling
Targeted Therapy - EGFR

How Do TKIs Work - Imatinib
http://www.hai-bin.net/images/CML03.jpg

Imatinib Clinical Activity

Measuring Response to CML Therapy

Imatinib Clinical Activity
Imatinib Clinical Activity

Imatinib & Survival in CML

Imatinib Concentration Response in CML

Efficacy of Imatinib in Advanced GIST - Dose Response
GIST Meta-Analysis Group JCO 2010

Clinical Benefit

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Complete Response</th>
<th>Cytogenetic Response</th>
<th>Major Response</th>
<th>Complete Cytogenetic Response</th>
<th>Minor Response</th>
<th>Overall Improvement</th>
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<td>750</td>
<td>1000</td>
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Adverse Effects

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<td>40%</td>
<td>15%</td>
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<tr>
<td>1</td>
<td>60%</td>
<td>30%</td>
<td>10%</td>
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Efficacy of Imatinib in Advanced GIST - Dose Response
GIST Meta-Analysis Group JCO 2010

Overall Survival

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<tr>
<td>200</td>
<td>80%</td>
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<tr>
<td>300</td>
<td>70%</td>
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<td>400</td>
<td>60%</td>
</tr>
<tr>
<td>500</td>
<td>50%</td>
</tr>
<tr>
<td>600</td>
<td>40%</td>
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Carlo De Angelis
Presentation Handouts pg4
Imatinib in Advanced GIST - Dose Response and Therapy - Dose Reduction and Discontinuation

<table>
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<tr>
<th>Grade</th>
<th>400 mg twice a day</th>
<th>800 mg twice a day</th>
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<tr>
<td>Treatment interruption</td>
<td>10/166 (6%)</td>
<td>36/308 (12%)</td>
</tr>
<tr>
<td>Non-hematological adverse effects</td>
<td>32/166 (20%)</td>
<td>32/308 (19%)</td>
</tr>
<tr>
<td>Severe adverse events</td>
<td>16/166 (10%)</td>
<td>57/308 (19%)</td>
</tr>
<tr>
<td>Hand-foot syndrome</td>
<td>24/166 (15%)</td>
<td>35/308 (11%)</td>
</tr>
<tr>
<td>Tumor progression</td>
<td>15/166 (9%)</td>
<td>38/308 (13%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>5/166 (3%)</td>
<td>9/308 (3%)</td>
</tr>
<tr>
<td>Not reported</td>
<td>1/166 (0.6%)</td>
<td>2/308 (0.7%)</td>
</tr>
</tbody>
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Imatinib Concentration Response in GIST
Demetri GD, et al. JCO 2009

Adherence to Imatinib
Tsang J et al. 2006 ASCO Annual Meeting - Abstract #6119

Can Plasma Concentrations of Imatinib be used to Identify Non-Adherence?

- Number of patients with full persistence was near 100% through month 6.
- Number of patients with full persistence declined from 94% at month 3 to 23% at month 18.
Probability of Non-Adherence versus Pharmacokinetic Variability

A Tale of Two TKIs - Gefitinib and Erlotinib


A Tale of Two TKIs - Gefitinib and Erlotinib


A Tale of Two TKIs - Gefitinib and Erlotinib

Gefitinib Unbound Trough Concentration and In Vitro IC\textsubscript{50}

Li J et al. JNCI 2006

Gefitinib 250 mg daily

Gefitinib 500 mg daily
Drug Interactions - Erlotinib Case Report
Mir O, et al. NEJM 2011

- 78 yo female with advanced lung adenocarcinoma
- Non-smoker
- Hx of depression and dyslipidemia
- Escitalopram 15 mg daily
- Alprazolam 0.5 mg three times daily
- Fenofibrate 20 mg daily
- Started on erlotinib 150 mg
  - At 2 months progressive disease
  - Not diarrhea or skin rash
  - Erlotinib concentration trough = 657 ng/mL
    (Mean concentration from phase I trials 1200 ng/mL)
  - Dose increased to 200 mg then 300 mg/day
  - Erlotinib trough concentration = 1360 ng/mL
  - Patient had grade 1 rash
  - CT scan showed improvement in disease

Systemic Exposure to Sunitinib and Response

Summary
- There is large inter/intra-patient variability in systemic exposure to orally administered TKIs
- Measures of systemic exposure to TKIs may predict response to therapy
- Optimizing treatment response to TKIs will require:
  - Selection of appropriate patient population based on tumor biology
  - Therapeutic Drug Monitoring to:
    - Optimize systemic exposure
    - Identify non-adherence and develop strategies to maintain adherence
    - Avoidance/management of drug interactions
**Speaker & Session Descriptions / Aperçu des séances et des présentateurs**

**MARIO DE LEMOS**  
Provincial Drug Information Coordinator, Systemic Therapy, BC Cancer Agency, Vancouver, BC

**BIOGRAPHY**

Mário de Lemos is the Provincial Drug Information Coordinator at the British Columbia Cancer Agency and a Clinical Assistant Professor of the Faculty of Pharmaceutical Sciences at the University of British Columbia. Mário was trained as a pharmacist in the UK, completing his BSc(Hons) in Pharmacy at Leicester Polytechnic and pre-registration training at King's College Hospital, London. He obtained his MSc in Clinical Pharmacy from Queen's University in Belfast, PharmD from the University of British Columbia, and MSc in Oncology from the University of Newcastle in UK.

**SYNOPSIS**

**PHARMACY RESEARCH BY “NON-RESEARCH” PHARMACISTS**

*Sunday, November 6th, 12:00 – 12:30 • Frontenac, Second Floor*

Conducting research is often viewed as ideal but non-essential outside of an organization devoted to research. This is partly due to the misconception of equating research with basic research undertaken primarily to acquire new knowledge without any particular application in view. This has two consequences. First, many pharmacists and pharmacy technicians see little relevance in research with their daily practice unless they are closely involved in the academia or residency programs. Second, practitioners may find it difficult to formulate everyday problems into researchable questions.

This presentation will share the experience of conducting various pharmacy-led projects at the British Columbia Cancer Agency.

**Learning Objectives:** At the end of the presentation, the participants should be able to:

- explain how to identify issues from daily practice for potential research questions
- explain how to formulate potential questions into research projects
- identify the key resources needed to conduct a research project
Pharmacy Research
For Non-Research Pharmacists

Mário de Lemos  
Provincial Drug Information (druginfo@bccancer.bc.ca)  
British Columbia Cancer Agency  
Vancouver, BC

Disclosure

• No real or apparent conflicts of interest

Is research for you?

• To solve practice-related problems
  – “non-career researcher”
• Research
  – systematic investigation to generate knowledge
    • Basic research: no particular application in view
    • Applied research: known application
• Development
  – systematic work based on existing knowledge
to develop or improve products and processes

My research history

• Azo dye degradation (1987)
  – mandatory: BSc thesis
  – not practice-related
• ACE inhibitors in CHF (1995)
  – mandatory: MSc thesis
  – (kind of) practice-related
• Pamidronate and renal failure (2003)
  – mandatory: drug information request
  – practice-related

Approach

• Who cares
• When
• How much

Who cares

• Timeliness – medium urgency
  – Very urgent: no time for research
  – Low urgency: no one cares?
• Importance
  – risk of NOT doing the research
  – impact on daily practice
• Unique
  – Would no one else look into it?
When

• How much evidence is enough?
  – Decision making (literature?, expert opinion?)
  – How long can you wait?
• How much time can you spare?
• What data do you already have?
  – Mental experiment
    • Convenient endpoint
    • Clinically significant difference
    • How to present the data
    • Defend assumptions

Money

• Keep it within current resources
  – Time: your own, student
  – Scope: to fit available data, make assumptions
• Grant money – not very helpful
  – Cyclic (e.g., annually)
  – Stimulates ambitious or "made-up" projects

Housekeeping

• Ethics – audit vs. research
• Principal Investigator – anchor
  – Co-investigators – share work, stakeholders
• Proposal – good for many things
  – Ethics, grant
  – Method guide
  – Final report
• BMJ Pocket Guide to Grant Applications

Examples

• Renal safety of pamidronate
  – 1-hour vs. 2-hour infusion
• Renal dosing of cancer drugs
  – MDRD vs. Cockcroft-Gault formulas
• Advising on natural health products
  – Clinical impact of a structured approach

Pamidronate – who cares

• Is 1-hr infusion of pamidronate safe?
• Timeliness – BCCA standard
  – based on 1 large RCT (ASCO 1999 abstract)
  – ASCO & manufacturers: 2-hr infusion (2002)
• Importance
  – Risk: renal dysfunction
  – Impact: 2-hr infusion ↑ workload
    • zoledronic acid: 15-min infusion, ↑ cost
• Unique – few people adopted 1-hr infusion

Pamidronate – when

• Evidence – literature, BCCA data audit
  – Answer within ~3 months
• How much time can you spare?
  – Investigators
• What data do you already have?
  – pharmacy orders, serum creatinine (SrCr)
    • Endpoint: renal dysfunction (RD) = SrCr, 2 x baseline
    • Clinical difference: >10% increase in RD vs. RCT
    • Presenting data: % of patients with RD
    • Assumptions: e.g., relative SrCr Δ, superiority study design
Pamidronate – money
• Within current resources
  – Time: 2 pharmacists, on and off x 2 months
  – Scope
    • Data: pts and Tx from pharmacy orders
    • Assumptions: renal dysfunction = 2 x baseline
• Grant money
  – ASCO deadline Dec 2003
  – CSHP: applied Oct 2003, $2500 Feb 2004

GFR – who cares
• Is lab reported GFR reasonable for dosing? 
• Timeliness – BC labs adopted MDRD eqn.
  – reporting GFR with SrCr (Oct 2003)
  – staff confused
• Importance
  – Dosing errors
  – Commonly used for drug dosing
• Unique – no expert advice
  – nephrologists used it for screening, not dosing

GFR – money
• Within current resources
  – Time:
    • 2 pharmacists + 1 student (Jan-Sep 04)
    • 2 pharmacists (Nov 2005-Dec 2006); 3 physicians
  – Scope
    • Data: pts and Tx from pharmacy orders, SrCr from lab, wt from pharmacy Tx records
    • Assumptions: missing patient data not systematically biased
• Grant money
  – Student project deadline: Jan 2005

Pamidronate – lessons
• Needs deadline (e.g., abstract submission)
• Feasible with current resources
  – Design based on available data
  – Some of your own time
• Takes time – literature review Sep 2003

GFR – lessons
• Needs deadline (e.g., summer student)
  – Designed in January, started in June
• Almost feasible with current resources
  – Design based on available data
  – Significant own time (weekends) + student(s)
• Takes time – literature review Nov 2003
**NHP – who cares**
- **Does structured counselling on natural health products benefit patients?**
- **Timeliness** – CAPhO grant Mar 2002
  - structured approach developed but no implementation date
- **Importance**
  - staff and patients confused about NHP use
- **Unique**
  - structured approach not published

**NHP – when**
- **Evidence** – one centre, prospective
  - Answer within ~12 months?
- **How much time can you spare?**
  - Investigators, general staff
- **What data do you already have?**
  - Anecdotal how many "new start" patients
  - Clinical difference: >15% in score
  - Presenting data: mean satisfaction score before and after
  - Assumptions: e.g., RCT vs. cohort, satisfaction vs. QoL

**NHP – money**
- **Current resources + grant money**
  - **Time:** Mar 2002-2007
    - PI, 4 co-investigators
    - two co-PI’s, 3 co-investigators, 4 collaborators
  - **Scope** – as wide as possible
    - Data: satisfaction, DRP’s, impact on decision, etc
    - Assumptions: similar demographics pre- and post-, implied consent, least impact with "new start" pts
- **Grant money - CAPhO**
  - applied Mar 2002, $15,000 Sep(?) 2002

**NHP – lessons**
- **Grant driven** - soft deadline, over ambitious
  - 2 mat leaves, staff & procedures changed
- **Needs to know how to use the money**
  - PI’s and CI’s did most of the work
- **Takes time** – grant proposal Mar 2002

### Summary – Applied Research
- **Who cares** – impact on **your practice**
  - Less generalisable
  - Less duplication/competition for resources
- **When** – minimize the need to research
  - Minimize data collection
  - Make assumptions (defend limitations)
- **How much** – more affordable
  - More likely to start
  - Easier to define scope

---

**Data collection/analysis**
- **Relax change:**
  - **Foster:** none
- **Publication:** J Oncol Pharm Pract (2008)

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**M de Lemos ML, S Taylor, J Barnett, F Hu, A Levin A, V Moravan V, S O'Reily,**

**M de Lemos, T Hseah, L Hamata, A Levin, K Swenerton, O Djurdjev, T Vu, F Hu, J Conklin, S Taylor,**

**S Jennings, M de Lemos, A Levin, N Murray,**

**S Taylor, M de Lemos, D Jang, J Man, D Ambable, S Mithani, L John, T Vu, R O'Brien,**
The following events will take place in the Exhibit & Poster Hall, located in the Sal de Bal Ballroom:

**Saturday, November 5th**
- 07:30: Hall opens
- 07:30 – 08:15: Breakfast
- 10:00 – 10:30: Refreshment Break
- 13:00 – 14:00: Lunch Dessert & Coffee
- 15:20 – 15:50: Refreshment Break
- 16:35 – 18:30: Exhibits and Posters Viewing Reception
- 18:30: Hall closes

**Sunday, November 6th**
- 07:30: Hall opens
- 08:00 – 08:30: Breakfast
- 10:15 – 10:30: Refreshment Break
- 10:30: Hall closes

Exhibitors’ map on next page
## Exhibitor Listing / Liste des exposants

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APPLYING LEAN PROCESS TO IMPROVE PATIENT WAIT TIME FOR AMBULATORY CHEMOTHERAPY IN A TERTIARY CANCER CENTRE

Patient wait time is a challenge for the Systemic Therapy Unit (STU) at the Princess Margaret Hospital which sees approximately 2,500 ambulatory chemotherapy visits per month using a combination of alternate day and same day bloodwork model.

Pharmacy and the STU staff applied the LEAN concept to conduct a week long rapid improvement event (RIE) to examine the process from the booking of systemic therapy appointment to the time pharmacy has the drug available for pickup. One of the event goals was to have drug ready for patient’s appointment time within 1 hour (Baseline = 1h 18min). Other event goals were to increase charts cleared by previous day to 75% (Baseline = 55%), clear all patient charts prior to patient's appointment time (Baseline = 59%) and to implement a visual & transparent system for real-time feedback at any given time to communicate back to the unit.

Two months after the RIE, Pharmacy achieved the goal of having drugs available within 1 hour of patient's appointment. Also, daily performance boards and team huddles were sustained to enable 66 more improvements to be recommended. All 8 recommendations from the week long RIE event and 80% of the subsequent recommendations were implemented.

Contact Author
Rita Kwong, Princess Margaret Hospital, Toronto, ON

Co-authors
Roy Lee, Princess Margaret Hospital, Toronto, ON
QUANTIFYING VALIDATION ACTIVITIES IN A CHEMOTHERAPY CLEAN ROOM

Background: An ISO Class 7 Clean Room is used for the preparation of chemotherapy. Typically, two pharmacy technicians prepare chemotherapy in biologic safety cabinets. A third technician is available to validate materials and procedures used, to ensure patient safety. We wanted to determine if the work done by the third technician could be accomplished using other means. We also wanted to quantify the non-validation activities taking place in the clean room.

Objectives:
1) Ensure patient safety needs are met, through provision of accurately prepared drugs.
2) Optimize technicians' time.
3) Explore other validation methods.

Design & Results: We conducted an environmental scan regarding methods of validation for chemotherapy doses. Two data collections were performed to determine what patient safety breeches were been captured by the current validation method, and what other tasks were accomplished by the validating technician.

It was found that few patient safety breeches were seen in comparison to the amount of chemotherapy prepared. It was also shown that having a third technician is vital to complete the set up and communication duties of the technicians in the Clean Room.

Conclusion: It was determined that three clean room technicians are required to meet the demands of chemotherapy preparation.

Contact Author
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Madeline Lemke, Sunnybrook Health Sciences Centre, Toronto, ON
Lisa Rotman, Sunnybrook Health Sciences Centre, Toronto, ON
Mari Mascioli, Sunnybrook Health Sciences Centre, Toronto, ON
OPTIMIZING CHEMOTHERAPY PREPARATION TIME BY CHANGING CURRENT QUEUING STRATEGIES

Objective: Assess the effectiveness of a changed chemotherapy preparation queuing strategy on preparation time.

Design: Mixing of chemotherapy is now prioritized by the patient's appointment time as opposed to the first-in-first-out system by approval time previously in place. Data was gathered from an internally developed booking system and two groups (before and after the process change) were compared.

Results: The median time change from approval to ready (AR) increased 3 minutes. The range fell by 53 minutes for all patients. For patients arriving one hour or more prior to appointment time, the median AR rose by one minute however the range dropped by 54 minutes. The median for delta time from ready to appointment time (RS) rose by three minutes however the range dropped by 5 minutes. A 4% decrease in the area under the curves for the RS before and after graphs was observed. The proportion of patients with chemotherapy ready within 30 minutes of their appointment time remained the same, 38%.

Conclusion: Despite a higher median time, the range and number of outliers dropped in nearly all metrics thus demonstrating our increased ability to deal with patients of varying complexity with the implementation of this process change.

Contact Author
Flay Charbonneau, Sunnybrook Health Sciences Centre, Toronto, ON

Co-authors
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Ben De Mendonca, Sunnybrook Health Sciences Centre, Toronto, ON
Tiffany Leung, Sunnybrook Health Sciences Centre, Toronto, ON
COMPARATIVE NET COST IMPACT OF THE UTILIZATION OF PANITUMUMAB VERSUS CETUXIMAB AS MONOTHERAPY FOR THE TREATMENT OF PATIENTS WITH METASTATIC COLORECTAL CANCER IN QUEBEC.

**Background:** The recently published CEPO EGRFI class review supports the use of panitumumab and cetuximab as a single agent treatment in metastatic colorectal cancer (mCRC) after failure of other chemotherapy regimens based on significant clinical benefits. The purpose of the analysis was to compare the costs of using panitumumab versus cetuximab in this patient population using a Net Impact Analysis (NIA) approach.

**Methods:** The NIA determined the total per patient cost of panitumumab versus cetuximab in Quebec. Utilization of healthcare resources was obtained through expert consultation. Direct costs related to infusions, follow-up monitoring, and treatment of AEs including drugs, medical supplies, laboratory testing, oncology chair and healthcare professionals’ time were incorporated.

**Results:** Based on pivotal study dosing, per patient drug acquisition costs of panitumumab and cetuximab were $21,000 and $27,523, respectively. Lower costs for infusion preparation/administration, patient monitoring and AE management were incurred with panitumumab. The total per patient cost of treating with panitumumab was 36% lower than with cetuximab ($22,869 vs. $35,776, respectively).

**Conclusion:** Treating chemotherapy-resistant mCRC patients with panitumumab rather than cetuximab reduces healthcare resource utilization and costs. This overall provincial healthcare saving could potentially be re-allocated to other cancer treatments.

**Key Words:** Panitumumab, cetuximab, mCRC, cost

**Contact Author**
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**Co-authors**
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Lucie Surprenant – St. Mary’s Hospital, Montreal, QC
Poster Listing / Liste des affiches

Administration

DRUG ACCESS NAVIGATOR DATABASE (DAND): IMPROVING THE MANAGEMENT OF DRUG ACCESS CASES THROUGH THE DEVELOPMENT AND IMPLEMENTATION OF A COMPUTERIZED DATABASE

Most oral chemotherapy and related support medications prescribed for oncology patients in Ontario are not routinely funded by the provincial drug programs. Navigating patient access is challenging and requires special request letters, private insurance investigations, or enrollment in assistance programs. Tracking case status and associated workload is equally difficult. As referrals and complexities increase, the need for a tool to facilitate processes was identified. Consequently, a Drug Access Navigator Database (DAND) was created using Microsoft Access software to support the process of tracking cases and generating reports on workload and outcomes.

The DAND links to forms, websites, costs, and contact information. Reports capture number of referrals, time spent, time for case resolution by drug, monthly or per cycle patient cost savings for new cases, approval expiry list, and pending case list. In the month of August 2011, there were 49 referrals, and 33 hours spent with an estimated patient cost diverted of $130,000.

After implementing DAND, tracking and managing drug access cases was found to be simpler and faster. It was also found to be an easy tool for workload tracking and solidifying the need for the role of a drug access navigator for Oncology drugs in Ontario.

Contact Author
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PROCESS ANALYSIS OF CHEMOTHERAPY DRUG PREPARATION IN NOVA SCOTIA HOSPITAL PHARMACY DEPARTMENTS

Objective: The 2010 report entitled “Improving the Safety of Ambulatory Intravenous Chemotherapy in Canada” identified practice processes which increase patient risk of receiving incorrect drugs or doses. CCNS conducted a process analysis of chemotherapy preparation areas in NS. The objective was to identify local practices which need improvement.

Design: This study was observational. An industrial engineering (IE) student employed process analysis techniques to describe and rank the risks observed in each setting. A process flow diagram was created for each site and compared to an ‘optimal’ flow design. A scoring system was designed, with 7 questions about risk to staff and 3 questions about occupational risks. Each question was rated on a 0 to 10 Likert scale by the IE student. Findings were summarized and pre-circulated to participants, to identify any errors.

Results: Eleven practice sites across Nova Scotia were assessed. Most (but not all) had adopted the one-dose-at-a-time process and had ‘real-time’ double check of all preparation steps by a second person. Other risk factors varied between the sites observed. Each site was given a final report for their site.

Conclusions:
Final results will be used to advise on local or provincial initiatives to address identified problems.

Contact Author
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Co-authors
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BUDGET IMPACT OF CHEMOTHERAPY FOR EARLY BREAST CANCER IN MANITOBA - USE OF A PROVINCIAL ONCOLOGY DRUG DATABASE TO EVALUATE COST PROJECTIONS

Background: In 2006, the Provincial Oncology Drug Program initiated prospective data collection for all chemotherapy administered in Manitoba via province-wide electronic order entry. This introduced an opportunity for improved access to data for characterizing drug utilization and clinical outcomes in Manitoba. In early 2008, the “TC regimen” (docetaxel plus Cyclophosphamide) was available on the Manitoba Oncology Drug Formulary. We present the results of a retrospective review of the actual budget impact of chemotherapy for early breast cancer and the impact of introducing the TC regimen in Manitoba.

Objectives:
- Calculate the actual annual drug acquisition costs of intravenous chemotherapy used for Stage I-III breast cancer patients diagnosed in 2007 and 2008.
- Compare the projected budget impact to the actual budget impact of introducing the TC regimen.

Design: Patients were identified using data from the Manitoba Cancer Registry and were cross-referenced with provincial oncology drug data. Only intravenously administered drugs were included in the cost calculations. Price used to calculate cost was the contract price at date of drug administration.

Results: Preliminary analyses indicated a significantly lower than predicted budget impact with the introduction of the TC regimen. Detailed results will be available at the time of presentation.

Contact Author
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Co-authors
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Kimi Guilbert, CancerCare Manitoba, Winnipeg, MB
Venetia Bourrier, CancerCare Manitoba, Winnipeg, MB
**DEVELOPMENT OF CLEANING AND DECONTAMINATION POLICY AND PROCEDURES FOR ONCOLOGY PHARMACY SERVICES AT THE SASKATCHEWAN CANCER AGENCY**

**OBJECTIVE:** Our purpose was to develop and implement evidence-based policy and procedures to support the appropriate cleaning and decontamination within our pharmacy facilities.

**METHODS:** Senior Pharmacy Technicians and Pharmacy Site Managers from both Saskatoon and Regina reviewed and selected guidelines, standards and the supportive scientific literature to then developed a draft policy and procedure. Input and approval was provided by SCA provincial pharmacy administration and the SCA Patient and Staff Safety Manager. The document was reviewed with pharmacy personnel, facilities managers, the safety consultant and the partnering environmental services providers.

**RESULTS:** Policy and procedures outlining standard cleaning and environmental services were developed and approved. Implementation is ongoing. The document forms the education, training and practice of the pharmacy and environmental personnel involved.

**CONCLUSION:** Implementation of a cleaning and decontamination policy requires significant collaboration and communication amongst personnel from the departments of pharmacy, facilities, environmental services and safety. Provision of supportive literature and environmental surface contamination results greatly assists in developing a shared vision prior to implementation.

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**REDUCING THE RISK OF ERRORS WITH ELASTOMERIC INFUSORS**

**Objective:** To identify the potential sources of error that can occur using Baxter elastomeric INFUSORS® (henceforth called infusors) and to develop a checklist to use to prevent these errors from occurring.

**Design:** The BCCA Pharmacy keeps a databank of oncology-related questions asked by community hospitals. A review of the databank revealed a high frequency of questions about rate errors occurring when administering infusional fluorouracil by infusor. The need to develop a process for preventing infusor errors was identified as a result of the rate error reports.

**Materials and Method:** A review of available educational materials about the infusors was completed. Possible causes of rate errors were identified and compiled into a checklist.

**Results:** Preventable sources of infusors errors identified include:
- infusor selection
- diluent selection
- flow obstruction
- access system selection
- storage temperature

**Conclusion:** Health Care Personnel involved in the provision of infusors for continuous fluorouracil administrations, and the patients who receive the infusions, should be educated about their role in preventing errors. Checklists can be useful aids for education about error prevention.

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ADHERENCE TO ADJUVANT ENDOCRINE THERAPY IN WOMEN WITH BREAST CANCER

Objectives: To determine how many patients with breast cancer who are prescribed adjuvant endocrine therapy discontinue early and to evaluate adherence in patients who persist with therapy. Secondary objectives were to explore possible trends to see if certain factors may correlate to early discontinuation of therapy.

Design: A retrospective review of charts and pharmacy dispensing records was conducted, including patients who initiated adjuvant endocrine therapy for breast cancer at the CCI from January 1 to December 31, 2006.

Results: 81 (22%) out of 346 included patients discontinued therapy within two years. Adherence rates calculated for the 265 patients who remained on therapy beyond two years showed that 247 (93%) of these patients had 80% or better adherence. Patients who did not undergo chemotherapy and patients with CCI follow up times of less than one year were significantly more likely to discontinue therapy.

Conclusions: The majority of patients who are prescribed adjuvant endocrine therapy for breast cancer at the CCI remain on therapy for at least two years and are adherent. Longer follow up by CCI practitioners may help to decrease discontinuation rates.

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PLERIXAFOR VS ANCESTIM FOR STEM CELL MOBILIZATION AFTER FAILURE OF CONVENTIONAL THERAPY

Hematological stem cell transplantation is a therapeutic option for the treatment of hematological malignancies. The feasibility of the haematological stem cell transplantation is dependent on the number of CD34+ cells collected. Approximately 5-30% of patients who are candidates for autologous stem cell transplantation fail to mobilize an adequate number of CD34+ cells. Mobilization agents such as ancestim or plerixafor have demonstrated efficacy in mobilizing haematological stem cells.

We have used at our center ancestim and plerixafor as mobilizing agents. The optimal mobilization strategy is still unknown. To our knowledge there is no comparative trial comparing ancestim and plerixafor nor is there any comparative efficacy or pharmacoeconomic data available. We have decided to retrospectively compare the use of ancestim and plerixafor at our center.

The primary objective of our retrospective study was to compare our populations that have received plerixafor or ancestim as a stem cell mobilization agent. We wanted to compare efficacy and cost variables.

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**BREAST CANCER AND BONE-RELATED EVENTS: TRENDS IN CLINICAL PRACTICE**

**Background:** In Metastatic Breast Cancer (mBrCA), bone is the most frequent site of disease, with 40% of patients first diagnosed with BM, and ~80% of women with mBrCa developing bone mets (BM). Currently there are no approved therapies to prevent BM. This project sought to determine the trend in development of BM in mBrCA at The Ottawa Hospital Cancer Centre (TOHCC).

**Methods:** Treatment data for patients diagnosed with Breast Cancer (BrCA) at TOHCC were extracted for the time periods 1994 to 2011. Date of referral to the centre and first date of initiation of intravenous bisphosphonates (IV-Bp) were grouped by year of each event.

**Results:** Since 1994, over 13,000 women have been referred with invasive BrCA. Of these women, 1139 have developed BM and received IV-Bp. Initiation of IV-Bp has increased rapidly since their availability, and ~77% of all patients treated with IV-Bp have been referred since 1994. 5- &10-year bone-event free rates have remained steady (~93% & ~90%, respectively).

**Conclusion:** Increases in BrCA survival have not translated into reductions in BM. Developing ways to identify women at high risk of BM as well as effective preventative measures should be a clinically important priority.

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ORALCHEMOTHERAPY.CA: A WEB REPOSITORY FOR PHARMACISTS TO IMPROVE CANCER PATIENT SAFETY

OBJECTIVE: With increasing availability and use of oral chemotherapeutics agents, a greater chance of prescribing error arises, especially when healthcare professionals involved have limited experience with these medications. We present an innovative solution to help pharmacists to quickly identify potential problems associated with oral chemotherapy to achieve timely resolution, and most importantly, avoid patient harm.

DESIGN: We have constructed a repository to disseminate information: “www.oralchemotherapy.ca”. This website features comprehensive, one-page monographs for each oral chemotherapeutic available in Canada, including risk stratification (high, moderate, low) associated with each medication, as well as drug interaction tables.

RESULTS: The website, oralchemotherapy.ca is now available. Monographs and drug interaction tables are now available through the website. Printable pdf versions of the monographs will be accessible in the near future.

CONCLUSION: It is hoped that the use of this simple yet innovative solution will empower non-oncology pharmacists and other healthcare professionals in the safer prescribing and dispensing of oral chemotherapeutic agents, optimise patient safety, and improve patient-centred care. We plan to host workshops to educate pharmacists on potential issues they when dispensing oral chemotherapy, and introducing them to oralchemotherapy.ca as an easy access, rapid and concise resource to improve patient safety.

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ERROR DETECTION AND PREVENTION BY PHARMACISTS IN AN AMBULATORY ONCOLOGY CLINIC

**Objective:** To capture and classify the types of near misses made in an ambulatory oncology clinic.

**Design:** This was a quality assurance study looking at near misses reported by pharmacists in an ambulatory oncology clinic. Data was collected between April 1, 2011 and September 30, 2011. Information was reported and extracted from the hospital's electronic event tracking system.

**Results:** The most common types of drug therapy problems prevented by pharmacists included chemotherapy orders where further drug therapy was needed, unnecessary drug therapy ordered and incorrect dosages (too high or too low). Low reporting rate was also noted.

**Conclusion:** Contributory causes included the use of incorrect pre-printed orders, lack of pre-printed orders in existence and dosage calculations done at every treatment visit. Recommendations to reduce these types of near misses include the implementation of a computerized order entry system and a checklist to ensure that take-home medications are prescribed. In addition, a local quality care committee at the Program level should be implemented to continue to analyze near misses in chemotherapy prescribing and administration. Fostering a non-punitive environment and education on event tracking tool may improve reporting rates.

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OCTREOTIDE DRUG USE EVALUATION AT THE BC CANCER AGENCY (BCCA)

**Objectives:** Long-acting octreotide (Sandostatin LARR) (OCTLAR) 30 mg IM monthly is funded at the BCCA for symptoms of carcinoid syndrome (CS) and peptide secretion in patients with gastrointestinal (GI) neuroendocrine tumors (NETs). Although the NETs incidence has remained stable, OCTLAR utilization has increased by 226% over 5 years.

**Design:** This was a retrospective review of OCTLAR prescriptions over a 6-month period.

**Results:** Significant numbers being asymptomatic or having unknown symptoms (see table). Most OCTLAR used outside eligibility criteria (indication or dose limit) did not receive special approval by BCCA.

<table>
<thead>
<tr>
<th>GI NETs</th>
<th>Non-GI NETs</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N = 100)</td>
<td>(N = 50)</td>
</tr>
<tr>
<td>Carcinoid syndrome at OCTLAR initiation</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>67 (67%)</td>
</tr>
<tr>
<td>Absent</td>
<td>26 (26%)</td>
</tr>
<tr>
<td>Treated beyond tumour progression</td>
<td>7</td>
</tr>
<tr>
<td>Unknown</td>
<td>25 (50%)</td>
</tr>
<tr>
<td></td>
<td>21 (42%)</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4 (8%)</td>
</tr>
<tr>
<td></td>
<td>&gt; 30 mg/month dose</td>
</tr>
<tr>
<td></td>
<td>Special approval 43 (43%)</td>
</tr>
<tr>
<td></td>
<td>32 19 (38%)</td>
</tr>
</tbody>
</table>

**Conclusions:** OCTLAR was often used outside funding eligibility. Since many patients were asymptomatic or continued therapy beyond disease progression, this leads to increasing prevalence (>150 patients/year). Usage outside eligibility may be due to two factors. New phase III data demonstrated improved progression free survival irrespective of presence of symptoms. Also, the benefit of therapy may have been commonly extrapolated beyond the study population.

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EVALUATION OF CLINICAL PHARMACISTS’ FOLLOW-UP SERVICE IN AN ONCOLOGY PAIN CLINIC

Background: Patients presenting with pain in an oncology setting are often complex and require a multidisciplinary approach. The Pain and Symptom Control Clinic at Tom Baker Cancer Center includes clinical pharmacists who participate in multidisciplinary clinics and provide a follow-up service to patients assessed.

Objective: This study assesses the impact of the pharmacists’ follow-up service with respect to activities performed as well as patient and health care professional satisfaction. The activities performed are also compared to defined objectives for pharmacy practice in a hospital setting.

Methods: Activities performed by the pharmacists over the study period were recorded. Surveys were completed by patients and health care professionals.

Results: Over six weeks, 44 patients required follow-up from a pharmacist. There was an average of 2.3 interactions per patient and an average time of 85 minutes was spent on each outside of clinic. All health care professionals felt that the pharmacists’ service was a valuable component of the Pain and Symptom Control Clinic and nearly all patients reported a positive experience with the service received.

Conclusion: The inclusion of pharmacists in the Pain & Symptom Control clinic is favored by patients and health care professionals and provides increased efficiency to the clinic.

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IMPACT OF PHARMACISTS’ INTERVENTIONS ON MEDICATION DISCREPANCIES AND DRUG-RELATED PROBLEMS IN NEW AMBULATORY CHEMOTHERAPY PATIENTS

Primary Objective: To determine the number of medication discrepancies in new ambulatory chemotherapy patients, using current chart checking and medication reviewing processes.

Secondary Objectives: To determine the types of medication discrepancies & numbers and types of drug-related problems (DRPs) identified and resolved.

To determine the cost associated with maintaining current pharmacy processes.

Design: Prospective, open-label, multi-centre study.

Results: 150 medication discrepancies were identified and 147 (98%) were resolved in 861 new ambulatory chemotherapy patients. 129 (86%) of discrepancies were unintentional, while 21 (14%) were undocumented intentional. 494 DRPs were identified, of which 477 (97%) were resolved. The most common DRPs included drug information/patient counseling interventions, missing labs, drug interactions, medication allergies, and incorrect doses. On average, 26 minutes were spent per patient assessment, resulting in $18,334 pharmacy resource expenditure for the entire study population.

Conclusion: Clinically important medication discrepancies and DRPs were identified and resolved in new ambulatory chemotherapy patients, using the current pharmacy chart checking and order reviewing processes.

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ORAL ANTI-CANCER AGENTS IN THE COMMUNITY SETTING: A CROSS COUNTRY SURVEY OF PHARMACISTS IN CANADA

Over the past decade, there has been a sharp rise in the use of oral anti-cancer agents (OAA). With this new trend comes the concern that community pharmacists may not have the training to safely dispense these agents and provide effective patient care. In order to identify the needs of community pharmacists with respect to oral anti-cancer therapy in this country, a cross-Canada survey was conducted. Using a structured electronic mailing strategy, standardized data collection forms were mailed to practising pharmacists in provinces where community pharmacists were dispensing the majority of OAA. Survey items included questions related to demographic information, current knowledge related to cancer therapy, access to educational resources, patient education, safety, and required elements of an OAA prescription. Of the 352 respondents to the survey, only 13.6% felt that they had received adequate oncology education at the undergraduate level, and approximately 19% had attended a continuing education event related to oncology in the past 2 years. Only 24% of respondents were familiar with the common doses of OAAs and a mere 10% felt comfortable educating patients on these medications.

This study has identified that a substantial portion of community pharmacists in Canada do not have a solid understanding of oral anti-cancer therapy.

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IS THE INCIDENT OF DELAYED-ONSET CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV) SIGNIFICANT IN ACUTE MYELOID LEUKEMIA (AML) PATIENTS RECEIVING REMISSION INDUCTION CHEMOTHERAPY (RIC)?

Objective: To determine the baseline incidence of CINV occurring in AML patients receiving RIC.

Design: A retrospective analysis of 40 consecutive newly diagnosed adult AML receiving treatment over a four-month period consisting of daunorubicin 60 mg/m2 IV push x 3 days, concurrently with 7 days of cytarabine continuous infusion IV at 200 mg/m2/day (100 mg/m2 for patients age 60 and over). Granisetron 1 mg IV as standard antiemetic. Breakthrough antiemetic as needed. Dexamethasone was contraindicated. Data obtained over 8 consecutive days of treatment.

Results: Frequency of CINV increased steadily over the first five days, reaching a peak at days 4-5. On each of these two days beyond day 3, vomiting incidence increased from 30 to 50% (a 40% increase) with 25% of all patients experiencing at least one episode of vomiting. Thereafter the frequency of vomiting decreased, but CINV persisted in some patients throughout day 8. The cumulative incidence increased at a steady rate, with new cases occurring, until the end of day 5; after which the incidence stabilized. By the end of day 5, 78% of patients had experienced CINV, while 50% had at least one episode of emesis.

Conclusion: Significant delayed CINV/retching is associated with post-daunorubicin infusion.

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PHYSICAL COMPATIBILITY OF CALCIUM GLUCONATE AND MAGNESIUM SULFATE INJECTIONS

Objective: To evaluate the physical compatibility of calcium gluconate (1 g) and magnesium sulphate (1 g) in NS and in D5W solutions for two frequently reported administration volumes (100 mL and 250 mL).

Design: Injection solutions were aseptically prepared using calcium gluconate (1 g) and magnesium sulfate (1 g) and all possible permutations of diluents (NS and D5W), volumes (100 mL vs. 250 mL) and orders of addition (calcium first or magnesium first). Similarly, calcium gluconate and magnesium sulfate controls were prepared without the other salt. Injection solutions were stored in environmental chambers at 25°C and 5°C up to 7 days. Visual examination and turbidity analyses were performed after 1 hour, 1 day and 7 days. The microscopic particle count test was performed after 7 days.

Results: No visible sign of precipitation was observed; no significant change in turbidity was measured; and microscopic evaluation of all samples complied with the USP specifications for particulate matter in injections. Another series of experiments performed using calcium chloride instead of calcium gluconate confirmed the stability-enhancing effect of the gluconate ion.

Conclusion: Calcium gluconate and magnesium sulphate injections were physically compatible at clinically relevant concentrations.

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THE LIFECYCLE VALUE OF ONCOLOGY MEDICINES

Background: Pharmaceuticals represent an important component of cancer care. When products come off patent, many continue to be used and may become the standard of care. However, society continues to gain value during this period. The objective of this study was to propose a framework to highlight this important aspect of determining the value of new drug innovation.

Methods: The drugs selected for the cases studies were paclitaxel and gemcitabine, both of which have come off patient. Pharmacoeconomics studies evaluating these agents were identified. The outcomes were reanalyzed based on the new off patient prices.

Results: Paclitaxel remains the standard of care in advanced ovarian and breast cancer. Using the new off-patent price, the cost was estimated to be less than $2,500 per QALY gained for both disease sites. Gemcitabine is used for the treatment of advanced pancreatic and lung cancer. Using the new off patent price, the cost was estimated to be less than $5,500 per life year gained for both patient groups.

Conclusions: Patients and society will continue to derive economic benefit from oncology medicines well past patent expiry. This framework suggests that current approach to determining value of new medicines should go beyond the initial patent period.

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PROSPECTIVE VALIDATION OF RISK PREDICTION SCORING SYSTEMS FOR ACUTE AND DELAYED CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV)

Background: We previously developed cycle based prediction models and associated scoring systems for acute and delayed CINV (Dranitsaris 2009, Petrella 2009). In this study, we prospectively assessed the scoring systems to accurately identify patients at high risk for ≥ grade 2 CINV.

Methods: Patients receiving CT were provided with symptom diaries for collecting CINV data. Prior to each cycle of chemotherapy (CT), the acute and delayed CINV scoring systems were applied to stratify patients into low and high risk groups. External validity was then assessed via a receiver operating characteristic curve (AUROC) analysis.

Results: CINV outcomes data were collected from 95 patients following 181 cycles of CT. The incidence of ≥ grade 2 acute and delayed CINV was 17.7% and 18.2% respectively. Major predictors for ≥ grade 2 CINV included; young age, platinum or anthracyline-based chemotherapy, low alcohol consumption, earlier cycles of CT, previous history of morning sickness and prior emetic episodes. Patients identified to be at high risk were 2.8 (p = 0.025) and 3.1 (p = 0.001) times more likely to developed ≥ grade 2 CINV.

Conclusion: This study demonstrates that our scoring systems are able to accurately identify patients at high risk for acute and delayed CINV.

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IDENTIFICATION OF GENES IN REGIONS OF RECURRENT GENOMIC AMPLIFICATION AS PUTATIVE THERAPEUTIC TARGETS IN PANCREATIC DUCTAL ADENOCARCINOMA

Objective: Pancreatic ductal adenocarcinoma (PDAC) presents with the worst prognosis of all solid tumors and novel therapies are urgently needed to combat this disease. Our aim was to integrate genomic data from PDAC tumors to identify candidate therapeutic targets.

Design: We sought to identify regions of recurrent genomic amplification in a cohort of PDAC samples through analysis of copy number alteration data from four independent pancreatic cancer genome datasets. We utilized array-based copy number data and gene expression analysis on 30 pancreatic cancer cell lines to define appropriate pre-clinical models for biological validation.

Results: We identified 20 genomic loci which are recurrently amplified among the four datasets. This resulted in a catalogue of 756 protein-coding genes and RNA genes which are candidates for further analysis. We further identified 50 candidate genes with high correlation of genomic amplification and gene expression in cell lines, as computed by a Spearman rank correlation coefficient.

Conclusion: Using this strategy, putative oncogenes which are recurrently amplified in PDAC have been identified and will subsequently be studied in drug-based assays on cell lines. The amplification will serve as a biomarker for tumors which may be amenable to treatment with a selective therapeutic agent.

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TEMOZOLOMIDE PLUS RADIOTHERAPY FOR GLIOBLASTOMA: EFFICACY VS. EFFECTIVENESS AND THE IMPACT OF MGMT METHYLATION

Background: Radiotherapy with concomitant and adjuvant temozolomide is standard first-line treatment for newly diagnosed glioblastoma in adults. The effectiveness of this regimen has not been evaluated in Canada. Additionally, the impact of O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation on survival has not been confirmed.

Objectives: Compare survival and MGMT predictive value between the Alberta and Stupp trial populations.

Design: Retrospective chart review of 215 adult glioblastoma patients who started radiotherapy and temozolomide between January 2007 and December 2010 at the Cross Cancer Institute (Edmonton, Alberta) or the Tom Baker Cancer Centre (Calgary, Alberta).

Results: In Alberta, median overall survival was 14.3 months (vs. 14.6 months in trial, p=NS) and median progression-free survival was 5.8 months (vs. 6.9 months in trial, p=NS). Unlike the trial, the Alberta MGMT subgroup analysis for overall survival was not statistically significant despite a hazard ratio of 0.65 in favour of the methylated group.

Conclusion: Current practice in Alberta enables patients to achieve survival outcomes similar to the clinical trial. Further follow-up is required to confirm the predictive value of the MGMT assay. Until that is clarified or better treatments are developed, it is reasonable to continue offering this treatment regimen to patients regardless of MGMT methylation status.

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The objective was to evaluate the stability of 10 and 25 mg/mL solutions of azacitidine.

For studies completed at 4°C and -20°C, azacitidine was reconstituted with cold (4°C) Sterile Water for Injection (SWFI). The concentration of azacitidine was determined by a validated, stability-indicating liquid chromatographic method in serial samples over 9.6 hours at 23°C, over 4 days at 4°C and over 23 days at -20°C. The expiry date was determined based on the time to achieve 90% of the initial concentration using the fastest limit of the 95% confidence interval of the observed degradation rate.

Azacitidine degradation was observed to be sensitive to temperature but not concentration (10 mg/mL or 25 mg/mL) or container (original glass vial or polypropylene syringe). At 23°C, 15% of the initial concentration is lost after 9.6 hours, 32% lost after 4 days at 4°C and less than 5% loss at -20°C after 23 days.

More than 90% of the initial azacitidine concentration will be retained, with 97.5% confidence, if following cold SWFI reconstitution, vials and syringes are placed in the refrigerator immediately, and storage does not exceed 2 hours at 23°C and 8 hours at 4°C and 4 days at -20°C. This recommendation reduces wastage.

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TRENDS IN ONCOLOGY CLINICAL TRIALS: THE IV-TO-@HOME SWITCH

**Background:** The trends of the @Home vs intravenous dispensing were analyzed at The Ottawa Hospital Cancer Centre (TOHCC) over a 14 year span to predict the future of clinical trials (CT) and clinical practice.

**Methods:** The clinical database at TOHCC was queried to extract CT based therapy from 1997 to the present. Medications were divided into intravenous (IV) vs non-IV therapy. Each preparation (IV/PO/SC/Other) was counted as a single event. The data was summarized by grouping the dispensing event within the year in which it occurred.

**Results:** From 1997 to present, the CT program expanded significantly but was highly variable in its volume (~100% difference between the slowest and the busiest year). IV medications made up the bulk of the workload (~69-83%) but were the most variable. At home therapy, while a smaller % of workload, continued to grow at a more rapid and consistent rate (~37% faster) compared to IV infusions.

**Conclusion:** The trends in oncology CT at TOHCC demonstrate that treatment @Home is increasing in frequency, with IV medications constituting the bulk of all cancer treatments. We will further analyze the success of the medications achieving marketed status.

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COMPARISON OF TWO CLOSED SYSTEM TRANSFER DEVICES FOR THE DELIVERY OF CANCER CHEMOTHERAPY: A CLINICAL STUDY GONE AWRY

**Objective:** This study was designed to compare two closed system drug transfer devices (CSTDs) in two cancer treatment facilities - the PhaSeal and ICU Medical ChemoClave systems. The objective was to measure surface contamination levels in each practice site after an adequate period of implementation at each site to identify any difference in outcomes between these two systems.

**Design:** This study is a Randomized Before-After Crossover effectiveness design, with each study site randomized for the implementation sequence. The CSTDs were limited to use with all doses of Cyclophosphamide.

**Results:** The first study site was randomized to the ChemoClave system. Within 4 weeks, the pharmacy technicians reported significant repetitive stress injuries to their wrists while using the Genie device for drug reconstitution. This device had to be discontinued until redesigned.

At the second site, we assessed the nursing procedures and discovered practices which increase surface contamination (contrary to advice received in advance). Implementation was held from the both sites until nursing and pharmacy practices could be adjusted.

**Conclusions:** The problems encountered during the study are now under resolution before we restart the implementation phase again.

This study was partially funded by the MedBuy Pharmacy Research Endowment Fund.

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CHEMOTHERAPY SELECTION AND UTILIZATION FOR EARLY BREAST CANCER IN MANITOBA - A RETROSPECTIVE EVALUATION

**Background:** In 2006, the Provincial Oncology Drug Program initiated prospective data collection for all chemotherapy administered in Manitoba via province-wide electronic order entry. This introduced an opportunity for improved access to data for characterizing drug utilization and clinical outcomes in Manitoba. This retrospective, multi-phase project applies the provincial drug data to characterize chemotherapy selection and outcomes of patients diagnosed with early stage breast cancer. Results for the initial phase of the project (drug utilization evaluation) will be presented.

**Objectives:**
- Determine the number of Stage I-III breast cancer patients diagnosed in Manitoba in 2007 and 2008 who received intravenous chemotherapy.
- Characterize the selection and pattern of use of intravenous chemotherapy regimens used for Stage I-III breast cancer patients diagnosed in Manitoba in 2007 and 2008.

**Design:** Patients were identified using data from the Manitoba Cancer Registry and were cross-referenced with provincial oncology drug data. Drug utilization was confirmed via electronic administration records and, when necessary, manual chart review of clinician documentation.

**Results:** A total of 644 patients were included in the cohort. Patient demographics and patterns of chemotherapy regimen selection by year and by disease factors (e.g. stage, nodal status, hormone receptor status, etc.) will be presented.

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PREVALENCE OF VENOUS THROMBOEMBOLISM PROPHYLAXIS IN HOSPITALIZED PATIENTS WITH CANCER

**Objectives:** The primary objective of the study is to determine the proportion of patients who have received appropriate thromboprophylaxis according to recognized, evidence-based consensus guidelines. The secondary objectives of the study include the proportions of patients with any of the following events:
1. One or more objectively documented episodes of DVT or PE during hospitalization
2. Bleeding events (serious or clinically relevant) during hospitalization
3. Contraindications to anticoagulant prophylaxis
4. Death during hospitalization

**Design:** This is a retrospective chart-review study.

**Results:** Of the 283 patients studied to date, 12.4% have received VTE prophylaxis with anticoagulants, 8.1% have developed symptomatic VTE, 2.5% have had bleeding complications, 17.0% have had contraindications to anticoagulation prophylaxis, and 3.9% have died during their hospital admission.

**Conclusion:** Based on the interim analysis of the 2008 and 2010 cohort data, VTE prophylaxis was not routinely provided to hospitalized patients with cancer at the Vancouver Cancer Centre. The results of this study have facilitated the implementation of effective VTE prophylaxis strategies for hospitalized cancer patients at BCCA.

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HEALTH CARE RESOURCE USE IN PATIENTS WITH PROGRESSIVE CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): A CANADIAN COST OF ILLNESS ANALYSIS

Background: A cost of illness analysis was conducted to estimate the overall cost of care for CLL patients in Canada who have progressed following first line therapy.

Methods: Costs of care were subdivided into patients who had relapsed following first line therapy and those who had become fludarabine refractory. Resource use estimates were obtained from six Canadian haematologists. The analysis considered direct costs for anticancer therapy, allogeneic stem cell transplantation, supportive care, medical consultations and visits, home care support, routine medical monitoring and admissions into a palliative care unit.

Results: Retreatment with fludarabine combined with cyclophosphamide and rituximab was the most commonly used second line regimen. In patients who became refractory to fludarabine, transplantation was the most commonly used intervention. Alemtuzumab was the most commonly used agent in patients who were transplant ineligible. Total direct costs for patients who had progressed following initial therapy were $26,645 (range: $4,103 to $46,439). In the fludarabine refractory setting, total direct costs for transplant eligible and ineligible patients were $341,811 and $28,244 respectively.

Conclusion: Progressive CLL is a highly resource intensive disease. Cost effective interventions are needed that would improve patient QOL, enhance survival and help contain total health care resource use.

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Saskatoon has been chosen as the city to host the 2012 National Oncology Pharmacy Symposium (NOPS 2012) from October 25th to 28th. The venue will be the Sheraton Cavalier Hotel conveniently located downtown and beautifully situated on the banks of the South Saskatchewan river. Saskatoon is Saskatchewan’s largest city and is currently listed as Canada’s fastest growing city and one of the sunniest places in our country!

Our city is home to the University of Saskatchewan, the only university in Canada to house all five health science colleges with a major teaching hospital on campus, and to Innovation Place, one of the most successful university-related research parks in North America where Canada’s only Synchrotron is located. We are leaders in agricultural biotechnology, the world’s largest exporter of uranium and have two-thirds of the world’s recoverable potash reserves in the Saskatoon region.

The South Saskatchewan river flows diagonally through the city and with seven bridges within city limits, Saskatoon has been referred to as the ‘City of Bridges’. Prepare to venture outside for a walk or jog around the amazing Meewasin Valley trail system meandering through more than 300 acres of riverbank parklands.

We would like everyone to accept our invitation and plan to attend NOPS 2012. Come and experience Saskatoon’s down home hospitality, vibrant essence and discover all the reasons Saskatoon is calling!

Kathy Gesy, NOPS 2012 Chair / Présidente du NOPS 2012