



NEWS FROM ACCRU

Word from the Director by Dr. Bernie Eigl

"Particle physics and tax law". These are two subjects I know nothing about. Experts can explain it to me, and although I think I might "get it", it doesn't take long to demonstrate that it's still Greek to me. We all have areas of "intellectual blindness" and should leave these subjects for more enlightened minds!

I have learned that clinical oncology and cancer research are such "Greek" subjects for some, and no matter how we might try to explain the principles of clinical cancer research and its frequent role as a standard treatment option ... it just

doesn't get through. Conversely, there are individuals -Mavens, if you like- from other walks of life who not only "get it" but can bring principles from their areas of expertise to bear upon improving ours. David Dilts is one of these people. His recent editorial in JCO speaks to one of the very real threats facing clinical cancer research in North America. I encourage all of you to read this and his original papers (see links).

Even without the manufactured challenges we face within our province, the future of clinical cancer research as we know it is at risk. Here in Alberta, the *en*

masse restructuring that health-care is undergoing has led to many people being thrust into positions of influence over domains that are irrevocably *Greek* to them. The fact that clinical research is often the only treatment option in advanced cancers; can improve quality, access and sustainability; and *is different* from clinical research in other specialties is presently still lost among many. Some of the pieces in this issue represent attempts to communicate this message.

If you know a local Maven who has influence, engage them with this or other messages.

Special points of interest:

- Research Advocacy
- Research Training Requirements
- SOCRA Exam
- Day in the Life
- Links

Trials Reduce Costs & Impact on AHS by Marlise Pelkey

With the rising costs of clinical trials, finding and maintaining funding can be difficult. There are many obvious reasons why trials are beneficial, including developing more effective treatments, increasing survival rates, improving patients' quality of life, gaining access to drugs, and patient autonomy. Despite these clear advantages, clinical trials are often viewed solely as an expense and ancillary benefits are frequently overlooked. These benefits include cost savings for patients being treated on a trial, future cost savings if a less expensive alternative is adopted in regular clinical practice, and reducing patient wait times and admissions.

The following studies are examples of trials undertaken in Alberta that exhibit some of these benefits:

- **MetaGIST** study compared 2 doses of imantinib, and found that a lower dose of 400 mg/day was just as effective as 800 mg/day standard care dose for most patients with metastatic GIST. This will result in lowered treatment costs.
- **RAPID** trial will determine if accelerated partial breast irradiation is as effective as whole breast irradiation in women who have had breast conserving surgery with ductal carcinoma or negative axillary lymph nodes. If partial breast irradiation is found to be as effective as whole, this will reduce treatment costs and doses and the patient may have fewer side effects and hospital visits.
- **TAILORx** study uses a molecular profiling test to determine if adjuvant chemotherapy in addition to hormone therapy will be beneficial or not in treating women with early stage breast

cancer. Unnecessary treatments and side effects may be spared if it is determined that chemotherapy is not an appropriate treatment for that patient, and may lower treatment costs.

- **NCIC PR.7** displayed that prostate cancer patients with PSA progression following radiotherapy, intermittent androgen suppression can be just as effective as standard treatment of continuous androgen suppression. Patients can spend time off hormone therapy while still being effectively treated, which may reduce their side effects, treatment costs and admissions.

There are many other examples in addition to those highlighted above; all can help advocate for research by displaying outcomes resulting in cost savings and reduced impact on the health care system.

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Recent ACCRU Clinical Trial Publications

Management of Merkel cell carcinoma with emphasis on small primary tumors--a case series and review of the current literature. [Tai P, Yu E, Assouline A, Lian JD, Kurian J, Krzisch C. J Drugs Dermatol. 2010 Feb;9\(2\):105-10.](#)

Nodal metastases occurred clinically at presentation in 9% patients with primary tumor size <1 cm. The rate of nodal metastases is too high to obviate sentinel node biopsies even for these small tumors. For the 87 patients with intermediate tumor size (>1 - <2 cm), nodal metastases occurred clinically in 13% at presentation and 26% during follow-up. Distant metastases occurred in 23% only at follow-up. The risks of nodal and distant failures for tumors of intermediate sizes were sufficient to be classified as high-risk for clinical study purposes.

Prognostic significance of number of positive nodes: a long-term study of one to two nodes versus three nodes in breast cancer patients. [Tai P, Yu E, Joseph K. Int J Radiat Oncol Biol Phys. 2010 May 1;77\(1\):180-7.](#)

The present study separately analyzed the survival outcomes of Stage T1-T2 breast cancer patients according to whether one, two, or three axillary nodes were pathologically positive. Patients with one or two positive nodes had a similar CSS. However, those with three positive nodes fared worse, with a significantly reduced CSS compared with those with one or two involved nodes. Thus, the survival data among patients with one to three nodes positive reveals clearly relevant differences when analyzed separately.

Can Images Obtained with High Field Strength Magnetic Resonance Imaging Reduce Contouring Variability of the Prostate? [Usmani N, Sloboda R, Kamal W, Ghosh S, Pervez N, Pedersen J, Yee D, Danielson B, Murtha A, Amanie J, Monajemi T. Int J Radiat Oncol Biol Phys. 2010 Jul 12. \[Epub ahead of print\]](#) Forty patients treated with prostate brachytherapy were accrued to a prospective study that included the acquisition of 1.5-T

MR and CT images at specified time points. Images from each of these patients were contoured by 5 radiation oncologists, with a random subset of patients repeated to quantify intraobserver contouring variability. Use of 3.0-T MRI does not demonstrate a significant improvement in contouring variability compared with 1.5-T MRI, although both magnetic strengths demonstrated less contouring variability compared with CT.

Clinical Trials Focusing on Cancer Pain Educational Interventions: Core Components to Include During Planning and Reporting. [Stiles CR, Biondo PD, Cummings G, Hagen NA. J Pain Symptom Manage. 2010 Jun 10. \[Epub ahead of print\]](#)

Development of a standardized reporting template for clinical trials in cancer pain educational interventions could advance knowledge transfer research and thereby increase effectiveness of national and international cancer control policy designed to support cancer pain control.

Interactions between breast cancer cells and bone marrow derived cells in vitro define a role for osteopontin in affecting breast cancer cell migration. [Koro K, Parkin S, Pohorelic B, Yang AD, Narendran A, Egan C, Magliocco A. 2010 Apr 17. \[Epub ahead of print\]](#)

In this study, we evaluated the suitability of bone cells derived from orthoplastic surgeries for use in an in vitro co-culture system representing a model of the bone microenvironment. Overall, we show that bone-derived cells enhance survival, proliferation, and migration of breast cancer cells, where migration is in part mediated by bone cell-produced osteopontin. Our in vitro co-culture model system provides a robust cost-effective method to study the various factors that mediate cancer/bone-derived cell interactions.

Referral and treatment rates of neoadjuvant chemotherapy in muscle-invasive bladder cancer before and after publication of a clinical practice

guideline [B.J.W. Miles, A.S. Fairey, M. Eliazziw, E.P. Estey, P. Venner, D. Finch, K. Trpkov, B.J. Egl. 2010 Aug 10; CUAJ 4\(4\): 263-7](#)

Referral to medical oncology regarding neoadjuvant chemotherapy occurred in 2.3% and 23.4% of patients in the pre- and post-Clinical Practice Guideline groups, respectively. Neoadjuvant referral and treatment rates increased after publication of the Clinical Practice Guideline. However, overall referral and treatment rates remained low, which warrants additional exploration.

Detection of c-KIT and PDGFRA gene mutations in gastrointestinal stromal tumors: comparison of DHPLC and DNA sequencing methods using a single population-based cohort. [Battochio A, Mohammed S, Winthrop D, Lefresne S, Mulder K, Chu Q, O'Hara C, Lai R. Am J Clin Pathol. 2010 Jan;133\(1\):149-55.](#)

Mutational analysis of c-KIT or PDGFRA has become an important laboratory assay for patients with gastrointestinal stromal tumors (GISTs) because the results are useful in predicting the responsiveness to imatinib. Our data suggest that DHPLC is a cost-effective, rapid, and sensitive test for screening for mutations of c-KIT and PDGFRA in GISTs

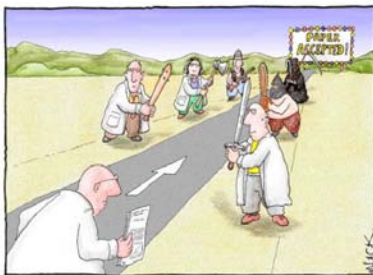
Other Recent Publications:

Promiscuity of translocation partners in multiple myeloma.

[Martin LD, Belch AR, Pilarski LM. J Cell Biochem. 2010 Apr 15;109\(6\):1085-94.](#)

Oncolytic viruses as experimental treatments for malignant gliomas: using a scourge to treat a devil. [Zemp FJ, Corredor JC, Lun X, Muruve DA, Forsyth PA. Cytokine Growth Factor Rev. 2010 Apr-Jun;21\(2-3\):103-17. Epub 2010 May 18](#)

Nutrition impact symptoms: key determinants of reduced dietary intake, weight loss, and reduced functional capacity of patients with head and neck cancer before treatment. [Kubrak C, Olson K, Jha N, Jensen L, McCargar L, Seikaly H, Harris J, Scrimger R, Parliament M, Baracos VE. Head Neck. 2010 Mar;32\(3\):290-300.](#)



Most scientists regarded the new streamlined peer-review process as 'quite an improvement.'

THIS JUST IN.....

PFIZER RECEIVES FDA WARNING LETTER

On June 28, 2010, the FDA issued a Warning Letter (also referred to as Form FDA 483) to a clinical investigator in Kansas for major consenting violations (investigator used out-dated versions of the informed consent), eligibility violations (e.g., a glucose level which fell below the lower limit of normal when the protocol inclusion criteria required a normal glucose level), and inability to produce electronic source data due to computer issues during the inspection.

In response to the 483, Pfizer Canada Inc., issued a commitment of actions for Pfizer Clinical Investigators. Below is an excerpt taken directly from the July 26, 2010 Pfizer letter to Investigators:

“To better ensure compliance with Good Clinical Practice and regulatory requirements, Pfizer is committed to further enhancing our processes and systems for conducting and managing clinical trials.

The purpose of this letter is to keep you informed of the process improvements that Pfizer is implementing that will affect Investigational sites working with Pfizer clinical trials as detailed below.

GCP Training for Investigators

Pfizer has developed and requires completion of a standard web-based GCP training module for investigators. A GCP knowledge check will be mandatory for all investigators; those who do not pass will be required to successfully complete the training module. Satisfactory completion will be documented. Investigators will need to meet these requirements once every two years irrespective of the number of studies conducted with Pfizer. This process will be implemented for investigators participating in new studies with an approved protocol after July 1, 2010. Investigators will be required to complete GCP training prior to enrolling patients into a Pfizer study.

For ongoing studies continuing into 2011, investigators will also be required to complete this training by 31 December 2010. Further details regarding the web-based GCP training will be provided by your study monitor.

Investigator data entry within specified timelines

Pfizer is developing a mechanism for measuring adherence to study-specific timelines as defined in the Case Report Form Completion Requirements document. A process will be implemented by December 2010 to enhance investigators’ compliance with appropriate timelines as defined by the study team in the CRF completion requirements.

Establish mechanisms for communication of new observations meeting ‘safe use’ criteria.

Additional requirements for clinical/study team assessment of protocol deviations have been implemented. Alert letters will be issued to sites when protocol deviations with substantial potential impact on safe use of study drug are detected. Investigators will be notified by routine communication of all other deviations relating to safe use of study drug.”

As with any communication from a trial Sponsor, a copy of that letter should be forwarded to the Research Ethics Board with the original filed in the site master study file.



LINKS

- <http://jco.ascopubs.org/cgi/content/full/28/24/3799>
- <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf>
- <http://www.socra.org/html/certific.htm>

Nurses in RT Complete Their Study by Donna Gies



In January 2008, I attended a presentation in the auditorium at the TBCC lead by Dr. Rachel Syme, then CRU manager, and Linda Watson, the Nursing Professional Practice Leader, encouraging Allied Health Care Professionals to become involved in front line research. This was being financially supported by the Research and Innovation Fund and with the reassurance of leadership and guidance to assist the novice researcher with the processes involved.

The nurses in Radiation Therapy decided that we would submit a research proposal titled "**A Randomized Control Study: Evaluating the Relation-**

ships between the use of Antiperspirant, Skin Reaction Intensity, and the Reported Quality of Life in Women Receiving External Beam Radiation for the Treatment of Stage 0, I, II Breast Cancer." This proposal was accepted and ethics approval obtained. Accrual of 198 patients took place between December 2008 and July 2010. We received support from the entire team in Radiation Therapy with Oncologists, Radiation Therapist and Unit clerks all playing some role in the successful accrual of these patients.

We are now in the process of having the data analyzed and will be presenting the results of this study at two national and one international confer-

ences this fall. It is an exciting time for us as we are confident that this study will provide sound evidence to support a change in practice that will allow women on treatment to make their own personal hygiene choices. It has been a privilege for us as front line nurses to have had the opportunity to conduct research that will make a difference to our patients.

We are very grateful to the Allied Health Care Professionals Fund, our colleagues in the Psychosocial and Radiation Therapy departments, our manager Fran Wilkin, and especially to Linda Watson, for the support they provided to us with this project.

Clinical Trial Registration

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Most investigator's conducting clinical trials are familiar with the registration standard established by the International Committee of Medical Journal Editors (ICMJE). But did you know that journal staff routinely check the National Institutes of Health database for trials that are being considered for future publication?

Trials must be registered on an acceptable trials registry prior to patient enrollment and further, the registration must be complete with required informative entries. Failure to comply can result in a study not being accepted for publication.

In the US, the FDA Amendments Act of 2007 mandates that applicable interventional studies of drugs, biologics and devices must be registered on the NIH registry—ClinicalTrials.gov.

These requirements are justified by the many benefits of registries, including reducing publication bias and selective reporting with negative trials, increasing participant recruitment, avoiding duplication of work, fostering collaboration, filling in gaps in research, and providing widespread access to information.

Investigator's who are conducting their own studies

need to ensure that their study is registered prior to study initiation. It is also the responsibility of investigators to provide updates every 6 months and to ensure that study status changes are reported in a timely manner. Fortunately in Alberta, the CRUs oversee this process.

Protocol registration forms can be obtained from the ACCRU office (403-521-3414). Once the forms are completed, the CRU staff at the CCI and the TBCC can then ensure that all studies will be registered and updated appropriately.

Regulatory Corner by Regulatory/Audit

In October 2009, the US Dept of Health and Human Services published a guidance document further defining investigator responsibilities concerning the rights, safety and welfare of trial subjects. The document contains nonbinding recommendations, but it is useful as a tool to provide further guidance in the tasks of the study team. The document also provides guidance for medical device trials. Below is a snapshot of its contents.

“Appropriate delegation” of study-related tasks.

As we know, GCP states that the investigator must ensure that individuals who are delegated tasks during the trial must be adequately informed about the protocol, the investigational product (s) and their trial-related duties (4.2.4), and are appropriately qualified (4.1.5). Health Canada’s Food and Drug Regulations Division 5 Part C.05.010(g) further states that these individuals must be qualified by education, training and experience to perform his/her respective duties.

So what do we do when we have nurse practitioners who are capable and can legally perform physical assessments and write prescriptions? What about our pharmacists who now have the ability to prescribe certain medications along with medical counseling to our

patients? The short answer? Despite what the law permits, we must follow the protocol and sponsor directions. If the protocol states that only a physician can perform a physical assessment with this task. Remember, though, that any medical decisions and care of the trial patient must be under the supervision of the qualified investigator (HC Division 5 Part C.05.010(f)).

What does “adequate training” mean?

The investigator bears the responsibility for staff training. If the sponsor has provided training to the investigator, that investigator must ensure that the staff receives the sponsor’s training (eg., training materials) that would be pertinent to their role in the trial. Training includes:

- familiarity with the purpose of the study and the protocol
- adequate understanding of the specifics of the protocol and attributes of the investigational product needed to perform their tasks
- aware of the regulatory requirements and acceptable standards for conducting the trial
- knowledgeable of

the regulations for protecting human subjects

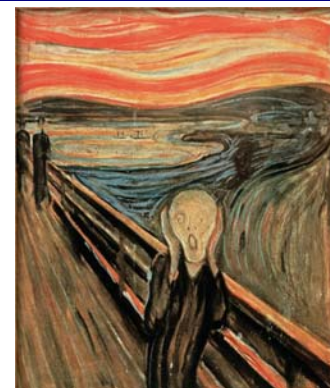
- competent to perform the tasks they are delegated
- aware of pertinent changes during the conduct of the trial and receive additional training as appropriate.

What does “adequate supervision” entail?

This guidance document is clear when it states that investigators need to develop a plan for supervision and oversight not only for less-experienced staff, but also for experienced and highly-qualified individuals.

Examples on how investigators can accomplish this are provided below:

- regular staff meetings to review the progress of the trial, any adverse events and to update staff on changes to the protocol or other procedures
- a procedure for the timely correction and documentation of problems identified by study staff, monitors, auditors, etc.
- a procedure to review staff performance of del-



gated tasks

- a procedure to ensure that consent is conducted in accordance with the regulations
- procedures to ensure that staff comply with the protocol
- procedures to address medical and ethical issues arising during the conduct of the trial.

If you would like to have a closer look at this document, it can be found at the following website:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf>

A Day in the Life SAE Reporting By Jessica Nickerson



“...who wouldn't want everyday to feel like Christmas?”

A strict schedule keeps the cogs of the Non-Local SAE process moving smoothly for the CRU at the CCI. Monday through Friday, you can find me at my desk, preparing all Non-Local SAE's for CCI submission to ACREC. Arriving in the morning to countless emails of new safety updates that requiring printing off; the number varies from one report to twenty something. Consider me lucky to get a dose of surprise every morning at 8am! Once my email is sorted through, I'll turn to my filing cabinet where the next bundle of safety reports awaits. And there begins my day of data entry.

Say that one of our studies receives a non-local SAE. What happens? They come to me! Some via email but the majority are dropped off in person as “gifts” which I like to consider

“Christmas presents” to take the joy of Christmas with me every minute of my day! The amount of reports I receive in a day varies; sometimes, it will be 0 and other days I can get 200. There has been an occasion where I was surprised with a whopping 500 reports! Through experience, I have found that this does occasionally happen when a new study opens.

The bulk of my day is spent entering actual SAE information into our database. This is comprised of reading through the reports and pulling Drug, Event, Relation and Date information. This creates a summary style letter (Non-Local Serious Adverse Event Reporting Form) that is then circulated to the Principal Investigators with the reports to be signed/acknowledged. The good thing about this is that the PI is only required to sign once as opposed to signing

each and every report that comes in. Signed letters are returned to me, which I submit to ACREC for acknowledgement. To complete this cycle I will distribute the completed forms back to the groups where they are filed.

In the past year I have entered over 19,000 SAE reports! To me, that number is surreal. Who knows one day I may reach 20,000. There is great efficiency in this process as the database has the capability to compile all SAE reports entered for a study in a matter of seconds. I often get a call or email requesting this information; every other day, in fact. I am told it comes in handy with monitor visits. All in all, my day can be very repetitive but the advantages are you always know what you're responsible for and who wouldn't want everyday to feel like Christmas?

Study/Accrual Updates

16 new studies have opened across the province during the months of June and July. These studies were opened in 7 different tumour groups including one Phase I study and one investigator-

initiated study. Five of these clinical trials are now open at both the CCI and TBCC:

- NCIC IND.195
- NCIC IND.200
- NCIC CO.21
- M10-757

- LUX BI 1200.32

June saw 68 patients enrolled in intervention based studies province-wide. Accruals were evenly spread between Cooperative, Industry & In-House.



SOCRA Exam Coming in October!

On Friday, October 15, 2010, the SOCRA exam is being held in Calgary.

To register, go directly to the SOCRA website where

you will find all the necessary details, registration forms and even sample exam questions.

The deadline to register for

this exam is Friday, September 3, 2010.

<http://www.socra.org/html/certific.htm>

NEWS FROM THE SITES: CCI by Sharon Knauer

We would like to take this opportunity to recognize and compliment the efforts by many groups who successfully delivered and responded to the audits in the months of June, July and Aug 2010: RTOG, Phase I (Ozmosis), Breast (Imclone, Schering Plough, NSABP), Lung (Torch), GU (Medivation), Hematology (Celgene MM020). In addition, the GI team has started preparation for an upcoming audit of PMH OSI-TAR-725 trial. CBIAR/IGAR/RT staff would like to underscore that with the operation of the 3TMRI all imaging studies are opened. The Symptom Control team are working hard on grant proposals for addi-

tional ESAS trials. A number of groups have been working with ICCN on ARIA implementation; the Lung group would like to report that they are making positive strides in this area. We would like to sincerely thank Tom Lam, ICCN Applications Specialist for his availability to the clinical research unit staff and for Romeo Felix for his efforts to travel to TBCC to help further advance ARIA at the CCI. Over the past number of weeks, we are delighted to bring on board new staff members. In addition, some current staff members have transitioned to different areas within the unit: Jess Chan Administrative Sup-

port Breast Group; Nancy Arlinghaus CRC Melanoma & RTOG; Cassandra Feader – CRU Admin Support; Taryn Shute CRN Hematology; Nicole Ell CRC Phase I; Usha Kumar - Research Assistant I Alberta Lymphoma Database Project. We would like to acknowledge the commitment and efforts of staff in professional development activities such as ACRP, SOCRA examinations, involvement in the CANO conference meeting in Edmonton, AB, Sept 11-15, 2010 and attendance to CCI Nursing In-services. Many thanks to Mary Fitzpatrick, Denise Harbora and John Loveseth for their contributions to the CRU as they depart to new frontiers.



Cross Cancer Institute

NEWS FROM THE SITES: TBCC by Carla Stiles

The Breast tumor group participated in a successful audit for the TRIO 012 study at the end of July. Congratulations to the breast team and our partnering departments in their. Ruth Gbewonyo has recently joined the TBCC CRU team as a casual CRC. She has been assisting with ethics applications, safety letters, and general assistance. Marleth Bernardo will be filling our Admin Assistant position for the remainder of Letitia's maternity leave.

With sick leaves and a vacations it is incumbent on remaining team members to step up to ensure that patient care remains outstanding. We'd like to recognize Laureen Johnson, Jane Gardner, Dianna Killick, Marilyn David, Barb Gawley, Heather Sissons, Kelly McLaughlan, Ralph Ablorh, Leanne Deman as well as Drs. Eigl, Hao and Heng for their outstanding support. In addition, all of the staff in the department have been very helpful and generous in

covering for their colleagues during vacation, etc. This summer we hosted three students. Britney Jones, Salim Ghondarah and Marlise Pelkey. Each student was working on clinical trial administration projects. Congratulations to Britney who received a \$10,000 research award for her research project "Cost of Care for prostate cancer patients: an observational cohort study comparing clinical trials to standard care".



Tom Baker Cancer Centre

NEWS FROM THE SITES: ACCs

The Research Coordinators from both the Medicine Hat and Lethbridge Cancer Centres recently traveled to Calgary to par-

ticipate in the departmental retreat hosted by the TBCC. This was a great opportunity for the staff of the CRUs to get to know

their counterparts in other parts of the province, share ideas and foster growth in cancer clinical trials across Alberta.



Medicine Hat Hospital. Home of the Medicine Hat Cancer Centre.



Lethbridge Hospital. Home of the Lethbridge Cancer Centre.