Ask a simple question, get a complex answer

We’ve all been there. Faced with a problem or situation, we step back and ask the simplest question, often to ourselves, and are astounded by either the lack of valid answer, or confronted by a very complex answer. That leaves us at a crossroads: do we try to answer the broader, simply-stated pragmatic question, or dive deep into the myriad of complexity that can come with breaking the question into a million little pieces?

Clinical investigation thrives on answering questions that answer both broad, far-reaching and practical questions, as well as inquiry based on precise, focused and discovery-based questions. In medicine, the two approaches co-exist on a spectrum and are both needed, as no two situations are identical. There is often a tension that exists when we design an experiment – in our world often a clinical trial with an intervention – and have to make a series of decisions that could ultimately dictate how explanatory or pragmatic the trial (and results) will be to the patients, practitioners, policy-makers and payers.

Indeed, the concept of translational medicine was initially built on discovery (“basic”) science developing a new potential biomarker or treatment, and then following forward in a number of precise experiments until it is tested in the largest of precise experiments – for example – a phase 3 trial. More recently, the observations made at the population level (and by patients), and with data science, have highlighted areas where discovery science should focus, and potential linkages not seen before – leading to translation from populations to benchtop.

To that end, we must continue to answer very explanatory questions, for example: does a short infusion of intravenous iron every 6 months, in patients with heart failure, reduce the risk of bad clinical outcomes? As this will apply to a specific population, under a specific situation, we may also wonder about broader questions for broader populations: are patients with an acute coronary syndrome managed equally well in a critical care unit or a regular cardiology ward? Answering each of the questions requires a different approach, a related but unique set of tools, and a committed investigative team and patient partners.

In early March, the CVC brought together partners from Canadian clinical trial sites, industry partners, colleagues from the Duke Clinical Research Institute and patient representation. I would personally like to thank the participants as this was clearly a dynamic discussion made richer by frank discussions on how and why we do what we do. More about the colloquium is appended.

As we consider the complexity of research, we should keep the 1977 Apple advertisement in mind “Simplicity is the ultimate sophistication”. Let’s work together, strive to simplify and provide sophisticated answers to simple questions.

Justin Ezekowitz
CVC Co-Director
On March 10th, 2019, the Canadian VIGOUR Centre welcomed 17 sites from 6 different provinces to participate in the 6th Annual CVC Clinical Trials Colloquium in Banff, AB. A sincere thank you to our sponsors Amgen, AstraZeneca, BMS-Pfizer Alliance, Boehringer-Ingelheim, CSL Behring, Novartis and Sanofi for their support to AstraZeneca, BMS-Pfizer Alliance, Boehringer-Ingelheim, CSL Behring, Novartis and Sanofi for their support towards making this event possible!

Building upon objectives and key feedback from previous colloquia, the focus of this year’s meeting was to seek out new opportunities for enhancing clinical research, including: enhancing best practices in conducting clinical trials, through an open forum of discussions, breakouts and sharing. Looking at trial designs, research infrastructure, cost effectiveness and privacy challenges within the current clinical trial environment, and considering how we can continue to adapt and enhance trials within a changing research environment. Learning from our patients and strategizing on successful ways to engage them in clinical trials conduct.

Enhancing best practices in conducting clinical trials, through an open forum of discussions, breakouts and sharing. Sharing and gaining knowledge from past and current trials experiences in order to achieve success in all aspects – from start-up through to closeout – including quality and training. Led by our Associate Director of Clinical Trials, Tracy Temple, we conducted our morning introductions by sharing our local research infrastructures, and learned of the various types and sizes of research teams as well as the myriad of research settings within our Canadian network. Lisa Berdan, Director of Mega Trials at DCRI, along with CVC Co-Directors Dr. Shaun Goodman and Dr. Justin Ezekowitz, began the day by reviewing some of the biggest challenges we face in conducting clinical trials, which affect all types of research design and study populations. This session concluded with a lively ‘Cost and Compensation’ debate where we explored some considerations and challenges – both from the research site’s and sponsor’s perspective – in determining adequate trial budgets and fair compensation.

In what was perhaps one of our most meaningful Colloquium topics to date, we were thrilled to welcome Mr. Ginter Hilbrecht, a current clinical trial research participant. Through his experience both as a research patient and representative of a study Patient Advisory Board affiliated with the DCRI and CSL Behring, Mr. Hilbrecht provided us a first-hand account of the research patient’s experience. From this invaluable patient perspective, we explored how to improve all aspects of trial design and conduct, with an aim to increase recruitment, minimize patient burden/concerns, keep patients engaged and committed to their trial participation, and ultimately optimize public awareness and perception of clinical research.

We began our afternoon with another important aspect of promoting research in the community: involving community GPs in clinical trials. Our colleague, Dr. Scott Garrison, shared his experience as a community family physician and provided us insight into some of the barriers to implementing traditional trial designs within the family practice setting. Dr. Garrison shared his innovative work in pragmatic clinical trial design and conduct, including the use of technology across multiple provinces as a novel way to help streamline recruitment and foster patient engagement.

We then turned our focus to training and the possibility of research site accreditation on the horizon. Our colleague, Ty Rorick, Interim Director, Industry Trials at DCRI, invited us to consider the pros and cons of accreditation, while noting site vs. institution requirements, country vs. global implications and, if implemented, whether this should be mandatory or voluntary. Closely related to accreditation is the topic of training and we examined the often daunting amount of training required in today’s research climate as well as the overlap that inevitably occurs across various trials and sponsors. We had a round-table deliberation about defining the minimum training requirements in order for sites to participate in clinical trials.

We closed our day with an innovative brainstorming session on how to build a research network and community. We learned more about which methods our sites currently use to stay connected to their research communities, including live conferences, trial-specific meetings, social media, and various professional researchers’ organizations, all ranging from local to international in scope. We had a useful discussion that helped identify both the unmet needs experienced by our sites as well as an initial determination of which methods and tools might be valuable to develop in the future. We look forward to enhancing CVC’s current resources for sites based on the information collected.

We wish to extend our appreciation to all investigators, coordinators, and sponsors who participated in this year’s gathering; their valuable experiences and contributions made this an engaging and unique event. While we can gather only a small group of sites to the Colloquium each year, our goal remains to continue learning from each of our sites how best to optimize the conduct and improve performance of clinical trials, as well as share key information within our entire network of sites.

If you are interested in hearing more about this year’s meeting or would like to inquire about participation in a future Colloquium, please contact Tracy Temple at tracy.temple@ualberta.ca or 780-492-1876.
STREAM-2

Globally there are 6 countries recruiting with an additional 4 countries coming on board very soon. The recent amendment to the protocol inclusion criteria has accelerated the number enrolled. Global enrollment is approaching 100 participants with a steady increase each month. Edmonton is currently the top recruiting site in the world with just over 20 participants enrolled! Amazing effort and collaboration by all the participating groups that continue to make this trial successful.

If you are interested in further information regarding this trial, please contact Clinical Trial Project Lead Courtney Gubbels at 1-800-707-9098 ext. 2 or via email at courtney.gubbels@ualberta.ca or Senior Regulatory Specialist Kalli Beleske, 1-800-707-9098 ext. 6 or via email at kalli@ualberta.ca.

SODIUM-HF

Our ongoing thanks to all sites for your continued efforts in screening, enrolling and following patients for the SODIUM-HF trial! With 2/3 of enrolment complete, your enthusiasm is needed more than ever to get us to the finish line...every patient counts!

If you have any suggestions, concerns or questions regarding increasing enrolment at your site, please reach out to Melisa Spaling (contact info below).

Congratulations to the following sites on their recent success:

- 1st patient randomized: Dr. Saldarrriaga, Paola Marcela Tobon, Adriana Maria Agudelo Perez, Elsa Gonzalez Sanchez (Medellin, Colombia)
- Finding your groove and enrolling several patients in March: Dr. Lavoie, Jo-Anne Kurenoff, Kendra Dawson, via email at kedawson@ualberta.ca
- Back at it!: Dr. Bourke, Romina Delgado (Orsono, Chile)

Welcome to the following new sites:

A warm welcome to the following sites. We look forward to continued strong enrolment from New Zealand!

- Dr. Doughty, Mardi Heath - University of Auckland (Auckland, NZ)
- Dr. Lund, Renee Raillton, Chaewoo Jun - Middlemore Clinical Trials (Auckland, NZ)

SODIUM-HF Website and Twitter

Don’t forget... the SODIUM-HF study has a trial website www.sodiumtrial.com and twitter handle! Follow @sodiumhf for posts featuring site personnel and their accomplishments as well as other exciting study-related news.

These platforms provide a different avenue for engaging with the SODIUM-HF operations team and other participating sites. Share your twitter handle and we will be sure to follow you!

If you are interested in receiving more information about the SODIUM-HF trial, please contact the Clinical Trials Project Lead, Melisa Spaling, via email at mspaling@ualberta.ca or 1-800-707-9098, ext. 1 or Regulatory Specialist, Kate Dawson, via email at kedawson@ualberta.ca or 1-800-707-9098, ext. 8.

Upcoming Independent Data Review:

Please continue to address queries, submit source documents and enter data in a timely manner as we anticipate an upcoming DSMB meeting in the spring of 2019. Recommendations of the DSMB will be shared with sites as needed, when available.

Sponsored by Leuven Research & Development (LRD) at University of Leuven, Belgium. STREAM-2 is a Phase 4 trial on Strategic Reperturbation in elderly Patients Early After Myocardial Infarction

ClinicalTrials.gov Identifier: NCT02775580

FEAST-HF

Recruitment into the FEAST-HF pilot is nearly complete at the University of Alberta. We look forward to learning more about the potential health benefits of dietary fiber supplementation as well as new avenues for treatment and future research for patients with Heart Failure.

If you are interested in further information about the FEAST-HF trial, please contact the Clinical Trial Project Lead, Karin Kushniruk, at 1-800-707-9098, ext. 7 or karin.kushniruk@ualberta.ca.

Sponsored by CSL Behring LLC, this is a Phase 3, Multicentre, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Investigate the Efficacy and Safety of CSL312 in Subjects with Acute Coronary Syndrome.

ClinicalTrials.gov Identifier: NCT03409926

AEGIS-II

We are off to a very good start in 2019! The start-up phase of AEGIS-II in Canada is very close to complete with just two sites left to hit the very important milestone of site activation, bringing our total number of sites in Canada to 32.

Our focus is now shifting to enrollment and we are proud to see our sites’ enthusiasm and motivation to contribute to this important study come to fruition. Canada has hit the ground running in 2019 with enrollment numbers exceeding projections each month!

Congratulations to the top three enrolling sites in Canada:

- Dr. Rodes-Cabau & Karine Maheux – IUCPQ (Quebec City, QC) 15 Patients
- Dr. Rainey & Norma Hogg - University of Alberta Hospital/Mazankowski Heart Institute (Edmonton, AB) 13 Patients
- Dr. Cheema & Khrystyna Kushniruk - St. Michael’s Hospital (Toronto, ON) 11 Patients

Mastering the details surrounding the local and central labwork required for infusion eligibility has proven challenging for some sites, so we encourage you to review the applicable sections of the protocol as well as the infusion eligibility tools very carefully prior to each infusion to avoid major protocol deviations. Your CVC team is always available for questions or clarifications as well.

As a reminder, the required time window for eCRF data entry is within 2 days of each visit, or within 24 hours for all Serious Adverse Events. Please ensure that you continue to enter data and answer open queries in a timely manner.

Thank you to all of the sites that have worked hard to keep their data consistently clean!

If you are interested in further information regarding this trial, please contact Clinical Trial Project Lead, Lyndsey Garrity at 1-800-707-9098, ext 8 or via email at lyndsey.garrity@ualberta.ca or Senior Regulatory Specialist Kalli Beleske, 1-800-707-9098 ext. 6 or via email at kalli@ualberta.ca.

Sponsored by Leuven Research and Development (LRD) at University of Leuven, Belgium, AEGIS-II is a Phase 2b, Multicentre, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Investigate the Efficacy and Safety of CSL312 in Subjects with Severe Unstable Angina.

ClinicalTrials.gov Identifier: NCT03450932

VICTORIA-HF Registry

The VICTORIA-HF Registry completed its enrollment earlier this year and is currently in the final stages of Close Out.

Thank you to our Canadian sites for a job well done! Many of our sites met their 50-patient target well ahead of schedule and we wish to thank each and every one of our sites for their excellent contribution to this important study.

We look forward to sharing the results with you in the future.

If you are interested in further information about the VICTORIA-HF Registry, please contact the VICTORIA Clinical Trial Project Lead, Karin Kushniruk, at 1-800-707-9098, ext. 7 or karin.kushniruk@ualberta.ca or the Regulatory Specialist, Kate Dawson, at kedawson@ualberta.ca or 1-800-707-9098, ext. 8.

Sponsored by Merck and Bayer this registry will assess the risk/benefit profile of Vericiguat in those patients with chronic heart failure.

VICTORIA Heart Failure Registry, please contact the Clinical Trial Project Lead, Karin Kushniruk, at 1-800-707-9098, ext. 7 or karin.kushniruk@ualberta.ca or the Regulatory Specialist, Kate Dawson, at kedawson@ualberta.ca or 1-800-707-9098, ext. 8.
There was a big push over the past few months to increase global enrollment. Thank you to all our sites that are diligently looking for participants leaving no stone unturned. All your hard work is translating into an upward trend in enrollment.

A special note of thanks to our Canadian top 3 enrolling sites:

- Dr. Pandey, Stephanie Buck and Patrick Toth – Cambridge Cardiac Care Centre (Cambridge, ON)
- Dr. Khosla and Tracy Cleveland – Surrey Memorial Hospital – Cardiology Clinical Trials (Surrey, BC)
- Dr. Swiggum and Sarah Nelson – Victoria Heart Institute (Victoria, BC)

**Trial Reminders:**

**6 Minute Walk Test**

The 6MWT is very important as it is part of the primary and secondary endpoints for the trial. If your participant is off study drug or has just agreed to telephone calls, please still ask them to return to the clinic to complete the walk. It is better to complete the walk out of window than not at all. Also, remember the participant does not need to walk the entire 6 minutes. At bare minimum, they just need to attempt the walk. As a reminder, there is a 6MWT administration video created for guidance. If you have not already watched the video, please do so.

**CEC Box**

When submitting your source documents please remember to remove all personal health identifiers. Clearly label each page with your site number and the subject number. When uploading to Box, please ensure you upload to the Heart-FID CEC Inbox otherwise the CEC will be unable to review your documents. Please upload your source documents within 10 days of knowledge of the event or as soon as possible.

**IND Safety Reports**

Review, sign, send and file! Please ensure you review the IND safety reports sent to you. After review, the PI is required to sign the report. Next, please send a copy of the signed report to the sponsor. Remember to write your site number on the report prior to sending. Send the report to your REB as per their reporting policy.

If you are interested in further information regarding this trial, please contact Clinical Trial Project Lead Courtney Gubbels at 1-800-707-9098 ext. 8 or via email at courtney.gubbels@ubalberta.ca or Regulatory Specialist Kate Dawson at 1-800-707-9098 ext. 8 or via email at kedawson@ubalberta.ca.

Sponsored by American Regent, Heart-FID is a Randomized, double-blind, placebo-controlled Study to investigate the Efficacy and Safety of Isoceler (Ferrocenacarboxylic acid) as Treatment for Heart Failure With Severe Dysfunction

ClinicalTrials.gov Identifier: NCT03837932

B2K Webinar Series

The Canadian VIGOUR Centre (CVC) and the Beyond 2018 (B2K18) educational program is pleased to host a Canadian Cardiologist-Sponsored and Accredited webinar series initiative that is being provided as an extension to the B2K18 Symposium (held annually during the Canadian Cardiovascular Congress). The next webinar (Oval Anti-platelet Therapy Post-ACS) will be held on May 1, 2019. More details and recordings of previous webinars can be found on the CVC website: https://thecvc.ca/beyond-2000/webinar-series.

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Publications


About the Chronicle

This newsletter is published periodically as a service to Canadian investigational sites. The purpose is to provide information of interest to individuals involved in cardiovascular clinical trials managed by the Canadian VIGOUR Centre, University of Alberta in Edmonton, Alberta, Canada.

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