

CBMTG Clinical Trials Network Quarter 3 Report, November 2009

The CBMTG CTN is comprised of a diverse range of specialized transplant health care professionals dedicated to conducting well-designed BMT-specific Canadian research. BMT is a widely accepted standard of care with the potential to offer cure to patients with otherwise incurable medical conditions. However, there remain numerous fundamental clinical questions and unmet medical needs. As a highly specialized professional organization, the CBMTG is ideally suited to provide guidance and infrastructure in the development and completion of BMT-specific clinical research in Canada. Although extremely important BMT trials remain a challenge as they often involve two subjects a donor and recipient. In addition the effects of transplant can carry on for months to years. We believe that the development of a strong Canadian-specific BMT research environment will overcome and address these challenges. In some respects because we are a coalition of smaller centers, we are dependent on a strong national CBMTG. Although much of our early efforts were aimed at identifying the pieces required to build a strong BMT-specific clinical trial network we are now clearly seeing the benefit of that early process. Our infrastructure is now paying off in a significant manner with all components playing a huge role in our success. Our trials are accruing at a record pace, management is impeccable and there is an instant recognition that the CBMTG is and will be a factor in international BMT trials.

Facts on the CBMTG CTN

- The CBMTG CTN has been in existence since 2000.
- There are currently 36 CTN board members representing all centers across Canada.
- The CTN holds monthly teleconferences as well as at least two face-to-face group meetings yearly.
- The current Chair of CBMTG CTN is Dr. Ronan Foley an Associate Professor in the Department of Pathology and Molecular Medicine, McMaster University, Hamilton Ontario, Canada.
- Our most recent website includes a section on the CTN to accommodate requests, e-dialogue and information about existing clinical studies. The website can be found at http://www.cbmtg.org/clinical_trials.
- The CTN is able to communicate online using the CTN Community of the CBMTG Online Discussion Board.

The CBMTG CTN aims to improve and consolidate Canadian transplant research, which will directly influence the quality of BMT care both at present and in the future. The CBMTG CTN directs and collaborates in a range of clinical studies that include the following:

1) Canadian-initiated studies (CBMTG-sponsored) Over the past 3 years more than 16 Canadian transplant sites have initiated a large multi-institutional phase III study comparing graft versus host disease in patients receiving GCSF-primed blood stem cells vs. G-CSF marrow stem cells. The grant proposal was funded by the NIH for a full 5 years. In addition to addressing an important fundamental question, the development of this trial and others has enabled our group to establish a comprehensive clinical trials infrastructure that enables Canada to become involved in a range of clinical research activities. Examples of this infrastructure range from Hematologists and Program Directors, Clinical and Research Fellows, transplant nursing staff, nurse practitioners and clinical trial nursing staff. Collaborators in the current NIH/CBMTG sponsored trial also include Vancouver General Hospital Trials Methodology, OneMatch Scientific / Canadian Blood Services, and several transplant registries. At present the 16 active Canadian centers have enrolled a total of 115 patients over the past year. Having established a high quality infrastructure we are now seeing direct evidence of successful collaboration and enthusiasm from all centers affiliated with the CBMTG/CTN. This trial is now accruing at a level that exceeds all prior predictions.

2) A second Canadian-initiated study has been developed and now funded by Canadian Institutes of Health Research (CIHR). This academic/industry blended study aims to fully evaluate whether a drug that blocks donor lymphocytes (ATG or Thymoglobulin) can significantly reduce the overwhelming and devastating complication of chronic graft vs. host disease. Development of this study has been greatly accelerated by the current collective infrastructure that includes experienced data management; trials methodology that is specific to allogeneic (donor and recipient) clinical trials and specialized trials nursing; transplant support staff and health care professionals. This important clinical study has the distinct advantage of building off prior experience in the study summarized above.

3) The trials described above aim to evaluate adult patients undergoing BMT; however, children are also well represented by highly recognized expert pediatric transplanters. We have recently secured peer-reviewed funding to complete a study in children trying to determine whether blood transfusions (either less or more) results in a better outcome. Everything is ready for the CBMTG 0603 transfusion trial to take off. The trial has opened in Sainte-Justine on June 1st, 2009.

4) Another recognized goal of the CBMTG CTN is to collaborate at an international level with transplant consortiums. To this end we are successfully collaborating with the US BMT CTN (Study 0201) and have 16 centers involved in a large 550 patient blood vs. marrow in the unrelated setting, as well as a Swedish study evaluating the benefit of Reduced Intensity Conditioning Transplant (RICT) in elderly patients with AML.

5) Canada directly supports some of the best-known basic science investigators in the world. With an increased scope and extent of clinical BMT trials we envision an opportunity to engage in potential collaborations with scientists that may help more fully understand why a new therapy works or, perhaps more importantly, why it doesn't work. These insights and mechanistic clues will help design and improve future trials so we can grow and develop in an incremental, logical manner. Our efforts to engage the scientific community will be highlighted at the 2010 CBMTG Biennial Meeting (April 7-10, 2010) where our headlining item will include basic stem cell research.

6) The CBMTG is comprised of a broad range of multidisciplinary professionals actively engaged in transplant care across Canada. From this the CBMTG recognizes the importance of providing funds to support smaller supportive care trials. In this regard the CBMTG is funding for 5 pilot studies. These studies are ideally suited for professional support staff. Proposals are peer-reviewed and awards of up to \$5000 have been selected by the CBMTG Executive Committee.

Accepted 2009 grants include:

- "Pertussis Problems: An investigation into pertussis vaccine immunogenicity after bone marrow transplantation in pediatric patients" (Conrad Fernandez)
- "Long-term cryopreservation of hematopoietic stem cells for autologous transplantation" (Donna Hogge)
- "Proteomics of Allogenic Blood or Marrow Grafts: A Pilot Study to Optimize Specimen Preparation for Mass Spectrometric Adjunct Studies for Patients in Prospective CBMTG Studies of Graft Source" (Harold Atkins)
- "Preclinical development of a natural killer cell line KHYG-1 as a novel therapeutic agent for high risk AML" (Armand Keating)
- "A prospective Study of the multidimensional quality of life in pediatric HSCT Recipients" (John Doyle)

Summary

The CBMTG CTN has successfully developed over a short period of time. This can be largely attributed to health care professionals at the CBMTG, the NIH (USA), the Vancouver Trials Methodology Group, and the CIHR. With these efforts our group now has the established track record and experience to advise and perform often complex transplant-related clinical trials. Moreover, the CBMTG is ideally positioned to conduct new trials and proposals. We see our in-house trials competition as successful and continue to foster a collaboration and support to our industry partners.

Current CBMTG Clinical Trials Network Members

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| Matthew Seftel | Harry Atkins |
| Ronan Foley | Lothar Huebsch |
| Clayton Smith | Karen Ballen |
| Jeff Lipton | Christian Fibich |
| Stephen Couban | Guy Cantin |
| Cindy Toze | Donna Wall |
| Holly Kerr | Michael Voralia |
| Thomas Kiss | John Doyle |
| James Russell | Jean Roy |
| Christopher Bredeson | Rena Buckstein |
| Marlis Schroeder | Evelina Tomas |
| Wanda Hasegawa | John Kuruvilla |
| Jeffrey Davis | Vikas Gupta |
| Brenda Sabo | Martin Champagne |
| Tammy Degelder | Michel Duval |
| Kirk Schultz | |
| Kang Howson-Jan | |
| Irwin Walker | |
| David Mitchell | |
| Ahmed Galal | |
| Pedro Lopez | |

Trials	NIH	Patients Enrolled
0601	G marrow vs G blood siblings	115
0801	CIHR (pending)	Not yet open
0201	BMT/CTN	230
KISS Trial	Sweden	97