

Memorandum

TO: All NCIC CTG Investigators

FROM: Dr. Ralph M. Meyer, Director

DATE: June 15, 2009

RE: Closure of NCIC CTG MA.5

As is indicated in this edition of *The Bulletin*, we are announcing the closure of three more trials. Since the Fall of 2008, the NCIC CTG has closed more than 150 phase III and IND trials. The reasons for announcing these trial closures are several. First, it is to ensure clarity among NCIC CTG Investigators and member centres with respect to which patients require ongoing follow-up and which trials require ongoing attention with your Research Ethics Boards. Second, we appreciate that the ongoing follow-up of patients represents a substantial workload and cost to our member centres. This issue may be particularly noteworthy when a high proportion of patients continue to be disease free and may be highly mobile and, thus, not routinely followed at the centre where their primary treatment was received. Third, ongoing follow-up represents a substantial workload and cost to the NCIC CTG Central Office. As a Group, we want to ensure that we are shifting our resources to the highest priority research topics.

In the process of closing trials, we will have decisions that involve tradeoffs; this will be particularly so when a trial has been extraordinarily successful and might continue to yield interesting scientific information.

The MA.5 trial is a stellar example of a high quality NCIC CTG trial. This trial was activated on December 1, 1989. The trial compared standard adjuvant therapy with CMF as compared with intensive CEF in premenopausal patients with newly diagnosed breast cancer and histologically involved axillary nodes. The experimental arm, CEF, was developed in Canada through pilot work conducted by the Ontario Clinical Oncology Group. Between December 1989 and July 1993, 716 women from across Canada entered this trial. The primary results were reported in the *Journal of Clinical Oncology* in 1998 and showed a 10% increase in 5-year relapse-free survival and a 7% increase in 5-year overall survival associated with the experimental treatment. These results led to regulatory approval of epirubicin for the treatment of breast cancer and adoption of CEF as a standard therapy. This CEF regimen has gone on to be tested further in the NCIC

CTG MA.21 trial, in which preliminary reporting demonstrated superior disease free survival as compared with standard treatment with Adriamycin, cyclophosphamide, and paclitaxel.

Furthermore, the MA.5 trial has been an outstanding example of attaching correlative-translational research work to our clinical trials. Groundbreaking work with respect to Her 2 expression and use of anthracycline therapy and most recently, topoisomerase II alpha and outcome according to anthracycline treatment are outstanding examples of such work. The MA.5 trial was the first NCIC CTG trial to be associated with a Quality of Life publication; in this instance, patient compliance was assessed. Finally, the results of MA.5 have been included in large individual-patient data meta-analyses assessing treatments of breast cancer.

The publication list associated with MA.5 is extensive, and is attached. Omitting abstract and review publications, 13 primary research papers have resulted from the MA.5 trial and have been published in high-impact journals that include the *New England Journal of Medicine*, the *Lancet*, the *Journal of Clinical Oncology*, and *Journal of the National Cancer Institute*.

In closing MA.5 it is important for the outstanding accomplishments that have resulted from this trial to be recognized. Special recognition goes to the Study Chair, Dr. Mark Levine, the Disease Site Chair during the conduct of MA.5, Dr. Kathy Pritchard, the NCIC CTG Physician Coordinator Dr. Lois Shepherd and Senior Biostatistician Dr. Dongsheng and to Kathy Bennett, Jon Ottaway and Nancy Paul who as study coordinators, oversaw the conduct of the trial for many years. Our thanks and congratulations go to each of these trial leaders and the many investigators, clinical research associates, and Central Office staff who have contributed to this outstanding project.

With future closure of NCIC CTG trials, we will strive to make note of those that have been associated with particularly outstanding research accomplishments. In addition, we will develop a user-friendly linkage on our website so that those interested can find the publications associated with a specific closed trial. As an addendum to this letter, the citation letter to MA.5 is attached.

Yours sincerely,



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Reference List for MA5 as of June 8, 2009

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