NCIC Clinical Trials Group
Data Safety Monitoring Committee Meeting
Summary of Meeting Minutes (April 28, 2006) and Summary of Post Meeting Teleconferences

BR. 24. Toxicity Issues and Treatment Related Deaths. The DSMC reviewed the toxicity experience on BR24 in detail because of concerns expressed by the trial committee and the NCIC CTG central office. The committee had available a detailed and up to date presentation of BR24 data as well as those from a phase I study of the investigational regimen in the trial. The committee reviewed data by treatment arm. Based on this review the committee made the following recommendation:

1) **Based on safety data observed to date, the DSMC recommended temporary suspension of trial accrual to BR.24 until all of the currently randomized patients have completed treatment and all of their data on toxicity, and compliance with protocol drug dose modifications has been received and reviewed by the trial committee and the DSMC. Further recommendations on the trial will then be made upon review of these data.**
2) **Patients currently on study must be informed and written documentation of this process obtained, and patients can choose to remain on or withdraw from study treatment.**
3) **Patients currently on study treatment do not need to be unblinded.**

Subsequent to this recommendation a detailed review of the existing study data was conducted. On the basis of that review a protocol amendment lowering the dose of AZD2171 and instituting more aggressive supportive care measures was adopted. The amendment and its rationale were discussed with and accepted by the DSMC with the following recommendations:

1. The DSMC members accept and strongly support the proposed amendments to the BR-24 study.
2. Once these amendments are incorporated into the protocol and approved by local ethics boards, accrual to the study can continue.
3. The DSMC chair should be informed immediately of any further treatment related deaths on this study.
4. The DSMC would like to see an updated toxicity analysis, by treatment arm, before the October conference call.

PR.3. Interim Analysis Results. Unfortunately, the representative from the MRC DSMC could not be part of the meeting. The NCIC DSMC felt it was very important for the MRC representative to be part of the review and discussion of the interim analysis, given the significant accrual contribution from the UK on this trial. A teleconference will therefore be arranged post-meeting for this purpose.

Recommendations:

1) **The decision on this interim analysis is deferred till a teleconference that is to be arranged shortly after the Spring Meeting.**
2) **At the subsequent conference call it was decided that the study should continue as planned.**

MA.12. Second Interim Analysis Results.

On the basis of a review of the current interim analysis, the DSMC made the following recommendation:

1) **The DSMC recommended that, based on the interim analysis, the study should continue as planned. The DSMC supports the merging of its data with other large intergroup trials to provide a more meaningful use of its results. The DSMC did not recommend releasing the results of the trial at this time.**

BR.20. Cardiac, QTc, Thromboembolic and Bleeding Disorders. The DSMC has been asked to monitor the safety data of this trial, specifically QTc prolongation. On the basis of this review the following recommendations were made:

1) **There are no safety concerns with this trial.**
2) **A breakdown of creatinine grades by fake arms is suggested at the next review.**

LY. 12. Slow Accrual. The DSMC reviewed this trial from the perspective of accrual. The committee had available data on accrual from the inception of the trial and was informed of the efforts that had been made in the past and recently to improve participation at existing sites and to recruit new sites. On the basis of this information, the DSMC made the following recommendation:

1) **Accrual has been very slow to this trial, despite efforts by the trial committee to increase participation. The DSMC would like to see a clear improvement in accrual in the next six months. This recommendation should be conveyed the trial committee.**

MAP.1 and MAP.2. Slow Accrual and Change of Study Endpoint. Both of these trials are not meeting their accrual objectives although MAP.2 is closer to its planned target. In a written response to these concerns, the study chair had acknowledged that the target sample size of MAP.1 would never be reached and the same might be true for MAP.2. He therefore proposed a change in the trial endpoint that would allow an analysis to be conducted with existing data. The DSMC considered this issue and made the following recommendations:

1) **The DSMC did not feel that it is appropriate to adjust a previously determined primary endpoint to enable earlier analysis of results, even though there is a lack of existent standard.**
2) **Toxicities on these 2 trials are acceptable.**
3) **MAP.1 should be closed due to slow accrual.**
4) **MAP.2 should continue as planned.**

SC.20. Slow Accrual and Consent Update. The DSMC had previously expressed concerns about accrual to this trial and about the lack of detailed information about toxicity from radiotherapy in the consent form. The DSMC reviewed recent accrual and the modified consent form and made the following recommendations:

1) **Toxicity on the trial is acceptable.**
2) **The current consent form is much improved.**
3) **SC.20 should continue accrual as planned.**

MAP. 3 and NSABP STAR Results. The DSMC had been asked to consider whether the recently released data from the NSABP STAR trial should affect the conduct of MA.P3. The Committee also reviewed toxicity and accrual to the trial. Based on this review, the DSMC made the following recommendations:

1) **Toxicity on this study is acceptable. MAP.3 should continue accrual as planned.**
2) **The consent form should be updated to reflect the STAR trial results when the data are released at the ASCO 2006 meeting.**

MY.10. First Interim Analysis.. Results from the first interim analysis of this trial were presented to and reviewed by the DSMC with the following recommendation:

1) **Toxicity is acceptable. MY.10 should continue as planned.**

Remaining Phase III Studies.

Study	Accrual	Toxicity
MA.17R	Drawn from letrozole arm of MA.17, so target population is finite. Acceptable but need follow-up	Acceptable
MA.20	Acceptable	Acceptable
MA.21	Completed	All patients have completed treatment
MA.27	Excellent	Acceptable
CO.17	Completed	Acceptable
PR.3	Completed	Acceptable
PR.7	Completed	Acceptable
PRP.1	Completed	Acceptable
EN.5	Completed	All patients have completed treatment
OV.16	Completed	Acceptable
BR.19	Closed April 22, 2005	Acceptable

Next Meeting. The next meeting of the committee will be in October 2006 via teleconference.

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Co-Chair