NCIC Clinical Trials Group
Data Safety Monitoring Committee Conference Call
Wednesday October 12, 2005
Summary of the Minutes

OV.16. This is a Phase III study of of cisplatin and topotecan followed by paclitaxel and carboplatin compared to paclitaxel and carboplatin alone in patients with advanced ovarian carcinoma. It completed its target enrolment in June 2005, having randomized 819 patients. The DSMC has been monitoring the safety data very closely, especially with respect to febrile neutropenia and thromboembolic events, both of which were more frequent on the experimental arm. The rates of both events as provided in the September 2005 safety update were similar to their rates in April 2005. The DSMC felt that the safety data presented were acceptable.

A request has been made by the Trial Committee to cancel the interim analysis of the progression-free survival (PFS) for this study, which was planned after observing 316 events. At this time, there have been 327 progressions logged.

Recommendations:
1) **Toxicity is acceptable. The true incidence of febrile neutropenia based on CTCAE criteria should be collected, as previous efforts to clarify has shown a lower than reported incidence of this toxicity.**
2) **The DSMC agrees that the previously planned interim analysis provides no value in changing the trial conduct or clinical practice, and furthermore since the final analysis is expected to occur within a year to 18 months, the Trial Committee should proceed with a protocol amendment to cancel the interim analysis.**

BR.20. This is a randomized Phase II study comparing ZD6474 to placebo in patients with small cell lung cancer who have had either a complete or partial response to initial chemotherapy, with or without radiation. The DSMC has been asked to monitor the safety data from this study, specifically those related to cardiac, QTc interval prolongation, thromboembolic and bleeding events. The DSMC reviewed the QTc parameters between the treatment arms and agreed that this trial is proceeding appropriately and safely.

Recommendations:
1) **Accrual is acceptable.**
2) **Toxicity is acceptable. The trial should proceed with continual stringent monitoring and appropriate management of QTc interval prolongation, a known toxicity of the study drug. Future reports on the safety data of this trial should include the distribution of patients in each arm who have a greater than 20% increase in QTc interval compared to baseline.**

LY.12. This is a Phase III study of gemcitabine, dexamethasone and cisplatin versus dexamethasone, cytarabine and cisplatin as salvage chemotherapy prior to autologous stem cell transplant in patients with relapsed or refractory non-Hodgkin's lymphoma, followed by maintenance rituximab versus observation. This trial was activated in August 2003, with a target sample size of 630 for the first randomization, and 240 for the second randomization. To date, 153 patients have been enrolled, at a rate much slower than anticipated.

Recommendations:
1) **Accrual has been slow despite several additional centres joining this trial.**

2) **The Study Chair is invited to present to the DSMC in the 2006 Spring Meeting, and submit to the DSMC plans and strategies for this protocol should accrual continue to be slow.**

MAP.1 and MAP.2. These two are randomized controlled studies in postmenopausal women at increased risk for development of breast cancer as evidenced by high breast density, comparing letrozole for one year versus placebo (MAP.1), or exemestane for one year versus placebo (MAP.2). MAP.1 has been activated since December 2000 and has accrued 67 of 120 patients to date. MAP.2 has been activated since August 2001 and has accrued 87 of 120 patients to date. The accrual of both trials have been slower than expected, with MAP.2 being slightly better due to the participating of several US sites in addition to Canadian sites. It was raised by the DSMC that perhaps the strong accruing sites of MAP.2 can join in MAP.1 to enhance its accrual should it continue to be slow. Alternatively, the Trial Committees may wish to consider performing conditional power analyses as futility analyses for one or both trials should completion of accrual be deemed unlikely. It was also discussed among DSMC members that given the small sample sizes of these studies, the yield from such analyses might be limited.

Recommendations:
1) **Accrual to both trials, especially MAP.1, has been slow.**
2) **The Study Chair is invited to present to the DSMC in the 2006 Spring Meeting, and put forward to the DSMC plans for these two protocols should their accruals continue to be slow. The above possible strategies have been suggested by the DSMC and may be considered by the Study Chair and Trial Committee.**

MY.10. This is a Phase III study of thalidomide and prednisone as maintenance therapy following autologous stem cell transplant in patients with multiple myeloma. This study has accrued 154 of the target 324 patients.

Recommendations:
1) **Accrual is slow but steady and acceptable.**
2) **Review of informed consent by the NCIC-CTG central staff at an upcoming safety conference to ensure that it contains an updated list of potential toxicities.**

SC.20. This is an International Phase III study of single versus multiple fractions for re-irradiation of painful bone metastases. This trial was activated in January 2004 and has accrued 131 of the target 650 patients to date.

Recommendations:
1) **The DSMC would like to ask the Study Chair to clarify the sites which are or will be participating in this study, and to present to the DSMC committee at the 2006 Spring Meeting the Trial Committee's plans to increase accrual.**
2) **Review of the informed consent form by the radiation quality assurance committee to ensure that accurate estimates and descriptions of toxicities and risks have been described.**

Remaining Phase III Studies.

Study	Accrual	Toxicity
CO.17	Completed	Acceptable
MA.12	Completed	Acceptable
MA.14	Completed	Acceptable
MA.20	Acceptable – picked up recently	Acceptable
MA.21	Completed	Acceptable
MA.27	Acceptable – picked up significantly recently	Acceptable
PR.7	Completed	Acceptable
PRP.1	Completed	Acceptable

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Lillian L. Siu, MD, FRCPC
Co-Chair