

## Recommendations of the ECOG Data Monitoring Committee, September 8, 2006

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group met by conference call on Sept. 8, 2006, and reviewed all ongoing phase III studies coordinated by ECOG. This report is being provided to ECOG investigators and to other participating groups for transmission to their local IRBs.

The DMC review included examination of aggregated adverse event data by treatment arm for each study, consideration of whether studies were making adequate progress towards completion, and, when appropriate, examination of interim outcome results. Results from other studies and other recent literature that might be relevant to the research were also considered. The complete ECOG DMC policy is available at <http://www.ecog.org/general/monitoring.html>. The adverse event data reviewed by the DMC is summarized in the interim reports contained in the agenda volume for the June 2006 ECOG Group Meeting. Local investigators should make copies of the relevant reports available to their local IRBs. ECOG members can obtain these reports from <http://www.ecog.org/agenda>. Copies are also provided to the operations offices of other participating groups. If an IRB requires additional information, please contact the ECOG Operations Office at (617) 632-3610.

The DMC accepted the reports on E1602, E2496, E2501, E2603, E2805, E2902, E4201, E4203, E4402, E4Z02, E5202, E5204 and TAILORx (PACCT-1) without discussion, recommending that these studies continue without modification. The DMC recommendations on the other studies are listed below.

***E1302 - Phase III randomized, placebo controlled, trial of docetaxel versus docetaxel+ZD1839 in PS2 patients or previously-treated patients with recurrent or metastatic head and neck cancer. Study Chair: Athanassios Argiris. Statistician: Musie Ghebremichael.***

**Recommendation:** The first planned interim analysis of survival was presented. Criteria for early stopping were not met, and the DMC recommended that this study continue with accrual and blinded follow-up.

***E1697 - A Randomized Study of Four Weeks of High Dose IFN Alpha2b in Stage T3-T4 or N1 (microscopic) Melanoma. Study Chair: Dr. Sanjiv Agarwala. Statistician: Sandra Lee.***

**Recommendation:** The first planned interim analysis of efficacy outcomes was presented. Criteria for early stopping were not met, and the DMC recommended that this study continue with accrual and follow-up.

***E1900 - A Phase III Trial in Adult Acute Myeloid Leukemia: Daunorubicin Dose-Intensification and Gemtuzumab-Ozogamicin Consolidation Therapy Prior to Autologous Stem Cell Transplantation.*** Study Chair: Dr. Hugo Fernandez. Statistician: Zhuoxin Sun.

**Recommendation:** Proposed changes to the statistical design to reflect protocol treatment compliance problems in the maintenance randomization were discussed. The proposed changes shift the primary endpoint to comparison of induction response, move the maintenance randomization to after the second cycle of consolidation therapy (instead of prior to consolidation), and increase the type I error rate on the maintenance comparison to 5% (one-sided). The DMC recommended not proceeding with proposed re-design, because the power for the maintenance comparison would be too low and results would be less meaningful to the leukemia community. Instead, the DMC would prefer increasing the overall number of patients to give slightly better power for the maintenance comparison than had been proposed, although they recognize that achieving the power planned in the original design will not be feasible.

***E3598 - A Phase III Trial of Carboplatin, Paclitaxel and Thoracic Radiotherapy, with or without Thalidomide, in Patients with Stage III Non-Small Cell Lung Cancer.*** Study Chair: Dr. Joan Schiller. Statistician: Suzanne Szwarc.

**Recommendation:** This study was amended to include low dose aspirin for DVT prophylaxis on the thalidomide arm in January 2005. The DMC reviewed updated information on thrombosis / embolism toxicity broken down by time period. The DMC recommended that this study continue as planned.

***E4697 - A Randomized Placebo-Controlled Phase III Trial of Yeast Derived GM-CSF vs. Peptide Vaccination vs. GM-CSF Plus Peptide Vaccination vs. Placebo in Patients with "No Evidence of Disease" after Complete Surgical Resection of "Locally Advanced" and/or Stage IV Melanoma.*** Study Chair: Dr. David Lawson. Statistician: Sandra Lee.

**Recommendation:** The results of the third interim analysis of outcome data were briefly discussed. The DMC recommended that this study continue as planned.

***E4A03 - A Randomized Phase III Study of CC-5013 plus Dexamethasone versus CC-5013 plus Low Dose Dexamethasone in Multiple Myeloma with Thalidomide plus Dexamethasone Salvage Therapy for Non-Responders.*** Study Chair: Dr. Vincent Rajkumar. Statistician: Susanna Jacobus.

**Recommendation 1:** The DMC recommended releasing data on baseline bone disease status for use in a lab project examining effects of various SNPs. This request does not involve either treatment or efficacy outcome data.

**Recommendation 2:** This study was suspended on September 14, 2005 because of the high rate of thrombosis / embolism toxicity on the standard dose dexamethasone arm, and it was reopened on November 23 with an amendment requiring DVT prophylaxis.

Updated data on thrombosis / embolism toxicity were reviewed. The DMC was concerned about the rate of thrombosis / embolism toxicity on the standard dose dexamethasone arm. Since some patients are continuing on treatment, the DMC requested further information on the number of patients continuing on standard dose dexamethasone treatment and on the timing of the thromboembolic events during the course of therapy. The DMC also requested that the study team and myeloma committee consider whether the recommended dose of dexamethasone should be reduced for patients continuing on treatment beyond the primary efficacy evaluation period.

***E5597 - Phase III Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non Small Cell Lung Cancer. Study Chair: Dr. Daniel Karp. Statistician: Sandra Lee.***

**Recommendation:** A request by Dr. Belinsky (the E5597 lab co-chair) to use analyses of lab data on methylation from this study in a grant renewal was reviewed. The DMC recommended releasing to Dr. Belinsky a statement that an interim analysis of the association of methylation of 6 genes with outcome had been performed and providing Dr. Belinsky a brief summary of the results. However, the DMC recommended that detailed information on the analyses not be released.