Report of the ECOG Data Monitoring Committee Meetings, March 9 and April 6, 2005

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group (ECOG) met by conference call on March 9 and April 6, 2005, 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 2005 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 studies reviewed at this meeting were E1199, E1302, E1697, E1900, E1D96, E1Z01, E2100, E2496, E2499, E2501, E2902, E3201, E3598, E3999, E4201, E4402, E4599, E4697, E4A03, E5597, and E6201. Interim analyses of outcome data were conducted on E2100, E3598, E3999, E4599, and E4697.

The DMC accepted the reports on E1199, E1302, E1900, E1Z01, E2499, E2501, E2902, E3201, E4402, E4A03, E5597, and E6201 without discussion, recommending that these studies continue without modification. The DMC recommendations on the other studies are listed below. Note that a recommendation to release the results means that the results will be released to the study team. The study team and the ECOG senior leadership will then decide on the appropriate course of action. Questions about these recommendations may be directed to Robert Gray, the ECOG Group Statistician (e-mail: gray@jimmy.harvard.edu; telephone number: 617-632-3012).

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 DMC recommended that this study continue, provided accrual continues to be above 160 patients per year. The DMC also encouraged vigorously pursuing discussions with EORTC on rapid resolution of the remaining issues for EORTC participation in this study. ECOG is encouraged to set a deadline for activation of this study by EORTC.

E1D96 - Phase III Study of Paclitaxel Versus Liposomal Doxorubicin for the Treatment of Advanced AIDS-Associated Kaposi's Sarcoma. *Study Chair: Dr. Jamie Von Roenn. Statistician: Sandra Lee.*

Recommendation: This study closed early due to slow accrual in May 2002 with a total of 89 patients entered. The DMC reviewed the problems related to incomplete data on this study. It is the DMC's understanding that ECOG will hold a conference call with the AIDS Malignancies Consortium (who enrolled most of the patients) and NCI to develop a plan to achieve final resolution of the data.

E2100 - A Randomized Phase III Trial of Paclitaxel versus Paclitaxel plus Bevacizumab (rhuMAb VEGF) as First-Line Therapy for Locally Recurrent or Metastatic Breast Cancer. *Study Chair: Dr. Kathy Miller. Statistician: Molin Wang.*

Recommendation: The first interim analysis of outcome data was discussed. Protocol criteria for early stopping based on the primary endpoint of progression-free survival were met, and the DMC recommended that the results be released to the investigators for possible presentation or publication, with public release as soon as feasible.

E2496 - Randomized Phase III Trial of ABVD vs. Stanford V +/- Radiation Therapy in Locally Extensive and Advanced Stage Hodgkin's Disease. *Study Chair: Dr. Sandra Horning. Statistician: Edie Weller.*

Recommendation: Originally, this study had been limited to patients with 0 – 2 risk factors. Eligibility was expanded to include patients with any number of risk factors in addendum 6. In response to a request from the study team, the DMC recommended that otherwise eligible patients with more than 2 risk factors, who were entered prior to addendum 6, be included in the primary analysis.

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: Donna Levy.*

Recommendation: The second planned interim analysis of outcome data was reviewed. The DMC recommended that results remain blinded and that this study continue as planned. The DMC will review toxicity data again at their next meeting.

E3999 - Phase III, Randomized, Placebo-Controlled, Double-Blind Trial of the MDR Modulator, LY335979, During Conventional Induction and Post-Remission Therapy in Patients Greater Than 60 Years of Age with Newly Diagnosed Acute Myeloid Leukemia, Refractory Anemia With Excess Blasts in Transformation or High-Risk Refractory Anemia with Excess Blasts. *Study Chair: Dr. Larry Cripe. Statistician: Haesook Kim.*

Recommendation: The first interim analysis of outcome data was discussed. The DMC recommended that results remain blinded and that this study continue as planned.

E4201 - A Randomized Phase III Study of Gemcitabine in Combination with Radiation Therapy versus Gemcitabine Alone in Patients with Localized, Unresectable Pancreatic Cancer. *Study Chair: Dr. Patrick Loehrer. Statistician: Weixiu Luo.*

Recommendation: This study opened in April 2003 and only 53 patients had been entered through the end of March 2005, with only 3 patients / month entered during February and March. The DMC recommended that this study continue. The DMC will review accrual at the next meeting. At that time, accrual will need to reach a rate of at least 10 patients per month, or it is very likely that the DMC will recommend closing this study.

E4599 - A Randomized Phase II/III Trial of Paclitaxel Plus Carboplatin with or without Bevacizumab (NSC#704865) in Patients with Advanced Nonsquamous Non-Small Cell Lung Cancer. *Study Chair: Dr. Alan Sandler. Statistician: Robert Gray.*

Recommendation: The second planned interim analysis was reviewed. The protocol criteria for stopping were met, and the DMC recommended that the results be released to the ECOG investigators for possible presentation and publication.

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 first interim analysis of outcome data was discussed. The DMC recommended that results remain blinded and that this study continue as planned. The DMC also recommended approving release of limited data on a subset of cases for use in developing preliminary analyses for a laboratory grant application (the data released will not include any information on treatment).