Report of the ECOG Data Monitoring Committee Meeting, April 27, 2004

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group (ECOG) met in Boston on April 27, 2004, 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 May 2004 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, E1292, E1301, E1697, E1899, E1900, E1996, E1D96, E2100, E2197, E2496, E2499, E2997, E3200, E3201, E3598, E3999, E4201, E4402, E4599, E4697, E5597, E5A93 and E6201. Interim analyses of outcome data were conducted on E2997 and E3200. The DMC accepted the reports on E1199, E1292, E1301, E1697, E1899, E1900, E1D96, E2100, E2197, E2496, E3201, E3598, E3999, E4201, E4402, E4599, and E5597 without discussion, recommending that these studies continue without modification. The DMC recommendations on the other studies are listed below. 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).

E1996 - Phase III Evaluation of EPO with or without G-CSF versus Supportive Therapy Alone in the Treatment of Myelodysplastic Syndromes. *Study Chair: Dr. Kenneth Miller. Statistician: Haesook Kim.*

Recommendation: There has only been one patient entered on this study since last August, and the ECOG Leukemia Committee had requested that this study be closed to further accrual. The DMC recommended that this be done. The DMC also recommended releasing the results of this study to the study team to consider for possible presentation or publication.

E2499 - Randomized Phase III Trial of Rutuximab (NSC #687451) and Autologous Stem Cell Transplantation for B Cell Diffuse Large Cell Lymphoma. *Study Chair: Dr. Ian Flinn. Statistician: Edie Weller.*

Recommendation: The DMC recommended proceeding with a modification to the design proposed by the ECOG Lymphoma Committee to address the slow accrual to this study. The modified design will give all patients rituximab pre-transplant and then randomize between maintenance rituximab vs. observation post transplant. The DMC will review accrual to this study again in one year. By that time, accrual needs to improve to at least 7 patients per month. Since patients randomized prior to changing the design cannot be included in the primary analysis of the modified design, accrual to this study had been suspended, pending approval of the modified design. The DMC recommended that this study remain suspended until the revised design activates.

E2997 - Phase III Randomized Trial of Fludarabine and Cyclophosphamide versus Fludarabine for Previously Untreated Chronic Lymphocytic Leukemia. *Study Chair: Dr. Ian Flinn. Statistician: Elizabeth Kumm.*

Recommendation: The second planned interim analysis was reviewed. This study has completed accrual, but some patients will remain on protocol treatment until September. Criteria for early stopping were met, and the DMC recommended that the results be released. The DMC also recommended that patients still on treatment and their physicians be notified of the interim results and that further treatment on protocol be left to their discretion.

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: Based on data so far, it appears the control arm survival rates in this study are different than anticipated in the design. The proportion of HLA positive patients is also lower than expected. The DMC recommended confidentially releasing information on the control arm survival rates to the study team to consider possible modifications to the design of this study, which will likely be necessary for this study to meet its objectives. If there is a proposed redesign this must be submitted to the DMC for review by the next DMC meeting. The DMC also recommended releasing preliminary results of the circulating DC and T-cell reactivity analyses to Dr. Kirkwood per study design.

E5A93 - The Treatment of Multiple Myeloma Utilizing VBMCP Chemotherapy Alternating with High-Dose Cyclophosphamide and Alpha2b-Interferon versus VBMCP. A Phase III Study of Previously Untreated Multiple Myeloma*. Study Chair: Dr. Robert Kyle. Statistician: Emily Blood.*

Recommendation: In response to a request from the Myeloma lab investigators, the DMC recommended that analyses combining lab data and the clinical outcome data be allowed to proceed, and that results of these analyses be confidentially released to the lab investigators. No public release of information from these analyses is allowed until approved by the DMC.

E6201 - A Phase III, Randomized Study of Gemcitabine (fixed-dose rate infusion) and Oxaliplatin versus Gemcitabine (fixed-dose rate infusion) versus Gemcitabine (30-minute infusion) in Pancreatic Cancer*. Study Chair: Dr. Elizabeth Poplin. Statistician: Donna Levy.*

Recommendation: The design of this study includes a planned increase in the accrual goal (from 666 to 789) if the accrual rate reaches at least 250 patients per year by the end of the first year of accrual. This study has now been open for one year, and the estimated accrual rate is 445 patients per year. The DMC therefore recommended increasing the accrual goal to 789 patients, in accordance with the design.

E3200 - Phase III Trial of Bevacizumab, Oxaliplatin, 5-FU, and Leucovorin vs. Oxaliplatin, 5-FU and Leucovorin vs. Bevacizumab Alone in Previously Treated Patients with Advanced Colorectal Cancer. *Study Chair: Dr. Bruce Giantonio. Statistician: Paul Catalano.*

Recommendation: The first scheduled interim analysis of outcome data was reviewed. The DMC recommended that this study continue in blinded follow-up in accordance with the design.