Report of the ECOG Data Monitoring Committee Meeting, April 22, 2003

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group (ECOG) met by conference call on April 22, 2003, 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 2003 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, E1496, E1697, E1900, E1996, E1A00, E1D96, E2100, E2197, E2496, E2898, E2997, E3200, E3598, E3999, E4494, E4599, E4697, E5597, and E5A93. Interim analyses of outcome data were conducted on E2197, E2997, E2898 and E4494. The DMC accepted the reports on E1199, E1292, E1900, E1996, E2197, E2496, E2898, E3598, E3999, E4697, E5597, and E5A93 without discussion, recommending that these studies continue without modification. The reports on E2197 and E2898 included planned interim analyses. In accepting the reports on these studies, the DMC recommended that these studies continue in blinded follow-up. 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).

E1496 - Randomized Phase III Study in Low Grade Lymphoma Comparing Maintenance Anti-CD20 Antibody versus Observation Following Induction Therapy. *Study Chair: Howard Hochster. Statistician: Edie Weller.*

Recommendation: A request for release of outcome data for planning purposes was considered. The DMC recommended that information on the maintenance comparisons not be released at this time, since many patients are still receiving protocol treatment, but did recommend approval for confidential release of induction response data.

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

Recommendation: SWOG, CALGB and the Sydney Melanoma Unit have recently been added to this study, but it is too early to evaluate the effect these groups will have on the overall accrual. The DMC recommended that this study continue, with the progress to be reviewed again in 6 months. By that time, the overall accrual rate needs to improve to at least 20 patients per month, or the DMC may recommend that this study be closed.

E1A00 - A Randomized Phase III Trial of Thalidomide (NSC#66847) Plus Dexamethasone Versus Dexamethasone in Newly Diagnosed Multiple Myeloma. *Study Chair: S. Vincent Rajkumar. Statistician: Emily Blood.*

Recommendation: The DMC reviewed the toxicity data on this study. The DMC recommended that this study continue as planned.

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

Recommendation: This study was terminated a year ago due to slow accrual, and it is currently in blinded follow-up. The outcome data is still incomplete, and the DMC recommended that this study continue in blinded follow-up, with the status of this study to be reviewed again in 6 months.

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 current toxicity data were reviewed. No significant problems were identified, and the DMC recommended this study continue. The DMC also recommended approval of a proposal from the study team for a design change to eliminate the planned suspension of accrual. Under this proposed change, the stopping rules will remain as planned, but accrual will remain open while the endpoints are evaluated.

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

Recommendation: The results of the first scheduled interim analysis were reviewed. The DMC recommended that this study continue. Because there was inadequate justification for the change, the DMC voted against a request from the study team to change the primary endpoint to clinical complete response.

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 toxicity data were reviewed. No significant problems were identified, and the DMC recommended that this study continue as planned. Survival data were also reviewed, and the DMC recommended that arm C (bevacizumab alone) remain permanently closed to patient entry (accrual to this arm had recently been suspended).

E4494 - Phase III Trial of CHOP vs CHOP and Chimeric Anti-CD20 Monoclonal Antibody in Older Patients with Diffuse Mixed, Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma. *Study Chair: Dr. Tom Habermann. Statistician: Edie Weller.*

Recommendation: Interim results from this study were reviewed. Although criteria for stopping were not met, in light of the results from the GELA study and the intense interest in the results of this study, the DMC recommended that the interim data be released for possible presentation and publication.

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: Patricia Stephenson.*

Recommendation: The current toxicity data were reviewed. No significant problems were identified, and the DMC recommended that this study continue. The DMC also recommended that this study be modified to drop the planned suspension of accrual prior to the first interim analysis, and that instead this study should remain open to accrual during this period.