Report of the ECOG Data Monitoring Committee Meeting, April 3, 2002

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group (ECOG) met on April 3, 2002, 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 2002 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, E1996, E1D96, E2100, E2190, E2193, E2197, E2496, E2597, E2898, E2997, E2Z96, E3193, E3200, E3598, E3695, E4494, E4599, E4697, E4897, E5597, and E5A93. E5397 was reviewed on a conference call on February 26, 2002. Interim analyses of outcome data were conducted on E1292, E2898, E3695, E4494, and E4897. The DMC accepted the reports on E1199, E1496, E1996, E2100, E2190, E2496, E2597, E2997, E3193, E3598, E4697, E5597, and E5A93 without discussion, recommending that they continue without modification. The DMC recommendations on the other studies are listed below.

E1292 - Phase III Prospectively Randomized Trial of Perioperative 5-FU After Curative Resection, Followed by 5-FU/Leucovorin for Patients with Colon Cancer. An interim analysis of outcome was reviewed. The DMC recommended this study continue in blinded follow-up.

E1697 - A Randomized Study of Four Weeks of High Dose IFN Alpha2b in Stage T3-T4 or N1 (Microscopic) Melanoma. Accrual is currently not adequate to meet the objectives of this study. However, commitments to participate have been obtained from the Sydney Melanoma Unit, SWOG and CALGB, and an amendment adding these groups is in preparation. The DMC therefore recommended that this study remain open to accrual. The DMC will review this study again in 1 year, at which time the study should be accruing at least 200 patients per year.

E1D96 - Phase III Study of Paclitaxel versus Liposomal Doxorubicin for the Treatment of Advanced AIDS-Associated Kaposi's Sarcoma. Accrual has slowed

further since the review at the last DMC meeting, and is not adequate to meet the objectives of this study. The DMC recommended that this study be closed to further accrual. The DMC also recommended that patients already on study continue to be treated and followed in accordance with the protocol, and that this study continue in blinded follow-up. The DMC will review the status of this study again in one year.

E2193 - A Phase III Prospective, Randomized Clinical Trial of Hormone Replacement Therapy in Post-Menopausal Women with a History of Node-Negative Breast Cancer or Ductal Carcinoma-In-Situ Who Are Receiving Adjuvant Tamoxifen. Accrual is currently not adequate to meet the objectives of this study. However, the Y-ME National Breast Cancer Organization is initiating a major effort to support recruitment of patients for this study. The DMC therefore recommended that this study remain open to accrual. The DMC will review the status of this study again in 1 year.

E2197 - Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytoxan in the Adjuvant Treatment of Node Positive and High Risk Node Negative Breast Cancer. The DMC considered a request from NSABP for confidential access to interim results from this study to aid in planning a new study. The DMC recommended releasing a statement to NSABP regarding the implications of the interim E2197 data for the new study, but recommended against providing interim data or analyses.

E2898 - Phase III Randomized Trial of Interferon Alfa-2b Alone versus Interferon Alfa-2b Plus Thalidomide in Patients with Previously Untreated Metastatic or Unresectable Renal Cell Carcinoma. The first scheduled interim analysis of outcome data was reviewed. The DMC recommended that this study remain blinded and continue as planned.

E2Z96 - Double Blind Randomized Trial of Methylphenidate for Alleviation of Fatigue and Lethargy Associated with Interferon Alpha 2b. This study is currently accruing too slowly to meet its objectives. The DMC recommended that this study be closed to further accrual. There are no patients currently on protocol therapy.

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. This study is currently suspended for a planned toxicity evaluation. The safety and efficacy monitoring plans were reviewed. The current toxicity data was also reviewed. There was insufficient data to make a recommendation on reopening this study. DMC therefore recommended that this study remain suspended, pending receipt of further data. DMC will review the report when it is received.

E3695 - A Randomized Phase III Trial of Concurrent Biochemotherapy with Cisplatin, Vinblastine, Dacarbazine, IL-2 and Interferon alpha-2b versus Cisplatin, Vinblastine, Dacarbazine Alone in Patients with Metastatic Malignant Melanoma. An interim analysis of outcome data was reviewed. This analysis was not part of the original design, but was requested by the DMC at their last meeting. The DMC recommended that this

study be terminated, because it was unlikely that the biochemotherapy arm of the study would result in the desired improvement in overall survival. The DMC also recommended that the results be released for possible presentation and publication In addition, the DMC recommended that further treatment of patients currently on the biochemotherapy arm be left to the discretion of the treating physician, following a discussion of the study's results between the physician and the patient. Materials to assist in these discussions have been posted on the ECOG web page.

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. Interim results from this study were reviewed. This analysis was not part of the original design, but was conducted because of the positive results from the GELA CHOP versus Rituximab+CHOP study in a similar population. After considering all available information, the DMC recommended that E4494 remain blinded and continue as planned. The DMC further recommended that the induction results to date could be released confidentially to a small group of ECOG Lymphoma Committee members for planning purposes, and that they be informed that the maintenance data are not yet mature. All individuals who will have access to the induction results will be required to sign confidentiality agreements. The DMC will continue to monitor this study closely.

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. This study is currently suspended for a planned toxicity evaluation. The safety and efficacy monitoring plans were reviewed. The current toxicity data was also reviewed. There was insufficient data to make a recommendation on reopening this study. DMC therefore recommended that this study remain suspended, pending receipt of further data.

E4897 - Phase III Trial of MVAC vs Carboplatin and Paclitaxel in Advanced Carcinoma of the Urothelium. The DMC recommended that the outcome data be released for possible presentation and publication.

E5397 – Randomized, Double Blind, Placebo Controlled Phase III Evaluation of Cisplatin+Placebo versus Cisplatin+C225 a Mouse/Human Monoclonal Antibody to the Epidermal Growth Factor Receptor, in Patients with Metastatic and/or Recurrent Squamous Cell Cancer of Head and Neck. The DMC recommended that the outcome data be released for possible presentation and publication.

Submitted by
Robert Gray, Ph.D.
ECOG Group Statistician
(617) 632-3012