Recommendations of the ECOG Data Monitoring Committee, November 5, 2003

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group met at the ECOG Coordinating Center on November 5, 2003, and reviewed all ongoing phase III studies coordinated by ECOG. The following voting members were present: Scott Bearman, Al Benson, Bruce Johnson, Pam McAllister, Joe Pater, DeJuran Richardson, Mitchell Smith, Jim Martenson, and Jim Stewart. Non-voting members present were Bruce Giantonio, Bob Gray, Margaret Mooney (substituting for Rick Kaplan) and Larry Rubinstein.

The DMC accepted the reports on E1292, E1899, E1900, E1996, E2197, E2496, E2499, E2997, E3999, E4201, E4697, E5A93, and E6201 without discussion, recommending that these studies continue without modification. The DMC recommendations on the other studies are listed below.

Voting: (in favor/opposed/abstain)

E1199 - A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive or High Risk Node-Negative Breast Cancer. *Study Chair: Dr. Joseph Sparano. Statistician: Molin Wang.*

Recommendation: A planned interim analysis of outcome data was presented. The protocol criteria for stopping were not met, and the committee recommended that this study continue in blinded follow-up. (9/0/0)

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

Recommendation: A planned interim analysis of the primary maintenance comparison was presented. The protocol criteria for stopping were met, and the committee recommended that the results be released for possible presentation and publication. (9/0/0) Although accrual to the initial induction step had closed in May, the randomization of patients to maintenance therapy was continuing. The DMC also recommended that that this randomization be closed. (9/0/0) The DMC further recommended that treatment of patients currently on protocol be left to physician discretion, that information on the results should be provided to participating patients and physicians, and that the physicians should discuss this information with the patients in planning the further course of therapy. (9/0/0)

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 Sydney Melanoma Unit has just activated this study. The DMC recommended that this study continue, with the progress to be reviewed again in 1 year. By that time, the overall accrual rate needs to improve to at least 20 patients per month, or the DMC will recommend that this study be closed. This should be achieved by the current participants, and the DMC will not be influenced by promises of additional groups entering at that time. (8/1/0)

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

Recommendation: The first planned interim analysis of outcome data was presented. Protocol criteria for early release were met, and the DMC recommended releasing the results for possible presentation and publication. (9/0/0) The DMC also recommended that information on the study results should be distributed to patients on this study and their physicians, and that the treating physicians should discuss this information with the patients and consider it in planning the further course of therapy. (9/0/0)

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 was terminated in May 2002 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. (9/0/0)

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: Based on a review of materials provided in the written report, the DMC agreed that there were no significant toxicity problems, and recommended that this study continue without modification. (9/0/0)

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. *Study Chair: Dr. Michael Gordon. Statistician: Judith Manola.*

Recommendation: A planned interim analysis of outcome data was presented. Criteria for early stopping in favor of the null hypothesis of no difference in survival were met,

and the DMC recommended release of the results of this study for possible presentation and publication. (9/0/0)

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: Based on a review of materials provided in the written report, the DMC agreed that there were no significant toxicity problems, and recommended that this study continue without modification. (9/0/0)

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: Lily Xu***.**

Recommendation: A planned interim analysis of outcome data was presented. Criteria for stopping were not met, and the committee recommended that this study continue as planned. (9/0/0) The DMC requested that additional details on the timing of thromboembolic events and on the amount of therapy delivered on the two arms be presented at the next meeting. (9/0/0)

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 DMC reviewed toxicity data for this study. Although there continues to be concern about the rate of bleeding events, the DMC did not believe changes to the protocol were required at this time. The DMC also recommended approval of a proposal to increase the sample size to approximately 900 patients to target a smaller treatment difference. (8/1/0) The consent form should also be modified to reflect updated toxicity information. (8/1/0)

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 recent paper in JNCI reported an increased rate of non-melanoma skin cancer in patients with a prior history of non-melanoma skin cancer receiving selenium supplementation (Duffield-Lillico *et. al*., JNCI, 95:1477-81, 2003). The DMC considered whether any changes to the E5597 protocol were required in light of this information. It was noted that the E5597 protocol already required submitting reports of all second cancers as adverse events. The DMC recommended modifying the wording to indicate specifically that this requirement includes basal cell and squamous cell skin cancers. The DMC also recommended that information given to patients on study and

added to the consent form regarding this risk should clearly discuss the risks and benefits in the context of the population studied in the JNCI paper. (9/0/0)