Recommendations of the ECOG Data Monitoring Committee, April 17, 2009 and April 28, 2009

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group met by conference call on April 17, 2009 and again on April 28, 2009 to review 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 for the June 2009 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 Mary Steele at the ECOG Operations Office at (617) 632-3610.

The DMC accepted the reports on E1105, E1305, E1505, E1697, E1A05, E1A06, E2905, E3805, E4203, and TAILORx (PACCT-1) without discussion, recommending that these studies continue without modification. The DMC recommendations on the other studies are listed below.

E1602 - A Randomized Phase II Trial of Multi-epitope Vaccination with Melanoma Peptides for Cytotoxic T Cells and Helper T Cells for Patients with Metastatic Melanoma. *Study Chair: Dr. Craig Slingluff. Statistician: Sandra Lee.*

Recommendation: Accrual and most treatment on this phase II protocol have been completed. Although further evaluation of the primary endpoint of CTL response is needed, the DMC recommended that this study be released to the study investigators.

E2603 - A Double-Blind, Randomized, Placebo-Controlled Phase III Trial of Carboplatin, Paclitaxel, and BAY 43-9006 versus Carboplatin, Paclitaxel and Placebo in Patients with Unresectable Locally Advanced or Stage IV Melanoma. *Study Chair: Dr. Keith Flaherty. Statistician: Sandra Lee.*

Recommendations:

1. The third planned interim analysis of overall survival was reviewed. Protocol criteria for stopping for futility were met and the DMC recommended that the study results be released.
2. Physicians should review the results with their patients. Each patient's treatment can be unblinded, and those assigned to BAY 43-9006 may continue to receive the drug from the NCI at the treating physician's discretion.

E2805 - ASSURE: Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma. *Study Chair: Dr. Naomi Balzer-Haas. Statistician: Judith Manola.*

Recommendation: The DMC reviewed the data on cardiac toxicity from this study. The DMC recommended that this study continue as planned. When the information required for the formal evaluation of the cardiac safety endpoint, the DMC will review the report before it is released to CTEP.

E2902 - A Phase III Study of Farnesyl Transferase Inhibitor R115777 in AML Patients in Second or Subsequent Remission or in Remission after Primary Induction Failure. *Study Chair: Dr. Selina Luger. Statistician: Xiaopan Yao.*

Recommendation: The fourth planned interim analysis of DFS was presented. Protocol criteria for stopping were not met, and the DMC recommended that this study continue with accrual and blinded follow-up as planned.

E4402 - Randomized Phase III Trial Comparing Two Different Rituximab Dosing Regimens for Patients with Low Tumor Burden Indolent non-Hodgkin's Lymphoma. *Study Chair: Dr. Brad Kahl. Statistician: Fangxin Hong.*

Recommendation: The DMC reviewed the third planned interim analysis of the primary endpoint of time to rituximab failure. The DMC recommended that his study continue with follow-up as planned.

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 ninth interim analysis of outcome data was presented. Although stopping boundaries were not crossed, the protocol design included provisions for releasing results 30 months after completion of accrual. Because of this provision, the DMC recommended that the study results be released to the investigators after the end of April, when the 30 months of follow-up will be completed.

E5103 - A Double-Blind Phase III Trial of Doxorubicin and Cyclophosphamide followed by Paclitaxel with Bevacizumab or Placebo in Patients with Lymph Node Positive and High Risk Lymph Node Negative Breast Cancer. *Study Chair: Dr. Kathy Miller. Statistician: Anne O'Neill.*

Recommendation: This study includes requirements for cardiac monitoring and early stopping rules for excessive cardiac toxicity. The DMC reviewed the data on cardiac toxicity and recommended that this study continue as planned.

E5202 - A Randomized Phase III Study Comparing 5-FU, Leucovorin and Oxaliplatin versus 5-FU, Leucovorin, Oxaliplatin and Bevacizumab in Patients with Stage II Colon Cancer at High Risk for Recurrence to Determine Prospectively the Prognostic Value of Molecular Markers. *Study Chair: Dr. Al B. Benson. Statistician: Paul Catalano.*

Recommendation: The DMC reviewed information on the results of NSABP C-08, which was a study examining a very similar treatment question to E5202 in the setting of stage II and III colon cancer (the NSABP C-08 population partially overlaps with the E5202 population). The DMC thought that the C-08 information did not raise substantial

safety or efficacy concerns for the E5202 study at this time and recommended that accrual to E5202 continue.

E5204 - Intergroup Randomized Phase III Study of Postoperative Oxaliplatin, 5-Fluorouracil and Leucovorin vs Oxaliplatin, 5-Fluorouracil, Leucovorin and Bevacizumab for Patients with Stage II or III Rectal Cancer Receiving Preoperative Chemoradiation. *Study Chair: Dr. Al Benson. Statistician: Paul Catalano.*

Recommendation: This study has been accruing much slower than planned. The DMC recommended that this study be closed.

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: The DMC considered a request from Dr. Steve Belinsky for release of information related to lab analyses for possible publication. The DMC recommended that this information not be released at this time.