Recommendations of the ECOG Data Monitoring Committee, October 21, 2009

The Data Monitoring Committee (DMC) of the Eastern Cooperative Oncology Group met by teleconference on October 21, 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 November 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 E1305, E1697, E1A05, E2805, E2905, E3805, E4203, E5202, E5204, and TAILORx (PACCT-1) without discussion, recommending that these studies continue without modification. The DMC recommendations on the other studies are listed below.

E1105 - A Randomized Phase III Double-Blind Placebo-Controlled Trial of First-line Chemotherapy and Trastuzumab with or without Bevacizumab for Patients with HER-2/NEU Over-expressing Metastatic Breast Cancer. *Study Chair: Dr. Ingrid Mayer. Statistician: Anne O'Neill.*

Recommendation: This study is nearing end of quarter 8 since activation and is accruing at well-below 50% of the planned rate. The DMC therefore recommended that this study be closed in accordance with the NCI policy on slowly accruing phase III studies.

E1505 – A Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients With Completely Resected Stage IB (>/= 4 cm) - IIIA Non-Small Cell Lung Cancer (NSCLC). *Study Chair: Dr. Heather Wakelee. Statistician: Suzanne Dahlberg.*

Recommendation: Information on treatment duration and reasons for discontinuation was reviewed and the DMC recommended that this study continue as planned.

E1A06 - An Intergroup Phase III Randomized Controlled Trial Comparing Melphalan, Prednisone and Thalidomide (MPT) versus Melphalan, Prednisone and

Lenalidomide (Revlimid)(MPR) in Newly Diagnosed Multiple Myeloma Patients who are not Candidates for High Dose Therapy. *Study Chair: Dr. Alexander Stewart. Statistician: Hajime Uno.*

Recommendation: The DMC recommended approval of a request to release toxicity information to another group interested in participating in this study, with appropriate confidentiality restrictions.

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

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. A monitoring rule on the rate of clinical CHF had been met and accrual had been suspended on September 24, 2009. The DMC reviewed the data on cardiac toxicity. The DMC recommended that the consent form be modified to reflect the current information on the risk of clinical CHF and that the study then be reopened to accrual. Intensive monitoring of cardiac toxicity will continue.

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 reviewed the first planned interim analysis of the primary endpoint of the incidence of new lung cancers. Based on the interim results, it was highly unlikely that this study could eventually show significant evidence of a benefit from selenium, so the DMC recommended that this study be terminated. The DMC also recommended that the patients be notified and that the intervention should be stopped.