



CANCER AND LEUKEMIA GROUP B
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RICHARD L. SCHILSKY, M.D.
CHAIRMAN

MEMORANDUM

Date: January 15, 2010

To: CALGB Principal Investigators and Lead CRAs

From: Richard L. Schilsky, MD, Group Chair

Re: CALGB Data and Safety Monitoring Board (DSMB) Report

The CALGB Data and Safety Monitoring Board (DSMB) met on November 13, 2009. Attached please find a listing of each study reviewed, the DSMB recommendation, and the action taken in response to the recommendation.

These statements may be submitted to your IRB per local IRB guidelines.

Questions may be directed to Kathleen S. Karas, Director of Protocol Operations (kkaras@uchicago.edu; 773-702-9674).

CANCER CONTROL

70305 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 70305, A randomized study to prevent lymphedema in women treated for breast cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring. If the accrual rate is not above 50% by the next meeting, then a recalculation of the statistical section to provide a modified estimate of the expected accrual rate and time to expected completion should be developed. The DSMB recommends that all adverse event data related to the protocol specified intervention should be included in all subsequent interim submissions to the DSMB.

Action: Recommendation accepted.

70604 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 70604, A randomized phase III study of standard dosing versus longer dosing interval of zoledronic acid in metastatic cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

ONCOLOGY NURSING

170601 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 170601, A phase III double blind trial of oral duloxetine for treatment of pain associated with chemotherapy-induced peripheral neuropathy (CIPN), during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring. The DSMB also supports the plan for expansion of the entry criteria to include patients receiving other neurotoxic agents [e.g., nab-paclitaxel and ixabepilone] during their anti-cancer therapy.

Action: Recommendation accepted.

LEUKEMIA COMMITTEE

10501 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 10501, A phase III intergroup CLL study of asymptomatic patients with untreated chronic lymphocytic leukemia randomized to early intervention versus observation with later treatment in the high risk genetic subset with IgVH unmutated disease, during a meeting on November 13, 2009. The DSMB recommended study closure based on chronic inadequate accrual. Salvaging the current study data to support a future trial in this area is strongly encouraged.

Action: Recommendation accepted. CALGB 10501 has been closed to new pre-registrations and randomizations. A protocol amendment is under development for the purpose of continuing data collection on patients who were pre-registered or randomized to the study. Patients who were previously randomized may continue to receive study therapy.

10603 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 10603, A phase III randomized, double-blind study of induction (daunorubicin/cytarabine) and consolidation (high dose cytarabine) chemotherapy + midostaurin (PKC412)(IND #101261) or placebo in newly diagnosed patients < 60 years of age with FLT3 mutated acute myeloid leukemia (AML), during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

SURGERY

140503 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 140503, A phase III randomized trial of lobectomy versus sublobar resection for small (≤ 2 cm) peripheral non-small cell lung cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring. If study accrual remains below the revised accrual rate provided in the proposed amendment, closure of this trial should be strongly considered.

Action: Recommendation accepted.

TRANSPLANT

100103 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 100103, A phase II study of allogeneic transplant for older patients with AML in first morphologic complete remission using a non-myeloablative preparative regimen, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

100104 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 100104, A phase III randomized, double-blind study of maintenance therapy with CC-5013 (NSC # 703813, IND # 70116) or placebo following autologous stem cell transplantation for multiple myeloma, during a meeting on November 13, 2009. The DSMB recommended releasing the study data to the study team and the Transplant Committee. There should be no further monitoring of this project by the DSMB.

Action: Recommendation accepted. Participating investigators were notified of the results via broadcast email on December 17, 2009 and provided with patient and physician letters. All patient treatment assignments were unblinded and instructions for patients currently receiving study therapy were provided.

RESPIRATORY

30506 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 30506, A randomized phase III trial of adjuvant therapy in early stage NSCLC evaluating the potential utility of a genomic prognostic model to identify patients as candidates for adjuvant chemotherapy, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

30607 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 30607, Randomized phase III double-blind placebo-controlled trial of sunitinib (NSC #736511, IND #74019) as maintenance therapy in non-progressing patients following an initial four cycles of platinum-based combination chemotherapy in advanced stage IIIB/IV non-small cell lung cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring. The DSMB recommends a careful review and modification of the consent document to address new survival data and the resulting FDA approval of a maintenance agent for non-squamous patients being managed in this specific treatment setting.

Action: Recommendation accepted. An amendment to revise the consent form will be prepared and submitted to CTEP for review and approval.

30610 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 30610, Phase III comparison of thoracic radiotherapy regimens in patients with limited small cell lung cancer also receiving cisplatin and etoposide, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

GI

80101 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 80101, Phase III intergroup trial of adjuvant chemoradiation after resection of gastric or gastroesophageal adenocarcinoma, during a meeting on November 13, 2009. The DSMB recommended continued monitoring.

Action: Recommendation accepted.

80405 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 80405, A phase III trial of irinotecan/5-FU/leucovorin or oxaliplatin/5-FU/leucovorin with bevacizumab, or cetuximab (C225), or with the combination of bevacizumab and cetuximab for patients with untreated metastatic adenocarcinoma of the colon or rectum, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

GU

90202 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 90202, A randomized double-blind, placebo-controlled phase III study of early versus standard zoledronic acid to prevent skeletal related events in men with prostate cancer metastatic to bone, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring without modification.

Action: Recommendation accepted.

90203 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 90203, A randomized phase III study of neo-adjuvant docetaxel and androgen deprivation prior to radical prostatectomy versus immediate radical prostatectomy in patients with high-risk, clinically localized prostate cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

90401 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 90401, A randomized double-blinded placebo-controlled phase III trial comparing docetaxel and prednisone with and without bevacizumab (IND #7921, NSC #704865) in men with hormone refractory prostate cancer, during a meeting on November 13, 2009. The DSMB recommended continued monitoring.

Action: Recommendation accepted.

LYMPHOMA

50303 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 50303, Phase III randomized study of R-CHOP versus dose-adjusted EPOCH-R with molecular profiling in untreated de novo diffuse large B-cell lymphomas, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

BREAST

40101 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 40101, Cyclophosphamide and doxorubicin (CA x 4 cycles) versus paclitaxel (4 cycles) as adjuvant therapy for breast cancer in women with 0-3 positive axillary lymph nodes: A phase III randomized study, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

40302 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 40302, Endocrine therapy with or without inhibition of EGF and HER2 growth factor receptors: A randomized, double-blind, placebo-controlled phase III trial of fulvestrant with or without lapatinib (GW572016) for postmenopausal women with hormone receptor positive advanced breast cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

40502 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 40502, A randomized phase III trial of weekly paclitaxel compared to weekly nanoparticle albumin bound NAB-paclitaxel or ixabepilone combined with bevacizumab as first-line therapy for locally recurrent or metastatic breast cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.

40503 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 40503, Endocrine therapy in combination with anti-VEGF therapy: A randomized, double-blind, placebo-controlled phase III trial of endocrine therapy alone or endocrine therapy plus bevacizumab (NSC 704865, IND 7921) for women with hormone receptor-positive advanced breast cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring. The DSMB also recommends accepting the amendment to convert the study to an open label design.

Action: Recommendation accepted. The amendment will be submitted to CTEP for review and approval.

40601 The CALGB Data and Safety Monitoring Board (DSMB) reviewed CALGB 40601, Randomized phase III trial of paclitaxel combined with trastuzumab, lapatinib, or both as neoadjuvant treatment of HER2-positive primary breast cancer, during a meeting on November 13, 2009. The DSMB recommended continued accrual and monitoring.

Action: Recommendation accepted.