NCCTG Data Monitoring Committee Adverse Events Report
Meeting Date: April 19, 2005

Committee Membership: Voting: C. Blanke, H. Burris, K. Huppler Hullsiek, C. Lawton, R. Marks, P. McAllister

Non-Voting: B. Friedlin, J. Kelaghan, M. Mooney, D. Sargent

On 4/19/05, the NCCTG Data Monitoring Committee met and reviewed the following phase-III trials. For each trial a complete report including accrual, baseline characteristics, toxicity, and blinded efficacy data was presented to and discussed by the NCCTG EDMC. The official action item for each trial is presented below, along with a notation of any specific issues raised or discussed regarding toxicity, if applicable.

CANCER CONTROL

#N00C1 (Phase III Placebo-Controlled, Randomized, Double-Blind Comparison of Etanercept (Enbrel) Versus Placebo for the Treatment of Cancer-Associated Weight Loss and Anorexia)

- *Action:* The DMC voted unanimously to release the data to the study team and to terminate DMC monitoring. The adverse event data were reviewed and no issues were identified.

#N00C9 (The Use of Ginkgo Biloba for the Prevention of Chemotherapy-Related Cognitive Dysfunction)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N00CA (Phase III Double-Blind Study of Depot Octreotide Versus Placebo in the Prevention of Acute Diarrhea in Patients Receiving Pelvic Radiation Therapy)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N00CB (A Phase III Randomized, Double-Blind, Placebo-Controlled Trial of Gabapentin in the Management of Hot Flashes in Men)

- *Action:* The DMC unanimously voted to notify the study team that if accrual does not reach 5 patients per month by the next DMC meeting, the trial will be recommended for closure. The adverse event data was reviewed and no issues were identified.

#N01C3 (The Efficacy of Lamotrigine in the Management of Chemotherapy-Induced Peripheral Neuropathy: A Phase III Randomized, Double Blind, Placebo-Controlled Trial)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N01C4 (Phase III Double-Blind, Placebo-Controlled Randomized Comparison of Zinc Sufate Versus Placebo for the Prevention of Altered Taste in Patients with Head and Neck Cancer During Radiation)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N01C5 (The Use of Valeriana Officinalis (Valerian) in Improving Sleep in Patients Who Are Undergoing Adjuvant Treatment for Cancer: A Phase III Randomized, Placebo-Controlled, Double-Blind Study)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N01C8 (Osteoporosis Prevention in Prostate Cancer Patients Receiving Androgen Ablation Therapy: A Phase III Randomized, Placebo-Controlled, Double-Blind Study)

- *Action:* The DMC voted unanimously to recommend that the trial be closed due to poor accrual. The adverse event data were reviewed and no issues were identified.

#N01C9 (Docetaxol and Infliximab/Placebo in Non-Small Cell Lung Cancer Patients)

- *Action:* The DMC unanimously voted to notify the study team that if accrual does not reach 6 patients per month by the next DMC meeting, the trial will be recommended for closure. The adverse event data was reviewed and no issues were identified.

#N01CB (The Efficacy of Lidocaine Patch in the Management of Postsurgical Neuropathic Pain in Patients with Cancer: A Phase III Double-Blind, Crossover Study)

- *Action:* The committee noted the slow accrual to the study, and recommended that the study continue with close attention paid to the accrual rate. The adverse event data was reviewed and no issues were identified.

#N02C1 (A Randomized Controlled Trial of Risedronate for Prevention of Bone Loss In Women Undergoing Chemotherapy for Primary Breast Cancer)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N02C3 (The Use of Low Dose Testosterone to Enhance Libido in Female Cancer Survivors: A Phase III Randomized, Placebo-Controlled, Double-Blind Crossover Study)

- *Action:* Release data to the study team and terminate DMC monitoring. The adverse event data were reviewed and no issues were identified.

#N02C4 (Phase III Double-Blind, Placebo-Controlled Randomized Comparison of Creatine for Cancer-Associated Weight Loss)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N03C5 (A Phase III Randomized Trial of Gabapentin Alone or in Conjunction With an Antidepressant in the Management of Hot Flashes in Women Who have Inadequate Control with an Antidepressant Alone)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

#N03CC (A Randomized, Controlled, Open-Label Trial of Empiric Prophylactic vs. Delayed Use of Zoledronic Acid for Prevention of Bone Loss in Postmenopausal Women With Breast Cancer Initiating Therapy with Letrozole After Tamoxifen)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

BREAST

#N9831 (Adjuvant AC + Paclitaxel +/- Trastuzumab in HER-2 Overexpressing Node-Positive Breast Cancer):

- *Action:* Dr. Larry Norton joined the committee via conference call for this discussion. The committee discussed the joint analysis of the N9831 and B-31 trials. It also reviewed the data from all three arms of the N9831 trial. The committee noted the significant difference in both disease free survival and overall survival between patients in the control and experimental arms of the two trials (in the joint analysis), and that the pre-specified stopping boundaries for efficacy had been met. The committee noted the consistency of the data between the two trials. The committee voted (5 to 1) to release the data from the pooled analysis to the study team for early reporting.

The committee noted that the data from the N9831 trial alone also show a clear trend toward increased disease free survival between the control arm (arm A) and the concurrently administered investigational arm (arm C). The committee noted that there is a difference in disease free survival between the sequential arm (arm B) and the concurrent arm (arm C) which favored concurrent administration of trastuzumab with paclitaxel, however this difference between arms B and C did not meet the pre-specified stopping boundaries. The committee voted (5 to 1) to release the data from arm B to the study team for early reporting.

Based on the totality of the data, the committee recommended that those patients on both arms A and B who have not yet completed their paclitaxel be offered the opportunity to cross over to the concurrent arm (arm C). All patients who crossover should be followed according to the test schedule for arm C, and patients currently on arm C should also continue to follow the test schedule. The DMC made no recommendation on how patients who have completed their adjuvant paclitaxel be managed and deferred to the study team on this question. The DMC noted that data from other trials may help to answer this question, as will comparison of the data from arms B and C of the N9831 trial as it matures.

The DMC noted that the data from the joint analysis would be reviewed by the DMC of the NSABP in two days time and that the data should not be released to the study team until a similar recommendation had been made by the NSABP DMC. This information will be communicated between DMC's by their respective chairs.

The DMC reviewed the adverse event data, including the 3rd interim cardiac toxicity analysis comparing arms A to C, and no issues were identified.

GI

#N0147 (A Randomized Phase III Trial of Irinotecan (CPT-11) and/or Oxaliplatin (OXAL) Plus 5-Fluorouracil (5-FU)/Leucovorin (CF) after Curative Resection for Patients for Patients with Stage III Colon Cancer)

- *Action:* The DMC unanimously recommended that the trial be reduced from 6 to 2 arms, based on the recommendation of and data presented by the study team. The adverse event data was reviewed and no issues were identified.

#MC9944 (Colorectal Cancer Screening: Fecal Blood vs. DNA)

- *Action:* The protocol progress and event data were reviewed and no issues were identified.

Notes: 1. Further information on accrual or adverse events for any of these trials is available by contacting the NCCTG Operations Office.

2. Additional information regarding the NCCTG DMC policy is available by contacting the NCCTG Operations Office.

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