Southwest
Oncology Group
A National Clinical Research Group

May 15, 2005

TO: ALL SOUTHWEST ONCOLOGY GROUP MEMBER, CCOP, UCOP AND AFFILIATE MEDICAL ONCOLOGISTS, SURGEONS, RADIATION ONCOLOGISTS, PATHOLOGISTS, SURGEONS AND CLINICAL RESEARCH ASSOCIATES; ECOG, CALGB, NCIC-CTG, NCCTG, RTOG, COG, ACOSOG, NSABP, CTSU AND EPP

FROM: Laurence H. Baker, D.O. - Chairman

RE: GUIDANCE ON REPORTING ADVERSE EVENTS TO INSTITUTIONAL REVIEW BOARDS FOR NIH-SUPPORTED MULTICENTER CLINICAL TRIALS (http://grants.nih.gov/grants/guide/notice-files/not99-107.html)

MEMORANDUM

All Southwest Oncology Group Phase III studies are monitored by our Data and Safety Monitoring Committee (DSMC). The Group policy regarding the function and composition of the DSMC is Policy #21 - which may be found on the public portion of the Group web site at http://swog.org/Visitors/download/policies/Policy21.pdf.

Copies of this document must be made available to local Institutional Review Boards (IRBs).

As outlined in the "GUIDANCE ON REPORTING ADVERSE EVENTS TO INSTITUTIONAL REVIEW BOARDS FOR NIH-SUPPORTED MULTICENTER CLINICAL TRIALS (http://grants.nih.gov/grants/guide/notice-files/not99-107.html)", the NIH requires that summary reports of adverse events be communicated from the DSMC to the IRBs at participating institutions. The interim reports for Southwest Oncology Group studies are posted in the Report of Studies area on the members side of the Group web site at https://swog.org/. This site also contains the deliberations of the DSMC from their most recent meetings. A copy of the deliberations from the April 7, 2005 meeting is attached. The information from these reports must be made available to your IRB.

If the DSMC has decided to make recommendations resulting in substantial changes to a study, those changes will be circulated in the form of a protocol amendment or a special notification (e.g., "Dear Physician" letter).

PC/dbs

Enclosure

cc: John J. Crowley, Ph.D.
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M E M O R A N D U M

TO: Dr. Baker and Data and Safety Monitoring Committee:
Drs. Piantadosi, Crowley, Kempin, Korn, Langer, MacDonald, Martin, Minasian, Petrylak, Thomas Jr. and Ms. Gottlieb

FROM: John Crowley, PhD

DATE: April 20, 2005

RE: SWOG DSMC – Final minutes of SWOG Data and Safety Monitoring Committee Meeting of Thursday, April 7, 2005

1. Accrual
    a. Breast S0221 - A Phase III Trial of Continuous Schedule AC + G vs. Q 2 Week Schedule AC, Followed by Paclitaxel Given Either Every 2 Weeks or Weekly for 12 Weeks as Post-Operative Adjuvant Therapy in Node-Positive or High Risk Node-Negative Breast Cancer. Accrual is still only about 50 patients per month, as against a planned accrual of 167 per month. Efforts are underway to get better participation from US Cooperative Groups outside of SWOG, and to convince the NCIC CTG to join (which would require free provision of filgrastim and pegfilgrastim). The NCIC CTG estimates that their accrual would be 50 patients per month. Accrual will be monitored over the next 6 months and an amendment reflecting the slower accrual and a smaller sample size will be prepared for the next meeting if need be.
    b. Breast / Cancer Control S0230 – A Phase III Trial of LHRH Analog Administration During Chemotherapy to Reduce Ovarian Failure Following Standard Adjuvant Chemotherapy in Early Stage Hormone-Receptor Negative Breast Cancer. This study is now open in CALGB and ECOG but has still accrued only 5 patients. Negotiations to have the International Breast Cancer Study Group join the trial should be concluded in another two months, and they estimate accrual of 100 patients per year, making the trial feasible. The DSMC will look at accrual again in six months.
    c. Melanoma S0008 – A Phase III Trial of High Dose Interferon Alpha-2b vs. Cisplatin, Vinblastine, DTIC+ IL-2 and Interferon in Patients with High Risk Melanoma. Accrual is at only 4 patients per month instead of the target of 11.4, but ECOG, CALGB and SWOG are all participating and there are no competing national trials. Accrual is now due for completion by September 2008. The study should continue.

2. External Evidence
    a. Breast / Cancer Control S0300 – A Randomized Placebo-Controlled Biomarker Modulation Trial Using Celecoxib in Premenopausal Women at High Risk for Breast Cancer. This trial was placed on temporary hold, before any subjects had been accrued, because of the recent release of data from several trials showing an increased risk of cardiovascular events associated with the use of Cox-2 inhibitors, including celecoxib. The FDA has decided to leave celecoxib on the market but with a stronger warning label. The DSMC believes that this small risk of cardiovascular events is more than offset by the potential benefit of celecoxib in preventing breast cancer, and recommended that this study reopen. The investigators are encouraged to add exclusion criteria regarding a history of thromboemboli or current hypertension.
    b. Lung S0023 – A Phase III Trial of Cisplatin/Etoposide/RT with Consolidation Docetaxel Followed by Maintenance Therapy with Gefitinib or Placebo in Patients with Inoperable Locally Advanced Stage III Non-Small Cell Lung Cancer. The company making gefitinib recently reported to the FDA and the NCI that the randomized trial of gefitinib vs. placebo in previously treated non-small cell lung cancer patients, mandated by their fast track approval from the FDA, was negative. The agent is still on the market but the NCI, through an expert review panel, urged SWOG to discontinue S0023. The DSMC felt that an informed response to this request required an unplanned look at the outcome data. An interim analysis was prepared and sent to the committee on April 11, and a conference call was convened on April 12. The data revealed that the hypothesis of a 33% improvement in survival with gefitinib in the present trial was untenable, and recommended that the trial be closed. (Two members reported a financial conflict of interest with the company and did not vote.) The SWOG Group Chair and the NCI agreed with the closure recommendation, closed the trial on April 15, and made unblinding information available to treating investigators on April 18.

3. Interim Analysis
    a. Lung S0124 – A Randomized Phase III Trial of Cisplatin and Irinotecan vs. Cisplatin and Etoposide in Patients with Extensive Stage Small Cell Lung Cancer. A formal planned interim analysis revealed no reason for stopping the trial early, so the study should proceed as planned to the next interim analysis in the Spring of 2006.

The following trials were reviewed by mail, not discussed at the meeting, and should proceed with no change:

Brain
S0001

Breast
S0012
S0226

Gastrointestinal
S0205

Genitourinary
S9346
S9917
S9921

HN
S9908

Leukemia
S0106
S0325

Lymphoma
S9704
S0016

Myeloma
S0232

The next meeting is scheduled for Thursday, September 29, 2005 at 5 pm at the Hyatt Regency New Orleans.