Southwest
Oncology Group
A National Clinical Research Group

November 1, 2006

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

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 October 5, 2006 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, Gaspar and Ms. Gottlieb

FROM: Cathy Tangen, DrPH and Jackie Benedetti, Ph.D.

DATE: October 19, 2006

RE: SWOG DSMC – Final minutes of SWOG Data and Safety Monitoring Committee Meeting of Thursday, October 5, 2006

1. Southwest Oncology Group's Conflict of Interest (COI) Policy:
   Dr. Vernon Sondak had presented the Southwest Oncology Group's COI policy at the April meeting, and the Data and Safety Monitoring Committee had expressed concern over its potential role in assessing COI of investigators. Dr. Sondak returned for further discussion. The committee expressed the opinion that it would prefer to assume that the Southwest Oncology Group had assessed and determined the COI issues. It was mentioned that the Central IRB (CIRB) was applying a much stricter interpretation of COI. The Committee felt that this was extending the power of the CIRB beyond its charge, and that the Group Chairs should take this issue up with CTEP.

2. Accrual
   a. Breast S0226 – A Phase III Randomized Trial of Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women with Breast Cancer. This study has had slow accrual, and a new statistical section was submitted to CTEP. Study was approved for continuation.
   b. Breast / Cancer Control S0230 – A Phase III Trial of LHRH Analog During Chemotherapy to Reduce Ovarian Failure Following Standard Adjuvant Chemotherapy for Early Stage Hormone-Receptor Negative Breast Cancer. CALGB and ECOG have recently started registering patients, and accrual reached 41 patients by the meeting, thus satisfying the goal of 40 set by the DSMC at the April meeting. The International Breast Cancer Study Group (Australia and New Zealand) has still not begun accruing. The Committee recommended continuation of the trial, but expects to see at least 25 to 30 additional patients by the next meeting.

c. Breast S0221 – A Phase III Trial of Continuous Schedule AC + G vs. Q 2 Week Schedule AC, Followed by Paclitaxel Every 2 Weeks or Weekly for 12 Weeks as Adjuvant Therapy in Node-Positive or High-Risk Node-Negative Breast Cancer. Based on weak accrual, CTEP required that the statistical section of the protocol be updated to account for more realistic accrual. This amendment has been approved by CTEP and the DSMC had no issues. The DSMC recommended that the study continue, with monitoring of the Grade 5 toxicities. At this point, the number of Grade 5's is low, but if it increased above 1% the study will be placed on the agenda of the DSMC for a more detailed discussion.
d. Leukemia S0106 – A Phase III Study of the Addition of Gemtuzumab Ozogamicin Induction Therapy Versus Standard Induction with Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy with Gemtuzumab Ozogamicin or No Additional Therapy for Patients Under Age 56 with Previously Untreated De Novo Acute Myeloid Leukemia. This study had been on probation by CTEP based on low accrual in quarters 5 and 6, but is now at 50% of estimated accrual, meaning no amendment is dictated by CTEP. The study has also been amended to include patients 56-60 years old. The committee reviewed toxicities and recommended careful monitoring of adverse events, particularly with the addition of older patients.
e. GU/CC S9917 – L-Selenium Based Chemoprevention of Prostate Cancer Among Men with High Grade Prostatic Intraepithelial Neoplasia. This study has received funding through a grant from DCP. The committee felt that additional information was required before endorsing the closure of this study. A conference call was held on October 19, 2006 to evaluate information about the lack of additional DCP funding, and the fact that there is no study supplement or matching placebo left for additional randomizations. However, there is enough for patients who are randomized by November 1, 2006. Because there appeared to be no reasonable alternative, the DSMC supported the closure of this study to accrual effective November 1, 2006. All patients will continue to be followed for three years after randomization.

3. Interim Analysis
    a. Lung S0124 – Cisplatin and Irinotecan Versus Cisplatin and Etoposide in Patients with Extensive Small Cell Lung Cancer. A formal planned interim analysis revealed no reason for stopping the trial early, so the study should proceed as planned. It is expected that the study will complete accrual in six months, and the data are expected to be mature for final analysis by early 2008.
4. Other
    a. GU S9921 – Adjuvant Androgen Deprivation Versus Mitoxantrone Plus Prednisone Plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy. The GU committee is in the process of getting longitudinal PSA data on all patients. It is expected that by the next meeting these data can be assessed and presented to the DSMC. The DSMC agreed with this plan.
    b. HN S0427 – This study was not scheduled for discussion, but concern was raised over accrual.

c. Breast S0307 – This study was not scheduled for discussion, but a question was raised as to whether there is language in the protocol regarding collect ion of information on osteonecrosis of the jaw.

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

Cancer Control
S0300

Genitourinary
S9346
S0421
S0437

Leukemia
S0325

Lymphoma
S9704
S0016

Melanoma
S0008

Myeloma
S0232

The next meeting is scheduled for Thursday, May 3, 2007 at 5 pm at The Hyatt Regency in Chicago.