Southwest
Oncology Group
A National Clinical Research Group

June 1, 2007

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 May 3, 2007 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: Cathy M. Tangen, Dr.P.H.
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M E M O R A N D U M

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

FROM: Cathy Tangen, DrPH

DATE: May 9, 2007

RE: SWOG DSMC – Final minutes of SWOG Data and Safety Monitoring Committee Meeting of Thursday, May 3, 2007

1. Southwest Oncology Group's reporting of adverse events and second primaries:

   Dr. Cathy Tangen provided a brief overview of SWOG's procedure for reporting adverse events and second primaries in study reports to the DSMC. The DSMC has requested for the next cycle of reports (fall 2007) that all Grade 4 and 5 adverse events should be reported in the adverse event tables, regardless of attribution.

   The DSMC has also requested that they receive a brief communication about each randomized trial that has had its final interim analysis, but has not yet reached the time of final analysis.

2. Accrual

   Cancer Control S0300 – A Randomized Placebo-Controlled Biomarker Modulation Trial Using Celecoxib in Premenopausal Women at High Risk for Breast Cancer. This study has had slow accrual although there are signs of an increase. An amendment is expected to be submitted to the NCI which should expand the pool of potential participants. The DSMC will monitor accrual in six months and carefully look at it again in one year. The DSMC would like to see 20 more patients registered in the next 12 months. In order to evaluate feasibility, the DSMC would also like to see some quantification of the reasons why women are choosing not to participate at one or more of the active sites.

3. Study Design Amendment

   Breast S0307 – A Phase III Trial of Bisphosphonates as Adjuvant Therapy for Primary Breast Cancer. Due to a lower than anticipated accrual rate, the DSMC evaluated a proposal to adjust the statistical design assumptions to be more in line with the currently observed accrual rate. The proposal calls for the accrual goal to be lowered from 6,000 to 4,500 women. The accrual period would be extended from 4 years to 6 years, but the follow-up period would be shortened by one year. The Bonferroni

corrected pairwise comparisons will be replaced by using the Fisher's Least Significant Difference for adjusting for multiple comparisons. The DSMC approved the proposed study design amendment. It will now be formally submitted to CTEP as an amendment for formal review.

4. Interim Analysis and Data Request

Lymphoma S0016 – A Phase III Randomized Trial of CHOP Chemotherapy Plus Rituximab versus CHOP Chemotherapy Plus Iodine-131 Tositumomab for the Treatment of Newly Diagnosed Follicular Non-Hodgkin's Lymphoma. The second formal interim analysis was presented. Based on those results, the DSMC voted that the study should continue as planned. With respect to a request by Lymphoma Committee leadership to see the progression-free survival curves by arm, the DSMC felt that since the study has approximately eight more months of accrual left and the number of events is relatively low, it is premature for the leadership to have access to the requested data. The disease committee leadership were informed that they could provide the DSMC an expanded rationale for access to outcome data if they still feel, in the light of the DSMC report on the interim analysis, that having access to PFS data is required.

5. Data Request

Lung S0124 – Randomized Phase III Trial of Cisplatin and Irinotecan versus Cisplatin and Etoposide in Patients with Extensive Small Cell Lung Cancer. Toxicity and pharmacogenomic data will be presented at ASCO. The Lung Committee leadership requested that progression-free survival and overall survival curves pooled across arms be allowed to be presented at ASCO. The DSMC felt there was no compelling justification for presenting these data, and the request has been denied. The final analysis should be conducted as planned in approximately one year.

6. Closure Status Revisited

Myeloma S0232 – A Phase III trial comparing Dexamethasone to the Combination of Dexamethasone + CC-5013 in Patients with Newly Diagnosed Multiple Myeloma. Based on external trial evidence, the appropriateness of both study arms of S0232 has been brought into question, and the study is concluded to no longer be feasible to conduct. The DSMC recommends that the current temporary closure be made permanent, and patients should be unblinded to treatment assignment.

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

Breast
S0221
S0226
S0500

Cancer Control
S0230

Genitourinary
S9346
S9917
S0421
S0437

Head and Neck
S0427

Leukemia
S0106
S0325

Lymphoma
S9704
S0410

Melanoma
S0008

The next meeting is scheduled for Thursday, October 4, 2007 at 5 pm at The Hyatt Regency in Huntington Beach, California.