Southwest
Oncology Group
A National Clinical Research Group

June 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 April 20, 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.
Elaine Armstrong, M.S.
Dana B. Sparks, M.A.T.
Nickey McCasland, R.N., M.P.H.
Marjorie A. Godfrey

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Statistical Center
Fred Hutchinson Cancer Research Center
1100 Fairview Avenue North, M3-C102
Seattle, Washington 98109-1024
Phone: 206/667-4623
FAX 206/667-4408

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

DATE: May 19, 2006

RE: SWOG DSMC – Final minutes of SWOG Data and Safety Monitoring Committee Meeting of Thursday, April 20, 2006

1. Southwest Oncology Group's Conflict of Interest (COI) Policy:
   Dr. Vernon Sondak presented the Southwest Oncology Group's COI policy, and he described the mechanism for expected interaction with the Data and Safety Monitoring Committee. Dr. Tangen will serve as the liaison with the COI Committee. This topic will be further clarified at our next meeting.

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. Accrual to this study is only about 25% of the rate anticipated. The requirement for mandatory pharmacokinetic sampling for the first 100 patients is being amended to make such sampling voluntary; NCIC CTG has also been approached to join the trial. Accrual will be assessed again in 6 months.
   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, but accrual is only 16 patients. Several members of The International Breast Cancer Study Group (Australia and New Zealand) joined the study on March 15, 2006, and they estimate accrual of 100 patients per year, making the trial feasible. The DSMC expects to see a total of 40 patients by the next meeting in six months or the study will be closed at that time.

3. Sample Size Amendment
   a. 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. Because of the lower than expected accrual rate, a new statistical section has been

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prepared which incorporates a smaller sample size and a longer duration of follow-up. The study statistician will work with the statisticians from CTEP to finalize the details, and a study amendment will be forthcoming. Accrual is still only about 50 patients per month, instead of the planned accrual of 167 per month. NCIC CTG has endorsed the study, but has not yet registered any patients. The investigators presented their concerns in regard to possible toxic deaths on this study. The Committee asked the investigators to fully evaluate the cases of possible toxic deaths and report to the committee the results of this evaluation within 3 months (end of July '06). If there are significant concerns about serious toxicity on the trial, the investigators should present the Committee with plans to manage the risks of any severe toxicity identified. The trial will definitely be reviewed in October 2006 for both accrual and toxicity.

4. Interim Analysis
    a. GU S9346 – Intermittent androgen deprivation in patients with Stage D2 prostate 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, expected in the Spring of 2009. The Committee suggested that the final analysis schedule be evaluated by the statistician since it may be possible to report the results earlier than originally specified due to the longer than expected accrual period.
    b. GU S9921 – Adjuvant androgen deprivation versus mitoxantrone plus prednisone plus androgen deprivation in selected high risk prostate cancer patients following radical prostatectomy. A first formal planned interim analysis indicated that the study had not crossed any statistical boundaries so the trial should continue. However, the study leadership should re-evaluate some of the original design assumptions and consider adjusting the trial specifications to better reflect what is being observed on the trial.
    c. Melanoma S0008 – A phase III trial of high dose interferon alpha-2b versus cisplatin, vinblastine, DTIC plus IL-2 and interferon in patients with high risk melanoma. 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 expected in the fall of 2007.

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

Breast
S0012
S0347
S0307

Cancer Control
S0230
S0300

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Gastrointestinal
S0205

Genitourinary
S9917
S0437

Leukemia
S0106
S0325

Lung
S0124

Lymphoma
S9704
S0016

Myeloma
S0232

The next meeting is scheduled for Thursday, October 5, 2006 at 5 pm at The Sheraton Hotel in Seattle.

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