Southwest
Oncology Group
A National Clinical Research Group

November 1, 2005

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 September 29, 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.
Elaine Armstrong, M.S.
Dana B. Sparks, M.A.T.
Nickey McCasland, R.N., M.P.H.
Marjorie A. Godfrey

Southwest Oncology Group

A National Clinical Research Group

Statistical Center
Fred Hutchinson Cancer Research Center
1100 Fairview Avenue North, MP-557
Seattle, Washington 98109-4417
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, Thomas Jr. and Ms. Gottlieb

FROM: John Crowley, PhD

DATE: October 19, 2005

RE: SWOG DSMC – Final minutes of SWOG Data and Safety Monitoring Committee Meeting of Thursday, September 29, 2005

1. Accrual
   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. Accrual is still only about 50 patients per month, as against a planned accrual of 167 per month. The NCIC CTG will soon join the trial, which could double the accrual. The study 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.
   b. 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.
   c. 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. This study is now open in CALGB and ECOG but has still accrued only 11 patients. The International Breast Cancer Study Group will join the trial within the next two months, and they estimate accrual of 100 patients per year, making the trial feasible. The DSMC expects to see a substantial increase in accrual or the study will be closed in 6 months.

d. Leukemia S0106 – A Phase III Study of the Addition of Gemtuzumab Ozogamicin (Mylotarg™) Induction Therapy Versus Standard Induction with Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy with Gemtuzumab Ozogamicin (Mylotarg™) or no Additional Therapy for Patients Under Age 56 with Previously Untreated de novo Acute Myeloid Leukemia (AML). The accrual rate has picked up but is at only 50-60 per year, about one-third of that planned. Discussions with NCIC CTG and several institutions in Sweden are ongoing. Wyeth is also considering strategies to increase accrual. The study will be looked at again in 6 months.

2. Sample Size Amendment
    a. GU / Cancer Control S9917 – L-Selenium-Based Chemoprevention of Prostate Cancer Among Men with High Grade Prostatic Intraepithelial Neoplasia. A proposed amendment increasing the sample size, to accommodate a lower than expected conversion rate to prostate cancer, was approved. In addition, release of some endpoint status information, collapsed over arm, to the study coordinator was approved, so that he can intervene to help increase compliance with the end of study biopsy compliance.

3. Interim Analysis
    a. Brain S0001 – A Phase III Study of Radiation Therapy (RT) and O6-Benzylguanine (O6-BG) Plus BCNU Versus RT and BCNU Alone for Newly Diagnosed Glioblastoma Multiforme (GBM) and Gliosarcoma. A formal planned interim analysis indicated that the hypothesis of a 40% improvement in survival for the O6-BG arm could be ruled out, and the study should close for negative results.
    b. Breast S0012 – A Randomized Comparison of Standard Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel Versus Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF Followed by Weekly Paclitaxel as Neoadjuvant Therapy for Inflammatory and Locally Advanced Breast Cancer. A formal planned interim analysis revealed no reason for stopping the trial early, so the study should proceed as planned to final accrual, final analysis and publication.
    c. Lymphoma S0016 – A Randomized Phase III Trial of CHOP Chemotherapy Plus Rituximab Versus CHOP Chemotherapy Plus Iodine-131-Tositumomab for the Treatment on Newly Diagnosed Follicular Non-Hodgkin's Lymphoma. 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 2006.

4. Other
    a. Head and Neck S9908 – A Double-Blind, Placebo-Controlled Trial to Study the Efficacy and Safety of L-Glutamine (in AES0014 Delivery Vehicle) Upon Radiation Therapy-Induced Oral Mucositis in Head and Neck Cancer Patients. MGI PHARMA withdrew support for this study and it was therefore closed on April 15, 2005.
    b. Myeloma S0232 – A Phase III Trial Comparing Dexamethasone (DEX) to the Combination of Dexamthasone + CC-5013 in Patients with Newly Diagnosed Multiple Myeloma. Due to observation of a higher incidence of thromboembolic events than expected, the study has been amended to add 325 milligrams of aspirin daily for all patients. This is based on data from the Mayo Clinic presented at the American Society of Hematology meetings in 2004, and also data from two studies presented at the American Society for Clinical Oncology presented this year.

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

Breast
S0012
S0347

Cancer Control
S0300

Gastrointestinal
S0205

Genitourinary
S9346
S9921

Leukemia
S0325

Lymphoma
S9704

Melanoma
S0008

The next meeting is scheduled for Thursday, April 20, 2006 at 5 pm at The Grand America Hotel in Salt Lake City.