SWOG
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GROUP CHAIR'S OFFICE
Laurence H. Baker, DO
CHAIR
24 Frank Lloyd Wright Dr
PO Box 483
Ann Arbor, MI 48106
734-998-7130
734-998-7118 FAX

OPERATIONS OFFICE
4201 Medical Dr
Suite 250
San Antonio, TX 78229
210-614-8808
210-614-0006 FAX

STATISTICAL CENTER
1730 Minor Ave
Suite 1900
Seattle, WA 98101
206-652-2267
206-342-1616 FAX

swog.org

November 15, 2010

TO: ALL SOUTHWEST ONCOLOGY GROUP MEMBER, CCOP, UCOP AND AFFILIATE MEDICAL ONCOLOGISTS, SURGEONS, RADIATION ONCOLOGISTS, PATHOLOGISTS AND CLINICAL RESEARCH ASSOCIATES; ACRIN, ECOG, CALGB, NCIC-CTG, NCCTG, RTOG, COG, ACOSOG, NSABP, EORTC, IBCSG, BMT-CTN, 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 22, 2010 meeting is attached. The information from this report 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).

This memorandum serves to notify the NCI and Southwest Oncology Group Statistical Center.

PC/dbs

Enclosure

cc: Cathy M. Tangen, Dr.P.H.
Nathan Erickson
Elaine Armstrong, M.S.
Dana B. Sparks, M.A.T.
Kati M. Stoermer, M.S.B.A.

Southwest Oncology Group

A National Clinical Research Group

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, Dr. Crowley, and Data and Safety Monitoring Committee

FROM: Cathy Tangen, DrPH

DATE: October 26, 2010

RE: SWOG DSMC – Final minutes of SWOG Data and Safety Monitoring Committee Meeting of Friday, October 22, 2010

1. Poor Accrual
   Genitourinary S0337 – Immediate post-TURBT instillation of gemcitabine versus saline in patients with newly diagnosed or occasionally recurring Grade I/II superficial bladder cancer. Accrual has been slower than expected for this trial, and there was even a more pronounced dip during the summer. However, accrual has stabilized again and the GU committee has expressed a strong commitment to this trial. The DSMC recommends the trial proceed as planned. They will continue to monitor the accrual.

2. Data Request
   Genitourinary S0421 – Docetaxel and atrasentan versus docetaxel and placebo for patients with advanced hormone refractory prostate cancer. This trial has two translational R01 grants affiliated with it. Their focus includes bone markers and circulating tumor cells. The investigators of these grants have asked for permission to perform prognostic marker analyses in the pooled treatment arms. The DSMC has given permission for these preliminary analyses to be conducted, and results can be reported on progress reports to the funding agency. However, the data are felt to be too preliminary for public reporting. The study coordinator has also asked to look at PSA dynamics and other endpoints on the control arm. This latter request was denied.

3. Poor Accrual
   Gastrointestinal S0600 – A phase III trial of irinotecan-based chemotherapy plus cetuximab with or without bevacizumab as second-line therapy for patients with metastatic colorectal cancer who have progressed on bevacizumab with either FOLFOX, OPTIMOX or XELOX. Since its redesign and re-activation one year ago, accrual has been poor. The goal is 620 patients, but only 13 were randomized in the past six months. This study will be reviewed at our April meeting, and if accrual does not significantly improve, the DSMC will recommend closure.

4. Interim Analysis
   Gastrointestinal S0727 – A phase I and randomized phase II trial of gemcitabine + erlotinib + IMC-A12 vs. gemcitabine + erlotinib as first-line treatment in patients with metastatic pancreatic cancer. The one interim analysis for this study was evaluated. No statistical boundaries were crossed, and the DSMC recommends the study continue as planned.

5. Proposed Study Design Change
   S0819 Lung – A randomized phase III study comparing carboplatin/paclitaxel or carboplatin/paclitaxel/bevacizumab with or without concurrent cetuximab in patients with advanced non-small cell lung cancer. Pemetrexed has been approved by the FDA as maintenance therapy for this patient population. To address the concern that patients on the control arm might be receiving pemetrexed once off protocol, the study leadership has proposed that the primary objective be changed from overall survival to progression-free survival. The DSMC recommends that the study leaders have a discussion with CTEP about a potential amendment for this study.

6. Interim Analyses
   Breast S0221 – A phase III trial of continuous schedule AC + G vs. Q2 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. The first planned interim analysis was reported. The futility boundary for continuous AC was crossed, and the DSMC recommends that the two arms containing the continuous schedule of AC be closed. No boundary was closed for the paclitaxel factor. The Breast Cancer Committee should evaluate the feasibility of completing the trial in light of this recommendation.

7. Breast S0226 – A phase III randomized trial of anastrozole versus anastrozole and fulvestrant as first line therapy for post menopausal women with metastatic breast cancer. The second formal interim analysis was reported. No boundaries were crossed, and the DSMC recommends the study continue as planned. The DSMC also reviewed a recently published paper in JCO that shows the 500 mg dose of fulvestrant is better than the 250mg dose. This trial uses the 250mg dose after loading with the 500mg dose, and it's combined with anastrozole unlike the published trial. The DSMC had no comments other than to suggest that, since the primary endpoint is progression-free survival, it is probably not unreasonable to allow patients to cross-over to 500 mg at the time of progression.

8. Final Analysis Request
   Melanoma S0008 – A Phase III Trial of high dose interferon Alpha-2b versus cisplatin, vinblastine, DTIC plus IL2 and interferon in patients with high risk melanoma. The study leadership has requested permission to perform an analysis of the pooled treatment arms to identify risk groups based on relapse-free survival, distant metastasis-free survival and overall survival. The request by the study leadership to report the primary results of the trial prior to the pre-specified final analysis schedule was declined.

9. External Information
   Breast S0800 – A randomized phase II trial of weekly nanoparticle albumin bound paclitaxel with or without bevacizumab, either preceded by or followed by Q 2 week AC as neoadjuvant therapy for inflammatory and locally advanced her-2/neu negative breast

cancer. The DSMC reviewed a slide set (AVANT trial) reporting no benefit of adding bevacizumab to a standard regimen as adjuvant treatment for colon cancer. The DSMC appreciated the information. No action needs to be taken.

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

Breast
S0307
S0500

Cancer Control
S0230
S0701

Gastrointestinal
S0518

Genitourinary
S9346

Gynecologic
S0904

Myeloma
S0777

The next DSMC meeting will be held via conference call 1-2 weeks prior to the SWOG Group Meeting in San Francisco (April 14-16, 2011). A query about availability for this call will follow.