SWOG CANCER RESEARCH NETWORK

June 15, 2023

TO: ALL NATIONAL CANCER CLINICAL TRIALS NETWORK (NCTN) MEMBERS AND NATIONAL COMMUNITY ONCOLOGY RESEARCH PROGRAM (NCORP) COMPONENTS AND SUBCOMPONENTS

FROM: Charles D. Blanke, M.D. - Chair

RE: GUIDANCE ON REPORTING ADVERSE EVENTS TO INSTITUTIONAL REVIEW BOARDS FOR NIH-SUPPORTED MULTICENTER CLINICAL TRIALS (https://grants.nih.gov/grants/guide/notice-files/not99-107.html)

MEMORANDUM

All SWOG 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 website at https://www.swog.org/about/policies-procedures.

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" (https://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 SWOG studies are posted in the Report of Studies area on the members side of the Group web site at www.swog.org/. This site also contains the deliberations of the DSMC from their most recent meetings. A copy of the deliberations from the October 25, 2022, February 24, 2023, and April 15, 2023 meetings are 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 SWOG Statistics and Data Management Center.

Enclosure

cc: Cathy M. Tangen, Dr.P.H.
Nathan Eriksen
Laura Gonzales BSN, MA, RN, OCN
Dana B. Sparks, M.A.T.

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M E M O R A N D U M

TO: Dr. Blanke, Dr. LeBlanc and Data and Safety Monitoring Committee

FROM: Cathy Tangen, DrPH

DATE: 10/25/2022

RE: SWOG DSMC – Minutes of SWOG Data and Safety Monitoring Committee Meeting of October 21, 2022

1. **Symptom Control/Quality of Life S1614** ***A Phase III Randomized Trial of Prophylactic Antiviral Therapy in Patients with Current or Past Hepatitis B Virus (HBV) Infection Receiving Anti-Cancer Therapy for Solid Tumors.*** The committee appreciates the communication from the study team that their intention is to permanently close this trial due to poor accrual. We note that the Division of Cancer Prevention (DCP) is also in agreement with this decision. We recognize the study team's tremendous effort to enroll to this trial.

2. **Lung S1701** ***A Randomized Phase II Trial of Carboplatin-Paclitaxel With or Without Ramucirumab in Patients with Unresectable Locally Advanced, Recurrent, or Metastatic Thymic Carcinoma.*** The committee acknowledges this study has been closed due to poor accrual, and we note that CTEP agrees with this action. We recognize this is a rare patient population, and we appreciate the effort by the study team to conduct this trial.

3. **Lung 1827** ***A Randomized Phase III Trial of MRI Surveillance with or without Prophylactic Cranial Irradiation (PCI) in Small-Cell Lung Cancer.*** The DSMC revisited the accrual to this trial after reviewing it last spring. Although the accrual rate has not increased in the last six months, it does remain stable, and the expected total accrual will provide useful information.

4. **Genitourinary S1937** ***A Phase III Randomized Trial of Eribulin with or without Gemcitabine versus Standard of Care (Physician's Choice) for Treatment of Metastatic Urothelial Carcinoma Refractory to, or Ineligible for, Anti PD1/PDL1 Therapy.*** The DSMC appreciated a member of the study team attending our meeting and providing background information regarding accrual challenges, and the activities that have been undertaken to increase it. The DSMC will review the accrual rate again at the spring 2023 meeting.

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5. **Breast S1418** ***"A Randomized, Phase III Trial to Evaluate the Efficacy and Safety of Pembrolizumab (MK-3475) as Adjuvant Therapy for Triple Receptor-Negative Breast Cancer with ≥ 1 cm Residual Invasive Cancer or Positive Lymph Nodes (ypN1mi, ypN1-3) after Neoadjuvant Chemotherapy."*** The study statistician attended our meeting and described the data elements that the pharmaceutical sponsor has requested in anticipation of the completion of this trial. The DSMC is supportive of this activity as described.

6. **Melanoma S2000** ***A Randomized Phase II Trial of Encorafenib + Binimetinib + Nivolumab vs Ipilimumab + Nivolumab in BRAF-V600 Mutant Melanoma with Brain Metastases.***
   The study statistician presented the redesign plans for this slowly accruing trial. The amendment still needs to be submitted to CTEP, but communications indicate they are supportive. The DSMC has concerns that this redesign may not be feasible in terms of accrual, but the committee is supportive of the lowering of the accrual goal.

7. **Genitourinary S1602** ***A Phase III Randomized Trial to Evaluate the Influence of BCG Strain Differences and T Cell Priming with Intradermal BCG Before Intravesical Therapy for BCG-Naïve High-Grade Non-Muscle Invasive Bladder Cancer.***
   The DSMC is supportive of SWOG sharing data elements that the FDA has requested from the CIS subset analysis. We encourage the SWOG study team to work with the FDA to plan the timing of any public release of any results by the FDA and a corresponding publication from SWOG. The DSMC would like to see a draft version of the CIS subset manuscript before they decide whether it can be submitted to a journal prior to the scheduled final analysis of the full trial.

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

NCTN
Breast: S1706
Gastrointestinal: S1613, S1815, S1922, S2001, S2104, S2107
Genitourinary: S1011, S1802, S1806, S1931, S2011, S2200
Leukemia: S1712, S1925
Lung: LUNGMAP, S1900E, S1900F, S1800D, S1914, S1929, S1934
Lymphoma: S1608, S1826, S1918
Myeloma: S1803, S2005
Early Therapeutics/Rare Cancers: S2012

NCORP
Prevention/Epidemiology: S0820, S1904
Symptom Control/Quality of Life: S1600
Survivorship: S1501

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Cancer Care Delivery Research: S1703, S1912CD, S2108CD
Palliative Care/End of Life: S1820

The next DSMC meeting is expected to be held tentatively on May 12, 2023, coinciding with the SWOG Group Meeting in San Francisco, CA. Details will be confirmed later.

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M E M O R A N D U M

TO: Dr. Blanke, Dr. LeBlanc and Data and Safety Monitoring Committee

FROM: Cathy Tangen, DrPH

DATE: 2/24/2023

RE: SWOG DSMC – Draft minutes of Off-Cycle SWOG Data and Safety Monitoring Committee Meeting of February 24, 2023

1. **Lymphoma S1826: A Phase III, Randomized Study of Nivolumab (Opdivo) plus AVD or Brentuximab Vedotin (Adcetris) plus AVD in Patients (Age >/= 12 Years) with Newly Diagnosed Advanced Stage Classical Hodgkin Lymphoma**
   S1826: The DSMC recommends that this study report primary results of this trial because of compelling progression-free survival (primary endpoint) that crossed a conservative statistical boundary. Follow-up in this patient population should be strongly encouraged to understand the long-term implication of treatment.

2. **Lymphoma S1918: A Phase II/III Randomized Study of R-miniCHOP with or without CC-486 (Oral Azacitidine) in Participants Age 75 Years or Older with Newly Diagnosed Diffuse Large B Cell Lymphoma, Grade IIIB Follicular Lymphoma, Transformed Lymphoma, and High-Grade B Cell Lymphomas with MYC and BCL2 and/or BCL6 Rearrangements**
   Members of the study team presented the results of the prespecified safety analysis for the pilot study, and they also provided clinical context. The DSMC agrees that the study should proceed to the phase II accrual portion of the trial. However, we recognize that the study team will also have a discussion with CTEP about these safety results. The protocol should be amended to provide additional background to justify why trial accrual will continue despite crossing the prespecified safety thresholds written in the analysis plan. The DSMC recognizes that the specified safety language was probably imprecise by including expected Grade 4 hematologic adverse events in the safety threshold. The DSMC will continue to monitor safety at our regularly scheduled meetings, and we note that the study team also monitors adverse events on a continuous basis.

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3. **Acquired Resistance Cohort of S1800D: A Phase II/III Study of N-803 plus Pembrolizumab versus Standard of Care in Participants with Stage IV or Recurrent Non-Small Cell Lung Cancer Previously Treated with Anti-PD-1 or Anti-PD-L1 Therapy (Lung-MAP Non-Match Sub-Study)**
   S1800D Acquired Resistance Cohort: Based on the initial futility assessment, the recommendation is that this cohort be closed to further accrual due to lack of activity in terms of disease control in the experimental arm. Because of the lack of activity in the Acquired Resistance Cohort, the DSMC also recommends that the Primary Resistant Cohort of S1800D be closed permanently to accrual.
   .
4. **Genitourinary S1806: A Phase III Randomized Trial of Concurrent Chemoradiotherapy with or without Atezolizumab in Localized Muscle Invasive Bladder Cancer**
   The DSMC reviewed the first formal interim analysis and recommends the trial continue as planned because no statistical threshold has been crossed. There was a request for confidential outcome data by a small group of investigators for planning purposes for the next trial in this patient population. Because this trial is still enrolling patients and only a minority of expected events have occurred to date, the DSMC feels this request is premature, and it is denied at the present time. The DSMC notes that the critical design assumption for the primary endpoint of bladder-intact event-free survival in the control arm appears reasonable, and that information may be useful for some trial design planning at the current time.

The next regularly scheduled DSMC meeting is expected to be held tentatively on Friday, May 12, 2023, coinciding with the SWOG Group Meeting in San Francisco, CA. Details will be confirmed later.

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M E M O R A N D U M

TO: Dr. Blanke, Dr. LeBlanc and Data and Safety Monitoring Committee

FROM: Cathy Tangen, DrPH

DATE: 5/15/2023

RE: SWOG DSMC – Minutes of SWOG Data and Safety Monitoring Committee Meeting of 5/12/2023

1. ***S0820: Preventing Adenomas of the Colon with Eflornithine and Sulindac (PACES***)
   The DSMC reviewed the planned interim futility analysis and recommends the trial continue as planned. We recognize the trial will close to accrual at the end of June, 2023. We are supportive of the study team's plan to relax certain time windows around endpoint ascertainment, particularly due to the impact of the COVID epidemic on disease screening.

2. ***S1706: A Phase II Randomized Trial of Olaparib (NSC-747856) Administered Concurrently with Radiotherapy versus Radiotherapy Alone for Inflammatory Breast Cancer***
   The DSMC appreciated the briefing we received on the proposed amendment that will, if approved by CTEP, allow for two different RT schedules in the experimental arm. We recognize this is a pragmatic decision considering the trial's accrual challenges.

3. ***S1925: Randomized, Phase III Study of Early Intervention with Venetoclax and Obinutuzumab Versus Delayed Therapy with Venetoclax and Obinutuzumab in Newly Diagnosed Asymptomatic High-Risk Patients with Chronic Lymphocytic Leukemia / Small Lymphocytic Lymphoma (CLL/SLL): EVOLVE CLL/SLL Study***
   The statistical team presented the feasibility assessment for this trial, and they explained that this will be an ongoing report at each DSMC meeting. The DSMC expressed no concerns and recommends the trial continue as planned.

4. ***S1937: A Phase III Randomized Trial of Eribulin with or without Gemcitabine versus Standard of Care (Physician's Choice) for Treatment of Metastatic Urothelial Carcinoma Refractory to, or Ineligible for, Anti PD1/PDL1 Therapy***
   The DSMC appreciated the update on the upcoming proposed protocol amendment that will broaden eligibility, increase options for the standard-of-care arm and reduce sample size if

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approved by CTEP. The Committee recognizes this trial is having significant accrual issues and is supportive of this design change.

5. ***S1418: A Randomized, Phase III Trial to Evaluate the Efficacy and Safety of Pembrolizumab (MK-3475) as Adjuvant Therapy for Triple Receptor-Negative Breast Cancer with ≥ 1 cm Residual Invasive Cancer or Positive Lymph Nodes (ypN1mi, ypN1-3) after Neoadjuvant Chemotherapy***
   The study statistician described a data request from Merck regarding baseline dates for the PDL-1 specimen tracking. The DSMC is supportive of this request, particularly because it does not involve any post-randomization information.

6. ***S1501: Prospective Evaluation of Carvedilol in Prevention of Cardiac Toxicity in Patients with Metastatic HER-2+ Breast Cancer, Phase III***
   The DSMC recognizes all the hard work put forth by the study team over a number of years. However, the current randomized trial design appears to be infeasible. We encourage the study team to make significant changes to the study or consider closing it due to poor accrual.

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

NCTN
Gastrointestinal- S1922, S2001, S2104, S2107
Genitourinary- S1602, S1802, S1806, S1931, S2011, S2200
Leukemia- S1712
Lung – S1701, S1827, S1914, S1934, S2302, LUNGMAP, S1900E, S1900F
Lymphoma- S1608, S1918, S2114
iMATCH- S2101
Melanoma- S2000
Myeloma- S1803, S2005
Early Therapeutics & Rare Cancers - S2012

NCORP
Prevention/Epidemiology- S1904
Symptom Control & Quality of Life- S1600, S2010
Cancer Care Delivery Research- S1703, S1912CD, S2108CD

The next DSMC meeting is expected to be held tentatively on 10/13/2023, coinciding with the SWOG Group Meeting in Chicago, IL. Details will be confirmed later.