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Monica M. Bertagnolli, MD
Alliance Group Chair

MEMORANDUM

Date: 15 June 2019

To: Alliance Principal Investigators and Lead CRAs

From: Monica M. Bertagnolli, MD, Alliance Group Chair

Re: Alliance Data and Safety Monitoring Board (DSMB) Report

The Alliance Data and Safety Monitoring Board (DSMB) met on May 10, 2019. Attached please find a listing of each study reviewed, the DSMB recommendation, and the action taken in response to the recommendation.

These statements may be submitted to your IRB per local IRB guidelines.

Questions may be directed to Michael Kelly, MA, Director of Protocol Operations (mkelly1@uchicago.edu)

Breast Committee

A011104 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A011104, Effect of preoperative breast MRI on surgical outcomes, costs and quality of life of women with breast cancer, during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

A011106 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A011106, Alternate approaches for clinical stage II or III estrogen receptor, positive breast cancer neoadjuvant treatment (ALTERNATE) in postmenopausal women: A phase III study, during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

A011202 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A011202, A randomized phase III trial evaluating the role of axillary lymph node dissection in breast cancer patients (cT1-3 N1) who have positive sentinel lymph node disease after neoadjuvant chemotherapy, during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB wanted clarification on the trial assumptions, how the slower than anticipated event rates impact the initial trial assumptions, how long it will take to meet the primary endpoint, given the observed hazard rate, and what revisions the study statistician might propose to address these issues. The DSMB requested to see this information in a month (June 15, 2019). The DSMB would also like to review the revised protocol plan incorporating changes to the eligibility and other enrollment criteria in light of the current evaluability prior to it going to CTEP. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A011203 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A011203, A randomized phase II trial of tamoxifen versus Z-endoxifen HCL in postmenopausal women with metastatic estrogen receptor positive, HER2 negative breast cancer, during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

A011401 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A011401, Randomized phase III trial evaluating the role of weight loss in adjuvant treatment of overweight and obese women with early breast cancer, during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

A011502 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A011502, A randomized phase III double blinded placebo controlled trial of aspirin as adjuvant therapy for node positive HER2 negative breast cancer: The ABC trial, during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

Z11102 The Alliance Data and Safety Monitoring Board (DSMB) reviewed Z11102, Impact of breast conservation surgery on surgical outcomes and cosmesis in patients with multiple ipsilateral breast cancers, during a meeting on May

10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

Cancer Care Delivery Research Committee

A191402CD The Alliance Data and Safety Monitoring Board (DSMB) reviewed A191402CD, Testing decision aids to improve prostate cancer decisions for minority men, during a meeting on May10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB requested more information on the study team's monitoring of inter-cluster correlation coefficient in order to better assess if the study will be adequately powered as planned originally. The DSMB requested page numbers to be added to the report. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A231701CD The Alliance Data and Safety Monitoring Board (DSMB) reviewed A231701CD, Increasing socioeconomically disadvantaged patients' engagement in breast cancer surgery decision making through a shared decision making intervention, during a meeting on May 10, 2019. The DSMB noted that the study has not accrued any patients as of the report date. The DSMB also reviewed and agreed with the proposed template for this report. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

Experimental Therapeutics and Rare Tumor Committee

A091302 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A091302, Randomized phase II study of sorafenib with or without everolimus in patients with radioactive iodine refractory Hurthle cell thyroid cancer, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events, and efficacy data and no issues requiring intervention were identified. The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

A091304 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A091304, A phase I/randomized phase II study of MLN0128 (TAK-228) vs. pazopanib in patients with locally advanced/unresectable and/or metastatic sarcoma, during a meeting in December 2018. The DSMB reviewed the interim futility analysis results and agreed with the study team to stop the trial due to the evidence that MLN0128 is no better than pazopanib in terms of improving PFS. The DSMB reviewed the current adverse event data and no issues requiring intervention were identified. The DSMB recommended that the study team work with CTEP on how best to address treatment options for patients who are currently on the MLN0128 arm, as well as patients in pre-registration. The DSMB voted unanimously to stop the trial for futility, terminate DSMB monitoring and release study results to the team.

Action: Recommendation Accepted

A091605 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A091605, A randomized phase II study of anti-PD1 antibody [MK-3475 (pembrolizumab)] alone versus anti-PD1 antibody plus stereotactic body radiation therapy in advanced Merkel cell carcinoma, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events, and no issues requiring intervention were identified. The DSMB noted that two large centers (Wash U and Duke) have recently activated the trial, and SWOG/ECOG have also agreed to participate. The DSMB will continute to monitor the accrual rate to this trial and voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

GI Committee

A021202 The Alliance Data and Safety Monitoring Board (DSMB) reviewed the final analysis on A021202, Prospective randomized phase II Trial of Pazopanib versus Placebo in Patients with Progressive Carcinoid Tumors, on March 5, 2019. Based on the primary and sensitivity analyses results demonstrating superior PFS for pazopanib, the DSMB voted unanimously to release these data to the study team, the sponsor, and present results at a scientific meeting / journal. With evaluation of the primary endpoint completed, the DSMB recommended termination of future DSMB monitoring and continuing follow-up of patients per protocol.

Action: Recommendation Accepted

A021502 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A021502, Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair, during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB noted that the accrual rate was slower than expected, and will continue to monitor the accrual to this trial. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A021602 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A021602, Randomized, double-blinded phase III study of cabozantinib versus placebo in patients with advanced neuroendocrine tumors after progression on everolimus, during a meeting on May 10, 2019. The DSMB noted that a potential study design change to allow crossover at the time of disease progression is under discussion. The DSMB reviewed the current adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

C80702 The Alliance Data and Safety Monitoring Board (DSMB) reviewed C80702, A phase III trial of 6 versus 12 treatments of adjuvant FOLFOX plus celecoxib or placebo for patients with resected Stage III colon cancer, during a meeting on May 10, 2019. The DSMB reviewed the adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB noted the increased data management efforts for the trial, and the improvement in the data delinquency rates and requested the study team to continue to keep abreast of the data clean up efforts. The DSMB reviewed the data on withdrawl of consent for follow-up, and remained concerned with the higher than usual rates in this trial. The DSMB appreciated the additional information provided and requested those be included in the report next time; specifically, the rates by site, availability of information on patients prior to withdrawl of consent, clarification on the type of withdrawl of consent (for all future data versus only to no further treatment versus no data collected on the trial). The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

N1048 The Alliance Data and Safety Monitoring Board (DSMB) reviewed N1048, A phase II/III trial of neoadjuvant FOLFOX with selective use of combined modality chemoradiation versus preoperative combined modality chemoradiation for locally advanced rectal cancer patients undergoing low anterior resection with total mesorectal excision, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB noted that the data release requests from February 2019 were for planning purposes and that those were not ready for review by the DSMB (see February 2019 recommendations for details). The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

GU Committee

A031102 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A031102, A randomized phase III trial comparing conventional-dose chemotherapy using paclitaxel, ifosfamide, and cisplatin (TIP) with high-dose chemotherapy using mobilizing paclitaxel plus ifosfamide followed by high-dose carboplatin and etoposide (TI-CE) as first salvage treatment in relapsed or refractory germ cell tumors (TIGER), during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A031501 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A031501, Phase III randomized adjuvant study of MK-3475 (Pembrolizumab) in muscle invasive and locally advanced urothelial carcinoma (AMBASSADOR) vs. observation, during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A031701 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A031701, A phase II study of dose-dense gemcitabine plus cisplatin (ddGC) in patients with muscle-invasive bladder cancer with bladder preservation for those patients whose tumors harbor deleterious DNA damage response (DDR) gene alterations, during a meeting on May 10, 2019. The DSMB reviewed the current study data, and no issues requiring intervention were identified. The DSMB accepted the study team's request to monitor this single arm trial, specifically due to the protocol requirements of withholding standard treatment with proven efficacy from a subset of patients. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

Leukemia Committee

A041501 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A041501, A phase III trial to evaluate the efficacy of the addition of inotuzumab ozogamicin (a conjugated anti-CD22 monoclonal Antibody) to frontline therapy in young adults (ages 16-39 years) with newly diagnosed precursor B-Cell ALL, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events, and no issues requiring intervention were identified. The DSMB noted that the phase III portion of the trial recently opened and is still in the ramp up phase. The DSMB will continute to monitor the accrual rate to this trial and voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

A041701 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A041701, A randomized phase II/III study of conventional chemotherapy +/- uproleselan (GMI-1271) in older adults with acute myeloid leukemia receiving intensive induction chemotherapy, during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A041702 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A041702, A randomized phase III study of ibrutinib plus obinutuzumab versus ibrutinib plus venetoclax and obinutuzumab in untreated older patients (>/= 70 years of age) with chronic lymphocytic leukemia (CLL), during a meeting on May 10, 2019. The DSMB reviewed current adverse events and efficacy data, and no issues reqiring intervention were identified. The DSMB recommended unanimously to continue per protocol.

Action: Recommendation Accepted

Lymphoma Committee

A051301 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A051301, A randomized double-blind phase III study of ibrutinib during and following autologous stem cell transplantation versus placebo in patients with relapsed or refractory diffuse large B-Cell lymphoma of the activated B-Cell subtype, during a meeting on May 10, 2019. The DSMB noted the submitted protocol amendment to CTEP (3/25/2019). The DSMB reviewed the current adverse events, and efficacy data and no issues requiring intervention were identified. The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

Myeloma Committee

A061202 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A061202, A phase I/II study of pomalidomide, dexamethasone, and ixazomib vs. pomalidomide and dexamethasone for patients with multiple myeloma refractory to lenalidomide and proteasome inhibitor-based therapy, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB noted the study team's efforts to increase accrual, including targeted e-mails to sites that have the trial open, monthly investigator calls, Alliance e-mail blast etc. The DSMB approved the release of the Phase I and Phase II data on the 12 patients who were enrolled onto the original configuration of the Phase II trial design (Pre-Update #4). The DSMB will continue to montior the accrual rate on this trial, and voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

Neuro Oncology Committee

A071102 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A071102, A phase II/III randomized trial of veliparib or placebo in combination with adjuvant temozolomide in newly diagnosed glioblastoma with MGMT promoter hypermethylation, during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted

N0577 The Alliance Data and Safety Monitoring Board (DSMB) reviewed N0577, Phase III intergroup study of radiotherapy versus temozolomide alone versus radiotherapy with concomitant and adjuvant temozolomide for patients with 1p/19q codeleted anaplastic glioma, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events, and no issues requiring intervention were identified. The DSMB requests the study team to include information on how many sites would be open at Australia and at EORTC at the time of the November 2019 meeting. The DSMB were also concerned with potentially competing trials (proton versus photon). The DSMB requests for an updated report outlining the Australian and EORTC study activation status and efforts made to increase accrual to the trial at the November meeting. The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

Prevention Committee

A211102 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A211102, Testing for atypia in random periareolar fine needle aspiration (RPFNA) cytology after 12 months metformin (1,1-dimethylbiguanide hydrochloride) chemoprevention versus placebo control in premenopausal women, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB noted an unexpected, unblinding incident that was reported on the trial, and would like to review the Alliance proposal to DCP on how this will be addressed, including perhaps a patient self-report

at the time of treatment completion if they knew the treatment that they were on. The DSMB was concerned with a slow accrual rate, but noted that two high volume sites recently activated the trial. The DSMB will continue to monitor the accrual rate on this trial, and voted unanimously to continue study per protocol.

Action: Recommendation Accepted

A211401 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A211401, Reducing surgical complications in newly diagnosed lung cancer patients who smoke cigarettes, during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB noted the efforts made by the study team to improve accrual, including reaching the goal of 10 patients by the time of the DSMB meeting. The DSMB was made aware of the logistical issues with drug distribution, which is being addressed. The DSMB will continue to monitor the accrual rate to this trial, and voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

Respiratory Committee

A081105 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A081105, Randomized double blind placebo controlled study of erlotinib or placebo in patients with completely resected epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC), during a meeting on May 10, 2019. The DSMB noted that the accrual to the trial has steadily improved and is now on target. The DSMB reviewed the current adverse event data and no issues requiring intervention were identified. The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

C30610 The Alliance Data and Safety Monitoring Board (DSMB) reviewed C30610, Phase III comparison of thoracic radiotherapy regimens in patients with limited small cell lung cancer also receiving cisplatin and etoposide, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB disapproved the request to close the trial for slow accrual reasons, and voted unanimously to continue to monitor the accrual rate, and continue the study per protocol.

Action: Recommendation Accepted

C140503 The Alliance Data and Safety Monitoring Board (DSMB) reviewed C140503, A phase III randomized trial of lobectomy versus sublobar resection for small (</=2 CM) peripheral non-small cell lung cancer, during a meeting on May 10, 2019. The DSMB reviewed the current adverse events and efficacy data, and no issues requiring intervention were identified. The DSMB noted the improvement in data delinquecy rates, and urged the study team to keep up the data clean up efforts. The DSMB voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

Symptom Intervention Committee

A221101 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A221101, A phase III randomized, double-blind placebo controlled study of armodafinil (Nuvigil) to reduce cancer-related fatigue in patients with glioblastoma multiforme, during a meeting on May 10, 2019. The DSMB noted the ~10% rate of non-evaluable patients on the trial. The DSMB reviewed the current adverse events and efficacy data, and noted that the study will fully mature on May 10, 2019. Based on the information presented, the DSMB accepted the study team's recommendation to release the data, and present/publish the findings once it is fully cleaned and analyzed. The DSMB recommended terminating further DSMB monitoring.

Action: Recommendation Accepted

A221504 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A221504, A randomized, double-blind, placebo-controlled pilot study of an oral, selective peripheral opioid receptor antagonist in advanced non-small

cell lung cancer (adenocarcinoma), during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB noted noted the efforts made by the study team to improve accrual, including presenting at other NCTN groups. The DSMB will continue to monitor the accrual rate to this trial, and voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

A221505 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A221505, Phase III randomized trial of hypofractionated post mastectomy radiation with breast reconstruction, during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB noted noted the changes made to the protocol to improve accrual. The DSMB will continue to monitor the accrual rate to this trial, and voted unanimously to continue the study per protocol.

Action: Recommendation Accepted

A221602 The Alliance Data and Safety Monitoring Board (DSMB) reviewed A221602, Olanzapine with or without fosaprepitant for the prevention of chemotherapy induced nausea and vomiting (CINV) in patients receiving highly emetogenic chemotherapy (HEC): A phase III randomized, double blind, placebo controlled trial , during a meeting on May 10, 2019. The DSMB reviewed the adverse event and efficacy data and no issues requiring intervention were identified. The DSMB noted that the accrual rate was slower than expected, and noted that the trial is now open to non-Alliance sites to help with accrual. The DSMB voted unanimously to continue study per protocol.

Action: Recommendation Accepted