DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
AD HOC TRANSLATIONAL RESEARCH STRATEGY SUBCOMMITTEE MEETING

Summary of Meeting
July 8, 2019

Webinar

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE
AD HOC TRANSLATIONAL RESEARCH STRATEGY SUBCOMMITTEE
Summary of Meeting
July 8, 2019

The second meeting of the Translational Research Strategy Subcommittee (TRSS) of the Clinical Trials and Translational Research Advisory Committee (CTAC) of the National Cancer Institute (NCI) was held by webinar on Monday, July 8, 2019, at 4:00 p.m. ET. The TRSS co-chair Dr. Dang presided.[1] The meeting was adjourned at 4:29 p.m.

Co-Chairs
Chi V. Dang
Nancy E. Davidson (absent)

Members
Francis Ali-Osman (absent)
Walter J. Curran, Jr.
David A. Mankoff (absent)
Lynn M. Matrisian (absent)
Roman Perez-Soler
Kevin M. Shannon
David A. Tuveson
Kevin P. White (absent)
Max S. Wicha

Ex Officio Members
James H. Doroshow, NCI

Executive Secretary
Peter Ujhazy

[1]A roster of TRSS members and their affiliations is included as an appendix.

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Monday, July 8, 2019

I. Welcome and Opening Statement

Peter Ujhazy, MD, PhD
Chi V. Dang, MD, PhD

Dr. Ujhazy called the second TRSS meeting to order and welcomed participants. He confirmed that a quorum of at least six subcommittee members was present.

Dr. Dang reviewed the confidentiality and conflict-of-interest practices required of TRSS members during their deliberations. He invited members of the public to send written comments on issues discussed during the meeting to Dr. Ujhazy within 10 days of the meeting.

II. Glioblastoma Working Group Final Report

Walter J. Curran, Jr., MD
Chi V. Dang, MD, PhD

Dr. Curran reminded the working group members that they had reviewed and discussed the report on glioblastoma multiforme (GBM) in detail during the May 8, 2019, TRSS meeting. He asked whether the members had any additional questions or suggestions upon review of the full working group report.

Suggested Change. Dr. Shannon said that the last paragraph within the "Research Capability 1: Preclinical Qualification of New Agents Targeting GBM" section on page 3 suggests that patient-derived xenograft (PDX) models are superior to other models. He is unaware of any data showing that PDX models are superior to genetically engineered mouse models (GEMMs) in accelerating drug discovery. PDX models and GEMMs are best used together because they complement each other. A recommendation at the end of the section says that the methods should be integrated, and that recommendation is accurate.

Dr. Dang agreed that PDX models are not better than GEMMs. The working group had even discussed this point. He suggested new text to say that PDX models and GEMMs are complementary experimental approaches that provide different information. This would require minor edits to the report.

Suggested Change. Dr. Wicha said that page 3 also alludes to the importance of tumor-initiating stem cells, but that statement was not included in the preclinical recommendations on page 13. He asked to include a recommendation that the biology of tumor-initiating stem cells, which is important to understanding therapeutic resistance, be investigated. This new text could be inserted within the recommendation on page 13 that references the PDX models and GEMMs, on page 14, the second bullet under "Clinical Trials" that calls for analyzing cell populations, including stem-like cell populations, before and after treatment.

Action Item. Dr. Dang asked Dr. Wicha to send his suggestions in writing for incorporation into the report. Dr. Wicha agreed to do so.

Suggested Change. Dr. Tuveson said that the report should include discussion about plasticity in initial presentation and response to treatment, as there is a high degree of genetic plasticity in GBM. Some patients respond to treatment initially and then develop resistance. Understanding the biology will lead to better therapies. Dr. Wicha said that this concept could be described in a few sentences to make it clear that genetic and epigenetic plasticity are important biological aspects of resistance.

Action Item. Dr. Dang asked that Dr. Tuveson and Dr. Wicha send their suggested changes on genetic plasticity and indicate where in the report the wording should be inserted.

Suggested Change. Dr. Shannon suggested an additional change to the first bullet point of the preclinical recommendations—"Develop and utilize better model systems for preclinical testing and qualification of novel compounds"—on page 5. He would add the phrase "with biologic studies of the role of stem cells and plasticity in response and resistance."

Suggested Change. Dr. Tuveson recommended that the report include infrastructure support.

Dr. Dang noted that the first sentence on page 13 begins, "Develop a national infrastructure for preclinical testing and qualification of novel therapeutics for patients with GBM that seamlessly integrates with an early phase clinical trials program and leverages existing NCI resources."

Suggested Change. Dr. Perez-Soler asked whether, given that GBM does not metastasize, the report should include a recommendation about topical treatment strategies at the time of the operation. He referenced treating the surgical bed with topical drugs that have the ability to penetrate and kill GBM cells.

Dr. Dang said that the Food and Drug Administration has approved a topical treatment, carmustine (Gliadel), which comes in the form of a wafer and is embedded in the surgical bed at the time of surgery. Current research to improve the effectiveness of topical treatments is ongoing.

Dr. Curran said that the working group included neurosurgical experts, and there was no discussion about expanding ongoing research in the field of topical treatments for GBM.

Dr. Dang said that there is a need to better understand the biology of contrast-enhancing and non-contrast–enhancing cells in order to develop more effective treatments. It may be possible to better design drugs to treat GBM once the mechanism is better understood.

Action Item. Dr. Curran thanked the subgroup members for their suggestions. He said that those who made suggestions should email them to the group, and he invited anyone who thinks of additional ideas to email them to the group. The report must be finalized within a few days. CTAC members will discuss the report at their meeting on Wednesday, July 17.

Motion: Dr. Dang asked for a motion to accept the report. Dr. Shannon made a motion to accept the report with minor modifications, and Dr. Tuveson seconded the motion. Dr. Dang asked whether there were any objections. There were none, and the motion passed unanimously.

Dr. Ujhazy said that Dr. Matrisian and Dr. Mankoff, who could not attend, went on record before the meeting as accepting the report.

Ms. Clark will send an email to all members of the working group to ensure that later emails include the entire group.

Action Items

- Dr. Wicha will submit his wording regarding the investigation of the biology of tumor-initiating stem cells, to be included in separate recommendations on pages 13 and 14.

- Dr. Tuveson and Dr. Wicha will provide language on GBM epigenetic/genetic plasticity and email their modifications to Dr. Dang and Dr. Curran, with copies to Tawny Clark and Dr. Ujhazy.
- Dr. Shannon will submit wording regarding the integration and complementarity of PDX model and GEMMs.
- Ms. Clark will send an email to all members of the working group to ensure that later emails include the entire group.
- Members with additional ideas should email them to the group.
- Abdul Tawab Amiri, PhD, will revise the report according to the proposed modifications and finalize it for distribution.

III. Wrap-Up and Adjournment

Chi V. Dang, MD, PhD

Dr. Dang thanked TRSS members for their input and suggestions. There being no further business, the second meeting of TRSS was adjourned at 4:29 p.m. on July 8, 2019.

11/9/2020 Chi Dang
Date Chi V. Dang, MD, PhD, Co-Chair

11/17/2020
Date Peter Ujhazy, MD, PhD, Executive Secretary

Appendix

NATIONAL INSTITUTES OF HEALTH
National Cancer Institute
Clinical Trials and Translational Research Advisory Committee

Ad Hoc Translational Research Strategy Subcommittee

CO-CHAIR
Chi V. Dang, M.D., Ph.D.
Scientific Director
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New York, New York
Professor
The Wistar Institute
Philadelphia, Pennsylvania

CO-CHAIR
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Senior Vice President, Director and Full Member
Clinical Research Division
Fred Hutchinson Cancer Research Center
President & Executive Director
Seattle Cancer Care Alliance
Head, Division of Medical Oncology
Department of Medicine
University of Washington
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MEMBERS

Francis Ali-Osman, D.Sc.
Margaret Harris and David Silverman
Distinguished Professor of Neuro-Oncology Research
Professor of Surgery
Professor of Pathology
Department of Surgery and Pathology
Duke University Medical Center
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Vice-Chair for Research
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Director
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