

National Cancer Advisory Board  
Subcommittee on Clinical Investigations

Gaithersburg Marriott Washingtonian Center  
9751 Washingtonian Boulevard  
Gaithersburg, MD 20878  
December 2, 2019  
7:30 – 9:00 p.m. EST

SUMMARY

Subcommittee Members:

Dr. Peter Adamson, Chair  
Dr. Margaret Mooney, Acting Executive Secretary  
Dr. Francis Ali-Osman  
Dr. Deborah Bruner (absent)  
Dr. David Christiani (absent)  
Dr. Judy Garber (absent)  
Dr. Elizabeth Jaffee (absent)  
Dr. Beth Karlan (absent)  
Dr. Timothy Ley  
Dr. Electra D. Paskett  
Dr. Nancy J. Raab-Traub (absent)  
Dr. Mack Roach  
Dr. Charles Sawyers (absent)  
Dr. Max Wicha (absent)

Other Participants:

Dr. Anna Barker, National Cancer Advisory Board (NCAB, pending)  
Dr. Carolyn Best, American Urological Association  
Dr. Howard Fingert, NCAB (pending)  
Dr. Andrea Hayes-Jordan, NCAB  
Dr. Timothy Ley, NCAB  
Dr. Douglas Lowy, National Cancer Institute (NCI)  
Dr. Edith Mitchell, President's Cancer Panel  
Dr. Norman E. Sharpless, NCI  
Dr. Susan Vadaparampil, NCAB (pending)  
Ms. Joy Wiszneauckas, NCI  
Dr. Amanda Cename, The Scientific Consulting Group, Rapporteur

**Opening Remarks**

Dr. Peter Adamson, Subcommittee Chair, welcomed the meeting participants. Dr. Norman Sharpless, Director, NCI, National Institutes of Health (NIH), conveyed that the Subcommittee's external advice is valued by the NCI. Members of the NCAB and other participants introduced themselves.

## **Update on Adult and Pediatric MATCH Trials and Plans for Future Basket and Umbrella Trials in the NCI National Clinical Trials Network (NCTN)**

*Dr. Margaret Mooney*

Dr. Margaret Mooney, Acting Associate Director and Chief, Clinical Investigations Branch, Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis, NCI, NIH, updated the participants on the Molecular Analysis for Therapy Choice (MATCH) trials. She explained that the trials were designed to screen patients with tumors that had not been treated successfully by other methods.

Dr. Mooney provided an overview of the MATCH trials, focusing on two areas of interest—use of laboratory networks and management of protocol structures—to inform future trials. She conveyed that the CTEP serves to test new investigational agents—or combinations of agents—to inform the understanding of the biology of tumors and their resistance to effective treatments. The CTEP is interested in early drug development research, particularly in biomarker assessment and evaluation.

Because development represents a collaborative effort, the NCI brings together three components: intramural investigators/funding, pharmaceutical and biotechnology companies, and extramural investigators. Dr. Mooney emphasized that the NCI supports an integrative infrastructure. She explained that CTEP clinical trials are separated by phase, research component, and specialty resources. Over the past 5 years, the NCI has shifted to a team-driven approach for early drug development.

At its start in 2015, the NCI-MATCH objective was to determine whether matching of agents (in adults whose tumors have specific genetic mutations) would treat certain cancers effectively. She described the early-phase national trial as a master protocol with individual arms that opened and closed independently. Genomic testing was carried out on biopsied tissue to direct patients to molecularly targeted treatments. Dr. Mooney explained that researchers were interested in rare tumors and subsets of common tumors.

Nearly 7,000 adult patients have been screened to date, and more than 1,000 patients have been matched to 37 treatment arms. Match rates have increased with the addition of new arms. Each arm is assessed by its objective response rate. Dr. Mooney presented an overview of the MATCH assay system and workflow, which consists of a four-network laboratory (The University of Texas MD Anderson Cancer Center, Massachusetts General Hospital, Frederick National Laboratory Molecular Characterization Laboratory, and Yale University).

Data are directed through a “MATCHBox,” which uses an algorithm to identify mutations for matching. Dr. Mooney explained that the tumor gene variants occurred less frequently than anticipated. To broaden the patient screening process, investigators developed a series of external laboratories connected to participating sites across a national network.

Dr. Mooney spoke briefly on the NCI-Children’s Oncology Group Pediatric MATCH trial, which includes patients ages 1 to 21. The goal of the trial was to screen 1,000 patients and to match 300 patients to treatment arms. She explained that the trial’s paradigm was largely consistent with its adult counterpart. Eligible participants underwent tissue biopsies previously; thus, additional biopsies were unnecessary for this trial. Germline testing was performed, and genetic counseling was made available for patients and their families.

More than 800 pediatric patients have been screened to date, and about 90 patients have been matched to treatment arms. Ten arms have been characterized, and three additional arms will be made available by early 2020. Among trial participants, 24 percent were assigned to a treatment arm and 10 percent enrolled in the study protocol. Challenges of the trial include risk determination, validation and interpretation, and

protocol development.

Dr. Mooney outlined future directions, identifying three potential successor trials currently under development:

- ComboMATCH would focus on drug combinations using pre-clinical data from *in vivo* models of drug combinations to predict clinical benefit in defined patient groups.
- Acute Myeloid Leukemia (AML)/Myelodysplastic Syndromes (MDS) Precision Medicine Initiative would focus on matching AML molecular subtypes to targeted therapies in different age and fitness groups, as well as throughout the course of the disease.
- iMATCH would focus on providing prospective immunologic profiling to design study arms defined by histology or molecular subgroups.

Dr. Mooney stated that the successor trials would operate within a similar infrastructure to the initial MATCH trials. She highlighted the value of consistent data screening, as well as coordinated communication and decision-making. To maximize the use of the network, a separate screening sub-protocol would be performed for each trial. Dr. Mooney highlighted widespread participation in the trial across the NCI community.

### ***Discussion***

Dr. Timothy Ley asked how the large resource of tissues collected during the MATCH trial could best be leveraged and managed. Dr. Mooney replied that work in this area is ongoing. She explained that the work represents a joint effort between the NCI and the NCTN; certain portions of the data will be made available in the future.

Dr. Howard Fingert asked whether the clinical data are sufficient to serve as a basis for future research. Dr. Mooney reiterated that data collection is performed systematically across MATCH trials. She added that she is uncertain whether the data elements specific to this study will be useful for external research. Dr. Adamson clarified that unique identifiers allow for tracking of pediatric patients across multiple studies. He agreed that a balance exists between quantity and quality of data collected. Dr. Mooney added that the AML/MDS study represents an effort toward longitudinal analysis.

Participants discussed how best to ensure accurate gender and ethnic representation in clinical trials. Dr. Edith Mitchell stated that the MATCH trial's diversity has been monitored continuously over its duration. Differences in gender among trial participants reflected differences in gender seen in the dominant cancers in several of the treatment arms. Additionally, insurance coverage influences access to clinical trials.

Dr. Ley pointed out that the mutation location and tumor architecture are critical to effectiveness of treatments. He suggested that recent findings should be incorporated into current trial designs, noting that commercial entities are employing more advanced approaches in drug development. Dr. Mack Roach pointed out that these treatment approaches are uncommon in standard care. Dr. Anna Barker stated that the scientific community should consider the best way to move forward.

In response to a comment from Dr. Sharpless regarding sample size and effectiveness, Dr. Adamson stated that an understanding of the molecular landscape of relapse offers value to researchers. He explained that some pediatric patients choose not to enroll in study arms because they pursue other treatments. To address this issue, the NCI is widening its window for reenrollment.

Dr. Adamson pointed out that combination therapy leads to an overwhelming number of permutations; thus, modeling must be employed to inform study designs. Dr. Mooney remarked on the importance of working with agent combinations that have been identified previously.

Dr. Roach stated the importance of providing support and backup options for patients whose treatment plans fail. Dr. Mitchell suggested that information from trials be expanded to clinical practice. She stated that patient advocacy groups could play a critical role in dissemination of knowledge.

**Adjournment**

Dr. Adamson adjourned the Subcommittee meeting at 8:58 p.m. EST.

  
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Dr. Peter Adamson  
Chair

3 DEC 2019  
Date

  
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Dr. Margaret Mooney  
Acting Executive Secretary

9 Dec 2019  
Date