The Biomarkers Consortium (BC)
Cancer Steering Committee (CSC)
Annual Scientific Symposium
Bethesda North Marriott Hotel, Bethesda, MD
November 4-5, 2019

Executive Summary

The Biomarker Consortium's (BC) Cancer Steering Committee (CSC) held its Annual Scientific Symposium on November 4-5, 2019, in Bethesda, Maryland. Each year, the CSC led by the Foundation for the NIH (FNIH) and its co-chairs Drs. Gary Kelloff, National Cancer Institute (NCI), and Eric Rubin, Merck, brings together experts from academia, pharmaceutical and biotechnology companies, non-profit organizations, and federal agencies to review advances in the fields of biomarker and regulatory science in cancer. The Annual Scientific Symposium serves as a yearly juncture for the BC CSC to assess and recalibrate potential projects for the future direction of biomarker discovery and development.

The goals of this year's meeting were to highlight cutting edge science, inform the field of the latest developments in biomarker science, and to guide CSC decision-making and project planning for the coming year. Presentations focused on key areas of interest including biomarkers in the immunotherapy landscape, advanced technologies in biomarker development, data science and machine learning in biomarker development, the microbiome in cancer, minimal residual disease, imaging biomarkers, and liquid biopsy.

The meeting was headlined by four keynote presentations. Dr. Monica Bertagnolli, Dana Farber Cancer Institute, spoke about the challenges and the need for developing a "learning health care system" that overlays research with clinical practice. Dr. Chi Van Dang, Ludwig Cancer Research Institute, described his work on the MYC oncogene and how its ability to disrupt circadian rhythms of metabolism plays a key role in the uncontrolled growth of cancer cells. Dr. Chris Boshoff, Pfizer, spoke about translating science into breakthrough therapies and how to choose combination therapies for maximum patient benefit. Dr. Gideon Blumenthal, Food and Drug Administration (FDA), discussed the FDA's new Oncology Center of Excellence, which was established as a result of the Cancer Moonshot in 2017.

New to this year's Scientific Symposium was the addition of a patient advocacy perspective.

Dr. Caitlyn Barrett spoke about the work that CureSeach for Children's Cancer is doing to bring more targeted therapy to pediatric oncology patients. Ms. Ann Ramer, RamerNation, a patient advocate, talked about the impact of cancer on her family, and her hopes for the future of pediatric cancer treatment and research.

Session 1: Biomarkers in the Immunotherapy Landscape chaired by Dr. Eric Rubin, outlined several ongoing efforts to develop biomarkers in immuno-oncology (IO). Dr. Jun Tang, Cancer Research Institute, gave an overview of the use of biomarkers in IO trials and the opportunities for trials to make better use of biomarkers to select patients and deliver better results. Dr. Bruce Johnson, Dana-Farber Cancer Institute, described the Human Tumor Atlas, an effort that came out of the Cancer Moonshot's Blue-Ribbon Panel recommendations. Dr. Priti Hegde, Foundation Medicine, described the potential and the challenges of using tumor mutational burden (TMB) as a biomarker for overall survival. Dr. Lyndsay Harris, NCI, outlined the goals and recent achievements of the Partnership for Accelerating Cancer Therapies group, which focuses on the validation and standardization of biomarker assays. Dr. Alessandra Cesano, Society for Immunotherapy of Cancer (SITC), described her organization's mission and structure, and the outcome of the recently convened SITC meetings about cancer biomarkers. Dr. Theresa LaVallee, spoke about the Parker Institute for Cancer Immunotherapy (PICI)'s mission to integrate clinical trial data into a database and use of deep informatic approaches to extract information that cannot be learned from any single trial.

Session 2: Challenges for Biomarker Development: Heterogeneity, Immunotherapy-related Toxicity, and Regulatory Issues was chaired by Dr. Bruce Johnson, Dana-Farber Cancer Institute. Dr. Alex Snyder, Merck, described the potential for using circulating tumor DNA (ctDNA) to assess disease burden and genomic information about the tumor in the context of immunotherapy. ctDNA is a noninvasive method that has the potential to be used for monitoring and could be developed as a surrogate endpoint akin to minimal/measurable residual disease (MRD). Dr. Kurt Schalper, Yale, described some of the challenges in measuring spatial tumor heterogeneity (the complex arrangement of tumor and immune cells) in the tumor microenvironment and identifying the features that matter most for clinical decision-making. Dr. Elad Sharon, NCI, spoke about a relatively new area of investigation: autoimmune disease that develops as a side-effect of immunotherapy and the need to track and study these immune related adverse events in a systematic way to better understand and address them. Dr. Marc Theoret, FDA, outlined the requirements for the FDA's accelerated approval pathway and some of the considerations for developing a biomarker (such as ctDNA) as an endpoint for approval.

Session 3: Advanced Technologies in Biomarker Development, led by Dr. Greg Friberg, Amgen, focused on new methods to measure the proteome, epigenome, and other features of cancer cells. Dr. Dan Liebler, Protypia, described a quantitative mass spectrometry method he developed for characterizing cancer proteotypes, which are the protein-level equivalent of a genotype. Dr. Jonathan Carlson, Massachusetts General Hospital, presented a new method to do sequential antibody staining of tumor cells using fine needle aspirates and requiring very small samples. Dr. Jim Heath, Institute for Systems Biology, focused on new techniques for

identifying the neoantigens that most effectively recruit immune cells to the tumor. Drs. Claudio Carini and Peter Parker, King's College London, presented their work on chromatin conformation signatures that aim to predict melanoma patients' responses to treatment.

Session 4: Data Science and Machine Learning in Biomarker Development chaired by Dr. Hisham Hamadeh, GenMab, focused on new algorithmic approaches to analyze data and identify meaningful biomarkers. Dr. David Patton, NCI, presented the NCI's vision for a Cancer Research Data Commons. Dr. Sean Khozin, FDA showcased outcomes from the FDA's Presidential Innovation Fellowship, which brought data scientists and entrepreneurs to FDA to work on data science challenges. Dr. Janusz Dutkowski, Data4Cure, talked about his organization's efforts to extract knowledge from research and literature data using machine learning. Dr. Pratik Shah, Massachusetts Institute of Technology , demonstrated how machine learning could be used to computationally stain tissue, thus ensuring that pathologists would not run out of biopsy material, and how machine learning could be used to improve clinical trial design. Dr. Shrujal Baxi, Flatiron Health, described how machine learning could help structure data in electric health records.

The breakout sessions on Day 2 provided an opportunity for investigators to present their work and receive feedback on progress and ideas for further exploration.

Breakout Session A was chaired by Dr. Greg Reaman, FDA, and focused on MRD as a biomarker and a clinical trial endpoint. Dr. Donald Berry, MD Anderson, presented statistical considerations for linking MRD with event-free survival (EFS). Although MRD negativity is a good prognostic factor in acute lymphocytic leukemia, it is not trivial to show statistically that MRD negativity translates to a benefit in EFS. Dr. Kenneth Anderson, Harvard, presented on the role of MRD in multiple myeloma. Dr. Jerry Radich, Fred Hutchinson Cancer Research Center, Dr. Robert Loberg, Amgen, and Dr. Kim Jessup all discussed the heterogeneous biology of acute myeloid leukemia (AML), which makes MRD assessment challenging. The advent of single-cell profiling by multiparametric flow cytometry or next-generation sequencing promises to enable an unbiased evaluation of disease burden and disease evolution in AML.

Breakout Session B focused on the microbiome in cancer. Dr. Yasmine Belkaid, National Institute of Allergy and Infectious Diseases, gave a high-level overview of the microbiome's effects on immunity, while Dr. Leopoldo Segal, New York University , spoke about ongoing work to develop microbiome biomarkers that could predict lung cancer patients' response to immunotherapy.

Breakout Session C, chaired by Dr. Carl Barrett, AstraZeneca, focused on liquid biopsy. Dr. Robert McCormack presented the progress of the BC-CSC ctDNA working group whose goal is to develop quality control materials for ctDNA testing. Dr. Mark Stewart, Friends of Cancer Research, highlighted the efforts of his organization to harmonize the measurement of complex biomarkers, including ctDNA and TMB. Dr. Lanny Kirsch, Adaptive Biotechnologies, focused on new immunosequencing technologies for measuring ctDNA for MRD assessment. Dr. Howard Scher, Memorial Sloan Kettering Cancer Center, emphasized the need for an analytical assay

validation network for a complex biomarker like ctDNA. Dr. Stan Hamilton, MD Anderson, touched on the clinical implementation challenges of liquid biopsies. Ms. Lauren Leiman, BloodPAC, explained the mission of BloodPAC, a nonprofit organization that came into existence as a result of the Cancer Moonshot, to accelerate the development and approval of liquid biopsy assays in cancer. The session concluded with Reena Philip from FDA explaining the FDA's perspective on liquid biopsy diagnostic tests.

Breakout Session D was chaired by Dr. Annette Schmid, Takeda, and focused on imaging biomarkers. Dr. Gregory Goldmacher, Merck, talked about the challenges of designing imaging biomarkers that can both scale down to small trials and scale up to large trials. Ideally the biomarker should not require expert interpretation, which is difficult to scale up to large trials, but it should be sensitive enough to detect a signal even in small trials. Dr. Tito Fojo, Columbia University, described his team's work modeling the kinetics of tumor growth and using this information to make earlier decisions about whether a therapy is effective or not. Dr. Larry Schwartz, Columbia University, presented the progress of the BC-CSC Vol-PACT project team's efforts to model tumor volumes, heterogeneity, and other features. Drs. Andrea Thiele and Bushi Wang from Boehringer Ingelheim described efforts to extract features from radiomic data, and Dr. Nozha Boujemaa, Median Technologies, described a novel whole organ AI-based approach to model tissue heterogeneity and predict disease severity.

Overall, the CSC's Annual Scientific Symposium successfully helped to define critical next steps in biomarker project development in the focus areas of the CSC