



GLOBAL SUMMIT AND BRAIN TRUST ON PRECISION DIAGNOSIS AND TREATMENT OF PROSTATE CANCER: Overview, Background and Current Plans

I. 1st, 2nd and 3rd Global Summit and Brain Trust on Precision Diagnosis and Treatment For Prostate Cancer (PC) and their Impact; and

II. Planning for the 4th Global Summit and Brain Trust - Scheduled For October 3-5, 2019, Boston (see Event Flyer attached or [view it here¹](#)).

Background

AdMeTech Foundation's Annual Global Summit and Brain Trust on Precision Diagnosis for PC took place starting in September 2016 and brought together – for the first time - the key international opinion leaders of multi-disciplinary diagnostic tools to bridge the current gap between the thought leaders of in-vivo quantitative imaging (radiomics) and in-vitro molecular diagnostics/genomics and expedite consensus for the development and implementation of the comprehensive approach to precision PC diagnosis and its impact on precision treatment. This event highlighted radiogenomics - integrating multi-modality diagnostics - as the groundbreaking emerging research and clinical field.²

Steering Committee, or Brain Trust, on Precision Diagnosis and treatment of PC, established following the 1st Summit, was convened in February and May 2017, October 2017 and August 2018 and included the key leaders of national and international programs in precision biomarkers from academia, industry, government and non-profit organizations¹

- 1) Our participants are the key pioneers and opinion leaders of multiple clinical disciplines (radiology, urology, radiation oncology, pathology and medical oncology), including, but not limited to:
 - a. Dr. Gerald Andriole, University of Washington, St. Louis;
 - b. Drs. Wassim Abida, Sigrid Carlsson, Amita Dave, Hedvig Hricak, Steve Larson, Michael Morris, Howard Scher and Andrew Vickers, Memorial Sloan Kettering Cancer Center;
 - c. Drs. Jelle Barentsz and Jurgen Futterer, Nijmegen/Radboud University, The Netherlands;
 - d. Drs. Matthew Cooperberg, Antonio Westphalen, Susan Noworolski, UCSF;
 - e. Dr. David Crawford, University of Colorado, Denver;
 - f. Drs. Angelo DeMarzo, Martin Pomper and Steven Rowe of Johns Hopkins;
 - g. Drs. Masoom Haider and Laurence Klotz, University of Toronto, Canada;
 - h. Drs. Ashesh Jani, Christopher Filson and Mehrdad Alemozaffar, Emory University;
 - i. Drs. Adam Kibel, Clare Tempany, Mukesh Harisinghani and Adam Feldman, Harvard;
 - j. Drs. Richard Babayan and Jennifer Rider, Boston University;
 - k. Dr. Eric Klein of Cleveland Clinic;
 - l. Drs. Daniel Margolis and David Nanus of Cornell Weill/Columbia;
 - m. Dr. Peter Nelson, Washington University;
 - n. Drs. Daniel Petrylak, Preston Sprenkle and Jeffrey Weinreb of Yale;
 - o. Drs. Alan Pollack, Sanoj Punnen and Radka Stoyanova, University of Miami;
 - p. Dr. Art Rastinehad, Mount Sinai School of Medicine.
 - q. Dr. Minhaj Siddiqui, University of Maryland;
 - r. Dr. Thomas Wheeler, Baylor College of Medicine; and
 - s. Drs. Peter Choyke, Peter Pinto and Baris Turkbey of the National Cancer Institute
- 2) Drs. Kibel, Sprenkle, Nelson, Vickers and others are members of the National Comprehensive Cancer Network's (NCCN) Panels on Prostate Cancer, developing influential, cutting-edge clinical guidelines for patient care;
- 3) Drs. Choyke, Pinto, Siddiqui, Turkbey, and Summit Chair Dr. Faina Shtern of the AdMeTech Foundation participate in the US VP Joseph Biden's \$1.8 Billion Cancer Moonshot Program, developing national strategy for cancer research and related infrastructure; and

- 4) Dr. Mark Buzzo, Director of Global Biomedical Research Programs for Movember Foundation (headquartered in Australia) leads international scientific strategy, with specific interest in advanced PC. The goal of the Brain Trust is to review the current and emerging data in imaging, fluid-based molecular diagnostics, tissue-based genomics and radiogenomics, drug development and novel approaches to treatment and observation strategies, and reach consensus on the best emerging clinical practices and priority needs in research, medical education, clinical training and public awareness¹. Our primary goal is to outline clinical, research and educational priorities, including statistically powered pilot studies on clinical role of radiogenomics in patient selection for appropriate care (observation strategy and focal, whole gland or systemic treatment).

The 2nd and 3rd Global Summit have emerged as seminal scientific and educational events in recognizing radiogenomics as the future of PC care. The program of these events, which took place on October 12-14, 2017 and August 3-5, 2018 respectively, was structured to review recent clinical advances and related scientific data in radiomics (quantitative imaging) and molecular diagnostics (including genomics), their integration into the emerging field of radiogenomics and its impact on patient selection for, design and monitoring of clinical interventions (e.g., biopsy and management strategy).

The scientific program for the 3rd Global Summit included population-based approach³ ([view here](#)):

- "Smart" approach to screening in asymptomatic general population, including patient selection;
- Diagnostic evaluation of men with abnormal screening or clinical suspicion of PC, to improve risk assessment in order to reduce unnecessary biopsies and improve tissue sampling/targeting;
- In men with proven localized PC:
 - 1) To improve early diagnosis, staging and biologic characterization of lethal prostate cancer, requiring immediate treatment;
 - 2) To increase confidence in sub-clinical (indolent) disease, requiring observation strategy (e.g., active surveillance) and related monitoring;
 - 3) To improve patient selection for, guidance, local outcomes and monitoring of minimally-invasive, image-guided focal treatment;
- In men with recurrent PC, to improve visualization, localization, prediction of progression and management strategy;
- In men with advanced PC, including oligometastatic disease and metastatic castrate resistant PC, to improve diagnosis, biologic characterization and treatment.

The 3rd Global Summit identified the best emerging clinical practices and recommended research priorities in order to expedite transfer of promising diagnostics and therapeutics from laboratories to patients - see attached Consensus Statement ([view Consensus Statement here](#)).⁴ In addition, the Industry Leadership Panel on Innovation discussed the challenges in and potential solutions for clinical adoption, including regulatory and reimbursement policy, clinical trials and guidelines.

The following [Emerging Important Trends have been highlighted by the 3rd Global Summit and will be expanded and updated in the 4th Global Summit](#):

1. "Radiogenomics, or integrated, multi-modality, comprehensive approach to precision diagnosis and its impact on precision care for men with PC;
2. Rapidly expanding discovery of new genetic and molecular targets for both early and advanced PC, which are critical for further development and integration of in vitro diagnostics, molecular imaging and dedicated drugs.
3. Impact of precision diagnosis on observation strategies and treatment, including patient selection for and design, administration and monitoring of clinical interventions for localized, recurrent and advanced prostate cancer.
4. "Smart" Screening, including baseline PSA as a critical tool for age-appropriate risk assessment;
5. Utilization of the validated PSA isomers (e.g., phi or 4K Score) and novel liquid biomarkers (e.g., germline testing) and their integration with imaging, especially multi-parametric (mp) MR for improved selection of patients for biopsy. During the Brain Trust, there was an intense debate which modality should come first (liquid biomarkers vs. mpMRI), and it has become clear this debate should be resolved through the related research and data rather than consensus. The related considerations need to include the ease of use, access, accuracy, anatomic and biologic information, and clinical utility/impact.
6. Fusion of Transrectal Ultrasound (TRUS) with mpMRI for improved biopsy tissue sampling for routine pathologic assessment (e.g., Gleason Pattern/Score) and genetic tissue profiling. Based on a preliminary

- data, high-resolution micro-ultrasound appears to represent a significant improvement compared to a standard TRUS – and is likely to impact clinical value of MRI/US Fusion Guidance.
7. Multiple promising in vitro novel liquid and tissue biomarkers and in vivo imaging tools have emerged recently for improved assessment of early and advanced prostate cancer that require further research.
 8. Further expert consensus and research is needed to define clinical indications for adding:
 - a. *Genetic cancer profiling to routine pathologic examination of biopsy tissue samples, with the goal to improve patient selection for precision care (e.g., Active Surveillance, Focal Interventions/"Male Lumpectomy", or Immediate Whole Gland Treatment); and*
 - b. *Genetic cancer profiling to routine pathologic examination of post-surgical tissue specimens, with the goal to optimize treatment planning.*
 9. Machine Learning and related tools for multi-factorial, multi-modality, information-intense data analysis.
 10. Several areas of imaging, including:
 - a. *mpMRI, which is currently the most promising and validated imaging tool before and after diagnosis of PC. However, the need for broader standardization of image acquisition, quality and interpretation has been recognized; and*
 - b. *Transition of molecular imaging (and related fusion with anatomic imaging, such as MRI or CT) from clinical use only for advanced PC (presented at the First and Second Global Summit) to early diagnosis of recurrence and biologic characterization of the early stages of localized disease (discussed at the Third Global Summit) ; and*
 11. Image-Guided Focal Treatment, emerging as a promising patient care option for localized disease, though further consensus and research is needed to define its clinical utility compared to Active Surveillance (AS) and Immediate Whole-Gland Treatment.⁵

Our Brain Trust met upon conclusion of the public program of the Third Summit and reached unanimous conclusion that the content of this event was extremely important and should be made public through two mechanisms:

- 1) To submit a Summit 2018 multi-disciplinary overview, including a Consensus Statement, to a peer-reviewed publication. Main paper editors and lead writers of the specific Summit session overviews have been secured (see attached); and
- 2) To publish Summit 2018 presentations online by the Grand Rounds of Urology, which has an international audience⁶;
- 3) To present Summit 2018 highlights at the International Prostate Cancer Update educational conference in January 2019.

The following recommendations have been made to expand the scope and content of the Summit 2019:

1. To expand a session on recurrent and advanced PC, including oligometastatic and castrate-resistant metastatic disease;
2. To expand a session on image-guided, minimally-invasive focal treatment for localized, recurrent and advanced disease (e.g., palliative interventions) and its role compared to other clinical approaches to patient care;
3. To invite organizations leading accreditation, regulatory and reimbursement policies and commercial product development to stimulate discussion on creating a facilitated pathway for clinical adoption of promising diagnostics and therapeutics (modeled after breast cancer and AIDS initiatives);
4. To expand the Summit Program to 2.5 - 3 days in order to increase the time for discussion and audience participation at the end of each session, Industry Leadership Panel, Poster Session, and Exhibit Tours; and
5. To ensure participation of the Prostate Cancer Foundation, the leading organization sponsoring research on advanced PC in the United States.

Impact on Clinical Community, National and International Scientific Strategy (2016-2018)

The First Global Summit and related "Brain Trust" meetings were instrumental in shifting integrated, multi-modality approach to PC Diagnosis (e.g., radiogenomics) and its impact on patient care from the fringe to the center of medical education and science and related strategic planning, both nationally and internationally.

As a direct result of this event, our outstanding faculty members ensured that US Vice President Joe Biden's \$1.8B Cancer Moonshot Program prioritized prostate cancer in general and precision oncology specifically, including radiogenomics, and invited AdMeTech to take part in a strategic planning for national research agenda and related infrastructure, starting in early 2017.

The Second and Third Annual Summit exceeded everyone's expectations even further. These events brought into a sharp focus the groundbreaking potential of the emerging field of radiogenomics for patient care:

- 1) Dr. Mark Buzzo of Movember participated in the 2nd Global Summit and expressed his intention to include participants of this event into the global strategic research planning that took place in late 2017;
- 2) Dr. Howard Soule, Executive VP and Chief Scientific Officer for Prostate Cancer Foundation, will take part in the 4th Global Summit on October 3-5, 2019;
- 3) Members of the National Comprehensive Network's Panels on Detection and Treatment of PC will continue to be involved in Summit 2019; and
- 4) Participants of the VP Biden's Cancer Moonshot Program will continue to take part in the 4th Global Summit.

Impact on Public Awareness/Opinion/Consumer Demand: Sharon Bagley of Boston Globe/STAT medical news (who attended our First Summit) delivered on her promise to write a feature article, which has had a groundbreaking impact on public awareness about the critical importance of novel diagnostic tools in transforming the current state of patient care and effectively addressing current concerns about PSA screening, including unnecessary procedures.⁷

Other major media (e.g., Associated Press, National Public Radio, Boston Business Journal) also covered Global Summit and the presented scientific data.

About AdMeTech Foundation: AdMeTech Foundation is a 501c3 non-profit organization, which has established the Manogram® Project and provides international leadership in creating a new standard of care for prostate cancer, including precision screening, diagnosis and treatment. To fulfill on this mission, the Manogram® Project has been leading design, development, management and implementation of groundbreaking programs in research, education, awareness and advocacy (see AdMeTech's Organizational Summary attached or visit www.admetech.org).

REFERENCES:

1. Summit 2019 Flyer: <http://www.admetech.org/4th-global-summit-flyer/>
2. About Annual Global Summit: <http://www.admetech.org/annual-global-summit-on-precision-diagnosis-for-prostate-cancer/>
3. Summit 2018 Program: <http://www.admetech.org/program-third-global-summit-on-precision-diagnosis-for-prostate-cancer/>
4. Summit 2018 Consensus Statement: <http://www.admetech.org/wp-content/uploads/2018/10/CONSENSUS.STATEMENT.10.15.18.Current.pdf>
5. Summit 2018 Highlights: <http://www.admetech.org/admetech-foundations-third-global-summit-on-precision-diagnosis-and-treatment-of-prostate-cancer/>
6. Grand Rounds in Urology: <https://grandroundsinurology.com/>
7. STAT News/Boston Globe Coverage: <https://www.statnews.com/2017/05/04/prostate-cancer-research-psa/>