Progress on Prostate Cancer Research December 2019

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Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man's prostate cancer and maximize his quality of life. This regular *Hot SHEET* supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

The PCF is the world's leading philanthropic organization funding and accelerating prostate cancer research. Founded in 1993, the PCF has raised more than $745 million and provided funding to more than 2,000 research programs at nearly 200 cancer centers and universities.

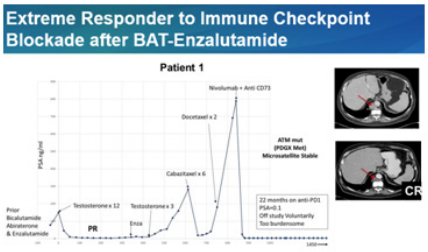
26th Annual PCF Scientific Retreat – Top New Discoveries for Patients

PCF held its 26th Annual Scientific Retreat in October. In attendance were 665 participants from 188 institutions from 18 countries. Scientific Retreat is an opportunity for PCF-funded investigators and other experts in the field of prostate cancer research to learn from each other through presentations and informal networking.

From 42 total panels and presentations, PCF's Director of Research, Dr. Andrea Miyahira, has curated the Top New Discoveries for Patients. Stay tuned for more next month!

Testosterone Effects on Innate Immunity: Implications for Combination Therapies

Bipolar androgen therapy (BAT) is an experimental treatment approach in which men are rapidly cycled between extremely high and extremely low (castrate) levels of testosterone (T). This is hypothesized to allow killing of both androgen receptor (AR)-expressing cells (vulnerable at extremely high T levels) and AR-low cells (vulnerable at castrate T levels). Dr. Samuel Denmeade and Dr. Sushant Kachhap of Johns Hopkins University presented promising results from BAT therapy clinical trials, which demonstrated that BAT therapy can resensitize men with mCRPC to enzalutamide, and improve PSA progression-free survival.



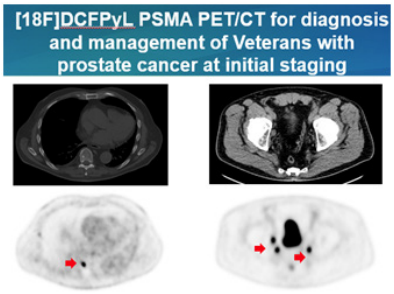
Interestingly, exceptional responses have been observed in some patients who were treated with checkpoint immunotherapy after BAT therapy. These results have led to a clinical trial testing BAT therapy in combination with vs. followed by nivolumab. The mechanisms which cause this sensitivity are being explored. Preliminary studies indicate that extremely high T levels activate the STING pathway, which activates immune responses and tumor infiltration by tumor-killing Natural Killer (NK) cells.

What this means to patients: Drs. Denmeade and Kachhap have made the startling observation that some patients treated with BAT therapy who progress go on to have exceptional responses when treated subsequently with checkpoint immunotherapy. This treatment approach is now being formally tested in clinical trials and the mechanisms which drive this are being studied.

Real World Validation of Deep Learning Algorithms in the Assessment of Metastasis by Medical Imaging of Veterans with Prostate Cancer

PSMA-PET imaging is a new imaging modality that is highly sensitive and specific for prostate cancer, and outperforms conventional imaging methods such as CT, bone scans, and MRI. Dr. Matthew Rettig and Dr. Nicholas Nickols of University of California, Los Angeles and the VA Greater Los Angeles Healthcare System, presented results from a study that compared PSMA-PET vs. conventional imaging (99mTc-MDP or NaF PET bone scan, CT or MRI of abdomen/pelvis) for diagnosis and management of 92 Veterans with high-risk prostate cancer at initial staging.

PSMA-PET imaging findings identified an altered risk group/stage that resulted in a major change in treatment recommendations in 35% of patients. Artificial intelligence (AI) algorithms are also being developed to evaluate PSMA-PET imaging. An AI algorithm using intraprostatic PSMA-PET imaging alone in veterans with prostate cancer was found to be highly predictive of co-existing metastatic disease. PSMA-PET AI prediction was superior to clinical predictors alone (clinical T stage, biopsy Gleason, % positive cores, PSA), and was not improved by the addition of clinical predictors.



What this means to patients: PSMA-PET imaging is a practice-changing imaging technology for prostate cancer that is highly sensitive and will likely soon be FDA-approved. These studies demonstrate significant clinical impact of PSMA-PET, including directing treatment recommendations, and having the ability to predict metastatic disease from prostate-only imaging.