



Team Progress Updates

SU2C Gynecologic Cancers Convergence Research Team:

“Connecting Immune Health and Tumor Biology in Gynecologic Cancers”



Mismatch repair (MMR) deficiency, the inability to repair faulty base pairing within the DNA helix, causes mutations to accumulate in DNA as cells replicate. In gynecologic cancers, the response to immune checkpoint inhibitors has been varied and may be related to the number of mutations carried by each tumor cell. The SU2C Gynecologic Cancers Convergence Research Team hypothesizes that some tumors with a high number of mutations fail to respond to checkpoint inhibition because of an immune dysfunction related to the mechanism for MMR deficiency.

The team is conducting two clinical trials that will test a) whether tumor-intrinsic factors affect the response to checkpoint inhibition; b) whether baseline immune function and quality affect this response; and c) whether there are blood biomarkers during treatment that may reflect the tumor-immune interaction.

Understanding the mechanism that causes some gynecologic cancers to fail to respond to checkpoint inhibition has the potential to dramatically impact those patients who do not respond to current treatments.

The team reported the following progress:

April 2019

- The team has opened two clinical trials: a phase II trial of nivolumab in patients with MSI^{Hi} or hypermutated uterine cancer (n=40) and a pilot study of neoadjuvant carboplatin and paclitaxel with nivolumab in patients with HGSOE (n=20).
- The researchers also plan to open an additional clinical trial for patients with MSI^{Hi} and DNA repair deficiencies undergoing standard of care at the University of Pennsylvania.
- A large set of cytometric assays has been established to characterize immune profiles, DNA damage, and T-cell biology from samples obtained in the clinical trials. Sets of assays have also been created from patients with MMR-D uterine cancer who have been treated with nivolumab, and from ovarian cancer patients treated with nivolumab plus chemotherapy.

