International research collaboration explores blood-based biomarker

Submitted by shawn on Sat, 05/25/2019 - 20:51 The study explores a potential non-invasive approach to identify tumor mutations
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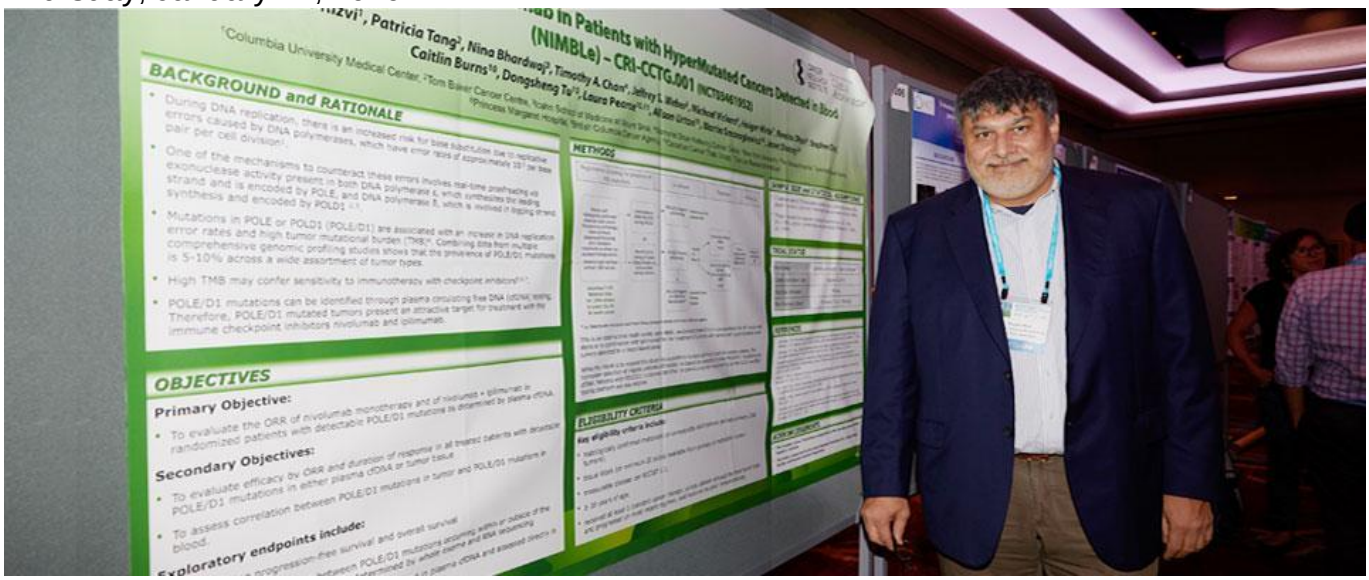

A new trial, *Nivolumab, Ipilimumab in Patients With Hyper Mutated Cancers Detected in Blood* (NIMBLe) will soon open at centers in the US and Canada. Trial researchers will initially explore the use of non-invasive approaches to confirm POLE and POLD1 mutations in solid tumors and to investigate whether those tumors are responsive to immunotherapy.

Responses and improved survival from treatment with immune checkpoint inhibitors have been observed in many types of tumors. However, not all patients benefit and biomarkers capable of better predicting how a patient will respond to immunotherapy are needed. POLE and POLD1 gene mutations have a high mutational burden, which is believed to cause tumors to appear more abnormal to the immune system. This means that cancers with this type of mutation may be more likely to be targeted by the immune system following treatment with immunotherapy. Researchers involved in the study believe that these mutations can be detected in the blood.

Nivolumab (anti-PD-1) and ipilimumab (anti-CTLA-4) are both approved agents shown to have activity in a number of tumor types, and have well characterized safety profiles. “The study will evaluate the efficacy and safety of these agents alone and in combination in patients with POLE and POLD1 mutations and will collect both blood and tumor tissue samples from patients to look at correlation between mutations detected in tumor itself and those detected in blood,” said Janet Dancey, Director of the Canadian Cancer Trials Group.

“It is challenging to identify these mutations in clinical practice, as traditional DNA analysis requires a tissue biopsy. Using a blood test to identify POLE and POLD1 mutations could provide a non-invasive alternative to biopsy procedures for patients,” said Naiyer Rizvi, International Study Chair and Principal Investigator at Columbia University in New York. The blood based assay will be used to identify patients positive for POLE and POLD1 mutations.

The adaptive study design allows for addition of new blood-based assays for other gene signatures as they become available. “Platform and other adaptive trial designs such as this support efficient evaluation of potential treatments in the right patient populations, and nonprofit-academic-industry collaboration is key,” said Jill O’Donnell-Tormey, CEO and Director of Scientific Affairs at the Cancer Research Institute.

Naiyer Rizvi, International Study Chair and Principal Investigator at Columbia University in New York

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Janet Dancey, Director of the Canadian Cancer Trials Group

POLE and POLD1 Hypermutation - Combined data from multiple comprehensive genomic profiling studies show that a wide variety of tumors are affected by these mutations. This trial will look at whether immune checkpoint blockade affects response in patients with these hypermutated phenotypes as well as whether detection of these phenotypes using a blood-based assay correlates with detection using traditional tissue assessment. It will involve repeat collections of blood during the study to allow for monitoring of potential changes in POLE/D1 mutation status over time, and will collect other bio samples for additional translational research studies such as whole exome sequencing.

Scientific Rationale for Investigation of Immune Checkpoint Blockade - Cancer immunotherapy rests on the premise that tumors can be recognized as foreign rather than as self and can be effectively attacked by an activated immune system. An effective immune response in this setting is thought to rely on immune surveillance of antigens expressed on cancer cells that ultimately results in an adaptive immune response and cancer cell death. These cancer-specific peptides can be targets for T-cell recognition and effector responses.