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Contact:
Nicole Oliverio, Dana-Farber Cancer Institute
nicole_oliverio@dfci.harvard.edu, 617-257-0454

Pilot study uses circulating tumor DNA to reliably predict relapse in patients with diffuse large B-cell lymphoma (DLBCL)

MAESTRO-Pool, a means of detecting circulating tumor DNA (ctDNA), could be sensitive and selective enough to help guide treatment decisions.

SAN DIEGO – Dana-Farber Cancer Institute investigators, in collaboration with researchers from the Broad Institute, demonstrated in a retrospective clinical study that a novel test for ctDNA was more sensitive and more specific than existing tools for detecting relapse in patients with DLBCL after autologous stem cell transplantation.

The findings were presented by Reid Merryman, MD, a clinician-scientist in the Lymphoma Program at Dana-Farber, at the 65th American Society for Hematology Annual Meeting and Exposition on December 10 in San Diego, CA.

The results suggest that the test, called MAESTRO-Pool, should be used in future prospective trials in DLBCL to further validate the findings. If successful, the test could help guide treatment decisions for patients after transplantation.

"We'd like to individualize treatment decisions for patients, for instance, escalating treatment for those at a high risk of relapse and de-escalating for those at a lower risk, with the goal of improving outcomes for patients," says Merryman. "To do that, we need a ctDNA test that is highly sensitive and specific."

Some patients with relapsed/refractory DLBCL who undergo autologous stem cell transplant will be cured of the disease. But many will relapse, sometimes years later. Relapse is currently

detected based on clinical symptoms and imaging scans, often after a patient already has a significant disease burden.

Relapse occurs when miniscule traces of cancer, called minimal residual disease (MRD), remain after treatment, and begin to grow. Existing ctDNA tests can identify MRD, but they detect relatively small numbers of mutations and therefore might lack sensitivity.

A novel ctDNA test called MAESTRO, which was developed in the lab of co-author Viktor Adalsteinsson, PhD, at the Broad Institute, is designed to identify hundreds or thousands of DNA mutations across the whole genome from a patient's tumor. The MAESTRO technology works by specifically probing for known mutations in a patient's cancer.

"MAESTRO enables us to sequence more deeply where we expect to find mutations, but overall to use much less sequencing and get similar results," says Merryman.

In this study, the team examined an extension of MAESTRO called MAESTRO-Pool, which probed for the mutations found in cancer cells of all patients in the study. Pooling helps guard against false positives.

"We expect to see only the mutations previously detected in the patient, but if we see mutations initially reported in other patients, it suggests we might have false positives," says Merryman.

This study examined 59 blood plasma samples from 9 patients with relapsed refractory DLBCL. The patients had been treated on a phase 2 clinical trial testing pembrolizumab as a maintenance drug after autologous stem cell transplantation. After three years of follow-up, five patients had relapsed and four had not.

The researchers retrospectively tested the samples, which had been taken at multiple time points from each patient, looking for signs of MRD. The study compared the MAESTRO-Pool results with those of a commercially available ctDNA detection test that employs immunoglobulin-based high-throughput sequencing (IgHTS).

Among the five patients who relapsed, MAESTRO-Pool detected ctDNA at the same time or sooner than IgHTS. MAESTRO-Pool detected ctDNA a median of 178 days earlier than detection of relapse via PET scan, compared to 44 days with IgHTS.

MAESTRO-Pool also detected extremely small traces of ctDNA, as low as 1 part per million, and was able to quantify the amount of ctDNA in each sample. Neither MAESTRO-Pool nor IgHTS detected ctDNA in patients who did not relapse.

“Both tests are very specific, with no false-positive results, but MAESTRO-Pool is significantly more sensitive,” says Merryman.

The MAESTRO technology does not identify new mutation acquired at the time of relapse. However, in this study, the investigators showed that by adding a panel test for genes of interest, it is possible characterize mutation changes as well.

As a next step, Merryman recommends the use of MAESTRO-Pool in prospective clinical trials involving a larger number of patients to validate the tool’s ability to predict relapse.

“The next step after that would be to design a trial that uses this ctDNA test to help guide therapy,” says Merryman.

About Dana-Farber Cancer Institute

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We provide the latest treatments in cancer for adults through Dana-Farber Brigham Cancer Center and for children through Dana-Farber/Boston Children’s Cancer and Blood Disorders Center. Dana-Farber is the only hospital nationwide with a top 5 *U.S. News & World Report* Best Cancer Hospital ranking in both adult and pediatric care.