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Dana-Farber Team Reports Progress with Precision Oncology Trial Matching Software

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NEW YORK – Investigators from the Dana-Farber Cancer Institute are making progress implementing an innovative computational program that they developed to match patients to precision medicine clinical trials based on results from genomic profiling tests.

Called MatchMiner, the open-source software is fueling clinical trial matches for increasing numbers of patients and has now been adopted by several other centers since it was first launched internally in 2017, investigators said during the second virtual session of the American Association for Cancer Research's annual meeting this week.

Researchers said they continue to collaborate with clinical groups at Dana-Farber and other institutions to understand the role the software can play in their clinical workflows and to evolve the tool to meet emerging needs.

As genomic profiling and molecularly guided treatment strategies become more widely adopted in cancer care, a major hurdle remains the difficulty of accurately and efficiently matching patients to therapies and clinical trials.

"Genomic sequencing of patient tumors is increasingly common. There are also an ever-growing number of clinical trials looking for patients with specific genomic features. With all this genomic data, and all these trials, it can be hard to find the right patient for the right trial at the right time," Dana-Farber scientist Tali Mazor said, speaking during the session on Wednesday.

In recently conducted studies exploring this "match rate" in precision oncology, investigators have found that while large numbers of patients test positive for actionable genomic alterations, only a fraction of them actually go on to receive a targeted agent.

Bioinformatic matching tools have emerged as one solution, offering a way to improve and standardize the translation of genomic test reports — often containing long lists of identified markers — into actionable next steps.

Researchers initially described the MatchMiner software in 2017, highlighting its potential in a preprint publication, and then released the open-source code on Github in 2018.

At AACR this week, the Dana-Farber team described in more detail how the program automates what can be a complex manual process, and the potential value this offers to clinical oncologic practice.

According to Mazor, MatchMiner is designed to work in two different directions and toward two complementary purposes: aiding and speeding clinical trial recruitment, and maximizing and optimizing precision oncology options for patients. As such, the program has two modes of access. In "patient-centric mode" an oncologist can search and rank clinical trial matches for a specific patient. In "trial-centric mode" a clinical trial investigator can identify and recruit patients for a specific trial.

In the three years the program has been operational at Dana-Farber, 300 trials have been curated into the system, along with genomic data from more than 37,000 patients.

Mazor said that over 81 percent of patients who have had their data entered into the software have matched to at least one open clinical trial, with an average of six trial matches per patient. And, to the group's knowledge, at least 115 patients so far have enrolled on a clinical trial based on the software's analysis.

Briefly, MatchMiner works through what Mazor described as a clinical trial markup language, which encodes detailed information about individual clinical trials and uses Boolean logic to define a trial's clinical, demographic, and genomic eligibility criteria.

"In order to identify a patient-trial match there are certain types of data we need, and because we are doing computational matching, we need that data to be in a specific format," she explained.

At Dana-Farber, the patient data fed into MatchMiner includes their clinical information and genomic profile from sequencing panels for solid tumors and hematologic malignancies. Mazor said the system as implemented within Dana-Farber currently supports the consideration of mutations, copy-number alterations, structural variants, mutational signatures, and tumor mutational burden, but it is flexible and can be extended to include any other relevant data type of interest.

The trial data that MatchMiner relies on is largely inclusion and exclusion criteria for enrollment, which is taken manually from trial descriptions and placed into a Boolean structure that can support the computational matching algorithm.

During a question and answer period, Mazor admitted that this manual curation step is time consuming, and it could be possible to use natural language processing to further automate so that things like trial eligibility criteria can be drawn directly from trial documentation. But she said that, at least right now, she and her colleagues have found that manual input "gives the … most accurate representation of what the true eligibility is."

When MatchMiner returns results from a patient-centric search, it also ranks the list of trials for which a patient is eligible. This is based on a few criteria, Mazor said, including how important a a detected genomic variant is to the patient's cancer. For example, if a variant is rated with a higher tier of pathogenicity, trials associated with it will rank higher than those for variants with more unclear links to disease or treatment response.

In addition, trials looking for patients with specific mutations will appear higher than those looking for any mutation in a gene of interest, she added.

As she and her colleagues have collaborated with various clinical groups, Mazor said, they have also experimented with adding human interpretation into this process, using molecular tumor board reports to influence the ranking of trial options.

"Right now, that's on a small scale, but we are thinking about how to implement this more broadly," she said.

Another ongoing goal is to add a functionality to search for or pool trials based on larger drug class, rather than specifying individual agents, which the current software requires.

Finally, Mazor said, the group is thinking about ways to make MatchMiner available more broadly. Although she said at least five other institutions have put it to use in its current form, the tool is designed to operate internally within each hospital system that implements it. Pooling patient and clinical trial recruiting across institutions might offer even greater benefits to patients. A first next step could be trying to integrate with other hospitals in the immediate area, Mazor said, though plans have not been formalized in any way.