Perthera's Virtual Molecular Tumor Board Can Improve Patient Outcomes, Overcome Access Barriers

Mar 12, 2020 | Charlotte Hu

NEW YORK – A new study has demonstrated the utility of an artificial intelligence-powered platform and virtual molecular tumor board by Perthera, a precision oncology firm based in Holliston, Massachusetts, to guide patients to the treatments they're most likely to benefit from.

The study, published earlier this month in *Lancet Oncology*, found that pancreatic cancer patients who received a targeted therapy recommended by Perthera on average survived one year longer than patients who received unmatched treatments like chemotherapy.

However, only a minority of patients with actionable markers were able to get on targeted therapies, demonstrating that access challenges continue to hamper evaluation of precision oncology approaches in the real world.

Testing in this study was performed as a collaboration between Perthera and the patient advocacy group Pancreatic Cancer Action Network as part of the Know Your Tumor Initiative. Based on the success of that program, Perthera is now partnering with health systems, cancer centers, oncologists, and other patient advocacy groups to help them integrate molecular profiling insights into cancer care with the help of its AI platform and virtual molecular tumor board.

PanCAN and Perthera launched the Know Your Tumor Initiative in 2014 to encourage more pancreatic cancer patients to get tumor profiling and improve the field's understanding of the molecular underpinnings of the disease. For pancreatic cancer, one-year survival rates are around 20 percent and drop to 7 percent at five years. However, as more patients are having their cancers molecularly profiled, expert bodies like the National Comprehensive Cancer Network have updated guidelines recommending genetic testing to assess patients' hereditary cancer risk, and there are now more personalized treatment options, particularly for those with alterations in BRCA1/2, NTRK, and overexpression of PD-L1.

Within the Know Your Tumor partnership, Perthera used its platform, AI, and the expertise of a virtual molecular tumor board to analyze the tumor profiles of pancreatic cancer patients who have gotten genomic or proteomic testing and comes up with targeted treatment options. Within the platform, Perthera organizes a molecular profiling protocol for patients, including ordering necessary tumor sequencing,

immunohistochemistry, and germline sequencing tests, and routing the samples to corresponding labs. Perthera does not perform any tests and is lab agnostic.

The test results, along with relevant treatment and medical history, are incorporated in Perthera's therapeutic engine, which is connected to various databases that it can scour for clinical trial, drug information, and more. The technology is further powered by artificial intelligence that can process all the information about the patient and come up with an initial list of ranked treatment recommendations including on-label drugs, off-label drugs, and open clinical trials.

That list then goes to the virtual molecular tumor board, where it can be edited or polished. The final product is the Perthera report, a summary of patient information and therapeutic recommendations that is sent back to the treating physician, who has the final say in the treatment course or clinical path.

The fact that the tumor board is virtual is also important in the context of bringing together busy healthcare professionals regularly. "Many of us, including myself, we're practicing oncologists at academic centers and we have had the experience where it can be difficult to make sure that everybody convenes in a physical room at the same time," said Michael Pishvaian, chief medical officer at Perthera and the lead author on the *Lancet Oncology* study.

Last year, the two groups published a study reporting that patients with actionable mutations who were matched to a targeted treatment using Perthera's platform had longer median progression-free survival compared to those who either did not have actionable mutations or had actionable mutations but didn't match to a targeted therapy.

In the latest study, the researchers performed a retrospective analysis of the data from the Know Your Tumor program. Approximately 25 percent of pancreatic cancer patients harbored an actionable genetic alteration, meaning that they could be targeted by an on- or off-label drug available on the market.

The treatments recommended by the tumor board and AI platform included immune checkpoint inhibitors for mismatch repair (MMR)-deficient tumors, anti-HER2 drugs for HER2-amplified or -activated tumors, TRK inhibitors for tumors that harbor ROS1, NTRK1, NTRK2, and NTRK3 gene fusions, RAF-MEK targeted therapies for BRAFV600E-mutated tumors, and PARP inhibitors for BRCA 1/2-mutated pancreatic cancers.

Out of the 1,082 patients who registered for the program and received molecular testing through Foundation Medicine, Caris Life Sciences, or other laboratories, 282 were found to have tumors with molecular changes that could be addressed by a targeted therapy. Treatment outcomes were available for 189 patients. Out of those, 46 patients received a targeted therapy that matched an alteration on their tumor, while 143 patients who were eligible for targeted therapy received an unmatched therapy standard chemotherapy. The median survival in the group who received targeted treatments that were highly ranked by Perthera's precision oncology platform and tumor board was 31 months, compared to 18 months in the group who received standard chemotherapy.

This study is one part of a larger effort to demonstrate the utility of Perthera's virtual molecular tumor board program, which allows multidisciplinary experts from across the country — scientists, cancer biologists, physicians, and computational biologists — to access a patient's molecular and treatment data in order to make personalized recommendations for on/off-label treatments or a clinical trial. The study showed that when patients followed the most highly ranked personalized treatment recommendations made by the tumor board, it led to improved outcomes.

The virtual molecular tumor board allows different experts to perform a centralized review for patients who may be scattered across the country. All patients that opt into Perthera's program go through the virtual molecular tumor board.

"It's not 5 to 10 percent, which is the norm for most hospitals. Every single patient benefits from our expert molecular tumor board. And it's done in an asynchronous manner," said Perthera CEO Gary Gregory. The case comes in and goes through the therapeutic engine, which generates the initial ranked therapies. Perthera then invites experts from across the country to participate in the tumor board. In a matter of 48 hours, there is an open discussion that can be done on the computer or via Perthera's application. Each expert provides feedback, then the leader of that case closes it out and the final report is generated.

The current record collection process is still very manual, with individual physician offices and treatment facilities forwarding information after patients give consent to access their medical records. Perthera's platform is not yet connected to any electronic medical record system. After the patient's case is reviewed, a report is generated, which summarizes the molecular findings and the recommendations of the virtual molecular tumor board in terms of treatments and trials, and is sent to the patient and treating physician.

Around 70 percent of physicians will use one of the recommendations put forth by the virtual molecular tumor board. When they don't, it usually has to do with access issues. "We may recommend as a treatment option an off-label therapy that the physicians don't feel that their patients can get access to, or a clinical trial that's difficult for patients to physically get to because of geography or other reasons," said Pishvaian.

Each patient provides consent for Perthera's ongoing non-interventional IRB registry studies within the platform, where Perthera can also collect their physicians' notes detailing treatment selections, as well as their clinical results every month after delivery of the report to track how they are doing on treatment.

From the patients who have opted into Perthera's program, researchers have also been able to glean insights into molecular aberrations that are consistent across tumor types but have not been previously studied. Gregory said that the platform harbors a collection of some of the industry's most comprehensive real-world evidence data.

For example, Pishvaian highlighted a pancreatic cancer study last year in *JCO Precision Oncology* where researchers demonstrated that patients who had a molecular test done and were found to have a defect in the DNA damage repair pathway DDR had better outcomes when they were treated with platinum-based chemotherapies than with non-platinum based therapies (2.37 years compared to 1.45 years).

"Those are the kinds of analysis that we're able to do through the data collected [within] … the platform and the virtual molecular tumor board," said Pishvaian. "We have definitely started to see recurrent patterns of specific markers where patients benefit from specific therapies. And those findings are spurring the designs of clinical trials that are aimed at ultimately getting FDA approval or [an] FDA label indication" for drugs that are currently used off label.

Gregory believes that Perthera, as one of the early champions of molecular profiling to match patients to treatments, is helping encourage the acceptance of this approach in the broader community. " When we started this project several years ago with PanCan, the use of molecular profiling was not the norm," he said. "Today, it's the standard of care to molecularly profile patients with advanced forms of pancreatic cancer. In many [other] types of cancer, it's still an emerging art form." However, Gregory acknowledged the pragmatic limits of implementing Perthera's technology. While it can highlight the best options through clinical information, medicine, and data, the therapy choice is ultimately left to the patient's own doctor.

"In terms of how to access on-label and off-label [drugs] and working through payors, it's the physician's call and direction," he said. "These drugs are very expensive, so physicians have to make sure the choices they make are on the mark and they then have to do the good fight of making sure the therapies are reimbursed."

To help from its end, Perthera has changed its model from working almost exclusively through patient advocacy groups to working directly with physicians, physician groups, and healthcare systems. They've

also reduced the cost of the service, which Gregory lists as one of the top access barriers previously.

Perthera's revenue streams come from various industry and pharmaceutical partnerships. The firm will provide molecular contract research services through their compilation of real-world data, clinical trial acceleration services, and post-market surveillance. Revenue can also come from collaborations in which an industry partner may want to employ their technology in the Perthera platform.

"In the past, we used to charge as much as $5,000 per patient for this service, and now we're offering this at limited to no charge to healthcare systems and physicians. That's a major accelerator, and the fact that we're working directly with physicians and health systems also allows us to align the service on a repeatable basis," he said.

Perthera estimates that its platform has been used in over 250 cancer centers across all 50 states and by 10 percent of US oncologists. "We've democratized and proven that it can go anywhere. It can go to one patient in North Dakota or hundreds of patients out of Cedars-Sinai," Gregory said.

The company is also helping other academic centers structure their internal faculty to host their own virtual molecular tumor boards, so physicians can still discuss patient cases despite not being able to be in the same room.

Perthera has seen some success with Thomas Jefferson University, which is using the program, especially the molecular tumor board, extensively in pancreatic cancer patients to advance the use of precision medicine.

Other hospitals have expressed interest in working with the firm, according to Gregory, and Perthera gives them the choice of using its platform with AI and virtual molecular tumor board in place of or in tandem with their in-house molecular tumor board.

Perthera also recently announced a partnership with the Lazarex Cancer Foundation, in which its precision oncology platform will be used in combination with Lazarex's own trial programs, IMPACT and CARE, to help enroll patients into clinical trials based on their molecular information. Lazarex's chairman Dana Dornsife highlighted in a statement that "Perthera’s platform has been proven to advance patient outcomes from both an overall and progression-free survival perspective, and also proven to accelerate clinical trial enrollment by five times the national average."

Lazarex is a public non-profit started in 2006 to help advanced cancer patients gain access to medical breakthroughs in clinical trials. While the group does not do trial matching, Lazarex helps patients navigate FDA-approved clinical trial options and provides financial assistance to cover out-of-pocket expenses, travel costs, and a travel companion.

Lazarex has relationships with over 200 investigational sites nationwide. It has supported patients across all of the comprehensive cancer centers in the US and has interfaced with other patient advocacy organizations and biotech industry partners like Perthera.

One of the programs that Lazarex is working on with Perthera is CARE, which aims to improve clinical trial enrollment, retention, and minority participation, and to create a platform of affordable access.

"The reason that we really like the partnership with Perthera is that Perthera can be much more specific regarding which clinical trials these patients could potentially benefit most from. Without the molecular profiling report that Perthera provides, we can't do that for our patients," Dornsife said.

In oncology clinical trials, patients can also rack up costs related to care and testing. Perthera, in this partnership, will facilitate molecular profiling for patients, precisely match and also accelerate clinical trial enrollment. It will also work with corresponding labs to minimize the patients' financial impact. "A lot of our

patients can't afford to have molecular profiling done. Many of them have government assistance with their healthcare, so their insurance will not cover the cost of molecular profiling," Dornsife said. "This partnership helps us to have that conversation with a patient, explain why [molecular testing] is important, and the fact that we can secure this test for the patient at no cost to them is a big deal."

Filed Under Cancer Clinical Sequencing North America pancreatic cancer tumor sequencing