Cellworks AI-Driven Modeling System Can Help Predict Response to AML, MDS Therapies

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NEW YORK (GenomeWeb) – The Cellworks Group has announced the results of clinical studies that showed how physicians could leverage the firm's computational biology modeling technology for genomic profiling of tumors and predicting patient response to chemotherapies.

In a prospective clinical study, called iCare 1, the Cellworks artificial intelligence-based technology was 90 percent accurate in predicting the response to standard-of-care treatments in patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS).

In a second study, Cellworks' technology predicted resistance to azacitidine (Vidaza) in newly diagnosed patients with MDS, a group of disorders caused by blood cells that are poorly formed or operating incorrectly. In a cohort of 37 intermediate- and high-risk MDS patients, Cellworks predicted azacitidine non-responders with 100 percent accuracy, the firm said.

Cellworks is providing details of the studies in poster presentations at the American Society of Hematology (ASH) annual meeting and exposition this week in San Diego.

The Cellworks technology helps oncologists "identify which patients have the greatest chance of responding to a treatment" and when it is worth the risk of exposing them to a therapy that will produce side effects, said Christopher Cogle, a medical oncologist at University of Florida Health and the principal investigator on the iCare 1 study. He noted that the computational system exposes activated pathways that are hidden for clinicians looking at only single-gene mutations. "By exposing activated pathways, the system opens up treatment opportunities for the patient and for the disease class itself," he said.

Cogle said that in current practice, oncologists generally treat refractory cancer patients by selecting among "salvage treatments" based on what hasn't already been tried. "That is a very dissatisfying way of picking the next therapy. As oncologists, we prefer to have a strong biologic rationale for a positive selection of treatment," he said.

A secondary advantage to using the Cellworks system, he said, is that it gives oncologists and patients a granular understanding of why a cancer is refractory, and it provides a biologic rationale for why the next therapy regimen is being chosen.

Since 2015 when he first began using Cellworks' technology, Cogle said that he has treated about 200 patients at UF and in a private company by leveraging guidance from the Cellworks system.

Similar to other groups of oncologists working with the Cellworks system, his team receives completed genetic test reports from several companies and hospitals offering FDA cleared tests, including Foundation Medicine, Guardant Health, and Memorial Sloan Kettering, as

well as other organizations conducting laboratory developed tests in CLIA-waived CAP accredited labs.

Cogel has also launched a company called CancerPop through which he provides oncology consultation using the Cellworks system, along with genetic testing.

While diagnostic tests provide important information about patient health and biopharma companies provide the therapies to treat diagnosed conditions, Cellworks' biological modeling system sits squarely in the middle, leveraging diagnostic data and guiding clinicians in their decision making and discussions with patients, said Cellworks CEO Yatin Mundkur.

The firm is engaged in discussions with the US Food and Drug Administration about the requirements for obtaining marketing clearance for clinical use of its computational modeling system.

Mundkur said it is too soon to provide guidance about the expected timing of clearance but he anticipates that the benefits its system provides to many different healthcare entities will factor into the FDA's decision.

A Cellworks system with regulatory approval might help oncologists predict whether a cancer treatment will produce a response by simulating the outcome of a drug therapy on a patient's genomic tumor profile.

For cancer patients, the system may help them to avoid the waste of precious time, medical costs, health risks, and side effects of taking cancer treatments that have no chance of working, he said. Oncologists could get a better understanding of the patient’s response to all drug options before treatment. The system could also increase the clinical utility of next-generation sequencing, because it provides clarity on cancer treatment decisions based on a patient's NGS report.

Healthcare payors also stand to benefit, he said. The Cellworks system helps reduce healthcare costs associated with cancer treatments that don't produce a response in patients but generate side effects that may require medical interventions.

Biopharma companies could use the system to improve patient enrichment in clinical trials, and improve target identification and lead validation, the firm said.

He noted that the results of the iCare 1 study demonstrated the promise of applying genomics-informed biosimulation predictions more broadly to other cancer indications.

As the firm validates its technology in advance of submitting it for FDA clearance, it is providing the system to community oncologists and academic medical centers for use in IRB-approved clinical studies.

Prospective study

In the iCare 1 study, Cogle and his colleagues working with Cellworks used the firm's computational biology modeling technology to understand the mechanisms of relapse after chemotherapy treatment and propose new re-induction treatment options for the 32 percent of patients that relapsed following the prescription of earlier therapies.

They recruited 120 patients with AML or MDS to compare computer predictions of treatment response to clinical outcomes. Of the 120 patients, 96 had full genomic testing profiles and 50 were eligible for evaluation based on length of follow-up.

The researchers reported that genomics-informed computational biology modeling accurately predicted response to standard of care in MDS and AML and identified mechanisms for induction failure.

For genomic profiling of patients' tumors and to create disease-specific protein network maps for each patient, the system obtained somatic mutation data through conventional cytogenetics, whole-exome sequencing, and array comparative genomic hybridization — a molecular technique for the detection of chromosomal copy number changes on a genome-wide and high-resolution scale.

By programming each disease agent's mechanism of action as determined from published literature, the clinician team generated a digital library of FDA-approved drugs.

The team tested digital drug models of the patients' therapy choices at varying dosages and predicted the efficacy of the drugs they were prescribing by calculating a disease inhibition score — defined as the degree to which disease pathways and phenotypes returned to a control state.

In the clinical study to test the system's prediction of resistance to azacitidine, Cellworks and the clinical investigators analyzed clinical, NGS, cytogenetics, and FISH data. With Cellworks technology they created a computational biology model for 37 out of 48 patients utilizing genomic data, and they created a predictive workflow complemented by a digital mechanistic model of azacitidine and other FDA-approved drugs.

The firm modeled the drugs by programming their mechanism of action on genomic pathways and simulating them individually and in combination. A disease inhibition score characterized the drug impact on inhibition of the disease phenotypes. For all azacitidine non-responder profiles, the firm identified unique combinations of drugs that could produce a response. Further, the Cellworks analysis uncovered possible mechanisms for azacitidine resistance that could be targeted to induce response, the firm said.

Only 40 to 50 percent of patients experienced clinical improvement from treatment with azacitidine, though it is the drug of choice for most of high-risk MDS patients, Mundkur said. As a result, oncologists are currently using the Cellworks predictive clinical decision support tool in research settings to identify MDS patients with a higher or lower likelihood of azacitidine response.