Evaluate Vantage

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Asco – Early liquid biopsy data hint at Grail's travails

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This weekend blood testing company Grail published data at Asco allowing oncologists to start to assess the value of its liquid biopsy technology.

The data show promise – but they also show the scale of the task ahead. Grail is already committed to two enormous clinical trials but with one of the Asco trials suggesting that DNA from white blood cells might also be sequenced to remove confounding data, ever vaster computing power will be needed to interpret the results.

Liquid biopsies are designed to detect circulating tumour DNA (ctDNA) – DNA shed by a tumour anywhere in the body into the patient's blood plasma. Since blood draws can be conducted much more easily and with less trauma than tissue biopsies, liquid biopsies are intended to be used to track the effects of cancer therapies and guide future interventions.

Concordance

Before any of that can happen they must be proven accurate. In one trial presented at the Asco meeting Grail compared results with its 508-gene plasma assay with tumour tissue samples taken from 124 patients with various cancers, including breast, prostate and non-small cell lung cancers.

Grail's tool detected 54 of 71 druggable mutations found in tumour tissue samples taken from the same patients. The tissue DNA was sequenced using the MSK-IMPACT assay, developed by the Memorial Sloan Kettering Cancer Center, which looks at mutations in 410 genes.

Some cancer-related mutations were detected in the bloodstream but not in tumour tissue. Grail is analysing this finding and intends to submit it for presentation at a future meeting.

Analysts from Leerink said this 76% concordance rate "appeared meaningful and promising", though they pointed out that many of the patients had mid- or late-stage disease, perhaps not offering the best assessment of a technology intended to catch cancer at the very earliest stages.

The trial is an early one, this panel will not be Grail's final product, and accuracy ought to improve. The researchers said that the study would inform development of a high-intensity sequencing approach for early cancer detection. But Grail says that the panel used in this study generated around 100 times more sequencing data than previous approaches, and another Asco study suggests this may get greater still.

So much data

That study, in 151 metastatic cancer patients, looked at whether clonal haematopoesis could confound liquid biopsy results. Clonal haematopoesis is a process in which a spontaneous mutation in blood cells spreads, creating a population of cells genetically distinct from the majority; it becomes more common as individuals age.

The trial showed that many mutations seen in circulating cell-free DNA in the blood – using the same Grail 508-gene panel – are not derived from cancer, but rather from the mutations arising in white blood cells. Consequently genomic DNA from white blood cells might also have to be sequenced, in addition to the ctDNA found in the plasma, to remove confounding data.

This will of course increase the amount of sequencing that must be done, and demand enormous computing power to crunch the numbers. And what numbers: Grail has begun its 10,000-patient CCGA study and is also enrolling an astonishing 120,000 breast cancer patients in the Strive trial.

With the best part of a billion dollars in recent funding, Grail is better positioned than many companies to be able to develop analytical capabilities on this scale. Even so, it is a big task.

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