First multi-gene NGS diagnostic kit approved

For the first time, the US Food and Drug Administration (FDA) has approved a next-generation sequencing (NGS)-based companion diagnostic that identifies multiple lung cancer mutations. The approval ushers in a new era in diagnostics, as the sequencing-based kit can be distributed to laboratories throughout the country, in contrast to 'home brew' tests, which are run only by the laboratory that developed it.

The new lung cancer diagnostic, the Oncomine Dx Target Test from Thermo Fisher Scientific in Waltham, Massachusetts, detects 369 variants in 23 genes in a single assay using one tumor specimen. Any of the variants on the panel can help a physician to make a treatment decision, but for three of those genes—*BRAF*, *ROS1* and *EGFR*—the test acts as a companion diagnostic for specific drugs. Oncomine results can be linked to Xalkori (crizotinib, from Pfizer) for *ROS1* mutations, Iressa (gefitinib, from AstraZeneca) for *EGFR* mutations, and the combination of the Novartis drugs Tafinlar (dabrafenib) and Mekinist (trametinib) for *BRAF* mutations. FDA approved the Tafinlar/Mekinist combination on June 22 to treat non-small-cell lung cancer patients with the *BRAF* V600E mutation at the same time as it gave the nod to Oncomine.

"It's the first NGS multi-marker success story," says Dan Rhodes, CEO of Strata Oncology, an Ann Arbor, Michigan startup focused on improving enrollment in cancer clinical trials by helping ensure that patients get comprehensive tumor sequencing (*Nat. Biotechnol.* **34**, 895, 2016). Rhodes is a former vice president, oncology strategy at Thermo Fisher, where he participated in the development of clinical research applications of Oncomine.

Thermo Fisher developed the *in vitro* diagnostic (IVD) version of Oncomine for lung cancer in collaboration with Basel, Switzerland–based Novartis and Pfizer, in New York. Lung cancer was a good indication to begin testing the IVD panel paradigm, notes Anne-Marie Martin, senior vice president, global head of precision medicine, at Novartis, because this indication has many different molecular subtypes, which are targeted by a number of drugs or drugs in development "We now have an analytically validated set of genes that allows you to test the hypothesis in a new indication or with a new drug," she says.

Armed with an approval in lung cancer, Thermo Fisher expects to quickly expand Oncomine use as a companion diagnostic in IVD kit form. Gaining approval for new uses for the test should be much quicker and less expensive than the first, says Joydeep Goswami, president of clinical next-generation sequencing and oncology at Thermo Fisher. "It doesn't really matter what the indication is," he says, it could be in lung, colon or any type of cancer covered by the genes on the panel. "We intend to quickly bring on a lot of different drugs that are in development and validate them on our panel," he says. For example, in May 2017 it began a collaboration with Cambridge, Massachusetts–based Agios to develop a companion diagnostic for Agios's phase 3 drug ivosidenib to identify isocitrate dehydrogenase 1 (*IDH1*) mutations in cholangiocarcinoma, a rare form of cancer that affects the bile duct system. (*IDH1* is not among the 23 genes on the current Oncomine panel.)

The Oncomine platform is based on Thermo Fisher's Ion AmpliSeq technology, which requires 10 ng of nucleic acid to screen tumor samples for multiple genetic markers. Although the technology is not as amenable to whole genome or whole exome sequencing, "it is very good at targeted sequencing from limited and challenging tumor specimens," says Rhodes. Metastatic lung cancer biopsy samples are uniquely challenging in this regard, he says. Because tumor biopsies often yield minute amounts, Oncomine's minimal DNA/RNA requirement makes panel testing for lung cancer feasible.

The Thermo Fisher kit could also encourage further testing in hospitals. At the moment, most diagnostic testing is done in-house, but by most accounts, also, only about 10% of cancer patients have their tumors sequenced. Even in academic medical centers, the number rises to only 15% or so of patients with metastatic disease, Rhodes says.

Mark Ratner *Boca Raton, Florida*

Thermo Fisher Scientific

The FDA has cleared Thermo Fisher's next-generation sequencing Oncomine assay, which screens for multiple cancer biomarkers at once.

> **"It's nice to know that there are steps we can take: we're not just winging it. Right now, there's a chance everything will line up. It's not a great chance, but a chance—so we have to take it."** Sam Sabky and his wife, parents of a 14-month-old son with Niemann-Pick disease, which typically results in death in early childhood, raised over half a million dollars through crowdfunding to support a gene therapy laboratory at Children's Hospital of Philadelphia. (*STAT*, 30 June 2017)

> **"Using CRISPR to make corn with a higher yield will not fix famines caused by bad economic systems or civil wars. If someone figures out how to use CRISPR to cure muscular dystrophy, they probably won't give the treatment away for free."** Science writer Carl Zimmer's reality check of the genetics revolution. (The Aspen Institute, 25 June 2017)