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# On Site: Sponsors look to the power of genomic profiling to screen, enroll patients in trials for targeted therapies

As patient centricity takes hold in drug development, more biopharmaceutical companies are turning to genomics profiling to screen large numbers of patients for enrollment into clinical trials for targeted therapies.

Sponsors are looking for the underlying causes of disease and the genetic triggers that cause symptoms. To do this, they have partnered with companies that will genotype thousands of volunteers who also fill out online surveys to provide researchers with their genetic profiles.

Launched in June, the Lung Cancer Master Protocol (Lung-MAP) trial will screen close to 1,000 lung cancer patients a year over a five-year period for alterations of more than 200 cancer-related genes. The trial will use genomic profiling to match patients with advanced squamous cell carcinoma to one of five investigational treatments designed to target those genomic alterations driving the growth of their cancer. Screening results will lead to assigning each patient to the trial arm that best matches his or her tumor's genomic profile.

Five pharmaceutical companies — Amgen, Genentech, Pfizer, AstraZeneca and Medimmune, AZ's global biologics R&D arm — are collaborating with Foundation Medicine, the National Cancer Institute, SWOG Cancer Research, Friends of Cancer Research, the Foundation for the NIH, and several lung cancer advocacy organizations for the unique trial.

"Working with large groups of patients and their genomics, we have the ability to rapidly acquire genetic data and understand their tumors better than with traditional methods," said Vincent Miller, M.D., chief medical officer of Foundation Medicine, whose clinical assays provide the informative genomic profile to identify molecular alterations in a patient's tumor and match them to relevant targeted therapies in clinical trials. "What once took 10 years from initial discovery of genomic alterations to establishing a therapy that showed efficacy and publishing the results now is condensed, in several scenarios, to a year. That's a profound change in accelerating timelines."

In a separate trial seeking to unravel the genetic ties to inflammatory bowel disease (IBD), Pfizer has turned to 23andMe, a home genetics company, to enroll 10,000 people with the hard-to-treat disease and study the DNA from their donated saliva samples.

Both companies hope to find genetic similarities in patients with the disease, which could serve as a roadmap to guide Pfizer's development of new targeted drugs. Two key goals of this large study are to understand the genetic factors related to risk for IBD and response to treatments, and environmental factors.

IBD is a catch-all term for Crohn's disease and ulcerative colitis (inflammation of the colon), for which current treatments include steroids and immune-suppressing drugs that reduce inflammation but cause serious side effects. An estimated 1.4 million people in the U.S. are diagnosed with IBD.

"Doing these kinds of studies with large patient populations, where understanding the underlying biology and genetics from each participant combines with extensive use of Big Data, is the wave of the future for exciting research and innovative projects," said Emily Drabant Conley, director of business development at 23andMe.

She said the IBD research with Pfizer is her company's largest partnership and is expected to appeal to many patients who may never have considered clinical trial participation.

Involving patients at the earliest stages of their understanding of genomics also can change their perceptions of clinical trials, she said. Participating IBD patients are enrolled with an at-home test kit that asks them to send a saliva sample and answer a short (15-minute) survey regarding their disease and its symptoms. Each patient receives free of charge the company's genome service, which includes his/her genetic ancestry and access to his/her uninterpreted genetic data.

"We are using a virtual platform and that gets the genetic information back to patients, keeps them engaged, and enables us to share discoveries, while they provide us their history of IBD, the medications they have used, and their response to treatments," said Drabant.

There is no cure for IBD, which is more common in developed countries. How the disease is triggered remains a mystery, as some scientists cite a virus or bacteria as the starting point, while others stress genetics as the root cause. The risk of getting IBD, according to the Centers for Disease Control and Prevention, "is found among first-degree relatives."

With a goal of developing new treatments based on genetics, Pfizer currently has two monoclonal antibodies for IBD in its pipeline and is working on other treatments for chronic inflammatory disease.

Jose Carlos Gutierrez-Ramos, Pfizer's senior vice president and head of biotherapeutics R&D, said in a statement, "By enhancing our understanding of the underlying biology of the disease, we hope to better support our clinical research activities and development programs."

— Ronald Rosenberg

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