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Decentralized Trials Ease Enrollment In Rare Disease Studies

by Alaric DeArment

Panel discussion illustrated how decentralized approaches can expand the possibilities of studies in rare diseases, such as cancers with rare genomic alterations.

Decentralized clinical trials have been touted for their greater convenience, for enabling clinical investigations during the COVID-19 pandemic and for their ability to increase clinical trial diversity. But decentralized trial technology provider Science 37 sees another benefit, which is that decentralization may help some studies get off the ground in the first place, particularly in diseases with few patients – including rare cancers, where people might not think of such studies as playing as big a role as in other indications.

Science 37, Inc. chief delivery officer Darcy Forman referred to a trial the the Culver City, CA-based company is participating in, which she described as a single-arm study among cancer patients with a rare genomic alteration, during a 26 July FierceMarkets-sponsored webinar.

“We are using a comprehensive genomic profiling registry to identify these very rare patients,” Forman said. “The study would have been very, very difficult for the sponsor to run because it would require thousands of brick-and-mortar sites because of how rare this patient population is.”

The rise of precision medicine and rare disease research in general have driven up the number of patients needed to screen to find enough clinical trial participants – and the digital approaches offered by decentralized (or virtual) trials can broaden the patient pool.

Large contract research organizations (CRO) like *Syneos Health* and *PPD, Inc.* have added to their decentralized trial offerings. And underscoring the growing importance of decentralized trials, specialist Science 37 said in June that it would go public through a merger with special purpose acquisition company (SPAC) LifeSci Acquisition II Corp., a deal that would value the company at

more than $1bn. (Also see "*Science 37 Blockbuster SPAC Valuation Points To Growth In Decentralized Trials*" - In Vivo, 1 Jun, 2021.)

Decentralization Opens Rare Disease Opportunity

To be sure, it can be hard to change practices in which people are deeply set in their ways, and rare diseases are no exception. At the US Food and Drug Administration's FDA Rare Disease Conference in March, Chris Austin, director of the National Institutes of Health's National Center for Advancing Translational Sciences, said innovations that aid decentralization of trials like remote monitoring were not widely accepted before COVID-19 limited physician-patient interaction. But many stakeholders, he noted, want the system to remain unchanged.

As such, Austin challenged the rare disease community to push for the pandemic to have lasting effects on research, since the rapid development of diagnostics, drugs and vaccines for COVID-19 prove that the translational research system can move faster than previously thought. (Also see "*Pandemic Perspectives: NCATS Director Urges Rare Disease Community To Push Against Return To Clinical Trial Status Quo*" - Pink Sheet, 9 Mar, 2021.)

Nevertheless, the small numbers of patients with rare diseases or rare cancer mutations still make it difficult to enroll clinical trials at a pace that can keep up with innovation.

While Forman of Science 37, speaking during the 26 July webinar, did not go into specifics about the particular genomic alteration the trial is targeting or what intervention it was using, it is clear that enrolling patients into studies of drugs meant to treat cancers in a tumor-agnostic way by targeting rare driver mutations represents a significant challenge to completing them.

"A lot of people don't think decentralized trials and oncology, in particular, go hand-in-hand because of that very strong physician-patient relationship with that oncologist that, again, is incredibly important," Forman said.

For example, the Phase II NAVIGATE study of *Bayer AG*'s NTRK inhibitor Vitrakvi (larotrectinib) opened in September 2015 and is recruiting as of 7 July, according to ClinicalTrials.gov, with a study completion estimate of September 2025. But in addition to allowing for a decade-long timeframe, the trial is designed to enroll 200 patients and has 154 sites spread across every continent except Africa, with just over 100 sites recruiting and another 36 preparing to open for recruitment. Only a single site in Russia – one of the five in Moscow alone – has withdrawn.

Virtual screening of patients could significantly speed up enrollment in such trials, however. Another member of the late July panel, Medable chief growth officer Sanskriti Thakur, said that in one trial her company took part in, the company remotely screened 11,000 patients for a rare genetic variant. In doing so, she said, the enrollment period was reduced from two years to one, and the number of sites required from 100 to 25, thus saving the sponsor $20m.

“While the pandemic has essentially provided momentum to all clinical trials from a decentralized and digitization perspective, what we’ve seen in the future is the opportunity not just to sustain this growth but to make it much broader,” Thakur said. “Not just about the clinical research, but about research in general; not just about bringing the technology to a site, making it virtual, but bringing it to the helm.”

No Signs Of Momentum Slowing Down

There’s no denying that COVID-19 significantly sped up the move to decentralized trials as a way to continue studies without face-to-face interaction. The pandemic caused decentralization to evolve from a luxury to a necessity, and de-risked the tools for virtual or hybrid trials in the process.

“[It was] no longer nice to have; we actually needed to maintain continuity and patient safety, so the pandemic certainly accelerated that process,” panelist and head of product and technology at PPD Digital Ravi Ramachandran said.

The consensus that has emerged since the darkest days of the pandemic is that there will probably be a hybrid model, with virtual participation supplementing brick-and-mortar sites, and panelists agreed with that view. (Also see "*Will Decentralized Trials Continue Growing After COVID-19 Pandemic Ends?*" - Scrip, 17 May, 2021.)

The greater flexibility of decentralized approaches has proven attractive, even in more serious diseases where that may not be expected, such as cancers. The US Food and Drug Administration has expressed an openness to fostering decentralized approaches in oncology trials post-pandemic as well, including encouraging sites to develop the necessary infrastructure to improve trial diversity. (Also see "*COVID-Era Trial Flexibilities, Equity Focus, Could Be Used To Reshape Cancer Study Enrollment*" - Pink Sheet, 18 Jun, 2021.)

Science 37’s Forman said that enrollment continues to be the biggest struggle, showing a slide estimating that only 8% of patients who would qualify for a study are available, along with only 5% of physicians participating. The poor participation rates are due to geographic limitations and the costs of setting up necessary infrastructure, she said.

Forman said her company’s experience is “why I feel so passionately that decentralized trials should be a part of every clinical trial, and that’s really because we’re seeing, and continue to see, that enrollment and patient identification for clinical trials continues to be the biggest struggle within the industry.”

“So decentralized trials are really about enabling patients and participants – anywhere – to participate, regardless of where their provider or their physician is, all while maintaining that really strong physician-patient relationship,” she said.