A patient-powered registry boosts the study of rare Castleman disease

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The study of a disease is inherently challenging when patients are few and far between, but doctors at the Perelman School of Medicine at the University of Pennsylvania have reported a new "patient-powered" approach that may help to revolutionize the study of rare diseases.

The Penn Medicine researchers, in a paper in *Cell Reports* Medicine, described a new type of patient registry they recently developed for Castleman disease, a rare disorder involving flu-like symptoms, enlarged lymph nodes, and sometimes life-threatening vital organ dysfunction.

The registry, called ACCELERATE, includes an approach in which Castleman disease patients can enroll directly. The researchers found that this patient-powered approach greatly boosted enrollment and the overall availability of data, compared to the traditional approach in which doctors at a few designated sites can enroll their patients. Another innovative component is that the study team requests and extracts data from the full medical record for each patient who enrolls rather than relying on physicians or patients to enter data, significantly increasing the quantity of data included.

"One of the greatest barriers to progress for rare diseases is the lack of high-quality, centralized data," said study senior author David Fajgenbaum, MD, an assistant professor of Translational Medicine and Human Genetics at the Perelman School of Medicine who directs the Center for Cytokine Storm Treatment & Laboratory (CSTL) and is a patient with Castleman disease. "Using this novel, patient-powered study design to centralize high-quality data through ACCELERATE has been transformative for Castleman disease tracking and clinical trial enrollment and may serve as a model for research on thousands of other rare diseases that have no approved therapies."

Rare diseases—which in the United States are defined as affecting fewer than 200,000 people—collectively afflict nearly five percent of the human population. However, in most cases they garner little attention from researchers because of the difficulties involved in enrolling enough patients and gathering associated clinical samples and other relevant data. Because of the dearth of research, only a small percentage of the diseases classified as rare diseases have specific approved treatments.

Research on Castleman disease, which is diagnosed in only several thousand people each year in the U.S., has been hampered by the same factors. Although a monoclonal antibody called siltuximab is approved for treating some forms of Castleman disease, it is not administered to all patients who are likely to receive benefit and is effective in only a portion of patients.

Following its approval of siltuximab, the European Medicines Agency (EMA) in 2016 directed the treatment's manufacturer, Janssen Pharmaceuticals, to establish a patient registry for Castleman disease. The company's research and development department partnered with Fajgenbaum and Penn Medicine to set up ACCELERATE, which includes a traditional doctor-directed arm but adds an online patient-powered arm.

The doctor-directed arm was run from nine medical centers in six European countries. Participating physicians enrolled their consenting Castleman disease patients and arranged for patients' clinical data and tissue samples to be added to a central database/repository. By contrast, the patient-powered arm used a website and social media to attract would-be patient participants—the registry team then contacted these patients' doctors to verify that they met registry criteria, and, if so, to obtain clinical data and samples.

The patient-powered arm resulted in the enrollment of more than 250 patients by the end of 2019, compared to fewer than 100 in the doctor-directed arm. The registry team also was able to gather a median of 683 clinical, laboratory, and imaging data elements per patient in the patient-powered group, compared to a median of just 37 in the doctor-directed arm. Thanks to the addition of the patient-powered arm, the registry was able to reach its five-year enrollment goal within two years.

"Beyond the direct value of this clinical data, we have also used these

data and tissue samples in multiple other studies that have led to improved treatment guidelines as well as new insights into the biology of Castleman disease—including potential targets for future treatments," said Sheila Pierson, MS, the first author of the study and the associate director for clinical research for the CSTL.

More information: Sheila K. Pierson et al. ACCELERATE: A Patient-Powered Natural History Study Design Enabling Clinical and Therapeutic Discoveries in a Rare Disorder, *Cell Reports Medicine* (2020). DOI: 10.1016/j.xcrm.2020.100158

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