When designing clinical trials for Huntington's disease, first ask the experts

April 23 2019

Progress in understanding the genetic mutation responsible for Huntington's disease (HD) and at least some molecular underpinnings of the disease has resulted in a new era of clinical testing of potential treatments. How best to design clinical trials in which HD patients are willing to participate and comply is a question faced by researchers. For that reason, investigators in the Perelman School of Medicine at the University of Pennsylvania (Penn) surveyed HD patients at different stages of the disease about their attitudes and treatment goals. The results, published in the *Journal of Huntington's Disease*, should be useful for designing future clinical trials of gene therapies for HD and other genetic disorders.

"Clinical trials in HD are creating a sense of optimism and hope within the HD community, with the majority of respondents [to our survey] reporting willingness to participate in trials. As new trials are developed and implemented, it is important to take the opinions and attitudes of the patient population into account," explained Tanya M. Bardakjian, MS, CGC, senior genetic counselor in the department of Neurology at Penn.

Treatments now being tested can be nontraditional, going beyond taking a daily pill. Some require repeated intravenous infusions, lumbar punctures, or brain surgery; some may be administered only at sites far from where the patient lives; and others may result in significant side effects. "In order to optimize feasibility, it is important to first understand how potential study participants feel about these new trial designs, with interventions that might involve a higher potential risk but

also higher potential reward," noted Ms. Bardakjian. The authors also wanted to determine whether responses differed if the respondent was a potential disease carrier, an asymptomatic genetic carrier, or showed HD symptoms.

Eighty-seven respondents completed an anonymous survey, including 36 patients diagnosed with HD, 18 pre-manifesting mutation carriers, and 33 asymptomatic participants at risk. The questionnaire included multiple-choice questions concerning hypothetical scenarios. For example, one question asked, "How likely are you to participate in gene therapy trials if treatment was an IV infusion in the arm requiring a clinic visit once a month?" Answers could range from not likely to very likely.

Another question assessed the respondent's willingness to participate in a clinical trial based on personal goals of therapy such as seeking a cure, slowing disease progress, or helping future generations. They were also asked about how they perceived the investigators' motivation to conduct trials, including whether they thought investigators were seeking financial gain or looking to advance their careers. Results were broken down according to the three disease-status groups described above. The questionnaire also collected demographic, clinical, and genetic background data.

The responses indicated that the majority of participants were very likely or likely to participate in clinical trials, regardless of study design or goals of therapy. However, individuals who know they carry the mutation and therefore will develop HD in the future but have no symptoms yet, had the most favorable views. Additionally, more invasive procedures and trials that include administration of a placebo were viewed less favorably across all groups. Ms. Bardakjian suggests that one way to counteract the negative effect of including a placebo group within a trial is to include the option of receiving active treatment

once the placebo period ends.

"We believe that a patient-centered trial design, through the inclusion of appropriate education and communication to ensure participants and advocates are informed and engaged, is likely to have a positive impact on recruitment," commented Ms. Bardakjian.

More information: Tanya M. Bardakjian et al, Attitudes of Potential Participants Towards Molecular Therapy Trials in Huntington's Disease, *Journal of Huntington's Disease* (2019). DOI: 10.3233/JHD-180328

Provided by IOS Press