Assessment of capacity to consent in a Huntington disease clinical trial: implications for future clinical trial design in neurodegenerative disease populations

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Background

Multiple factors impact the ability to give informed consent in people with Huntington disease (HD). Patients with HD experience progressive cognitive deficits and neuropsychiatric symptoms, not typically captured by the treatment of chorea, and HD, an open label extension/switch study of dTBZ.

Independent capacity assessments were used to augment the informed consent process for the first time in HD clinical trials in First-HD, a double-blind, placebo controlled study of deutetrabenazine (dTBA) for the treatment of chorea, and ARC-HD, an open label extension/study switch of dTBZ.

In the absence of prior data regarding capacity assessment in HD research, the current analysis aims to describe the First-HD / ARC-HD experience in order to inform and improve the process for future trials in HD and in other neurodegenerative disorders.

Design & Methods

Clinical trial information

• First-HD: Randomized (1:1), double-blind, placebo-controlled, parallel-group study; 34 sites in the United States and Canada; 123 people screened after consent, 90 subjects enrolled.
• ARC-HD: open-label dTBZ study with two cohorts
  • First-HD participants could opt to join the ARC-HD open-label extension after completion of First-HD
  • ARC-HD new study participants changed overnight from stable doses of deutetrabenazine to open label dTBZ, 13 sites US (some also First-HD sites) and Australia, 53 people screened after consent with 37 enrolled.

Capacity assessment study participants were potential pre-consent study participants.

• Motor manifest HD with chorea, CAGn > 37
• UHDRS Total Functional Capacity (TFC) score ≥50
• Live in caregiver if TFC > 5
• No specified cognitive symptom inclusion or exclusion criteria
• Able to give (at least) assent to participate in trials
• Exclusions included serious, untreated or undertreated psychiatric illness; stable antidepressant therapy was permitted

Capacity assessors were medical professionals chosen by the site because of their experience in conducting clinical capacity to consent evaluations

• Independent of the study site personnel and not otherwise involved with First-HD or ARC-HD trial
• While experience with HD was preferred, it was not mandatory
• Assessors were approved via First-HD/ARC-HD PI and co-PI review of experience, statement of work, credentials and licensure documentation.

First-HD/ARC-HD Capacity Assessment Process

All participants underwent capacity assessment at key decision making points for participation in First-HD/ARC-HD Capacity assessment focused on the capacity to consent only for the specific clinical trial in question, First-HD or ARC-HD.

Results

Data source:

• 23 sites provided forms completed by 31 assessors.
• Forms from 110 capacity assessments of potential research participants were reviewed.
  • Missing data from 16 assessments
  • Major reasons for non-response:
    • Time burden or cost of retrieving source documents
    • Local IRB concerns about analyzing these data
  • 1 site no forms: no capacity assessments were completed

Capacity assessor characteristics:

• Most sites (70%) used the same assessor for all participants
• One site used 3 different capacity assessors
• Sites used 2 different capacity assessors
• Physicians, (52%) non-MD mental health professionals (35%) and ancillary providers (10%) performed the assessments:
  • 15 MD and 1 PA
  • One consult liaison psychiatrist
  • Neuropsychology subspecialties: movement disorders (5), cognitive/behavioral (3), general neurology (2), clinical geneticist (2), unknown (2), epilepsy (1)
• 9 PhD and 2 PsyD
• 8 neuropsychologists (8), clinical psychologist (1), psychologist/gerontologist (1), unknown (1)
• 2 MSW licensed social worker, 1 MA psychometrist, 1 BA clinical nurse specialist

Use of tools beyond structured interview:

• One site used 3 different capacity assessors
• Forms from 110 capacity assessments of potential research participants were reviewed.
  • Missing data from 16 assessments
  • In two assessments, someone else sat in on interview

Results of capacity assessment:

• 96% of patients were capable of giving informed consent
• 4% of patients were unable to participate without an LAR because of inability to provide informed consent:
  • 3 patients used LARs and enrolled in the trials
  • 1 patient did not understand that he/she had HD, after treatment was able to return, complete assessment, and give consent to participate

Conclusions

Independent assessment of capacity to consent is a dynamic, interactive, individualized process that may detect specific issues.

Despite expected cognitive impairments, patients with HD in these trials were capable of providing informed consent.

Capacity assessors can be a variety of different types of medical professionals. Most were physicians or PhD level psychologists.

Consort consideration for capacity assessors to ensure common areas of evaluation and documentation. A flexible process with a common foundation of evaluation areas and optional tools is recommended.

Addition of independent capacity assessment to the consent process is feasible. However, this addition to study protocols adds burden to sites participants, investigators, trial team members, and to patients to either travel to the site an extra time or undergo two interviews (capacity assessment and informed consent) in one day.

This analysis cannot determine if our system reduced bias compared to having site study personal assessing capacity as part of the consent process.

Future studies are encouraged to build the capacity assessment process into the study database to enhance individual study consent process and enhance understanding of capacity to consent in HD clinical trials. Capturing pre-consent data is feasible.

Disclosures

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