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

CM Testa, M Edmondson, P Agarwal, K Blindauer, C Gray, J Jankovic, R Kumar, D Shprecher, P Siragusa, J Whaley, S Frank for the Huntington Study Group First-HD and ARC-HD Investigators and Coordinators

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 captured by screening tool cut-offs. The existence and type of symptoms are highly variable from patient to patient and over time. Chronic disease patients and site personnel may have longstanding clinical care relationships that could bias towards trial enrollment.

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 (dTBZ) for the treatment of chorea, and ARC-HD, an open label extention/switch study 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 tetrabenazine to open label dTBA, 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 ≥5
- Live in caregiver if TFC 5 to 7
- No specific 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

Design & Methods

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 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.

Pre-Assessment

*Opportunity to review trial information with study personnel

*Purpose of capacity assessment and outcomes explained

Capacity Assessment

*Structured in-person interview occurred within 30 days of screening

*Assessment tools were encouraged but not specified

*Information obtained from caregiver or other informant was encouraged but not mandatory

*Capacity assessor provided written comments on reasoning behind their decision making on de-identified forms kept in site source documents

Post-Assessment Outcome

Patient has capacity

*Informed consent process

*Consents to or declines screening visit

Patient lacks capacity

LAR identified and educated:

*Informed consent process with LAR plus patient provides assent

*LAR consents to or declines screening

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

- Six 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
- Neurology 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 clinical social worker, 1 MA psychometrician, 1 BA clinical nurse specialist

Use of tools beyond structured interview:

Number of assessors using scales to assess cognition:

- 4 Montreal Cognitive Assessment (MoCA)
- 3 Mini Mental Status Exam (MMSE), 1 modified MMSE
- 1 Kokmen short test of mental status

Number of assessors using scales to assess capacity:

- 3 Aid to Capacity Evaluation (ACE), 2 modified ACE
- 6 UCSD Brief Assessment of Capacity to Consent (UBACC)
- 1 MacArthur Competence Assessment Tool

Use of other informants:

No one else interviewed with potential participants in 27 cases:

7 assessors (23%) at 6 sites exclusively used participant-only interviews covering 17 assessments.

7 assessors at 7 other sites with 10 such assessments; In two assessments, someone else sat in on interview

Results

Comments from the assessors on potential participants:

- Specifically cited patients understanding of (# assessments):
  Their ability to withdraw from study (24), voluntary nature of study (22), coercion (3), risks (54) benefits (40), placebo concept and/or randomization (26)
- Comment areas on patient characteristics:
  Overall cognitive status, functioning at home (9), ability to ask pertinent questions (12), rational decision making about study (8)

Capacity Assessment Outcomes:

- 96% of patients were capable to give 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.

Consider training 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.

Adding independent capacity assessment to the consent process is feasible. However, this addition to study protocols adds burden to sites particularly scheduling another team member, 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 conduct, and enhance understanding of capacity to consent in HD clinical trials. Capturing pre-consent data is feasible.

Disclosures

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