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THE INTERNATIONAL SOCIETY FOR CNS CLINICAL TRIALS AND METHODOLOGY

WELCOME

International Society for CNS Clinical Trials and Methodology

Orphan Diseases Working Group

21 February 2020

The Grand Hyatt – Washington DC

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Today's Objectives

Discuss points 1 and 2 from the 4 topics identified as key issues at previous meetings followed by determining point person for ongoing work in each of the 4 sub groups

1. Approaches to endpoint development and validation for Orphan Diseases – recent examples of data in the public domain with endpoints
2. Methods for obtaining stakeholder feedback on study design
3. Methods for improving access to clinical trials in orphan disease
4. Best practices for training and standardizing assessments for orphan disease trials

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Decision reached to combine topics 2 and 3, and 1 and 4, due to overlap in content

- Resulted in 2 Topics for Focus
  - 1) Obtaining stakeholder input and improving patient access to trials
  - 2) Approaches to endpoint development and best practices for training and standardization

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Discussion of Topic 1: Obtaining stakeholder feedback on study design

- Involve multiple stakeholders, avoid a single source (ie, the “only” world expert…)
- Advocacy / patient associations (may be best source, most expert)
- Others parent/caregiver, patient, clinician, researcher, etc.
- Consider skills of the team to adapt technique to improve participant experience (eg, pt experience coord.)
- Do a stakeholder assessment – follow tx pathway to identify ALL relevant stakeholders
- Consider an externally led Patient-Focused Drug Development Meeting
  - Examples: Autism meeting hosted by FDA (was available to EMA), SLE – caregiver / division
- In very rare disorders, may be more challenging. Aggregate disorders? (examples: Columbia – “Genes”).
- May be differential experience globally in regulatory environment in rare disorders (could be a shared call to discuss between others)
- Sometimes controversy can make engagement challenging
- Community Engage studios (Vanderbilt)
  - literally ask a panel, either in person or WebEx, good moderator to bring out all voices.
  - Can do this w/ draft protocol, also if there are problems
- Community Ad Board
  - Standing group of community members
- Involve a community member of the protocol team
- When involving caregivers, parents, advocates, scientists must use lay language and assure understanding of protocol / treatment goals
- Consider ISCTM as hosting as a stand-alone meeting or TC (Bipolar, Suicide as examples)

Discussion of Topic 2 -Approaches to endpoint development and best practices for training and standardization

- Approaches to endpoint development and validation for Orphan Dis. recent examples, public domain data w. EP
- Global perspective: regulators from US, EU are collaborative partners - reach out to FDA – COA staff to participate
- Add identification of domains, selection of endpoints or domains of interest
- Are there available measures (and shortcomings), gap analysis, adapt accordingly
- Clearly document and define the selection process in the protocol
- IND / Phase 2 meeting discussions, part of your development discussion w/ regulator
- Develop validation strategy. Not a classical, gold standard approach. Treatment sensitivity difficult to demonstrate in indication where no treatment exists. As alternative, scale able to detect changes in severity?
- What is clinically meaningful to a family (feels, functions, or survives – how is this done over short-term, in patient who cannot communicate)? Avoid composite measures.

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Discussion of Topic 2 -Approaches to endpoint development and best practices for training and standardization, continued

- Developmental component (age), impact may be different
- Individual differences – use goal-attainment (in all distressing parts of the disease)
- Impact development, and may be deteriorating at phase of illness
- Caregiver-rated: may require extensive interactions with the investigator, clear understanding
- Measure defined syndrome/symptoms, not (just) the IMPACT on caregiver, consider look-back period
- Developing adaptive instruments
- Examples
- CGIs with disease-specific anchors – training across sites and cross culturally.
- ICARS (modified)
- Multiple Sclerosis Individual Outcome Assessment
- Measuring cognitive component in non-verbal / difficulty articulating population with motor/degenerative disorder

Target Deliverables

- **White paper from each topic**
- **Inform discussions at ISCTM Autumn Meeting sessions; 22-23 September 2020- Boston**

Work model/Timelines

- **Subgroups meet March – August via telecons**
- **Present draft of White Paper at WG session in Boston for review by full group**