

Clinical Evaluations in Trials

Tina Duong

Stanford University

PPMD Annual Meeting 2018

Disclosures

- *Scientific Advisory Board:*
 - *Biogen, Cytokinetics, Roche, Acceleron*
- *Consultation:*
 - *Roche, Audentes, ATOM International, Solid Bio, Seismic, Trinds, Pfizer, Audentes*

Clinical Outcome Assessment (COA)

- Symptoms, overall mental state, or the effects of a disease or condition on how the patient functions
- COAs may be **used to determine whether or not a drug has been demonstrated to provide a treatment benefit**

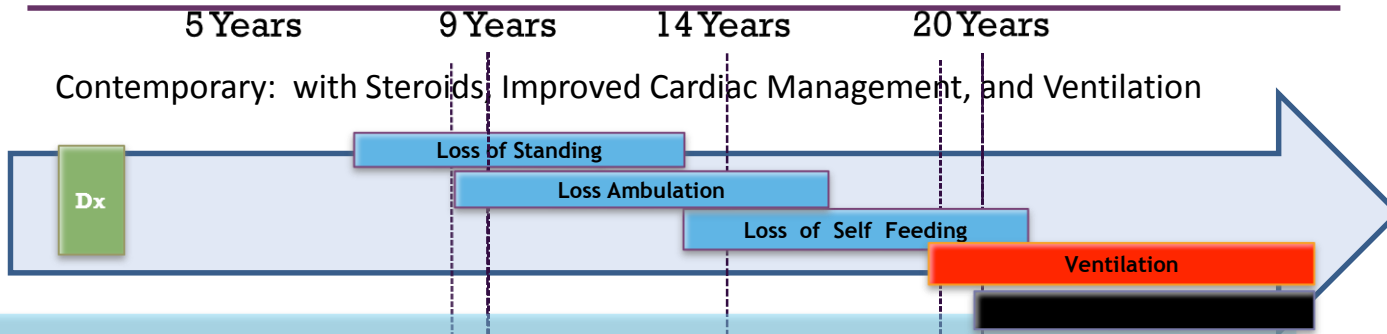
FDA Defines 4 Types of Clinical Outcome Assessments^{1,2}

- Patient-Reported Outcome (PRO) Measure
 - A report that comes from direct patient responses without amendment or interpretation of the patient's report by a clinician or anyone else
- Clinician-Reported Outcome (ClinRO) Measure
 - A report that comes from a trained healthcare professional after observation of a patient's health condition
- Observer-Reported Outcome (ObsRO) Measure
- **Performance Outcome (PerfO) Measure**
 - Observe an actual demonstration of functional performance in a clinical setting

What companies consider when they choose outcomes

- Mechanism of therapeutic agent
 - What is the drug suppose to do?
- Endpoints: Does it require that the patient remain ambulatory
 - Ie: inclusion of ≤ 8 sec to climb stairs, 300 meters 6MWT etc.
 - Length of the study
- Psychometric Properties of the outcome: Are the changes due to the instrument or actual clinical changes?
 - Reliability
 - Validity
 - Sensitivity

Schematic Natural History of DMD



Clinical Endpoints with Validation and Existing Longitudinal Data

Griffiths

Bayley III

Northstar Ambulatory Assessment (NSAA)

Timed Function Tests

6MWT

Strength: Manual muscle testing

Strength: Quant. Lower limb

Strength: Quant. Upper limb (proximal and distal)

Pulmonary Function Testing

Performance of Upper Limb Scale (PUL)

Patient Reported Outcomes (PROs): PODCI, PROM

How long does it take to perform these outcomes?

Strength Assessments

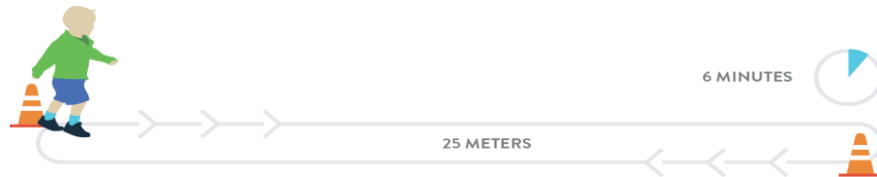
- Manual Muscle tests (10-20min)
 - CE describes strength using a 10 point scale
 - Start ~ 5-6 years
- Quantitative Muscle Tests (10-20min)
 - Handheld myometry
 - Start ~ 5-6 years



How long does it take to perform these outcomes?

Functional Tests

- Pulmonary Function Tests: (15 min)
- 6 Minute Walk Test (6MWT) (16 min)
 - Walk around a 25 meter course for 6 minutes
- Northstar Assessment (NSAA): (15 min)
 - 17 items that consist of:
 - Standing, sit up, get up from the floor, hop, jump, run/walk
- Stair Climb (2 min)
- Performance Upper Limb Scale (PUL) (15 min)
 - 22 Items
 - Performed in sitting
 - Bringing hands over head, onto table, cup to mouth, turning on a light, tearing paper, manipulating coins, tracing a path



Video Examples of Functional Tests

