Newborn Screening for Duchenne Muscular Dystrophy: Phase 2 Update

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Evidence Review Group (ERG)

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Update on Activities

Activities

- TEP Call 1: October 27, 2023
- TEP Call 2: Plan for Feb or March
- Literature Review: In Progress
- Public Health System Impact Assessment
  - Webinar held on January 17, 2024
  - Survey open for the next month
  - Key informant interviews during this period
- Decision-Analytic Modeling
  - Will be the focus of TEP 2, to be convened in February
- Final presentation at the next meeting of the ACHDNC

Update on Screening Activity

Screening Update

- States with legislation for DMD newborn screening
  - Ohio
  - New York
- In addition
  - Minnesota: DMD newborn screening approved by the state's advisory committee, now pending final approval by the State Commissioner
  - Arizona and Illinois: Legislation introduced

Treatment

Treatment

- Main outcome – mean change in dystrophin
- Each received accelerated approval by the FDA

Drug	Year Approved	Exon Skipped	Pivotal Study	Clinical Outcome
Eteplirsen	2016	51	Open-label, 48 weeks, mean age 9 years	Not reported
Golodirsen	2019	53	Open-label , 168 weeks, median age 8 years	6MWT and FVC% worsened (no control group)
Viltolorsen	2020	53	Open-label, 20 weeks, comparison to historical controls, mean age 7 years	No difference in NSAA and other measures
Casimersen	2021	45	Double-blind, placebo controlled for 96 weeks, 48-week extension, mean age 9 years	Not reported

Gene Therapy

- Delandistrogene moxeparovec
  - Accelerated FDA Approval for children age 4 and 5 years – 2023
    - Diagnosis after age 5 years, the average age of diagnosis, currently precludes gene therapy
    - Minoritized children have a longer average time to diagnosis, which could lead to disparities in access to gene therapy
  - 3 main studies, including a double-blind placebo-controlled trial
    - The trial had a dosing error, reducing the sample size
    - Mean age 6.3 years (range: 4-7 years)
  - Pooled data
    - Range: 4-5 years
  - Overall, change in North Star Ambulatory Assessment (NSAA) at 48 weeks was not statistically significant
  - Trend at 48 weeks among subjects 4-5 years toward improvement in NSAA
  - NSAA declined in subjects ≥6 years

Glucocorticoid Therapy

- Deflazacort
  - FDA Approved in 2017
  - Randomized double-blind placebo-controlled trial for 12 weeks, with comparator treatment through 52 weeks
    - Age: 5-15 years
    - Improved muscle strength compared to placebo
  - Randomized double-blind placebo-controlled trial until 104 weeks or loss of ambulation
    - Age 6-12 years
    - Difference in loss of ambulation was 63 months in deflazacort compared with 32 months in the placebo group
- Prednisone
  - Typically started before the plateau phase, around 4-5 years of age, to improve strength and pulmonary function

Areas of Focus for the Review

- Link between the amount of dystrophin and functional outcomes
- Treatment benefits from presymptomatic identification

Non-Pharmacologic Interventions

Benefits to the Individual and the Family

- Still reviewing articles from the search
- Have not identified peer-reviewed published sibling studies
- Three meeting abstracts
  - Contacting authors for additional information
- This is a major focus

Next Steps

Summary of Ongoing Activity

- Focus on the impact of presymptomatic identification compared with clinical identification
    - Individual and family benefit
    - Inequities in diagnosis and treatment
    - Understanding the relationship between biomarkers and patient-centered outcomes
- Assessing screening accuracy and outcomes
    - CK-MM screened once or twice
    - Gene sequencing through the newborn screening lab or as part of diagnostic referral
- Understanding perspectives from newborn screening programs
- Modeling expected outcomes from screening all newborns

Questions