# ADEPT7 Workshop
# Assessing Disease Similarity in Adult and Pediatric Patients with Multiple Sclerosis

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# Multiple Sclerosis

- Multiple sclerosis (MS) is an autoimmune disease that affects the brain and spinal cord
- A diagnosis of MS at any age is based on criteria incorporating physician examination, history, laboratory studies and neuroimaging
- MS affects more than 2.5 million individuals in the world
  - MS is the leading cause of non-traumatic acquired neurological disability

# Pediatric MS is a Rare Form of MS

- Estimates vary but ~2-10% of patients with MS present with a diagnosis before age 18
  - <5000 pediatric patients with MS in the United States
  - Worldwide incidence <1 per 100,000

- Genetic and other risk factors may predispose to pediatric onset

- Before 2018, there were no approved treatments for patients with MS younger than 18 years old

# Diagnostic Criteria

- Adult diagnosis of MS: Revised McDonald criteria
  - Dissemination of relapses and lesions in time and space
- Pediatric diagnosis of MS: International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis
  - Incorporate revised McDonald criteria and reflect unique aspects of pediatric onset of MS

# Pediatric vs. Adult MS: Demographics

| | Pediatric MS | Adult MS |
|---|---|---|
| Age of First Relapse | <16 years of age | 20-40 years of age |
| Biological Sex Ratio (F:M) | Before puberty=1:1<br>After puberty=2-3:1 | 3:1 |
| Race and Ethnicity | Many are White/non-Hispanic but Hispanic and Black may have earlier onset | Majority of diagnosed are European White/Non-Hispanic |
| Age of Onset of Disability | ~28 years of age | ~38 years of age |
| Onset of Secondary Progressive MS | ~15 years after onset | ~20 years after onset |

# Pediatric vs. Adult MS: Pathophysiology

| | Pediatric MS | Adult MS |
|---|---|---|
| Presentation | Can be ADEM-like with more initial brainstem/spinal cord involvement | Optic neuritis and sensory disturbances |
| Phenotype | Greater than 98% Relapsing | Relapsing>Progressive |
| Annualized Relapse Rate (untreated) | Greater than 1 | Less than 1 |
| Prevalence of Cognitive Symptoms | May be present at onset in 20% of patients | Age of onset, duration of disease, disability correlate with risk |

# Assessment of Efficacy in Pediatric MS

- Extrapolation
- Placebo-controlled trials
- Active controlled trials

# What Data Do Pediatric Trials Provide?

- Pharmacokinetic and pharmacodynamic evaluations
- Evaluations of outcomes not relevant or obtainable in the adult population
- Safety database

# Conclusions (1)

- Pediatric and adult MS are phenotypes of the same autoimmune disease

- There are important clinical differences between pediatric and adult MS

# Conclusions (2)

- Existing adult data can be leveraged to reduce trial numbers and inform trial design

- Data from clinical trials in pediatric patients with MS will inform future trials