Introduction to Pediatric Aspects of Drug Development

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Where are we with Pediatric DD in 2020?

- More sophisticated understanding of the early, developmental underpinnings of almost all CNS disorders

- Common episodic and non-episodic disorders can/do occur in childhood
  - E.g. mood disorders, psychotic disorders including schizophrenia
  - 5-10% of all multiple sclerosis cases commence prior to 18 y.o.
  - Clinical stigmata of most CNS disorders are present in childhood/adolescence but have often been understudied

- Childhood disorders persist into adulthood and continue to cause impairment/morbidity, or worsen impairment/morbidity
  - E.g. ADHD, Autism Spectrum Disorder, Down syndrome, migraine headache

Where are we with Pediatric DD in 2020? (continued)

- Familial nature of disorders and the role of genetic anticipation
  - Many disorders occur earlier with each generation and cause more morbidity/mortality
    - E.g. Type 1 myotonic dystrophy, bipolar disorder, Huntington's disorder, Fragile X syndrome

- Preventive aspects to intervening/treating early
  - Decrease lifetime morbidity – multiple examples in psychiatry and neurology
  - Change the trajectory of the disorder and in doing so change the outcome

Where are we with Pediatric DD in 2020? (continued)

- Virtually all medicines approved for adult use are used by clinicians, post-approval, in children
  - On-label and off-label
    - Especially in tertiary clinical settings
  - Contemporary prescribing information can be helpful in dose selection
  - Pediatric regulatory initiatives have diminished the risk of children lingering as “therapeutic orphans”

Where are we with Pediatric DD in 2020? (continued)

- Pediatric drug development is now required and also incentivized

- Need to be mindful of unique safety/tolerability concerns
  - E.g. bone, brain, reproductive organs
    - Partially mitigated through juvenile preclinical tox studies
  - Clinicians that treat across the lifespan understand that children often tolerate CNS medicines better than adults (e.g. clonidine for ADHD)
  - Expanding role of pharmacogenetic testing (especially if the disorder is familial)

- Pediatric clinical assessments/outcome measures often lean more heavily on observational features, caregiver report
  - Diminished insight and lower expressive language capability in children

Advantages of including children early

- Children often have more obvious signs/symptoms (than adults) that are more amenable to direct observation
  - E.g. hyperactivity, visual hallucinations, generalized seizures
  - More tractable signs/symptoms to assess drug effects
  - “Independent observer” (e.g. caregiver) available for corroboration

- Children are more often treatment-naïve
  - Caregiver motivation to participate in studies is high, especially if there is a lack of an adequate pharmacopeia
  - Downside: more “expectancy” (can drive up placebo response rate), and randomization to placebo is less appealing (particularly once a drug is available for prescription)

- It’s not easy, and there are specific challenges to pediatric drug development that you will hear about from the next speakers, but it’s worth it