

Translating Real-World Data into Real-World Evidence

Pam Vig, PhD

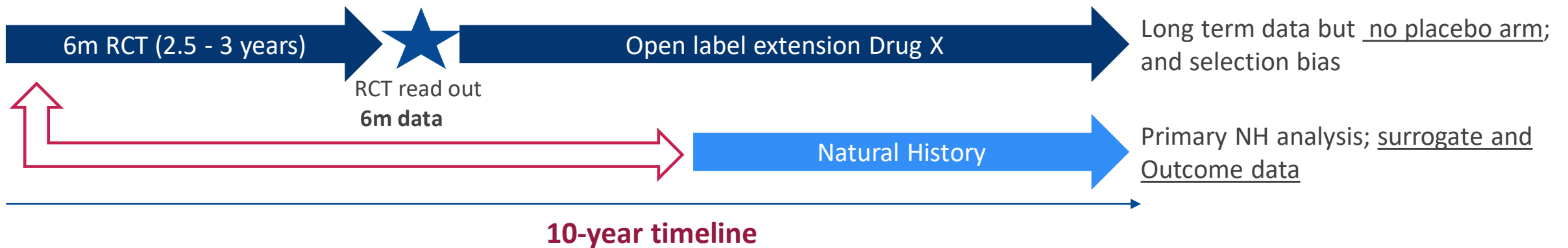
CSO, Mirum Pharmaceuticals

Natural history comparisons: Challenges with long-term data collection

Natural History Comparison Challenges



- In ALGS and PFIC placebo-controlled studies to date consist of a maximum of 6-month primary endpoints
- Long-term data collection required for definitive clinical outcomes (e.g., transplantation, death)
 - Longer-term placebo-controlled studies not feasible
 - Retention, recruitment and ethics around long-term placebo arms
 - Can continue to collect outcome observations for years, but absence of long-term comparator arm
- How do we provide comparative outcome data for a treatment without running the impossible several years-long placebo controlled randomized study?
 - The timelines for studies must overlap with useful information over the same timeline from natural history data



- Global accumulation of patient history allows real world data, larger numbers and more comprehensive view of disease not possible in a clinical trial
- NH registries are not prospectively planned for regulatory submissions (no regulatory input)
 - Cannot be prospectively planned for future treatment comparisons
 - Gaps in data collection (past collection vs what is required in the future)
 - Example: sBA are not universally collected in pediatric cholestatic liver diseases; No uniform and validated scoring method used for severity of pruritus, globally
- A well-selected, appropriate cohort can be identified, which is representative of the treatment population
 - Pre-specified SAP (cohort selection process, statistical methods, sensitivity analyses to eliminate potential biases and confounders)
 - Evaluate comparability of study populations on key disease characteristics after cohort selection

Challenges of prospective long-term data collection

Pediatrics to Adult



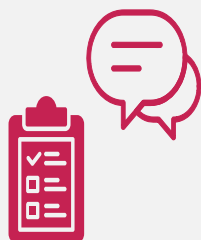
- Long-term data collection required for definitive clinical outcomes (e.g., transplantation, death)
- Are we losing patient data when they transition from Pediatrics to Adult
 1. Transition from pediatrics to adult care (does it happen?)
 2. Continued collection by adult hepatologist (IRB approval needed and if prospective collection, then ICF require)
 3. Ensure connectivity of patient identifier from peds to adult
 4. Variability of collection as well as data entry (less familiarity with disease, new coordinator etc)
 5. What if they go to a transplant center (how to minimize loss of follow up)?
 6. Are there additional data that we want to collect into adulthood?
 7. Interruptions in data collection
- How do we ensure a smooth transition and continued collection?
- Can there be a standard process when patient hits adulthood by the registry coordinator (for prospective continued collection)?

- If continue on-study, then collection is robust
- Company efforts to collect follow-up data from discontinued clinical trial patients for a comprehensive outcome analysis
- Follow up for discontinued patients who are no longer in the study
 - In order to collect follow up/outcomes IRB approval required
 - Re-consent patient/family to collect hard outcome (death, transplant etc)
 - Missing data
- Plan ahead: Prospectively consent patient at time of study start or at the time they discontinue

To improve disease understanding from pediatrics to adulthood

ONGOING

Natural History Database retrospective and prospective



Natural History
database coordination



Industry and regulatory
input for future clinical
trials or comparisons



Pediatric and adult
physicians for
commitment of
continued collection



THANK YOU!