External controls for pediatric cancer clinical trials

2023 Childhood Cancer Data Initiative Annual Symposium
Breakout Session #4

NIH NATIONAL CANCER INSTITUTE

3/29/2023

External Controls Breakout Session
Overview

Definition: An externally controlled trial (ECT) measures outcomes in participants receiving the investigational treatment according to a protocol compared to outcomes in a group of people external to the trial who did not receive the same treatment.

Appropriateness: The suitability of an externally controlled trial design depends on the clinical setting. Consult the relevant FDA review division early in drug development to determine if an externally controlled trial is reasonable.

Study Elements

Overall Study and RWD Source Information

Study Design

- Temporality
- Population
- Exposure
- Comparator
- Covariates
- Endpoint

Data Processes

- Provenance
- QA/QC
- Missing Data
- Auditing

- Time Periods
  - Standard of Care
- Geographic Region
  - Access to Care
- Diagnosis
  - Expected variation
- Prognosis
  - Factors available and similar
- Treatments
  - Factors such as dose and duration
- Other Treatment-Related Factors
  - LOT, Concurrent Treatment Regimen
- Follow-up periods
  - Index date
- Intercurrent events
- Outcome
  - Measurement
- Missing Data

How can CCDI develop a use case?

Appropriate Clinical Setting (randomization not feasible)

- Neuro (DMG)
- Heme (AML)
- Solid (Neuroblastoma)

Available Data

- CHOP
- COG
- CBTN

Barriers

- Data sharing
  - Use NCI Data Archive?

Feasibility assessment

- Data Availability (including confounders)
- Data Fit-for-purpose
- Data completeness and quality
- Contemporaneity

Next steps

Incorporate patient perspective
Technical- getting data to CCDI
Early meetings to evaluate utility
Hybrid designs

Discussion Questions

- What are the appropriate clinical settings for an external control?
- What data sets are ready for potential use?
- What are the potential barriers?
- How can these use cases best fit in the CCDI infrastructure?
- How can this be actionable?

U.S. Department of Health & Human Services

National Institutes of Health | National Cancer Institute

cancer.gov

1-800-4-CANCER