March 21, 2018

Common Challenges & Solutions in Analysis & Reporting of PROs in Oncology Clinical Trials
• Key Learning Objectives:
  – The specific challenges associated with the analysis of data from oncology studies.
  – Why traditional statistical methods for clinical trials can lead to biased results when applied to oncology studies.
  – Possible analytic methods to help account for potential biases and help you better understand your patients.
  – Why safety and patient-reported outcome endpoints may appear contradictory in oncology trials.
Assessment schedule may not be optimal

- Is beginning of cycle the most appropriate time?

- Dose adjustment / interruption may delay treatment cycles.

- How about more assessments during the early cycles while the majority of patients are still in the study?
Imperfect measures may be redundant

- Currently used measures are static.
- Impact of new therapies are missed.
  - Skin rash
  - Vitiligo
  - Photosensitivity
- Summary scores may be misleading.
- Questionable content validity.
Missing Data are just annoying

• Common and rarely random.
• No one cares about exploratory endpoints.
• Suboptimal analytical methods.
PROs are rarely presented in context of efficacy and safety

- Demonstrating Tx-A (PRO) = Tx-B (PRO) is unique to cancer.

- Proving the null hypothesis using imperfect instruments in an underpowered study is nothing to shout about.

- Often this conclusion is not supported by safety data.
Current state of PROs in cancer studies

- PRO instruments may not be capturing what is needed
- Data capture itself as a process is not ideal
- Missing Data
PRO Instruments Are Not Ideal

• PRO instruments should:
  – Measure what is needed
  – Be sensitive enough

• New immuno-oncology therapies may have completely different symptom profile.

• Important to invest time upfront to plan PRO strategy.
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<th>Dependent variable</th>
<th>Explanatory variable</th>
<th>Total effects</th>
<th>Direct effects</th>
<th>Total indirect effects</th>
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<td>NS</td>
<td>-0.345***</td>
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<td>NS</td>
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</table>
Data Capture Is Not Ideal

- PRO data collection frequency and around events of interest.
- Patient burden
- Analysis: Experimental to observational mindset
  - Fixed visits vs. continuous time
  - Data-driven analytic decisions
  - Importance of sensitivity analyses
Missing Data

• Very common and usually not at random.
• Traditional mixed effects models and imputation methods do not work well.
• Need to account for the informative nature of missing data.
  – Selection Models / Shared Parameter Models
  – Pattern Mixture Models
  – Extended Pattern Mixture Models
Kaplan-Meier Overall Survival Estimate

- **Survival Probability**
- **Overall Survival Time (Months)**

95% CI  
Survivor function

- The Kaplan-Meier estimate provides an overview of the survival probability over time, with the shaded area representing the 95% confidence interval.
Kaplan-Meier Survival Estimates

Overall Survival Time

Increasing Fatigue
Total High Fatigue
Total Low Fatigue
Generating knowledge and providing greater understanding so that you—and those who regulate, pay for, prescribe, and use your products—can make better decisions.

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