Discussion:
Jim Neaton -
How to Construct an Optimal Interim Report:
What a DSMC Does and Doesn’t Need to Know

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## Personal Perspectives

### View from:

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<th>DSMC Member</th>
<th>Study Statistician</th>
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<td><strong>Industry</strong></td>
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<td><strong>Academia [NIH, other funded]</strong></td>
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Does ‘one size fit all?’

- Trial Design
  - Active vs Placebo Controlled
  - Superiority vs Noninferiority vs Equivalence
- Disease [severity]
- Risk to Trial Participants
- Seriousness of Outcome of Interest
- Trial Duration
- Potential for Impact on Trial Conduct
- Other considerations
Interim Monitoring: How Often? Of What?

- Safety Monitoring
  - Frequency of monitoring [e.g., every 6 months]
  - Unmasked (coded) treatment group assignment
  - Known, unknown adverse events

- Efficacy Monitoring
  - Success / Futility
  - Masked / Unmasked (coded) treatment group
  - Frequency of monitoring
    - At all DSMC meetings
    - At planned interim analysis times; how often
  - Interim analysis boundaries
    Formal / informal
Example: Placebo Controlled Masked RCT

- Non-life threatening
- Primary outcome: first recurrence by 12 months end of treatment period
- Accrual over 4 years, 18 months of followup
- Multi-center
- DSMC meetings 2x/year
  - Safety monitoring
  - Efficacy Monitoring
Example:

**Efficacy Monitoring**

**DSMC / Investigator Views**

- **DSMC**
  - Monitor unmasked efficacy at every meeting (approximately 8 times)
  - Stopping boundaries at p very low
  - One formal planned interim analysis: O’Brien Fleming boundaries for efficacy; no futility boundaries

- **Investigators**
  - One formal planned interim analysis: O’Brien Fleming boundaries for efficacy and futility
  - No interim analyses
Impacts on Study Conduct

- **DSMC**
  - Stated goal ‘not to stop the study’
  - Needs efficacy to evaluate safety

- **Investigators**
  - Would not like to stop study
  - Efficacy would always be available to DSMC if any safety concerns at all
  - Concerns re impact of repeated looks
    - On final p-value for efficacy
    - Influence on behavior
Informal Survey

- Respondents confidentiality preserved
- Very small convenience sample
- Responses
  - Initial response:
    - DSMC needs to see everything
  - Thoughtful responses:
    - Depends on trial and implications
Acknowledgements

- Thank you to my statistical and clinical colleagues for thoughtful discussions of these issues
- Thank you to the speaker and panelists for a provocative discussion