Data Monitoring Committees: Promoting Best Practices

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Mission of the DMC

- To Safeguard the Interests of the Study Participants
- To Preserve Trial Integrity and Credibility to enable the clinical trial to provide timely and reliable insights to the broader clinical community

Uli Burger
Paul Gallo
Some Fundamental Principles in Achieving the DMC Mission

To assist the DMC in achieving its Mission, procedures are needed…

- To reduce pre-judgment of interim data
  ⇒  *Maintaining confidentiality of interim data*

- To guide the interpretation of interim data
  ⇒  Group sequential monitoring boundaries
  ⇒  Unbiased judgment
      ...  *Well-informed*
      ...  *Independent*

... Motivates fundamental principles for DMC functioning and composition…
Some Fundamental Principles

- DMC should have *Sole Access* to interim results on relative efficacy & relative safety of interventions

- DMC should have *Multidisciplinary* representation having experience in the DMC process

- DMC should be *Independent* with freedom from apparent significant conflicts of interest ... financial, professional, regulatory
An Opinion: The DMC process for monitoring randomized clinical trials is *not* better than it was 10 years ago!

In particular, ongoing and emerging challenges threaten the DMC’s *independence* and effectiveness…

Best practices and operating principles for effective functioning of DMCs have been proposed to address these challenges.
DMC: Best Practices

• An expert panel of representatives from academia, industry and government sponsors, and regulatory agencies met in June 2015 to discuss ongoing and emerging challenges potentially threatening DMC’s independence and effectiveness.

• A position paper was published in 2017 in *Clinical Trials* to summarize these discussions and to offer the authors’ recommendations to improve the DMC process.

• The authors of the *Clinical Trials* article:
  TR Fleming, DL DeMets, MT Roe, J Wittes, KA Carim, AN Vora, A Meisel, RP Bain, MA Konstam, MJ Pencina, DJ Gordon, KW Mahaffey, CH Hennekins, JD Neaton, GD Pearson, TLG Andersson, MA Pfeffer, SS Ellenberg

Proposed Best Practices and Operating Principles

• Achieving adequate training/experience in DMC process
  Didactic instruction; *Apprenticeship model*
• Indemnification
• Addressing confidentiality issues
  — Maintaining confidentiality: ↓ pre-judgment ⇒ ↑ trial integrity
  — DMC needs *ongoing* access to *unblinded* efficacy & safety data
  — Access by others should be limited to a ‘need-to-know’ basis
  — Need for a Mediator, balancing ethical & legal responsibilities

• Implementing procedures to enhance DMC independence
  — DMC Meeting Format *Closed / Open / Closed Sessions*
  — Creating an Effective DMC Charter:
    …providing *guiding principles*, not *rigid requirements*
  — DMC recommendations through *consensus*, not by *voting*

• Defining the role of the Independent / Reporting Statistician
  “Data monitoring committees: Promoting Best Practices *Clinical Trials* 2017; 14: 115-123

Linked DMCs: Thomas Jaki
Frontloading: Lisa Squassante

Steven Teerenstra

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