Short Overview:
Pharmaceutical Industry COVID-19 Biostatistics Working Group

BBS virtual Seminar on "Impact of COVID-19 on clinical trials"
May 6, 2020

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This presentation is based on materials from the working group but has been adapted by the presenter. It should not be construed to represent the views of all working group members or their affiliated institutions and companies.
### Working group members

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Working group output

• **Manuscript**: "Statistical issues and recommendations for clinical trials conducted during the COVID-19 pandemic"
  • Submitted to *SBR special edition on COVID-19* (with discussion)
  • Core sections:
    • Pandemic-related factors, impacts, and risk assessment
    • Implications and mitigations for estimands, missing data, and analysis
    • Study-level issues and mitigations

• **Slide deck**: "Study and data integrity considerations for clinical trials impacted by COVID-19"
  • Presented as *DIA webinar* on May 13, 5:00-6:15PM CET
  • A small teaser of the material is presented on the next slides
Key steps to assess, define and understand the impact of COVID-19 on study and data integrity

**ASSESS IMPACT**
- Impact on data quality
- Impact on recruitment and retention
- Impact on treatment effects and study power
- Blinded/Unblinded Review

**DEFINE RISK**
- Lack of interpretability
- Confounding or inconclusive results
- Loss of power

**MITIGATION & CONTINGENCY MEASURES**
- Different ways of collecting data
- Analysis methods, missing data, sensitivity analyses
- Documentation in Protocol, SAP and CSR
- Consult with regulatory agencies
Blinded/unblinded aggregate impact & risk assessment

• **Blinded review by sponsor**
  • Extent and pattern of intercurrent events and missing data
  • Enrollment change and shift in population
  • Reassessment of protocol assumptions
  • Probability of success for achieving pre-specified goals

• **Role of IDMC**
  • Carefully consider the need and feasibility of IDMC to lead/participate in the risk assessment
  • Amend the IDMC charter to document communication plan for outcomes of the unblinded risk assessment
  • **Exercise caution** in unblinded assessment to avoid biases
Does the COVID-19 pandemic change my trial?

• Answer depends on **impact & risk assessment** and **mitigation measures**

• **Research question** frequently unchanged
  • How would Drug A compare to Drug B in the absence of the acute, systematic disruptions to the healthcare systems due to the **COVID-19 pandemic**?

• **Estimand**: assess impact on all 5 attributes, in particular ICE
  • Different strategies may be appropriate for pandemic & non-pandemic ICE

• **Missing data & analysis**:
  • Missing data in many situations MCAR or MAR
  • Previously planned primary and sensitivity analyses need to be reviewed
Recommendations

- **Assess**: Diligently assess every impact of COVID-19 on the clinical trial conduct and interpretation.
- **Act**: Fully understand the risks, have a fit-for-purpose mitigation plan and act correspondingly.
- **Consult**: Engage early with Health Authorities and keep the communication channel open.
- **Document**: If mitigation is required, clearly document the actions and the rationales.