Clinical Development & Analytics
Oncology and Hematology

Short overview of COVID-19 discussions in the Industry Working Group* on Estimands in Oncology

Evgeny Degtyarev

BBS Virtual Seminar, May 6

***PSI/EFSPI Special Interest Group and Scientific Working Group of the ASA Biopharmaceutical Section**

NOVARTIS | Reimagining Medicine

Assessing the impact of COVID-19: What do we want to know?

- Original scientific objective implicitly assumed a world without ongoing pandemic:
  - Absence of a disease that characterizes through being severe (high proportion of hospitalizations and deaths), being highly infectious, and for which no effective therapy is available
  - No major disruption of the healthcare systems
- Assuming that the pandemic will be over, original scientific objective should remain of primary interest
- In light of unforeseen complications due to COVID-19:
  - Estimate from the initially planned analysis still provides the right answer?
  - Will trial results be useful for informing clinical practice in a world without ongoing pandemic?

Assessing the impact of COVID-19: Still getting the right answer?

- Enrolled patients representative of the target **population**?
- Received **treatment** and its duration in the trial representative of what would have been administered without the pandemic?
- Currently defined **endpoint** reflecting the treatment effect in the original scientific objective?
- **Intercurrent events** due to COVID-19 meaningfully handled with current analysis conventions to reflect the treatment effect in the original scientific objective?
- Interpretability of the **summary measure** still valid?

→ if at risk of not getting sufficiently precise answer, consider:

- clarifying the estimand taking into account intercurrent events due to COVID-19
- modifying the estimator (e.g. handling missing data differently)
- introducing a new estimand (supplementary analysis) or sensitivity analysis

Assessing the impact of COVID-19: Few points to consider

- Some cancer types often directly compromise immune system (e.g. blood cancers) and many treatments are immunosuppressive
- **IV treatments**: increased risk of discontinuations in indications with available oral medications
- **Durable responses**: Patients may prefer to avoid travelling to receive additional treatment (e.g. maintenance therapy)
- **Open-label trials**: increased risk of discontinuations after randomization to SoC if patients can receive it closer to their home
- Treatment often a **sequence of interventions** with a risk of delays due to hospital capacity
- Data after such discontinuation/delay always relevant to evaluate original scientific objective?
  - What if **start of new therapy considered as event** and patient switched from IV to oral medication?

Conclusions

- Estimand framework useful to structure assessment of COVID-19 impact
- If the estimate from initially planned analysis not informative in a world without ongoing pandemic, consider clarifying the estimand accounting for intercurrent events due to COVID-19
- Key factors to consider choosing the strategy:
  - potential relationship of intercurrent event to disease or treatment
  - interpretability of the data after intercurrent event to address original scientific objective
- Hypothetical strategy appears reasonable for events caused by healthcare system disruption
- Principal stratification may be valuable to assess treatment effect in patients who would not experience severe complications of COVID-19 infections on either arm
- Slides summarizing key considerations released on Apr 16 on our homepage https://oncoestimand.github.io/home/oncoestimand.html
  - Update planned based on further discussions and initial feedback – we welcome your input!
  - Manuscript close to submission