Summaries of COVID-19 Infections in Clinical Trials

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Agenda

- Background
- Recommendations in guidance documents
- Thoughts on implementation

Background

- COVID-19 pandemic started and has varying degrees of impact on study conduct for ongoing studies
  - Study teams developed mitigation plans to address immediate needs
- Now, there are ongoing discussions and strategic planning initiatives to determine the impact on the analysis of data
- This presentation will focus on proposed tables and listings that enumerate, describe, or summarize COVID-19 infections occurring in trial participants

Main Message

- For Clinical Study Reports and Submissions, stay focused on establishing the benefit/risk of the investigational product

Avoid unnecessary complication

The pandemic is not the featured discussion

TransCelerate Guidance

- May 2020 TransCelerate CSR Guidance
  - The primary purpose of a CSR is to report results of the trial
  - In most cases, the pandemic should not be the featured discussion
  - As part of the summary of impact, describe COVID-19 illness that occurred in trial participants during the trial

EMA COVID Guidance

- June 2020 Points to consider on implications of Coronavirus disease (COVID-19) on methodological aspects of ongoing clinical trials
  - On the individual participant level, any available information concerning COVID-19 testing or infection status should be recorded in trial documentation whenever possible

PHUSE Blog

- June 2020 PHUSE Blog: Adverse Events – PHUSE COVID-19 Guidance for Data Scientists
  - All COVID-19 infections and positive tests should be collected as adverse events in a study
  - It is important to understand the prevalence of COVID-19 related adverse events in a clinical study and to investigate whether there is an imbalance in the distribution of these events between treatment arms

COVID Safety Manuscript

- July 2020 Manuscript Clinical Trial Drug Safety Assessment for Studies and Submissions Impacted by COVID-19
  - For some compounds, considering the COVID-19 infection itself as a safety topic of interest could be warranted; In these situations, a separate summary enumerating all patients with COVID-19 infections would be useful

FDA Trial Conduct Guidance

- July 2020 Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency
  - Recommends a comparison between the rate of observed SAEs among COVID-19 infected trial participants in the investigational drug arm to COVID-19 infected trial participants in the control arm
  - In the context of IND SAE reporting of COVID infections

COVID-19 MedDRA SMQ

- MedDRA 23.0 (in production April 2020)
  - Approximately 70 new COVID-19 related terms
  - New High Level Term (HLT) Coronavirus infections in the System Organ Class (SOC) Infections and infestations.
  - Other terms under different SOCs
- MedDRA 23.1 (September 2020)
  - A COVID-19 Standardized MedDRA Query (SMQ) will contain a list of MedDRA Preferred Terms (PTs) associated with the COVID-19 clinical condition

https://www.meddra.org/COVID-19-terms-and-MedDRA

COVID-19 Impact Assessment

- Recommendation
  - Listing of participants with COVID-19 infections, using the MedDRA SMQ
    - Severity, seriousness included in listing
  - Summary of COVID-19 infections (if a lot of participants with COVID-19)
  - Listing of participants who discontinued due to a COVID-related reason
  - Listing of protocol deviations related to COVID-19

Scenario 1 (Most Studies)

- Situation
  - **No biological reason** to suspect an increased risk of infection with study drug
  - Number of COVID-19 infections **is small**
- Recommendation
  - No need for additional summaries or listings beyond what is done for the COVID-19 impact section of a CSR/submission
  - If after reviewing data, there is concern that the study drug increases risk of infection, then follow-up is needed (as with any unexpected finding); with the number of infections small, follow-up would likely be through individual case review (e.g., through graphical patient profiles)

Scenario 2

- Situation
  - **No biological reason** to suspect an increased risk of infection with study drug
  - Number of COVID-19 infections is **not small**
- Recommendation
  - Include a summary table of infections in addition to the listing in the COVID-19 impact section
  - If after reviewing data, there is concern that the study drug increases risk of infection, then follow-up is needed (as with any unexpected finding), and should be discussed, such as the safety section

Scenario 3

- Situation
  - **There is a biological reason** to suspect an increased risk of infection with study drug (e.g., suppresses immune system)
  - Number of COVID-19 infections **is small**
- Recommendation
  - No need for additional summaries or listings beyond what is done for the COVID-19 impact section of a CSR/submission
  - Infections is likely already identified as a safety topic of interest, so there will likely be an Infection section already planned for the CSR/submission
    - COVID-19 infections will likely already be included in the planned infection summaries
    - A textual statement on the number of COVID-19 infections would likely be warranted

Scenario 4

- Situation
  - **There is a biological reason** to suspect an increased risk of infection with study drug (e.g., suppresses immune system)
  - Number of COVID-19 infections is **not small**
- Recommendation
  - Include a summary table of infections in addition to the listing in the COVID-19 impact section
  - Infections is likely already identified as a safety topic of interest, so there will likely be an Infection section already planned for the CSR/submission
    - COVID-19 infections will likely already be included in the planned infection summaries
    - Considering COVID-19 infections as a pre-specified subset of infections is likely warranted; If the SMQ doesn't reflect COVID-19 infections adequately, a customized MedDRA PT list might be warranted

Generally not needed in any situation

- Separate *summary* of medications used to treat COVID-19 infections
  - Review of medication data used to treat COVID-19 infections is critical for individual case reviews, that allows for the review of medications relative to adverse events and/or lab abnormalities
- Re-run of general safety analyses among those infected with COVID-19 during the study

Potential Separate Efforts

- What are the risk factors for COVID-19 infection?
  - Through medical history and demographic collection
- Prevalence of COVID-19 infections across geographical regions
- Effectiveness of treatments for COVID-19 infection
  - Through concomitant medication collection

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Questions?