Medically Attended Visits (MAVs): Is it Time to Expand the Primary Endpoint for Trials in Participants with Mild-to-Moderate COVID-19?

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Background

- To date, EUAs and drug approvals for products for the treatment of mild-to-moderate COVID-19 have been based on the following primary endpoint:
  - Hospitalization or death
- Given the high uptake of vaccines, increased natural immunity, and overall lower risk of hospitalization and death in patients with COVID-19 demonstrating an effect on hospitalization or death is currently challenging

Potential Revised Primary Efficacy Endpoint

- One or more of the following from randomization through 1 month:
  - COVID-19-related MAV
  - All-cause or COVID-19-related hospitalization
  - All-cause death

Trial Design Considerations

- The use of a composite primary endpoint that includes COVID-19 related MAVs may be considered in the following trial settings:
  - A double-blind, placebo-controlled trial in a population in which the use of a placebo (without SOC) is considered ethically acceptable
  - A double-blind, placebo-controlled, add-on trial (study drug + SOC vs SOC) in a high-risk population

Proposed MAV Definition

- Any unscheduled, non-routine healthcare visit where the participant is evaluated by a licensed healthcare provider, including visits at or with:
  - Emergency room for < 24hrs
  - Urgent care center
  - Outpatient clinic or primary care provider
  - Telehealth (if a licensed healthcare provider evaluated the patient during the visit)

Proposed Criteria for Classifying an MAV as COVID-19 Related

- A MAV will be considered COVID-19 related if the reason for the visit is one of the following:
  - A worsening of one or more COVID-19 signs or symptoms such that it is at least moderate severity and interferes with the participant's daily activities
  - A persistent COVID-19 sign or symptom that is severe and interferes with the participant's daily activities
  - A complication of COVID-19 (e.g., a thrombotic event)*
  - An exacerbation of underlying conditions due to COVID-19*

*Specific criteria to be defined

Additional Considerations

- MAVs that lead to an intervention (e.g., supplemental oxygen, intravenous fluids, and need for nebulizer treatments) are of particular interest
- The potential role of an adjudication committee:
  - Improve consistency and accuracy in MAV assessment across different regions with varying resources and standards of care
  - Assess worsening/persistence of COVID-19 signs and symptoms and link these signs/symptoms to medically attended visits
  - Use a checklist to objectively and consistently identify COVID-19-related medically attended visits and resultant interventions