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Investigator: Paul Bollyky Associate Professor, Infectious Disease and Immunology

Title: Design for the INHALE Clinical Trial: Avoidance of Lung Events in COVID-19

Summary:
In December 2019, a series of pneumonia cases emerged in Wuhan, Hubei, China. Sequencing subsequently identified a novel coronavirus, which was named COVID-19. On March 11th 2020, the World Health Organization declared a pandemic and as of April 18th 2020, approximately 2.5 million people have been infected and at least 158,000 have died.

The primary driver of COVID-19 morbidity and mortality is respiratory compromise. This is thought to be linked with increases of certain elements of the extracellular matrix, one of which is a matrix polymer known to drive inflammation in multiple other tissues and disease models.

We are planning a proof-of-concept study to evaluate the clinical utility of a repurposed agent that inhibits the synthesis of an extracellular matrix polymer which may be a means of managing the respiratory morbidity of COVID-19 infection. The repurposed agent was developed in the 1970s and approved in Europe. However, it has been neither reviewed nor approved by the FDA. If successful, this may prove to be a low cost and easily adhered to medication with significant benefit in both the USA and the developing world.

For the study design, we are considering an international, multi-center, 3-week, 2:1 randomized, phase 1/2 study of this repurposed agent as treatment versus standard of care with at most 40–45 subjects. One of the primary objectives is to identify the safe and effective dose. Other endpoints, that will be looked on in a largely exploratory manner, will include the ability of the repurposed agent to improve time to worsening in oxygenation requirement, time to mechanical ventilation, duration of hospital stay, and mortality.

Questions:
1. Should this positioned as a Phase 1 (EP: safety) vs Phase 2 (EP: efficacy) study?
2. If we frame as a Phase 1 study, should this contain a dose finding portion?
3. What is the most effective way of including a comparison group (SOC) given the likely complication of placebo double-blinded studies and risk of drop-out if open-label is pursued?
4. Should we allow antivirals to be co-administered?
5. If so, should this be exclusively a study for patients on remdesivir?
6. Are there other endpoints we should consider?
7. Is there benefit to studying these in a hierarchical fashion?
8. What form of multiple comparison adjustments would you suggest for these tests?
Zoom Meeting Information

Topic: Workshop: Data Studio
Time: May 6, 2020 13:30 Pacific Time (US and Canada)
Meeting ID: 976 8841 7197

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