Clinical Trials Endpoints for COVID-19 Studies

Marco Cavaleri, PhD, European Medicines Agency
William Fischer, MD, University of North Carolina SoM
Michael G. Ison, MD MS, Northwestern University Feinberg SoM
Shmuel Shoham, MD, Johns Hopkins University SoM
Davey Smith, MD MAS, University of California San Diego

ISIRV AVG – Therapeutics for COVID-19
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Endpoints for Influenza in Outpatients

**Influenza A**

**Influenza B**

## Endpoints for Studies of Hospitalized Influenza and RSV

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sponsor</th>
<th>Status</th>
<th>Outcome measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baloxivir</td>
<td>Roche</td>
<td>Completed</td>
<td>Time to Clinical Improvement (Hospital Discharge OR NEWS2 ≤ 2 for 24 hours)</td>
</tr>
<tr>
<td>Danarixin</td>
<td>GSK</td>
<td>Completed</td>
<td>Time to Clinical Resolution (discharge or (temp, O2 sat, and (2 of 3 RR, HR, SBP)</td>
</tr>
<tr>
<td>IVIG</td>
<td>NIAID</td>
<td>Completed</td>
<td>Day 7 Ordinal scale</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>NIAID</td>
<td>Completed</td>
<td>% negative viral RNA day 5</td>
</tr>
<tr>
<td>Peramivir</td>
<td>Biocryst</td>
<td>Completed</td>
<td>Time to Clinical Resolution (4 of 5)</td>
</tr>
<tr>
<td>Peramivir</td>
<td>Biocryst</td>
<td>Completed</td>
<td>Change viral titer in 48 h</td>
</tr>
<tr>
<td>Peramivir</td>
<td>Biocryst</td>
<td>Completed</td>
<td>Time to Clinical Resolution (4 of 5)</td>
</tr>
<tr>
<td>Peramivir</td>
<td>CUHK</td>
<td>Completed</td>
<td>change in influenza RNA load</td>
</tr>
<tr>
<td>Pimodivir</td>
<td>Janssen</td>
<td>Suspended</td>
<td>Day 6 Ordinal scale -Hospital Recovery Scale</td>
</tr>
<tr>
<td>Plasma</td>
<td>NIAID</td>
<td>Completed</td>
<td>Day 7 Ordinal scale</td>
</tr>
<tr>
<td>Plasma</td>
<td>NIAID</td>
<td>Completed</td>
<td>Time to Normalization of Respiratory Status (hypoxia and tachypnea)</td>
</tr>
<tr>
<td>Vis410</td>
<td>Visterra</td>
<td>Completed</td>
<td>Day 7 Ordinal scale</td>
</tr>
<tr>
<td>Zanamivir</td>
<td>GSK</td>
<td>Completed</td>
<td>Time to Clinical Resolution : ( 4 of the 5 vital signs (temp, O2 sat, RR, HR, SBP) or hospital discharge)</td>
</tr>
<tr>
<td>Presatovir</td>
<td>Gilead</td>
<td>Completed</td>
<td>Time-Weighted Average Change in Respiratory Syncytial Viral (RSV) Load From Baseline to Day 5</td>
</tr>
</tbody>
</table>
# National Early Warning Score (NEWS)

<table>
<thead>
<tr>
<th>PHYSIOLOGICAL PARAMETERS</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration Rate</td>
<td>≤8</td>
<td>9 - 11</td>
<td>12 - 20</td>
<td>21 - 24</td>
<td>≥25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen Saturations</td>
<td>≤91</td>
<td>92 - 93</td>
<td>94 - 95</td>
<td>≥96</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Supplemental Oxygen</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>≤35.0</td>
<td>35.1 - 36.0</td>
<td>36.1 - 38.0</td>
<td>38.1 - 39.0</td>
<td>≥39.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP</td>
<td>≤90</td>
<td>91 - 100</td>
<td>101 - 110</td>
<td>111 - 219</td>
<td>≥220</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Rate</td>
<td>≤40</td>
<td>41 - 50</td>
<td>51 - 90</td>
<td>91 - 110</td>
<td>111 - 130</td>
<td>≥131</td>
<td></td>
</tr>
<tr>
<td>Level of Consciousness</td>
<td>A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>V, P, or U</td>
</tr>
</tbody>
</table>

*NOTE: The high NEWS score reflects the highest level of clinical observation and intervention.*
Ordinal Scale: Developed for Flu but Applied to COVID-19

- Ordinal Scale
  - Not hospitalized with resumption of normal activities (1)
  - Not hospitalized, but unable to resume normal activities (2)
  - Hospitalized, not requiring supplemental oxygen (3)
  - Hospitalized, requiring supplemental oxygen (4)
  - Hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation (5)
  - Hospitalized, requiring ECMO, invasive mechanical ventilation, or both (6)
  - Death (7)

Ordinal Scale: Developed for Flu but Applied to COVID-19

- Time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only

Mortality Endpoint

A All Participants (N=6425)

B Invasive Mechanical Ventilation (N=1007)

C Oxygen Only (N=3883)

D No Oxygen Received (N=1535)

Ambulatory Outcomes for COVID-19

• Duration of COVID-19 symptoms (Phase 2)
  o Fever or feeling feverish; cough, shortness of breath or difficulty breathing at rest or with activity; sore throat; body pain or muscle pain/aches; fatigue; headache, chills, nasal obstruction or congestion; nasal discharge (runny nose); nausea or vomiting; and diarrhea
  o Each symptom is scored daily by the participant as absent (score 0), mild (1), moderate (2) or severe (3)

• Duration of viral shedding (Phase 2)

• Cumulative incidence of death from any cause or hospitalization (Phase 3)

• Proportion of participants with new adverse event (AE) ≥ Grade 3 (Phase 3)

• Nonscheduled medical visits (ED, office)

• Other complications

• Objective measures (PFTs)

• Functional status
Ambulatory Outcomes for COVID-19

Daily Symptom Score

Group Discussion

- Endpoints for prophylaxis with monoclonals/antivirals and early treatment
  - Reduced transmission
  - Reduced development of clinically significant infection

- Challenges with current endpoints for COVID-19
  - Can you combine patients requiring O2 with those that do not
  - Ordinal Scale: time to event or fixed time points
  - How to incorporate non-pulmonary events

- Antivirals vs. Immune modulator and timing

- Return to normal activity after recovery – how to capture the data

- What data do we need to inform endpoints

- Role of virology, resistance and biomarkers (Serostatus, Cytokine levels, CRP)

- Next steps
Questions?

Michael G. Ison, MD MS
+1-312-695-4186
mgison@northwestern.edu

Are you a registered organ donor?
I am!