

# **Clinical Trials Endpoints for COVID-19 Studies**

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#### **Endpoints for Influenza in Outpatients**



Northwestern Medicine<sup>\*</sup> Treanor *et al. JAMA*. 2000; 283: 1016-1024. Ison *et al. Lancet Inf Dis.* 2020; 20: 1204-1214.

# Endpoints for Studies of Hospitalized Influenza and RSV

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



#### **National Early Warning Score**

National Early Warning Score (NEWS)\*

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



# 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





Northwestern Medicine<sup>\*</sup> Beigel *et al.* N Eng J Med. 2020: doi.org/10.1056/NEJMoa2007764.

#### **Mortality Endpoint**



Northwestern Medicine<sup>\*</sup> The RECOVERY Collaborative Group. *N Engl J Med*. 2020. DOI: 10.1056/NEJMoa2021436.

# **Ambulatory Outcomes for COVID-19**

- Duration of COVID-19 symptoms (Phase 2)
  - 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
  - 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)  $\geq$  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
  - $_{\circ}~$  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)



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# **Questions?**

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