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History of Changes for Study: NCT04280705

Adaptive COVID-19 Treatment Trial (ACTT)

Latest version (submitted May 6, 2020) on ClinicalTrials.gov

Study Record Versions

Version	A	B	Submitted Date	Changes
1	○	○	February 20, 2020	None (earliest Version on record)
2	○	○	February 21, 2020	Recruitment Status, Study Status, Contacts/Locations and Oversight
3	○	○	February 27, 2020	Study Status and Contacts/Locations
4	○	○	March 3, 2020	Contacts/Locations and Study Status
5	○	○	March 5, 2020	Contacts/Locations and Study Status
6	○	○	March 6, 2020	Contacts/Locations and Study Status
7	○	○	March 12, 2020	Contacts/Locations and Study Status
8	○	○	March 18, 2020	Contacts/Locations and Study Status
9	○	○	March 19, 2020	Contacts/Locations and Study Status
10	◉	○	March 20, 2020	Outcome Measures, Contacts/Locations, Study Design, Study Description, Eligibility, Arms and Interventions, Study Status and Study Identification
11	○	○	March 24, 2020	Contacts/Locations and Study Status
12	○	○	March 24, 2020	Contacts/Locations and Study Status
13	○	○	March 26, 2020	Contacts/Locations and Study Status
14	○	○	April 2, 2020	Contacts/Locations and Study Status
15	○	○	April 16, 2020	Contacts/Locations, Outcome Measures, Arms and Interventions, Study Description, Study Status, Eligibility and Study Design
16	○	◉	April 23, 2020	Contacts/Locations, Study Status, Arms and Interventions and Study Design
17	○	○	April 30, 2020	Conditions and Study Status
18	○	○	May 6, 2020	Contacts/Locations and Study Status

Compare

Comparison Format: ○ Merged ◉ Side-by-Side

- A study version is represented by a row in the table.
- Select two study versions to compare. One each from columns A and B.
- Choose either the "Merged" or "Side-by-Side" comparison format to specify how the two study versions are to be displayed. The Side-by-Side format only applies to the Protocol section of the study.
- Click "Compare" to do the comparison and show the differences.
- Select a version's Submitted Date link to see a rendering of the study for that version.
- The yellow A/B choices in the table indicate the study versions currently compared below. A yellow table row indicates the study version currently being viewed.
- Hover over the "Recruitment Status" to see how the study's recruitment status changed.
- Study edits or deletions are displayed in red.
- Study additions are displayed in *green*.

Scroll up to access the controls

Changes (Side-by-Side) for Study: NCT04280705
March 20, 2020 (v10) -- April 23, 2020 (v16)

Changes in: Outcome Measures, Contacts/Locations, Arms and Interventions, Study Description, Study Status, Eligibility and Study Design

☐ **Show only changed modules**

	March 20, 2020	April 23, 2020
Study Identification		
Unique Protocol ID:	20-0006	20-0006
Brief Title:	Adaptive COVID-19 Treatment Trial (ACTT)	Adaptive COVID-19 Treatment Trial (ACTT)
Official Title:	A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults	A Multicenter, Adaptive, Randomized Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults
Secondary IDs:		
Study Status		
Record Verification:	February 20, 2020	*April 16, 2020*
Overall Status:	Recruiting	Recruiting
Study Start:	February 21, 2020	February 21, 2020
Primary Completion:	April 1, 2023 [Anticipated]	April 1, 2023 [Anticipated]
Study Completion:	April 1, 2023 [Anticipated]	April 1, 2023 [Anticipated]
First Submitted:	February 20, 2020	February 20, 2020
First Submitted that Met QC Criteria:	February 20, 2020	February 20, 2020
First Posted:	February 21, 2020 [Actual]	February 21, 2020 [Actual]
Last Update Submitted that Met QC Criteria:	March 20, 2020	*April 23, 2020*
Last Update Posted:	March 24, 2020 [Actual]	*April 27, 2020* [Actual]
Sponsor/Collaborators		
Sponsor:	National Institute of Allergy and Infectious Diseases (NIAID)	National Institute of Allergy and Infectious Diseases (NIAID)
Responsible Party:	Sponsor	Sponsor
Collaborators:		
Oversight		
U.S. FDA-regulated Drug:	Yes	Yes
U.S. FDA-regulated Device:	No	No
Product Exported from U.S.:	No	No
Data Monitoring:		
Study Description		
Brief Summary:	This study is an adaptive, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of novel therapeutic agents in hospitalized adults diagnosed with COVID-19. The study is a multicenter trial that will be conducted in up to	This study is an adaptive, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of novel therapeutic agents in hospitalized adults diagnosed with COVID-19. The study is a multicenter trial that will be conducted in up to

	approximately 75 sites globally. The study will compare different investigational therapeutic agents to a control arm. There will be interim monitoring to introduce new arms and allow early stopping for futility, efficacy, or safety. If one therapy proves to be efficacious, then this treatment may become the control arm for comparison(s) with new experimental treatment(s). Any such change would be accompanied by an updated sample size. Because background standards of supportive care may evolve/improve over time as more is learned about successful management of COVID-19, comparisons of safety and efficacy will be based on data from concurrently randomized subjects. An independent data and safety monitoring board (DSMB) will actively monitor interim data to make recommendations about early study closure or changes to study arms. Subjects will be assessed daily while hospitalized. Discharged subjects will be asked to attend study visits at Days 15 and 29. All subjects will undergo a series of efficacy, safety, and laboratory assessments. The primary objective of the study is to evaluate the clinical efficacy of different investigational therapeutics relative to the control arm in adults hospitalized with COVID-19.	approximately *100* sites globally. The study will compare different investigational therapeutic agents to a control arm. There will be interim monitoring to introduce new arms and allow early stopping for futility, efficacy, or safety. If one therapy proves to be efficacious, then this treatment may become the control arm for comparison(s) with new experimental treatment(s). Any such change would be accompanied by an updated sample size. Because background standards of supportive care may evolve/improve over time as more is learned about successful management of COVID-19, comparisons of safety and efficacy will be based on data from concurrently randomized subjects. An independent Data and Safety Monitoring Board (DSMB) will actively monitor interim data to make recommendations about early study closure or changes to study arms. To evaluate the clinical efficacy*, as assessed by time to recovery,* of different investigational therapeutics *as compared* to the control arm*.*
Detailed Description:	This study is an adaptive, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of novel therapeutic agents in hospitalized adults diagnosed with COVID-19. The study is a multicenter trial that will be conducted in up to approximately 75 sites globally. The study will compare different investigational therapeutic agents to a control arm. There will be interim monitoring to introduce new arms and allow early stopping for futility, efficacy, or safety. If one therapy proves to be efficacious, then this treatment may become the control arm for comparison(s) with new experimental treatment(s). Any such change would be accompanied by an updated sample size. Because background standards of supportive care may evolve/improve over time as more is learned about successful management of COVID-19, comparisons of safety and efficacy will be based on data from concurrently randomized subjects. An independent data and safety monitoring board (DSMB) will actively monitor interim data to make recommendations about early study closure or changes to study arms. The initial sample size is calculated to be approximately 440 subjects, and if any additional therapeutic arms are added, the sample size will be recalculated. Subjects will be assessed daily while hospitalized. Discharged subjects will be asked to attend study visits at Days 15 and 29. All subjects will undergo a series of efficacy, safety, and laboratory assessments. The primary objective of the study is to evaluate the clinical efficacy of different investigational therapeutics relative to the control arm in adults hospitalized with COVID-19. The secondary objectives of the study are to 1) evaluate the clinical	*This study is an adaptive, randomized, double-blind, placebo-controlled trial to evaluate the safety and efficacy of novel therapeutic agents in hospitalized adults diagnosed with COVID-19. The study is a multicenter trial that will be conducted in up to approximately 100 sites globally. The study will compare different investigational therapeutic agents to a control arm. There will be interim monitoring to introduce new arms and allow early stopping for futility, efficacy, or safety. If one therapy proves to be efficacious, then this treatment may become the control arm for comparison(s) with new experimental treatment(s). Any such change would be accompanied by an updated sample size. Because background standards of supportive care may evolve/improve over time as more is learned about successful management of COVID-19, comparisons of safety and efficacy will be based on data from concurrently randomized subjects. An independent Data and Safety Monitoring Board (DSMB) will actively monitor interim data to make recommendations about early study closure or changes to study arms. The initial sample size is projected to be 572 subjects to achieve 400 subjects with a "recovered" status (per the primary objective). The primary analysis will be based on those subjects enrolled in order to 400 recoveries. An additional analysis of the moderate severity subgroup (those with baseline status of "Hospitalized, requiring supplemental oxygen" or "Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care") is also of public health importance. Hence, enrollment will be permitted until the date of April 20, 2020 to ensure*

efficacy of different investigational therapeutics as compared to the control arm as assessed by clinical severity, hospitalization, and mortality, and 2) evaluate the safety of different investigational therapeutics as compared to the control arm.	*400 recoveries and provide additional data about this important subgroup. With recent enrollment rates, the total sample size may be 600 to over 800.* *Subjects will be assessed daily while hospitalized. If the subjects are discharged from the hospital, they will have a study visit at Days 15, 22, and 29 as an outpatient. For discharged subjects, it is preferred that the Day 15 and 29 visits are in person to obtain safety laboratory tests and OP swab and blood (serum only) samples for secondary research as well as clinical outcome data. However, infection control or other restrictions may limit the ability of the subject to return to the clinic. In this case, Day 15 and 29 visits may be conducted by phone, and only clinical data will be obtained. The Day 22 visit does not have laboratory tests or collection of samples and may also be conducted by phone.* *All subjects will undergo a series of efficacy, safety, and laboratory assessments. Safety laboratory tests and blood (serum and plasma) research samples and oropharyngeal (OP) swabs will be obtained on Days 1 (prior to infusion) and Days 3, 5, 8, and 11 (while hospitalized). OP swabs and blood (serum only) plus safety laboratory tests will be collected on Day 15 and 29 (if the subject attends an in-person visit or are still hospitalized).* *The primary outcome is time to recovery by Day 29. A key secondary outcome evaluates treatment-related improvements in the 8-point ordinal scale at Day 15. As little is known about the clinical course of COVID-19, a pilot study will be used for a blinded sample size reassessment.*

Conditions

Conditions:	Corona Virus Infection	Corona Virus Infection
Keywords:	Adaptive COVID-19 Efficacy Multicenter novel coronavirus Safety	Adaptive COVID-19 Efficacy Multicenter novel coronavirus Safety

Study Design

Study Type:	Interventional	Interventional
Primary Purpose:	Treatment	Treatment
Study Phase:	Phase 3	Phase 3
Interventional Study Model:	Parallel Assignment	Parallel Assignment
Number of Arms:	2	2
Masking:	Double (Participant, Investigator)	Double (Participant, Investigator)
Allocation:	Randomized	Randomized
Enrollment:	440 [Anticipated]	*800* [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator	Placebo

Placebo 200 mg of Remdesivir placebo administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir placebo *while hospitalized* for the duration of the hospitalization up to a 10 days total course. n= 220. *286.*	The supplied matching placebo lyophilized formulation is identical in physical appearance to the active lyophilized formulation and contains the same inactive ingredients. *Alternatively, a placebo of normal saline of equal volume may be given if there are limitations on matching placebo supplies.*
Experimental: Remdesivir 200 mg of Remdesivir administered intravenously on Day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir *while hospitalized* for the duration of the hospitalization up to a 10 days total course. n= 220. *286.*	Drug: Remdesivir Drug Remdesivir is a single diastereomer monophosphoramidate prodrug designed for the intracellular delivery of a modified adenine nucleoside analog GS-441524. In addition to the active ingredient, the lyophilized formulation of Remdesivir contains the following inactive ingredients: water for injection, sulfobutylether beta-cyclodextrin sodium (SBECD), and hydrochloric acid and/or sodium hydroxide.

Outcome Measures

Primary Outcome Measures:

1. Percentage of subjects reporting each severity rating on an 8-point ordinal scale
   The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities.

   [Time Frame: Day 15]

   Time to recovery
   Day of recovery is defined as the first day on which the subject satisfies one of the following three categories from the ordinal scale: 1) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 2) Not hospitalized, limitation on activities and/or requiring home oxygen; 3) Not hospitalized, no limitations on activities.

   [Time Frame: *Day 1 through Day 29*]

Secondary Outcome Measures:

2. Change from baseline in alanine transaminase (ALT)
   Day 1 through Day 29

   Change from baseline in alanine transaminase (ALT)
   Day 1 through Day 29
3. Change from baseline in aspartate transaminase (AST)
   Day 1 through Day 29

   Change from baseline in aspartate transaminase (AST)
   Day 1 through Day 29
4. Change from baseline in creatinine
   Day 1 through Day 29

   Change from baseline in creatinine
   Day 1 through Day 29
5. Change from baseline in glucose
   Day 1 through Day 29

   Change from baseline in glucose
   Day 1 through Day 29
6. Change from baseline in hemoglobin
   Day 1 through Day 29

   Change from baseline in hemoglobin
   Day 1 through Day 29
7. Change from baseline in platelets
   Day 1 through Day 29

   Change from baseline in platelets
   Day 1 through Day 29
8. Change from baseline in prothrombin time (PT)
   Day 1 through Day 29

   Change from baseline in prothrombin time (PT)
   Day 1 through Day 29
9. Change from baseline in total bilirubin
   Day 1 through Day 29

   Change from baseline in total bilirubin
   Day 1 through Day 29
10. Change from baseline in white blood cell count with differential

    Change from baseline in white blood cell count *(WBC)* with differential

Day 1 through Day 29	Day 1 through Day 29
11. Change in National Early Warning Score (NEWS) from baseline The NEW score has demonstrated an ability to discriminate patients at risk of poor outcomes. This score is based on 7 clinical parameters (respiration rate, oxygen saturation, any supplemental oxygen, temperature, systolic blood pressure, heart rate, level of consciousness). The NEW Score is being used as an efficacy measure. [Time Frame: Day 1 through Day 29]	Change in National Early Warning Score (NEWS) from baseline The NEW score has demonstrated an ability to discriminate patients at risk of poor outcomes. This score is based on 7 clinical parameters (respiration rate, oxygen saturation, any supplemental oxygen, temperature, systolic blood pressure, heart rate, level of consciousness). The NEW Score is being used as an efficacy measure. [Time Frame: Day 1 through Day 29]
12. Clinical status using ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 3 through Day 29]	Clinical status using ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 3 through Day 29]
13. Cumulative incidence of Grade 3 and 4 adverse events (AEs) Grade 3 AEs are defined as events that interrupt usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention. Severe events are usually incapacitating. Grade 4 AEs are defined as events that are potentially life threatening. [Time Frame: Day 1 through Day 29]	Cumulative incidence of Grade 3 and 4 *clinical and/or laboratory* adverse events (AEs) Grade 3 AEs are defined as events that interrupt usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention. Severe events are usually incapacitating. Grade 4 AEs are defined as events that are potentially life threatening. [Time Frame: Day 1 through Day 29]
14. Cumulative incidence of serious adverse events (SAEs) An SAE is defined as an AE or suspected adverse reaction is considered serious is, in the view of either the investigator or the sponsor, if results in death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. [Time Frame: Day 1 through Day 29]	Cumulative incidence of serious adverse events (SAEs) An SAE is defined as an AE or suspected adverse reaction is considered serious *if*, in the view of either the investigator or the sponsor, *it* results in death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. [Time Frame: Day 1 through Day 29]
15. Discontinuation or temporary suspension of infusions For any reason. [Time Frame: Day 1 through Day 29]	Discontinuation or temporary suspension of *investigational therapeutics* For any reason. [Time Frame: Day 1 through Day *10*]

16. Duration of hospitalization Measured in days. [Time Frame: Day 1 through Day 29]	Duration of hospitalization Measured in days. [Time Frame: Day 1 through Day 29]
17. Duration of new non-invasive ventilation or high flow oxygen use [Time Frame: Day 1 through Day 29]	Duration of new non-invasive ventilation or high flow oxygen use *Measured in days.* [Time Frame: Day 1 through Day 29]
18. Duration of new oxygen use [Time Frame: Day 1 through Day 29]	Duration of new oxygen use *Measured in days.* [Time Frame: Day 1 through Day 29]
19. Duration of new ventilator or extracorporeal membrane oxygenation (ECMO) use [Time Frame: Day 1 through Day 29]	Duration of new ventilator or extracorporeal membrane oxygenation (ECMO) use *Measured in days.* [Time Frame: Day 1 through Day 29]
20. Incidence of new non-invasive ventilation or high flow oxygen use Day 1 through Day 29	Incidence of new non-invasive ventilation or high flow oxygen use Day 1 through Day 29
21. Incidence of new oxygen use Day 1 through Day 29	Incidence of new oxygen use Day 1 through Day 29
22. Incidence of new ventilator or extracorporeal membrane oxygenation (ECMO) use Day 1 through Day 29	Incidence of new ventilator or extracorporeal membrane oxygenation (ECMO) use Day 1 through Day 29
23. Mean change in the ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 1 through Day 29]	Mean change in the ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 1 through Day 29]
24. Number of non-invasive ventilation/high flow oxygen free days Day 1 to Day 29	
25. Number of oxygenation free days [Time Frame: Day 1 to Day 29]	*Percentage of subjects reporting each severity rating on an 8-point ordinal scale* *The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen -*

		requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: *Day 15*]
26.	Subject 14-day mortality Date and cause of death (if applicable). [Time Frame: Day 1 through Day 15]	Subject 14-day mortality Date and cause of death (if applicable). [Time Frame: Day 1 through Day 15]
27.	Subject 28-day mortality Date and cause of death (if applicable). [Time Frame: Day 1 through Day 29]	Subject *29-* day mortality Date and cause of death (if applicable). [Time Frame: Day 1 through Day 29]
28.	Time to an improvement of one category using an ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 1 through Day 29]	Time to an improvement of one category using an ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 1 through Day 29]
29.	Time to an improvement of two categories using an ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 1 through Day 29]	Time to an improvement of two categories using an ordinal scale The ordinal scale is an assessment of the clinical status at the first assessment of a given study day. The scale is as follows: 1) Death; 2) Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO); 3) Hospitalized, on non-invasive ventilation or high flow oxygen devices; 4) Hospitalized, requiring supplemental oxygen; 5) Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise); 6) Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care; 7) Not hospitalized, limitation on activities and/or requiring home oxygen; 8) Not hospitalized, no limitations on activities. [Time Frame: Day 1 through Day 29]
30.	Time to discharge or to a National Early Warning Score (NEWS) of The NEW score has demonstrated an ability to discriminate patients at risk of poor outcomes. This score is based on 7 clinical parameters (respiration rate, oxygen saturation, any	Time to discharge or to a National Early Warning Score (NEWS) of The NEW score has demonstrated an ability to discriminate patients at risk of poor outcomes. This score is based on 7 clinical parameters (respiration rate, oxygen saturation, any

	supplemental oxygen, temperature, systolic blood pressure, heart rate, level of consciousness). The NEW Score is being used as an efficacy measure. [Time Frame: Day 1 through Day 29]	supplemental oxygen, temperature, systolic blood pressure, heart rate, level of consciousness). The NEW Score is being used as an efficacy measure. [Time Frame: Day 1 through Day 29]
31.	Ventilator/extracorporeal membrane oxygenation (ECMO) free days Day 1 through Day 29	

Eligibility

Minimum Age:	18 Years	18 Years
Maximum Age:	99 Years	99 Years
Sex:	All	All
Gender Based:		
Accepts Healthy Volunteers:	No	No
Criteria:	Inclusion Criteria:	Inclusion Criteria:

1. Admitted to a hospital with symptoms suggestive of COVID-19 infection.
2. Subject (or legally authorized representative) provides written informed consent prior to initiation of any study procedures.
3. Understands and agrees to comply with planned study procedures.
4. Agrees to the collection of oropharyngeal (OP) swabs.
5. Male or non-pregnant female adult > / = 18 years of age at time of enrollment.
6. Has laboratory-confirmed SARS-CoV-2 infection as determined by polymerase chain reaction (PCR) or other commercial or public health assay in any specimen collected < 72 hours prior to randomization.
   Note - 72 hours is not necessarily time from initial diagnosis. If > / = 72 hours since positive PCR, the PCR may be repeated to assess eligibility.
7. Illness of any duration, and at least one of the following:
   - Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR
   - Clinical assessment (evidence of rales/crackles on exam) AND SpO2 < / = 94% on room air, OR
   - Requiring supplemental oxygen, OR
   - Requiring mechanical ventilation.
8. Women of childbearing potential must agree to either abstinence or use at least one primary form of contraception not including hormonal contraception from the time of screening through Day 29.
9. Agrees to not participate in another clinical trial for the treatment of COVID-19 or SARS-CoV-2 through Day 29.

Exclusion Criteria:

1. Admitted to a hospital with symptoms suggestive of COVID-19 infection.
2. Subject (or legally authorized representative) provides informed consent prior to initiation of any study procedures.
3. *Subject (or legally authorized representative)* understands and agrees to comply with planned study procedures.
4. Male or non-pregnant female adult > / = 18 years of age at time of enrollment.
5. *Has laboratory-confirmed SARS-CoV-2 infection as determined by polymerase chain reaction (PCR) or other commercial or public health assay in any specimen, as documented by either or the following:*
   - *PCR positive in sample collected < 72 hours prior to randomization; OR*
   - *PCR positive in sample collected >/= 72 hours prior to randomization, documented inability to obtain a repeat sample (e.g. due to lack of testing supplies, limited testing capacity, results taking >24 hours, etc.) AND progressive disease suggestive of ongoing SARS-CoV-2 infection.*
6. Illness of any duration, and at least one of the following:
   - Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR
   - SpO2 < / = 94% on room air, OR
   - Requiring supplemental oxygen, OR
   - Requiring mechanical ventilation.
7. Women of childbearing potential must agree to either abstinence or use at least one primary form of contraception not including hormonal contraception from the time of screening through Day 29.
8. Agrees to not participate in another clinical trial for the treatment of COVID-19 or SARS-CoV-2

1. Alanine Transaminase (ALT)/Aspartate Transaminase (AST) > 5 times the upper limit of normal.
2. Estimated glomerular filtration rate (eGFR) < 50 or requiring dialysis.
3. Pregnancy or breast feeding.
4. Anticipated transfer to another hospital which is not a study site within 72 hours.
5. Allergy to any study medication.

through Day 29.

Exclusion Criteria:

1. Alanine Transaminase (ALT) *or* Aspartate Transaminase (AST) > 5 times the upper limit of normal.
2. Estimated glomerular filtration rate (eGFR) < *30 ml/min (including patients receiving hemodialysis* or *hemofiltration)*.
3. Pregnancy or breast feeding.
4. Anticipated *discharge from the hospital or* transfer to another hospital which is not a study site within 72 hours.
5. Allergy to any study medication.

Contacts/Locations

Central Contact: John Beigel
Telephone: 13014519881
Email: DMIDClinicalTrials@niaid.nih.gov

20-0006 Central Contact
Telephone: *13017617948*
Email: DMIDClinicalTrials@niaid.nih.gov

Locations:

United States, Alabama

University of Alabama at Birmingham School of Medicine - Infectious Disease
[Not yet recruiting]
Birmingham, Alabama, United States, 35294

United States, Alabama

University of Alabama at Birmingham School of Medicine - Infectious Disease
[Recruiting]
Birmingham, Alabama, United States, *35233*

United States, California

University of California San Diego Health - Jacobs Medical Center
[Not yet recruiting]
La Jolla, California, United States, 29037

United States, California

University of California San Diego Health - Jacobs Medical Center
[Recruiting]
La Jolla, California, United States, 29037

UCLA MedCtr. - Westwood Clinic
[Recruiting]
Los Angeles, California, United States, 90095

University of California Los Angeles Medical Center - Westwood Clinic
[Recruiting]
Los Angeles, California, United States, 90095

U. of California Irvine MedCtr. - InfDis.
[Not yet recruiting]
Orange, California, United States, 92868-3298

University of California Irvine *Medical Center* - *Infectious Disease*
[Recruiting]
Orange, California, United States, 92868-3298

VA Palo Alto Hlth. Care System - InfDis.
[Not yet recruiting]
Palo Alto, California, United States, 94304-1207

VA Palo Alto *Health* Care System - *Infectious Diseases*
[Recruiting]
Palo Alto, California, United States, 94304-1207

Stanford University - Stanford Hospital and Clinics - Pediatrics - Infectious Diseases
[Not yet recruiting]
Palo Alto, California, United States, 94304-1503

Stanford University - Stanford Hospital and Clinics - Pediatrics - Infectious Diseases
[Recruiting]
Palo Alto, California, United States, 94304-1503

University of California Davis Medical Center - Internal Medicine - Infectious Disease
[Recruiting]
Sacramento, California, United States, 95817-1460

University of California Davis Medical Center - Internal Medicine - Infectious Disease
[Recruiting]
Sacramento, California, United States, 95817-1460

Naval Medical Center San Diego - Infectious Disease Clinic
[Not yet recruiting]
San Diego, California, United States, 92314

Naval Medical Center San Diego - Infectious Disease Clinic
[Recruiting]
San Diego, California, United States, 92314

University of California San Francisco - Zuckerberg San Francisco General Hospital - Division of HIV, ID, and Global Medicine
[Recruiting]
San Francisco, California, United States, 94110-2859

University of California San Francisco - Zuckerberg San Francisco General Hospital - Division of *Human Immunodeficiency Virus*, *Infectious Disease*, and Global Medicine
[Recruiting]
San Francisco, California, United States, 94110-2859

Cedars Sinai Medical Center
[Recruiting]
West Hollywood, California, United States, 90048-1804

United States, Colorado

Rocky Mountain Regional Veteran Affairs Medical Center - Department of Infectious Diseases
[Recruiting]
Aurora, Colorado, United States, 80045

United States, Colorado

Denver Health Division of Hospital Medicine - Main Campus
[Not yet recruiting]
Denver, Colorado, United States, 80204

Denver Health Division of Hospital Medicine - Main Campus
[Recruiting]
Denver, Colorado, United States, 80204

United States, Florida

University of Florida Health - Shands Hospital - Division of Infectious Diseases and Global Medicine
[Recruiting]
Gainesville, Florida, United States, 32610

United States, Georgia

Emory Vaccine Ctr. - The Hope Clinic
[Recruiting]
Decatur, Georgia, United States, 30030-1705

United States, Georgia

Emory Vaccine *Center* - The Hope Clinic
[Recruiting]
Decatur, Georgia, United States, 30030-1705

Atlanta VA Medical Center - Infectious Diseases Clinic
[Not yet recruiting]
Decatur, Georgia, United States, 30033

United States, Illinois

Northwestern Hospital - Infectious Disease
[Not yet recruiting]
Chicago, Illinois, United States, 60611-2908

United States, Illinois

Northwestern Hospital - Infectious Disease
[Recruiting]
Chicago, Illinois, United States, 60611-2908

University of Illinois at Chicago College of Medicine - Division of Infectious Diseases
[Recruiting]
Chicago, Illinois, United States, 60612

United States, Louisiana

Southeast Louisiana Veterans Health Care System (SLVHCS) - Section of Infectious Diseases
[Recruiting]
New Orleans, Louisiana, United States, 70119

United States, Maryland

U. of Maryland Sch. of Med. - Ctr. for Vaccine Dev. - Baltimore
[Not yet recruiting]
Annapolis, Maryland, United States, 21401-1527

United States, Maryland

University of Maryland *School* of *Medicine* - *Center* for Vaccine *Development* - Baltimore
[Recruiting]
Annapolis, Maryland, United States, 21401-1527

Johns Hopkins Hospital - Medicine - Infectious Diseases [Not yet recruiting] Baltimore, Maryland, United States, 21287-0005	Johns Hopkins Hospital - Medicine - Infectious Diseases [Recruiting] Baltimore, Maryland, United States, 21287-0005
	Walter Reed National Military Medical Center [Recruiting] *Bethesda, Maryland, United States, 20889*
NIH - Clinical Ctr., NIAID Lab. Of Immunoregulation, Clinical Research Section [Not yet recruiting] Bethesda, Maryland, United States, 20892-1504	*National Institutes of Health* - Clinical *Center*, *National Institute* of *Allergy and Infectious Diseases Laboratory Of* Immunoregulation, Clinical Research Section [Recruiting] Bethesda, Maryland, United States, 20892-1504
United States, Massachusetts	**United States, Massachusetts**
Massachusetts General Hospital - Infectious Diseases [Recruiting] Boston, Massachusetts, United States, 02114-2621	Massachusetts General Hospital - Infectious Diseases [Recruiting] Boston, Massachusetts, United States, 02114-2621
	University of Massachusetts Medical School - Infectious Diseases and Immunology [Recruiting] *Worcester, Massachusetts, United States, 01655-0002*
United States, Minnesota	**United States, Minnesota**
University of Minnesota Medical Center, Fairview - Infectious Diseases and International Medicine [Recruiting] Minneapolis, Minnesota, United States, 55455-0341	University of Minnesota Medical Center, Fairview - Infectious Diseases and International Medicine [Recruiting] Minneapolis, Minnesota, United States, 55455-0341
United States, Missouri	**United States, Missouri**
Saint Louis U. - Ctr. for Vaccine Development [Not yet recruiting] Saint Louis, Missouri, United States, 63104-1015	Saint Louis *University* - *Center* for Vaccine Development [Recruiting] Saint Louis, Missouri, United States, 63104-1015
United States, Nebraska	**United States, Nebraska**
University of Nebraska Medical Center - Infectious Diseases [Recruiting] Omaha, Nebraska, United States, 68198-5400	University of Nebraska Medical Center - Infectious Diseases [Recruiting] Omaha, Nebraska, United States, 68198-5400
United States, New York	**United States, New York**
Montefiore MedCtr. - InfDis. [Recruiting] Bronx, New York, United States, 10467-2401	Montefiore *Medical Center* - *Infectious Diseases* [Recruiting] Bronx, New York, United States, 10467-2401
New York University School of Medicine - Langone Medical Center - Microbiology - Parasitology [Not yet recruiting] New York, New York, United States, 10016	New York University School of Medicine - Langone Medical Center - Microbiology - Parasitology [Recruiting] New York, New York, United States, 10016-*6402*
U. of Rochester MedCtr. - Vaccine Rsrch. Unit [Not yet recruiting] Rochester, New York, United States, 14642	*University* of Rochester *Medical Center* - Vaccine *Research* Unit [Recruiting] Rochester, New York, United States, 14642-*0001*

United States, North Carolina	**United States, North Carolina**
Duke Human Vaccine Institute - Duke Vaccine and Trials Unit [Not yet recruiting] Durham, North Carolina, United States, 27704	Duke Human Vaccine Institute - Duke Vaccine and Trials Unit [Recruiting] Durham, North Carolina, United States, 27704
	United States, Pennsylvania
	Penn State Health Milton S. Hershey Medical Center - Division of Infectious Diseases *[Recruiting]* *Hershey, Pennsylvania, United States, 17033*
United States, Pennsylvania	
Hosp. of the U. of Pennsylvania - InfDis. [Not yet recruiting] Philadelphia, Pennsylvania, United States, 19104	*Hospital* of the *University* of Pennsylvania - *Infectious Diseases* [Recruiting] Philadelphia, Pennsylvania, United States, 19104-*4238*
	University of Pennsylvania Perelman School of Medicine - Penn Institute for Immunology *[Not yet recruiting]* *Philadelphia, Pennsylvania, United States, 19104-4863*
United States, Tennessee	**United States, Tennessee**
Vanderbilt Univ MC - Inf Dis [Not yet recruiting] Nashville, Tennessee, United States, 37232-0011	Vanderbilt *University Medical Center* - *Infectious Diseases* [Recruiting] Nashville, Tennessee, United States, 37232-0011
United States, Texas	**United States, Texas**
Brooke Army Medical Center [Not yet recruiting] Fort Sam Houston, Texas, United States, 78234	Brooke Army Medical Center [Recruiting] Fort Sam Houston, Texas, United States, 78234
University of Texas Medical Branch - Division of Infectious Disease [Recruiting] Galveston, Texas, United States, 77555-0435	University of Texas Medical Branch - Division of Infectious Disease [Recruiting] Galveston, Texas, United States, 77555-0435
BCM - Micro Virol and Microbio [Not yet recruiting] Houston, Texas, United States, 77030-3411	*Baylor College of Medicine* - *Molecular Virology* and *Microbiology* [Recruiting] Houston, Texas, United States, 77030-3411
	University of Texas Health Science Center at San Antonio - Infectious Diseases *[Recruiting]* *San Antonio, Texas, United States, 78229-3901*
	United States, Virginia
	University of Virginia - Acute Care Surgery *[Recruiting]* *Charlottesville, Virginia, United States, 22908-0816*
United States, Virginia	
Naval Medical Center Portsmouth - Infectious Disease Division [Not yet recruiting] Portsmouth, Virginia, United States, 23708	Naval Medical Center Portsmouth - Infectious Disease Division [Recruiting] Portsmouth, Virginia, United States, 23708

United States, Washington

EvergreenHealth Infectious Disease Service
[Recruiting]
Kirkland, Washington, United States, 98034

The University of Washington - Virology Research Clinic
[Recruiting]
Seattle, Washington, United States, 98104-2433

Providence Sacred Heart Medical Center
[Recruiting]
Spokane, Washington, United States, 99204

Madigan Army Medical Center - Infectious Disease Clinic
[Not yet recruiting]
Tacoma, Washington, United States, 98431

United States, Washington

EvergreenHealth Infectious Disease Service
[Recruiting]
Kirkland, Washington, United States, 98034

The University of Washington - Virology Research Clinic
[Recruiting]
Seattle, Washington, United States, 98104-2433

Providence Sacred Heart Medical Center
[Recruiting]
Spokane, Washington, United States, 99204

Madigan Army Medical Center - Infectious Disease Clinic
[Recruiting]
Tacoma, Washington, United States, 98431

Denmark

University of Copenhagen - Centre of Excellence for Health, Immunity and Infections (CHIP) - Department of Infectious Diseases
[Recruiting]
Copenhagen, Denmark, 2100

Germany, Nordrhein-Westfalen

Universitatsklinikum Bonn, Medizinische Klinik I - Bereich Infektiologie/HIV der Medizinischen Klinik
[Recruiting]
Bonn, Nordrhein-Westfalen, Germany, 53127

Germany

Universitatsklinikum Koeln Klinik I fur Innere Medizin Klinisches Studienzentrum fur Infektiologie I
[Recruiting]
Cologne, Germany, 50937

Universitätsklinikum Frankfurt -Medizinische Klinik II - Infektiologie
[Recruiting]
Frankfurt, Germany, 60590

Greece, Central Macedonia

AHEPA University Hospital - 1st Department of Internal Medicine
[Recruiting]
Thessaloniki, Central Macedonia, Greece, P.O. 54636

Greece

Medical School of Athens University - Evangelismos Hospital - Department of Critical Care and Pulmonary Services
[Recruiting]
Athens, Greece, GR-10675

Japan

National Center for Global Health and Medicine Hospital - Disease Control and Prevention Center
[Not yet recruiting]
Tokyo, Japan, 162-8655

Japan

National Center for Global Health and Medicine Hospital - Disease Control and Prevention Center
[Recruiting]
Tokyo, Japan, 162-8655

Korea, Republic of, Gyeonggi-do

Seoul National University Bundang Hospital - Division of Infectious Diseases
[Recruiting]
Bundang-gu Seongnam-si, Gyeonggi-do, Korea, Republic of, 13620

Korea, Republic of, Jongno-gu

Seoul National University Hospital
[Recruiting]
Seoul, Jongno-gu, Korea, Republic of, 03080

Singapore

National Centre for Infectious Diseases (NCID)
[Recruiting]
Singapore, Singapore, 308442

Korea, Republic of, Gyeonggi-do

Seoul National University Bundang Hospital - Division of Infectious Diseases
[Recruiting]
Bundang-gu Seongnam-si, Gyeonggi-do, Korea, Republic of, 13620

Korea, Republic of, Jongno-gu

Seoul National University Hospital
[Recruiting]
Seoul, Jongno-gu, Korea, Republic of, 03080

Mexico

Instituto Nacional de Ciencias Medicas y Nutrición Salvador Zubirán - Departamento de Infectologia
[Recruiting]
Mexico City, Mexico, 14080

Instituto Nacional de Enfermedades Respiratorias (INER) - Ismael Cosío Villegas
[Recruiting]
Mexico City, Mexico, 14080

Singapore

National University Health System - Division of Infectious Diseases
[Not yet recruiting]
Singapore, Singapore, 119228

Singapore General Hospital - Department of Infectious Diseases
[Not yet recruiting]
Singapore, Singapore, 169608

Singapore

National Centre for Infectious Diseases (NCID)
[Recruiting]
Singapore, Singapore, 308442

Changi General Hospital - Clinical Trials and Research Unit (CTRU)
[Not yet recruiting]
Singapore, Singapore, 529889

Ng Teng Fong General Hospital - Infectious Disease Service
[Not yet recruiting]
Singapore, Singapore, 609606

Khoo Teck Puat Hospital - Clinical Research Unit
[Not yet recruiting]
Singapore, Singapore, 768828

Spain, Cataluña

Hospital Clinic Barcelona, Servicio de Salud Internacional
[Recruiting]
Barcelona, Cataluña, Spain, 08036

Hospital Germans Trias i Pujol - Servei Malalties Infeccioses
[Recruiting]
Barcelona, Cataluña, Spain, 08916

United Kingdom, Brighton

Royal Sussex County Hospital - Department of Intensive Care Medicine
[Recruiting]
East Sussex, Brighton, United Kingdom, BN2 5BE

United Kingdom, London, City Of

Saint Thomas' Hospital - Directorate of Infection
[Recruiting]
London, London, City Of, United Kingdom, SE1 7EH

United Kingdom, Newcastle Upon Tyne

Royal Victoria Infirmary - Department of Infectious Diseases
[Recruiting]
Level 6, Ward 19, Newcastle Upon Tyne, United Kingdom, NE1 4LP

United Kingdom, West Yorkshire

St. James's University Hospital - Infectious Diseases
[Recruiting]
Leeds, West Yorkshire, United Kingdom, LS9 7TK

United Kingdom

John Radcliffe Hospital
[Recruiting]
Headington, Oxford, United Kingdom, OX3 9DU

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