COVID-19 is an emerging, rapidly evolving situation.
Get the latest public health information from CDC: https://www.coronavirus.gov.
Get the latest research information from NIH: https://www.nih.gov/coronavirus.

Adaptive COVID-19 Treatment Trial (ACTT)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04280705

Recruitment Status : Recruiting
First Posted : February 21, 2020
Last Update Posted : April 20, 2020

See Contacts and Locations

Sponsor:
National Institute of Allergy and Infectious Diseases (NIAID)

Information provided by (Responsible Party):
National Institute of Allergy and Infectious Diseases (NIAID)

Study Details Tabular View No Results Posted Disclaimer How to Read a Study Record

Study Description

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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 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.

Condition or disease	Intervention/treatment	Phase
Corona Virus Infection	Other: Placebo Drug: Remdesivir	Phase 3

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 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 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.

Study Design

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Study Type ☐ :	Interventional (Clinical Trial)
Estimated Enrollment ☐ :	572 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Double (Participant, Investigator)
Primary Purpose:	Treatment
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
Actual Study Start Date ☐ :	February 21, 2020
Estimated Primary Completion Date ☐ :	April 1, 2023
Estimated Study Completion Date ☐ :	April 1, 2023

Arms and Interventions

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Arm ☐	Intervention/treatment ☐
Placebo Comparator: Placebo 200 mg of Remdesivir placebo administered intravenously on Day	Other: Placebo The supplied placebo lyophilized formulation is identical in physical

1, followed by a 100 mg once-daily maintenance dose of Remdesivir placebo while hospitalized for up to a 10 days total course. n=286.	appearance to the active lyophilized formulation and contains the same inactive ingredients. Alternatively, a matching placebo of normal saline of equal volume may be given if there are limitations on 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 up to a 10 days total course. n=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

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Primary Outcome Measures ☐ :

1. Time to recovery [Time Frame: Day 1 through Day 29]

   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.

Secondary Outcome Measures ☐ :

1. Change from baseline in alanine transaminase (ALT) [Time Frame: Day 1 through Day 29]
2. Change from baseline in aspartate transaminase (AST) [Time Frame: Day 1 through Day 29]
3. Change from baseline in creatinine [Time Frame: Day 1 through Day 29]
4. Change from baseline in glucose [Time Frame: Day 1 through Day 29]
5. Change from baseline in hemoglobin [Time Frame: Day 1 through Day 29]
6. Change from baseline in platelets [Time Frame: Day 1 through Day 29]
7. Change from baseline in prothrombin time (PT) [Time Frame: Day 1 through Day 29]
8. Change from baseline in total bilirubin [Time Frame: Day 1 through Day 29]
9. Change from baseline in white blood cell count (WBC) with differential [Time Frame: Day 1 through Day 29]
10. Change in National Early Warning Score (NEWS) from baseline [Time Frame: Day 1 through Day 29]

    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.

11. Clinical status using ordinal scale [Time Frame: Day 3 through Day 29]

    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.

12. Cumulative incidence of Grade 3 and 4 clinical and/or laboratory adverse events (AEs) [Time Frame: Day 1 through Day 29]

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.

13. Cumulative incidence of serious adverse events (SAEs) [Time Frame: Day 1 through Day 29]

    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.

14. Discontinuation or temporary suspension of investigational therapeutics [Time Frame: Day 1 through Day 10]

    For any reason.

15. Duration of hospitalization [Time Frame: Day 1 through Day 29]

    Measured in days.

16. Duration of new non-invasive ventilation or high flow oxygen use [Time Frame: Day 1 through Day 29]

    Measured in days.

17. Duration of new oxygen use [Time Frame: Day 1 through Day 29]

    Measured in days.

18. Duration of new ventilator or extracorporeal membrane oxygenation (ECMO) use [Time Frame: Day 1 through Day 29]

    Measured in days.

19. Incidence of new non-invasive ventilation or high flow oxygen use [Time Frame: Day 1 through Day 29]
20. Incidence of new oxygen use [Time Frame: Day 1 through Day 29]
21. Incidence of new ventilator or extracorporeal membrane oxygenation (ECMO) use [Time Frame: Day 1 through Day 29]
22. Mean change in the ordinal scale [Time Frame: Day 1 through Day 29]

    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.

23. Percentage of subjects reporting each severity rating on an 8-point ordinal scale [Time Frame: Day 15]

    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.

24. Subject 14-day mortality [Time Frame: Day 1 through Day 15]

    Date and cause of death (if applicable).

25. Subject 29-day mortality [Time Frame: Day 1 through Day 29]

Date and cause of death (if applicable).

26. Time to an improvement of one category using an ordinal scale [Time Frame: Day 1 through Day 29]

    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.

27. Time to an improvement of two categories using an ordinal scale [Time Frame: Day 1 through Day 29]

    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.

28. Time to discharge or to a National Early Warning Score (NEWS) of </= 2 and maintained for 24 hours, whichever occurs first [Time Frame: Day 1 through Day 29]

    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.

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 99 Years (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion 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 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 and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT04280705***

Contacts

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

Locations

Show 68 study locations

Sponsors and Collaborators

National Institute of Allergy and Infectious Diseases (NIAID)

More Information

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Responsible Party:	National Institute of Allergy and Infectious Diseases (NIAID)
ClinicalTrials.gov Identifier:	NCT04280705 History of Changes
Other Study ID Numbers:	20-0006
First Posted:	February 21, 2020 Key Record Dates
Last Update Posted:	April 20, 2020
Last Verified:	April 8, 2020

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Product Manufactured in and Exported from the U.S.: No

Keywords provided by National Institute of Allergy and Infectious Diseases (NIAID):

- Adaptive
- COVID-19
- Efficacy
- Multicenter
- novel coronavirus
- Safety

Additional relevant MeSH terms:

- Coronavirus Infections
- Severe Acute Respiratory Syndrome
- Virus Diseases
- Coronaviridae Infections
- Nidovirales Infections
- RNA Virus Infections
- Respiratory Tract Infections
- Respiratory Tract Diseases

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