Novel Experimental COVID-19 Therapies Affecting Host Response

Status: Recruiting

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion criteria 1. Hospitalized for COVID-19 2. ≥18 years of age 3. SARS-CoV-2 infection, documented by: 1. a nucleic acid test (NAT) or equivalent testing within 3 days prior to randomization OR 2. documented by NAT or equivalent testing more than 3 days prior to randomization AND progressive disease suggestive of ongoing SARS-CoV-2 infection per the responsible investigator (For non-NAT tests, only those deemed with equivalent specificity to NAT by the protocol team will be allowed. A central list of allowed non- NAT tests is maintained in Appendix E. Appendix E. Non-NAT Tests Deemed with Equivalent Specificity to NAT by the Protocol Team). 4. Hypoxemia, defined as SpO2 <92% on room air, new receipt of supplemental oxygen to maintain SpO2 ≥92%, or increased supplemental oxygen to maintain SpO2 ≥92% for a patient on chronic oxygen therapy 5. Symptoms or signs of acute COVID-19, defined as one or more of the following: 1. cough 2. reported or documented body temperature of 100.4 degrees Fahrenheit or greater 3. shortness of breath 4. chest pain 5. infiltrates on chest imaging (x-ray, CT scan, lung ultrasound) Exclusion criteria 1. Onset of COVID-19 symptom fulfilling inclusion criterion #5 >14 days prior to randomization 2. Hospitalized with hypoxemia (as defined in inclusion #4) for >72 hours prior to randomization (the 72-hour window for randomization begins when the patient first meets the hypoxemia inclusion criteria after hospital admission) 3. Pregnancy 4. Breastfeeding 5. Prisoners 6. End-stage renal disease (ESRD) on dialysis 7. Patient undergoing comfort care measures only such that treatment focuses on end-of-life symptom management over prolongation of life. 8. The treating clinician expects inability to participate in study procedures or participation would not be in the best interests of the patient 9. Known allergy/hypersensitivity to IMP or its excipients The following exclusion criteria differ from the master protocol criteria: TXA127-specific exclusion criteria(4/20/2022 Closed to Accrual): 1. Patient unable to participate or declines participation in the TXA127/Ang(1-7) arm. 2. History of sensitivity (including angioedema) or allergic reaction to medication targeting the RAAS system including study medications or other allergy in the opinion of the investigator that contraindicates participation (not applicable to fostamatinib arm) 3. Hemodynamic instability

•defined as MAP < 65 mmHg at time of randomization confirmed on two measurements 5 minutes apart OR vasopressors at or above norepinephrine equivalent of 0.1 mcg/kg/min in prior 4 hours to maintain MAP > 65 mmHg. 4. Known severe renal artery stenosis. 5. Known significant left ventricular outflow obstruction, such as obstructive hypertrophic cardiomyopathy or severe aortic or mitral stenosis. 6. Randomized in another trial evaluating RAAS modulation in the prior 30 days TRV027-specific exclusion criteria (4/20/2022 Closed to Accrual): 1. Participants on ARBs will be excluded from this study arm. 2. Patient unable to participate or declines participation in the TRV027 arm. 3. History of sensitivity (including angioedema) or allergic reaction to medication targeting the RAAS system including study medications or other allergy in the opinion of the investigator that contraindicates participation (not applicable to fostamatinib arm) 4. Hemodynamic instability

•defined as MAP < 65 mmHg at time of randomization confirmed on two measurements 5 minutes apart OR vasopressors at or above norepinephrine equivalent of 0.1 mcg/kg/min in prior 4 hours to maintain MAP > 65 mmHg. 5. Known severe renal artery stenosis. 6. Known significant left ventricular outflow obstruction, such as obstructive hypertrophic cardiomyopathy or severe aortic or mitral stenosis. 7. Randomized in another trial evaluating RAAS modulation in the prior 30 days Fostamatinib specific exclusion criteria: The following exclusion criteria differ from the master protocol criteria: 1. Randomized in another trial evaluating fostamatinib in the prior 30 days Study arm exclusion criteria measured within 24 hours prior to randomization: 1. AST or ALT ≥ 5 × upper limit of normal (ULN) or ALT or AST ≥ 3 × ULN and total bilirubin ≥ 2 × ULN 2. SBP > 160 mmHg or DBP > 100 mmHg at the time of screening and randomization 3. ANC < 1000/mL 4. Patient is anticipated to require a strong CYP3A inhibitor (Atazanavir, Certinib, Clarithromycin, Cobicistat and cobicistat-containing coformulations, Idelalisib,Indinavir, Itraconazole, Ketoconazole, Levoketoconazole, Lonafarnib, Lopinavir, Mifeprostone, Mibefradil, Nefazodone, Nelfinavir, Ombitasvir-paritaprevir-ritonavir plus dasabuvir, Posaconazole, Ribociclib Ritonavir, Saquinavir, Telithromycin, Troleandomycin, Tucatinib, Voriconazole) from randomization to 21 days post-randomization. For a full list of CYP3A4 substrates, please reference this regularly updated list: https://drug-interactions.medicine.iu.edu/MainTable.aspx. 5. Patient unable to participate or declines participation in the fostamatinib arm.

Conditions & Interventions

Interventions:

Drug: TXA127, Drug: TRV027, Drug: Placebo, Drug: Fostamatinib

Conditions:

COVID-19, SARS-CoV-2 Infection, Coronavirus Infection

Keywords:

COVID-19 drug treatment, RAAS

More Information

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IRB

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