STOP-COVID19 | Superiority Trial Of Protease inhibition in COVID-19

Eligibility

V3 19-10-20

Assessing Eligibility

- Pre-screening eligibility assessments:
  - Routine clinical care
  - Retrospective clinical assessment / medical record review
  - Most recent result - within 72 hours
  - No result available
    - ➢ Post-consent trial staff request / carry out assessment.
- Any exclusion identified = stop screening
    - ➢ Screening log
- Confirm eligibility when all screening results are available
  - Meet all IC & no EC
  - PI / Medic confirm eligibility pre-randomisation
    - ➢ Medical Record PI confirmation

Inclusion criteria (1)

- Male or female
- ≥16 years
- SARS-CoV-2infection (clinically suspected[+] or laboratory confirmed*).
- Admitted to hospital as in-patient
- Illness of any duration, and **at least one of the following**:
    - Radiographic infiltrates (e.g. chest x-ray, CT scan)
    - Rales/crackles on physical examination
    - SpO2 ≤94% on room air pre-randomisation
    - Requiring supplemental oxygen
    - Lymphocyte count <1 x 10^9 cells per L.
- Participant (or legally authorized representative) provides written informed consent
- Able to take oral medication
- Understands & agrees to comply with planned trial procedures

Inclusion criteria (2)

SARS-CoV-2infection (clinically suspected[+] or laboratory confirmed*).

- ***Laboratory-confirmed**: SARS-CoV-2 infection as determined by polymerase chain reaction (PCR), or other commercial or public health assay in any specimen **< 96 hours prior to randomization**.
- [+]**Clinically suspected**: in general, SARS-CoV-2 infection should be suspected when a patient presents with (i) **typical symptoms** (e.g. influenza-like illness with fever and muscle pain, or respiratory illness with cough and shortness of breath); and (ii) **compatible chest X-ray findings** (consolidation or ground-glass shadowing); and (iii) **alternative causes have been considered unlikely or excluded** (e.g. heart failure, influenza). However, the diagnosis remains a clinical one based on the opinion of the managing doctor

Exclusion criteria – Excluded medications

- Itraconazole, ketoconazole, diltiazem, verapamil, phenytoin or rifampicin
- HIV treatments - current treatment with protease/integrase inhibitors or non-nucleoside reverse transcriptase inhibitors*
- *The Liverpool HIV checker (https://www.hiv-druginteractions.org/checker) should be used to check for any HIV drug interactions. Simvastatin could be used as a surrogate for Brensocatib as it metabolised similarly by CYP 3A4 pathway.
- **ensure all medications are checked including different formulations e.g. sustained release and brand names.**

Exclusion criteria

Results within 72 hrs of randomisation (most recent result)

- ALT and/or AST greater than five times upper limit of normal
- History of severe liver disease
- Stage 4 severe CKD(eGFR < 30) or requiring dialysis
- Absolute neutrophil count less than 1.0 x 10^9 cells per L
- Pregnant or breast feeding
- Anticipated transfer to non-trial site hospital within 24hrs
- Allergy to Brensocatib
- Use of any investigational drug within five times of the elimination half-life after the last trial dose or within 30 days, whichever is longer. Co-enrolment with COVID-19 trials is allowed as per co-enrolment agreements and/or individual decision by the CI.

Co-enrolment (1)

- Co-enrolment into COVID-19 CTIMPs will be described in individual agreements between STOP-COVID19 and other trials.
- Where agreements are not in place for specific trials the site should contact the CI and co-enrolment will be decided on an individual participant basis. This decision will be documented in the participant's medical record.
- Co-enrolment into COVID-19 non-CTIMP intervention trials will be allowed.
- Co-enrolment to other non-COVID-19 Clinical Trials of Investigational Medicinal Product (CTIMPs) will not be allowed.
- Enrolment in observational trials or studies will be allowed.

Co-enrolment (2)

RECOVERY and STOP-COVID19 have agreed that:

- Patients admitted to a hospital participating in both studies can be initially screened for participation in STOP-COVID19.
- If a patient is randomised to STOP-COVID19 they may then be co-enrolled into RECOVERY
- All randomisation options in RECOVERY are available.
- RECOVERY and STOP-COVID19 will work closely together to share information on participating sites, interventions, and co-enrolments.

Pregnancy test & Contraception

- Women of child-bearing potential must be willing to have pregnancy testing prior to trial entry - urine or blood.
- Females of childbearing potential and males must be willing to use a highly effective method of contraception (hormonal or barrier method of birth control; abstinence). Contraception should be continued until at least 30 days after final dose of IMP taken.
- Highly effective contraception examples:
  - combined or progestogen-only hormonal methods associated with inhibition of ovulation
  - IUD
  - IUS
  - bilateral tubal occlusion
  - vasectomy
  - abstinence

Eligibility Questions

- RN discuss with PI
- RN contact STOP-COVID19 Trial Manager
  - Stop-covid19@dundee.ac.uk
  - Escalate to CI
- PI contact CI:
  - Prof James Chalmers