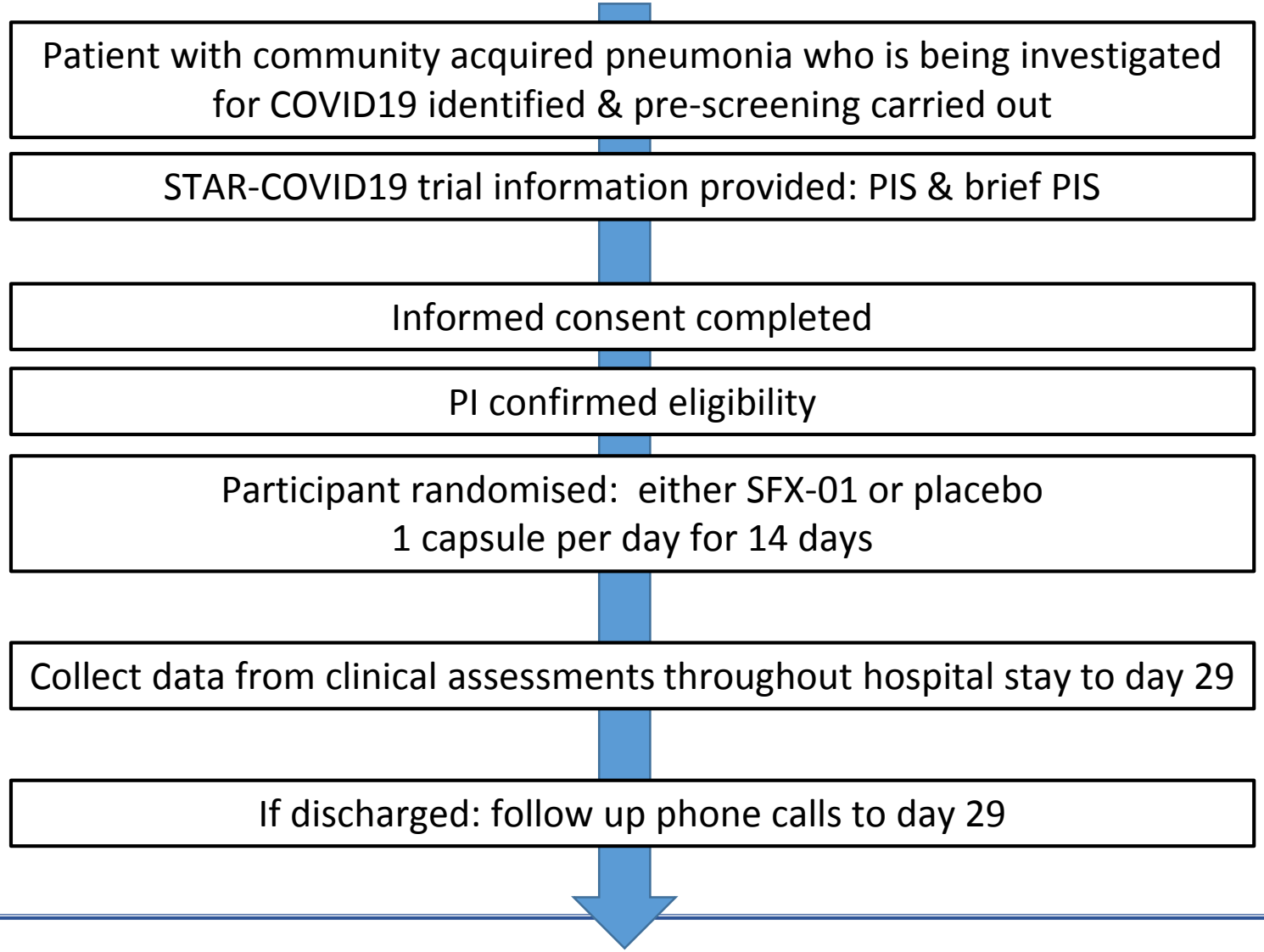
SFX-01 **t**reatment for **Acute Respiratory Infections** (STAR-Covid19)

Participant Pathway

Participant pathway



Pre-screen and participant identification

- Patients with community acquired pneumonia, suspected to be caused by COVID-19 disease
- Patient lists from clinical team
- Check inclusion/exclusion via electronic or paper medical records
- Screening done by a delegated & named member of the trial team

Assessing Eligibility

- Eligibility slides provide detailed information
- Likely that assessments to determine eligibility will be carried out by the clinical team/routine care.
- Investigations/assessments carried out within previous 72 hours – use the most recent result
- Where not available research team request/collect samples after obtaining informed consent
- Local lab analysis and ranges
- Where any result/finding is outwith inclusion/exclusion criteria the participant is not eligible and will not be randomised.
- Eligibility must be confirmed by a delegated medical doctor in the medical record

Screening assessments

- X-ray or computed tomography scan review: Community acquired pneumonia is defined as a new radiographic infiltrate on chest x-ray or CT scan in a patient presenting with respiratory symptoms both of which are clinically evident less than 48 hours after hospitalization.

- CURB65 score calculated using the worst values obtained on admission or in the 24 hours prior to randomization

SYMPTOM	**POINTS**
C= confusion (Abbreviated mental test score less than 8 or clinically diagnosed delirium),	1
U= blood urea greater than7mmol/L	1
R= respiratory rate greater than 30 breaths/min	1
B= blood pressure, systolic less than 90mmHg and/or diastolic blood pressure less than 60mmHg	1
Age greater than or equal to **65** years	1

Screening assessment

- Tested for suspected SARS-CoV-2 infection via RT-PCR or another approved laboratory method.
  For the avoidance of doubt, this trial permits inclusion of patients presenting with acute respiratory infections whether or not the test for SARS-CoV-2 is positive. Patients can be randomised to the study while awaiting the results of the test for SARS-CoV-2
- Focused medical history, taken from medical records, including the following information:
  - Approximate day of onset of respiratory symptoms
  - History of chronic medical conditions related to inclusion and exclusion criteria
  - Medication allergies (SFX-01)
  - Review concomitant medications and therapies for this current illness
- Physical examination findings
- PaO2/FiO2 ratio
- Obtain blood for screening laboratory evaluations if not done in the preceding 72 hours:
  - ALT and/or AST
  - Creatinine
  - eGFR
- Pregnancy test for women of child bearing potential (blood or urine)

Informed Consent

- Informed consent slides provide detailed information about the consent process, including for adults who lack capacity to consent for themselves
- Informed consent should be carried out by delegated staff who are experienced in obtaining consent for CTMP trials
- The consent process is face to face and requires adequate PPE and adherence to local infection control policies
- Participants will be given the PIS and the brief PIS before being given time to consider their participation
- Due to the urgency of beginning treatment patients may have less than 24 hours to decide
- Patients can give optional consent to future research on their data and stored samples

Confirmation of eligibility

Eligibility will be confirmed once all screening results are available.

- Patients are ineligible and will not be randomised if:
- Any result/finding is out-with inclusion/exclusion criteria
- They are likely to be transferred within 24 hours to another hospital which is not a trial site
- They have used an investigational drug within a period equal to 5 times the elimination half life of the drug, or 30 days whichever is longer. Record screening assessment in medical record and enter into STAR-COVID19 database/eCRF.

Eligibility should be confirmed by a delegated doctor in the medical record PRIOR to randomisation

Recruitment documentation

- **Screening log** – if a participant is found to be ineligible document the first inclusion/exclusion criterion that is failed
- Provide potential participant with a **brief PIS** (or provide legal representative specific brief PIS)
- Also provide **full-length PIS**. There are 4 PIS: participant PIS, PIS for professional legal representative, PIS for personal legal representative and PIS for participant who recovers capacity to consent. There are separate PIS for the Tayside site.
- There are **4 ICF**: for participant, professional legal representative, personal legal representative & participant who recovers capacity
- Eligibility and the consent process must be documented in the **Medical record**
- Consent and randomisation are recorded on the **Enrolment & Randomisation Log**
- **Optional worksheets** can be used to collect data from the medical record. Source data remains the medical record and worksheets will not be audited or monitored
- Data taken from the medical record will be entered into the **electronic CRF**. This should be done within 7 days of the final assessment

Baseline (pre-treatment) assessments

It is likely that these clinical assessments will be carried out by the clinical team.

- Vital signs:
  - Blood pressure and pulse (lying or seated)
  - Tympanic temperature
  - SpO_2
  - Record if SpO_2 measured on air or what O_2 concentration the patient was receiving
- Clinical status (7 point ordinal scale)
- NEWS score

Baseline (pre-treatment) assessments

Research assessments for exploratory objectives – must be carried out POST-consent.

- Nasal/throat swabs or sputum – stored at site at -80°C. This should be taken at baseline but can be taken up to 72 hours later

TAYSIDE ONLY

- Blood taken for exploratory studies

Randomisation

The Randomisation slides detail the randomisation process.

- Participants will be randomized immediately following confirmation of eligibility
- TRuST online randomisation system will be used
- The date and time of randomisation should be recorded in the medical record
- GP letter should be sent to the patient's GP

Intervention

The trial is double blinded

- Participants will receive one capsule per day (300mg SFX-01 or placebo) in addition to standard of care treatment
- IMP should be given up to 2 hours after food
- 14 day course of treatment
- IMP should be refrigerated (2-8°C)
- If patient is discharged within 14 days they will be given the tablets to take at home

IMP issue

- Clinical Trials Pharmacy will issue IMP to research team member
- Research team member will ensure that IMP is available for dosing
- Clinical team responsible for IMP storage from receipt until Day 14/discharge
- IMP will be stored securely within the clinical area as per local policy and procedure
- Storage will be 2-8°C
- Prescription chart completion by clinician
- Daily IMP administration recorded by clinical staff

Dosing

- Day of first dose = **Day 1**
- One capsule to be taken daily, up to 2 hours after food
- Capsule should be swallowed whole with water
- If NG tube: open the capsule, dissolve contents in 20mL water, use syringe to push through NGT, flush with 10 mL water (or saline), and clamp NGT for 30 mins.
- Missed doses should be given within 12 hours of the missed dose
- Maximum duration of treatment is 14 days. If a dose is missed the treatment duration will not be extended

Daily assessments while in hospital 1

Clinical Support Status 7-point score; worst score that day to be recorded retrospectively.

1. Not hospitalised, no limitations on activities
2. Not hospitalised, limitation on activities
3. Hospitalised, not requiring supplemental oxygen
4. Hospitalised, requiring supplemental oxygen
5. Hospitalised, on non-invasive ventilation or high flow oxygen devices
6. Hospitalised, on invasive mechanical ventilation or ECMO
7. Death.

If discharged, telephone call assessment on Days 3, 5, 8, 11, 15 and 29

Daily assessments while in hospital 2

NEWS2 score

1. Evaluated from assessments; closest to 8AM
2. Record total score; maximum 20

Physiological parameter	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9-11	12-20		21-24	≥25
SpO_2 Scale 1 (%)	≤91	92-93	94-95	≥96			
Air or Oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Pulse (per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Conciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

Daily assessments while in hospital 3

- Record Concomitant medications
- Record supplemental oxygen and requirement for mechanical ventilation
- Record adverse events
- Collect results of any local laboratory tests done locally to infection – this can be collected at any timepoint while the patient is in hospital

Further assessments while hospitalised

DAY 3

- Record results of blood tests done by the clinical team for clinically indicated reasons
    - full blood count
    - urea and electrolytes
    - liver function tests

If these tests not done on Day 3 (not clinically indicated), results of tests done within a window of +/- 2 days are acceptable

Further assessments while hospitalised TAYSIDE ONLY

IN TAYSIDE ONLY

DAY 8 & DAY 15

- Research blood samples taken. Must be taken within a window +/- 2 days

DAY 15

- Record results of blood tests done by the clinical team for clinically indicated reasons
    - full blood count
    - urea and electrolytes
    - liver function tests

If these tests not done on Day 3 (not clinically indicated), results of tests done within a window of +/- 2 days are acceptable

Assessments once discharged from hospital

Once discharged participants should be given a participant diary and asked to record any adverse events.

DAY 3, 5, 8, 11, 15, 29

- Participant telephoned
    - record concomitant medications
    - record clinical status on analogue scale
    - record adverse events

If the team are unable to contact the participant on the designated day, e.g. it falls at the weekend, the research team will contact them afterwards and record the data retrospectively.

Assessments once discharged from hospital TAYSIDE ONLY

In Tayside discharged participants will be invited to attend the hospital for the Day 15 visit.

- collect blood for safety blood assessment (full blood count, urea and electrolytes, liver function tests)
- collect blood for research exploratory assessments
- record concomitant medications
- record clinical status on analogue scale
- record adverse events

A window of +/- days is acceptable for blood samples. If patient cannot attend the hospital e.g. due to COVID restrictions or because they are not well enough, the visit will be a telephone call. Reasonable travel expenses will be met for hospital visits

Drug return and compliance check

- Day 15 on telephone or in person (Tayside)
- Participants asked how many tablets remaining, record in eCRF
- If there are any tablets remaining these should be mailed back to the research team (or taken in person if attending hospital).