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Identifying candidates for early respiratory failure treatment based on Interleukin-6 levels

Submission date
07/10/2025

Recruitment status
Recruiting

Registration date
09/10/2025

Overall study status
Ongoing

Last Edited
09/10/2025

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute hypoxemic respiratory failure (AHRF) occurs when the lungs are unable to absorb enough oxygen. The bloodstream is deprived of oxygen which can eventually lead to more severe conditions like multiorgan failure (MOF) and death. AHRF accounts for over 30% of patients to critical care units, so new treatments are sorely needed. Research has shown that blood levels of the inflammatory biomarker Interlukin-6 (IL-6) may be a reliable marker for predicting which patients with AHRF will progress into requiring intensive care unit (ICU) admission, MOF, and eventually death. Il-6 levels were shown to reliably peak several days before MOF, ICU admission, and death. Identifying patients before their peak IL-6 levels may therefore provide us with a window to administer a new treatment to prevent the patient's condition from worsening. The aim of this study is to test the feasibility of a treatment strategy for AHRF based on IL-6 measurement in patients who are admitted to hospital care with AHRF.

Who can participate?
Patients aged 18 years and over who arrive at the emergency department with respiratory symptoms and are admitted to inpatient care

What does the study involve?
Patients will have their plasma IL-6 levels measured over 2 days. Patients with elevated IL-6 levels will be randomly allocated into one of three treatment groups: standard of care only, standard of care plus a single IV infusion of tocilizumab, or standard of care plus treatment with oral dexamethasone for 10 days. Patients will then be observed till discharge or up to 28 days, and a follow-up phone interview will be conducted 6 months of the end of the observation period.

What are the possible benefits and risks of participating?
Potential benefits to the study include the possibility of improved health outcomes, and contributing to research that may benefit others in the future. Potential risks include the burden undergoing study assessments outside of those needed for standard treatment, and the potential side effects of the study medication.

Where is the study run from?
University Health Network (Canada)

When is the study starting and how long is it expected to run for?
May 2024 to February 2027

Who is funding the study?
UHN AMO Innovation Fund (Canada)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
296418

Study information

Scientific Title
Interleukin-6 guided treatment with dexamethasone or tocilizumab in patients hospitalized with acute respiratory symptoms - a feasibility study (IDENTIFY)

Acronym
IDENTIFY

Study objectives
The hypothesis is that in adult hospital inpatients with acute hypoxemic respiratory failure (AHRF) and elevated interleukin-6 (IL-6) levels, early immunomodulatory treatment with dexamethasone or tocilizumab may reduce progression of disease. This proposed pilot feasibility trial aims to investigate the feasibility of an IL-6 based predictive enrichment strategy to initiate treatment with dexamethasone or tocilizumab in inpatients with respiratory symptoms and elevated IL-6.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 24/06/2025, University Health Network Research Ethics Board (700 University Ave, 4th Floor, Toronto, ON, M5G 1Z5, Canada; +1 (0)416 581 7849; reb@uhn.ca), ref: 25-5269

Study design
Single-centre Phase II randomized controlled pilot feasibility study

Primary study design
Interventional

Study type(s)

Other, Treatment

Health condition(s) or problem(s) studied
Acute hypoxemic respiratory failure

Interventions
Patient's blood IL-6 levels will be measured at 2 timepoints, with samples taken 24-48 hours apart. Patients will be monitored for 28 days, or until discharge from hospital, and data will be gathered from their medical charts.

Patients with elevated IL-6 levels will be randomized in a 1:1:1 ratio into one of three study arms. The three study arms are Control, tocilizumab, and dexamethasone. Patients will be randomized via a web-based, allocation-concealed randomization with random block sizes (accessible 24 hours per day).

Patients in the control arm will receive on routine care for their specific condition, and no study intervention.

Patients in the tocilizumab arm will receive a single intravenous (IV) infusion of tocilizumab, in addition to the routine for their specific condition. Tocilizumab will be infused over 1 hour, at a dosage of 4 mg per kg of body weight, up to a maximum dose of 400 mg.

Patients in the dexamethasone arm will receive dexamethasone orally or through an equivalent access, in addition to the routine for their specific condition. Dexamethasone will be given in tablet form at a dosage of 6 mg per day, for up to 10 days. Dexamethasone will be discontinued if the patient is discharged from the hospital.

A follow-up interview assessing patient's health-related quality of life will be conducted at 6 months from the end of the 28-day observation period, or hospital discharge (whichever comes first).

Intervention Type
Mixed

Primary outcome(s)
1. Participant recruitment measured using the number of enrolled participants at study closeout.
2. Feasibility of daily IL-6 measurements measured using the number of participants who successfully completed daily IL-6 measurements at study closeout.
3. Proportion of patients meeting eligibility criteria and not randomized measured using number of eligible patients randomized compared to the number of eligible patients not randomized at study closeout.
4. Compliance with the treatment protocol measured using the number of patients who completed the study treatment a outline in the protocol and the amount of associated protocol deviations at study closeout.
5. Time from hospital admission to randomization measured for each randomized patient study closeout.

Key secondary outcome(s))
1. All-cause 28-day mortality measured at the end of the 28-day observation period.
2. SOFA score increase of greater than or equal to 2, or death over the 28-day observation period.

3. Development of ARDS or death recorded at the end of the 28-day observation period.
4. ICU admission or death recorded at the end of the 28-day observation period.
5. Hospital length of stay recorded at the end of the 28-day observation period.
6. ICU length of stay recorded at the end of the 28-day observation period.
7. Need for invasive mechanical ventilation or death at the end of the 28-day observation period.
8. Duration of invasive mechanical ventilation occurring from the time of enrollment to the end of the 28-day observation period.
9. Health-related quality of life measured using the 36-Item Short Form Survey (SF-36) at 6 months following the 28-day observation period or hospital discharge
10. Survival at 6 months following the 28-day observation period or hospital discharge.
11. Complications of steroids or tocilizumab measured using the number of adverse events of special interest (AESI) related to the study intervention during the 28-day observation period . These AESIs include:
11.1. Hypersensitivity or allergic reaction to tocilizumab
11.2. Nosocomial infections
11.3. Neuromuscular weakness
11.4. Gastrointestinal perforations
11.5. Hypernatremia (serum sodium >150 mmol/L)
11.6. Hyperglycemia (requiring new insulin or increased insulin dose)
11.7. Hepatic dysfunction
11.8. Demyelinating disorders
11.9. Myocardial infarction or acute coronary syndrome
11.10. Malignancies
11.11. Stroke
11.12. New delirium
11.13. Neuromuscular weakness
11.14. Clinically significant gastrointestinal bleeding (requiring transfusion or endoscopy)
11.15. Fetal and infant harm
11.16. Death

Completion date
26/02/2027

Eligibility

Key inclusion criteria
1. Age >18 years
2. New onset or worsening of respiratory symptoms (cough, dyspnea, and/or requirement of oxygen supplementation) in the past 14 days
3. Requirement for inpatient hospital management

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 years

Sex
All

Key exclusion criteria
1. Inability to provide informed consent
2. Patients with known contraindications to dexamethasone or tocilizumab, or any of their components
3. Allergic reaction to tocilizumab or other monoclonal antibodies
4. Patients who are using azathioprine or cyclophosphamide
5. Active tuberculosis infection
6. Patients who have active hepatic disease or hepatic impairment
7. ALT or AST >3x upper limit of normal
8. Neutrophil count <1000/mcl
9. Platelet count <50,000/mm3
10. Hemoglobin (Hb) below 8.5 g/dL
11. White blood cell count (WBC) below 3000/mm3
12. Absolute Neutrophil Count (ANC) below 2.0 x 109/L
13. Absolute lymphocyte count below 500/mm3
14. Total bilirubin above ULN
15. Triglycerides (TG) above 10 mmol/L (above 900 mg/dL)
16. Serum creatinine above 1.4 mg/dL in female patients and above 1.6 mg/dL in male patients
17. Patients already receiving systemic steroids, monoclonal antibodies or other immunosuppressive medications at the time of presentation
18. Inability to comply with the regulations to avoid conception within 28 days after enrollment
19. Admission to ICU prior to randomization
20. Immediate need for intubation
21. Imminent death
22. Clinical team refusal
23. Participation in other drug clinical trials (this criterion will be discussed with the PI)
24. Reaching >72 h since hospital admission
25. Pregnancy (positive pregnancy test) or breastfeeding (which is a contraindication to tocilizumab)

Date of first enrolment
13/10/2025

Date of final enrolment
13/10/2026

Locations

Countries of recruitment
Canada

Study participating centre
Toronto General Hospital
200 Elizabeth Street

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Sponsor information

Organisation
University Health Network

ROR
https://ror.org/042xt5161

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Mount Sinai Hospital

Funder Name
University Health Network

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date