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Compassionate use of tocilizumab in hantavirus pulmonary syndrome: a pre- and post-study

Submission date	Recruitment status	[ ] Prospectively registered
14/05/2024	Recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
26/06/2024	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
26/06/2024	Respiratory	[ ] Record updated in last year

Plain English summary of protocol
Background and study aims
Hantavirus Pulmonary Syndrome (HPS) is a severe and sometimes fatal respiratory disease caused by infection with hantavirus. Current treatments are primarily supportive, and there is a need for more effective therapies. This study investigates whether tocilizumab, a drug used to reduce inflammation in other diseases, can improve survival rates in patients with HPS.

Who can participate?
Adults aged 18 years or older who have been diagnosed with Hantavirus Pulmonary Syndrome and are admitted to the hospital

What does the study involve?
Participants will receive a single dose of tocilizumab administered intravenously (through a vein) within the first 24 hours of their hospital admission. Their health will be monitored closely throughout their hospital stay to observe the effectiveness and safety of the treatment.

What are the possible benefits and risks of participating?
The potential benefit of participating in this study is the possible reduced risk of death from HPS. The risks include side effects related to tocilizumab, such as possible allergic reactions and increased susceptibility to infections. All participants will receive standard medical care for HPS in addition to the study treatment.

Where is the study run from?
Hospital Zonal Bariloche "Ramón Carrillo" (Argentina)

When is the study starting and how long is it expected to run for?
February 2024 to August 2029

Who is funding the study?
1. Hospital Zonal Bariloche "Ramón Carrillo" (Argentina)
2. Rio Negro National University (Argentina)

Who is the main contact?
Dr Fernando Tortosa, fgtortosa@unrn.edu.ar

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
TOCIHPS2024

Study information

Scientific Title
A pre- and post-intervention study to assess the efficacy of tocilizumab in reducing mortality in hantavirus pulmonary syndrome

Acronym
HPS-TOCI-Reduction

Study objectives
The hypothesis of this study is that the administration of tocilizumab will reduce the mortality rate among patients with Hantavirus Pulmonary Syndrome (HPS) by 25% compared to the historical mortality rate without this treatment.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 07/05/2024, Comisión ética de Evaluación de Protocolos de Estudios de Investigación en Salud Humana de la Provincia de Río Negro (CEEPISH) (Viedma, Rio Negro, Viedma, 8400, Argentina; +54 (0)92944578364; investigacionrionegro@gmail.com), ref: 185470-S-2024

Study design
Pre-post intervention study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hantavirus pulmonary syndrome

Interventions
In this pre-post intervention study, all participants diagnosed with Hantavirus Pulmonary Syndrome (HPS) receive tocilizumab in addition to standard care. The study assesses the mortality rate before and after the intervention, comparing historical mortality data from patients with similar demographic and clinical profiles who did not receive tocilizumab. Tocilizumab is administered as a single intravenous dose of 8 mg/kg, up to a maximum of 800 mg, within the first 24 hours of hospital admission. The primary outcome measure is the mortality rate at 28 days post-intervention. The study is conducted in a hospital setting, ensuring that all participants are monitored for safety and efficacy outcomes.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Tocilizumab

Primary outcome(s)
Mortality measured using medical records at 28 days post-intervention

Key secondary outcome(s))
1. Incidence of mechanical ventilation measured using medical records at the time of hospital admission, daily during hospital stay, and at discharge
2. Duration of mechanical ventilation, measured using medical records from the initiation to the cessation of mechanical ventilation during the hospital stay
3. Incidence of inotropic support measured using medical records at the time of hospital admission, daily during hospital stay, and at discharge

Completion date
31/08/2029

Eligibility

Key inclusion criteria
1. Diagnosis confirmation: participants must be clinically diagnosed with Hantavirus Pulmonary Syndrome. Diagnosis should be confirmed through one or more of the following:
1.1. Detection of hantavirus-specific IgM antibodies in serum.
1.2. A four-fold rise in hantavirus-specific IgG antibody titers in paired serum samples.
1.3. Positive RT-PCR test for hantavirus RNA in blood or tissue samples.
2. Age: participants must be aged 18 years or older. This age criterion ensures that all participants can legally consent to the study and are within the adult age range most commonly affected by HPS.
3. Severity of condition: participants must be exhibiting symptoms severe enough to require hospitalization, ensuring the study targets those most likely to benefit from tocilizumab treatment.
4. Ability to provide informed consent: participants must be capable of giving informed consent or have a legal guardian who can consent on their behalf if they are incapacitated.
5. Treatment window: participants must be eligible to receive the study intervention (tocilizumab) within 24 hours of hospital admission to ensure the treatment is administered in a timely manner, which is critical for its potential efficacy.
6. Health status: participants must have no known allergies to tocilizumab or its excipients.
7. No severe co-morbid conditions that could interfere with the study outcomes or significantly increase the risk of adverse effects from tocilizumab, such as severe chronic liver disease, known active tuberculosis, or other severe active infections.
8. No prior treatment: participants must not have received tocilizumab or other investigational treatments for HPS before enrollment in this study to ensure that any observed effects can be attributed to the study drug.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Key exclusion criteria
1. Previous treatment with tocilizumab or related therapies: participants who have previously received tocilizumab or other monoclonal antibodies targeting IL-6 or IL-6 receptors for any condition.
2. Severe allergic reactions: individuals with a history of severe allergic reactions to tocilizumab

or any of its excipients.
3. Active or latent infections: participants with active, severe infections at the time of screening, such as tuberculosis, HIV, or hepatitis.
4. Individuals with a known history of chronic or recurrent infections.
5. Pregnancy or lactation: pregnant or breastfeeding women due to the unknown effects of tocilizumab on fetuses or infants.
6. Severe comorbid conditions: individuals with uncontrolled cardiovascular, liver, renal, or metabolic diseases that could complicate treatment outcomes.
7. Patients with a known history of gastrointestinal perforation within the last 6 months.
8. Recent vaccinations: participants who have received live vaccines within 30 days prior to the intended start of treatment.
9. Participation in other clinical trials: individuals currently participating in another clinical trial or who have participated in a clinical trial involving an investigational product within the last 30 days.
10. Substance abuse: current or recent (within the last year) history of significant alcohol or drug abuse that could interfere with adherence to study protocols.
11. Immunosuppression: patients with conditions or on treatments that significantly suppress immune function, such as chemotherapy or high-dose corticosteroids.
12. Psychiatric illness: individuals with psychiatric illnesses or conditions that could interfere with their ability to understand or comply with the requirements of the study.

Date of first enrolment
01/06/2024

Date of final enrolment
31/12/2028

Locations

Countries of recruitment
Argentina

Chile

Study participating centre
Hospital Zonal Bariloche "Ramón Carrillo"
Moreno 601
San Carlos de Bariloche
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Sponsor information

Organisation
Ministerio de Salud de Rio Negro

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
"Ramon Carrillo" Bariloche Hospital

Funder Name
Rio Negro National University

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study will be stored in a publicly available repository to ensure transparency and accessibility.

The datasets will also be available upon request from qualified researchers to facilitate further research and validation of the findings.
Contact name and email address: Dr Fernando Tortosa fgtortosa@unrn.edu.ar

Datasets generated during the study will be published as a supplement to the results publication to provide comprehensive access to the research data.

Future data-sharing plans are not finalized at this stage. The details will be established based on the study's progression and outcomes and will be made available at a later date.

Type of Data: The study will collect clinical data, treatment outcomes, and adverse event reports related to the use of tocilizumab in treating Hantavirus Pulmonary Syndrome.
Timing of Data Availability: Data will be available after the completion of the study and publication of the main results, expected to be around the end of 2028.
Access Criteria: Data will be accessible to researchers who provide a methodologically sound proposal that is approved by an independent review committee associated with the data repository.
Data Sharing Mechanism: Interested researchers will be required to sign a data access agreement to ensure the confidentiality and proper use of the data.
Consent for Data Sharing: Participants will be informed about the data sharing plan, and their consent will include permission to share de-identified data with external researchers under controlled conditions.
Ethical Considerations and Legal Compliance:

All data sharing will comply with ethical standards, legal requirements, and guidelines set forth by regulatory bodies. Data will be anonymized or de-identified to protect participant privacy.

IPD sharing plan summary

Stored in publicly available repository, Available on request, Published as a supplement to the results publication