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Using oxygen-deprived red blood cells to treat burns and blood cancers at Haukeland University Hospital

Submission date 24/01/2025	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 18/03/2025	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 26/03/2025	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Anaemia results from either the acquired loss of red blood cells due to disease, injury, or surgery or the inability of the patient to produce their own red blood cells due inherited disorders. Substantial evidence suggests decreased quality of red blood cells from substances that accumulate during red blood cell storage. Hypoxic storage, where the oxygen content is reduced to low levels, has been indicated by data from in vitro and pre-clinical studies to improve red blood cell quality. The use of hypoxic red blood cells for blood transfusion may result in improved outcomes, both in acute and chronic transfusion settings. It could lead to improved oxygen delivery and contribute to a decrease in the required number of red blood cell transfusions and decreased risk of iron overload. Furthermore, hypoxic blood may improve recovery in burn patients.
The Hemanext ONE system can be used to manufacture and store hypoxic red blood cells in special blood bags that do not allow any oxygen into the blood. Thus, the cells are not damaged during storage. This investigation aims to study safety of hypoxic red blood cells in 2 patient groups: acute burn and haematologic malignancies.

Who can participate?
Male and female adult patients (at least 18 years) with acute burn or haematologic malignancies, who require transfusion of red blood cells.

What does the study involve?
The study involves transfusion of two units of hypoxic red blood cells manufactured with the Hemanext ONE System. Patients will be enrolled, transfused and followed-up until their subsequent transfusion or 28 days (+/- 1 day) after transfusion, whichever comes first. There are 5 scheduled visits during the study including physical examination, vital signs and blood samples.

What are the possible benefits and risks of participating?
There are no clear immediate benefits to participate in this study, but preclinical data support the hypothesis that hypoxic blood has the potential to be of benefit to patients suffering from hematological malignancies. The results of the study may eventually lead to improved

transfusion treatment of patients with hematological malignancies. There are no clear disadvantages to participating in the study. No further risk is expected with the transfusion of Hemanext ONE System beyond what is already known with blood transfusion in general, including:
• Transfusion-associated graft versus host disease
• Transfusion-related acute lung injury (TRALI)
• Post transfusion purpura
• Transfusion-associated circulatory overload (TACO)
• Transfusion-transmitted infection (TTI)
• Allergic reaction
• Transfusion-associated dyspnea (TAD)
• Febrile non-hemolytic transfusion reaction (FNHTR)
• Hypotensive transfusion reaction
• Delayed hemolytic transfusion reaction (DHTR)
• Delayed serologic transfusion reaction (DSTR)
• Acute hemolytic transfusion reaction (AHTR)
• Major cardiac event (MCE)
• Haematoma (bruise)
• Arterial puncture
• Delayed bleeding (re-bleeding)
• Nerve injury/irritation
• Localized infection/inflammation
• Deep venous thrombosis (DVT)
• Arteriovenous fistula
• Compartment syndrome
• Brachial artery pseudoaneurysm
• Vasovagal reactions

Where is the study run from?
The study is run from Haukeland University Hospital, Bergen, Norway.

When is the study starting and how long is it expected to run for?
February 2022 to May 2024

Who is funding the study?
The study is funded by Hemanext Inc. (USA), the company that produces the blood bags.

Who is the main contact?
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Contact information

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ClinicalTrials.gov (NCT)
NCT05549232

Protocol serial number
PRO-CLIN-0012

Study information

Scientific Title
A single center, pilot clinical investigation of surgical bleeding in burn patients, and chronically transfused patients with haematological malignancies, who are transfused with hypoxic red blood cells manufactured with Hemanext ONE system

Study objectives
Anaemia results from either the acquired loss of red blood cells (RBCs) due to disease, injury, or surgery or the inability of the patient to produce their own RBCs due inherited disorders. The primary therapeutic goal of RBC transfusion is to increase the oxygen-carrying capacity of the blood and prevent tissue hypoxia. Substantial evidence suggests decreased quality of RBCs from substances that accumulate during RBC storage.
Hypoxic storage, where the oxygen content of RBC units is reduced to low levels (e.g., less than 20% oxy-haemoglobin prior to refrigeration and maintained throughout storage), has been indicated by data from in vitro and pre-clinical studies to reduce oxidative stress, counteract RBC metabolic impairments, and improve RBC deformability and oxygen delivery. The use of hypoxic RBCs for blood transfusion may result in improved outcomes, both in acute and chronic transfusions settings.
The Hemanext ONE system can be used to manufacture and store hypoxic RBCs for any patient requiring a blood transfusion. It received its CE Mark in April 2021. The Post Market Clinical Evaluation Plan for Hemanext ONE requires collection of safety and efficacy data for the device.

This pilot investigation was conducted to begin to inform on the safety of the blood product resulting from processing leukocyte reduced RBCs with the device.
The investigation aimed to study safety of hypoxic RBCs in 2 patient groups: acute burn and haematologic malignancies. Burn patients undergoing surgical excision routinely require large quantities of blood to be transfused. Patients with haematological malignancies often require regular transfusions.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 27/06/2022, REK sør-øst B (Regional Ethics Committee South East B) (Gullhaugveien 1-3, Oslo, 0484, Norway; +4722845511; rek-sorost@medisin.uio.no), ref: 381996

Study design
Single-center prospective open-label single treatment clinical investigation

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Safety of hypoxic RBCs in 2 patient groups: acute burn and haematologic malignancies.

Interventions
Transfusion of two units of Red Blood Cells, Leukocytes reduced, O2/CO2 reduced (single transfusion course) manufactured with the Hemanext ONE System, combined with PRN standard Red Blood Cells, as applicable. Patients will be enrolled, transfused and followed-up until their subsequent transfusion or 28 days (+/- 1 day) post-transfusion, whichever comes first.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Hemanext ONE

Primary outcome(s)
Adverse events in patients are monitored by investigators during transfusion visit and by phone 24 hours and 7 days (+/- 1) after the transfusion visit.

Key secondary outcome(s))
1. Blood pH, pO2, pCO2, HCO3 and base (excess) is measured by following the standard practice at the site before, during and after the transfusion (Burn patients group only).
2. Haemoglobin level is measured by following the standard practice at the site before the following transfusion.
3. Frequency of all AEs, including transfusion related AEs are monitored by investigators up to 7

days (+/- 1) post-transfusion.
4. AEs are monitored by investigators up to 28 days after the initial transfusion, or up to subsequent transfusion episode, whichever comes first.
5. Frequency of all AEs are monitored, through the assessment of patient's diary, when applicable, from enrolment up to 7 days (+/-1 day) post-transfusion.
6. Vital signs are monitored by investigators over the course of the transfusion and up to 15 minutes post-transfusion.

Completion date
16/05/2024

Eligibility

Key inclusion criteria
A. Hematological malignancies patients group:
1. Male or female patients at least 18 years of age
2. Patients expected to require > 2 units of red blood cells in a single transfusion event
3. Patients who have the capacity to consent to particpate and are willing to comply with the study procedures.
4. Patients identified by a Transfusion hemoglobin trigger of less than 9 g/dL
5. Patients with a documented diagnosis of leukemia, myelomatosis or MDS requiring chronic transfusions

B. Burn patients group:
1. Male or female patients at least 18 years of age
2. Patients who have the capacity to consent by themselves to participate to the clinical investigation
3. Smaller burn patients, hospitalized with a Total Body Surface Area (TBSA%) burn ≥ 10% and ≤ 50%
4. Patients expected to require > 2 unit of red blood cells in a single transfusion event

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
22

Key exclusion criteria

A. Both patients groups:
1. Patients with any positive antibody screening test
2. Patients for whom consent has not been obtained
3. Patients with a known haemolytic anemia (congenital or acquired)
4. Patients < 18 years old
5. Patients with a known or suspected pregnancy
6. Patients with a history of major transfusion reactions
7. Patients whom the Investigator deems clinical trial participation is not in their best interest.

B. Burn patients specific exclusion criteria:
1. Patients who do not have the capacity to consent by themselves to participate to the clinical investigation
2. Patients hospitalized with a Total body surface area (TBSA%) burn more than 50%
3. Patients with combined trauma in need of blood transfusions for treatment other than the burn excision

Date of first enrolment
30/08/2022

Date of final enrolment
16/04/2024

Locations

Countries of recruitment
Norway

Study participating centre
Haukeland University Hospital
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Sponsor information

Organisation
Hemanext Inc.

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request
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IPD sharing plan summary
Available on request