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Treatment of acute liver failure in children with liver cells and support cells suspended in a gel

Submission date 12/02/2025	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol
Registration date 16/07/2025	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 16/07/2025	**Condition category** Digestive System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Acute Liver Failure in children is associated with high mortality without liver transplantation. In addition, donor organ shortage makes it difficult to provide this treatment to every potential patient. Liver transplantation is life-saving but it carries the risk of major surgery and complications from lifelong anti-rejection drugs to suppress the immune system. If bridged across the immediate crisis following acute liver failure, the immense regenerative potential of the liver means that the patient's liver may 're-grow'. This period is very time-sensitive. Unfortunately, if the vital synthetic and detoxification function of the liver is not provided, the patient will often die before the liver can re-grow. Transplantation of liver cells (hepatocytes) can provide this 'bridge' with considerable advantages over whole organ transplantation. Firstly, hepatocytes are derived from donor livers which are otherwise unsuitable for transplantation. Secondly, unlike whole organs, they can be frozen and stored, thus acting as an 'off the shelf' treatment. Thirdly, the technique of hepatocyte transplantation within microbeads coated with alginate (a gel originating from seaweed) and infused into the abdominal cavity is much less invasive than liver transplantation. Finally, the alginate protects the cells against the body's immune system, avoiding the need for immunosuppressive drugs and the associated major risks. Furthermore, preclinical work in King's College Hospital has shown that the addition of support cells called mesenchymal stromal cells (MSCs), can significantly improve the ability of hepatocytes to survive and function within the alginate microbead. The HELP trial is a phase I/II safety and tolerability study of infusion of HMB002 (an optimal combination of hepatocytes and mesenchymal stromal cells put together in peptide-alginate microbeads) into paediatric patients with acute liver failure. This novel cellular therapy may act as a bridge treatment to liver transplant or lead to regeneration of the native liver. The trial aims to evaluate the safety, biological activity and tolerability of transplantation of a single dose of microbeads made from the optimum combination of peptide-alginate, mesenchymal stromal cells (MSCs) and hepatocytes in paediatric patients with acute liver failure.

Who can participate?

Infants and children under the age of 16 years old with acute liver failure.

What does the study involve?

Enrolled participants will have pre-infusion checks and monitoring in the paediatric high

dependency unit (HDU) or Paediatric intensive care unit (PICU), as this degree of monitoring will be required for children with acute liver failure.
Following successful pre-infusion checks, the HMB002 solution containing beads will be infused manually into the peritoneal cavity under ultrasound guidance, as a single infusion or several infusions, dependent on body weight.
Participants will be continuously monitored before and for at least 24 hours after infusion in PICU/HDU. Once clinical condition permits and after 24 hours post infusion they will be monitored in the paediatric wards. Participants will undergo daily examination until Day 7 while still an inpatient, and then be followed up at weeks 2, 4, 8, 12, 16, 24 and 52. Participants will be discharged following a liver organ transplant or upon recovery of their native liver.

Participants will also be followed up annually (at a minimum) for another 9 years after HMB0002 infusion for monitoring of long-term safety, and aligned with routine care.

What are the possible benefits and risks of participating?
The benefits to the participants in the study are currently unknown. Although our earlier experience with similar microbeads (made from liver cells without any mesenchymal stromal cells) has shown promising results, it is unknown how effective this treatment will be in children with acute liver failure. It is hoped that the study may provide a bridging therapy for children awaiting a liver transplant and/or an alternative treatment for those children who may not be eligible for a transplant.

Possible risks from HMB0002 microbead infusion include allergic reaction, fever, increased intrabdominal pressure, bleeding and infection at the site of infusion. These complications will be managed with careful monitoring within the pediatric intensive care setting.

Where is the study run from?
King’s College Hospital NHS Trust, UK

When study is the starting and how long is it expected to run for?
March 2022 to September 2037 (including long-term safety follow-up)

Who is funding the study?
Medical Research Council, UK

Who is the main contact?
Prof Anil Dhawan, anil.dhawan@kcl.ac.uk
Dr Barath Jagadisan, barath.jagadisan@nhs.net

Contact information

Type(s)
Public

Contact name
Prof Anil Dhawan

ORCID ID
https://orcid.org/0000-0002-4942-0845

Contact details

Hepatocyte Biology and Transplantation Group, Institute of Liver Studies, 3rd floor Cheyne Wing, King's College Hospital, Bessemer Road
London
United Kingdom
SE5 9PJ
+44 (0)203 2994408
anil.dhawan@kcl.ac.uk

Type(s)
Public

Contact name
Dr Barath Jagadisan

ORCID ID
https://orcid.org/0000-0002-2108-9054

Contact details
Hepatocyte Biology and Transplantation Group, Institute of Liver Studies, 3rd floor Cheyne Wing, King's College Hospital, Bessemer Road
London
United Kingdom
SE5 9PJ
-
barath.jagadisan@nhs.net

Type(s)
Scientific

Contact name
Dr Celine Filippi

ORCID ID
https://orcid.org/0000-0002-4679-3275

Contact details
Hepatocyte Biology and Transplantation Group, Institute of Liver Studies, 3rd floor Cheyne Wing, King's College Hospital, Bessemer Road
London
United Kingdom
SE5 9PJ
+44 (0)2032993137
celine.filippi@kcl.ac.uk

Additional identifiers

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2019-000316-29

IRAS number

199623

ClinicalTrials.gov number
NCT05491135

Secondary identifying numbers
CPMS 52663, Medical Research Council (MRC) grant code MR/V038583/1

Study information

Scientific Title
Hepatocytes co-Encapsulated with mesenchymal stromal cells in alginate microbeads for the treatment of acute Liver failure in Paediatric patients (HELP)

Acronym
HELP

Study objectives
The main hypothesis of the proposed study is that co-encapsulation of hepatocytes with MSCs, in alginate microbeads which allow the appropriate cell anchorage, will substantially improve the survival and function of hepatocytes and be a feasible, safe and effective form of cellular therapy for paediatric acute liver failure.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/06/2022, London – West London & GTAC Research Ethics Committee (The Old Chapel Royal Standard Place , Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8098, (0) 2071048075; westlondon.rec@hra.nhs.uk), ref: 22/LO/0292

Study design
Phase I/II open-label single-centre first-in-man study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, Medical and other records

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Hepatocyte transplantation in paediatric acute liver failure

Interventions
This is an open-label, single-centre study first-in-man study. The study will be conducted using the Simon two-stage design. Nine patients will be recruited during stage 1 of the study. Once 9 patients have completed their 24-week visit, the study will stop for futility if only 2 or fewer patients have survived with the native liver. Otherwise, the study will progress to Stage 2 of recruitment, where the trial will continue to enrol a further 8 patients. A total of 17 patients will be recruited into the study (at the end of stages 1 and 2). At the end of the second stage, 7 or more patients out of the 17 enrolled should have survived with the native liver at 24 weeks post HMB002 treatment, to show evidence of the efficacy of this novel hepatocyte transplantation that would support a larger randomised controlled trial.

Following signed informed consent from the parent/legal guardian, the following screening tests and procedures will be undertaken to ensure the patient is eligible to take part in the study (some of these may be part of routine care).
• Medical and Medication History
• Physical examination
• Height and weight monitoring
• Vital signs (body temperature, blood pressure, Pulse rate and Oxygen saturation)
• Urine or serum pregnancy test in females of childbearing potential
• Clinical blood tests and additional research bloods
• Recording of neurological parameters
• Ultrasound of the abdomen
• Quality of Life - Parent and where appropriate patient questionnaires (optional)

Enrolled participants will have pre-infusion checks and monitoring in the paediatric high dependency unit (HDU) or Paediatric intensive care unit (PICU). Children with acute liver failure generally require this degree of monitoring in any case. The child may be intubated and ventilated as part of routine care. This involves ventilation using a machine to help move air into and out of the lungs. If a suitable donor liver becomes available within 12 hours of the planned study treatment, the patient will go on to receive a liver transplant.

Following successful pre-infusion checks, the solution containing beads will be infused manually into the peritoneal cavity with usually a 50ml syringe, as a single infusion or several infusions, to achieve more than 25 million hepatocytes per kilogram of body weight. HMB002 infusion will be done under ultrasound guidance.
• Participants will be continuously monitored before and for at least 24 hours after infusion in PICU/HDU. Some of these tests outlined below will be as per the HDU and PICU standard of care. Once clinical condition permits and after 24 hours post-infusion, the child may be stepped down to the paediatric wards.
o Physical and neurological examination
o Intra-abdominal pressure will be measured using a urinary catheter where possible, at regular intervals both before and after infusion.
o Regular review of the IMP infusion site
o regular Vital signs (body temperature, blood pressure, Pulse rate and Oxygen saturation) • Clinical bloods at regular intervals both pre and post-infusion.
o Additional research bloods
o Recording of ventilator settings and additional supportive therapy given as part of the standard of care • Ultrasound of the abdomen

o Recording of side effects
o Recording of change in medications
• Participants will undergo daily examination until Day 7 while still an inpatient, and then be followed up at weeks 2, 4, 8, 12, 16, 24 and 52. Participants will be discharged following a liver organ transplant or upon recovery of their native liver. Therefore some of the follow-up visits will be done in the outpatient clinics at King's College Hospital. Patients will have some or all of the assessments below at each follow-up visit. Some of these visits will be part of standard routine care.
o Physical and neurological examination
o Height and weight monitoring,
o Monitoring of Vital signs (body temperature, blood pressure, Pulse rate and Oxygen saturation)
o Clinical Blood tests and additional bloods for research (at some visits; optional)
o Recording of the level of ventilator settings and supportive treatment as given with routine care.
o Recording of side effects
o Recording of changes to Medication
o Parent and where appropriate patient questionnaires at the final visit (optional parents/legal guardian consent
o Ultrasound of the abdomen at specified time points in the protocol.

Microbeads will ideally be removed within 4 weeks of infusion. This will be done at the time of liver transplant or upon recovery of the native liver prior to discharge (using laparoscopy, a small keyhole surgery of the abdomen).

Participants will also be followed up for another 9 years after HMB0002 infusion for monitoring of long-term safety. This will be aligned with routine care and will be conducted annually as a minimum but may be more frequent depending on the clinical condition of the child or young person. Clinical blood tests and abdominal ultrasound data will be collected annually during the long-term follow-up period (years 2 to 5 as per routine care). SAEs (with exceptions) will be collected for the duration of the follow-up period as outlined in the study protocol.

Intervention Type
Biological/Vaccine

Pharmaceutical study type(s)
Therapy

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
HMB002 (co-encapsulated hepatocytes with mesenchymal stromal cells in alginate microbeads)

Primary outcome measure
1. Safety will be measured using data collected on moderate to severe (including life-threatening and death) adverse event occurrences due to the product in the first 52 weeks post-procedure (Baseline to 52 weeks)
2. Tolerability will be measured using data collected on the proportion of initiated infusion

where >80% of the infusion is received by the patient (Day of infusion)
3. Biological activity will be measured using data collected on survival with a native liver at 24 weeks post-treatment (baseline to 24 weeks)

Secondary outcome measures
1. Change in blood marker levels including haematological, biochemical and coagulation measured using standard medical laboratory methods at baseline to 52 weeks post-treatment. This includes changes in full blood count and differentials, INR, APTT, fibrinogen, Serum levels of ALT, AST, Creatine Kinase, Total bilirubin, Conjugated bilirubin, Alkaline phosphatase, Albumin, total protein, serum urea, serum levels of sodium, potassium, chloride, urea, creatinine and plasma Ammonia.
2. Change in Quality of life measures from baseline to week 52 measured using the PedsQLTM Quality of Life Inventory questionnaires for parent and child completed at screening and at week 52 visit
3. Patient survival with a native liver measured using data collected from patient medical records at 52 weeks post-treatment
4. Patient survival with transplanted or native liver measured using data collected from patient medical records at 24 and 52 weeks post-treatment

Overall study start date
01/03/2022

Completion date
30/09/2037

Eligibility

Key inclusion criteria
1. Infant or child (male or female) under 16 years of age at recruitment
2. Written informed consent obtained from a parent / legal guardian
3. Presence of ALF, defined as a multisystemic disorder in which severe impairment of liver function with or without encephalopathy occurs in association with hepatocellular necrosis reflected as synthetic liver failure in a child with no recognised underlying chronic liver disease. Children must fit one of the ALF categories
4. Willing and able to comply with the study visit schedule

Participant type(s)
Patient

Age group
Child

Upper age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 17; UK Sample Size: 17

Key exclusion criteria
1. Severe ascites causing high intra-abdominal pressure and / or respiratory compromise
2. Intra-abdominal sepsis suspected or proven
3. Clinical condition too unstable to tolerate procedure without compromise
4. Proven preexisting allergy or intolerance to alginate on medical history
5. Proven pre-existing allergy to gentamicin on medical history;
6. Intraperitoneal or intra-abdominal malignancy
7. Adhesions or fistulae to anterior abdominal wall
8. Children who weigh in excess of 33kg
9. Pregnant or lactating patients
10. Female patients of childbearing potential who are not willing to use highly effective methods of contraception to prevent pregnancy or abstain from heterosexual activity for 52 weeks post treatment.
11. Male patients who are not willing to use an effective method of contraception (condom, vasectomy, sexual abstinence) for 52 weeks post treatment, when engaging in sexual activity with a female of childbearing potential
12. Participation in concurrent therapeutic trial for ALF
13. Imminent Liver transplantation expected within 12 hours of infusion
14. Total Hepatectomy
15. Dependent on Extracorporeal Membrane Oxygenation (ECMO)
16. Previous liver transplant

Date of first enrolment
01/06/2025

Date of final enrolment
01/09/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Kings College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Sponsor information

Organisation

King's College Hospital NHS Foundation Trust

Sponsor details
Denmark Hill
London
England
United Kingdom
SE5 9RS
+44 (0)2032991980
kch-tr.research@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.kch.nhs.uk/

ROR
https://ror.org/01n0k5m85

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
It is intended that the results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals.

Intention to publish date
31/03/2030

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	version 3.2	25/07/2023	19/02/2025	Yes	No
Protocol file		15/12/2022	19/02/2025	No	No