ISRCTN85274829 https://doi.org/10.1186/ISRCTN85274829

A controlled clinical trial investigating the clinical and cost-effectiveness of early Transjugular Intrahepatic Portosystemic Stent-Shunt (TIPSS) procedure to insert a stent (tube) in the liver to reduce pressure versus endoscopic plus drug therapy in patients with cirrhosis and acute variceal bleeding after initial control of bleeding by variceal band ligation (VBL)

Submission date
15/06/2023

Recruitment status
Recruiting

Registration date
30/06/2023

Overall study status
Ongoing

Last Edited
19/11/2025

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims

Cirrhosis (scarring of the liver) can lead to varices (abnormally enlarged veins) developing in the lower gullet (food pipe) or stomach causing the varices to bleed. Variceal bleeding is a serious complication of liver cirrhosis. The currently accepted treatment for patients who bleed from varices is known as the standard of care (SOC) and includes using an endoscope (a bendy tube incorporating light and a tiny video camera) to tie off an enlarged vein with a rubber ring (variceal banding) or injecting a drug, with a needle, directly into the swollen vein, causing the vein to clot and stop the bleeding. Patients may also be prescribed antibiotics and other drugs like beta-blockers to lower pressure in the enlarged veins to reduce the risk of further bleeding. For some patients, a device called a transjugular intrahepatic portosystemic stent-shunt (TIPSS) is used. The TIPSS procedure involves placing a special small metal tube, roughly 10mm in diameter, inside the liver using a wire passed through a vein in the neck and down through the liver. The procedure is done under sedation or general anaesthetic. TIPSS may be used to treat severe variceal bleeding in an emergency to stop bleeding where SOC has not worked or in patients that are at high risk of bleeding again after satisfactory stabilisation with SOC. This is called “early” TIPSS. The REACT-AVB trial will compare “early” TIPSS with SOC in severe variceal

bleeding patients to see if “early” TIPSS treatment is better than SOC in improving the survival of these patients. It will also compare cost-effectiveness and quality of life for the patients for both treatments. REACT-AVB will be recruiting patients from hospitals throughout the UK.

Who can participate?
Patients, aged 18 years and over who have liver cirrhosis and have been admitted to the hospital with variceal bleeding and have undergone an emergency endoscopy procedure for gastrointestinal bleeding

What does the study involve?
Once the patient has consented they will be randomly selected by a computer to one of the treatment arms. The treatment will continue for at least one year.

During the trial, patients will be seen at 3 separate time points, 6 weeks, 6 and 12 months (these normally coincide with their usual standard appointments) to assess their health. Patients will also be asked, by a research nurse to complete a health questionnaire form, (EQ5D-5L) on three separate occasions.

What are the possible benefits and risks of participating?
Whilst there is no guarantee that there will be any direct benefit to the patient, by taking part in the trial, they may feel empowered knowing that their contribution to the results of the trial should in the future, lead to the best treatment for variceal bleeding in patients with liver cirrhosis.

The TIPSS procedure has been in use for over 30 years and carries few complications. Variceal banding has been used for over 30 years and is generally considered very safe. For further details, please refer to the patient information sheet which can be accessed via the trial website https://www.birmingham.ac.uk/react-avb.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
December 2021 to November 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Mrs Sukhi Sehmi (REACT-AVB Senior Trial Manager), S.sehmi@bham.ac.uk (UK)

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 54613, IRAS 314108/327501

Study information

Scientific Title
Randomised controlled trial of EArly transjugular intrahepatiC porTosystemic stent-shunt in Acute
Variceal Bleeding (REACT-AVB)

Acronym
REACT-AVB

Study objectives
Current study objectives as of 19/11/2025:
Early transjugular intrahepatic portosystemic stent-shunt (TIPSS) within 5 days of acute variceal bleed results in improved transplant-free patient survival when compared with standard of care

Previous study objectives:
Early transjugular intrahepatic portosystemic stent-shunt (TIPSS) within 4 days of acute variceal bleed results in improved transplant-free patient survival when compared with standard of care

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 29/09/2023, Scotland A Ethics Committee (NHS Lothian, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; None available; Manx.Neill@nhslothian.scot.nhs.uk), ref: 23/SS/0050

2. approved 04/07/2023, West Midlands - Coventry & Warwickshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8009; coventryandwarwick.rec@hra.nhs.uk), ref: 23/WM/0085

Study design
Randomized interventional treatment device imaging study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Complications of cirrhosis

Interventions
Cirrhosis (scarring of the liver) can lead to varices (abnormally enlarged veins) developing in the lower gullet (food pipe) or stomach. Variceal bleeding is a serious complication of liver cirrhosis. Patients with variceal bleeding need treatment with one of the following:

• Medicines (beta-blockers which slow down the heart and lower pressure in the enlarged veins, this reduces the risk of further bleeding) and endoscopic treatment (using a bendy tube incorporating light and a tiny video camera to tie off varices with rubber bands or inject a drug) to stop the bleeding and prevent further bleeding. This is known as standard of care (SOC).
• For patients at high risk of bleeding again, an “early” Transjugular Intrahepatic Portosystemic Stent-Shunt (TIPSS) is offered to reduce the risk of further bleeding. The TIPSS procedure involves placing a special small metal tube, roughly 10mm in diameter (about the size of a grain of rice), inside the liver using a wire passed through a vein in the neck and down through the liver. The procedure is done under sedation (you will be sleepy) or general anaesthetic (you will be asleep). The procedure is done with X-ray imaging guidance. There have only been a few clinical trials comparing early TIPSS with SOC in a small number of patients. The results from these trials are not clear as to which patients benefit from early TIPSS and whether it works. Current guidelines recommend further research. Nobody so far has compared early TIPSS with SOC in a large clinical trial and obtained clear results. This trial is being conducted to find out if early TIPSS is better than SOC.

This trial will randomly assign (like flipping a coin) patients to either SOC or early TIPSS to avoid any bias and ensure patients in both treatment groups are well matched and similar. Once the treatment group (either SOC or early TIPSS) is assigned, the participant and research staff will know which treatment have been given. Potential participants with liver cirrhosis and admitted to the hospital with bleeding from varices will be invited to take part and given a patient information sheet to read. The decision to take part in the trial will be entirely voluntary. If a patient decides to participate, the research staff will ask the patient to read and sign the consent form. The signed consent form will stay on record in the participant's trial file and medical records and be available for review by the trial monitors. A copy will also be given to the participant and with their permission, a copy will also be sent to the REACT-AVB Trial Office at the University of Birmingham. During the trial, participants will be asked to confirm their willingness to continue in the trial. If they decide not to take part, their normal treatment will not be affected in any way and they will continue to be cared for by your normal care team who will ensure that they receive treatment for bleeding varices.

Where potential participants are critically ill and lack the capacity to consent for themselves because of sedation, infection and delirium, advice will be sought from a consultee (for sites in England, Wales and Northern Ireland) or consent will be sought from a legal representative (for sites in Scotland). When the participant regains capacity during the study, the site will need to confirm ongoing consent at the earliest opportunity. To protect the interest of patients, no trial procedure will take place until advice/consent has been sought.

During the trial, at 3 separate time points (baseline, 6 months, and 12 months), participants will be asked to complete a health questionnaire form, (EQ5D-5L). This may be carried out face-to-face with the research staff or remotely. With permission from the participant, a copy of the completed form will also be sent to the REACT-AVB Trial Office.

All patients who take part in the trial will be seen as usual clinical practice either in the clinic or over the telephone/video conference, every few months to assess well-being and to look for untoward effects. Patients in the early TIPSS group will have an ultrasound to check that the TIPSS is working well on 2-7 days. These patients do not require further endoscopies or beta-blockers. Patients in the SOC group will be prescribed regular beta-blockers and have endoscopies to treat the varices every few weeks to months depending on how well the varices respond to treatment.

The trial will seek to recruit just under 300 patients nationally over 4 years. It includes a 12-month pilot trial to address any problems early. The trial will also compare cost-effectiveness and quality of life for the patients for both treatments. If it is concluded that early TIPSS is more effective in terms of survival, cost, and quality of life than SOC, this could lead to a major change in clinical practice.

Intervention Type
Other

Primary outcome(s)
Transplant-free survival measured using the discharge and follow-up forms at one year (post-randomisation)

Key secondary outcome(s))
Current secondary outcome measures as of 10/07/2023:

1. Transplant-free survival measured using the discharge and follow-up forms at 6 weeks (post-randomisation)
2. Rebleeding* measured using the discharge and follow-up forms (post-randomisation):
2.1. Early (less than or equal to 6 weeks)
2.2. Late (greater than 6 weeks)
3. Serious adverse events (SAE) related to treatment measured using the SAE form (up to 12 months post-randomisation)
4. Other complications of cirrhosis measured using the discharge and follow-up forms (up to 12 months post-randomisation):
4.1. New onset ascites
4.2. New onset encephalopathy
4.3. Spontaneous bacterial peritonitis
4.4. Hepatocellular carcinoma
4.4. Any renal dysfunction
5. Mortality prediction measured using Child-Pugh scoring at 6 and 12 months (post-randomisation)
6. Survival prediction measured using the Model for End-Stage Liver Disease (MELD) scoring at 6 and 12 months (post-randomisation)
7. Health-related quality of life measured using the EuroQol EQ-5D-5L at 6 and 12 months (post-randomisation)
8. Use of healthcare resources, costs and cost-effectiveness based on cost per Quality-Adjusted Life-Year (QALY) estimated measured using the EQ-5D-5L and cost per life year gained at one year, and modelled cost per QALY over a patient lifetime
9. Crossover therapies measured using the discharge and follow-up forms up to 12 months post-randomisation

*Rebleeding is defined as hematemesis and/or melena with either:
1. Endoscopic evidence of variceal bleeding or stigmata of recent haemorrhage and at least a 2 g /L reduction in haemoglobin within 24 hours of admission
2. Massive upper gastrointestinal bleeding leading to death. The definition includes bleeding from banding ulceration.

Previous secondary outcome measures:

1. Transplant-free survival measured using the discharge and follow-up forms at 6 weeks (post-randomisation)
2. Rebleeding* measured using the discharge and follow-up forms (post-randomisation):
2.1. Early (within 6 weeks)
2.2. Late (6 weeks to 1 year)

3. Serious adverse events (SAE) related to treatment measured using the SAE form (up to 12 months post-randomisation)
4. Other complications of cirrhosis measured using the discharge and follow-up forms (up to 12 months post-randomisation):
4.1. New onset ascites
4.2. New onset encephalopathy
4.3. Spontaneous bacterial peritonitis
4.4. Hepatocellular carcinoma.
4.4. Any renal dysfunction
5. Mortality prediction measured using Child-Pugh scoring at 6 and 12 months (post-randomisation)
6. Survival prediction measured using the Model for End-Stage Liver Disease (MELD) scoring at 6 and 12 months (post-randomisation)
7. Health-related quality of life measured using the EuroQol EQ-5D-5L at 6 and 12 months (post-randomisation)
8. Use of healthcare resources, costs and cost-effectiveness based on cost per Quality-Adjusted Life-Year (QALY) estimated measured using the EQ-5D-5L and cost per life year gained at one year, and modelled cost per QALY over a patient lifetime
9. Crossover therapies measured using the discharge and follow-up forms up to 12 months post-randomisation

*Rebleeding is defined as hematemesis and/or melena with either:
1. Endoscopic evidence of variceal bleeding or stigmata of recent haemorrhage and at least a 2 g /L reduction in haemoglobin within 24 hours of admission
2. Massive upper gastrointestinal bleeding leading to death. The definition includes bleeding from banding ulceration.

Completion date
30/11/2027

Eligibility

Key inclusion criteria
1. Liver cirrhosis as defined clinically, radiologically (ultrasound scan (USS) and/or transient elastography) or on histology
2. Acute variceal bleed (oesophageal or gastric) with haemostasis following initial endoscopic therapy
3. Child-Pugh score 7-13
4. Age > = 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Failure to control acute bleeding (as per Baveno 7 criteria) prior to randomisation.
2. Previous portosystemic shunt or TIPSS.
3. Known occlusive portal vein thrombosis precluding TIPSS.
4. Active cancer including hepatocellular carcinoma affecting 1-year survival.
5. Clinically significant encephalopathy causing recurrent hospital admissions.
6. Pregnant or lactating women.
7. Evidence of heart failure refractory to treatment.
8. Severe active septicaemia refractory to treatment.

Date of first enrolment
08/03/2024

Date of final enrolment
30/09/2027

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
England
B15 2GW

Study participating centre

Royal Free Hospital
Pond Street
London
England
NW3 2QG

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Edinburgh
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Scotland
EH16 4SA

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
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G4 0SF

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
Queens Medical Centre
Derby Road
Nottingham
England
NG7 2UH

Study participating centre
The Whittington Hospital
Highgate Hill
London

England
N19 5NF

Study participating centre
Derriford Hospital
Derriford Road
Derriford
Plymouth
England
PL6 8DH

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
Scotland
G51 4TF

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney
Norwich
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NR4 7UY

Study participating centre
Good Hope Hospital
Rectory Road
Sutton Coldfield
England
B75 7RR

Study participating centre
Northern General Hospital
Northern General Hospital NHS Trust
C Floor, Huntsmnan Building
Herries Road
Sheffield
England
S5 7AU

Study participating centre
Heartlands Hospital
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Birmingham
England
B9 5ST

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
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BS10 5NB

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
Cheltenham General Hospital
Sandford Road
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GL53 7AN

Study participating centre
Queen Alexandra Hospital
Southwick Hill Road
Cosham
Portsmouth
England
PO6 3LY

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
England
WV10 0QP

Study participating centre
Northwick Park Hospital
Watford Road
Harrow
England
HA1 3UJ

Study participating centre
University Hospital Aintree
Fazakerley Hospital
Lower Lane
Liverpool
England
L9 7AL

Study participating centre
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Oxford Road
Manchester
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M13 9WL

Study participating centre
Royal Liverpool University Hospital
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Liverpool
England
L7 8XP

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication. The trial data will be entered into a secure trial-specific database and data will not be publicly available prior to publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		22/03/2024	25/03/2024	Yes	No
Protocol file	version 4.0	29/07/2025	19/11/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes