Clinical trial results:
MAcrophage Therapy for Liver Cirrhosis (MATCH)

Summary

EudraCT number	2015-000963-15
Trial protocol	GB
Global end of trial date	24 August 2022

Results information

Result version number	v1 (current)
This version publication date	30 May 2025
First version publication date	30 May 2025
Summary attachment (see zip file)	Autologous macrophage therapy for liver cirrhosis: a phase 2 open-label randomized controlled trial (Autologous macrophage therapy for liver cirrhosis a phase 2 open-label randomized controlled trial.pdf)

Trial information

Trial identification

Sponsor protocol code	MATCH0.1

Additional study identifiers

ISRCTN number	ISRCTN10368050
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Edinburgh/NHS Lothian:ACCORD
Sponsor organisation address	QMRI, 47 Little France Crescent, Edinburgh, United Kingdom, EH16 4TJ
Public contact	Professor Stuart Forbes, University of Edinburgh, +44 0131 651 9500, stuart.forbes@ed.ac.uk
Scientific contact	Professor Stuart Forbes, University of Edinburgh, +44 0131 651 9500, stuart.forbes@ed.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 April 2018
Global end of trial reached?	Yes
Global end of trial date	24 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I (dose escalation study):
The primary objective of this study is to demonstrate safety and the maximum tolerated dose of autologous monocyte derived macrophages in participants with advanced liver cirrhosis.

Phase II (randomised control trial):
The primary objective of the randomised control trial is to demonstrate an improvement in the severity of liver disease over 3 months.

Protection of trial subjects:

The Phase I dose escalation arm was a 3+3 design, progressing to higher dose after safety review of the IDMC. The dose used in the RCT was limited to the maximum achieved dose of 1x10^9, the highest dose tested in the dose escalation phase. To minimise discomfort and reduce the potential for a transfusion reaction during cell infusion 10mg IV Chlorphenamine and 100mg IV Hydrocortisone was administered before pre-hydration with 250mls normal saline. During the SARS CoV2 pandemic additional safety measures were in place to protect participants during study visits.

Background therapy:

Other than standard care, no background therapy was used.

Evidence for comparator:

No comparator was used In the dose escalation phase, in the RCT phase the cell product was compared to standard care as no comparative treatment is available for this patient group.

Actual start date of recruitment	08 August 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	11
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	9
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment opened on the dose escalation phase on 03/08/2016, the last patient in the Phase I dose escalation arm was enrolled 23/03/2017. Recruitment on the RCT arm opened 13/09/2017 recruitment was closed 22/11/2021, once the minimum target of 23 participants in each randomised group had achieved the 3 month primary end point threshold.

Pre-assignment

Screening details:

The study was conducted in two different phases.
After determining the recommended Phase II RCT dose, in the Phase I dose escalation part. Subjects were enrolled in Phase II RCT to estimate the safety and efficacy of autologous monocyte derived macrophages in participants with advanced liver cirrhosis.

Pre-assignment period milestones

Number of subjects started	11
Intermediate milestone: Number of subjects	Dose escalation screening: 11
Number of subjects completed	9

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Failed screening: 2

Period 1

Period 1 title	Phase I Dose Escalation (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase I Dose Escalation 10^7

Arm description:

Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose of up to 10^7

Arm type	Experimental
Investigational medicinal product name	Cell infusion dose 10^7
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose 10^7

Arm title	Phase I Dose Escalation 10^8

Arm description:

Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose of up to 10^8

Arm type	Experimental

Investigational medicinal product name	Cell infusion dose 10^8
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose 10^8

Arm title	Phase I Dose Escalation 10^9

Arm description:

Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose of up to 10^9

Arm type	Experimental
Investigational medicinal product name	Cell infusion dose 10^9
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose 10^9

Number of subjects in period 1[1]	Phase I Dose Escalation 10^7	Phase I Dose Escalation 10^8	Phase I Dose Escalation 10^9
Started	3	3	3
Completed	3	3	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Discrepancies due to participants failing screening

Baseline characteristics

Reporting groups

Reporting group title	Phase I Dose Escalation

Reporting group description: -

Reporting group values	Phase I Dose Escalation	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	8	8	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous			
Age at recruitment			
Units: years			
arithmetic mean	57.6		
standard deviation	± 5.7	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	5	5	
Dominant aetiology of liver disease			
Investigators were directed to indicate the dominant aetiology of liver disease			
Units: Subjects			
Alcoholic liver diease	6	6	
primary biliary cirrhosis	1	1	
non-alcoholic fatty liver disease	1	1	
Previous Hepatitis C	1	1	
cryptogenic cirrhosis		0	
Haemochromotosis		0	

Subject analysis sets

Subject analysis set title	Dose Escalation
Subject analysis set type	Safety analysis

Subject analysis set description:

All recruited participants in the dose escalation phase

Subject analysis set title	Dose Escalation1x10^7
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants in the dose escalation phase allocated to receive 1x10^7

Subject analysis set title	Dose Escalation 1x10^8
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants in the dose escalation phase allocated to receive 1x10^8

Subject analysis set title	Dose Escalation 1x10^9
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants in the dose escalation phase allocated to receive 1x10^9

Reporting group values	Dose Escalation	Dose Escalation1x10^7	Dose Escalation 1x10^8
Number of subjects	11	3	3
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	9	2	3
From 65-84 years	2	1	
85 years and over	0		
Age continuous			
Age at recruitment			
Units: years			
arithmetic mean	58.55	59.3	55.7
standard deviation	± 5.85	± 8.5	± 6.4
Gender categorical Units: Subjects			
Female	4	2	0
Male	7	1	3
Dominant aetiology of liver disease			
Investigators were directed to indicate the dominant aetiology of liver disease			
Units: Subjects			
Alcoholic liver diease	7	2	2
primary biliary cirrhosis	1	1	
non-alcoholic fatty liver disease	2		
Previous Hepatitis C	1		1
cryptogenic cirrhosis	0		
Haemochromotosis	0		

Reporting group values	Dose Escalation 1x10^9		
Number of subjects	3		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	3		
Age continuous			
Age at recruitment			
Units: years arithmetic mean standard deviation	57.7 ± 2.9		
Gender categorical Units: Subjects			
Female Male	2 1		
Dominant aetiology of liver disease			
Investigators were directed to indicate the dominant aetiology of liver disease			
Units: Subjects			
Alcoholic liver diease primary biliary cirrhosis non-alcoholic fatty liver disease Previous Hepatitis C cryptogenic cirrhosis Haemochromotosis	2 1		

End points

End points reporting groups

Reporting group title	Phase I Dose Escalation 10^7
Reporting group description:	
Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose of up to 10^7	
Reporting group title	Phase I Dose Escalation 10^8
Reporting group description:	
Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose of up to 10^8	
Reporting group title	Phase I Dose Escalation 10^9
Reporting group description:	
Given cell infusion of the autologous monocyte derived macrophage product up to a maximum dose of up to 10^9	
Subject analysis set title	Dose Escalation
Subject analysis set type	Safety analysis
Subject analysis set description:	
All recruited participants in the dose escalation phase	
Subject analysis set title	Dose Escalation1x10^7
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants in the dose escalation phase allocated to receive 1x10^7	
Subject analysis set title	Dose Escalation 1x10^8
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants in the dose escalation phase allocated to receive 1x10^8	
Subject analysis set title	Dose Escalation 1x10^9
Subject analysis set type	Safety analysis
Subject analysis set description:	
All participants in the dose escalation phase allocated to receive 1x10^9	

Primary: Macrophage Activation Syndrome

End point title	Macrophage Activation Syndrome[1]
End point description:	
Macrophage Activation Syndrome occurring during the infusion visit	
End point type	Primary
End point timeframe:	
During infusion visit	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative analysis performed, percentage of participants with the primary end point presented

End point values	Dose Escalation1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: Participants				
Present	0	0	0	
Absent	3	3	3	

Statistical analyses

No statistical analyses for this end point

Primary: Dose limiting toxicity

End point title	Dose limiting toxicity[2]

End point description:

Presence of a dose limiting toxicity (as defined in study protocol) from infusion to 14 post-infusion

End point type	Primary

End point timeframe:

From infusion to 14 days post infusion

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative analysis performed, percentage of participants with the primary end point presented

End point values	Dose Escalation1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: Participants				
Presence	0	0	0	
Absence	3	3	3	

Statistical analyses

No statistical analyses for this end point

Primary: Acute transfusion reaction

End point title	Acute transfusion reaction[3]

End point description:

Presence of acute transfusion reactions during the period of infusion

End point type	Primary

End point timeframe:

During infusion

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative analysis performed, percentage of participants with the primary end point presented

End point values	Dose Escalation1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: Participants				
Present - clinically significant	0	0	0	
Present - not clinically significant	1	0	0	
Absent	2	3	3	

Statistical analyses

No statistical analyses for this end point

Primary: Acute transfusion reaction post infusion

End point title	Acute transfusion reaction post infusion[4]

End point description:

Presence of acute transfusion reaction 0 to 2 hours post infusion

End point type	Primary

End point timeframe:

0 to 2 hours post infusion

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparative analysis performed, percentage of participants with the primary end point presented

End point values	Dose Escalation1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: Participant				
Present - clinically significant	0	0	0	
Present - not clinically significant	1	0	0	
Absent	2	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in MELD

End point title	Change in MELD

End point description:

Change in MELD score at 90 days from baseline

End point type	Secondary

End point timeframe:

Baseline to 90 day change in MELD score

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed	9[5]			
Units: score				
arithmetic mean (standard deviation)	-1.12 (± 1.87)			

Notes:

[5] - Figures only available for participants who received infusion

Statistical analyses

No statistical analyses for this end point

Secondary: Change in serum albumin

End point title	Change in serum albumin

End point description:

End point type	Secondary

End point timeframe:

Baseline to 90 day change

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: g dl-1				
arithmetic mean (standard deviation)	-0.20 (± 0.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in UKELD

End point title	Change in UKELD

End point description:

End point type	Secondary

End point timeframe:

Baseline to 90 day change

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: score				
arithmetic mean (standard deviation)	-0.42 (± 2.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in INR

End point title	Change in INR

End point description:

End point type	Secondary

End point timeframe:

Baseline to 90 day change

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: ratio				
arithmetic mean (standard deviation)	-0.04 (± 0.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ELF

End point title	Change in ELF

End point description:

End point type	Secondary

End point timeframe:

Baseline to 90 day change

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: score				
arithmetic mean (standard deviation)	-0.24 (± 0.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PRO-C3M

End point title	Change in PRO-C3M

End point description:

End point type	Secondary

End point timeframe:

Baseline to 90 day change

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: score				
arithmetic mean (standard deviation)	-14.86 (± 14.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in C3M

End point title	Change in C3M

End point description:

End point type	Secondary

End point timeframe:

Baseline to 90 day change

End point values	Dose Escalation			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: score				
arithmetic mean (standard deviation)	-10.95 (± 13.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Transplant free survival

End point title	Transplant free survival

End point description:

End point type	Secondary

End point timeframe:

Baseline to one year follow-up

End point values	Dose Escalation1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	3	3	3	
Units: participants				
Alive, transplant free	3	3	3	
Dead or transplanted	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
consent to 12 month follow up	
Adverse event reporting additional description:	
participants were asked to report adverse events that may have occurred since the previous visit, at every visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20

Reporting groups	
Reporting group title	Dose Escalation 1x10^7
Reporting group description:	
Cell infusion at maximum dose of up to 1x10^7	
Reporting group title	Dose Escalation 1x10^8
Reporting group description:	
Cell infusion at maximum dose of up to 1x10^8	
Reporting group title	Dose Escalation 1x10^9
Reporting group description:	
Cell infusion at maximum dose of up to 1x10^9	

Serious adverse events	Dose Escalation 1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary lesion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea and vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal discomfort			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Dose Escalation 1x10^7	Dose Escalation 1x10^8	Dose Escalation 1x10^9
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
General disorders and administration site conditions			
Fatigue	Additional description: including increase in lethargy		
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	1	3
Malaise			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Right side pressure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sweats			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Vaginal prolapse			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Coryzal illness			

subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Shortness of breath, chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Toe injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
lightheaded			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort	Additional description: This includes, discomfort, cramp or pain		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ademonas Colon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Varices oesophageal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0

Endocrine disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	1	2	2
Musculoskeletal and connective tissue disorders			
Pain			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	4	8	4
Tightness of jaw			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 March 2016	Inclusion criteria changed to include new government guidelines for alcohol intake (14 units per week) for both males and females) Previously government guidance included 21 units per week for men and 14 units for females.
23 May 2017	Hepatitis E virus testing added to the inclusion criteria Changes to the manufacturing process, following evidence that a single change was sufficient for cell growth, the protocol was modified to a one change of media rather than two.
12 August 2017	Blood tests change to include magnesium in baseline investigations
20 November 2017	Addition of the Protein fingerprint Biomarker test to the blood samples from the Dose Escalation Phase Clarification that for the RCT phase participants are required to fast for up to 4 hours prior to visit Clarification that for clinical visits MELD score is determined by the study team using the online calculator adopted by the Scottish Liver Transplant unit.
13 February 2018	Screening for eligibility was modified to allow time for clinical investigations where required, to be concluded prior to determining eligibility. Where possible all information was collected at the same visit however for some participants additional information was required, in such circumstances screening could be conducted up to 30days pre apheresis and the randomisation visit to be conducted 7 days pre apheresis. All patients will have paired MRI scans
18 July 2018	Treatment schedule changed from 3 infusions to 1 for participants allocated to the cell group, consequently the apheresis, infusion and safety visits for infusions two and three were removed from the protocol resulting in the number of visits for treatment group being reduced from 17 to 11 The upper bound for the inclusion criteria of MELD was changed from a maximum of 16 to requiring a maximum of 17.
05 November 2018	Change from a single to multicentre study. With the addition of two study sites in Scotland, both of which are situated in large University Hospitals. Participants were recruited from all three study sites, however apheresis and infusion visits were conducted at the lead study site. Due to logistical requirements only participants recruited at the lead site underwent MRI investigations.
21 May 2020	Addition of SARS-CoV-2 testing for all participants at screening visit and apheresis visit for participants allocated to the treatment group. Additional manufacturing site at Jack Copland Centre, Scottish National Blood Transfusion Service HQ.
31 March 2021	Updates to the Protocol and PIS to ensure 7 days between any vaccination for COVID-19 and apheresis, to reflect the guidance from the United Kingdom Blood Transfusion & Tissue Transplantation Services and the Joint Professional Advisory Committee (JPAC).

10 August 2021	Change in IMP shelf life from 48 to 24hrs based on new Scottish Blood Transfusion stability data, it should be noted that all Autologous Macrophage Cell Products released on the MATCH01 trial were administered within the 24hours.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 March 2017	Recruitment in the Phase I dose escalation arm was completed 23/03/2017, recruitment was then paused to allow the pre planned analysis of the data collected. The randomised control trial opened 13/09/2017 after the IDMC had reviewed the dose escalation data report and agreed progression to the RCT arm of the study.	13 September 2017
20 March 2020	During the SARS-CoV-2 pandemic all study recruitment was halted for a period of four months, however all follow-up visits continued uninterrupted. No participants dropped out of the study or were lost to follow-up during this period.	31 July 2020

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31591593

http://www.ncbi.nlm.nih.gov/pubmed/34750149