



## Clinical trial results:

### Adoptive Immunotherapy with CD25/71 allodepleted donor T cells to improve immunity after unrelated donor stem cell transplant (ICAT)

#### Summary

EudraCT number	2013-000872-14
Trial protocol	GB
Global end of trial date	30 January 2020

#### Results information

Result version number	v1 (current)
This version publication date	02 November 2022
First version publication date	02 November 2022

#### Trial information

##### Trial identification

Sponsor protocol code	UCL/11/0519
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01827579
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Cancer Research UK and UCL Cancer Trials Centre
Sponsor organisation address	90 Tottenham Court Road , London, United Kingdom, W1T 4TJ
Public contact	ATIMP trials group, Cancer Research UK and UCL Cancer Trials Centre, 44 2076799797, ctc.icat@ucl.ac.uk
Scientific contact	ATIMP trials group, Cancer Research UK and UCL Cancer Trials Centre, 44 2076799797, ctc.icat@ucl.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	18 December 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 January 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to determine whether adoptive immunotherapy with CD25/71 allodepleted donor T-cells can be safely used to improve T-cell reconstitution after unrelated donor SCT.

Protection of trial subjects:

Patient safety was monitored through eligibility criteria and regular patient assessments during treatment and follow up as well as regular review of safety data by Independent Data Monitoring Committee (IDMC) and Trial Management Group (TMG).

All adverse events that occurred between Day 30 to Day 120 post-transplant (or after this date if the site investigator felt the event was related to the trial treatment) were recorded in the patient notes and the trial CRFs. Those meeting the definition of a Serious Adverse Event (SAE) were also be reported to UCL CTC.

Background therapy:

All patients underwent 9/10 or 10/10 HLA matched unrelated donor peripheral blood stem cell transplantation with an Alemtuzumab based conditioning regimen as per standard local institutional protocols. Conditioning regimens were either myeloablative or reduced intensity.

Evidence for comparator:

The control group in the ICAT trial received standard of care therapy as well as identical supportive care to the ATIMP arm. The rationale for the use of comparators is as follows:

- The primary end-point is the circulating CD3 count at 4 months post-SCT and this has been compared between the treatment and control cohorts.
- The following secondary efficacy end-points have been compared between the treatment and control cohorts:
  1. Time to recovery of normal T-cell ( $> 700/\text{mkl}$ ) and CD4 ( $> 300/\text{mkl}$ ) counts and normal TCR diversity as assessed by V spectratyping post-SCT
  2. In vitro anti-viral responses of circulating PBMC
  3. TRM and DFS at 1 year post-SCT
- The safety secondary end-point is the incidence of significant (grade II-IV) acute and moderate/severe chronic GVHD. This has been compared between the 2 cohorts.

Actual start date of recruitment	01 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

Notes:

<b>Subjects enrolled per age group</b>	
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)	32
From 65 to 84 years	5
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Between Aug2014-Feb2019, 37 patients were enrolled, 21 patients were treated and included in analysis (control 8, ATIMP 13)

15 were withdrawn before treatment(donor refusal(7), patient unwell(3), developed GVHD(3), ATIMP not manufactured (1)), and 2 patients were replaced as 1withdrew consent and 1 died before reaching primary end point.

### Pre-assignment

Screening details:

History and physical examination including weight

Histological or bone marrow confirmation of haematological malignancy and disease status pre-transplant

Serological testing for HIV, HTLV, Hepatitis B and C, syphilis, EBV and CMV

Pregnancy test, if appropriate

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Active intervention (ATIMP)

Arm description:

Adoptive immunotherapy with allodepleted donor T-cells (ATIMP)

Arm type	Experimental
Investigational medicinal product name	CD25/71 allodepleted donor T-cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous injections of allodepleted donor T-cells at increasing doses (105/kg at day 30 post-SCT [+/- 10 days\*], 3 x 105/kg at day 60 [+/- 10 days\*] and 106/kg at day 90 [+/- 10 days\*]) at monthly intervals post-SCT until either their circulating CD3 count is normal (> 700/L) or they develop acute GVHD >Grade I.

<b>Arm title</b>	Control
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Arm description:

Patients in the control arm received standard of care treatment.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 1</b>	Active intervention (ATIMP)	Control
Started	27	10
Completed	13	8
Not completed	14	2
Developed grade II GVHD	3	-
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	1
Patient declined due to feeling too unwell	1	-
Patient required supplemental oxygen	1	-
Problem with ATIMP manufacture	1	-
Donor refused participation	7	-
Patient too cytopenic	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Active intervention (ATIMP)
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Reporting group description:

Adoptive immunotherapy with allodepleted donor T-cells (ATIMP)

Reporting group title	Control
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Reporting group description:

Patients in the control arm received standard of care treatment.

Reporting group values	Active intervention (ATIMP)	Control	Total
Number of subjects	27	10	37
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	23	9	32
From 65-84 years	4	1	5
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	10	5	15
Male	17	5	22
Disease type			
Type of haematological malignancy patient had when registered into the trial			
Units: Subjects			
ALL	2	0	2
AML	16	2	18
CLL	2	0	2
CML	0	2	2
NHL	4	4	8
HL	0	1	1
Myelodisplasia	3	1	4
Disease status			
Patient disease status at time of registration into the study			
Units: Subjects			
Complete remission	20	4	24
Partial remission	6	2	8
Stable disease	0	2	2
Progressive disease	0	2	2
Not recorded	1	0	1



## End points

### End points reporting groups

Reporting group title	Active intervention (ATIMP)
Reporting group description: Adoptive immunotherapy with allodepleted donor T-cells (ATIMP)	
Reporting group title	Control
Reporting group description: Patients in the control arm received standard of care treatment.	

### Primary: Circulating CD3+ve T cell count at 4 months post-SCT

End point title	Circulating CD3+ve T cell count at 4 months post-SCT
End point description: The primary end-point is the circulating CD3 count at 4 months post-SCT and this will be compared between the treatment and control cohorts. A standardized difference (or difference between two medians) will be estimated, with 95% confidence interval and p-value (compared against the 15% level from the sample size calculation). The results for the primary endpoint of the study (T-cell reconstitution at month 4 post-transplant) are shown in the uploaded ppt 'ICAT_EudraCT_Results_upload' Figure 2A. The mean circulating CD3+ T-cell at month 4 were higher in the ADT cohort (730/ $\mu$ L, range 10-4080) than in the control cohort (212.5/ $\mu$ L, range 10-500). However, data were not normally distributed and non-parametric tests did not show a significant difference in the median T-cell count between both cohorts: 230/ $\mu$ L (range 10-4080) in treatment cohort and 145/ $\mu$ L (range 10-500) in controls (one-sided p=0.18)	
End point type	Primary
End point timeframe: The primary end-point is the circulating CD3 count at 4 months post-SCT	

End point values	Active intervention (ATIMP)	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	8		
Units: cells/microlitre				
median (full range (min-max))	230 (10 to 4080)	145 (10 to 500)		

Attachments (see zip file)	ICAT_EdraCT_Results_Upload_2021_February/ICAT_EudraCT_r
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### Statistical analyses

Statistical analysis title	Data analysis
Statistical analysis description: With an 80% power and one-sided test of statistical significance of 15%, this 2:1 randomised trial required 16 patients in the experimental treatment and 8 in the control to detect a standardized difference of $\geq 0.85$ in the circulating CD3 count at 4 months post-SCT. Statistical analysis in this study was mostly descriptive. Wilcoxon signed-rank test was used to compare	



median values for lymphocyte recovery at 4 months, as data was not normally distributed.

Comparison groups	Active intervention (ATIMP) v Control
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
P-value	≤ 0.15 <sup>[2]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Wilcoxon signed-rank test

Notes:

[1] - Statistical analysis was mostly descriptive.

37 patients were recruited, 16 were withdrawn due to donor refusal (7), GVHD (3), death, consent withdrawal, manufacture problem & clinical decision. Out of the 21 patients, 13 were treated on the ATIMP arm and 8 on the control arm. All 21 patients were evaluable for the primary endpoint (T cell recovery at 4 months postSCT); 18 patients completed the 12 month follow up (3 patients died before 12month: relapse(2) in ATIMP arm; TRM(1) in control arm.

[2] - one-sided p

## Secondary: Time to recovery of normal T-cell

End point title	Time to recovery of normal T-cell
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End point description:

Survival analysis and Kaplan-Meier plot was used to display the time to patients achieve CD3 counts greater than 700.

We observed a trend towards T cell recovery (>700/ $\mu$ L) in the ADT cohort (uploaded ppt 'ICAT\_Figures\_for\_EudraCT\_results\_upload', Figure 2D), though this was not statistically significant: HR= 1.83 (95%CI: 0.52 to 6.41), p=0.35.

End point type	Secondary
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End point timeframe:

Time to recovery of normal CD3 counts at 4, 6 and 12 months post-SCT

End point values	Active intervention (ATIMP)	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	8		
Units: percent				
Month 0	0	0		
Month 4	23	0		
Month 6	39	0		
Month 9	48	13		
Month 12	48	27		

## Statistical analyses

No statistical analyses for this end point

## Secondary: DFS at 1 year post-SCT

End point title	DFS at 1 year post-SCT
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End point description:

DFS will be analysed using Kaplan-Meier curves and Cox regression.

1-year disease-free survival rate was 67.7% in ADT vs 62.5% in controls.

End point type	Secondary
End point timeframe:	
At 1 year	

End point values	Active intervention (ATIMP)	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	8		
Units: percent				
number (not applicable)	67.7	62.5		

### Statistical analyses

No statistical analyses for this end point

### Secondary: TRM at 1 year postSCT

End point title	TRM at 1 year postSCT
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End point description:

Mortality will be analysed using Kaplan-Meier curves and Cox regression.

The one-year overall survival rate for patients treated with allodepleted T cells was 92% compared to 88% in the controls.

A total of 4 deaths were reported in the ADT group and 1 death in the control group.

Three patients died during the 12-month follow-up: 2/13 in the ADT group due to disease progression/relapse and 1/8 controls due to TRM (viral infection). Two further patients died after 12-month follow-up, both in the ADT arm: one due to relapse at 21 months post-transplant and one due to pneumonia at 14 months post-transplant.

End point type	Secondary
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End point timeframe:

At 1 year postSCT

End point values	Active intervention (ATIMP)	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	8		
Units: percent				
number (not applicable)	92	88		

### Statistical analyses

No statistical analyses for this end point

**Secondary: Incidence of grade II-IV acute and chronic GVHD**

End point title	Incidence of grade II-IV acute and chronic GVHD
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End point description:

GVHD and toxicity will be reported in terms of frequencies and percentages by treatment group. (Excel named 'ICAT\_AE\_Dat\_18\_12\_2020 listing all adverse events reported for the study (max grade / number of patients) has been also uploaded with the ICAT results for completeness)

End point type	Secondary
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End point timeframe:

Up to 12months postSCT

End point values	Active intervention (ATIMP)	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	8		
Units: number of patients				
Acute GVHD grade II or higher	7	4		
Acute GVHD grade III	3	2		
Acute GVHD grade IV	0	0		
Chronic GVHD - mild	1	3		
Chronic GVHD - moderate	1	0		
Chronic GVHD - severe	1	0		

<b>Attachments (see zip file)</b>	ICAT_AE_Data_18_12_2020/ICAT_ae data_2020_12_18.xlsx
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**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

GVHD between 1 and 12 months post-transplant.

All other AEs between 1 and 4 months post-transplant

Adverse event reporting additional description:

GVHD and toxicity are reported in terms of frequencies and percentages by treatment group.

The most common AEs (experienced by 5 or more patients) have been entered into the EudraCT database. A complete list of all AEs with frequencies and percentages by treatment group is provided in the upload excel 'ICAT\_AE\_data\_18\_12\_2020'.

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.03
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### Reporting groups

Reporting group title	Active intervention (ATIMP)
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Reporting group description:

Adoptive immunotherapy with allodepleted donor T-cells (ATIMP)

Reporting group title	Control
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Reporting group description:

Patients in the control arm received standard of care treatment.

Serious adverse events	Active intervention (ATIMP)	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	2 / 8 (25.00%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events	0	0	
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haemorrhage into temporal AVM			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Heart failure			

subjects affected / exposed	0 / 13 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 13 (7.69%)	2 / 8 (25.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
GVHD			
subjects affected / exposed	5 / 13 (38.46%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	6 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest			
subjects affected / exposed	1 / 13 (7.69%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

<b>Non-serious adverse events</b>	Active intervention (ATIMP)	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	8 / 8 (100.00%)	
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	7 / 13 (53.85%)	1 / 8 (12.50%)	
occurrences (all)	7	1	
Neutrophil count decreased			
subjects affected / exposed	6 / 13 (46.15%)	2 / 8 (25.00%)	
occurrences (all)	6	2	
White blood cell count decreased			
subjects affected / exposed	6 / 13 (46.15%)	1 / 8 (12.50%)	
occurrences (all)	6	1	
Platelet count decreased			
subjects affected / exposed	4 / 13 (30.77%)	2 / 8 (25.00%)	
occurrences (all)	4	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 13 (23.08%)	3 / 8 (37.50%)	
occurrences (all)	3	3	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 13 (30.77%)	2 / 8 (25.00%)	
occurrences (all)	4	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 13 (23.08%)	2 / 8 (25.00%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 13 (61.54%)	2 / 8 (25.00%)	
occurrences (all)	8	2	
Nausea			
subjects affected / exposed	3 / 13 (23.08%)	2 / 8 (25.00%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 4	1 / 8 (12.50%) 1	
Infections and infestations Infection subjects affected / exposed occurrences (all)	8 / 13 (61.54%) 8	4 / 8 (50.00%) 4	
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 4	1 / 8 (12.50%) 1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2013	<p>Protocol v2.0 19/12/2013</p> <p>Summary of changes:</p> <ul style="list-style-type: none"><li>• Sec on 2.2 Clarification on how the CD25/71 ADTs will be produced from the starting material. Addition of +2/ day flexibility for when infusing the ATIMP in case d30, 60 or 90 fell on a weekend. Change made throughout protocol.</li><li>• Sec on 4 Clarification that only donors for patients randomised to receive the ATIMP will be approached for consent to the trial and confirmation that donors can withdraw up to the point where ADTs are infused into the patient.</li><li>• Sec on 5.2 Clarification that starting material will only be obtained by donors if the patient is randomised to receive the ATIMP.</li><li>• Sec on 7.2.2 Clarification that if the products do not meet the release criteria, the case will be discussed with the CI, CTC, and manufacturer as it may be in the best interest of the patient to infuse the cells.</li><li>• Sec on 7.4 Addition of circulating T cell count &gt;700/<math>\mu</math>l as an inclusion criteria for consistency reasons.</li><li>• Sec on 10.2.2 Clarification that sites must have procedures in place to notify donor collect on centres for a SAR which could be linked to the quality and safety of the donor blood/leucapheresis. Furthermore that the blood collection centre must have systems in place to notify the site of an SAE in a donor which could affect the safety of the patient. This is in line with HTA guidance.</li><li>• Other typographical changes throughout the protocol, addition of CTA number to the title page, removal of full contact details for the statistician, amending figures to state that the starting donor material may be donor leucapheresis/blood, minor changes throughout to ensure the protocol is consistent with the new CTC protocol template.</li></ul>
08 December 2014	<p>Protocol v3.0 25/11/2014</p> <p>Summary of changes:</p> <ul style="list-style-type: none"><li>• Inclusion Criteria changed from patients with 'underlying acute myeloid or acute lymphoblastic leukaemia' to patients with 'underlying haematological malignancy'</li><li>• EBV and CMV serology added to the screening assessments for patients</li><li>• '+/2 working days' changed to '+/7 days' when referring to the infusion schedules (D30, D60 and D90 posttransplant)</li><li>• Clarification that any delays to ATIMP infusion for clinical reasons need to be agreed in advance with the trials office.</li><li>• Addition that surplus ATIMP (CD25/71 ADTs) may be stored at the manufacturing site for use in future ethically approved research related solely to ICAT, following obtaining patient and donor consent.</li><li>• Removal of the list of 'expected adverse events' following allodepleted donor T cell infusion, as they are no longer exempt from SAE reporting.</li></ul>
17 December 2015	<p>Protocol 4.0 17/12/2015</p> <p>NOTE: this amendment was approved by both REC and MHRA but MRC in their role as funder did not approve, therefore this amendment was not implemented at sites and the latest document versions in use before the submission of the amendment remained in use.</p>



04 May 2016	<p>Protocol v5.0 04/05/2016</p> <p>Summary of changes:</p> <ul style="list-style-type: none"> <li>• '+/- 7 days' changed to '+/- 10 days' when referring to the infusion schedules (D30, D60 and D90 posttransplant).</li> <li>• "A minimum of 25 days should be given between consecutive doses to ensure no GVHD has developed" has been added throughout for clarification in light of the above change</li> </ul>
12 December 2016	<p>Protocol v6.0 12/12/2016</p> <p>The trial protocol was amended to clarify that it is not always possible for the laboratory to manufacture enough allodepleted donor T cells for the patient to be able to receive 3 doses of the ATIMP. In such cases, after discussion with the patient, only 1 or 2 doses may be administered (depending on the number of cells manufactured). The last substantial amendment approved by the ethics committee on 04/10/2016 amended the patient information sheet to account for this but it was omitted from the trial protocol in error.</p> <p>The randomisation section was amended to outline that patients on both the ATIMP arm and control arm of the trial should receive a patient contact card to ensure the trial adheres to good clinical practice guidelines for advanced therapies.</p> <p>The statistics section was amended so that the predicted dropout rate has been changed from 35% to 50% and the potential target recruitment total amended from 32 to 50 patients to account for this. This has been done as the dropout rate was greatly underestimated and the current recruitment total is 26 patients. The target treatment total remains at 24 patients but recruitment is expected to run until July 2017 and so it is likely that the trial will meet the target recruitment total before meeting the target treatment total. Therefore, this has been amended to allow for the original target treatment total to be met even if the original estimated target recruitment total is surpassed.</p>
12 July 2017	<p>Protocol v7.0 12/07/2017</p> <p>Summary of changes:</p> <ol style="list-style-type: none"> <li>1. Twelve month extension to recruitment from 3 to 4 years (section 1.1'Summary of Trial Design')</li> <li>2. Section 15.1 'Sample size calculation' now clarifies that once the required 8 patients in the control arm reach 4 months (primary end point assessment), any remaining patients will be registered into the ATIMP arm until the target of 16 treated ATIMP patients is achieved and the trial will close to recruitment.</li> </ol> <p>In addition the following clarifications regarding the serology tests required to be performed at screening have been added to sections 5.1 'Pre-randomisation evaluation' and 5.3.2 'Exclusion Criteria' (no new tests have been added):</p> <ul style="list-style-type: none"> <li>• results from HBV, HCV, syphilis and HIV tests are required prior to randomisation of patient into the study to assess eligibility, while EBV, CMV and HTLV results are needed for information</li> <li>• patients with 'active' HBV, HCV and HIV infection are excluded from the trial and PCR should be used to rule out 'active infection' if serology result is positive.</li> </ul>

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported (?)

Notes: