



Clinical trial results:

A multi-center phase I/II safety and feasibility study using CliniMACS TCR/ and CD19 depleted stem cell grafts from haploidentical donors for haematopoietic progenitor cell transplantation in children and adults

Summary

EudraCT number	2011-005562-38
Trial protocol	DE NL
Global end of trial date	21 December 2018

Results information

Result version number	v1 (current)
This version publication date	07 July 2019
First version publication date	07 July 2019

Trial information

Trial identification

Sponsor protocol code	M-2011-238
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Miltenyi Biotec GmbH
Sponsor organisation address	Friedrich-Ebert-Str. 68, Bergisch Gladbach, Germany, 51429
Public contact	Clinical Trial Manager, Dr. Sandra Karitzky, Miltenyi Biotec GmbH, 0049 220483066560, sandrak@miltenyibiotec.de
Scientific contact	Clinical Trial Manager, Dr. Sandra Karitzky, Miltenyi Biotec GmbH, 0049 220483066560, sandrak@miltenyibiotec.de

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	21 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2018
Global end of trial reached?	Yes
Global end of trial date	21 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the safety/tolerability and feasibility of haploidentical PBSC grafts depleted of TCR α / β + and CD19+ cells using the CliniMACS TCR α / β and CD19 Systems in adult and paediatric patients with hematological and non-hematological malignancies and specific non-malignant diseases, defined as the incidence of grade II–IV acute graft-versus-host disease (GVHD) on Day 100 post-transplantation.

Protection of trial subjects:

1. Monitoring incidence and severity of acute GVHD and acute NRM and type of adverse events.
2. Immediate reporting of each case of GVHD grade III-IV and each case of NRM.
3. Implementation of statistical stopping guidelines for GVHD grade III-IV and NRM to allow immediate reaction in case of elevated incident rates.
4. Assessment and analysis of graft failure by DSMB for decision on conditioning regimen after treatment of the first 10 patients who had not received ATG Fresenius.
5. Evaluation of changes in findings of physical examination, vital signs and clinical laboratory results (complete blood count, differential and platelet count and blood chemistry).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2012
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	Germany: 59
Country: Number of subjects enrolled	Netherlands: 1
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	2
Children (2-11 years)	18

Adolescents (12-17 years)	10
Adults (18-64 years)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All patients who signed the informed consent are considered enrolled into the trial.

Pre-assignment period milestones

Number of subjects started	74 ^[1]
Number of subjects completed	60

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Patients did not undergo transplantation with IMP: 14
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Patients who started the pre-assignment period are considered all patients who signed the ICF. A patient is considered enrolled into the trial once he received the IMP. Among the patients who started the pre-assignment period are 14 screening-failures who could not receive IMP, therefore the number of patients who started the pre-assignment period and those who were enrolled into the trial differs.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pediatric cohort

Arm description:

Patients aged ≥ 8 weeks to 17 years

Arm type	Experimental
Investigational medicinal product name	TCRabCD19PBSC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Mobilized peripheral blood stem cells from allogeneic donors depleted of TCR α/β ⁺ and CD19⁺ cells using the CliniMACS TCR α/β -Biotin and CD19 Systems; Viable CD34⁺ cells: target cell number $\geq 4 \times 10^6$ /kg BW, percentage of viable cells $\geq 95\%$; TCR α/β ⁺ cells: target cell number $\leq 25 \times 10^3$ /kg BW).

The number of transfusions depended on the number of individual stem cell apheresis cycles needed to reach a content of $\geq 4 \times 10^6$ CD34⁺CD45⁺ cells/kg BW of the patient for transplantation. The IMP could be administered with up to three transfusions on three subsequent days (Day 0, Day +1 and Day +2) or could be cryopreserved after processing for subsequent single transfusion of the pooled product

Arm title	Adult cohort
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Arm description:

Patients aged ≥ 18 years

Arm type	Experimental
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Investigational medicinal product name	TCRabCD19PBSC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Mobilized peripheral blood stem cells from allogenic donors depleted of TCR α / β + and CD19+ cells using the CliniMACS TCR α / β -Biotin and CD19 Systems; Viable CD34+ cells: target cell number $\geq 4 \times 10^6$ /kg BW, percentage of viable cells $\geq 95\%$; TCR α / β + cells: target cell number $\leq 25 \times 10^3$ /kg BW).

The number of transfusions depended on the number of individual stem cell apheresis cycles needed to reach a content of $\geq 4 \times 10^6$ CD34+CD45+ cells/kg BW of the patient for transplantation. The IMP could be administered with up to three transfusions on three subsequent days (Day 0, Day +1 and Day +2) or could be cryopreserved after processing for subsequent single transfusion of the pooled product

Number of subjects in period 1	Pediatric cohort	Adult cohort
Started	30	30
Completed	30	30

Baseline characteristics

Reporting groups

Reporting group title	Pediatric cohort
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Reporting group description:

Patients aged ≥ 8 weeks to 17 years

Reporting group title	Adult cohort
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Reporting group description:

Patients aged ≥ 18 years

Reporting group values	Pediatric cohort	Adult cohort	Total
Number of subjects	30	30	60
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
adult patients (≥ 18 years)	0	30	30
pediatric patients (≥ 8 weeks to 17 years)	30	0	30
Age continuous			
Units: years			
arithmetic mean	8.7	38.2	
standard deviation	± 5.3	± 13.8	-
Gender categorical			
Units: Subjects			
Female	13	13	26
Male	17	17	34

Subject analysis sets

Subject analysis set title	Safety Analysis Set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Safety analysis set:

Reporting group values	Safety Analysis Set		
Number of subjects	60		
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)	0		
From 65-84 years	0		
85 years and over	0		
adult patients (≥ 18 years)	30		
pediatric patients (≥ 8 weeks to 17 years)	30		
Age continuous			
Units: years			
arithmetic mean	23.5		
standard deviation	± 18.2		
Gender categorical			
Units: Subjects			
Female	26		
Male	34		

End points

End points reporting groups

Reporting group title	Pediatric cohort
Reporting group description:	
Patients aged ≥ 8 weeks to 17 years	
Reporting group title	Adult cohort
Reporting group description:	
Patients aged ≥ 18 years	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety analysis set:	

Primary: Incidence of grade II–IV acute GVHD

End point title	Incidence of grade II–IV acute GVHD ^[1]
End point description:	
End point type	Primary
End point timeframe:	
day 100 post-transplantation	

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: The statistical analyses in this study will be exploratory since the study is not powered to address any pre-defined statements but to generate valid hypotheses on safety/tolerability and feasibility issues. A formal sample size calculation was therefore not done. Thus, all resulting p-values and confidence intervals are to be interpreted in the exploratory sense only.

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with grade II–IV aGVHD	1	5	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of grade I aGVHD

End point title	Incidence of grade I aGVHD
End point description:	
End point type	Secondary
End point timeframe:	
day 100 post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with grade I aGVHD	17	12	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of cGVHD, 1 year

End point title	Incidence and severity of cGVHD, 1 year
End point description: multiple responses possible	
End point type	Secondary
End point timeframe: 1 year post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	22 ^[2]	25 ^[3]	47 ^[4]	
Units: patients with cGVHD				
clinically limited cGVHD	4	9	13	
clinically extended cGVHD	2	4	6	
Total	4	10	14	

Notes:

[2] - multiple responses possible for cGVHD

[3] - multiple responses possible for cGVHD

[4] - multiple responses possible for cGVHD

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of cGVHD, 2 years

End point title	Incidence and severity of cGVHD, 2 years
End point description: multiple responses possible	
End point type	Secondary
End point timeframe: 2 years post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	22	25	47	
Units: patients with cGVHD				
clinically limited cGVHD	4	10	14	
clinically extended cGVHD	2	5	7	
Total	4	12	16	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of NRM

End point title	Incidence of NRM
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End point description:

End point type	Secondary
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End point timeframe:

day 100, 1 and 2 years post-transplantation

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with NRM				
day 100	1	2	3	
1 year	4	5	9	
2 years	5	5	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of acute infusional toxicity

End point title	Incidence of acute infusional toxicity
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End point description:

End point type	Secondary
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End point timeframe:

day 0 to day 2

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with infusional toxicities	3	4	7	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of graft failure

End point title	Incidence of graft failure
End point description:	
Patients with primary and secondary graft failure	
End point type	Secondary
End point timeframe:	
day 0 to day 28	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with graft failure	6	2	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophil and platelet engraftment

End point title	Neutrophil and platelet engraftment
End point description:	
End point type	Secondary
End point timeframe:	
day 28 past-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with engraftment				
neutrophil engraftment	25	27	52	
platelet engraftment	25	23	48	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to neutrophil and platelet engraftment

End point title	Time to neutrophil and platelet engraftment
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 28	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: days				
arithmetic mean (standard deviation)				
time to neutrophil engraftment	12.2 (± 1.9)	12.9 (± 2.9)	12.6 (± 2.5)	
time to platelet engraftment	14.8 (± 3.3)	15.6 (± 2.1)	15.1 (± 2.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
End point description:	
End point type	Secondary
End point timeframe:	
day 100, 1 and 2 years post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: alive patients				
day 100	28	28	56	
1 year	19	23	42	
2 years	17	21	39	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease free survival

End point title Disease free survival

End point description:

End point type Secondary

End point timeframe:

day 100, 1 and 2 years post-transplantation

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: alive, disease-free patients				
day 100	26	27	53	
1 year	17	21	38	
2 years	13	18	31	

Statistical analyses

No statistical analyses for this end point

Secondary: Transfusion requirement

End point title Transfusion requirement

End point description:

End point type Secondary

End point timeframe:

day 0 to day 100 post-transplantation

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	30	
Units: patients with infusion				
thrombocyte infusion	30	30	60	
erythrocyte infusion	29	30	59	
other blood product	11	4	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Transfusion requirement - time to last infusion

End point title	Transfusion requirement - time to last infusion
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 100 post-transfusion	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: days				
arithmetic mean (standard deviation)				
time to erythrocyte infusion	24.0 (± 26.6)	21.4 (± 21.8)	22.7 (± 24.1)	
time to thrombocyte infusion	16.8 (± 23.5)	18.9 (± 18.1)	17.9 (± 20.8)	
time to infusion of other blood product	41.4 (± 37.3)	26.9 (± 29.5)	40.3 (± 26.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of relapse

End point title	Incidence of relapse
End point description:	
End point type	Secondary
End point timeframe:	
day 100, 1 and 2 years post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30		
Units: patients with relapse				
day 100	3	1	4	
1 year	9	4	13	
2 years	11	7	18	

Statistical analyses

No statistical analyses for this end point

Secondary: Days of hospitalization

End point title	Days of hospitalization
End point description:	
End point type	Secondary
End point timeframe:	
day 28	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	25	27	52	
Units: days				
arithmetic mean (standard deviation)	27.2 (± 3.2)	24.5 (± 5.4)	25.8 (± 4.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Days of re-hospitalization

End point title	Days of re-hospitalization
End point description:	
End point type	Secondary
End point timeframe:	
day 100	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	7	23	
Units: days				
arithmetic mean (standard deviation)	13.5 (± 6.2)	13.9 (± 11.1)	13.6 (± 7.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - bone marrow, day 28

End point title	Chimerism - bone marrow, day 28
End point description:	
End point type	Secondary
End point timeframe:	
day 28 post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	22	37	
Units: patients with chimerism				
mixed chimerism	2	2	4	
complete chimerism	13	20	33	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - bone marrow, day 100

End point title	Chimerism - bone marrow, day 100
End point description:	
End point type	Secondary
End point timeframe:	
day 100 post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	15	20	35	
Units: patients with chimerism				
mixed chimerism	3	1	4	
complete chimerism	12	19	31	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - TCRgamma/delta+ cells

End point title	CliniMACS performance - TCRgamma/delta+ cells
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End point description:

End point type	Secondary
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End point timeframe:

day 0 to day 2 post-transplantation

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29	30	59	
Units: x10e6 cells/kg BW				
arithmetic mean (standard deviation)	16.8 (± 13.3)	9.7 (± 7.6)	13.2 (± 11.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - Haematocrit volume in graft

End point title	CliniMACS performance - Haematocrit volume in graft
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End point description:

End point type	Secondary
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End point timeframe:

day 0 to day 2 post-transplantation

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: percent volume/volume				
arithmetic mean (standard deviation)	4.2 (± 3.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - Number of grafts with $\geq 4 \times 10^6$ CD34+CD45+ stem cells/kg BW achieved

End point title	CliniMACS performance - Number of grafts with $\geq 4 \times 10^6$ CD34+CD45+ stem cells/kg BW achieved
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2 post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)	96.7	100	98.3	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - Number of grafts $\leq 25 \times 10^3$ TCRab+ cells/kg BW achieved

End point title	CliniMACS performance - Number of grafts $\leq 25 \times 10^3$ TCRab+ cells/kg BW achieved
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2 post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)	83.3	83.3	83.3	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - Number of grafts $\leq 1 \times 10^5$ CD20+ cells/kg BW achieved

End point title	CliniMACS performance - Number of grafts $\leq 1 \times 10^5$ CD20+ cells/kg BW achieved
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2 post-transplantation	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)	73.3	96.7	85.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of all infections, year 1

End point title	Incidence of all infections, year 1
End point description:	
Incidence of CMV, ADV, EBV and aspergillus as well as other viral bacterial and fungal infections	
End point type	Secondary
End point timeframe:	
1 year post-transplantation (≤ 379 days after first PBSC infusion)	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	22	25	47	
Units: percent				
number (not applicable)	40.9	28.0	34.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of all infections, year 2

End point title	Incidence of all infections, year 2
End point description:	Incidence of CMV, ADV, EBV and aspergillus as well as other viral bacterial and fungal infections
End point type	Secondary
End point timeframe:	2 years post-transplantation (<= 758 days after first PBSC infusion)

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)	56.7	43.3	50.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of all infections, day 100

End point title	Incidence of all infections, day 100
End point description:	Incidence of CMV, ADV, EBV and aspergillus as well as other viral bacterial and fungal infections
End point type	Secondary
End point timeframe:	<=105 days after first PBSC infusion

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	30	
Units: percent				
number (not applicable)	86.7	80.0	83.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of virus reactivation - CMV

End point title	Number of virus reactivation - CMV
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End point description:

End point type	Secondary
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End point timeframe:

days 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 100

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with virus reactivation				
day 7	2	1	3	
day 14	1	2	3	
day 21	3	4	7	
day 28	1	6	7	
day 35	0	8	8	
day 42	1	8	9	
day 49	3	7	10	
day 56	2	7	9	
day 63	1	5	6	
day 70	1	7	8	
day 100	3	5	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of virus reactivation - ADV

End point title	Number of virus reactivation - ADV
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End point description:

End point type	Secondary
End point timeframe:	
days 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 100	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with virus reactivation				
day 7	3	0	3	
day 14	4	0	4	
day 21	8	0	8	
day 28	7	0	7	
day 35	8	0	8	
day 42	9	0	9	
day 49	12	0	12	
day 56	10	3	13	
day 63	9	2	11	
day 70	11	2	13	
day 100	11	1	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of virus reactivations - EBV

End point title	Number of virus reactivations - EBV
End point description:	
End point type	Secondary
End point timeframe:	
days 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 100	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with virus reactivations				
day 7	0	0	0	
day 14	0	0	0	
day 21	0	0	0	
day 28	0	0	0	
day 35	0	1	1	
day 42	0	0	0	

day 49	0	0	0	
day 56	0	1	1	
day 63	0	0	0	
day 70	0	0	0	
day 100	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: PedsQL - Change of physical health summary score

End point title	PedsQL - Change of physical health summary score ^[5]
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End point description:

End point type	Secondary
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End point timeframe:

baseline to day 100, 1 and 2 years

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Peds-QL was only assessed in pediatric patients <18 years old. Therefore no data are available for adult arm.

End point values	Pediatric cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: physical health summary score				
arithmetic mean (standard deviation)				
day 100	53.9 (± 27.8)			
1 year	54.9 (± 35.1)			
2 years	50.6 (± 33.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PedsQL - Change of psychosocial health summary score

End point title	PedsQL - Change of psychosocial health summary score ^[6]
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End point description:

End point type	Secondary
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End point timeframe:

baseline to day 100, 1 and 2 years

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Peds-QL was only assessed in pediatric patients <18 years old. Therefore no data are available for adult arm.

End point values	Pediatric cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: psychosocial health summary score				
arithmetic mean (standard deviation)				
day 100	60.5 (± 16.2)			
1 year	63.4 (± 15.9)			
2 years	20.2 (± 57.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: PedsQL - Change of total score

End point title PedsQL - Change of total score^[7]

End point description:

End point type Secondary

End point timeframe:

from baseline to day 100, 1 and 2 years

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Peds-QL was only assessed in pediatric patients <18 years old. Therefore no data are available for adult arm.

End point values	Pediatric cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: total score				
arithmetic mean (standard deviation)				
day 100	57.5 (± 19.9)			
1 year	59.5 (± 23.5)			
2 years	54.6 (± 24.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-3L Quality of life, baseline

End point title EQ-5D-3L Quality of life, baseline^[8]

End point description:

End point type Secondary

End point timeframe:

baseline

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: percent				
number (not applicable)				
I have no problems in walking	73.3			
I have some problems in walking	6.7			
I have no problems with self-care	76.7			
I have problems with self-care	3.3			
I have no problems with performing my usual activi	56.7			
I have some problems with performing usual activit	16.7			
I am unable to perform usual activities	3.3			
I have no pain or discomfort	46.7			
I have moderate pain or discomfort	30.0			
I have extrem pain or discomfort	3.3			
I am not anxious or depressed	46.7			
I am moderately anxious or depressed	26.7			
I am extremely anxious or depressed	6.7			

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-3L Quality of life questionnaire, day 100

End point title	EQ-5D-3L Quality of life questionnaire, day 100 ^[9]
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End point description:

End point type	Secondary
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End point timeframe:

day 100

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Pediatric cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: percent				
number (not applicable)				
I have no problems in walking about	60.0			
I have some problems in walking about	16.7			

I have no problems with self-care	70.0			
I have some problems with self-care	6.7			
I have no problems with performing usual activiti	46.7			
I have some problems with performing usual activit	20.0			
I am unable to perform my usual activities	6.7			
I have no pain or discomfort	33.3			
I have moderate pain or discomfort	40.0			
I have xtreme pain or discomfort	3.3			
I am not anxious or depressed	43.3			
I am moderately anxious or depressed	30.0			
I am extremely anxious or depressed	3.3			

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-3L Quality of life questionnaire, year 1

End point title	EQ-5D-3L Quality of life questionnaire, year 1 ^[10]
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End point description:

End point type	Secondary
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End point timeframe:

year 1

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: percent				
number (not applicable)				
I have no problems in walking around	40.0			
I have some problems in walking around	10.0			
I have no problems with self-care	50.0			
I have no problems with performing usual activities	33.3			
I have some problems with performing usual activit	16.7			
I have no pain or discomfort	26.7			
I have moderate pain or discomfort	16.7			
I have xtreme pain or discomfort	6.7			
I am not ancious or depressed	30.0			
I am moderately anxious or depressed	20.0			

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-3L Quality of life questionnaire, 2 years

End point title	EQ-5D-3L Quality of life questionnaire, 2 years ^[11]
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End point description:

End point type	Secondary
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End point timeframe:

2 years

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: percent				
number (not applicable)				
I have no problems in walking about	36.7			
I have some problems in walking about	10.0			
I have no problems with self care	43.3			
I have some problems with self care	3.3			
I have no problems with performing usual activitie	33.3			
I have some problems with performing unusual activ	13.3			
i have no pain or discomfort	20.0			
I have moderate pain or discomfort	26.7			
I am not anxious or depressed	20.0			
I am moderately anxious or depressed	20.0			
I am extremely anxious or depressed	6.7			

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D-3L - Change of VAS

End point title	EQ-5D-3L - Change of VAS ^[12]
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End point description:

End point type	Secondary
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End point timeframe:

change from baseline to day 100, 1 and 2 years

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: VAS Health state				
arithmetic mean (standard deviation)				
day 100	-8.1 (\pm 20.8)			
1 year	3.6 (\pm 19.3)			
2 years	7.8 (\pm 22.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: FACT BMT - Change of trial outcome index score

End point title	FACT BMT - Change of trial outcome index score ^[13]
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End point description:

End point type	Secondary
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End point timeframe:

change from baseline to day 100, 1 and 2 years

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Trial outcome index score				
arithmetic mean (standard deviation)				
day 100	-2.8 (\pm 15.7)			
1 year	0.3 (\pm 13.2)			
2 years	3.5 (\pm 9.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: FACT BMT - Change of FACT-G total score

End point title	FACT BMT - Change of FACT-G total score ^[14]
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End point description:

End point type	Secondary
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End point timeframe:

from baseline to day 100, 1 and 2 years

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: FACT-G total score				
arithmetic mean (standard deviation)				
day 100	-3.4 (\pm 13.3)			
1 year	-0.1 (\pm 14.7)			
2 years	3.2 (\pm 11.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: FACT BMT - Change of FACT BMT total score

End point title	FACT BMT - Change of FACT BMT total score ^[15]
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End point description:

End point type	Secondary
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End point timeframe:

from baseline to day 100, 1 and 2 years

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: FACT-BMT was only assessed for adult patients ≥ 18 years old. Therefore no data are available for pediatric arm.

End point values	Adult cohort			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: FACT BMT- total score				
arithmetic mean (standard deviation)				
day 100	-4.4 (± 17.3)			
1 year	1.0 (± 18.4)			
2 years	4.6 (± 13.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Transfusion - New treatment with cellular products, 1 year

End point title	Transfusion - New treatment with cellular products, 1 year
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End point description:

End point type	Secondary
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End point timeframe:

only transfusions with start date >105 and <=379 days after first PBSC infusion are included -

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	22	25	47	
Units: patients with new transfusions				
Total	9	4	13	
Erythrocyte	1	1	2	
Thrombocyte	2	2	4	
DLI	2	2	4	
Antigen specific T-cell infusion	1	1	2	
Other	6	0	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Transfusions - New treatment with cellular products, 2 years

End point title	Transfusions - New treatment with cellular products, 2 years
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End point description:

End point type	Secondary
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End point timeframe:

only transfusions with start date >379 and <=758 days after first PBSC infusion are included

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	14	20	34	
Units: patients with new transfusions				
Total	1	7	8	
Erythrocytes	0	1	1	
Thrombocytes	0	1	1	
DLI	0	6	6	
Other	0	1	1	
Second transplantation	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Enrollment in another clinical trial

End point title	Enrollment in another clinical trial
End point description:	
End point type	Secondary
End point timeframe:	
after day 100	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	30	
Units: patients enrolled in another trial	2	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Concomitant medication - standard prophylactic treatment

End point title	Concomitant medication - standard prophylactic treatment
End point description:	
End point type	Secondary
End point timeframe:	
only medications with start date ≤ 105 days after first PBSC infusion are included	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with concomitant medication				
Immunosuppressants	30	30	60	
Antimycotics	30	29	59	
Antibacterials	29	28	57	
Antivirals	26	30	56	
Immune sera + Immunoglobulins	27	19	46	
Drugs for acid related disorders	6	10	16	
Antihistamines	4	7	11	
Corticosteroids	2	7	9	
Antidiarrheals, intestinal antiinflammatory	2	1	3	
Antiprotozoals	0	2	2	
Stomatological preparations	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Concomitant medication - non-standard treatment

End point title	Concomitant medication - non-standard treatment
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End point description:

End point type	Secondary
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End point timeframe:

only medications with start date <=105 days after first PBSC infusion are included

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with concomitant medication				
Analgesics	30	30	60	
Antibacterials	30	30	60	
Drugs for acid related disorders	30	30	60	
Antiemetics + Antinauseants	29	26	55	
Antihistamines	27	26	53	
Diuretics	27	25	52	
Antivirals	27	20	47	

Psycholeptics	21	25	46	
Mineral supplements	16	26	42	
Antihemorrhagics	18	21	39	
Corticosteroids	19	19	38	
Drugs for functional gastrointestinal disorders	12	24	36	
Antianemic preparations	25	8	33	
Vitamins	11	22	33	
Antithrombic agents	12	19	31	
Blood substitutes + perfusion solutions	14	12	26	
Antimycotics	15	8	23	
Corticosteroids, dermatologic preparations	13	10	23	
Drugs for constipation	12	10	22	
Antigout preparations	17	4	21	
Immunostimulants	10	11	21	
Anesthetics	14	3	17	
Antineoplastic agents	12	4	16	
Other dermatological agents	11	4	15	
Drugs for obstructive airway disease	11	3	14	
Antidiarrheals, Intestinal Inflammatory agents	2	10	12	
Cough + cold preparations	6	6	12	
Cardiac therapy	7	4	11	
Psychoanaleptics	4	7	11	
Unspecified herbal + traditional medicine	9	2	11	
Immunosuppressants	6	4	10	
Thyroid therapy	3	6	9	
Urologicals	6	3	9	
All other therapeutic products	2	6	8	
Antiprotozoals	2	6	8	
Endocrine therapy	2	6	8	
Ophthalmologicals	4	4	8	
Stomatological preparations	4	4	8	
Agents acting on renin-angiotensin system	2	5	7	
Antiinflammatory + antirheumatic products	3	4	7	
Beta blocking agents	3	4	7	
Antiepileptics	5	1	6	
Bile + Liver therapy	4	4	6	
Calcium channel blockers	3	3	6	
Drugs used in diabetes	0	6	6	
Nasal preparations	3	3	6	
Antipruritics	2	3	5	
Emollients + protectives	2	3	5	
Immune sera + immunoglobulins	1	4	5	
Sex hormones + modulators of genital system	1	4	5	
lipid modifying agents	3	1	4	
pituitary + hypothalamic hormones + analogues	1	3	4	
Antibiotics + chemotherapeutics for dermal use	1	2	3	

Antifungals for dermatological use	0	3	3	
antiseptics + disinfectants	2	1	3	
Preparations + treatment of wounds + ulcers	2	1	3	
Antihypersensitives	0	2	2	
Digestives incl. enzymes	1	1	2	
General nutrients	0	2	2	
Muscle relaxants	0	2	2	
Other nervous system drugs	0	2	2	
Drugs for treatment of bone disease	1	0	1	
Gynecological antiinfectives + antiseptics	0	1	1	
Other alimentary tract + metabolism products	1	0	1	
Throat preparations	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Therapy related toxicities of conditioning

End point title	Therapy related toxicities of conditioning
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End point description:

End point type	Secondary
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End point timeframe:

during conditioning and prior to stem cell transplantation

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with therapy related toxicities	30	30	60	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 14

End point title	Chimerism - peripheral blood, day 14
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End point description:

End point type	Secondary
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End point timeframe:
day 14

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
Mixed chimerism	20.0	6.7	13.3	
Complete chimerism	60.0	83.3	71.7	
not established	0	3.3	1.7	
missing	20.0	6.7	13.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 7

End point title	Chimerism - peripheral blood, day 7
End point description:	
End point type	Secondary
End point timeframe: day 7	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	10.0	6.7	8.3	
mixed chimerism	16.7	16.7	16.7	
complete chimerism	20.0	43.3	31.7	
missing	53.3	33.3	43.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 21

End point title	Chimerism - peripheral blood, day 21
End point description:	
End point type	Secondary
End point timeframe:	
day 21	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	3.3	3.3	3.3	
mixed chimerism	16.7	6.7	11.7	
complete chimerism	63.3	80.0	71.7	
missing	16.7	10.0	13.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 28

End point title	Chimerism - peripheral blood, day 28
End point description:	
End point type	Secondary
End point timeframe:	
day 28	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	10.0	3.3	6.7	
complete chimerism	56.7	80.0	68.3	
missing	33.3	16.7	25.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 35

End point title Chimerism - peripheral blood, day 35

End point description:

End point type Secondary

End point timeframe:
day 35

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	0	3.3	1.7	
complete chimerism	70.0	73.3	71.7	
missing	30.0	23.3	26.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 42

End point title Chimerism - peripheral blood, day 42

End point description:

End point type Secondary

End point timeframe:
day 42

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	3.3	1.7	
mixed chimerism	0	3.3	1.7	
complete chimerism	100.0	80.0	78.3	

missing	0	13.3	18.3	
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Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 49

End point title	Chimerism - peripheral blood, day 49
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End point description:

End point type	Secondary
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End point timeframe:

day 49

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	3.3	1.7	
mixed chimerism	0	0	0	
complete chimerism	76.7	73.3	75.0	
missing	23.3	23.3	23.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 56

End point title	Chimerism - peripheral blood, day 56
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End point description:

End point type	Secondary
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End point timeframe:

day 56

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	3.3	0	1.7	
complete chimerism	63.3	70.0	66.7	
missing	33.3	30.0	31.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 63

End point title	Chimerism - peripheral blood, day 63
End point description:	
End point type	Secondary
End point timeframe:	
day 63	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	10.0	0	5.0	
complete chimerism	63.3	63.3	63.3	
missing	26.7	36.7	31.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 70

End point title	Chimerism - peripheral blood, day 70
End point description:	
End point type	Secondary

End point timeframe:

day 70

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	3.3	0	1.7	
complete chimerism	73.3	76.7	75.0	
missing	23.3	23.3	23.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, day 100

End point title	Chimerism - peripheral blood, day 100
End point description:	
End point type	Secondary
End point timeframe:	
day 100	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	10.0	6.7	8.3	
mixed chimerism	6.7	3.3	5.0	
complete chimerism	66.7	80.0	73.3	
missing	16.7	10.0	13.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, month 6

End point title	Chimerism - peripheral blood, month 6
End point description:	
End point type	Secondary
End point timeframe:	
month 6 (day 180)	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	3.3	0	1.7	
complete chimerism	56.7	66.7	61.7	
missing	40.0	33.3	36.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Chimerism - peripheral blood, month 9

End point title	Chimerism - peripheral blood, month 9
End point description:	
End point type	Secondary
End point timeframe:	
month 9 (day 207)	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: percent				
number (not applicable)				
not established	0	0	0	
mixed chimerism	3.3	0	1.7	
complete chimerism	53.3	60.0	56.7	
missing	43.3	40.0	41.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - CD3+ T-cells

End point title Reconstitution - CD3+ T-cells

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	12.5 (± 16.2)			
d 14	114.2 (± 143.4)			
d 21	149.1 (± 160.2)			
d 28	179.1 (± 212.4)			
d 63	230.8 (± 236.4)			
d 100	303.4 (± 305.6)			
m 6	590.1 (± 587.3)			
y 1	1048.4 (± 738.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - CD4+ T-cells

End point title Reconstitution - CD4+ T-cells

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	1.0 (± 1.9)			
d 14	5.4 (± 8.4)			
d 21	19.2 (± 27.5)			
d 28	35.0 (± 83.4)			
d 63	39.4 (± 56.0)			
d 100	55.0 (± 50.0)			
m 6	161.1 (± 154.2)			
y 1	403.2 (± 297.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - CD8+ T-cells

End point title	Reconstitution - CD8+ T-cells
End point description:	
End point type	Secondary
End point timeframe:	
day 7, 14, 21, 28, 63, 100, month 6, year 1	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	1.6 (± 2.2)			
d 14	14.8 (± 34.2)			
d 21	20.7 (± 38.2)			
d 28	39.1 (± 83.9)			
d 63	87.0 (± 150.1)			
d 100	125.8 (± 196.7)			
m 6	264.4 (± 374.3)			
y 1	456.2 (± 513.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - B-cells

End point title Reconstitution - B-cells

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	2.6 (± 8.7)			
d 14	5.5 (± 16.0)			
d 21	2.6 (± 2.6)			
d 28	15.4 (± 49.7)			
d 63	255.6 (± 308.6)			
d 100	228.3 (± 237.2)			
m 6	261.8 (± 216.1)			
y 1	379.2 (± 239.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - Monocytes

End point title Reconstitution - Monocytes

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	23.9 (± 29.0)			
d 14	1216.7 (± 851.4)			
d 21	1002.7 (± 570.0)			
d 28	749.0 (± 440.6)			
d 63	351.5 (± 216.6)			
d 100	333.0 (± 188.0)			
m 6	421.9 (± 217.4)			
y 1	447.1 (± 138.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - NK cells

End point title Reconstitution - NK cells

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	42.8 (± 50.0)			
d 14	267.2 (± 212.7)			

d 21	346.9 (± 223.5)			
d 28	336.3 (± 233.9)			
d 63	267.1 (± 159.6)			
m 6	565.3 (± 1883.6)			
y 1	240.8 (± 128.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - CD3+CD56+ T-cells

End point title	Reconstitution - CD3+CD56+ T-cells
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End point description:

End point type	Secondary
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End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	3.2 (± 4.6)			
d 14	26.8 (± 52.8)			
d 21	34.8 (± 61.4)			
d 28	34.2 (± 61.4)			
d 63	28.1 (± 36.7)			
d 100	33.2 (± 38.1)			
m 6	35.6 (± 46.1)			
y 1	37.2 (± 45.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - Neutrophils

End point title	Reconstitution - Neutrophils
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End point description:

End point type	Secondary
End point timeframe:	
day 7, 14, 21, 28, 63, 100, month 6, year 1	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	4.7 (± 5.5)			
d 14	1298.8 (± 2313.7)			
d 21	2230.7 (± 2109.1)			
d 28	2561.7 (± 2795.6)			
d 63	2177.1 (± 2065.6)			
d 100	2019.4 (± 1377.9)			
m 6	2420.9 (± 1422.9)			
y 1	3102.0 (± 1927.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - Eosinophiles

End point title	Reconstitution - Eosinophiles
End point description:	
End point type	Secondary
End point timeframe:	
day 7, 14, 21, 28, 63, 100, month 6, year 1	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	10.9 (± 16.3)			
d 14	841.5 (± 1075.7)			

d 21	443.1 (± 700.5)			
d 28	669.6 (± 913.9)			
d 63	210.9 (± 207.6)			
d 100	214.5 (± 227.6)			
m 6	277.0 (± 417.0)			
y 1	294.9 (± 479.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - CD3+TCRab+ T-cells

End point title	Reconstitution - CD3+TCRab+ T-cells
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End point description:

End point type	Secondary
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End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.6 (± 1.3)			
d 14	6.1 (± 12.7)			
d 21	25.6 (± 40.4)			
d 28	54.1 (± 125.7)			
d 63	127.1 (± 232.8)			
d 100	167.7 (± 214.7)			
m 6	410.8 (± 475.4)			
y 1	991.6 (± 860.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - CD3+TCRgd+ T-cells

End point title	Reconstitution - CD3+TCRgd+ T-cells
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End point description:

End point type	Secondary
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End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	10.7 (± 15.7)			
d 14	89.8 (± 119.7)			
d 21	115.5 (± 142.6)			
d 28	111.1 (± 150.1)			
d 63	116.9 (± 132.2)			
d 100	135.8 (± 136.1)			
m 6	180.9 (± 210.9)			
y 1	224.6 (± 187.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - naive CD4+ TCRab+

End point title	Reconstitution - naive CD4+ TCRab+
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End point description:

End point type	Secondary
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End point timeframe:

day 7, 14, 21, 28, 63, 100, month 6, year 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.0 (± 0.0)			
d 14	0.0 (± 0.0)			
d 21	0.0 (± 0.1)			
d 28	2.8 (± 19.7)			
d 63	0.1 (± 0.5)			
d 100	1.6 (± 4.1)			
m 6	42.9 (± 83.4)			
y 1	218.1 (± 267.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - memory CD4+ TCRab+

End point title	Reconstitution - memory CD4+ TCRab+
End point description:	
End point type	Secondary
End point timeframe:	
day 7, 14, 21, 27, 63, 100, m6, y 1	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.2 (± 0.8)			
d 14	3.1 (± 7.3)			
d 21	16.1 (± 25.6)			
d 28	23.4 (± 54.1)			
d 63	36.3 (± 53.9)			
d 100	49.3 (± 47.3)			
m 6	119.1 (± 100.6)			
y 1	287.8 (± 428.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - naive CD8+ TCRab+

End point title	Reconstitution - naive CD8+ TCRab+
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End point description:

End point type	Secondary
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End point timeframe:

d 7, 14, 21, 28, 63, 100, m 6, y 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.0 (± 0.0)			
d 14	0.0 (± 0.2)			
d 21	0.4 (± 2.0)			
d 28	2.5 (± 16.0)			
d 63	2.2 (± 7.6)			
d 100	4.5 (± 11.2)			
m 6	40.3 (± 60.9)			
y 1	149.9 (± 186.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - memory CD8+ TCRab+

End point title	Reconstitution - memory CD8+ TCRab+
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End point description:

End point type	Secondary
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End point timeframe:

day 7, 14, 21, 28, 63, 100, m6, y 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.0 (± 0.1)			
d 14	2.1 (± 4.9)			
d 21	7.4 (± 22.0)			
d 28	22.5 (± 63.4)			
d 63	83.7 (± 185.7)			
d 100	103.9 (± 178.9)			
m 6	179.6 (± 328.6)			
y 1	292.8 (± 399.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - DN TCRab+

End point title	Reconstitution - DN TCRab+
End point description:	
End point type	Secondary
End point timeframe:	
day 7, 14, 21, 28, 63, 100, m6, y 1	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.1 (± 0.4)			
d 14	0.3 (± 0.5)			
d 21	0.5 (± 0.7)			
d 28	1.3 (± 3.3)			
d 63	1.7 (± 2.8)			
d 100	4.1 (± 14.5)			
m 6	17.9 (± 55.4)			
y 1	18.6 (± 31.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - TCR Vd2+ TCRgd+

End point title Reconstitution - TCR Vd2+ TCRgd+

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, m6, y 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	7.5 (± 14.2)			
d 14	55.9 (± 82.2)			
d 21	76.1 (± 106.1)			
d 28	68.7 (± 93.2)			
d 63	57.5 (± 72.2)			
d 100	59.0 (± 72.3)			
m 6	57.2 (± 69.3)			
y 1	79.0 (± 110.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - TCR Vd2- TCRgd+

End point title Reconstitution - TCR Vd2- TCRgd+

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, m6, y 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	3.2 (± 3.8)			
d 14	33.8 (± 51.4)			
d 21	39.4 (± 60.5)			
d 28	42.2 (± 76.3)			
d 63	59.4 (± 93.0)			
d 100	76.8 (± 115.2)			
m 6	123.7 (± 198.0)			
y 1	145.8 (± 162.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - naive Treg

End point title	Reconstitution - naive Treg
End point description:	
End point type	Secondary
End point timeframe:	
day 7, 14, 21, 28, 63, 100, m6, y 1	

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.0 (± 0.0)			
d 14	0.0 (± 0.1)			
d 21	0.0 (± 0.3)			
d 28	0.2 (± 1.3)			
d 63	0.5 (± 1.7)			
d 100	0.2 (± 0.7)			
m 6	2.6 (± 6.0)			
y 1	9.2 (± 10.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Reconstitution - memory Treg

End point title Reconstitution - memory Treg

End point description:

End point type Secondary

End point timeframe:

day 7, 14, 21, 28, 63, 100, m 6, y 1

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	60			
Units: cells/microlitre				
arithmetic mean (standard deviation)				
d 7	0.1 (± 0.3)			
d 14	1.0 (± 3.0)			
d 21	4.1 (± 10.1)			
d 28	4.3 (± 8.9)			
d 63	9.2 (± 14.3)			
d 100	10.8 (± 11.8)			
m 6	11.9 (± 10.1)			
y 1	23.2 (± 15.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - CD34+ CD45+ cells

End point title CliniMACS performance - CD34+ CD45+ cells

End point description:

End point type Secondary

End point timeframe:

day 0 to day 2

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29	30	59	
Units: x 10 ⁶ cells/kg BW				
arithmetic mean (standard deviation)	17.9 (± 10.9)	9.5 (± 4.1)	13.6 (± 9.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - CD20+ cells

End point title	CliniMACS performance - CD20+ cells
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29	30	59	
Units: x10 ⁵ cells/kg BW				
arithmetic mean (standard deviation)	0.7 (± 0.5)	0.6 (± 1.3)	17.4 (± 13.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - CD56+ CD16+ cells

End point title	CliniMACS performance - CD56+ CD16+ cells
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29	30	59	
Units: $\times 10^6$ cells/kg BW				
arithmetic mean (standard deviation)	74.6 (\pm 49.8)	42.1 (\pm 18.5)	58.1 (\pm 40.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - CD3+ cells

End point title	CliniMACS performance - CD3+ cells
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29	30	59	
Units: $\times 10^6$ cells/kg BW				
arithmetic mean (standard deviation)	15.4 (\pm 12.5)	9.8 (\pm 7.7)	12.5 (\pm 10.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: CliniMACS performance - WBCs or CD45+ cells

End point title	CliniMACS performance - WBCs or CD45+ cells
End point description:	
End point type	Secondary
End point timeframe:	
day 0 to day 2	

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	29	30	59	
Units: $\times 10^8$ cells				
arithmetic mean (standard deviation)	4.5 (\pm 3.1)	3.9 (\pm 2.0)	4.2 (\pm 2.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Transfusion - New treatment with cellular product, day 100

End point title	Transfusion - New treatment with cellular product, day 100
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End point description:

End point type	Secondary
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End point timeframe:

only transfusions with start date \leq 105 days after first PBSC infusion are included

End point values	Pediatric cohort	Adult cohort	Safety Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	30	30	60	
Units: patients with new infusions				
erythrocytes	14	29	43	
thrombocytes	30	30	60	
DLI	1	0	1	
Other	18	2	20	
second transplantation	4	3	7	
Antigen-specific T cell infusions	2	0	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events collected during total study period (from Visit 1 to Visit 18)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	Total
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Reporting group description: -

Reporting group title	Adults
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Reporting group description: -

Reporting group title	Children
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Reporting group description: -

Serious adverse events	Total	Adults	Children
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 60 (90.00%)	28 / 30 (93.33%)	26 / 30 (86.67%)
number of deaths (all causes)	23	9	14
number of deaths resulting from adverse events	22	9	13
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	4 / 60 (6.67%)	0 / 30 (0.00%)	4 / 30 (13.33%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Acute myeloid leukaemia recurrent			
subjects affected / exposed	7 / 60 (11.67%)	4 / 30 (13.33%)	3 / 30 (10.00%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 6	0 / 3	0 / 3
Kaposi's sarcoma			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukaemia recurrent			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Malignant pleural effusion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyosarcoma			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Rhabdomyosarcoma recurrent			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Vascular disorders			
Aortitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microangiopathy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive disease			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
General disorders and administration site conditions			

Disease progression			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Acute graft versus host disease in skin			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cell-mediated immune deficiency			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic graft versus host disease			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic graft versus host disease in intestine			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic graft versus host disease in liver			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytokine release syndrome			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Engraftment syndrome			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 2
Dyspnoea			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obliterative bronchiolitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	5 / 60 (8.33%)	3 / 30 (10.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	1 / 6	1 / 4	0 / 2
deaths causally related to treatment / all	1 / 2	1 / 2	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus test positive			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

White blood cell count decreased subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Engraft failure			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative fever			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transplant failure			
subjects affected / exposed	10 / 60 (16.67%)	3 / 30 (10.00%)	7 / 30 (23.33%)
occurrences causally related to treatment / all	8 / 10	3 / 3	5 / 7
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			

subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	1 / 3	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Neurological symptom			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Paraesthesia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune thrombocytopenic purpura			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Blindness			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Hepatitis acute			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis exfoliative			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenoviral hepatitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenoviral upper respiratory infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	14 / 60 (23.33%)	3 / 30 (10.00%)	11 / 30 (36.67%)
occurrences causally related to treatment / all	11 / 24	4 / 4	7 / 20
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 3
Aspergillus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical mycobacterial infection			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BK virus infection			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral septic infarct			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cerebral toxoplasmosis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus hepatitis			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	5 / 60 (8.33%)	3 / 30 (10.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	6 / 11	6 / 8	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis viral			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	4 / 60 (6.67%)	2 / 30 (6.67%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 influenza			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex pneumonia			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	3 / 4	3 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human herpesvirus 6 infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Listeriosis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			

subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis enterococcal			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningococcal infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papilloma viral infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal infection			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 60 (8.33%)	3 / 30 (10.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	1 / 5	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia adenoviral			

subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pneumonia bacterial			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	6 / 60 (10.00%)	5 / 30 (16.67%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	3 / 6	3 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonas infection			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	5 / 60 (8.33%)	1 / 30 (3.33%)	4 / 30 (13.33%)
occurrences causally related to treatment / all	2 / 5	1 / 1	1 / 4
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Sinobronchitis			

subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection bacterial			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxoplasmosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	5 / 60 (8.33%)	2 / 30 (6.67%)	3 / 30 (10.00%)
occurrences causally related to treatment / all	0 / 8	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 60 (1.67%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 60 (3.33%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Total	Adults	Children
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 60 (100.00%)	30 / 30 (100.00%)	30 / 30 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia recurrent			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	3	2	1
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	2
Hypertension			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Hypotension			

subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	4	3	1
Jugular vein thrombosis			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Catheter site erythema			
subjects affected / exposed	12 / 60 (20.00%)	7 / 30 (23.33%)	5 / 30 (16.67%)
occurrences (all)	14	8	6
Catheter site pain			
subjects affected / exposed	9 / 60 (15.00%)	7 / 30 (23.33%)	2 / 30 (6.67%)
occurrences (all)	9	7	2
Catheter site swelling			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	2
Chest pain			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	5	4	1
Chills			
subjects affected / exposed	11 / 60 (18.33%)	4 / 30 (13.33%)	7 / 30 (23.33%)
occurrences (all)	12	4	8
Fatigue			
subjects affected / exposed	21 / 60 (35.00%)	12 / 30 (40.00%)	9 / 30 (30.00%)
occurrences (all)	24	13	11
General physical health deterioration			
subjects affected / exposed	5 / 60 (8.33%)	3 / 30 (10.00%)	2 / 30 (6.67%)
occurrences (all)	5	3	2
Inflammation			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	3	2	1
Mucosal inflammation			

subjects affected / exposed	44 / 60 (73.33%)	21 / 30 (70.00%)	23 / 30 (76.67%)
occurrences (all)	51	26	25
Oedema			
subjects affected / exposed	4 / 60 (6.67%)	2 / 30 (6.67%)	2 / 30 (6.67%)
occurrences (all)	4	2	2
Oedema peripheral			
subjects affected / exposed	18 / 60 (30.00%)	15 / 30 (50.00%)	3 / 30 (10.00%)
occurrences (all)	19	16	3
Pain			
subjects affected / exposed	8 / 60 (13.33%)	5 / 30 (16.67%)	3 / 30 (10.00%)
occurrences (all)	9	6	3
Pyrexia			
subjects affected / exposed	48 / 60 (80.00%)	22 / 30 (73.33%)	26 / 30 (86.67%)
occurrences (all)	85	36	49
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	14 / 60 (23.33%)	6 / 30 (20.00%)	8 / 30 (26.67%)
occurrences (all)	22	12	10
Acute graft versus host disease in skin			
subjects affected / exposed	12 / 60 (20.00%)	4 / 30 (13.33%)	8 / 30 (26.67%)
occurrences (all)	17	5	12
Chronic graft versus host disease			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	6	4	2
Drug hypersensitivity			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	3	0	3
Engraftment syndrome			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	2
Graft versus host disease			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	7	3	4
Graft versus host disease in skin			

subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 11	3 / 30 (10.00%) 6	4 / 30 (13.33%) 5
Reproductive system and breast disorders Vulvovaginal erythema subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 30 (0.00%) 0	2 / 30 (6.67%) 2
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	25 / 60 (41.67%) 31	13 / 30 (43.33%) 16	12 / 30 (40.00%) 15
Dry throat subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	2 / 30 (6.67%) 2	1 / 30 (3.33%) 1
Epistaxis subjects affected / exposed occurrences (all)	13 / 60 (21.67%) 16	9 / 30 (30.00%) 12	4 / 30 (13.33%) 4
Oropharyngeal pain subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 6	3 / 30 (10.00%) 3	3 / 30 (10.00%) 3
Pharyngeal erythema subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	1 / 30 (3.33%) 1	2 / 30 (6.67%) 2
Pleural effusion subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Productive cough subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Psychiatric disorders Depressed mood subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	2 / 30 (6.67%) 2	2 / 30 (6.67%) 2
Depression			

subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Hallucination			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Insomnia			
subjects affected / exposed	6 / 60 (10.00%)	3 / 30 (10.00%)	3 / 30 (10.00%)
occurrences (all)	6	3	3
Panic attack			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	2
Restlessness			
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Sleep disorder			
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Investigations			
Adenovirus test positive			
subjects affected / exposed	7 / 60 (11.67%)	2 / 30 (6.67%)	5 / 30 (16.67%)
occurrences (all)	7	2	5
Alanine aminotransferase increased			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Blood bilirubin increased			
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
C-reactive protein increased			

subjects affected / exposed	13 / 60 (21.67%)	9 / 30 (30.00%)	4 / 30 (13.33%)
occurrences (all)	21	15	6
Cytomegalovirus test positive			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Enterococcus test positive			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	3	2	1
Haemoglobin decreased			
subjects affected / exposed	3 / 60 (5.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	3	1	2
Hepatic enzyme increased			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	3	2	1
Lymphocyte count decreased			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Neutrophil count decreased			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	3	0	3
Protein total decreased			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	3	0	3
Weight decreased			
subjects affected / exposed	7 / 60 (11.67%)	3 / 30 (10.00%)	4 / 30 (13.33%)
occurrences (all)	7	3	4
White blood cell count decreased			
subjects affected / exposed	6 / 60 (10.00%)	1 / 30 (3.33%)	5 / 30 (16.67%)
occurrences (all)	6	1	5
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	3 / 60 (5.00%)	0 / 30 (0.00%)	3 / 30 (10.00%)
occurrences (all)	3	0	3
Cardiac disorders			

Tachycardia subjects affected / exposed occurrences (all)	18 / 60 (30.00%) 21	10 / 30 (33.33%) 11	8 / 30 (26.67%) 10
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	8 / 60 (13.33%) 10	5 / 30 (16.67%) 7	3 / 30 (10.00%) 3
Dysgeusia subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	3 / 30 (10.00%) 3	1 / 30 (3.33%) 1
Headache subjects affected / exposed occurrences (all)	24 / 60 (40.00%) 35	14 / 30 (46.67%) 19	10 / 30 (33.33%) 16
Hypoaesthesia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	3 / 30 (10.00%) 3	0 / 30 (0.00%) 0
Neuropathy peripheral subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 30 (0.00%) 0	2 / 30 (6.67%) 2
Paraesthesia subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	2 / 30 (6.67%) 2	2 / 30 (6.67%) 2
Polyneuropathy subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	2 / 30 (6.67%) 2	1 / 30 (3.33%) 1
Febrile neutropenia			

subjects affected / exposed	5 / 60 (8.33%)	4 / 30 (13.33%)	1 / 30 (3.33%)
occurrences (all)	6	5	1
Leukopenia			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	6	5	1
Neutropenia			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	4	3	1
Pancytopenia			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Thrombocytopenia			
subjects affected / exposed	5 / 60 (8.33%)	4 / 30 (13.33%)	1 / 30 (3.33%)
occurrences (all)	5	4	1
Eye disorders			
Dry eye			
subjects affected / exposed	6 / 60 (10.00%)	4 / 30 (13.33%)	2 / 30 (6.67%)
occurrences (all)	6	4	2
Eyelid oedema			
subjects affected / exposed	4 / 60 (6.67%)	2 / 30 (6.67%)	2 / 30 (6.67%)
occurrences (all)	4	2	2
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Abdominal pain			
subjects affected / exposed	31 / 60 (51.67%)	11 / 30 (36.67%)	20 / 30 (66.67%)
occurrences (all)	50	16	34
Abdominal pain upper			
subjects affected / exposed	9 / 60 (15.00%)	6 / 30 (20.00%)	3 / 30 (10.00%)
occurrences (all)	11	8	3
Constipation			
subjects affected / exposed	6 / 60 (10.00%)	3 / 30 (10.00%)	3 / 30 (10.00%)
occurrences (all)	7	4	3
Diarrhoea			

subjects affected / exposed	32 / 60 (53.33%)	21 / 30 (70.00%)	11 / 30 (36.67%)
occurrences (all)	42	28	14
Dry mouth			
subjects affected / exposed	7 / 60 (11.67%)	4 / 30 (13.33%)	3 / 30 (10.00%)
occurrences (all)	7	4	3
Dyspepsia			
subjects affected / exposed	4 / 60 (6.67%)	3 / 30 (10.00%)	1 / 30 (3.33%)
occurrences (all)	4	3	1
Dysphagia			
subjects affected / exposed	9 / 60 (15.00%)	7 / 30 (23.33%)	2 / 30 (6.67%)
occurrences (all)	9	7	2
Flatulence			
subjects affected / exposed	2 / 60 (3.33%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	2	0	2
Gastrointestinal pain			
subjects affected / exposed	2 / 60 (3.33%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 60 (5.00%)	3 / 30 (10.00%)	0 / 30 (0.00%)
occurrences (all)	3	3	0
Haematemesis			
subjects affected / exposed	3 / 60 (5.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	3	2	1
Nausea			
subjects affected / exposed	41 / 60 (68.33%)	23 / 30 (76.67%)	18 / 30 (60.00%)
occurrences (all)	63	33	30
Oesophagitis			
subjects affected / exposed	5 / 60 (8.33%)	2 / 30 (6.67%)	3 / 30 (10.00%)
occurrences (all)	5	2	3
Stomatitis			
subjects affected / exposed	10 / 60 (16.67%)	5 / 30 (16.67%)	5 / 30 (16.67%)
occurrences (all)	11	6	5
Vomiting			
subjects affected / exposed	41 / 60 (68.33%)	19 / 30 (63.33%)	22 / 30 (73.33%)
occurrences (all)	75	29	46
Hepatobiliary disorders			

Hepatotoxicity subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	2 / 30 (6.67%) 2	1 / 30 (3.33%) 1
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	2 / 30 (6.67%) 2	1 / 30 (3.33%) 1
Drug eruption subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 4	0 / 30 (0.00%) 0	2 / 30 (6.67%) 4
Erythema subjects affected / exposed occurrences (all)	16 / 60 (26.67%) 20	6 / 30 (20.00%) 6	10 / 30 (33.33%) 14
Hyperhidrosis subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 6	3 / 30 (10.00%) 3	3 / 30 (10.00%) 3
Petechiae subjects affected / exposed occurrences (all)	11 / 60 (18.33%) 12	7 / 30 (23.33%) 7	4 / 30 (13.33%) 5
Pruritus subjects affected / exposed occurrences (all)	18 / 60 (30.00%) 24	6 / 30 (20.00%) 9	12 / 30 (40.00%) 15
Pruritus allergic subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 30 (0.00%) 0	2 / 30 (6.67%) 3
Pruritus generalised subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 7	1 / 30 (3.33%) 1	6 / 30 (20.00%) 6
Rash subjects affected / exposed occurrences (all)	19 / 60 (31.67%) 22	11 / 30 (36.67%) 12	8 / 30 (26.67%) 10
Rash erythematous subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Rash macular			

subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 30 (0.00%) 0	2 / 30 (6.67%) 2
Rash maculo-papular subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 8	1 / 30 (3.33%) 1	6 / 30 (20.00%) 7
Rash pruritic subjects affected / exposed occurrences (all)	15 / 60 (25.00%) 15	5 / 30 (16.67%) 5	10 / 30 (33.33%) 10
Skin hyperpigmentation subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 7	4 / 30 (13.33%) 5	1 / 30 (3.33%) 2
Oliguria subjects affected / exposed occurrences (all)	10 / 60 (16.67%) 10	3 / 30 (10.00%) 3	7 / 30 (23.33%) 7
Renal failure subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 30 (0.00%) 0	2 / 30 (6.67%) 2
Renal impairment subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	1 / 30 (3.33%) 1	2 / 30 (6.67%) 2
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 7	4 / 30 (13.33%) 7	0 / 30 (0.00%) 0
Bone pain subjects affected / exposed occurrences (all)	11 / 60 (18.33%) 13	7 / 30 (23.33%) 9	4 / 30 (13.33%) 4
Musculoskeletal pain subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 8	4 / 30 (13.33%) 5	3 / 30 (10.00%) 3
Myalgia			

subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	2 / 30 (6.67%) 2	1 / 30 (3.33%) 1
Pain in extremity subjects affected / exposed occurrences (all)	12 / 60 (20.00%) 14	6 / 30 (20.00%) 7	6 / 30 (20.00%) 7
Spinal pain subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	3 / 30 (10.00%) 3	0 / 30 (0.00%) 0
Infections and infestations			
Adenovirus infection subjects affected / exposed occurrences (all)	6 / 60 (10.00%) 6	0 / 30 (0.00%) 0	6 / 30 (20.00%) 6
BK virus infection subjects affected / exposed occurrences (all)	8 / 60 (13.33%) 8	3 / 30 (10.00%) 3	5 / 30 (16.67%) 5
Candida infection subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	2 / 30 (6.67%) 2	2 / 30 (6.67%) 2
Clostridium difficile infection subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	0 / 30 (0.00%) 0	2 / 30 (6.67%) 3
Conjunctivitis subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	2 / 30 (6.67%) 3	0 / 30 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Cytomegalovirus infection subjects affected / exposed occurrences (all)	11 / 60 (18.33%) 13	9 / 30 (30.00%) 10	2 / 30 (6.67%) 3
Cytomegalovirus viraemia subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 7	6 / 30 (20.00%) 6	1 / 30 (3.33%) 1
Febrile infection subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	0 / 30 (0.00%) 0	3 / 30 (10.00%) 3

Gastroenteritis adenovirus subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	1 / 30 (3.33%) 1	2 / 30 (6.67%) 2
Human herpesvirus 6 infection subjects affected / exposed occurrences (all)	19 / 60 (31.67%) 20	10 / 30 (33.33%) 10	9 / 30 (30.00%) 10
Infection subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	3 / 30 (10.00%) 3	1 / 30 (3.33%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	2 / 30 (6.67%) 2	0 / 30 (0.00%) 0
Oral candidiasis subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4	3 / 30 (10.00%) 3	1 / 30 (3.33%) 1
Rhinitis subjects affected / exposed occurrences (all)	11 / 60 (18.33%) 11	4 / 30 (13.33%) 4	7 / 30 (23.33%) 7
Sepsis subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	1 / 30 (3.33%) 1	2 / 30 (6.67%) 2
Sinusitis subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 4	1 / 30 (3.33%) 1	2 / 30 (6.67%) 3
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3	1 / 30 (3.33%) 1	2 / 30 (6.67%) 2
Metabolism and nutrition disorders			
Cachexia subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 2	0 / 30 (0.00%) 0	2 / 30 (6.67%) 2
Decreased appetite subjects affected / exposed occurrences (all)	12 / 60 (20.00%) 12	10 / 30 (33.33%) 10	2 / 30 (6.67%) 2
Hypokalaemia			

subjects affected / exposed	11 / 60 (18.33%)	3 / 30 (10.00%)	8 / 30 (26.67%)
occurrences (all)	12	3	9
Malnutrition			
subjects affected / exposed	9 / 60 (15.00%)	4 / 30 (13.33%)	5 / 30 (16.67%)
occurrences (all)	9	4	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 December 2013	<p>Amendment I:</p> <ol style="list-style-type: none"> 1. Donor suitability was specified more clearly and inclusion of patients for whom an HLA-identical donor was available but haploidentical HSCT was considered to be in the patient's best interest for medical reasons was allowed. Medical reasons were defined as, e.g., medical urgency of transplantation or a high risk of relapse for patients with a history of previous HSCT. Wording of inclusion criteria 2 and 3 was changed accordingly. 2. In the safety outcome objective and parameter referring to mortality wording was changed from TRM to NRM. The rationale for this change was that NRM is the term recommended by the European group for Blood and Marrow transplantation. TRM and NRM are closely related, therefore, this change does not compromise interpretation of study results. It was implemented throughout the protocol wherever applicable. 3. Timing of donor consent was specified more precisely. In some cases (e.g., if the donor lived far away) it had been very difficult to obtain the study-specific consent and the blood sample of the donor prior to enrollment of the patient and at one visit. However, it had to be ensured that conditioning of the patient was not started before the donor had signed the study-specific consent form. Wording was changed accordingly in all relevant sections. 4. The schedule for anti-allergic prophylaxis in patients receiving ATG Fresenius S during conditioning was allowed to be performed according to hospital routine of study centers and adapted to the individual patient's needs. 5. Recommendations regarding prophylaxis of viral, bacterial and fungal infections were changed to allow for different hospital routines at the study centers. Furthermore, required eCRF documentation was changed to give more details. 6. Laboratory assessments: A number of procedural changes regarding performance of laboratory assessments were implemented 7. Assessment of cell chimerism after transplantation: procedural changes were implemented
10 March 2014	<p>Amendment II:</p> <ol style="list-style-type: none"> 1. Provisions were included to account for the risk of graft failure arising of the presence of donor-specific anti-HLA-antibodies in patients. It was recommended to choose an alternative donor in case of positive cross-match results. If no alternative donor was available and the apheresis product from a donor with positive cross-match results had to be used, treatment against donor-specific anti-HLA-antibodies (e.g., with rituximab, plasmapheresis) before SCT was highly recommended to improve the chances for successful donor engraftment. 2. Initially, adult patients with therapy-refractory disease were not allowed to be treated with ATG Fresenius S for conditioning. Instead use of TNI (7 Gy on Day -1) was mandatory. This was changed to enable investigator's decision on the best course for the individual patient and application of TNI according to hospital routine. 3. In some study centers G-CSF was administered to shorten duration of neutropenia after conditioning. The benefit of this treatment, however, was controversial. Therefore, and to ensure comparability of outcomes, a strong recommendation not to administer G-CSF was added. 4. Handling of patients receiving another HSCT for treatment of graft failure or relapse had not been defined in previous protocol versions. It was therefore regulated that in case a second HSCT from the same or an alternative donor for the treatment of graft failure or relapse was to be performed patients were to be considered as having discontinued the study prematurely and an early termination visit was to be performed. Nevertheless, safety monitoring of the patients had to be ensured and SAE follow-up was to be performed according to protocol until the regular final follow-up visit after two years. 5. Laboratory assessments: A number of procedural changes regarding performance of laboratory assessments were implemented 6. Assessment of cell chimerism after transplantation: Procedural changes were implemented.

12 September 2014	<p>Amendment III:</p> <ol style="list-style-type: none"> 1. The number of study centers was adjusted. 2. Assessment of donor chimerism by PCR analysis of bone marrow samples was to be performed on samples of patients with hematological malignancies. 3. To account for the increased risk of graft failure in patients with non-malignant diseases cryopreservation of an autologous graft as potential back-up treatment in the case of graft failure was recommended. 4. Use of TNI according to hospital routine in chemotherapy-naïve patients and patients with non-malignant diseases, except of patients with immunodeficiencies was allowed independent of their state of remission according to investigator's assessment of the most appropriate approach for each patient. Rationale for this change was the observation that in patients with an increased risk of graft failure, graft rejection can be overcome by more intensified conditioning regimens, e.g., using TNI. 5. Following occurrence of four cases of graft failure in patients receiving ATG Fresenius S during conditioning it was decided to increase the dose of ATG Fresenius S to 30 mg/kg BW in total. Rationale of this change were previous clinical experiences and results of an ATG kinetic study showing that an increase of the ATG dose to 30 mg/kg BW led to higher maximum ATG serum concentrations on Day -8 while returning to ATG serum concentrations on Day 0 comparable to those observed after administration of 15 mg/kg BW. 6. Clarification of procedures in case a patient receives another HSCT for treatment of graft failure or relapse. 7. Laboratory assessments: A number of procedural changes regarding performance of laboratory assessments were implemented 8. Clarification that routine local assessment of cell chimerism was to be performed for patients with hematological malignancies, only.
21 May 2015	<p>Amendment IV:</p> <ol style="list-style-type: none"> 1. Exclusion criterion 8 was changed to account for differences in clinical routine for adult and pediatric patients. The ejection fraction is measured in adult patients according to hospital routine but not routinely in pediatric patients. Therefore, assessment of the shortening fraction to monitor cardiac function was added as alternative for pediatric patients. 2. The definition of the term "screening failure" was specified in more detail as "patient who had a screening examination (Visit 1), but who for any reason did not receive the IMP. 3. The sentence demanding temperature monitoring and documentation during transport in case of transport time longer than 10 minutes was deleted. Transport had to follow local routine practice and monitoring was to be performed according to local standard. 4. Conditioning was to be adjusted to account for medical needs of patients with a BMI <18 or >25 according to the adapted body surface area calculations as per center routine. 5. Regulations of SAE reporting were clarified. Rationale for this change was that a high number of SAEs was expected throughout the trial because of the life-threatening indications included. The majority of SAEs occurring after Day 100 was expected to be related to disease progress and not to IMP administration. Since such SAEs do not provide additional information on IMP safety documentation and reporting of all SAEs observed was to be limited to the main part of the trial ending with Visit XIV. During the follow-up phases SAEs were to be documented, but only SARs were to be reported to the sponsor. 6. Documentation of concomitant medication during follow-up phases was changed because patients included in the study received a large variety of medication due to the various morbidities of the underlying diseases. During follow-up concomitant medication required for treatment of SARs, only, was to be documented.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported