



Clinical trial results: Cyclophosphamide as graft-versus-host prophylaxis after allogeneic stem cell transplantation for multiple myeloma. A phase II study.

Summary

EudraCT number	2016-002557-38
Trial protocol	DE
Global end of trial date	01 December 2022

Results information

Result version number	v1 (current)
This version publication date	09 October 2026
First version publication date	09 October 2026
Summary attachment (see zip file)	Summary results (Allo-MM-PostCy-Study Synopsis CSR 2025_03_26.pdf)

Trial information

Trial identification

Sponsor protocol code	Allo-MM-PostCy-Study
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03700450
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Center Hamburg Eppendorf
Sponsor organisation address	Martinistr. 52, Hamburg, Germany, 20246
Public contact	Study Investigator, Department of Stem Cell Transplantation University Medical Center Hamburg-Eppendorf, bmt@uke.de
Scientific contact	Study Investigator, Department of Stem Cell Transplantation University Medical Center Hamburg-Eppendorf, bmt@uke.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	01 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2022
Global end of trial reached?	Yes
Global end of trial date	01 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of the study is chronic GvHD and progression-free survival at 2 years after transplantation.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines, the general principles indicated in the Declaration of Helsinki, and all applicable regulatory requirements. Prior to study initiation the study protocol was reviewed and approved by an Independent Ethics Committee (IEC). The study, all study procedures and the risks and benefits were explained to the subjects by responsible investigators and written informed consent were collected prior to any study related examinations.

A clinical monitor visited the Investigator at regular time intervals during the course of the study to review the progress and conduct of the study and verifies the protection of subject's rights and safety.

Background therapy:

Graft Source for Allogeneic SCT: Peripheral blood stem cells (PBSC) or bone marrow stem cells (BM)

The patient received the following conditioning regime before SCT:

< 60 years of age: thiotepa 2 x 5 mg/kg BW, busulfan 3 x 3.2 mg/kg BW a day

> 60 years of age: thiotepa 2 x 5 mg/kg BW, busulfan 2 x 3.2 mg/kg BW a day

In case of haploidentical transplantation additional fludarabine 5 x 30 mg/m² was given.

Busulfan was administered as intravenous application once daily. Anti-epileptic drug should have been used to prevent seizure with busulfan. Fludarabine at a dose of 30 mg/m² was given intravenously as short infusion from day -6 to day -2.

Evidence for comparator: -

Actual start date of recruitment	10 April 2018
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: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	35
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in Germany. 3 active study centers were involved.

Pre-assignment

Screening details:

Screening period: up to 28 days before Day 0 (Allo SCT)

Main Inclusion Criteria: Multiple myeloma newly diagnosed with deletion 17p or translocation 4;14 or multiple myeloma with 1. or 2. relapse after auto SCT; Patients age: 18 - 65 years; ECOG $\leq$ 2;

Availability of haploidentical, matched or mismatched relative or unrelated donor

Pre-assignment period milestones

Number of subjects started	36
Number of subjects completed	36

Period 1

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

Blinding implementation details:

unblinded, all patients received on day 3 and 4 after allogeneic stem cell transplantation (day 0) 50 mg/kg BW cyclophosphamide.

Arms

Arm title	additional GvHD prophylaxis: Cyclophosphamid
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Arm description:

cyclophosphamide 50 mg/kg BW at day +3 and day +4 and as outlined:

- in case of haploidentical SCT/MMRD: plus tacrolimus (day +5 until +180) and MMF (day +5 until day +35)
- in case of MUD: plus cyclosporine A (day +5 until +120) and MMF (day +5 until day +35)
- in case of MMUD: plus cyclosporine A (day +5 until +180) and MMF (day +5 until day +35)
- in case of MRD: plus cyclosporine A (day +5 until +120)

Arm type	Experimental
Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	not applicable, since Cyclophosphamide was applied
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dose: 2 x 50 mg/kg body weight (BW) on day +3 and +4 after allo SCT

Mode of administration: intravenously (iv)

Number of subjects in period 1	additional GvHD prophylaxis: Cyclophosphamid
Started	36
Completed	26
Not completed	10
Adverse event, serious fatal	9
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	36	36	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	34	34	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	53.2		
standard deviation	± 7.1	-	
Gender categorical			
Safety Population			
Units: Subjects			
Female	14	14	
Male	22	22	
Results of cytogenic abnormalities			
Units: Subjects			
Normal	3	3	
Abnormalities	26	26	
Missing data	7	7	
Specifications of abnormalities			
Units: Subjects			
Translocation t(4; 14) (alone or with further abn.	5	5	
Deletion 17p (del17p) (alone or with further abn.	2	2	
both: t(4;14), del17p	1	1	
+1q21 (alone or with further abnormalities)	6	6	
Other abnormalities	12	12	
Missing data	10	10	
Relapse after 1. autologous stem cell transplantation			
Units: Subjects			
Yes	26	26	
No	10	10	

Relapse after 2. autologous stem cell transplantation Units: Subjects			
Yes	6	6	
No	3	3	
NA	27	27	
Number of patients of previous auto SCT (autograft)			
The value for "Number 2.auto SCT" is "9", not "0". Due to a system error, the value could not be entered. Error message: "The total number of subjects for all categories in the study specific categorical characteristic are not the same as the total number of subjects in the baseline period. Ensure the number of subjects recorded for the categories account for all subjects in the baseline period". However, the value "9" is correct, as these patients receive both the first and the second SCT.			
Units: Subjects			
1. auto SCT	36	36	
2. auto SCT	0	0	
Relationship between stem cell donor and recipient Units: Subjects			
MRD	6	6	
MUD	22	22	
MMUD	4	4	
MMRD	0	0	
Haploidentical	4	4	
Sorrow Risk Score Units: Subjects			
<= 3	33	33	
> 3	3	3	
Conditioning age group			
unit Thiotepe and Busulfan: mg/ Kg body weight i.v.			
Units: Subjects			
> 60 years: Thiotepe (2x5mg), Busulfan (2x3.2mg)	6	6	
<= 60 years: Thiotepe (2x5mg), Busulfan (3x3.2mg)	30	30	
ECOG status at study inclusion Units: Subjects			
Fully active	18	18	
Restricted in physically strenuous activity	17	17	
Ambulatory and capable of all self-care	1	1	
Capable of only limited self-care	0	0	
Completely disabled	0	0	
Dead	0	0	
Type of Myeloma Units: Subjects			
IgG	19	19	
IgA	11	11	
IgD	0	0	
IgE	0	0	
Light Chain	6	6	
nonsecretory	0	0	
Time from auto SCT to relapse (<= 12 months vs >12 months)			

Units: Subjects			
<= 12 months	9	9	
>12 months	16	16	
Missing	11	11	
Time from auto SCT to relapse (<= 15 months vs >15 months)			
Units: Subjects			
<= 15 months	12	12	
>15 months	13	13	
Missing	11	11	
Age median			
Units: Years			
median	54.0		
full range (min-max)	35 to 66	-	

End points

End points reporting groups

Reporting group title	additional GvHD prophylaxis: Cyclophosphamid
Reporting group description:	
cyclophosphamide 50 mg/kg BW at day +3 and day +4 and as outlined:	
- in case of haploidentical SCT/MMRD: plus tacrolimus (day +5 until +180) and MMF (day +5 until day +35)	
- in case of MUD: plus cyclosporine A (day +5 until +120) and MMF (day +5 until day +35)	
- in case of MMUD: plus cyclosporine A (day +5 until +180) and MMF (day +5 until day +35)	
- in case of MRD: plus cyclosporine A (day +5 until +120)	

Primary: Chronic GvHD and progression-free survival at 2 years after allogeneic SCT

End point title	Chronic GvHD and progression-free survival at 2 years after allogeneic SCT ^[1]
End point description:	
Efficacy analyses will be done using the FAP population (and possibly additionally the PPP population). All statistical tests, including the statistical test of the primary efficacy endpoint, will be two-sided at a significance level of 5%. All reported confidence intervals will be two-sided with confidence level 95%. Chronic GvHD and progression-free survival is defined as the probability of being alive with no sign of relapse or progression and without any chronic GvHD of grade 'moderate' or 'severe'. The associated time span is defined as the interval from Day 0 to relapse or progression or death due to any cause or chronic GvHD of grade 'moderate' or 'severe', whatever comes first. To compare cGRFS at 2 years after allogeneic SCT between the single arm 'MultMyelom' of this study and historical reference data, a two-sided z-test with a 5.0% significance level will be performed and the corresponding two-sided p-value will be presented.	
End point type	Primary
End point timeframe:	
2 years after 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: Please refer to "End point description"

End point values	additional GvHD prophylaxis: Cyclophosphamid			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Proportion				
number (confidence interval 95%)				
2 years after SCT	0.389 (0.258 to 0.586)			
1 year from start of salvage therapy	0.846 (0.718 to 0.997)			
2 years from start of salvage therapy	0.615 (0.454 to 0.834)			

Attachments (see zip file)	Chronic GvHD and progression-free survival /Allo-MM-PostCy-
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Statistical analyses

No statistical analyses for this end point

Secondary: Non-relapse mortality (NRM) at 2 years after allogeneic SCT

End point title	Non-relapse mortality (NRM) at 2 years after allogeneic SCT
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End point description:

Non-relapse mortality will be defined as the probability of dying without previous occurrence of a relapse or progressive disease. The associated time span is defined as the interval from date of SCT (Day 0) (Database: f_allo-sct: i_tx-sct-date) to death, without previous relapse or progressive disease. Relapse or progressive disease is considered a competing event with the associated time span from date of SCT (Day 0) to relapse or progressive disease. Patients alive without relapse or progressive disease are censored

at last contact. A patient experienced a relapse/progressive disease (first relapse/progressive disease) if the documented response status at any time is relapse/progressive disease. Cumulative incidence functions will be estimated for the competing events

- relapse (first relapse) or progressive disease (first progressive disease)
- death before any relapse/progressive disease

for treatment arm 'MultMyelom' over 2 years after allo-SCT. The NRM rate as well as the

End point type	Secondary
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End point timeframe:

2 years after allogeneic SCT

End point values	additional GvHD prophylaxis: Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Proportion				
number (confidence interval 95%)				
100 days: Non-relapse mortality	0.111 (0.035 to 0.238)			
100 days: Relapse	0.000 (0 to 0)			
1 year: Non-relapse mortality	0.111 (0.035 to 0.238)			
1 year: Relapse	0.139 (0.050 to 0.273)			
2 years: Non-relapse mortality	0.111 (0.035 to 0.238)			
2 years: Relapse	0.472 (0.301 to 0.626)			

Attachments (see zip file)	NRM at 2 year after allogeneic SCT/Allo-MM-PostCy-Study
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Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of acute GvHD on Day +100 after allogeneic SCT

End point title	Incidence of acute GvHD on Day +100 after allogeneic SCT
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End point description:

Incidence of acute GvHD of grade II-IV until Day +100 after allogeneic SCT: Incidence of acute GvHD of grade II-IV until Day +100 after allogeneic SCT will be defined as the probability of experiencing any acute GvHD event of grade II-IV within 100 days after allogeneic SCT. The associated time span is defined as the interval from date of SCT (Day 0)

End point type	Secondary
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End point timeframe:

Day +100 after allogeneic SCT

End point values	additional GvHD prophylaxis: Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Proportion				
number (confidence interval 95%)				
Acute GvHD of grade II-IV (100 days)	0.111 (0.034 to 0.238)			
Death before acute GvHD of grade II-IV (100 days)	0.083 (0.021 to 0.203)			
Acute GvHD of grade III/IV (100 days)	0.056 (0.010 to 0.165)			
Death before acute GvHD of grade III-IV (100days)	0.083 (0.021 to 0.203)			

Attachments (see zip file)	Incidence of acute GvHD/Allo-MM-PostCy-Study Secondary
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Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of chronic GvHD at 1 and 2 years after allogeneic SCT

End point title	Incidence of chronic GvHD at 1 and 2 years after allogeneic SCT
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End point description:

Incidence of chronic GvHD until 1 year (2 years) after allogeneic SCT will be defined as the probability of experiencing any chronic GvHD event within 1 year (2 years) after allogeneic SCT. The associated time span is defined as the interval from date of SCT (Day 0) to the first chronic GvHD event.

End point type	Secondary
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End point timeframe:

1 and 2 years after allogeneic SCT

End point values	additional GvHD prophylaxis: Cyclophospha mid			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Proportion				
number (confidence interval 95%)				
1 year: chronic GvHD	0.417 (0.253 to 0.573)			
1 year: Death before chronic GvHD	0.194 (0.084 to 0.339)			
2 years: Chronic GvHD	0.417 (0.253 to 0.573)			
2 years: Death before chronic GvHD	0.222 (0.102 to 0.371)			

Attachments (see zip file)	Incidence of chronic GvHD/Allo-MM-PostCy-Study Secondary
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Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity according to NCI

End point title	Toxicity according to NCI
End point description:	
P1: Study period until first IMP intake	
P2: Study period after IMP intake	
The endpoint '5. Toxicity according to NCI' will be evaluated as a safety endpoint.	
End point type	Secondary
End point timeframe:	
entire study period	

End point values	additional GvHD prophylaxis: Cyclophospha mid			
Subject group type	Reporting group			
Number of subjects analysed	33 ^[2]			
Units: Number of patients				
P1: Pts. with any AE of tox. grade III or higher	9			
P1: Pts. with severe AEs of tox. grade III or high	0			
P2: Pts. with any AE of tox. grade III or higher	27			
P2: Pts. with severe AEs of tox. grade III or high	2			

Notes:

[2] - Safety Population (SP): include all patients who are registered and received SCT.

Attachments (see zip file)	Toxicity according to NCI/Allo-MM-PostCy-Study Secondary
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Statistical analyses

No statistical analyses for this end point

Secondary: Complete remission rate (including sCR and MRD negativity)

End point title	Complete remission rate (including sCR and MRD negativity)
End point description: Incidence of complete remission or stringent complete remission until 1 year (2 years) after allogeneic SCT will be defined as the probability of experiencing complete remission or stringent complete remission within 1 year (2 years) after allogeneic SCT. The associated time span is defined as the interval from date of SCT (Day 0)) to complete remission or stringent complete remission, whatever comes first.	
End point type	Secondary
End point timeframe: entire study period	

End point values	additional GvHD prophylaxis: Cyclophospha mid			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Proportion				
number (confidence interval 95%)				
1 year: Complete remission (including sCR)	0.639 (0.454 to 0.775)			
1 year: Death before complete remission (incl. sCR)	0.139 (0.049 to 0.274)			
2 years: Complete remission (including sCR)	0.778 (0.593 to 0.886)			
2 years: Death before complete remission (inc. sCR)	0.139 (0.049 to 0.274)			

Attachments (see zip file)	Complete remission rate/Allo-MM-PostCy-Study Secondary
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Statistical analyses

No statistical analyses for this end point

Secondary: Overall and progression-free survival at 2 years

End point title	Overall and progression-free survival at 2 years
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End point description:

Overall survival (OS) will be defined as the probability of surviving a specific time. Survival time is defined as the time from Day 0 to death due to any cause.

Progression-free survival (PFS) is defined as the probability of being alive with no sign of relapse or progression. The associated time span is defined as the interval from Day 0 to relapse or progression or death due to any cause, whatever comes first. A relapse / progression, and death from any cause will be considered an event. Patients alive without progression or relapse are censored at the last time without indication of an event.

Firstly, the Kaplan-Meier estimate for the survivor function will be calculated to assess the progression-free survival rate for treatment group 'MultMyelom' at 2 years after allogeneic

SCT. Secondly, the standard error for this survival rate will be calculated using Greenwood's formula.

The survival rate for treatment group 'MultMyelom' at 2 years after allogeneic SCT [...]

End point type	Secondary
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End point timeframe:

2 years

End point values	additional GvHD prophylaxis: Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	36			
Units: Proportion				
number (confidence interval 95%)				
Overall Survival 1 year after SCT	0.806 (0.686 to 0.946)			
Overall Survival 2 years after SCT	0.722 (0.590 to 0.884)			
Progression-free Survival 1 year after SCT	0.750 (0.621 to 0.906)			
Progression-free Survival 2 years after SCT	0.417 (0.283 to 0.613)			

Attachments (see zip file)	Overall and progression-free survival at 2 years/Allo-MM-
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs CTCAE grade 3-5 were collected and recorded in the eCRF from the time point of signed informed consent until the end of the study. Exceptions were defined by protocol.

Adverse event reporting additional description:

Immediate SAE reporting (within 24h) until 28d after SCT.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Adverse events - Period 1 (until first IMP intake)
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Reporting group description:

Period 1= from date of eligibility to date of first intake of IMP. This includes SCT and days 1 and 2 after Allo SCT as per protocol flow chart. The number "Subjects affected by serious adverse events": 0 is incorrect but must be provided due to an system error. Only AEs are presented.

Reporting group title	Adverse events - Period 2 (after IMP intake)
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Reporting group description:

Period 2= from date of first intake of IMP until end of study visit. The number "Subjects affected by serious adverse events": 0 is incorrect but must be provided due to an system error. Only AEs are presented.

Serious adverse events	Adverse events - Period 1 (until first IMP intake)	Adverse events - Period 2 (after IMP intake)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	
number of deaths (all causes)	4	10	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adverse events - Period 1 (until first IMP intake)	Adverse events - Period 2 (after IMP intake)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 36 (41.67%)	33 / 36 (91.67%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Any			
subjects affected / exposed	0 / 36 (0.00%)	6 / 36 (16.67%)	
occurrences (all)	0	6	

Vascular disorders Any subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	5 / 36 (13.89%) 5	
General disorders and administration site conditions Any subjects affected / exposed occurrences (all) Mucosal inflammation subjects affected / exposed occurrences (all) Prexia subjects affected / exposed occurrences (all)	5 / 36 (13.89%) 5 3 / 36 (8.33%) 3 3 / 36 (8.33%) 3	17 / 36 (47.22%) 17 13 / 36 (36.11%) 13 10 / 36 (27.78%) 10	
Immune system disorders Any subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 36 (5.56%) 2	
Investigations Any subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	7 / 36 (19.44%) 7	
Injury, poisoning and procedural complications Any subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	2 / 36 (5.56%) 2	
Nervous system disorders Any subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	4 / 36 (11.11%) 4	
Blood and lymphatic system disorders Any	Additional description: The statistician did not specify the number of affected subjects, but only the number of events/ occurrences. However, due to a system error, this entry is required. Therefore, the same number as that for the "occurrences all number" was entered.		
subjects affected / exposed occurrences (all) Anemia	4 / 36 (11.11%) 4	4 / 36 (11.11%) 4	

subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	2 / 36 (5.56%) 2	
Febrile Neutropenia subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	1 / 36 (2.78%) 1	
Gastrointestinal disorders Any subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2	5 / 36 (13.89%) 5	
Diarrhoe subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	3 / 36 (8.33%) 3	
Hepatobiliary disorders Any subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	3 / 36 (8.33%) 3	
Renal and urinary disorders Any subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	5 / 36 (13.89%) 5	
Infections and infestations Any subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3	20 / 36 (55.56%) 20	
Atypical pneumonia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	3 / 36 (8.33%) 3	
Cytomegalovirus infection reactivation subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 1	5 / 36 (13.89%) 5	
Pneumonia subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	3 / 36 (8.33%) 3	
Metabolism and nutrition disorders Any			

subjects affected / exposed	0 / 36 (0.00%)	5 / 36 (13.89%)	
occurrences (all)	0	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported