Clinical trial results:
Autologous-Allogeneic Tandem Stem Cell Transplantation and Maintenance Therapy with Thalidomide / DLI for patients with Multiple Myeloma (MM) and age <= 60 years: A phase II-study

Summary

EudraCT number	2007-004928-21
Trial protocol	DE
Global end of trial date	17 April 2018

Results information

Result version number	v1 (current)
This version publication date	22 October 2022
First version publication date	22 October 2022
Summary attachment (see zip file)	Auto-Allo TSCT in MM_Integrated Study Report - Synopsis V1.0 2020-04-07, signed (Auto-Allo TSCT in MM_Integrated Study Report - Synopsis V1.0 2020-04-07, signed.pdf)

Trial information

Trial identification

Sponsor protocol code	Auto-Allo-TSCT in MM

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00777998
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department of Stem Cell Transplantation, University Medical Center Hamburg-Eppendorf
Sponsor organisation address	Martinistrasse 52, Hamburg, Germany, 20246
Public contact	Coordinating Principal Investigator, Prof. Dr. Nicolaus Kröger, Department of Stem Cell Transplantation, University Medical Center Eppendorf, +49 40741054850, nkroeger@uke.uni-hamburg.de
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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	15 April 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Event-free survival four years after auto-allo tandem-transplantation and maintenance therapy with thalidomide in comparison to those patients without a suitable donor, who will receive tandem autologous stem cell transplantation followed by thalidomide maintenance therapy.
Any of the following occurrences will be considered an endpoint event:
•recurrence or progression of the primary disease,
•disease related mortality, or
•treatment related mortality.

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 and authorized investigators and written informed consent were collected prior to any study related examinations. The patientes were assured maximum confidentiality of their data. The information was guided by the Patient Information Form and the Declaration of Consent provided in German language. The patients were to be given sufficient time for decision-making. Patient's participation in the study was entirely voluntary and could be revoked at any time without having to specify a reason and without adversely affecting their further therapy.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2008
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: 217
Worldwide total number of subjects	217
EEA total number of subjects	217

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	217
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed in 20 active hospital sites in Germany (3 additional centers participated but did not enroll any patients).
Recruitment period: May 2008 - May 2013

Pre-assignment

Screening details:

Inclusion: myeloma stage II or III according to Salmon and Durie, age between 18 and 60 years, and a maximum of 8 cycles chemotherapy prior to registration independently of the response

Exclusion: more than 8 cycles chemotherapy, severe irreversible renal, hepatic, pulmonary, or cardiac diseases, positive serology for HIV, and prior transplant

Pre-assignment period milestones

Number of subjects started	178[1]
Number of subjects completed	178

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: Enrolled were total of 217 patients before first autogologous transplant. Before first autograft, 3 patients died, 1 experienced screening failure, 4 patients were excluded due to patient or investigator decision, and 1 patient because of missing data.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1

Arm description:

Tandem autologous

Arm type	Active comparator
Investigational medicinal product name	Autologous hematopoietic stem cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Infusion of autologous hematopoietic stem cells, dosage depends of amount of cells collected from the patient

Arm title	Arm 2

Arm description:

tandem autologous-allogeneic

Arm type	Active comparator

Investigational medicinal product name	Allogeneic hematopoietic stem cells
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Infusion of allogeneic hematopoietic stem cells, dosage depends on amount of donated stem cells

Number of subjects in period 1[2]	Arm 1	Arm 2
Started	46	132
Completed	46	132

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: From 217 initially included patients 208 received first autograft, of whom then 132 received second allogeneic transplant and 46 a second autograft. Before second transplant, 30 patients withdrew, of whom 3 died, 5 withdrew from consent, 4 had progressive disease, 12 re excluded due to patient or investigator decision, 2 were lost to follow-up, and 4 patients were excluded due to unknown reasons.

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1
Reporting group description: Tandem autologous	
Reporting group title	Arm 2
Reporting group description: tandem autologous-allogeneic	

Reporting group values	Arm 1	Arm 2	Total
Number of subjects	46	132	178
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
Age continuous Units: years			
median	53	51	
full range (min-max)	34 to 61	26 to 61	-
Gender categorical Units: Subjects			
Female	19	74	93
Male	27	58	85

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description: Tandem autologous	
Reporting group title	Arm 2
Reporting group description: tandem autologous-allogeneic	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: The Full Analysis data set (FAS) include all patients who were included in the safety analysis. However, a blinded analysis meeting was authorized to decide whether any study participants had to be excluded from the FAS in cases of very severe protocol violations that prevented a valid assessment of treatment efficacy.	

Primary: Progression-free survival

End point title	Progression-free survival
End point description:	
End point type	Primary
End point timeframe: 4-years	

End point values	Arm 1	Arm 2	Full analysis	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	46	132	0[1]	
Units: year				
number (confidence interval 95%)	35 (21 to 49)	47 (38 to 55)	(to)	

Notes:

[1] - only results for comparators reported

Statistical analyses

Statistical analysis title	PFS
Comparison groups	Arm 1 v Arm 2
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Logrank
Parameter estimate	Median difference (final values)
Point estimate	12

Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	17
Variability estimate	Standard deviation
Dispersion value	6

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from the time of informed consent until end of study.

Only SAEs that were observed in at least three patients are shown in this report.

Adverse event reporting additional description:

A total of 12 SAEs reported by 12 patients in the Auto-Allo group (12.0% of 100 who received thalidomide after the second SCT) and four SAEs reported by three patients in the Auto-Auto group (7.9% of 28 who received thalidomide) were assessed to be potentially related to thalidomide by the local investigators.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Auto-Allo TCST group
Reporting group description: -	
Reporting group title	Auto-Auto TSCT group

Reporting group description: -

Serious adverse events	Auto-Allo TCST group	Auto-Auto TSCT group	
Total subjects affected by serious adverse events			
subjects affected / exposed	103 / 132 (78.03%)	32 / 46 (69.57%)	
number of deaths (all causes)	45	15	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Recurrence or persistence of primary disease	Additional description: Plasma Cell Myeloma		
subjects affected / exposed	17 / 132 (12.88%)	8 / 46 (17.39%)	
occurrences causally related to treatment / all	0 / 17	0 / 8	
deaths causally related to treatment / all	0 / 12	0 / 8	
Surgical and medical procedures			
Surgery			
subjects affected / exposed	2 / 132 (1.52%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			

subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Mucosal inflammation			
subjects affected / exposed	5 / 132 (3.79%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	5 / 132 (3.79%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	24 / 132 (18.18%)	3 / 46 (6.52%)	
occurrences causally related to treatment / all	0 / 26	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 132 (1.52%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	10 / 132 (7.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	1 / 10	0 / 0	
deaths causally related to treatment / all	0 / 7	0 / 0	
Graft versus host disease in gastrointestinal tract			

subjects affected / exposed	4 / 132 (3.03%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 132 (7.58%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 12	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 132 (0.76%)	2 / 46 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute kidney injury			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteolysis			

subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection			
subjects affected / exposed	9 / 132 (6.82%)	4 / 46 (8.70%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 8	0 / 0	
Pneumonia			
subjects affected / exposed	12 / 132 (9.09%)	8 / 46 (17.39%)	
occurrences causally related to treatment / all	0 / 16	1 / 8	
deaths causally related to treatment / all	0 / 2	0 / 0	
Sepsis			
subjects affected / exposed	9 / 132 (6.82%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 10	0 / 0	
deaths causally related to treatment / all	0 / 8	0 / 0	
Bronchitis			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	4 / 132 (3.03%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	3 / 132 (2.27%)	0 / 46 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	4 / 132 (3.03%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			

subjects affected / exposed	2 / 132 (1.52%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 132 (1.52%)	1 / 46 (2.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Auto-Allo TCST group	Auto-Auto TSCT group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 132 (98.48%)	46 / 46 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma	Additional description: Recurrence or persistence of primary disease		
subjects affected / exposed	26 / 132 (19.70%)	9 / 46 (19.57%)	
occurrences (all)	28	11	
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 132 (12.88%)	2 / 46 (4.35%)	
occurrences (all)	28	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 132 (9.85%)	6 / 46 (13.04%)	
occurrences (all)	16	8	
Mucosal inflammation			
subjects affected / exposed	47 / 132 (35.61%)	25 / 46 (54.35%)	
occurrences (all)	68	35	
Oedema peripheral			
subjects affected / exposed	19 / 132 (14.39%)	6 / 46 (13.04%)	
occurrences (all)	29	6	
Pyrexia			
subjects affected / exposed	49 / 132 (37.12%)	15 / 46 (32.61%)	
occurrences (all)	78	17	
Pain			

subjects affected / exposed	5 / 132 (3.79%)	3 / 46 (6.52%)	
occurrences (all)	5	3	
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	9 / 132 (6.82%)	1 / 46 (2.17%)	
occurrences (all)	10	1	
Hypersensitivity			
subjects affected / exposed	7 / 132 (5.30%)	1 / 46 (2.17%)	
occurrences (all)	7	1	
Graft versus host disease in skin			
subjects affected / exposed	11 / 132 (8.33%)	0 / 46 (0.00%)	
occurrences (all)	12	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 132 (10.61%)	1 / 46 (2.17%)	
occurrences (all)	16	1	
Dyspnoea			
subjects affected / exposed	9 / 132 (6.82%)	1 / 46 (2.17%)	
occurrences (all)	11	1	
Dyspnoea exertional			
subjects affected / exposed	4 / 132 (3.03%)	3 / 46 (6.52%)	
occurrences (all)	5	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 132 (6.06%)	2 / 46 (4.35%)	
occurrences (all)	9	2	
Investigations			
Blood creatinine increased			
subjects affected / exposed	13 / 132 (9.85%)	0 / 46 (0.00%)	
occurrences (all)	14	0	
Blood potassium decreased			
subjects affected / exposed	3 / 132 (2.27%)	3 / 46 (6.52%)	
occurrences (all)	5	3	
C-reactive protein increased			
subjects affected / exposed	5 / 132 (3.79%)	4 / 46 (8.70%)	
occurrences (all)	6	4	

Gamma-glutamyltransferase increased			
subjects affected / exposed	9 / 132 (6.82%)	1 / 46 (2.17%)	
occurrences (all)	11	1	
Weight increased			
subjects affected / exposed	3 / 132 (2.27%)	3 / 46 (6.52%)	
occurrences (all)	4	3	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 132 (2.27%)	3 / 46 (6.52%)	
occurrences (all)	4	3	
Nervous system disorders			
Headache			
subjects affected / exposed	23 / 132 (17.42%)	7 / 46 (15.22%)	
occurrences (all)	25	9	
Paraesthesia			
subjects affected / exposed	7 / 132 (5.30%)	4 / 46 (8.70%)	
occurrences (all)	12	5	
Peripheral sensory neuropathy			
subjects affected / exposed	9 / 132 (6.82%)	5 / 46 (10.87%)	
occurrences (all)	10	6	
Polyneuropathy			
subjects affected / exposed	36 / 132 (27.27%)	13 / 46 (28.26%)	
occurrences (all)	54	22	
Hypoaesthesia			
subjects affected / exposed	3 / 132 (2.27%)	4 / 46 (8.70%)	
occurrences (all)	3	4	
Neuropathy peripheral			
subjects affected / exposed	2 / 132 (1.52%)	4 / 46 (8.70%)	
occurrences (all)	2	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	17 / 132 (12.88%)	3 / 46 (6.52%)	
occurrences (all)	25	6	
Febrile neutropenia			
subjects affected / exposed	30 / 132 (22.73%)	12 / 46 (26.09%)	
occurrences (all)	45	20	

Neutropenia			
subjects affected / exposed	12 / 132 (9.09%)	2 / 46 (4.35%)	
occurrences (all)	16	2	
Pancytopenia			
subjects affected / exposed	7 / 132 (5.30%)	0 / 46 (0.00%)	
occurrences (all)	8	0	
Thrombocytopenia			
subjects affected / exposed	17 / 132 (12.88%)	6 / 46 (13.04%)	
occurrences (all)	24	8	
Febrile bone marrow aplasia			
subjects affected / exposed	19 / 132 (14.39%)	11 / 46 (23.91%)	
occurrences (all)	29	18	
Leukopenia			
subjects affected / exposed	6 / 132 (4.55%)	4 / 46 (8.70%)	
occurrences (all)	6	7	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	13 / 132 (9.85%)	4 / 46 (8.70%)	
occurrences (all)	15	6	
Abdominal pain upper			
subjects affected / exposed	8 / 132 (6.06%)	2 / 46 (4.35%)	
occurrences (all)	8	2	
Constipation			
subjects affected / exposed	16 / 132 (12.12%)	14 / 46 (30.43%)	
occurrences (all)	21	16	
Diarrhoea			
subjects affected / exposed	55 / 132 (41.67%)	25 / 46 (54.35%)	
occurrences (all)	80	34	
Gastritis			
subjects affected / exposed	7 / 132 (5.30%)	3 / 46 (6.52%)	
occurrences (all)	7	3	
Nausea			
subjects affected / exposed	26 / 132 (19.70%)	5 / 46 (10.87%)	
occurrences (all)	35	7	
Stomatitis			

subjects affected / exposed	8 / 132 (6.06%)	1 / 46 (2.17%)	
occurrences (all)	9	1	
Vomiting			
subjects affected / exposed	9 / 132 (6.82%)	3 / 46 (6.52%)	
occurrences (all)	14	4	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	7 / 132 (5.30%)	4 / 46 (8.70%)	
occurrences (all)	8	6	
Pruritus			
subjects affected / exposed	7 / 132 (5.30%)	1 / 46 (2.17%)	
occurrences (all)	8	1	
Rash			
subjects affected / exposed	28 / 132 (21.21%)	12 / 46 (26.09%)	
occurrences (all)	42	17	
Drug eruption			
subjects affected / exposed	0 / 132 (0.00%)	3 / 46 (6.52%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	7 / 132 (5.30%)	1 / 46 (2.17%)	
occurrences (all)	7	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	15 / 132 (11.36%)	3 / 46 (6.52%)	
occurrences (all)	16	3	
Back pain			
subjects affected / exposed	15 / 132 (11.36%)	9 / 46 (19.57%)	
occurrences (all)	16	11	
Bone pain			
subjects affected / exposed	8 / 132 (6.06%)	2 / 46 (4.35%)	
occurrences (all)	8	2	
Muscle spasms			
subjects affected / exposed	13 / 132 (9.85%)	4 / 46 (8.70%)	
occurrences (all)	15	6	
Pain in extremity			

subjects affected / exposed	9 / 132 (6.82%)	5 / 46 (10.87%)	
occurrences (all)	10	6	
Spinal pain			
subjects affected / exposed	1 / 132 (0.76%)	3 / 46 (6.52%)	
occurrences (all)	1	3	
Infections and infestations			
Bronchitis			
subjects affected / exposed	15 / 132 (11.36%)	5 / 46 (10.87%)	
occurrences (all)	21	5	
Cytomegalovirus infection			
subjects affected / exposed	28 / 132 (21.21%)	0 / 46 (0.00%)	
occurrences (all)	34	0	
Epstein-Barr virus infection			
subjects affected / exposed	11 / 132 (8.33%)	1 / 46 (2.17%)	
occurrences (all)	13	1	
Herpes zoster			
subjects affected / exposed	20 / 132 (15.15%)	6 / 46 (13.04%)	
occurrences (all)	22	6	
Infection			
subjects affected / exposed	17 / 132 (12.88%)	11 / 46 (23.91%)	
occurrences (all)	21	15	
Nasopharyngitis			
subjects affected / exposed	40 / 132 (30.30%)	9 / 46 (19.57%)	
occurrences (all)	50	10	
Pneumonia			
subjects affected / exposed	23 / 132 (17.42%)	15 / 46 (32.61%)	
occurrences (all)	34	15	
Sepsis			
subjects affected / exposed	14 / 132 (10.61%)	2 / 46 (4.35%)	
occurrences (all)	15	2	
Sinusitis			
subjects affected / exposed	7 / 132 (5.30%)	1 / 46 (2.17%)	
occurrences (all)	7	1	
Cystitis			
subjects affected / exposed	5 / 132 (3.79%)	3 / 46 (6.52%)	
occurrences (all)	5	4	

Oral candidiasis			
subjects affected / exposed	6 / 132 (4.55%)	3 / 46 (6.52%)	
occurrences (all)	6	4	
Urinary tract infection			
subjects affected / exposed	3 / 132 (2.27%)	3 / 46 (6.52%)	
occurrences (all)	3	3	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	11 / 132 (8.33%)	5 / 46 (10.87%)	
occurrences (all)	14	7	

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