



Clinical trial results:

Optimising Renal outcome in Myeloma renal failure

A pilot study of Thalidomide, Bendamustine, and Dexamethasone (TBD) vs Bortezomib, Bendamustine, and Dexamethasone (BBD) in patients with renal failure defined as a GFR below 30 mls/ min.

Summary

EudraCT number	2012-003947-31
Trial protocol	GB
Global end of trial date	20 April 2020

Results information

Result version number	v1 (current)
This version publication date	23 May 2021
First version publication date	23 May 2021

Trial information

Trial identification

Sponsor protocol code	26866138-MMY2070
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Additional study identifiers

ISRCTN number	ISRCTN32505664
ClinicalTrials.gov id (NCT number)	NCT02424851
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Oxford University Hospitals NHS Foundation Trust
Sponsor organisation address	Research & Development Department, Joint Research Office, Block 60, Churchill Hospital, Oxford, United Kingdom, OX3 7LE
Public contact	Dr Karthik Ramasamy, Oxford University Hospitals NHS Trust, 44 01865235882, kramasamy@nhs.net
Scientific contact	Dr Karthik Ramasamy, Oxford University Hospitals NHS Trust, 44 01865235882, kramasamy@nhs.net

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 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2020
Global end of trial reached?	Yes
Global end of trial date	20 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives is to compare the amount of serum free light chain circulating in the body, the rate of renal recovery and overall survival in response to two cycles of therapy with either thalidomide or bortezomib in patients presenting with myeloma and renal failure.

The co-primary objective is to determine if the response to treatment of the myeloma tumour burden is mirrored in the renal response at the end of cycle 4.

Protection of trial subjects:

tbc

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 31
Worldwide total number of subjects	31
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	29
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

In total 88 patients were screened for the trial, of which 31 patients were consented and randomised across 7 sites in the UK by the 9th March 2019.

Pre-assignment

Screening details:

In total 88 patients were screened for the trial, 57 patients were screen failures. Most frequent reasons for screen failure were participant fragility or renal function improvement.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Bortezomib, Bendamustine and Dexamethasone

Arm description:

Bortezomib, Bendamustine and Dexamethasone

Arm type	Active comparator
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3 mg/m²

Arm title	Thalidomide, Bendamustine and Dexamethasone
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Arm description:

Thalidomide, Bendamustine and Dexamethasone

Arm type	Experimental
Investigational medicinal product name	Thalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

2.5 mg/ml

Number of subjects in period 1	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone
Started	16	15
Completed	16	15

Baseline characteristics

Reporting groups

Reporting group title	Bortezomib, Bendamustine and Dexamethasone
Reporting group description: Bortezomib, Bendamustine and Dexamethasone	
Reporting group title	Thalidomide, Bendamustine and Dexamethasone
Reporting group description: Thalidomide, Bendamustine and Dexamethasone	

Reporting group values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone	Total
Number of subjects	16	15	31
Age categorical Units: Subjects			
70 years and under	8	8	16
Over 70 years	8	7	15
Gender categorical Units: Subjects			
Female	8	6	14
Male	8	9	17

End points

End points reporting groups

Reporting group title	Bortezomib, Bendamustine and Dexamethasone
Reporting group description:	Bortezomib, Bendamustine and Dexamethasone
Reporting group title	Thalidomide, Bendamustine and Dexamethasone
Reporting group description:	Thalidomide, Bendamustine and Dexamethasone

Primary: Serum Free Light Chain Response to Treatment - Defined as >50% Reduction From Baseline in sFLC

End point title	Serum Free Light Chain Response to Treatment - Defined as >50% Reduction From Baseline in sFLC
End point description:	
End point type	Primary
End point timeframe:	End of week 6 (after receiving two cycles of therapy)

End point values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	14		
Units: Participants	13	3		

Statistical analyses

Statistical analysis title	Primary outcome 1
Comparison groups	Bortezomib, Bendamustine and Dexamethasone v Thalidomide, Bendamustine and Dexamethasone
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.006
Method	Fisher exact

Primary: Renal Response to Treatment Using the International Myeloma Working Group (IMWG) Renal Response Criteria

End point title	Renal Response to Treatment Using the International Myeloma
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End point description:

End point type Primary

End point timeframe:

End of week 12 (after receiving 4 cycles of therapy)

End point values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: Participants				
Complete/partial response	5	1		
Minor response	3	7		
No response	3	1		
Not evaluable	5	6		

Statistical analyses

Statistical analysis title	Primary outcome 2
Comparison groups	Bortezomib, Bendamustine and Dexamethasone v Thalidomide, Bendamustine and Dexamethasone
Number of subjects included in analysis	31
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.02
Method	Fisher exact

Secondary: Overall survival

End point title Overall survival

End point description:

End point type Secondary

End point timeframe:

1 month post end of treatment and 1 year post randomisation

End point values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: Participants	9	13		

Statistical analyses

Statistical analysis title	Secondary outcome 2
Comparison groups	Bortezomib, Bendamustine and Dexamethasone v Thalidomide, Bendamustine and Dexamethasone
Number of subjects included in analysis	31
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.31
Method	Logrank

Secondary: Haematological and Non-haematological Toxicity in Both Treatment Arms

End point title	Haematological and Non-haematological Toxicity in Both Treatment Arms
End point description:	
End point type	Secondary
End point timeframe:	
End of weeks 3, 6, 9, 12 (after receiving 4 cycles of therapy), 30 days after final treatment and 12 months after randomisation	

End point values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	15		
Units: Events				
Serious adverse events	2	0		
Adverse events	3	6		

Statistical analyses

Statistical analysis title	Secondary outcome 4
Comparison groups	Bortezomib, Bendamustine and Dexamethasone v Thalidomide, Bendamustine and Dexamethasone
Number of subjects included in analysis	31
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.48 ^[1]
Method	Fisher exact

Notes:

[1] - No statistically significant differences were detected between SAEs or AEs by treatment arm, Fisher's Exact p=0.48 and p=0.25 respectively.

Secondary: Comparison of Renal Response, Using the IMWG Renal Response Criteria, at the End of the Second and Fourth Cycles of Therapy

End point title	Comparison of Renal Response, Using the IMWG Renal Response Criteria, at the End of the Second and Fourth Cycles of Therapy
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End point description:

End point type	Secondary
End point timeframe:	
End of weeks 6 and 12	

End point values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: Participants				
Partial response	2	0		
Minor response	9	7		
No response	4	6		

Statistical analyses

Statistical analysis title	Secondary outcome 3
Comparison groups	Bortezomib, Bendamustine and Dexamethasone v Thalidomide, Bendamustine and Dexamethasone
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.45
Method	Fisher exact

Secondary: Quality of Life Measured by the EQ-5D-3L Questionnaire

End point title	Quality of Life Measured by the EQ-5D-3L Questionnaire
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End point description:

End point type	Secondary
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End point timeframe:

End of week 1 cycles 1-4 and at 1 month follow up

End point values	Bortezomib, Bendamustine and Dexamethasone	Thalidomide, Bendamustine and Dexamethasone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0.72 (± 0.15)	0.69 (± 0.35)		
1 month follow up	0.69 (± 0.19)	0.80 (± 0.28)		

Statistical analyses

Statistical analysis title	Secondary outcome 5
Comparison groups	Bortezomib, Bendamustine and Dexamethasone v Thalidomide, Bendamustine and Dexamethasone
Number of subjects included in analysis	17
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.33
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation to 30 days following last administration of IMP

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.0
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Reporting groups

Reporting group title	Bortezomib, bendamustine and dexamethasone
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Reporting group description: -

Reporting group title	Thalidomide, bendamustine and dexamethasone
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Reporting group description: -

Serious adverse events	Bortezomib, bendamustine and dexamethasone	Thalidomide, bendamustine and dexamethasone	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	9 / 15 (60.00%)	
number of deaths (all causes)	7	2	
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
fever			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Syncope			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischemic attacks			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vomiting			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematuria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bone infection			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 16 (6.25%)	3 / 15 (20.00%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper respiratory infection			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Bortezomib, bendamustine and dexamethasone	Thalidomide, bendamustine and dexamethasone	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 16 (93.75%)	11 / 15 (73.33%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
labial cyst			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Superficial thrombophlebitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Thromboembolic event			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Edema limbs			
subjects affected / exposed	4 / 16 (25.00%)	3 / 15 (20.00%)	
occurrences (all)	4	3	
Fatigue			
subjects affected / exposed	4 / 16 (25.00%)	5 / 15 (33.33%)	
occurrences (all)	4	9	
Infusion site extravasation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all) Laryngeal hemorrhage subjects affected / exposed occurrences (all) Dyspnea subjects affected / exposed occurrences (all) Upper respiratory infection subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0 1 / 16 (6.25%) 1 2 / 16 (12.50%) 2 2 / 16 (12.50%) 2 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0	1 / 15 (6.67%) 4 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1 1 / 16 (6.25%) 1	0 / 15 (0.00%) 0 0 / 15 (0.00%) 0	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Alkaline Phosphatase Increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0 0 / 16 (0.00%) 0	1 / 15 (6.67%) 1 1 / 15 (6.67%) 1	

Weight Loss subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 15 (6.67%) 1	
Neutrophil count decreased subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	2 / 15 (13.33%) 2	
Creatinine increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 15 (13.33%) 2	
White blood cell decreased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 15 (13.33%) 2	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	1 / 15 (6.67%) 1	
Cardiac disorders Left Ventricular systolic dysfunction subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Nervous system disorders Tremor subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	3 / 15 (20.00%) 4	
Syncope subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 15 (6.67%) 1	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	2 / 15 (13.33%) 5	

Paresthesia subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	3 / 15 (20.00%) 3	
Presyncope subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	3 / 15 (20.00%) 4	
Febrile neutropenia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Blurred vision subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
visual disturbance subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Gastrointestinal disorders Mucositis oral subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	1 / 15 (6.67%) 1	
Nausea subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 5	1 / 15 (6.67%) 1	
Diarrhoea			

subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 6	2 / 15 (13.33%) 3	
Constipation subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 11	3 / 15 (20.00%) 3	
Dysphagia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Oral Dysesthesia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Stomach pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 15 (13.33%) 2	
Skin and subcutaneous tissue disorders			
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	3 / 15 (20.00%) 8	
Skin ulceration subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 15 (0.00%) 0	
Skin infection subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 15 (6.67%) 1	
Dry skin subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Scalp pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Erythroderma subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Palmar-plantae erythrodysesthesia syndrome			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 15 (6.67%) 1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Chronic kidney disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chest wall pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Other			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Infections and infestations			
Bone infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Bronchial Infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Catheter related infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Enterocolitis infectious			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Mucosal infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Papulopustular rash			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Lung infection			
subjects affected / exposed	2 / 16 (12.50%)	3 / 15 (20.00%)	
occurrences (all)	5	5	
Unknown source			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Oral thrush			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hypokalemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hyperkalemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyponatremia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

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