Clinical trial results:
A Phase Ib/II, open-label, multicenter study of oral HDM201 in combination with oral LEE011 in adult patients with liposarcoma

Summary

EudraCT number	2014-003604-75
Trial protocol	ES DE FR
Global end of trial date	16 October 2019

Results information

Result version number	v1 (current)
This version publication date	02 October 2020
First version publication date	02 October 2020

Trial information

Trial identification

Sponsor protocol code	CHDM201X2103C

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02343172
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 614231111, novartis.email@novartis.com

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	16 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective for this trial was to determine the maximum tolerated dose (MTD) and/or the recommended phase two dose (RP2D) of HDM201 in combination with LEE011 in one or more of the pre-defined regimens

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 March 2015
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	Canada: 14
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Singapore: 6
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 6
Worldwide total number of subjects	74
EEA total number of subjects	48

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)	41
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study did not enter the initially planned phase 2 part.

Pre-assignment

Screening details:

Three different dosing regimen were tested : regimen 1, 4 and 5 (see detailed description for the definitions of these 3 different dosing regimen)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Regimen 1: 2.5mg HDM201+400mg LEE011

Arm description:

escalation

Arm type	escalation cohort
Investigational medicinal product name	HDM201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

HDM201 was supplied as capsules of dosage strengths of 2.5, 10 and 100 mg. This information applies for all dosing cohorts

Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

LEE011 was supplied as capsules of dosage strengths of 50 and 200 mg This information applies for all dosing cohorts

Arm title	Regimen 1: 5mg HDM201+400mg LEE011

Arm description:

escalation

Arm type	escalation cohort

No investigational medicinal product assigned in this arm

Arm title	Regimen 1: 10mg HDM201+400mg LEE011

Arm description:

escalation

Arm type	escalation cohort

No investigational medicinal product assigned in this arm

Arm title	Regimen 1: 15mg HDM201+400mg LEE011

Arm description:

escalation

Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 4: 50mg HDM201+400mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 4: 150mg HDM201+400mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 4: 200mg HDM201+400mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 4: 150mg HDM201+300mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 4: 120mg HDM201+200mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 5: 100mg HDM201+300mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 5: 120mg HDM201+300mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 5: 150mg HDM201+300mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 5: 200mg HDM201+300mg LEE011
Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	
Arm title	Regimen 5: 120mg HDM201+400mg LEE011

Arm description: escalation	
Arm type	escalation cohort
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Regimen 1: 2.5mg HDM201+400mg LEE011	Regimen 1: 5mg HDM201+400mg LEE011	Regimen 1: 10mg HDM201+400mg LEE011
Started	4	10	5
Completed	0	0	0
Not completed	4	10	5
Adverse event, serious fatal	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	-	1	-
progressive disease	4	9	4
Subject/guardian decision	-	-	1

Number of subjects in period 1	Regimen 1: 15mg HDM201+400mg LEE011	Regimen 4: 50mg HDM201+400mg LEE011	Regimen 4: 150mg HDM201+400mg LEE011
Started	7	4	11
Completed	0	0	0
Not completed	7	4	11
Adverse event, serious fatal	-	1	-
Physician decision	1	-	-
Adverse event, non-fatal	2	-	4
progressive disease	4	2	6
Subject/guardian decision	-	1	1

Number of subjects in period 1	Regimen 4: 200mg HDM201+400mg LEE011	Regimen 4: 150mg HDM201+300mg LEE011	Regimen 4: 120mg HDM201+200mg LEE011
Started	4	4	6
Completed	0	0	0
Not completed	4	4	6
Adverse event, serious fatal	-	-	-
Physician decision	-	1	-
Adverse event, non-fatal	2	1	-
progressive disease	2	2	6
Subject/guardian decision	-	-	-

Number of subjects in period 1	Regimen 5: 100mg HDM201+300mg LEE011	Regimen 5: 120mg HDM201+300mg LEE011	Regimen 5: 150mg HDM201+300mg LEE011

Started	4	6	4
Completed	0	0	0
Not completed	4	6	4
Adverse event, serious fatal	-	-	1
Physician decision	-	1	-
Adverse event, non-fatal	-	1	-
progressive disease	4	4	3
Subject/guardian decision	-	-	-

Number of subjects in period 1	Regimen 5: 200mg HDM201+300mg LEE011	Regimen 5: 120mg HDM201+400mg LEE011
Started	1	4
Completed	0	0
Not completed	1	4
Adverse event, serious fatal	-	-
Physician decision	-	-
Adverse event, non-fatal	1	2
progressive disease	-	2
Subject/guardian decision	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Regimen 1: 2.5mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 1: 5mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 1: 10mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 1: 15mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 50mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 150mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 200mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 150mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 120mg HDM201+200mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 100mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 120mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 150mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 200mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 120mg HDM201+400mg LEE011
Reporting group description: escalation	

Reporting group values	Regimen 1: 2.5mg HDM201+400mg LEE011	Regimen 1: 5mg HDM201+400mg LEE011	Regimen 1: 10mg HDM201+400mg LEE011
Number of subjects	4	10	5

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)	4	6	3
From 65-84 years	0	4	2
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	50.3	61.1	61.4
standard deviation	± 10.24	± 13.50	± 13.35
Sex: Female, Male Units: participants			
Female	1	3	4
Male	3	7	1
Race/Ethnicity, Customized Units: Subjects			
Asian	1	2	1
Caucasian	3	8	4
Unknown	0	0	0

Reporting group values	Regimen 1: 15mg HDM201+400mg LEE011	Regimen 4: 50mg HDM201+400mg LEE011	Regimen 4: 150mg HDM201+400mg LEE011
Number of subjects	7	4	11
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)	4	2	6
From 65-84 years	3	2	5
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	61.9	61.5	61.4
standard deviation	± 6.84	± 9.33	± 11.51
Sex: Female, Male Units: participants			
Female	3	2	2
Male	4	2	9

Race/Ethnicity, Customized Units: Subjects			
Asian	2	1	3
Caucasian	4	3	8
Unknown	1	0	0

Reporting group values	Regimen 4: 200mg HDM201+400mg LEE011	Regimen 4: 150mg HDM201+300mg LEE011	Regimen 4: 120mg HDM201+200mg LEE011
Number of subjects	4	4	6
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)	1	2	3
From 65-84 years	3	2	3
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	67.8	67.5	67.5
standard deviation	± 11.44	± 10.02	± 10.02
Sex: Female, Male Units: participants			
Female	4	1	2
Male	0	3	4
Race/Ethnicity, Customized Units: Subjects			
Asian	1	1	1
Caucasian	3	2	5
Unknown	0	1	0

Reporting group values	Regimen 5: 100mg HDM201+300mg LEE011	Regimen 5: 120mg HDM201+300mg LEE011	Regimen 5: 150mg HDM201+300mg LEE011
Number of subjects	4	6	4
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)	2	3	2
From 65-84 years	2	3	2
85 years and over	0	0	0

Age Continuous Units: years			
arithmetic mean	65.5	62.0	67.0
standard deviation	± 4.80	± 16.46	± 10.10
Sex: Female, Male Units: participants			
Female	1	3	3
Male	3	3	1
Race/Ethnicity, Customized Units: Subjects			
Asian	1	1	1
Caucasian	3	5	3
Unknown	0	0	0

Reporting group values	Regimen 5: 200mg HDM201+300mg LEE011	Regimen 5: 120mg HDM201+400mg LEE011	Total
Number of subjects	1	4	74
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	3	41
From 65-84 years	1	1	33
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	67.0	53.0	
standard deviation	± 0	± 10.95	-
Sex: Female, Male Units: participants			
Female	1	2	32
Male	0	2	42
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	17
Caucasian	1	3	55
Unknown	0	0	2

Subject analysis sets	
Subject analysis set title	2.5mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	5mg HDM201
Subject analysis set type	Sub-group analysis

Subject analysis set description: escalation	
Subject analysis set title	10mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	15mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	50mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	100mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	120mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	150mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	200mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	

Reporting group values	2.5mg HDM201	5mg HDM201	10mg HDM201
Number of subjects	4	9	5
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	1.5	3.1	4.1
standard deviation	±	±	±

Sex: Female, Male Units: participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Caucasian Unknown			

Reporting group values	15mg HDM201	50mg HDM201	100mg HDM201
Number of subjects	7	4	4
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	6.1	7.8	11
standard deviation	±	±	±
Sex: Female, Male Units: participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Caucasian Unknown			

Reporting group values	120mg HDM201	150mg HDM201	200mg HDM201
Number of subjects	15	18	5
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years			

85 years and over			

Age Continuous Units: years arithmetic mean standard deviation	 12 ±	 13 ±	 10 ±
Sex: Female, Male Units: participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
Asian Caucasian Unknown			

End points

End points reporting groups

Reporting group title	Regimen 1: 2.5mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 1: 5mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 1: 10mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 1: 15mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 50mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 150mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 200mg HDM201+400mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 150mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 4: 120mg HDM201+200mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 100mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 120mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 150mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 200mg HDM201+300mg LEE011
Reporting group description: escalation	
Reporting group title	Regimen 5: 120mg HDM201+400mg LEE011
Reporting group description: escalation	
Subject analysis set title	2.5mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	5mg HDM201

Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	10mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	15mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	50mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	100mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	120mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	150mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	
Subject analysis set title	200mg HDM201
Subject analysis set type	Sub-group analysis
Subject analysis set description: escalation	

Primary: Incidence of Dose Limiting Toxicities (DLTs) during the first cycle of treatment.

End point title	Incidence of Dose Limiting Toxicities (DLTs) during the first cycle of treatment.[1]
End point description: DLTs in the first cycle of treatment.	
End point type	Primary
End point timeframe: 5 years	

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: no statistical Analysis was performed

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	8	4	7
Units: participants				

Total	0	0	0	2
neutropenia	0	0	0	0
thrombocytopenia	0	0	0	0
anemia	0	0	0	0
platelet count decreased	0	0	0	2
neutrophil count decreased	0	0	0	1
white blood cell count decreased	0	0	0	0
Febrile neutropenia	0	0	0	0

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	11	4	4
Units: participants				
Total	0	4	3	1
neutropenia	0	2	1	0
thrombocytopenia	0	1	2	0
anemia	0	0	1	0
platelet count decreased	0	2	1	1
neutrophil count decreased	0	1	1	0
white blood cell count decreased	0	1	1	0
Febrile neutropenia	0	0	0	0

End point values	Regimen 4: 120mg HDM201+200 mg LEE011	Regimen 5: 100mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	6	3
Units: participants				
Total	1	0	0	2
neutropenia	0	0	0	1
thrombocytopenia	0	0	0	0
anemia	1	0	0	0
platelet count decreased	1	0	0	1
neutrophil count decreased	0	0	0	0
white blood cell count decreased	0	0	0	0
Febrile neutropenia	0	0	0	0

End point values	Regimen 5: 200mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: participants				
Total	1	2		
neutropenia	0	1		
thrombocytopenia	0	1		
anemia	0	0		
platelet count decreased	1	1		
neutrophil count decreased	1	0		
white blood cell count decreased	1	0		
Febrile neutropenia	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Exposure to HDM201 and LEE011 as measured by AUC 0-24h

End point title	Exposure to HDM201 and LEE011 as measured by AUC 0-

End point description:

as measured by AUC0-24h

End point type	Primary

End point timeframe:

5 years

Notes:

[2] - 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: no statistical Analysis was performed

[3] - 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: no statistical Analysis was performed

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	4	6
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
HDM201	267.2 (± 66.2)	587.6 (± 127.0)	1339.3 (± 14.8)	1458.2 (± 13.6)
LEE011	11290.0 (± 85.6)	5537.4 (± 138.1)	6314.2 (± 38.8)	3675.0 (± 21.8)

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	9	3	2
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
HDM201	6547.9 (± 47.2)	26066.2 (± 37.7)	45670.5 (± 20.4)	28307.2 (± 11.2)
LEE011	8669.1 (± 80.5)	8152.8 (± 64.6)	9006.9 (± 18.7)	5264.5 (± 17.7)

End point values	Regimen 4: 120mg HDM201+200 mg LEE011	Regimen 5: 100mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	4	4
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
HDM201	26294.4 (± 45.5)	22069.8 (± 31.9)	15473.7 (± 67.4)	36102.4 (± 96.6)
LEE011	3859.2 (± 70.7)	5958.0 (± 71.6)	3387.1 (± 88.8)	7259.2 (± 106.0)

End point values	Regimen 5: 120mg HDM201+400 mg LEE011			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng*hr/mL				
geometric mean (geometric coefficient of variation)				
HDM201	25249.2 (± 37.1)			
LEE011	11185.4 (± 67.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with dose interruptions and reduction

End point title	Number of patients with dose interruptions and reduction

End point description:

To assess tolerability of HDM201 in combination with LEE011

End point type	Secondary

End point timeframe:

5 years

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	5	7
Units: participants				
HDM201 at least 1 dose reduction	0	0	1	2
LEE011 at least 1 dose interruption	1	0	1	0
HDM201 at least 1 dose delay	3	5	3	5
LEE011 at least 1 dose delay	3	5	3	5

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	11	4	4
Units: participants				
HDM201 at least 1 dose reduction	0	7	2	3
LEE011 at least 1 dose interruption	0	2	1	2
HDM201 at least 1 dose delay	2	10	3	3
LEE011 at least 1 dose delay	2	11	4	3

End point values	Regimen 4: 120mg HDM201+200 mg LEE011	Regimen 5: 100mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	6	4
Units: participants				
HDM201 at least 1 dose reduction	3	0	3	0
LEE011 at least 1 dose interruption	0	0	0	0
HDM201 at least 1 dose delay	5	1	4	1
LEE011 at least 1 dose delay	5	1	5	3

End point values	Regimen 5: 200mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: participants				
HDM201 at least 1 dose reduction	1	1		

LEE011 at least 1 dose interruption	0	2		
HDM201 at least 1 dose delay	1	3		
LEE011 at least 1 dose delay	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose intensity

End point title	Dose intensity

End point description:

To assess tolerability of HDM201 in combination with LEE011 SD of 999999 means not evaluable (only 1 participant in the subgroup)

End point type	Secondary

End point timeframe:

5 years

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	5	7
Units: mg				
arithmetic mean (standard deviation)				
LEE011	411.5 (± 22.92)	384.0 (± 25.36)	368.0 (± 57.01)	374.5 (± 39.09)
HDM201	2.6 (± 0.16)	4.8 (± 0.31)	8.5 (± 2.41)	13.5 (± 2.28)

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	11	4	4
Units: mg				
arithmetic mean (standard deviation)				
LEE011	392.8 (± 13.14)	318.9 (± 60.72)	293.1 (± 141.34)	257.6 (± 29.31)
HDM201	67.9 (± 27.82)	116.3 (± 42.92)	159.8 (± 88.84)	113.1 (± 65.96)

End point values	Regimen 4: 120mg HDM201+200	Regimen 5: 100mg HDM201+300	Regimen 5: 120mg HDM201+300	Regimen 5: 150mg HDM201+300

	mg LEE011	mg LEE011	mg LEE011	mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	6	4
Units: mg				
arithmetic mean (standard deviation)				
LEE011	189.6 (± 14.15)	300.0 (± 0.00)	256.6 (± 46.62)	289.0 (± 21.95)
HDM201	117.7 (± 7.71)	181.3 (± 37.50)	131.8 (± 41.58)	275.0 (± 43.30)

End point values	Regimen 5: 200mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: mg				
arithmetic mean (standard deviation)				
LEE011	300.0 (± 999999)	338.4 (± 72.34)		
HDM201	128.6 (± 999999)	205.3 (± 60.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 1

End point title	Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 1[4]

End point description:

to evaluate PK parameters of HDM201 and LEE011

End point type	Secondary

End point timeframe:

day 1, day 14

Notes:

[4] - 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: no statistical Analysis was performed

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	8	5	6
Units: ng/mL				
geometric mean (geometric coefficient of variation)				

HDM201 day 1	21.0 (± 48.5)	41.0 (± 61.3)	92.4 (± 5.0)	107.3 (± 18.8)
LEE011 day 1	1117.2 (± 66.4)	664.2 (± 114.5)	609.6 (± 53.2)	459.5 (± 35.0)
HDM201 day 14	52.3 (± 88.7)	54.5 (± 62.5)	131.7 (± 52.4)	167.9 (± 36.0)
LEE011 Day 14	1581.6 (± 61.3)	635.8 (± 55.1)	609.9 (± 92.9)	447.0 (± 46.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 4

End point title	Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 4[5]

End point description:

to evaluate PK parameters of HDM201 and LEE011

End point type	Secondary

End point timeframe:

day 1, day 21

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: no statistical Analysis was performed

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	3	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	275.9 (± 30.6)	1277.6 (± 43.7)	1982.7 (± 34.4)	1475.9 (± 10.6)
LEE011 day 1	685.7 (± 80.9)	652.8 (± 88.5)	932.9 (± 25.9)	477.8 (± 24.8)
HDM201 day 21	201.2 (± 13.1)	991.9 (± 77.5)	2180.0 (± 0)	1320.0 (± 0)
LEE011 Day 21	516.0 (± 0)	0 (± 0)	2630.0 (± 0)	0 (± 0)

End point values	Regimen 4: 120mg HDM201+200 mg LEE011			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	1284.4 (± 33.7)			

LEE011 day 1	491.0 (± 84.3)			
HDM201 day 21	1412.5 (± 24.8)			
LEE011 Day 21	338.1 (± 36.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 5

End point title	Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 5[6]

End point description:

to evaluate PK parameters of HDM201 and LEE011

End point type	Secondary

End point timeframe:

day 1, day 28

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: no statistical Analysis was performed

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	3	4
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	1043.3 (± 62.1)	1103.1 (± 43.3)	1544.7 (± 70.2)	1180.4 (± 10.2)
LEE011 day 1	614.6 (± 63.4)	494.6 (± 88.5)	805.2 (± 72.5)	967.9 (± 89.0)
HDM201 day 28	1023.1 (± 33.5)	1010.7 (± 50.6)	1170.9 (± 50.5)	1170.1 (± 40.4)
LEE011 Day 28	533.9 (± 54.0)	465.6 (± 56.9)	613.0 (± 30.3)	547.1 (± 8.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response (BOR), Overall response rate (ORR) as per RECIST v1.1, assessed by investigator

End point title	Best overall response (BOR), Overall response rate (ORR) as per RECIST v1.1, assessed by investigator

End point description:

to assess the preliminary anti-tumor activity of HDM201 in combination with LEE011 in liposarcoma: BOR (complete response, partial response, stable disease), ORR (complete response + partial response) , assessed by investigator

End point type	Secondary

End point timeframe:
5 years

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	5	7
Units: participants				
confirmed complete response	0	0	0	0
confirmed partial response	0	0	0	0
stable disease	1	5	2	3
overall response rate	0	0	0	0

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	11	4	4
Units: participants				
confirmed complete response	0	0	0	0
confirmed partial response	0	1	1	0
stable disease	2	7	2	4
overall response rate	0	1	1	0

End point values	Regimen 4: 120mg HDM201+200 mg LEE011	Regimen 5: 100mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	6	4
Units: participants				
confirmed complete response	0	0	0	0
confirmed partial response	0	0	1	0
stable disease	2	2	4	1
overall response rate	0	0	1	0

End point values	Regimen 5: 200mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: participants				
confirmed complete response	0	0		
confirmed partial response	0	0		
stable disease	1	2		
overall response rate	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 1

End point title	Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 1[7]

End point description:

to evaluate PK parameters of HDM201 and LEE011

End point type	Secondary

End point timeframe:

day 1, day 14

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: no statistical Analysis was performed

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	8	5	6
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	372.8 (± 59.8)	547.6 (± 73.4)	1289.7 (± 12.1)	1495.1 (± 13.7)
LEE011 day 1	11929.6 (± 67.8)	5456.9 (± 103.8)	5804.6 (± 38.5)	3668.9 (± 21.7)
HDM201 day 14	989.7 (± 106.8)	857.3 (± 64.5)	1854.5 (± 64.5)	2088.9 (± 31.5)
LEE011 Day 14	22807.5 (± 90.8)	9247.0 (± 54.2)	7589.5 (± 88.7)	4833.7 (± 35.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 4

End point title	Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 4[8]

End point description:

to evaluate PK parameters of HDM201 and LEE011

End point type	Secondary

End point timeframe:

day 1, day 21

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: no statistical Analysis was performed

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	3	2
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	8316.9 (± 47.2)	26039.0 (± 38.3)	45554.1 (± 19.4)	28048.9 (± 11.3)
LEE011 day 1	7728.8 (± 68.4)	6427.9 (± 78.6)	8735.9 (± 18.7)	5116.5 (± 17.3)
HDM201 day 21	3652.1 (± 15.1)	14617.1 (± 65.6)	34451.4 (± 0)	13209.5 (± 0)
LEE011 Day 21	4249.0 (± 0)	0 (± 0)	19212.3 (± 0)	0 (± 0)

End point values	Regimen 4: 120mg HDM201+200 mg LEE011			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	25570.9 (± 40.6)			
LEE011 day 1	3815.3 (± 69.8)			
HDM201 day 21	19065.0 (± 30.9)			
LEE011 Day 21	3389.4 (± 34.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast

Regimen 5

End point title	Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 5[9]

End point description:

to evaluate PK parameters of HDM201 and LEE011

End point type	Secondary

End point timeframe:

day 1, day 28

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: no statistical Analysis was performed

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	3	4
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
HDM201 day 1	22014.2 (± 74.0)	21593.8 (± 80.6)	36044.8 (± 97.1)	25086.4 (± 30.2)
LEE011 day 1	5947.3 (± 71.9)	4175.7 (± 109.3)	7214.2 (± 108.1)	11048.0 (± 68.3)
HDM201 day 28	16136.7 (± 37.2)	14516.4 (± 51.2)	18343.0 (± 52.6)	14214.2 (± 9.6)
LEE011 Day 28	5803.3 (± 63.0)	4622.2 (± 42.5)	5381.0 (± 41.4)	6149.6 (± 1.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline of Pharmacodynamics (PD) markers in blood (GDF-15)

End point title	Changes from baseline of Pharmacodynamics (PD) markers in blood (GDF-15)

End point description:

measure of GDF-15 fold-change in protein levels (PD direct targets of p53)

End point type	Secondary

End point timeframe:

5 years

End point values	2.5mg HDM201	5mg HDM201	10mg HDM201	15mg HDM201
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	9	5	7
Units: mg				
arithmetic mean (full range (min-max))	1.5 (1.2 to 1.7)	3.1 (1.4 to 8.8)	4.1 (1.4 to 6.4)	6.1 (3.9 to 9.2)

End point values	50mg HDM201	100mg HDM201	120mg HDM201	150mg HDM201
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	4	15	18
Units: mg				
arithmetic mean (full range (min-max))	7.8 (2.1 to 13)	11 (9.1 to 13)	12 (5.7 to 21)	13 (4.9 to 25)

End point values	200mg HDM201			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: mg				
arithmetic mean (full range (min-max))	10 (7.6 to 13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from baseline of Pharmacodynamics (PD) markers in tumor tissue (p21, MDM2)

End point title	Changes from baseline of Pharmacodynamics (PD) markers in tumor tissue (p21, MDM2)

End point description:

measure of MDM2 H-score versus HDM201 dose - all regimen. The H-score is a method of assessing the extent of nuclear immunoreactivity, applicable to steroid receptors. The score is obtained by the formula: 3 x percentage of strongly staining nuclei + 2 x percentage of moderately staining nuclei + percentage of weakly staining nuclei, giving a range of 0 to 300.

End point type	Secondary

End point timeframe:

5 years

End point values	2.5mg HDM201	5mg HDM201	10mg HDM201	15mg HDM201
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	9	5	7
Units: H-score				
arithmetic mean (full range (min-max))				
MDM2	98 (60 to 115)	55 (0.0 to 250)	38 (0.0 to 70)	83 (30 to 150)
p21	123 (30 to 195)	73 (0.0 to 250)	50 (0.0 to 140)	60 (0.0 to 190)

End point values	50mg HDM201	100mg HDM201	120mg HDM201	150mg HDM201
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	4	15	18
Units: H-score				
arithmetic mean (full range (min-max))				
MDM2	155 (90 to 220)	157 (70 to 220)	92 (0.0 to 215)	134 (20 to 170)
p21	110 (0.0 to 220)	202 (130 to 240)	70 (0.0 to 163)	147 (0.0 to 240)

End point values	200mg HDM201			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: H-score				
arithmetic mean (full range (min-max))				
MDM2	275 (270 to 280)			
p21	243 (130 to 255)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS) as per RECIST v1.1, assessed by investigator

End point title	Progression free survival (PFS) as per RECIST v1.1, assessed by investigator

End point description:

to assess the preliminary anti-tumor activity of HDM201 in combination with LEE011 in liposarcoma: PFS as per RECIST v1.1, assessed by investigator. PFS rate is the estimated probability that a patient will remain progression-free up to the specified time point. PFS rates are obtained from the Kaplan-Meier survival estimates for all treatment groups; Greenwood formula is used for CIs of KM estimates. 999999 value for the CI means not evaluable

End point type	Secondary

End point timeframe:

5 years

End point values	Regimen 1: 2.5mg HDM201+400 mg LEE011	Regimen 1: 5mg HDM201+400 mg LEE011	Regimen 1: 10mg HDM201+400 mg LEE011	Regimen 1: 15mg HDM201+400 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	5	7
Units: months				
median (confidence interval 95%)	2.5 (1.2 to 999999)	5.5 (2.7 to 8.2)	1.9 (1.4 to 19.1)	2.8 (1.4 to 999999)

End point values	Regimen 4: 50mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+400 mg LEE011	Regimen 4: 200mg HDM201+400 mg LEE011	Regimen 4: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	11	4	4
Units: months				
median (confidence interval 95%)	5.5 (0.3 to 9.8)	4.8 (4.2 to 35.9)	4.2 (1.5 to 999999)	0 (0 to 0)

End point values	Regimen 4: 120mg HDM201+200 mg LEE011	Regimen 5: 100mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+300 mg LEE011	Regimen 5: 150mg HDM201+300 mg LEE011
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	4	6	4
Units: months				
median (confidence interval 95%)	2.7 (1.6 to 4.0)	1.8 (1.3 to 4.2)	6.1 (4.0 to 14.1)	1.4 (1.0 to 999999)

End point values	Regimen 5: 200mg HDM201+300 mg LEE011	Regimen 5: 120mg HDM201+400 mg LEE011		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: months				
median (confidence interval 95%)	9.2 (0 to 999999)	5.8 (1.4 to 5.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from the first patient first visit until the last patient last visit, plus a 30 day safety follow up period. The total duration for the collection of adverse events for this trials was approximately 4.5 years.

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Regimen 1@2.5 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 1@2.5 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 1@5 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 1@5 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 1@10 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 1@10 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 1@15 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 1@15 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 4@50 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 4@50 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 4@150 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 4@150 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 4@200 mg HDM201+ @400 mg LEE011

Reporting group description:

Regimen 4@200 mg HDM201+ @400 mg LEE011

Reporting group title	Regimen 4@150 mg HDM201+ @300 mg LEE011

Reporting group description:

Regimen 4@150 mg HDM201+ @300 mg LEE011

Reporting group title	Regimen 4@120 mg HDM201+ @200 mg LEE011

Reporting group description:

Regimen 4@120 mg HDM201+ @200 mg LEE011

Reporting group title	Regimen 5@100 mg HDM201+ @300 mg LEE011

Reporting group description:

Regimen 5@100 mg HDM201+ @300 mg LEE011

Reporting group title	Regimen 5@120 mg HDM201+ @300 mg LEE011

Reporting group description:

Regimen 5@120 mg HDM201+ @300 mg LEE011

Reporting group title	Regimen 5@150 mg HDM201+ @300 mg LEE011

Reporting group description:

Regimen 5@150 mg HDM201+ @300 mg LEE011

Reporting group title	Regimen 5@200 mg HDM201+ @300 mg LEE011

Reporting group description:
Regimen 5@200 mg HDM201+ @300 mg LEE011

Reporting group title	Regimen 5@120 mg HDM201+ @400 mg LEE011

Reporting group description:
Regimen 5@120 mg HDM201+ @400 mg LEE011

Reporting group title	Total

Reporting group description:
Total

Serious adverse events	Regimen 1@2.5 mg HDM201+ @400 mg LEE011	Regimen 1@5 mg HDM201+ @400 mg LEE011	Regimen 1@10 mg HDM201+ @400 mg LEE011
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	2 / 10 (20.00%)	3 / 5 (60.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creutzfeldt-Jakob disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Regimen 1@15 mg HDM201+ @400 mg LEE011	Regimen 4@50 mg HDM201+ @400 mg LEE011	Regimen 4@150 mg HDM201+ @400 mg LEE011
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	4 / 11 (36.36%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal infection			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creutzfeldt-Jakob disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Regimen 4@200 mg	Regimen 4@150 mg	Regimen 4@120 mg

	HDM201+ @400 mg LEE011	HDM201+ @300 mg LEE011	HDM201+ @200 mg LEE011
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intestinal perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creutzfeldt-Jakob disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Regimen 5@100 mg HDM201+ @300 mg LEE011	Regimen 5@120 mg HDM201+ @300 mg LEE011	Regimen 5@150 mg HDM201+ @300 mg LEE011
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from	0	0	1

adverse events			
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creutzfeldt-Jakob disease			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Regimen 5@200 mg HDM201+ @300 mg LEE011	Regimen 5@120 mg HDM201+ @400 mg LEE011	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	2 / 4 (50.00%)	29 / 74 (39.19%)
number of deaths (all causes)	0	0	4
number of deaths resulting from adverse events	0	0	1
Investigations			
Neutrophil count decreased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	5 / 74 (6.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	2 / 74 (2.70%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	5 / 74 (6.76%)
occurrences causally related to treatment / all	0 / 0	1 / 1	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	5 / 74 (6.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creutzfeldt-Jakob disease			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
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			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Septic shock			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
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	Regimen 1@2.5 mg HDM201+ @400 mg LEE011	Regimen 1@5 mg HDM201+ @400 mg LEE011	Regimen 1@10 mg HDM201+ @400 mg LEE011
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	10 / 10 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Vascular disorders			

Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 4 (50.00%)	2 / 10 (20.00%)	1 / 5 (20.00%)
occurrences (all)	2	4	1
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	4 / 10 (40.00%)	2 / 5 (40.00%)
occurrences (all)	2	4	3
Feeling cold			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Malaise			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	2
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	2	2	1
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Epistaxis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pulmonary infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Psychomotor retardation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Basophil count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood albumin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase decreased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	7 / 10 (70.00%)	1 / 5 (20.00%)
occurrences (all)	0	10	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lipase increased			

subjects affected / exposed	2 / 4 (50.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	7	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 10 (20.00%)	2 / 5 (40.00%)
occurrences (all)	5	4	2
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	2	3	1
Vitamin B12 decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 10 (20.00%)	2 / 5 (40.00%)
occurrences (all)	0	5	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Procedural pain			

subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Product use complaint			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiovascular disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Anosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Balance disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Dysaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Haemorrhage intracranial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	3 / 4 (75.00%)	3 / 10 (30.00%)	2 / 5 (40.00%)
occurrences (all)	5	4	2
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Lymphopenia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	3	1	1
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	2 / 5 (40.00%)
occurrences (all)	0	1	3
Thrombocytosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Vision blurred			

subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	2 / 10 (20.00%)	2 / 5 (40.00%)
occurrences (all)	4	2	2
Abdominal pain lower			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Breath odour			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 4 (50.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	3	2	1
Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	2 / 10 (20.00%)	1 / 5 (20.00%)
occurrences (all)	1	2	1

Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	2 / 5 (40.00%)
occurrences (all)	0	1	2
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gingival discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Loose tooth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 4 (50.00%)	7 / 10 (70.00%)	5 / 5 (100.00%)
occurrences (all)	3	11	6
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Subileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Tooth discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	3 / 10 (30.00%)	2 / 5 (40.00%)
occurrences (all)	2	4	3
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Cold sweat			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	2 / 5 (40.00%)
occurrences (all)	0	0	2
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain of skin			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Penile ulceration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Psoriasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Purpura			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Skin discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Leukocyturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nocturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Limb discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 10 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	4 / 10 (40.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastroenteritis norovirus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Soft tissue infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	3 / 4 (75.00%)	3 / 10 (30.00%)	1 / 5 (20.00%)
occurrences (all)	3	4	1
Dehydration			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypertriglyceridaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Iron overload			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lack of satiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Regimen 1@15 mg HDM201+ @400 mg LEE011	Regimen 4@50 mg HDM201+ @400 mg LEE011	Regimen 4@150 mg HDM201+ @400 mg LEE011
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tumour pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pallor			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 4 (50.00%)	1 / 11 (9.09%)
occurrences (all)	1	5	1
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	5 / 7 (71.43%)	2 / 4 (50.00%)	8 / 11 (72.73%)
occurrences (all)	5	4	11
Feeling cold			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	5
Mucosal inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	3
Dyspnoea			

subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	3
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Lung disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pulmonary infarction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Psychomotor retardation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Basophil count increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood albumin increased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 4 (25.00%)	5 / 11 (45.45%)
occurrences (all)	2	1	8
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	4
Lymphocyte count decreased			
subjects affected / exposed	3 / 7 (42.86%)	1 / 4 (25.00%)	3 / 11 (27.27%)
occurrences (all)	6	3	8
Lymphocyte count increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	3 / 11 (27.27%)
occurrences (all)	4	0	24
Platelet count decreased			
subjects affected / exposed	5 / 7 (71.43%)	0 / 4 (0.00%)	4 / 11 (36.36%)
occurrences (all)	8	0	10
Vitamin B12 decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	3 / 7 (42.86%)	2 / 4 (50.00%)	5 / 11 (45.45%)
occurrences (all)	6	2	16
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Fall			

subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Product use complaint			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Cardiovascular disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	7
Dysaesthesia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	3
Haemorrhage intracranial			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Head discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	1 / 11 (9.09%)
occurrences (all)	0	4	1
Hypoaesthesia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Parosmia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	3
Syncope			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Taste disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tremor			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	7 / 11 (63.64%)
occurrences (all)	3	0	11
Leukopenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	3
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	5 / 7 (71.43%)	0 / 4 (0.00%)	6 / 11 (54.55%)
occurrences (all)	8	0	10
Thrombocytopenia			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	3 / 11 (27.27%)
occurrences (all)	2	0	4
Thrombocytosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Abdominal discomfort			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	2
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	3 / 11 (27.27%)
occurrences (all)	0	1	5
Abdominal pain lower			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Breath odour			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	2 / 4 (50.00%)	7 / 11 (63.64%)
occurrences (all)	2	2	12
Dry mouth			
subjects affected / exposed	2 / 7 (28.57%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	3	0	2
Dyspepsia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Epigastric discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gingival discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Loose tooth			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	7 / 7 (100.00%)	4 / 4 (100.00%)	8 / 11 (72.73%)
occurrences (all)	12	11	52
Odynophagia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Subileus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Tongue ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	4 / 7 (57.14%)	2 / 4 (50.00%)	7 / 11 (63.64%)
occurrences (all)	8	4	26
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Cold sweat			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Onycholysis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Penile ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Psoriasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin discolouration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Leukocyturia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Flank pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			

subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal viral infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Tracheitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	3 / 7 (42.86%)	0 / 4 (0.00%)	3 / 11 (27.27%)
occurrences (all)	3	0	3
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 4 (25.00%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Hypocalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Iron overload			
subjects affected / exposed	1 / 7 (14.29%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lack of satiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 4 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Regimen 4@200 mg HDM201+ @400 mg LEE011	Regimen 4@150 mg HDM201+ @300 mg LEE011	Regimen 4@120 mg HDM201+ @200 mg LEE011
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Lipoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Chills			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	4 / 4 (100.00%)	2 / 6 (33.33%)
occurrences (all)	1	10	2
Feeling cold			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gait disturbance			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	2
Swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychomotor retardation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	6
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Basophil count increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood albumin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	2	0	3
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	3	2
Blood potassium increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	11
Lymphocyte count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	1 / 6 (16.67%)
occurrences (all)	1	15	2
Lymphocyte count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 4 (25.00%)	3 / 4 (75.00%)	1 / 6 (16.67%)
occurrences (all)	2	10	2
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	3 / 4 (75.00%)	3 / 6 (50.00%)
occurrences (all)	1	5	4
Vitamin B12 decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	2 / 6 (33.33%)
occurrences (all)	2	6	3
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Product use complaint			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiovascular disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Dysaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemorrhage intracranial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Taste disorder			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	3 / 4 (75.00%)	4 / 6 (66.67%)
occurrences (all)	2	5	8
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	5
Thrombocytopenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	4
Thrombocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	8	0
Abdominal pain lower			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	1	4	1
Breath odour			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3

Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	0 / 6 (0.00%)
occurrences (all)	2	4	0
Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gingival discomfort			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Loose tooth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 4 (100.00%)	2 / 4 (50.00%)	4 / 6 (66.67%)
occurrences (all)	4	28	10
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Subileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tooth discolouration			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	4 / 6 (66.67%)
occurrences (all)	3	13	13
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cold sweat			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Onycholysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Penile ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Xeroderma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint swelling			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Gastroenteritis norovirus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Staphylococcal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tracheitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vaginal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vulvitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	3 / 4 (75.00%)	0 / 6 (0.00%)
occurrences (all)	1	3	0
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	5
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Iron overload			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lack of satiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Regimen 5@100 mg HDM201+ @300 mg LEE011	Regimen 5@120 mg HDM201+ @300 mg LEE011	Regimen 5@150 mg HDM201+ @300 mg LEE011
Total subjects affected by non-serious adverse events			

subjects affected / exposed	4 / 4 (100.00%)	6 / 6 (100.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 6 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	4 / 4 (100.00%)	4 / 6 (66.67%)	2 / 4 (50.00%)
occurrences (all)	4	6	5
Feeling cold			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Swelling			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Thirst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Psychomotor retardation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Amylase increased			

subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Basophil count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood albumin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
occurrences (all)	2	4	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Blood potassium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	6	0
Lymphocyte count increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	2	3	2
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	1	5	1
Vitamin B12 decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

White blood cell count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	1	3	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Product use complaint			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiovascular disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Balance disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
Dysaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haemorrhage intracranial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	2	0

Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	3 / 6 (50.00%)	0 / 4 (0.00%)
occurrences (all)	1	6	0
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	0	6	0
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	1	0	2
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Thrombocytosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry eye			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	3 / 4 (75.00%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	3	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Breath odour			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Constipation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	4	3	1
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gingival discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Loose tooth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 4 (100.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
occurrences (all)	6	7	2
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Subileus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	3 / 6 (50.00%)	3 / 4 (75.00%)
occurrences (all)	2	33	5
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Cold sweat			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Penile ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Xeroderma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Flank pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal viral infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Soft tissue infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vulvitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	3 / 6 (50.00%)	1 / 4 (25.00%)
occurrences (all)	1	10	1
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dyslipidaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Iron overload			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lack of satiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Regimen 5@200 mg HDM201+ @300 mg LEE011	Regimen 5@120 mg HDM201+ @400 mg LEE011	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	4 / 4 (100.00%)	74 / 74 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	6 / 74 (8.11%)
occurrences (all)	0	0	8
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	4
Pallor			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	10 / 74 (13.51%)
occurrences (all)	0	0	16
Chills			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	5
Face oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Fatigue			

subjects affected / exposed	0 / 1 (0.00%)	2 / 4 (50.00%)	42 / 74 (56.76%)
occurrences (all)	0	6	63
Feeling cold			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	1	0	4
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	5
Mucosal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	8 / 74 (10.81%)
occurrences (all)	0	0	8
Pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	2 / 74 (2.70%)
occurrences (all)	0	2	3
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	10 / 74 (13.51%)
occurrences (all)	0	0	13
Swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Thirst			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Immune system disorders			

Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	8 / 74 (10.81%)
occurrences (all)	0	0	13
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	8 / 74 (10.81%)
occurrences (all)	0	0	9
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Interstitial lung disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Lung disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	4 / 74 (5.41%)
occurrences (all)	0	1	5
Oropharyngeal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	3
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Productive cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Pulmonary embolism			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Pulmonary infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	5 / 74 (6.76%)
occurrences (all)	0	0	6
Psychomotor retardation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	3
Amylase increased			

subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	1	0	10
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	4
Basophil count increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Blood albumin increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Blood alkaline phosphatase decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	4 / 74 (5.41%)
occurrences (all)	0	2	10
Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Blood cholesterol increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	24 / 74 (32.43%)
occurrences (all)	0	0	34
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	6
Blood potassium increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	2 / 74 (2.70%)
occurrences (all)	0	1	2
Blood urea increased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	3
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Lipase increased			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	5 / 74 (6.76%)
occurrences (all)	1	0	23
Lymphocyte count decreased			
subjects affected / exposed	1 / 1 (100.00%)	1 / 4 (25.00%)	15 / 74 (20.27%)
occurrences (all)	1	1	44
Lymphocyte count increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 1 (100.00%)	2 / 4 (50.00%)	22 / 74 (29.73%)
occurrences (all)	1	2	63
Platelet count decreased			
subjects affected / exposed	1 / 1 (100.00%)	1 / 4 (25.00%)	25 / 74 (33.78%)
occurrences (all)	1	1	43
Vitamin B12 decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Weight increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2

White blood cell count decreased			
subjects affected / exposed	1 / 1 (100.00%)	2 / 4 (50.00%)	26 / 74 (35.14%)
occurrences (all)	3	3	54
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Product use complaint			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Road traffic accident			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Cardiovascular disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Anosmia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1

Balance disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	9 / 74 (12.16%)
occurrences (all)	1	0	19
Dysaesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	4 / 74 (5.41%)
occurrences (all)	0	2	8
Haemorrhage intracranial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Head discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	10 / 74 (13.51%)
occurrences (all)	0	3	16
Hypoaesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	5

Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Taste disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 1 (100.00%)	3 / 4 (75.00%)	35 / 74 (47.30%)
occurrences (all)	2	4	53
Leukopenia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	8 / 74 (10.81%)
occurrences (all)	0	1	11
Lymphopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	6 / 74 (8.11%)
occurrences (all)	0	0	11
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 4 (50.00%)	22 / 74 (29.73%)
occurrences (all)	0	4	35
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 4 (50.00%)	17 / 74 (22.97%)
occurrences (all)	0	5	24
Thrombocytosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dry eye			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	3
Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	4
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	18 / 74 (24.32%)
occurrences (all)	0	1	28
Abdominal pain lower			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	6 / 74 (8.11%)
occurrences (all)	0	0	9
Breath odour			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1

Constipation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	11 / 74 (14.86%)
occurrences (all)	0	1	13
Dental caries			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	23 / 74 (31.08%)
occurrences (all)	0	0	34
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	10 / 74 (13.51%)
occurrences (all)	0	0	11
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	5 / 74 (6.76%)
occurrences (all)	0	0	5
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Epigastric discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gingival discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Loose tooth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 1 (100.00%)	4 / 4 (100.00%)	56 / 74 (75.68%)
occurrences (all)	1	8	161
Odynophagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1

Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	4 / 74 (5.41%)
occurrences (all)	0	1	4
Subileus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Tongue ulceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Tooth discolouration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	1 / 1 (100.00%)	2 / 4 (50.00%)	38 / 74 (51.35%)
occurrences (all)	1	6	123
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	4
Cold sweat			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	5
Hyperhidrosis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Onychoclasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Onycholysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Pain of skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Penile ulceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	5 / 74 (6.76%)
occurrences (all)	0	0	5
Psoriasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Purpura			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	4
Skin discolouration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Xeroderma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	3
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Leukocyturia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Nocturia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	3
Flank pain			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Limb discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	3
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	6 / 74 (8.11%)
occurrences (all)	0	1	7
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1

Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gastroenteritis norovirus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gastrointestinal viral infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Laryngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1

Soft tissue infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Staphylococcal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Tracheitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Vaginal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Vulvitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	23 / 74 (31.08%)
occurrences (all)	0	5	35
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Dyslipidaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	3
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	3
Hypertriglyceridaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	5
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	5
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 4 (25.00%)	2 / 74 (2.70%)
occurrences (all)	0	1	2
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	3 / 74 (4.05%)
occurrences (all)	0	0	4
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	5
Hyponatraemia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	2	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	4 / 74 (5.41%)
occurrences (all)	0	0	5
Iron overload			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Lack of satiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 4 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2015	• To add a new regimen which investigates intermittent dosing of HDM201. This new regimen combines HDM201 administered once every 3 weeks (q3w) and LEE011 administered daily for two weeks followed by one week off treatment • Clarification of inclusion criteria, to specify that patients who have received more than one prior line of treatment, are eligible to enroll in the study • Introduce an HDM201 new drug product variant using a drug substance of smaller particle size with improved in vitro dissolution rate characteristics. • Include analysis of PK/safety relationships as an exploratory endpoint, to highlight its importance in guiding the selection of the appropriate dose and regimen in terms of efficacy and safety • Incorporate, in GDF-15 sampling, a 24 hr profile at Cycle 1 Day 1 for a more robust assessment of GDF-15 kinetics in exploratory PK/PD and PK/safety modeling, and reduce pre-dose samples at Days 8 and 14
01 October 2015	• To update and reinforce safety measures. This amendment aligns the cardiac and liver safety measures with guidance implemented in the LEE011 program. Moreover, in order to prevent the bleeding risk associated with HDM201–related thrombocytopenia, the exclusion criteria and concomitant medications were updated.
07 July 2016	• to implement additional safety measures for the monitoring of tumor lysis syndrome (TLS)
08 March 2019	• to add language to allow the transfer of on-treatment patient to a Novartis rollover clinical study that continues to provide study treatment (CLEE011X2X01B), considering that there no new patients will be enrolled into the study. In addition, the timing requirements for the primary and final CSR were updated to remove reference to the phase II part of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

After evaluation of the data collected in the phase Ib part of the study, Novartis decided to not open the Phase II part. This decision was not based on safety concerns and patients who benefit from the treatment were allowed to remain on study.

Notes: