



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 standard deviation | 65.5 ± 4.80 | 62.0 ± 16.46 | 67.0 ± 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 standard deviation | 67.0 ± 0 | 53.0 ± 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

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

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

| | | | |
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| 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 |

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

| | | | |
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| 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 occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Vaginal infection subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Vulvitis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Cachexia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Decreased appetite subjects affected / exposed occurrences (all) | 3 / 4 (75.00%) 3 | 3 / 10 (30.00%) 4 | 1 / 5 (20.00%) 1 |
| Dehydration subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Dyslipidaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 10 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 10 (10.00%) 2 | 0 / 5 (0.00%) 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 occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 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 occurrences (all) | 1 / 7 (14.29%) 1 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 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 occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 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 occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Tooth discolouration subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 7 (57.14%) 8 | 2 / 4 (50.00%) 4 | 7 / 11 (63.64%) 26 |
| Hepatobiliary disorders Hepatocellular injury subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 11 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Cold sweat subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Dermatitis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Dry skin subjects affected / exposed occurrences (all) | 1 / 7 (14.29%) 2 | 0 / 4 (0.00%) 0 | 1 / 11 (9.09%) 1 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 0 |
| Onychoclasia subjects affected / exposed occurrences (all) | 0 / 7 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 11 (0.00%) 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 |

| | | | |
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| 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 | | | |

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

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|---|----------------|---------------|-----------------|
| 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 occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Psychomotor retardation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 2 | 0 / 6 (0.00%) 0 |
| Amylase increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 6 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 2 | 0 / 6 (0.00%) 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 occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Tremor subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 3 / 4 (75.00%) 5 | 4 / 6 (66.67%) 8 |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 0 / 4 (0.00%) 0 | 2 / 6 (33.33%) 5 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 0 / 4 (0.00%) 0 | 2 / 6 (33.33%) 4 |
| Thrombocytosis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Dry eye subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 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 |
| Onychoclasia | | | |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| 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 occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Pulmonary infarction subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 4 (0.00%) 0 |
| Psychomotor retardation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 4 (0.00%) 0 |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 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 occurrences (all) | 1 / 4 (25.00%) 1 | 2 / 6 (33.33%) 3 | 1 / 4 (25.00%) 2 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Product use complaint subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Road traffic accident subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Wound subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Cardiovascular disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nervous system disorders | | | |
| Ageusia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Anosmia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 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 occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Taste disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Tremor subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 3 / 6 (50.00%) 6 | 0 / 4 (0.00%) 0 |
| Leukopenia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 2 / 6 (33.33%) 6 | 0 / 4 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 | 2 / 4 (50.00%) 2 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 2 / 6 (33.33%) 2 | 0 / 4 (0.00%) 0 |
| Thrombocytosis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 2 | 0 / 4 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 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 |
| Onychoclasia | | | |
| 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 occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 4 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Leukocyturia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Micturition urgency subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Renal failure subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 | 1 / 4 (25.00%) 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 occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 8 / 74 (10.81%) 13 |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 8 / 74 (10.81%) 9 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Hiccups subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Interstitial lung disease subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Lung disorder subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 4 (25.00%) 1 | 4 / 74 (5.41%) 5 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 2 / 74 (2.70%) 3 |
| Pleural effusion subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Productive cough subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 2 / 74 (2.70%) 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 occurrences (all) | 1 / 1 (100.00%) 3 | 2 / 4 (50.00%) 3 | 26 / 74 (35.14%) 54 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Fall subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Procedural pain subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 2 / 74 (2.70%) 2 |
| Product use complaint subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Road traffic accident subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Wound subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 2 / 74 (2.70%) 2 |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Cardiovascular disorder subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 2 |
| Nervous system disorders | | | |
| Ageusia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Anosmia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 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 occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 2 |
| Taste disorder subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Tremor subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 4 (25.00%) 1 | 1 / 74 (1.35%) 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 1 (100.00%) 2 | 3 / 4 (75.00%) 4 | 35 / 74 (47.30%) 53 |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 4 (25.00%) 1 | 8 / 74 (10.81%) 11 |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 6 / 74 (8.11%) 11 |
| Neutropenia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 2 / 4 (50.00%) 4 | 22 / 74 (29.73%) 35 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 2 / 4 (50.00%) 5 | 17 / 74 (22.97%) 24 |
| Thrombocytosis subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 2 / 74 (2.70%) 3 |
| Ear and labyrinth disorders | | | |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 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 |
| Onychoclasia | | | |
| 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 occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 3 / 74 (4.05%) 3 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Leukocyturia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Micturition urgency subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Renal failure subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 74 (1.35%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 2 / 74 (2.70%) 2 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 1 (0.00%) 0 | 0 / 4 (0.00%) 0 | 3 / 74 (4.05%) 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 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• to implement additional safety measures for the monitoring of tumor lysis syndrome (TLS) |
| 08 March 2019 | <ul style="list-style-type: none">• 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: