



Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

HDM201

Trial Indication(s)

Liposarcoma

Protocol Number

CHDM201X2103C

Protocol Title

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

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase I

Study Start/End Dates

Study Start Date: March 2015 (Actual)

Primary Completion Date: October 2019 (Actual)

Study Completion Date: October 2019 (Actual)

Reason for Termination (If applicable)

The study was completed. 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.

Study Design/Methodology

This was a multi-center, open-label, Phase Ib/II study of HDM201 in combination with LEE011, administered orally, in patients with liposarcoma who progressed on/or despite prior therapy.

Three regimens were evaluated in this study and the tested dose levels details are provided below.

- Regimen 1: HDM201 and LEE011 administered once a daily (qd), 2 weeks on, 2 weeks off in a 4-week cycle.
- Regimen 4: HDM201 administered once every 3 weeks (Q3W) and LEE011 qd, 2 weeks on, 1 week off in a 3-weeks cycle.
- Regimen 5 (alternative regimen to Regimen 4): HDM201 was dosed once every 4 weeks (Q4W) and LEE011 qd, 2 weeks on, 2 weeks off in a 4-weeks cycle

Centers

9 centers in 6 countries: Canada(1), France(2), Spain(2), Singapore(1), Germany(2), Taiwan(1)

Objectives:

Primary objective: To determine the maximum tolerated dose (MTD) and/or recommended phase two dose (RP2D) of HDM201 in combination with LEE011 in one or more of the pre-defined regimens

Secondary objectives:

- To characterize the safety and tolerability of HDM201 in combination with LEE011
- To characterize the pharmacokinetic (PK) properties of HDM201 in combination with LEE011 and potential metabolite/s when feasible

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- To assess the pharmacodynamic (PD) effect of HDM201 in combination with LEE011 and a potential relationship with clinical outcome
- To assess preliminary anti-tumor activity of HDM201 in combination with LEE011 in liposarcoma

Test Product (s), Dose(s), and Mode(s) of Administration

The investigational treatment used in this study was HDM201, supplied as capsules of dosage strengths of 2.5, 10 and 100 mg and LEE011, supplied as capsules of dosage strengths of 50 and 200 mg. Both the investigational drugs were administered orally.

Statistical Methods

The descriptive statistics of HDM201 and LEE011 primary PK parameters were provided for each dosing regimen.

Evaluation of anti-tumor activity was based on investigator assessment of overall lesion response according to RECIST v1.1. Progression-free survival is defined as the time from the date of randomization/treatment start to the date of first radiologically documented disease progression by investigator assessment per RECIST 1.1 or death due to any cause. If a patient has not had an event at the time of the analysis cut-off, PFS was censored at the date of last adequate tumor evaluation (see RECIST 1.1 guidelines in Section 14.4 of the protocol). Clinical deterioration without objective radiological evidence was not considered as documented disease progression.

The assessment of safety was based on the type and frequency of Adverse Events (AEs) as well as on the number of laboratory values that fall outside of pre-determined ranges (Common Toxicity Criteria for AEs [CTCAE] version 4.03 grading limits or normal ranges as appropriate). Other safety data included electrocardiogram, vital signs and ECOG performance status.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Patients with histologically documented, locally advanced or metastatic WD/DD liposarcoma who have received at least one prior systemic therapy

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- Patients with radiologic progression, defined by RECIST v.1.1, occurring while on/or within 6 months after last systemic treatment, prior to enrollment
- ECOG performance status of 0-1

Exclusion Criteria:

- Prior treatment with compounds with the same mode of action
- Patients with TP53 mutated tumors, if the molecular status is known
- Symptomatic central nervous system metastases
- Inadequate organ function
- Previous and concomitant therapy that precludes enrollment, as defined by protocol

Other protocol-defined inclusion/exclusion criteria may apply.

Participant Flow Table

Overall Study

| | Regimen 1: 2.5mg HDM20 1+400 mg LEE01 1 | Regimen 1: 5mg HDM20 1+400 mg LEE01 1 | Regimen 1: 10mg HDM20 1+400 mg LEE01 1 | Regimen 1: 15mg HDM20 1+400 mg LEE01 1 | Regimen 4: 50mg HDM20 1+400 mg LEE01 1 | Regimen 4: 150mg HDM20 1+400 mg LEE01 1 | Regimen 4: 200mg HDM20 1+400 mg LEE01 1 | Regimen 4: 150mg HDM20 1+300 mg LEE01 1 | Regimen 4: 120mg HDM20 1+200 mg LEE01 1 | Regimen 5: 100mg HDM20 1+300 mg LEE01 1 | Regimen 5: 120mg HDM20 1+300 mg LEE01 1 | Regimen 5: 150mg HDM20 1+300 mg LEE01 1 | Regimen 5: 200mg HDM20 1+300 mg LEE01 1 | Regimen 5: 120mg HDM20 1+400 mg LEE01 1 | Total |
|------------------------------|---|---|--|--|--|---|---|---|---|---|---|---|---|---|-------|
| Arm/Group Description | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | |
| Started | 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 | 74 |
| Completed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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| | | | | | | | | | | | | | | | |
|--|---|----|---|---|---|----|---|---|---|---|---|---|---|---|---|
| Not Completed | 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 | 7 |
| progr essiv e disea se | 4 | 9 | 4 | 4 | 2 | 6 | 2 | 2 | 6 | 4 | 4 | 3 | 0 | 2 | 5 |
| Adver se Event | 0 | 1 | 0 | 2 | 0 | 4 | 2 | 1 | 0 | 0 | 1 | 0 | 1 | 2 | 1 |
| Subje ct/gua rdian decisi on | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 |
| Physi cian Decisi on | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 3 |
| Death | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 |

Baseline Characteristics

| | Regim en 1: 2.5mg HDM20 1+400 mg LEE01 1 | Regim en 1: 5mg HDM20 1+400 mg LEE01 1 | Regim en 1: 10mg HDM20 1+400 mg LEE01 1 | Regim en 1: 15mg HDM20 1+400 mg LEE01 1 | Regim en 4: 50mg HDM20 1+400 mg LEE01 1 | Regim en 4: 150mg HDM20 1+400 mg LEE01 1 | Regim en 4: 200mg HDM20 1+400 mg LEE01 1 | Regim en 4: 150mg HDM20 1+300 mg LEE01 1 | Regim en 4: 120mg HDM20 1+200 mg LEE01 1 | Regim en 5: 100mg HDM20 1+300 mg LEE01 1 | Regim en 5: 120mg HDM20 1+300 mg LEE01 1 | Regim en 5: 150mg HDM20 1+300 mg LEE01 1 | Regim en 5: 200mg HDM20 1+300 mg LEE01 1 | Regim en 5: 120mg HDM20 1+400 mg LEE01 1 | Tota l |
|----------------------|---|---|--|--|--|---|---|---|---|---|---|---|---|---|-----------|
| Arm/ Grou | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | |

Clinical Trial Results Website

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|---|----|---|---|---|----|---|---|---|---|---|---|---|---|----|
| 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 | 74 |
|---|----|---|---|---|----|---|---|---|---|---|---|---|---|----|

Age Continuous

(units: years)

Mean ± Standard Deviation

| | | | | | | | | | | | | | | |
|----------------|----------------|----------------|---------------|---------------|----------------|----------------|----------------|----------------|---------------|----------------|----------------|--------|----------------|--------------------|
| 50.3±1 0.24 | 61.1±1 3.50 | 61.4±1 3.35 | 61.9±6. 84 | 61.5±9. 33 | 61.4±1 1.51 | 67.8±1 1.44 | 67.5±1 0.02 | 67.5±1 0.02 | 65.5±4. 80 | 62.0±1 6.46 | 67.0±1 0.10 | 67.0±0 | 53.0±1 0.95 | 61.8 ±11. 29 |
|----------------|----------------|----------------|---------------|---------------|----------------|----------------|----------------|----------------|---------------|----------------|----------------|--------|----------------|--------------------|

Sex: Female, Male

(units: participants)

Count of Participants (Not Applicable)

Fe
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| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| 1 | 3 | 4 | 3 | 2 | 2 | 4 | 1 | 2 | 1 | 3 | 3 | 1 | 2 | 32 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|

Mal
e

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| 3 | 7 | 1 | 4 | 2 | 9 | 0 | 3 | 4 | 3 | 3 | 1 | 0 | 2 | 42 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|

Race/Ethnicity, Customized

(units: participants)

Count of Participants (Not Applicable)

Asi
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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| 1 | 2 | 1 | 2 | 1 | 3 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 17 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|

Ca
uca

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|
| 3 | 8 | 4 | 4 | 3 | 8 | 3 | 2 | 5 | 3 | 5 | 3 | 1 | 3 | 55 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----|

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|------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Unkn wn | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
|------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

Primary Outcome Result(s)

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

(Time Frame: 5 years)

| | Regim en 1: 2.5mg HDM20 1+400 mg LEE01 1 | Regim en 1: 5mg HDM20 1+400 mg LEE01 1 | Regim en 1: 10mg HDM20 1+400 mg LEE01 1 | Regim en 1: 15mg HDM20 1+400 mg LEE01 1 | Regim en 4: 50mg HDM20 1+400 mg LEE01 1 | Regim en 4: 150mg HDM20 1+400 mg LEE01 1 | Regim en 4: 200mg HDM20 1+400 mg LEE01 1 | Regim en 4: 150mg HDM20 1+300 mg LEE01 1 | Regim en 4: 120mg HDM20 1+200 mg LEE01 1 | Regim en 5: 100mg HDM20 1+300 mg LEE01 1 | Regim en 5: 120mg HDM20 1+300 mg LEE01 1 | Regim en 5: 150mg HDM20 1+300 mg LEE01 1 | Regim en 5: 200mg HDM20 1+300 mg LEE01 1 | Regim en 5: 120mg HDM20 1+400 mg LEE01 1 |
|--|---|---|--|--|--|---|---|---|---|---|---|---|---|---|
| Arm/Group Description | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on |
| Number of Participants Analyzed [units: participants] | 4 | 8 | 4 | 7 | 3 | 11 | 4 | 4 | 6 | 4 | 6 | 3 | 1 | 4 |

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

(units: participants)

Count of Participants (Not Applicable)

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| | | | | | | | | | | | | | | |
|----------------------------------|----------|----------|----------|---------------|----------|---------------|------------|------------|---------------|----------|----------|---------------|-------------|------------|
| Total | 0 (%) | 0 (%) | 0 (%) | 2 (28.57%) | 0 (%) | 4 (36.36%) | 3 (75%) | 1 (25%) | 1 (16.67%) | 0 (%) | 0 (%) | 2 (66.67%) | 1 (100%) | 2 (50%) |
| neutropenia | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 2 (18.18%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (33.33%) | 0 (%) | 1 (25%) |
| thrombocytopenia | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (9.09%) | 2 (50%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (25%) |
| anemia | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (25%) | 0 (%) | 1 (16.67%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| platelet count decreased | 0 (%) | 0 (%) | 0 (%) | 2 (28.57%) | 0 (%) | 2 (18.18%) | 1 (25%) | 1 (25%) | 1 (16.67%) | 0 (%) | 0 (%) | 1 (33.33%) | 1 (100%) | 1 (25%) |
| neutrophil count decreased | 0 (%) | 0 (%) | 0 (%) | 1 (14.29%) | 0 (%) | 1 (9.09%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (100%) | 0 (%) |
| white blood cell count decreased | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (9.09%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (100%) | 0 (%) |
| Febrile neutropenia | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (25%) |

Exposure to HDM201 and LEE011 as measured by AUC 0-24h
(Time Frame: 5 years)

| Regime n 1: 2.5mg | Regime n 1: 5mg | Regime n 1: 10mg | Regime n 1: 15mg | Regime n 4: 50mg | Regime n 4: 150mg | Regime n 4: 200mg | Regime n 4: 150mg | Regime n 4: 120mg | Regime n 5: 100mg | Regime n 5: 120mg | Regime n 5: 150mg | Regime n 5: 120mg |
|----------------------|--------------------|---------------------|---------------------|---------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|----------------------|--------------------|---------------------|---------------------|---------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|

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| | HDM201 +400mg LEE011 | HDM201 +400mg LEE011 | HDM201 +400mg LEE011 | HDM201 +400mg LEE011 | HDM201 +400mg LEE011 | HDM201 +400mg LEE011 | HDM201 +400mg LEE011 | HDM201 +300mg LEE011 | HDM201 +200mg LEE011 | HDM201 +300mg LEE011 | HDM201 +300mg LEE011 | HDM201 +300mg LEE011 | HDM201 +400mg LEE011 |
|---|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| Arm/Group Description | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n | escalatio n |
| Number of Participants Analyzed [units: participants] | 3 | 4 | 4 | 6 | 3 | 9 | 3 | 2 | 6 | 4 | 4 | 4 | 4 |
| Exposure to HDM201 and LEE011 as measured by AUC 0-24h (units: ng*hr/mL) Geometric Mean (Geometric Coefficient of Variation) | | | | | | | | | | | | | |
| HDM201 | 267.2 (6.2%) | 587.6 (27.0%) | 1339.3 (14.8%) | 1458.2 (13.6%) | 6547.9 (47.2%) | 26066.2 (37.7%) | 45670.5 (20.4%) | 28307.2 (11.2%) | 26294.4 (45.5%) | 22069.8 (31.9%) | 15473.7 (67.4%) | 36102.4 (96.6%) | 25249.2 (37.1%) |
| LEE011 | 11290.0 (85.6%) | 5537.4 (138.1%) | 6314.2 (38.8%) | 3675.0 (21.8%) | 8669.1 (80.5%) | 8152.8 (64.6%) | 9006.9 (18.7%) | 5264.5 (17.7%) | 3859.2 (70.7%) | 5958.0 (71.6%) | 3387.1 (88.8%) | 7259.2 (106.0%) | 11185.4 (67.0%) |

Secondary Outcome Result(s)

Number of patients with dose interruptions and reduction

(Time Frame: 5 years)

| Regime n 1: 2.5mg HDM20 1+400 | Regime n 1: 5mg HDM20 1+400 | Regime n 1: 10mg HDM20 1+400 | Regime n 1: 15mg HDM20 1+400 | Regime n 4: 50mg HDM20 1+400 | Regime n 4: 150mg HDM20 1+400 | Regime n 4: 200mg HDM20 1+400 | Regime n 4: 150mg HDM20 1+300 | Regime n 4: 120mg HDM20 1+200 | Regime n 5: 100mg HDM20 1+300 | Regime n 5: 120mg HDM20 1+300 | Regime n 5: 150mg HDM20 1+300 | Regime n 5: 200mg HDM20 1+300 | Regime n 5: 120mg HDM20 1+400 |
|---|---|--|--|--|---|---|---|---|---|---|---|---|---|
|---|---|--|--|--|---|---|---|---|---|---|---|---|---|

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| | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 | mg LEE011 |
|--|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Arm/ Group Description | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on |
| Number of Participant s Analy zed [units : partic ipant s] | 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 |
| Number of patients with dose interruptions and reduction (units: participants) Count of Participants (Not Applicable) | | | | | | | | | | | | | | |
| HDM2 01 at least 1 dose reduct ion | 0 (%) | 0 (%) | 1 (20%) | 2 (28.57%) | 0 (%) | 7 (63.64%) | 2 (50%) | 3 (75%) | 3 (50%) | 0 (%) | 3 (50%) | 0 (%) | 1 (100%) | 1 (25%) |
| LEE0 11 at least 1 dose interru ption | 1 (25%) | 0 (%) | 1 (20%) | 0 (%) | 0 (%) | 2 (18.18%) | 1 (25%) | 2 (50%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 2 (50%) |
| HDM2 01 at | 3 (75%) | 5 (50%) | 3 (60%) | 5 (71.43%) | 2 (50%) | 10 (90.91%) | 3 (75%) | 3 (75%) | 5 (83.33%) | 1 (25%) | 4 (66.67%) | 1 (25%) | 1 (100%) | 3 (75%) |

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least
1
dose
delay

| | | | | | | | | | | | | | | |
|------------------------------|------------|------------|------------|---------------|------------|--------------|-------------|------------|---------------|------------|---------------|------------|-------------|------------|
| LEE011 at least 1 dose delay | 3 (75%) | 5 (50%) | 3 (60%) | 5 (71.43%) | 2 (50%) | 11 (100%) | 4 (100%) | 3 (75%) | 5 (83.33%) | 1 (25%) | 5 (83.33%) | 3 (75%) | 1 (100%) | 3 (75%) |
|------------------------------|------------|------------|------------|---------------|------------|--------------|-------------|------------|---------------|------------|---------------|------------|-------------|------------|

Dose intensity

(Time Frame: 5 years)

| | Regime n 1: 2.5mg HDM20 1+400 mg LEE011 | Regime n 1: 5mg HDM20 1+400 mg LEE011 | Regime n 1: 10mg HDM20 1+400 mg LEE011 | Regime n 1: 15mg HDM20 1+400 mg LEE011 | Regime n 4: 50mg HDM20 1+400 mg LEE011 | Regime n 4: 150mg HDM20 1+400 mg LEE011 | Regime n 4: 200mg HDM20 1+400 mg LEE011 | Regime n 4: 150mg HDM20 1+300 mg LEE011 | Regime n 4: 120mg HDM20 1+200 mg LEE011 | Regime n 5: 100mg HDM20 1+300 mg LEE011 | Regime n 5: 120mg HDM20 1+300 mg LEE011 | Regime n 5: 150mg HDM20 1+300 mg LEE011 | Regime n 5: 200mg HDM20 1+300 mg LEE011 | Regime n 5: 120mg HDM20 1+400 mg LEE011 |
|---|--|--|---|---|---|--|--|--|--|--|--|--|--|--|
| Arm/Group Description | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 |

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Dose intensity

(units: mg)

Mean ± Standard Deviation

| | | | | | | | | | | | | | | |
|--------|---------------|---------------|---------------|---------------|---------------|---------------|----------------|---------------|---------------|---------------|---------------|---------------|----------------------------|---------------|
| LEE011 | 411.5 ± 22.92 | 384.0 ± 25.36 | 368.0 ± 57.01 | 374.5 ± 39.09 | 392.8 ± 13.14 | 318.9 ± 60.72 | 293.1 ± 141.34 | 257.6 ± 29.31 | 189.6 ± 14.15 | 300.0 ± 0.00 | 256.6 ± 46.62 | 289.0 ± 21.95 | 300.0 ± NA ^[12] | 338.4 ± 72.34 |
| HDM201 | 2.6 ± 0.16 | 4.8 ± 0.31 | 8.5 ± 2.41 | 13.5 ± 2.28 | 67.9 ± 27.82 | 116.3 ± 42.92 | 159.8 ± 88.84 | 113.1 ± 65.96 | 117.7 ± 7.71 | 181.3 ± 37.50 | 131.8 ± 41.58 | 275.0 ± 43.30 | 128.6 ± NA ^[12] | 205.3 ± 60.04 |

[1] there was only 1 patient analyzed, 1 value. available. Therefore SD cannot be calculated

[2] there was only 1 patient analyzed, 1 value. available. Therefore SD cannot be calculated

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

(Time Frame: day 1, day 14)

| Arm/Group Description | Regimen 1: 2.5mg HDM201+400mg LEE011 | Regimen 1: 5mg HDM201+400mg LEE011 | Regimen 1: 10mg HDM201+400mg LEE011 | Regimen 1: 15mg HDM201+400mg LEE011 |
|---|---|---|--|--|
| escalation | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 8 | 5 | 6 |

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

(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%) |

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

(Time Frame: day 1, day 21)

| Regimen 4: 50mg | Regimen 4: 150mg | Regimen 4: 200mg | Regimen 4: 150mg | Regimen 4: 120mg |
|--------------------|---------------------|---------------------|---------------------|---------------------|
|--------------------|---------------------|---------------------|---------------------|---------------------|

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| | HDM201+400mg LEE011 | HDM201+400mg LEE011 | HDM201+400mg LEE011 | HDM201+300mg LEE011 | HDM201+200mg LEE011 |
|---|------------------------|------------------------|------------------------|------------------------|------------------------|
| Arm/Group Description | escalation | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 10 | 3 | 2 | 6 |
| Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 4 (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%) | 1284.4 (33.7%) |
| LEE011 day 1 | 685.7 (80.9%) | 652.8 (88.5%) | 932.9 (25.9%) | 477.8 (24.8%) | 491.0 (84.3%) |
| HDM201 day 21 | 201.2 (13.1%) | 991.9 (77.5%) | 2180.0 (0%) | 1320.0 (0%) | 1412.5 (24.8%) |
| LEE011 Day 21 | 516.0 (0%) | | 2630.0 (0%) | | 338.1 (36.4%) |

Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 5
(Time Frame: day 1, day 28)

| | Regimen 1: 2.5mg HDM201+400mg LEE011 | Regimen 5: 120mg HDM201+300mg LEE011 | Regimen 5: 150mg HDM201+300mg LEE011 | Regimen 5: 120mg HDM201+400mg LEE011 |
|---|---|---|---|---|
| Arm/Group Description | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 6 | 3 | 4 |
| Pharmacokinetics (PK) parameters of HDM201 and LEE011: Cmax Regimen 5 (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%) |

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

(Time Frame: 5 years)

| | Regime n 1: 2.5mg HDM20 1+400 mg LEE011 | Regime n 1: 5mg HDM20 1+400 mg LEE011 | Regime n 1: 10mg HDM20 1+400 mg LEE011 | Regime n 1: 15mg HDM20 1+400 mg LEE011 | Regime n 4: 50mg HDM20 1+400 mg LEE011 | Regime n 4: 150mg HDM20 1+400 mg LEE011 | Regime n 4: 200mg HDM20 1+400 mg LEE011 | Regime n 4: 150mg HDM20 1+300 mg LEE011 | Regime n 4: 120mg HDM20 1+200 mg LEE011 | Regime n 5: 100mg HDM20 1+300 mg LEE011 | Regime n 5: 120mg HDM20 1+300 mg LEE011 | Regime n 5: 150mg HDM20 1+300 mg LEE011 | Regime n 5: 200mg HDM20 1+300 mg LEE011 | Regime n 5: 120mg HDM20 1+400 mg LEE011 |
|--|---|---|--|--|--|---|---|---|---|---|---|---|---|---|
| Arm/ Group Description | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on |
| Number of Participants Analyzed [units : partic ipant s] | 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 |
| Best overall response (BOR), Overall response rate (ORR) as per RECIST v1.1, assessed by investigator | | | | | | | | | | | | | | |
| (units:) | | | | | | | | | | | | | | |
| Count of Participants (Not Applicable) | | | | | | | | | | | | | | |
| confir med compl ete respo nse | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |

Clinical Trial Results Website

| | | | | | | | | | | | | | | |
|----------------------------|------------|------------|------------|---------------|------------|---------------|------------|-------------|---------------|------------|---------------|------------|-------------|------------|
| confirmed partial response | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (9.09%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 1 (16.67%) | 0 (%) | 0 (%) | 0 (%) |
| stable disease | 1 (25%) | 5 (50%) | 2 (40%) | 3 (42.86%) | 2 (50%) | 7 (63.64%) | 2 (50%) | 4 (100%) | 2 (33.33%) | 2 (50%) | 4 (66.67%) | 1 (25%) | 1 (100%) | 2 (50%) |
| overall response rate | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (9.09%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 1 (16.67%) | 0 (%) | 0 (%) | 0 (%) |

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

(Time Frame: day 1, day 14)

| | Regimen 1: 2.5mg HDM201+400mg LEE011 | Regimen 1: 5mg HDM201+400mg LEE011 | Regimen 1: 10mg HDM201+400mg LEE011 | Regimen 1: 15mg HDM201+400mg LEE011 |
|--|---|---|--|--|
| Arm/Group Description | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 8 | 5 | 6 |
| Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 1 (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%) |

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

(Time Frame: day 1, day 21)

| | Regimen 4: 50mg HDM201+400mg LEE011 | Regimen 4: 150mg HDM201+400mg LEE011 | Regimen 4: 200mg HDM201+400mg LEE011 | Regimen 4: 150mg HDM201+300mg LEE011 | Regimen 4: 120mg HDM201+200mg LEE011 |
|--|--|---|---|---|---|
| Arm/Group Description | escalation | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 10 | 3 | 2 | 6 |
| Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 4 (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%) | 25570.9 (40.6%) |
| LEE011 day 1 | 7728.8 (68.4%) | 6427.9 (78.6%) | 8735.9 (18.7%) | 5116.5 (17.3%) | 3815.3 (69.8%) |
| HDM201 day 21 | 3652.1 (15.1%) | 14617.1 (65.6%) | 34451.4 (0%) | 13209.5 (0%) | 19065.0 (30.9%) |
| LEE011 Day 21 | 4249.0 (0%) | | 19212.3 (0%) | | 3389.4 (34.4%) |

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

(Time Frame: day 1, day 28)

| | Regimen 1: 2.5mg HDM201+400mg LEE011 | Regimen 5: 120mg HDM201+300mg LEE011 | Regimen 5: 150mg HDM201+300mg LEE011 | Regimen 5: 120mg HDM201+400mg LEE011 |
|--|---|---|---|---|
| Arm/Group Description | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 6 | 3 | 4 |
| Pharmacokinetics (PK) parameters of HDM201 and LEE011: AUClast Regimen 5 (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%) |

Clinical Trial Results Website

| | | | | |
|---------------|-----------------|-----------------|-----------------|-----------------|
| 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%) |

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

(Time Frame: 5 years)

| | 2.5mg HDM201 | 5mg HDM201 | 10mg HDM201 | 15mg HDM201 | 50mg HDM201 | 100mg HDM201 | 120mg HDM201 | 150mg HDM201 | 200mg HDM201 |
|---|---------------------|---------------------|---------------------|---------------------|--------------------|-------------------|-------------------|-------------------|-------------------|
| Arm/Group Description | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation |
| Number of Participants Analyzed [units: participants] | 4 | 9 | 5 | 7 | 4 | 4 | 15 | 18 | 5 |
| Changes from baseline of Pharmacodynamics (PD) markers in blood (GDF-15) (units: mg) Mean (Full Range) | 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) | 7.8 (2.1 to 13) | 11 (9.1 to 13) | 12 (5.7 to 21) | 13 (4.9 to 25) | 10 (7.6 to 13) |

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

(Time Frame: 5 years)

| | 2.5mg HDM201 | 5mg HDM201 | 10mg HDM201 | 15mg HDM201 | 50mg HDM201 | 100mg HDM201 | 120mg HDM201 | 150mg HDM201 | 200mg HDM201 |
|-------------------------------|-----------------|---------------|----------------|----------------|----------------|-----------------|-----------------|-----------------|-----------------|
| Arm/Group Description | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation | escalation |
| Number of Participants | 4 | 9 | 5 | 7 | 4 | 4 | 15 | 18 | 5 |

Clinical Trial Results Website

Analyzed [units:
participants]

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

(units: H-score)

Mean (Full Range)

| | | | | | | | | | |
|------|--------------------|--------------------|--------------------|--------------------|---------------------|---------------------|--------------------|---------------------|---------------------|
| MDM2 | 98 (60 to 115) | 55 (0.0 to 250) | 38 (0.0 to 70) | 83 (30 to 150) | 155 (90 to 220) | 157 (70 to 220) | 92 (0.0 to 215) | 134 (20 to 170) | 275 (270 to 280) |
| p21 | 123 (30 to 195) | 73 (0.0 to 250) | 50 (0.0 to 140) | 60 (0.0 to 190) | 110 (0.0 to 220) | 202 (130 to 240) | 70 (0.0 to 163) | 147 (0.0 to 240) | 243 (130 to 255) |

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

(Time Frame: 5 years)

| | Regime n 1: 2.5mg HDM20 1+400 mg LEE011 | Regime n 1: 5mg HDM20 1+400 mg LEE011 | Regime n 1: 10mg HDM20 1+400 mg LEE011 | Regime n 1: 15mg HDM20 1+400 mg LEE011 | Regime n 4: 50mg HDM20 1+400 mg LEE011 | Regime n 4: 150mg HDM20 1+400 mg LEE011 | Regime n 4: 200mg HDM20 1+400 mg LEE011 | Regime n 4: 150mg HDM20 1+300 mg LEE011 | Regime n 4: 120mg HDM20 1+200 mg LEE011 | Regime n 5: 100mg HDM20 1+300 mg LEE011 | Regime n 5: 120mg HDM20 1+300 mg LEE011 | Regime n 5: 150mg HDM20 1+300 mg LEE011 | Regime n 5: 200mg HDM20 1+300 mg LEE011 | Regime n 5: 120mg HDM20 1+400 mg LEE011 |
|--|---|---|--|--|--|---|---|---|---|---|---|---|---|---|
| Arm/ Group Description | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on | escalati on |
| Number of Participant Analyzed [units: participants] | 4 | 10 | 5 | 7 | 4 | 11 | 4 | 4 | 6 | 4 | 6 | 4 | 1 | 4 |

Clinical Trial Results Website

Progression free survival (PFS) as per RECIST v1.1, assessed by investigator
(units: months)
Median (95% Confidence Interval)

| | | | | | | | | | | | | | | |
|--------------|--------------------------------------|---------------------|----------------------|--------------------------------------|---------------------|----------------------|--------------------------------------|---------------------------------|---------------------|---------------------|----------------------|--------------------------------------|----------------------------------|---------------------|
| confirmation | 2.5 (1.2 to NA) ^[1235] | 5.5 (2.7 to 8.2) | 1.9 (1.4 to 19.1) | 2.8 (1.4 to NA) ^[1235] | 5.5 (0.3 to 9.8) | 4.8 (4.2 to 35.9) | 4.2 (1.5 to NA) ^[1235] | NA (NA to NA) ^[4] | 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 NA) ^[1235] | 9.2 (NA to NA) ^[6] | 5.8 (1.4 to 5.8) |
|--------------|--------------------------------------|---------------------|----------------------|--------------------------------------|---------------------|----------------------|--------------------------------------|---------------------------------|---------------------|---------------------|----------------------|--------------------------------------|----------------------------------|---------------------|

[1] the upper CI limit could not be calculated
 [2] the upper CI limit could not be calculated
 [3] the upper CI limit could not be calculated
 [4] The PFS could not be calculated
 [5] the upper CI limit could not be calculated
 [6] the CI could not be calculated (only 1 patient)

Safety Results

All-Cause Mortality

| | Regimen 1@2.5 mg HDM20 1+ @400 mg LEE01 1 N = 4 | Regimen 1@5 mg HDM2 01+ @400 mg LEE01 1 N = 10 | Regimen 1@10 mg HDM2 01+ @400 mg LEE01 1 N = 5 | Regimen 1@15 mg HDM2 01+ @400 mg LEE01 1 N = 7 | Regimen 4@50 mg HDM20 1+ @400 mg LEE01 1 N = 4 | Regimen 4@15 0 mg HDM2 01+ @400 mg LEE01 1 N = 11 | Regimen 4@20 0 mg HDM2 01+ @400 mg LEE01 1 N = 4 | Regimen 4@15 0 mg HDM2 01+ @300 mg LEE01 1 N = 4 | Regimen 4@120 mg HDM20 1+ @200 mg LEE01 1 N = 6 | Regimen 5@10 0 mg HDM2 01+ @300 mg LEE01 1 N = 4 | Regimen 5@12 0 mg HDM2 01+ @300 mg LEE01 1 N = 6 | Regimen 5@150 mg HDM20 1+ @300 mg LEE01 1 N = 4 | Regimen 5@20 0 mg HDM2 01+ @300 mg LEE01 1 N = 1 | Regimen 5@12 0 mg HDM2 01+ @400 mg LEE01 1 N = 4 | Total N = 74 |
|-----------------------------|--|---|---|---|---|--|---|---|--|---|---|--|---|---|-----------------|
| Arm/Group Description | Regimen 1@2.5 mg HDM20 1+ @400 mg LEE01 1 | Regimen 1@5 mg HDM2 01+ @400 mg LEE01 1 | Regimen 1@10 mg HDM2 01+ @400 mg LEE01 1 | Regimen 1@15 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@50 mg HDM20 1+ @400 mg LEE01 1 | Regimen 4@15 0 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@20 0 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@15 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 4@120 mg HDM20 1+ @200 mg LEE01 1 | Regimen 5@10 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@12 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@150 mg HDM20 1+ @300 mg LEE01 1 | Regimen 5@20 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@12 0 mg HDM2 01+ @400 mg LEE01 1 | Total |
| Total participants affected | 1 (25.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.6%) | 0 (0.0%) | 0 (0.0%) | 1 (25.0%) | 0 (0.0%) | 0 (0.0%) | 4 (5.4%) |

Serious Adverse Events by System Organ Class

| | |
|--|---------------------------|
| Time Frame | Timeframe for AE |
| Additional Description | AE additional description |
| Source Vocabulary for Table Default | MedDRA (22.1) |
| Assessment Type for Table Default | Systematic Assessment |

| | Regimen 1@2.5 mg HDM2 01+ @400 mg LEE01 | Regimen 1@5 mg HDM2 01+ @400 mg LEE01 | Regimen 1@10 mg HDM2 01+ @400 mg LEE01 | Regimen 1@15 mg HDM2 01+ @400 mg LEE01 | Regimen 4@50 mg HDM2 01+ @400 mg LEE01 | Regimen 4@15 mg HDM2 01+ @400 mg LEE01 | Regimen 4@20 mg HDM2 01+ @400 mg LEE01 | Regimen 4@15 mg HDM2 01+ @300 mg LEE0 | Regimen 4@12 mg HDM2 01+ @200 mg LEE01 | Regimen 5@10 mg HDM2 01+ @300 mg LEE01 | Regimen 5@12 mg HDM2 01+ @300 mg LEE01 | Regimen 5@15 mg HDM2 01+ @300 mg LEE01 | Regimen 5@200 mg HDM20 1+ @300 mg LEE01 | Regimen 5@12 mg HDM2 01+ @400 mg LEE01 | Total |
|------------------------------------|---|---------------------------------------|--|--|--|--|--|---------------------------------------|--|--|--|--|---|--|-------------|
| | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 11 | 1 | 1 | 1 | 1 | 1 | 1 | N = 74 |
| | N = 4 | N = 10 | N = 5 | N = 7 | N = 4 | N = 11 | N = 4 | N = 4 | N = 6 | N = 4 | N = 6 | N = 4 | N = 1 | N = 4 | |
| Arm/Group Description | Regimen 1@2.5 mg HDM2 01+ @400 mg LEE01 | Regimen 1@5 mg HDM2 01+ @400 mg LEE01 | Regimen 1@10 mg HDM2 01+ @400 mg LEE01 | Regimen 1@15 mg HDM2 01+ @400 mg LEE01 | Regimen 4@50 mg HDM2 01+ @400 mg LEE01 | Regimen 4@15 mg HDM2 01+ @400 mg LEE01 | Regimen 4@20 mg HDM2 01+ @400 mg LEE01 | Regimen 4@15 mg HDM2 01+ @300 mg LEE0 | Regimen 4@12 mg HDM2 01+ @200 mg LEE01 | Regimen 5@10 mg HDM2 01+ @300 mg LEE01 | Regimen 5@12 mg HDM2 01+ @300 mg LEE01 | Regimen 5@15 mg HDM2 01+ @300 mg LEE01 | Regimen 5@200 mg HDM20 1+ @300 mg LEE01 | Regimen 5@12 mg HDM2 01+ @400 mg LEE01 | Total |
| | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 11 | 1 | 1 | 1 | 1 | 1 | 1 | |
| Total participants affected | 3 (75.00%) | 2 (20.00%) | 3 (60.00%) | 2 (28.57%) | 2 (50.00%) | 4 (36.36%) | 3 (75.00%) | 0 (0.00%) | 2 (33.33%) | 1 (25.00%) | 3 (50.00%) | 1 (25.00%) | 1 (100.00%) | 2 (50.00%) | 29 (39.19%) |
| Blood and lymphatic | | | | | | | | | | | | | | | |

Clinical Trial Results Website

system disorders

| | | | | | | | | | | | | | | | |
|---------------------|------------|------------|------------|------------|-----------|-----------|------------|-----------|-----------|-----------|-----------|------------|-----------|------------|-----------|
| Anaemia | 2 (50.00%) | 1 (10.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 5 (6.76%) |
| Febrile neutropenia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 1 (25.00%) | 2 (2.70%) |
| Leukopenia | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Neutropenia | 0 (0.00%) | 1 (10.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (4.05%) |
| Thrombocytopenia | 1 (25.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (50.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 5 (6.76%) |

Cardiac disorders

| | | | | | | | | | | | | | | | |
|--------------|-----------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Pericarditis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
|--------------|-----------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|

Gastrointestinal disorders

| | | | | | | | | | | | | | | | |
|------------------------------|------------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|------------|------------|-----------|-----------|-----------|-----------|
| Abdominal pain | 2 (50.00%) | 1 (10.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 5 (6.76%) |
| Ascites | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Constipation | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Gastrointestinal haemorrhage | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Intestinal perforation | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |

Clinical Trial Results Website

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|---|----------------|----------------|----------------|---------------|----------------|---------------|---------------|---------------|---------------|----------------|---------------|---------------|----------------|-----------------|---------------|---------------|
| Subileus | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Vomiting | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |
| General disorders and administration site conditions | | | | | | | | | | | | | | | | |
| Asthenia | 1 (25. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |
| Chest pain | 0 (0.0 0%) | 0 (0.0 0%) | 1 (20. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |
| Pyrexia | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.0 9%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |
| Infections and infestations | | | | | | | | | | | | | | | | |
| Abdominal infection | 1 (25. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |
| Aspergillus infection | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.0 9%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |
| Creutzfeldt-Jakob disease | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (100. 00%) | 0 (0.0 0%) | 1 (1.35 %) |
| Pneumonia | 0 (0.0 0%) | 1 (10. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.00 %) | 0 (0.0 0%) | 2 (2.70 %) |
| Sepsis | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.00 %) | 0 (0.0 0%) | 2 (2.70 %) |
| Septic shock | 0 (0.0 0%) | 1 (10. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (1.35 %) |

Clinical Trial Results Website

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|--|----------|------------|----------|------------|----------|-----------|----------|----------|----------|----------|------------|------------|-------------|----------|-----------|
| Tracheobronchitis | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Investigations | | | | | | | | | | | | | | | |
| Neutrophil count decreased | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Platelet count decreased | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 2 (28.57%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 4 (5.41%) |
| White blood cell count decreased | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Metabolism and nutrition disorders | | | | | | | | | | | | | | | |
| Dehydration | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 2 (2.70%) |
| Musculoskeletal and connective tissue disorders | | | | | | | | | | | | | | | |
| Fistula | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Nervous system disorders | | | | | | | | | | | | | | | |
| Aphasia | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (100.00%) | 0 (0.0%) | 1 (1.35%) |

Clinical Trial Results Website

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|--|----------|----------|------------|----------|----------|-----------|------------|----------|----------|----------|------------|----------|-------------|----------|-----------|
| Disturbance in attention | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (100.00%) | 0 (0.0%) | 1 (1.35%) |
| Dizziness | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Memory impairment | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (100.00%) | 0 (0.0%) | 1 (1.35%) |
| Renal and urinary disorders | | | | | | | | | | | | | | | |
| Renal failure | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Respiratory, thoracic and mediastinal disorders | | | | | | | | | | | | | | | |
| Dyspnoea | 0 (0.0%) | 0 (0.0%) | 1 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Vascular disorders | | | | | | | | | | | | | | | |
| Hypotension | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |
| Peripheral arterial occlusive disease | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (1.35%) |

Other Adverse Events by System Organ Class

Time Frame

Timeframe for AE

Clinical Trial Results Website

| | |
|--|---------------------------|
| Additional Description | AE additional description |
| Source Vocabulary for Table Default | MedDRA (22.1) |
| Assessment Type for Table Default | Systematic Assessment |
| Frequent Event Reporting Threshold | 5% |

| | Regimen 1@2.5 mg HDM2 01+ @400 mg LEE0 11 N = 4 | Regimen 1@5 mg HDM2 01+ @400 mg LEE01 1 N = 10 | Regimen 1@10 mg HDM2 01+ @400 mg LEE0 11 N = 5 | Regimen 1@15 mg HDM2 01+ @400 mg LEE0 11 N = 7 | Regimen 4@50 mg HDM2 01+ @400 mg LEE0 11 N = 4 | Regimen 4@150 mg HDM2 01+ @400 mg LEE01 1 N = 11 | Regimen 4@20 0 mg HDM2 01+ @400 mg LEE01 1 N = 4 | Regimen 4@15 0 mg HDM2 01+ @300 mg LEE01 1 N = 4 | Regimen 4@12 0 mg HDM2 01+ @200 mg LEE01 1 N = 6 | Regimen 5@10 0 mg HDM2 01+ @300 mg LEE01 1 N = 4 | Regimen 5@12 0 mg HDM2 01+ @300 mg LEE01 1 N = 6 | Regimen 5@15 0 mg HDM2 01+ @300 mg LEE01 1 N = 4 | Regimen 5@20 0 mg HDM2 01+ @300 mg LEE01 1 N = 1 | Regimen 5@12 0 mg HDM2 01+ @400 mg LEE01 1 N = 4 | Total N = 74 |
|---|--|---|---|---|---|---|---|---|---|---|---|---|---|---|-----------------|
| Arm/Group Description | Regimen 1@2.5 mg HDM2 01+ @400 mg LEE01 1 | Regimen 1@5 mg HDM2 01+ @400 mg LEE01 1 | Regimen 1@10 mg HDM2 01+ @400 mg LEE01 1 | Regimen 1@15 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@50 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@150 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@20 0 mg HDM2 01+ @400 mg LEE01 1 | Regimen 4@15 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 4@12 0 mg HDM2 01+ @200 mg LEE01 1 | Regimen 5@10 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@12 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@15 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@20 0 mg HDM2 01+ @300 mg LEE01 1 | Regimen 5@12 0 mg HDM2 01+ @400 mg LEE01 1 | Total |
| Total participants affected | 4 (100.00%) | 10 (100.00%) | 5 (100.00%) | 7 (100.00%) | 4 (100.00%) | 11 (100.00%) | 4 (100.00%) | 4 (100.00%) | 6 (100.00%) | 4 (100.00%) | 6 (100.00%) | 4 (100.00%) | 1 (100.00%) | 4 (100.00%) | 74 (100.00%) |
| Blood and lymphatic system disorders | | | | | | | | | | | | | | | |
| Anaemia | 3 (75.00%) | 3 (30.00%) | 2 (40.00%) | 3 (42.86%) | 0 (0.00%) | 7 (63.64%) | 2 (50.00%) | 3 (75.00%) | 4 (66.67%) | 1 (25.00%) | 3 (50.00%) | 0 (0.00%) | 1 (100.00%) | 3 (75.00%) | 35 (47.30%) |

Clinical Trial Results Website

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|------------------------------------|------------|------------|------------|------------|------------|------------|------------|-----------|------------|------------|------------|------------|-----------|------------|-------------|
| Leukopenia | 0 (0.00%) | 1 (10.00%) | 1 (20.00%) | 1 (14.29%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 8 (10.81%) |
| Lymphopenia | 2 (50.00%) | 1 (10.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (33.33%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 6 (8.11%) |
| Neutropenia | 0 (0.00%) | 1 (10.00%) | 1 (20.00%) | 5 (71.43%) | 0 (0.00%) | 6 (54.55%) | 2 (50.00%) | 0 (0.00%) | 2 (33.33%) | 1 (25.00%) | 0 (0.00%) | 2 (50.00%) | 0 (0.00%) | 2 (50.00%) | 22 (29.73%) |
| Thrombocytopenia | 0 (0.00%) | 1 (10.00%) | 2 (40.00%) | 2 (28.57%) | 0 (0.00%) | 3 (27.27%) | 2 (50.00%) | 0 (0.00%) | 2 (33.33%) | 1 (25.00%) | 2 (33.33%) | 0 (0.00%) | 0 (0.00%) | 2 (50.00%) | 17 (22.97%) |
| Thrombocytosis | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Cardiac disorders | | | | | | | | | | | | | | | |
| Angina pectoris | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Cardiovascular disorder | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Ear and labyrinth disorders | | | | | | | | | | | | | | | |
| Vertigo | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Endocrine disorders | | | | | | | | | | | | | | | |
| Hypothyroidism | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Eye disorders | | | | | | | | | | | | | | | |
| Cataract | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Dry eye | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |

Clinical Trial Results Website

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|-----------------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|-------------|
| Eye pain | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Periorbital oedema | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Vision blurred | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Vitreous floaters | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (100.00%) | 0 (0.00%) | 1 (1.35%) |
| Gastrointestinal disorders | | | | | | | | | | | | | | | |
| Abdominal adhesions | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Abdominal discomfort | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Abdominal distension | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 4 (5.41%) |
| Abdominal pain | 2 (50.00%) | 2 (20.00%) | 2 (40.00%) | 0 (0.00%) | 1 (25.00%) | 3 (27.27%) | 0 (0.00%) | 2 (50.00%) | 0 (0.00%) | 3 (75.00%) | 0 (0.00%) | 2 (50.00%) | 0 (0.00%) | 1 (25.00%) | 18 (24.32%) |
| Abdominal pain lower | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Abdominal pain upper | 0 (0.00%) | 1 (10.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 1 (25.00%) | 1 (25.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 6 (8.11%) |
| Breath odour | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Constipation | 2 (50.00%) | 1 (10.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 3 (50.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 11 (14.86%) |
| Dental caries | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Diarrhoea | 1 (25.00%) | 2 (20.00%) | 1 (20.00%) | 2 (28.57%) | 2 (50.00%) | 7 (63.64%) | 2 (50.00%) | 2 (50.00%) | 0 (0.00%) | 1 (25.00%) | 2 (33.33%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 23 (31.08%) |

Clinical Trial Results Website

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|-----------------------------|-----------------|----------------|------------------|------------------|------------------|----------------|------------------|-----------------|-----------------|------------------|-----------------|-----------------|------------------|------------------|------------------|
| Dry mouth | 0 (0.0 0%) | 1 (10.0 0%) | 2 (40.0 00%) | 2 (28.5 7%) | 0 (0.0 0%) | 2 (18.1 8%) | 1 (25.0 00%) | 1 (25.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16.6 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 10 (13.5 51%) |
| Dyspepsia | 1 (25.0 00%) | 2 (20.0 0%) | 0 (0.0 0%) | 1 (14.2 29%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 5 (6.76 %) |
| Dysphagia | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (18.1 8%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (2.70 %) |
| Epigastric discomfort | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Gingival bleeding | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (25.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Gingival discomfort | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 1 (25.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Loose tooth | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25.0 00%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Nausea | 2 (50.0 00%) | 7 (70.0 0%) | 5 (100.0 00%) | 7 (100.0 00%) | 4 (100.0 00%) | 8 (72.7 3%) | 4 (100.0 00%) | 2 (50.0 00%) | 4 (66.6 67%) | 4 (100.0 00%) | 3 (50.0 00%) | 1 (25.0 00%) | 1 (100.0 00%) | 4 (100.0 00%) | 56 (75.6 68%) |
| Odynopha gia | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25.0 00%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Stomatitis | 0 (0.0 0%) | 0 (0.00 %) | 1 (20.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 1 (25.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25.0 00%) | 4 (5.41 %) |
| Subileus | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16.6 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Tongue ulceration | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16.6 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Tooth discolourat ion | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 1 (25.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Toothache | 0 (0.0 0%) | 1 (10.0 0%) | 1 (20.0 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (2.70 %) |
| Vomiting | 1 (25.0 00%) | 3 (30.0 0%) | 2 (40.0 00%) | 4 (57.1 14%) | 2 (50.0 00%) | 7 (63.6 4%) | 2 (50.0 00%) | 2 (50.0 00%) | 4 (66.6 67%) | 2 (50.0 00%) | 3 (50.0 00%) | 3 (75.0 00%) | 1 (100.0 00%) | 2 (50.0 00%) | 38 (51.3 35%) |

Clinical Trial Results Website

General disorders and administrative on site conditions

| | | | | | | | | | | | | | | | |
|------------------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|-------------|------------|------------|-------------|------------|-------------|
| Asthenia | 2 (50.00%) | 2 (20.00%) | 1 (20.00%) | 1 (14.29%) | 2 (50.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 10 (13.51%) |
| Chills | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 4 (5.41%) |
| Face oedema | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Fatigue | 2 (50.00%) | 4 (40.00%) | 2 (40.00%) | 5 (71.43%) | 2 (50.00%) | 8 (72.73%) | 1 (25.00%) | 4 (100.00%) | 2 (33.33%) | 4 (100.00%) | 4 (66.67%) | 2 (50.00%) | 0 (0.00%) | 2 (50.00%) | 42 (56.76%) |
| Feeling cold | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Gait disturbance | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Influenza like illness | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (100.00%) | 0 (0.00%) | 4 (5.41%) |
| Malaise | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Mucosal inflammation | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Non-cardiac chest pain | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Oedema peripheral | 1 (25.00%) | 0 (0.00%) | 2 (40.00%) | 1 (14.29%) | 0 (0.00%) | 1 (9.09%) | 1 (25.00%) | 2 (50.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 8 (10.81%) |
| Pain | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 2 (2.70%) |

Clinical Trial Results Website

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|-------------------------------------|------------|------------|------------|------------|------------|------------|------------|-----------|------------|------------|------------|------------|-----------|-----------|-------------|
| Pyrexia | 3 (75.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 2 (50.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 10 (13.51%) |
| Swelling | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Thirst | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Hepatobiliary disorders | | | | | | | | | | | | | | | |
| Hepatocellular injury | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Immune system disorders | | | | | | | | | | | | | | | |
| Haemophagocytic lymphohistiocytosis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Infections and infestations | | | | | | | | | | | | | | | |
| Device related infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Ear infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Gastroenteritis | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Gastroenteritis norovirus | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Gastrointestinal viral infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |

Clinical Trial Results Website

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|--|----------------|----------------|----------------|---------------|----------------|----------------|---------------|----------------|----------------|----------------|----------------|---------------|---------------|----------------|---------------|
| Gingivitis | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Influenza | 0 (0.0 0%) | 0 (0.00 %) | 1 (20. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (2.70 %) |
| Laryngitis | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Nasophary ngitis | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (2.70 %) |
| Oral herpes | 0 (0.0 0%) | 1 (10.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Respirator y tract infection | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (18.1 8%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (2.70 %) |
| Rhinitis | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Sinusitis | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Skin infection | 1 (25. 00%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Soft tissue infection | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 1 (1.35 %) |
| Staphyloco ccal infection | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Tracheitis | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Upper respiratory tract infection | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Urinary tract infection | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (16. 67%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |

Clinical Trial Results Website

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|---|------------|------------|------------|------------|-----------|------------|-----------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|
| Vaginal infection | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Viral upper respiratory tract infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Vulvitis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Injury, poisoning and procedural complications | | | | | | | | | | | | | | | |
| Contusion | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Fall | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Procedural pain | 1 (25.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Product use complaint | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Road traffic accident | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Wound | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Investigations | | | | | | | | | | | | | | | |
| Alanine aminotransferase increased | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |

Clinical Trial Results Website

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|--------------------------------------|----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|-------------|
| Amylase increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 1 (100.00%) | 0 (0.0%) | 4 (5.41%) |
| Aspartate aminotransferase increased | 0 (0.0%) | 0 (0.00%) | 1 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |
| Basophil count increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Blood albumin increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Blood alkaline phosphatase decreased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Blood alkaline phosphatase increased | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 4 (5.41%) |
| Blood bilirubin increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 1 (1.35%) |
| Blood cholesterol increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Blood creatinine increased | 0 (0.0%) | 7 (70.00%) | 1 (20.00%) | 1 (14.29%) | 1 (25.00%) | 5 (45.45%) | 1 (25.00%) | 0 (0.0%) | 3 (50.00%) | 1 (25.00%) | 3 (50.00%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 24 (32.43%) |
| Blood lactate dehydroge | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |

Clinical Trial Results Website

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|-------------------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|-------------|
| nase increased | | | | | | | | | | | | | | | |
| Blood potassium increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 2 (2.70%) |
| Blood urea increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Electrocardiogram QT prolonged | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |
| Gamma-glutamyltransferase increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Haemoglobin decreased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Lipase increased | 2 (50.00%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (100.00%) | 0 (0.0%) | 5 (6.76%) |
| Lymphocyte count decreased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 3 (42.86%) | 1 (25.00%) | 3 (27.27%) | 1 (25.00%) | 2 (50.00%) | 1 (16.67%) | 1 (25.00%) | 1 (16.67%) | 0 (0.0%) | 1 (100.00%) | 1 (25.00%) | 15 (20.27%) |
| Lymphocyte count increased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Neutrophil count decreased | 1 (25.00%) | 2 (20.00%) | 2 (40.00%) | 2 (28.57%) | 0 (0.0%) | 3 (27.27%) | 1 (25.00%) | 3 (75.00%) | 1 (16.67%) | 1 (25.00%) | 2 (33.33%) | 1 (25.00%) | 1 (100.00%) | 2 (50.00%) | 22 (29.73%) |
| Platelet count decreased | 1 (25.00%) | 1 (10.00%) | 1 (20.00%) | 5 (71.43%) | 0 (0.0%) | 4 (36.36%) | 1 (25.00%) | 3 (75.00%) | 3 (50.00%) | 1 (25.00%) | 2 (33.33%) | 1 (25.00%) | 1 (100.00%) | 1 (25.00%) | 25 (33.78%) |
| Vitamin B12 decreased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |

Clinical Trial Results Website

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|---|------------|-----------|-----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|-------------|
| Weight decreased | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (2.70%) |
| Weight increased | 0 (0.0%) | 1 (10.0%) | 1 (20.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (2.70%) |
| White blood cell count decreased | 0 (0.0%) | 2 (20.0%) | 2 (40.0%) | 3 (42.86%) | 2 (50.0%) | 5 (45.45%) | 1 (25.00%) | 2 (50.00%) | 2 (33.33%) | 1 (25.00%) | 2 (33.33%) | 1 (25.00%) | 1 (100.00%) | 2 (50.00%) | 26 (35.14%) |
| Metabolism and nutrition disorders | | | | | | | | | | | | | | | |
| Cachexia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Decreased appetite | 3 (75.00%) | 3 (30.0%) | 1 (20.0%) | 3 (42.86%) | 0 (0.0%) | 3 (27.27%) | 1 (25.00%) | 3 (75.00%) | 0 (0.0%) | 1 (25.00%) | 3 (50.00%) | 1 (25.00%) | 0 (0.0%) | 1 (25.00%) | 23 (31.08%) |
| Dehydration | 1 (25.00%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 2 (2.70%) |
| Dyslipidaemia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Hyperglycaemia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (2.70%) |
| Hyperkalaemia | 0 (0.0%) | 1 (10.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (2.70%) |
| Hypertriglyceridaemia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Hypoalbuminaemia | 1 (25.00%) | 1 (10.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 4 (5.41%) |
| Hypocalcaemia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 2 (2.70%) |
| Hypokalaemia | 0 (0.0%) | 1 (10.0%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |

Clinical Trial Results Website

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|--|------------|------------|------------|------------|-----------|------------|-----------|------------|------------|------------|------------|------------|-------------|-----------|-----------|
| Hypomagnesaemia | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 4 (5.41%) |
| Hyponatraemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (100.00%) | 0 (0.00%) | 1 (1.35%) |
| Hypophosphataemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 1 (16.67%) | 1 (25.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 4 (5.41%) |
| Iron overload | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Lack of satiety | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Musculoskeletal and connective tissue disorders | | | | | | | | | | | | | | | |
| Arthralgia | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Back pain | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 3 (4.05%) |
| Flank pain | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Joint swelling | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Limb discomfort | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Muscle spasms | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Muscular weakness | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Musculoskeletal chest pain | 0 (0.00%) | 2 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |

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|--|----------|-----------|-----------|------------|----------|------------|------------|------------|------------|----------|------------|----------|-------------|------------|------------|
| Musculoskeletal pain | 0 (0.0%) | 1 (10.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Musculoskeletal stiffness | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Myalgia | 0 (0.0%) | 1 (10.0%) | 1 (20.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |
| Pain in extremity | 0 (0.0%) | 4 (40.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (25.00%) | 6 (8.11%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | | | | | | | | | | | | |
| Lipoma | 0 (0.0%) | 0 (0.0%) | 1 (20.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Tumour pain | 0 (0.0%) | 1 (10.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 3 (50.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 6 (8.11%) |
| Nervous system disorders | | | | | | | | | | | | | | | |
| Ageusia | 0 (0.0%) | 0 (0.0%) | 1 (20.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Anosmia | 0 (0.0%) | 0 (0.0%) | 1 (20.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Balance disorder | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Dizziness | 0 (0.0%) | 2 (20.0%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 2 (18.18%) | 0 (0.0%) | 1 (25.00%) | 1 (16.67%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 1 (100.00%) | 0 (0.0%) | 9 (12.16%) |
| Dysaesthesia | 0 (0.0%) | 1 (10.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |

Clinical Trial Results Website

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|------------------------------|----------------|----------------|---------------|----------------|----------------|---------------|----------------|----------------|----------------|----------------|----------------|----------------|---------------|----------------|-----------------|
| Dysgeusia | 0 (0.0 0%) | 1 (10.0 0%) | 0 (0.0 0%) | 1 (14. 29%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 4 (5.41 %) |
| Haemorrhage intracranial | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (14. 29%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Head discomfort | 0 (0.0 0%) | 1 (10.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Headache | 1 (25. 00%) | 1 (10.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 1 (9.09 %) | 0 (0.0 0%) | 2 (50. 00%) | 1 (16. 67%) | 1 (25. 00%) | 0 (0.0 0%) | 1 (25. 00%) | 0 (0.0 0%) | 1 (25. 00%) | 10 (13. 51%) |
| Hypoaesthesia | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (14. 29%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Neuropathy peripheral | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 1 (14. 29%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Parosmia | 0 (0.0 0%) | 1 (10.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Sciatica | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Somnolence | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 2 (33. 33%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 3 (4.05 %) |
| Syncope | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Taste disorder | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 1 (25. 00%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Tremor | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (25. 00%) | 1 (1.35 %) |
| Psychiatric disorders | | | | | | | | | | | | | | | |
| Anxiety | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |
| Confusional state | 0 (0.0 0%) | 0 (0.00 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (9.09 %) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 0 (0.0 0%) | 1 (1.35 %) |

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|------------------------------------|----------|------------|------------|------------|----------|------------|----------|------------|------------|----------|------------|----------|----------|----------|-----------|
| Depression | 0 (0.0%) | 0 (0.00%) | 1 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Insomnia | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (18.18%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 5 (6.76%) |
| Psychomotor retardation | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Sleep disorder | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Renal and urinary disorders | | | | | | | | | | | | | | | |
| Acute kidney injury | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Dysuria | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 2 (33.33%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |
| Haematuria | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Leukocyturia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Micturition urgency | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Nocturia | 0 (0.0%) | 0 (0.00%) | 1 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Pollakiuria | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Renal failure | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (14.29%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |

Respiratory, thoracic and mediastinal disorders

Clinical Trial Results Website

| | | | | | | | | | | | | | | | |
|---------------------------|------------|------------|------------|------------|-----------|------------|-----------|------------|------------|-----------|------------|------------|-----------|------------|------------|
| Cough | 1 (25.00%) | 1 (10.00%) | 1 (20.00%) | 1 (14.29%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 8 (10.81%) |
| Dyspnoea | 1 (25.00%) | 2 (20.00%) | 0 (0.00%) | 2 (28.57%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 8 (10.81%) |
| Epistaxis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Hiccups | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Interstitial lung disease | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Lung disorder | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Nasal congestion | 1 (25.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 4 (5.41%) |
| Oropharyngeal pain | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Pleural effusion | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Productive cough | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.70%) |
| Pulmonary embolism | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Pulmonary infarction | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Rhinitis allergic | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Rhinorrhoea | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |

Skin and subcutaneo

Clinical Trial Results Website

us tissue disorders

| | | | | | | | | | | | | | | | |
|--------------------|------------|------------|------------|------------|----------|-----------|------------|------------|----------|----------|------------|----------|----------|----------|-----------|
| Alopecia | 0 (0.0%) | 0 (0.00%) | 1 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 3 (4.05%) |
| Cold sweat | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Dermatitis | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Dry skin | 0 (0.0%) | 0 (0.00%) | 2 (40.00%) | 1 (14.29%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 4 (5.41%) |
| Hyperhidrosis | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Onychoclasia | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Onycholysis | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Pain of skin | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Penile ulceration | 0 (0.0%) | 1 (10.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Pruritus | 1 (25.00%) | 2 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 5 (6.76%) |
| Psoriasis | 0 (0.0%) | 0 (0.00%) | 1 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Purpura | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Rash | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (16.67%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (1.35%) |
| Rash maculopapular | 0 (0.0%) | 2 (20.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (9.09%) | 0 (0.0%) | 1 (25.00%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 4 (5.41%) |

Clinical Trial Results Website

| | | | | | | | | | | | | | | | |
|---------------------------|-----------|-----------|-----------|------------|-----------|-----------|------------|------------|------------|-----------|------------|-----------|-----------|-----------|-----------|
| Skin discolouration | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Xeroderma | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Vascular disorders | | | | | | | | | | | | | | | |
| Haematoma | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Hot flush | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |
| Hypertension | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (50.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (4.05%) |
| Pallor | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (14.29%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.35%) |

Other Relevant Findings

Not Applicable

Conclusion:

- Based on the data collected during the phase Ib part of this study in liposarcoma patients, the combination of HDM201 120 mg Q3W and LEE011 200mg qd, 2 weeks on, 1 week off (Regimen 4) was declared as RP2D (recommended phase 2 dose).
- Regimen 4 showed some signs of clinical activity, including patients with prolonged PRs.
- The safety profile of combination of HDM201 and LEE011 was manageable and consistent with the previous experience with either single agent.

Clinical Trial Results Website

- PK data of HDM201 in combination with LEE011 in Regimen 4 was generally consistent with the single agent HDM201 PK, albeit with mean exposures tending slightly higher compared to single agent, and suggesting that LEE011 has a mild impact on the PK of HDM201 in the regimen selected as RP2D (Regimen 4).
- Dose-dependent pharmacodynamic changes in direct transcriptional targets of p53 were seen in a majority of patients but did not correlate with clinical activity.

Date of Clinical Trial Report

27 May 2020