



Clinical trial results:

A Multicenter, Open-Label Extension Study of WVE-210201 in Patients Previously Enrolled in WVE-DMDX51-001

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2018-000975-34 |
| Trial protocol | GB FR NL BE IT |
| Global end of trial date | 20 January 2020 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 13 September 2020 |
| First version publication date | 13 September 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | WVE-DMDX51-002 |
|-----------------------|----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Wave Life Sciences UK Limited |
| Sponsor organisation address | 1 Chamberlain Square CS, Birmingham, United Kingdom, B3 3AX |
| Public contact | Chief Medical Officer, Wave Life Sciences, +617 949-2900, info@wavelifesci.com |
| Scientific contact | Chief Medical Officer, Wave Life Sciences, +617 949-2900, info@wavelifesci.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 February 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 January 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of WVE-210201

Protection of trial subjects:

Written informed consent from each patient or patient's parent(s) or legal guardian(s), if applicable, and written assent from each patient, if applicable, were obtained before any study-specific screening or baseline period evaluations were performed. The anonymity of participating patients was maintained to the extent required by applicable laws and in accordance with current HIPAA standards. This study was designed and monitored in accordance with Sponsor procedures, which complied with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

The unblinded, independent Safety Monitoring Committee (SMC) reviewed aggregate safety data periodically and unblinded, aggregate safety data periodically and on an ad hoc basis should any emergent safety concerns have arisen during the course of the study. Recommendations based on these reviews were to be provided to the Sponsor

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 14 August 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 1 |
| Country: Number of subjects enrolled | Italy: 5 |
| Country: Number of subjects enrolled | United States: 10 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | Belgium: 8 |
| Country: Number of subjects enrolled | France: 5 |
| Worldwide total number of subjects | 37 |
| EEA total number of subjects | 26 |

Notes:

| Subjects enrolled per age group | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 33 |
| Adolescents (12-17 years) | 4 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 6 countries (Belgium, France, Italy, United Kingdom, Canada and United States from 14 August 2018 to 20 January 2020).

Pre-assignment

Screening details:

The patients successfully completed the Phase I study (WVE-DMDX51-001) were eligible to participate in this open-label extension study (OLE study). They were re-evaluated for certain eligibility criteria. Patients started screening for this OLE study after a minimum of 2 weeks from the last follow-up visit in the Phase I study.

Period 1

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

Blinding implementation details:

This is an open-label study.

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 1 mg/kg WVE-210201 |

Arm description:

Dose at enrollment, 1 mg/kg WVE-210201 administered via IV infusion

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | suvodirsen |
| Investigational medicinal product code | WVE-210201 |
| Other name | |
| Pharmaceutical forms | Powder for infusion, Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received weekly IV infusions of suvodirsen. WVE-210201 was provided either as a lyophilized powder or as an isotonic solution for dilution for infusion.

| | |
|------------------|--------------------|
| Arm title | 2 mg/kg WVE-210201 |
|------------------|--------------------|

Arm description:

Dose at enrollment, 2 mg/kg WVE-210201 administered via IV infusion

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | suvodirsen |
| Investigational medicinal product code | WVE-210201 |
| Other name | |
| Pharmaceutical forms | Solution for infusion, Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received weekly IV infusions of suvodirsen. WVE-210201 was provided either as a lyophilized powder or as an isotonic solution for dilution for infusion.

| | |
|------------------|----------------------|
| Arm title | 3.5 mg/kg WVE-210201 |
|------------------|----------------------|

Arm description:

Dose at enrollment, 3.5 mg/kg WVE-210201 administered via IV infusion

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | suvodirsen |
| Investigational medicinal product code | WVE-210201 |
| Other name | |
| Pharmaceutical forms | Solution for infusion, Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received weekly IV infusions of suvodirsen. WVE-210201 was provided either as a lyophilized powder or as an isotonic solution for dilution for infusion.

| | |
|------------------|--------------------|
| Arm title | 5 mg/kg WVE-210201 |
|------------------|--------------------|

Arm description:

Dose at enrollment, 5 mg/kg WVE-210201 administered via IV infusion

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | suvodirsen |
| Investigational medicinal product code | WVE-210201 |
| Other name | |
| Pharmaceutical forms | Powder for infusion, Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Patients received weekly IV infusions of suvodirsen. WVE-210201 was provided either as a lyophilized powder or as an isotonic solution for dilution for infusion.

| Number of subjects in period 1 | 1 mg/kg WVE-210201 | 2 mg/kg WVE-210201 | 3.5 mg/kg WVE-210201 |
|---------------------------------------|--------------------|--------------------|----------------------|
| Started | 14 | 5 | 5 |
| Completed Dose Modification Visit | 13 | 5 | 0 |
| Target Dose 3.5 mg/kg | 1 | 4 | 0 |
| Target Dose 5 mg/kg | 12 | 1 | 0 |
| Completed | 0 | 0 | 0 |
| Not completed | 14 | 5 | 5 |
| Physician decision | 1 | - | - |
| Study Terminated by Sponsor | 13 | 5 | 5 |

| Number of subjects in period 1 | 5 mg/kg WVE-210201 |
|---------------------------------------|--------------------|
| Started | 13 |
| Completed Dose Modification Visit | 0 |
| Target Dose 3.5 mg/kg | 0 |
| Target Dose 5 mg/kg | 0 |
| Completed | 0 |
| Not completed | 13 |
| Physician decision | - |
| Study Terminated by Sponsor | 13 |

Baseline characteristics

Reporting groups

| | |
|---|----------------------|
| Reporting group title | 1 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 1 mg/kg WVE-210201 administered via IV infusion | |
| Reporting group title | 2 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 2 mg/kg WVE-210201 administered via IV infusion | |
| Reporting group title | 3.5 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 3.5 mg/kg WVE-210201 administered via IV infusion | |
| Reporting group title | 5 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 5 mg/kg WVE-210201 administered via IV infusion | |

| Reporting group values | 1 mg/kg WVE-210201 | 2 mg/kg WVE-210201 | 3.5 mg/kg WVE-210201 |
|--|--------------------|--------------------|----------------------|
| Number of subjects | 14 | 5 | 5 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 12 | 4 | 5 |
| Adolescents (12-17 years) | 2 | 1 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 14 | 5 | 5 |

| Reporting group values | 5 mg/kg WVE-210201 | Total | |
|--|--------------------|-------|--|
| Number of subjects | 13 | 37 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 12 | 33 | |
| Adolescents (12-17 years) | 1 | 4 | |
| Adults (18-64 years) | 0 | 0 | |

| | | | |
|-------------------|---|---|--|
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |

| | | | |
|---------------------------------------|----|----|--|
| Gender categorical Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 13 | 37 | |

Subject analysis sets

| | |
|----------------------------|-------------------|
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All patients who received at least 1 dose of WVE-210201

| Reporting group values | Safety population | | |
|---|-------------------|--|--|
| Number of subjects | 37 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 33 | | |
| Adolescents (12-17 years) | 4 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Gender categorical Units: Subjects | | | |
| Female | 0 | | |
| Male | 37 | | |

End points

End points reporting groups

| | |
|---|----------------------|
| Reporting group title | 1 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 1 mg/kg WVE-210201 administered via IV infusion | |
| Reporting group title | 2 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 2 mg/kg WVE-210201 administered via IV infusion | |
| Reporting group title | 3.5 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 3.5 mg/kg WVE-210201 administered via IV infusion | |
| Reporting group title | 5 mg/kg WVE-210201 |
| Reporting group description: | |
| Dose at enrollment, 5 mg/kg WVE-210201 administered via IV infusion | |
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All patients who received at least 1 dose of WVE-210201 | |

Primary: Number of Patients who Experienced a Serious TEAE

| | |
|---|--|
| End point title | Number of Patients who Experienced a Serious TEAE ^[1] |
| End point description: | |
| An SAE was defined as any event that resulted in death, was immediately life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or was a congenital anomaly/birth defect not present at Screening. Important medical events that did not result in death, were life threatening, or required hospitalization were considered SAEs when, based upon appropriate medical judgment, they jeopardized the patient or required medical or surgical intervention to prevent one of the outcomes listed in this definition. No patients were withdrawn due to a serious or intolerable AE that in the Investigator's opinion required discontinuation of study drug. 3 patients experienced severe adverse events (2 in 3.5 mg/kg WVE-210201 arm and 1 in 5 mg/kg WVE-210201 arm). This may include patients whose doses were modified. | |
| End point type | Primary |
| End point timeframe: | |
| Day 1 to Early Termination | |
| Notes: | |

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis has been used.

| End point values | 1 mg/kg WVE-210201 | 2 mg/kg WVE-210201 | 3.5 mg/kg WVE-210201 | 5 mg/kg WVE-210201 |
|---|--------------------|--------------------|----------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 14 | 5 | 5 | 13 |
| Units: Subjects | | | | |
| number (not applicable) | | | | |
| Number of Patients who Experienced an SAE | 0 | 0 | 1 | 5 |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Early Termination

Adverse event reporting additional description:

For the patients who had a dose modification during the course of the study, events that occurred prior to dose modification are counted in the dose arm that the patient received at the time of enrollment, and events that occurred after dose modification are counted in the dose arm that the patient received after dose modification.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | 1 mg/kg WVE-210201 |
|-----------------------|--------------------|

Reporting group description:

1 mg/kg WVE-210201 administered via IV infusion

| | |
|-----------------------|--------------------|
| Reporting group title | 2 mg/kg WVE-210201 |
|-----------------------|--------------------|

Reporting group description:

2 mg/kg WVE-210201 administered via IV infusion

| | |
|-----------------------|----------------------|
| Reporting group title | 3.5 mg/kg WVE-210201 |
|-----------------------|----------------------|

Reporting group description:

3.5 mg/kg WVE-210201 administered via IV infusion.

| | |
|-----------------------|--------------------|
| Reporting group title | 5 mg/kg WVE-210201 |
|-----------------------|--------------------|

Reporting group description:

5 mg/kg WVE-210201 administered via IV infusion

| Serious adverse events | 1 mg/kg WVE-210201 | 2 mg/kg WVE-210201 | 3.5 mg/kg WVE-210201 |
|---|--------------------|--------------------|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gamma-glutamyltransferase increased | | | |

| | | | |
|--|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|--------------------|--|--|
| Serious adverse events | 5 mg/kg WVE-210201 | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 26 (19.23%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Tachycardia | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | 1 mg/kg WVE-210201 | 2 mg/kg WVE-210201 | 3.5 mg/kg WVE-210201 |
|---|--------------------|--------------------|----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 14 (100.00%) | 5 / 5 (100.00%) | 10 / 10 (100.00%) |
| Vascular disorders | | | |
| Flushing | | | |

| | | | |
|--|----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 0 | 5 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pallor | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Catheter site erythema | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Feeling abnormal | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperthermia | | | |

| | | | |
|---|----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infusion site erythema | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site papule | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 6 / 10 (60.00%) |
| occurrences (all) | 1 | 0 | 29 |
| Immune system disorders | | | |
| Allergy to arthropod bite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| Cough | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 3 / 10 (30.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 5 (20.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 1 | 2 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Sputum discoloured | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Attention deficit/hyperactivity disorder | | | |

| | | | |
|--------------------------------|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Restlessness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood fibrinogen increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood lactic acid increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Body temperature increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Complement factor C3 increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|----------------|---------------|-----------------|
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Monocyte count increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Protein urine present | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Troponin increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod sting | | | |

| | | | |
|-----------------------------|-----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Fall | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Heat exhaustion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Laceration | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Soft tissue injury | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound complication | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Wound secretion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Cyanosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------|---------------------|-----------------------|
| Palpitations subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 2 |
| Tachycardia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 2 / 10 (20.00%) 2 |
| Dysstasia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 4 | 1 / 5 (20.00%) 1 | 6 / 10 (60.00%) 37 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Tympanic membrane hyperaemia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Eye disorders Eye pruritus subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 5 (20.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 2 | 1 | 6 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 4 / 10 (40.00%) |
| occurrences (all) | 1 | 0 | 4 |
| Defaecation urgency | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 3 / 10 (30.00%) |
| occurrences (all) | 0 | 0 | 9 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Food poisoning | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Loose tooth | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Nausea | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|----------------------|
| Vomiting subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 3 / 10 (30.00%) 3 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 5 (20.00%) 1 | 0 / 10 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 2 / 5 (40.00%) 2 | 0 / 10 (0.00%) 0 |
| Livedo reticularis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 5 (20.00%) 1 | 2 / 10 (20.00%) 2 |
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 5 (20.00%) 1 | 0 / 10 (0.00%) 0 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Rash pruritic subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Renal and urinary disorders | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| Dysuria subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 5 (20.00%) 3 | 0 / 10 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 2 / 10 (20.00%) 3 |
| Haemarthrosis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 5 (20.00%) 1 | 0 / 10 (0.00%) 0 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Myalgia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Osteoporosis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Infections and infestations | | | |
| Asymptomatic bacteriuria subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Candida infection | | | |

| | | | |
|------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 1 | 0 | 4 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin bacterial infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|--------------------|---------------------|
| Insulin resistance subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
|--|---------------------|--------------------|---------------------|

| | | | |
|---|--------------------|--|--|
| Non-serious adverse events | 5 mg/kg WVE-210201 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 26 / 26 (100.00%) | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | | |
| occurrences (all) | 13 | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Pallor | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Catheter site erythema | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 5 | | |
| Chest pain | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | | |
| occurrences (all) | 9 | | |
| Chills | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | | |
| occurrences (all) | 8 | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 4 | | |

| | | | |
|--|-------------------------|--|--|
| Feeling abnormal subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Feeling cold subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Hyperthermia subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Infusion site erythema subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Infusion site papule subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 2 | | |
| Malaise subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Non-cardiac chest pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Peripheral swelling subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 22 / 26 (84.62%) 113 | | |
| Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Seasonal allergy | | | |

| | | | |
|--|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 5 / 26 (19.23%) 7 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 4 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Hypoxia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Nasal congestion subjects affected / exposed occurrences (all) | 3 / 26 (11.54%) 3 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 5 | | |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Sputum discoloured subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Throat irritation | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Mood altered | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Restlessness | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood fibrinogen increased | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Blood lactic acid increased | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Body temperature increased | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 3 | | |
| C-reactive protein increased | | | |

| | | | |
|-------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Complement factor C3 increased | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 4 / 26 (15.38%) | | |
| occurrences (all) | 4 | | |
| Heart rate increased | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Monocyte count increased | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Neutrophil count increased | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Protein urine present | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 4 | | |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|-----------------------|--|--|
| White blood cell count increased subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | | |
| Arthropod sting subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Fall subjects affected / exposed occurrences (all) | 9 / 26 (34.62%) 14 | | |
| Heat exhaustion subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Laceration subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Ligament sprain subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Limb injury subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 2 | | |
| Procedural pain subjects affected / exposed occurrences (all) | 6 / 26 (23.08%) 6 | | |
| Skin abrasion subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Soft tissue injury subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Wound complication | | | |

| | | | |
|---|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Wound secretion subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Cardiac disorders | | | |
| Cyanosis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Palpitations subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Tachycardia subjects affected / exposed occurrences (all) | 7 / 26 (26.92%) 31 | | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Dysstasia subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Headache subjects affected / exposed occurrences (all) | 14 / 26 (53.85%) 58 | | |
| Lethargy subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Ear and labyrinth disorders | | | |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Tympanic membrane hyperaemia | | | |

| | | | |
|--|-----------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Eye disorders Eye pruritus subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 6 / 26 (23.08%) 14 | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 4 / 26 (15.38%) 7 | | |
| Defaecation urgency subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 8 / 26 (30.77%) 8 | | |
| Dysphagia subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Flatulence subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Food poisoning subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Gastritis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Haemorrhoids | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Loose tooth | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 8 / 26 (30.77%) | | |
| occurrences (all) | 17 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 14 / 26 (53.85%) | | |
| occurrences (all) | 46 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Erythema | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Livedo reticularis | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 5 | | |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|----------------------|--|--|
| Rash maculo-papular subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Rash pruritic subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 9 | | |
| Urticaria subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Back pain subjects affected / exposed occurrences (all) | 5 / 26 (19.23%) 5 | | |
| Haemarthrosis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 7 | | |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Osteoporosis subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Pain in extremity | | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed | 6 / 26 (23.08%) | | |
| occurrences (all) | 11 | | |
| Infections and infestations | | | |
| Asymptomatic bacteriuria | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| Candida infection | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 4 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 26 (7.69%) | | |
| occurrences (all) | 2 | | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin bacterial infection | | | |
| subjects affected / exposed | 1 / 26 (3.85%) | | |
| occurrences (all) | 1 | | |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 26 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 26 (11.54%) | | |
| occurrences (all) | 3 | | |

| | | | |
|--|---------------------|--|--|
| Wound infection subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 2 / 26 (7.69%) 6 | | |
| Dehydration subjects affected / exposed occurrences (all) | 1 / 26 (3.85%) 1 | | |
| Insulin resistance subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 25 May 2018 | Amendment 3.0, dated 25 May 2018 - Addition of liquid formulation of WVE-210201 |
| 01 August 2018 | Amendment 5.0, dated 01 August 2018 - Baseline needle biopsy collection was removed and end-of-treatment needle biopsy was clarified. |
| 22 January 2019 | Amendment 6.0, dated 22 January 2019 - Study was extended from 14 weeks to 96 weeks. Dose modification to the highest tolerated doses (3.5 and 5 mg/kg) was added. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Not applicable

Notes: