



Clinical trial results:

NSGO-OV-UMB1; ENGOT-OV30: A phase II umbrella trial in patients with relapsed ovarian cancer.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-002805-36 |
| Trial protocol | DK FI NO |
| Global end of trial date | 30 November 2021 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 10 September 2023 |
| First version publication date | 10 September 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | ENGOT-OV30/NSGO |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03267589 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Nordic Society of Gynaecological Oncology - Clinical Trial Unit (NSGO-CTU) |
| Sponsor organisation address | Blegdamsvej 9 , Copenhagen , Denmark, 2100 |
| Public contact | Medical Director, Mansoor Raza Mirza, Nordic Society of Gynaecological Oncology - Clinical Trial Unit (NSGO-CTU), +45 35453311, mansoor.raza.mirza@regionh.dk |
| Scientific contact | Medical Director, Mansoor Raza Mirza, Nordic Society of Gynaecological Oncology - Clinical Trial Unit (NSGO-CTU), +45 35453311, mansoor.raza.mirza@regionh.dk |

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 | 30 September 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 October 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 November 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The overall objective is to obtain preliminary evidence of efficacy of novel agents for the management of relapsed ovarian cancer.

Protection of trial subjects:

The IDSMC was established to provide independent review and assessment of the efficacy and safety data in a systematic manner and to safeguard the interest and safety of the participating patients in the study. The composition of the IDMC consisted of 3 independent individuals, and made recommendations to the Sponsor based on their review to continue or stop the trial based on their assessment of safety information. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the ICH-GCP guidelines. The local principal investigators were responsible for ensuring that the study was conducted in accordance with the protocol, the ethical principles of the Declaration of Helsinki, current ICH guidelines on Good Clinical practice (GCP) and applicable local regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 14 May 2018 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 3 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Norway: 8 |
| Country: Number of subjects enrolled | Denmark: 12 |
| Country: Number of subjects enrolled | Finland: 5 |
| Worldwide total number of subjects | 25 |
| EEA total number of subjects | 25 |

Notes:

Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

| | |
|--|----|
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 12 |
| From 65 to 84 years | 13 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Candidates were identified by a member of the treatment team. The investigator screened patients' medical records for suitable candidates. Patients had to sign a specific CD73 ICF. Enrolment occurred only after the patient had signed the ICF and screening assessments and eligibility criteria were completed. Recruitment from Q2 2018 - Q2 2019.

Pre-assignment

Screening details:

Subjects underwent CD73 expression evaluation to ensure positive tumor cell CD73 expression. During pre-screening, patients were required to sign the ICF, fulfil the eligibility criteria and consent to give an archival tumor sample for CD73 screening. Re-screening at a later date at investigator's discretion was possible, though not more than once.

Period 1

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

Arms

| | |
|-----------|----------|
| Arm title | Cohort A |
|-----------|----------|

Arm description:

25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab.

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI9447 |
| Investigational medicinal product code | |
| Other name | Oleclumab |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received MEDI9447 3000 mg every 2 weeks via IV infusion. Subjects will remain on therapy until unacceptable toxicity, documentation of disease progression, subject withdrawal, or completion of the study.

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received durvalumab 1500 mg every 4 weeks via IV infusion. A dose of 1500 mg (for patients >30kg in weight) was administered using an IV bag containing 0.9% (w/v) saline or 5% (w/v) dextrose, with a final durvalumab concentration ranging from 1 to 20 mg/mL, and delivered through an IV administration set with a 0.2- or 0.22-µm in-line filter. Subjects will remain on therapy until unacceptable toxicity, documentation of disease progression, subject withdrawal, or completion of the study.

| Number of subjects in period 1 | Cohort A |
|---------------------------------------|----------|
| Started | 25 |
| Completed | 2 |
| Not completed | 23 |
| Death | 19 |
| Other | 4 |

Baseline characteristics

Reporting groups

| Reporting group title | Overall period |
|--|----------------|
| Reporting group description: 25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab. | |

| Reporting group values | Overall period | Total | |
|--|----------------|-------|--|
| Number of subjects | 25 | 25 | |
| 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) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 12 | 12 | |
| From 65-84 years | 13 | 13 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 64.7 | | |
| standard deviation | ± 8.8 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 25 | 25 | |
| Male | 0 | 0 | |
| Race | | | |
| Units: Subjects | | | |
| White | 23 | 23 | |
| Asian | 2 | 2 | |
| Previous cancer | | | |
| Units: Subjects | | | |
| No | 25 | 25 | |
| Yes | 0 | 0 | |
| Any comorbidity | | | |
| Units: Subjects | | | |
| No | 24 | 24 | |
| Yes | 1 | 1 | |
| Number of relapses | | | |
| Units: Subjects | | | |
| 1st relapse | 5 | 5 | |
| ≥2 relapses | 20 | 20 | |
| FIGO | | | |
| Units: Subjects | | | |

| | | | |
|---------------------------|----|----|--|
| Stage IV A | 6 | 6 | |
| Stage IV B | 5 | 5 | |
| Unknown | 1 | 1 | |
| Stage I | 3 | 3 | |
| Stage III | 10 | 10 | |
| Prior chemotherapy | | | |
| Units: Subjects | | | |
| No | 0 | 0 | |
| Yes | 25 | 25 | |
| Prior chemo type | | | |
| Units: Subjects | | | |
| Adjuvant | 4 | 4 | |
| 1st line | 11 | 11 | |
| 2nd line | 3 | 3 | |
| 3rd line | 1 | 1 | |
| Not reported | 6 | 6 | |
| BRCA mutation | | | |
| Units: Subjects | | | |
| No | 19 | 19 | |
| Yes | 3 | 3 | |
| Missing | 3 | 3 | |
| ECOG Performance Status | | | |
| Units: Subjects | | | |
| ECOG Performance Status 0 | 10 | 10 | |
| ECOG Performance Status 1 | 15 | 15 | |

End points

End points reporting groups

| | |
|--|----------|
| Reporting group title | Cohort A |
| Reporting group description: 25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab. | |

Primary: Disease control rate (DCR) (CR+PR+SD)

| | |
|--|--|
| End point title | Disease control rate (DCR) (CR+PR+SD) ^[1] |
| End point description: The analysis of DCR will be performed by calculating the point estimate of the percentage of patients which achieve complete or partial response or stable disease for at least 16 weeks, assessed according to RECIST 1.1 criteria. | |
| End point type | Primary |
| End point timeframe: Disease Control Rate (DCR = Complete Response (CR), Partial Response (PR) or Stable Disease (SD) at 16 weeks). | |

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: Only endpoint data from one arm (arm A) is reported. According to the EudraCT manual, it is therefor not mandatory to report the statistical analysis related to an endpoint (only one arm).

| End point values | Cohort A | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 0.32 (0.14 to 0.55) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-Free Survival (PFS)

| | |
|--|--|
| End point title | Median Progression-Free Survival (PFS) |
| End point description: PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status. Median PFS estimated by Kaplan-Meier method using RECIST v. 1.1 | |
| End point type | Secondary |
| End point timeframe: Median Progression-Free Survival (PFS) by RECIST v1.1 until end of observation. | |

| End point values | Cohort A | | | |
|-----------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: month | | | | |
| median (standard error) | 2.73 (\pm 0.533) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

| | |
|-----------------|-----------------------|
| End point title | Overall survival (OS) |
|-----------------|-----------------------|

End point description:

Patients who were alive at the time of the analysis were censored at the date of their last follow-up assessment. Patients without follow-up assessment were censored at the day of their last dose and patients with no post baseline information were censored at the time of their first administration of treatment drugs. OS was be estimated and tested along the same lines as PFS.

Overall survival estimated by Kaplan-Meier methods

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

OS is defined as the time from the date of inclusion/randomization to the date of death, regardless of the cause of death, or until end of observation.

| End point values | Cohort A | | | |
|-----------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: month | | | | |
| median (standard error) | 9.59 (\pm 2.198) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) according to RECIST v1.1

| | |
|-----------------|--|
| End point title | Objective Response Rate (ORR) according to RECIST v1.1 |
|-----------------|--|

End point description:

Objective response rate defined as the proportion of subjects achieving a best overall objective response according to RECIST v1.1 of PR or CR.

The analysis of the response rate is performed by calculating the point estimate of the percentage of patients which achieved complete or partial response assessed according to RECIST 1.1.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Objective Response Rate (ORR) according to RECIST v1.1 at 16 weeks.

| End point values | Cohort A | | | |
|----------------------------------|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 0.045 (0.001 to 0.228) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

| | |
|---|----------------------------|
| End point title | Duration of Response (DoR) |
| End point description: | |
| NB: Duration of Response (DoR) endpoint is not reported, as there is only one responder. | |
| End point type | Secondary |
| End point timeframe: | |
| DoR is the time between the initial response to therapy and subsequent disease progression or relapse. DoR can be estimated and tested along the same lines as PFS. | |

| End point values | Cohort A | | | |
|-----------------------------|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 ^[2] | | | |
| Units: month | | | | |
| median (standard error) | 0 (\pm 0) | | | |

Notes:

[2] - DoR is not reported, as there was only one responder

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 6 months by RECIST v. 1.1

| | |
|---|--|
| End point title | Progression-free survival (PFS) at 6 months by RECIST v. 1.1 |
| End point description: | |
| PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status. | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Progression-Free Survival (PFS) by RECIST v1.1 at 6 months | |

| | | | | |
|----------------------------------|---------------------|--|--|--|
| End point values | Cohort A | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: Percent | | | | |
| number (confidence interval 95%) | 0.20 (0.07 to 0.37) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 12 months by RECIST v. 1.1

| | |
|-----------------|---|
| End point title | Progression-free survival (PFS) at 12 months by RECIST v. 1.1 |
|-----------------|---|

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.

12-month PFS by Immune-RECIST estimated by Kaplan-Meier method

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Progression-Free Survival (PFS) by RECIST v1.1 12 months | |

| | | | | |
|----------------------------------|-----------------------|--|--|--|
| End point values | Cohort A | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: N/A | | | | |
| number (confidence interval 95%) | 0.04 (0.003 to 0.170) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-free survival (PFS) by Immune-RECIST

| | |
|-----------------|---|
| End point title | Median Progression-free survival (PFS) by Immune-RECIST |
|-----------------|---|

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.

Median PFS estimated by Kaplan-Meier method using Immune-RECIST.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Median PFS by Immune-RECIST until end of observation.

| End point values | Cohort A | | | |
|-----------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: month | | | | |
| median (standard error) | 3.29 (\pm 0.625) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 6 months by Immune-RECIST

| | |
|-----------------|--|
| End point title | Progression-free survival (PFS) at 6 months by Immune-RECIST |
|-----------------|--|

End point description:

PFS is defined as the time from start of treatment/observation until investigator assessed disease progression or death. The progression events are defined by well-documented and verifiable imaging data. PFS will be censored if the patient is lost to follow-up or refuses to continue in the trial (i.e. withdraws consent). For patients alive and without progression at the time of analysis, PFS will be censored. In any case of censoring, the date of censoring will be the last time point documenting survival status.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PFS by Immune-RECIST at 6 months.

| End point values | Cohort A | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: month | | | | |
| number (confidence interval 95%) | 0.24 (0.10 to 0.42) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) at 12 months by Immune-RECIST

| | |
|-----------------|---|
| End point title | Progression-free survival (PFS) at 12 months by Immune-RECIST |
|-----------------|---|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

PFS by Immune-RECIST at 12 months.

| End point values | Cohort A | | | |
|----------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: month | | | | |
| number (confidence interval 95%) | 0.04 (0.003 to 0.170) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events must be reported to sponsor from day 1 of the treatment and until 28 days after the last date of treatment.

Adverse event reporting additional description:

The investigator is responsible for ensuring that all adverse events observed by the investigator or reported by subjects are properly recorded in the subjects' medical records and the electronic case report form.

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

Dictionary used

| | |
|-----------------|------|
| Dictionary name | None |
|-----------------|------|

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Cohort A |
|-----------------------|----------|

Reporting group description:

25 CD73 positive relapsed ovarian cancer patients in cohort A were enrolled and received a combination of MEDI9447 and Durvalumab

| Serious adverse events | Cohort A | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 25 (60.00%) | | |
| number of deaths (all causes) | 19 | | |
| number of deaths resulting from adverse events | 1 | | |
| General disorders and administration site conditions | | | |
| Fever | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Pain | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Other | | | |
| subjects affected / exposed | 9 / 25 (36.00%) | | |
| occurrences causally related to treatment / all | 3 / 10 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|----------------|--|--|
| Neutropenia | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Gastrointestinal perforation | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Ileus | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 19 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 25 (4.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 19 | | |

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

| Non-serious adverse events | Cohort A | | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 24 / 25 (96.00%) | | |
| Investigations Blood creatine increased subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) Peripheral motor neuropathy subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 2 / 25 (8.00%) 2 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 7 / 25 (28.00%) 8 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Fever subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Decreased appetite subjects affected / exposed occurrences (all) Edema subjects affected / exposed occurrences (all) Other subjects affected / exposed occurrences (all) | 9 / 25 (36.00%) 17 4 / 25 (16.00%) 6 14 / 25 (56.00%) 20 3 / 25 (12.00%) 9 7 / 25 (28.00%) 8 23 / 25 (92.00%) 76 | | |

| | | | |
|---|-----------------|--|--|
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | | |
| occurrences (all) | 7 | | |
| Constipation | | | |
| subjects affected / exposed | 4 / 25 (16.00%) | | |
| occurrences (all) | 5 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 25 (20.00%) | | |
| occurrences (all) | 5 | | |
| Ileus | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 3 | | |
| Nausea | | | |
| subjects affected / exposed | 8 / 25 (32.00%) | | |
| occurrences (all) | 11 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 25 (8.00%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 7 / 25 (28.00%) | | |
| occurrences (all) | 8 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 10 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 3 / 25 (12.00%) | | |
| occurrences (all) | 4 | | |
| Renal and urinary disorders | | | |
| Proteinuria | | | |
| subjects affected / exposed | 6 / 25 (24.00%) | | |
| occurrences (all) | 6 | | |
| Urinary tract infection | | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 2 | | |
| Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) | 3 / 25 (12.00%) 4 | | |
| Metabolism and nutrition disorders Hypomagnesaemia subjects affected / exposed occurrences (all) Hyponatraemia subjects affected / exposed occurrences (all) | 2 / 25 (8.00%) 3 4 / 25 (16.00%) 5 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported