



## Clinical trial results:

### Multicenter phase II trial of Nintedanib plus docetaxel in second line of treatment in patients with no squamous non small cell lung cancer refractory to first line chemotherapy (REFRACT study)

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-000475-27    |
| Trial protocol           | FR                |
| Global end of trial date | 16 September 2020 |

#### Results information

|                                   |                                           |
|-----------------------------------|-------------------------------------------|
| Result version number             | v1 (current)                              |
| This version publication date     | 14 May 2021                               |
| First version publication date    | 14 May 2021                               |
| Summary attachment (see zip file) | Refract_manuscript (REFRACT_Article.docx) |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | I14041 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02531737 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                         |
|------------------------------|---------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | CHU de Limoges                                                                                          |
| Sponsor organisation address | 25 Avenue Martin Luther King, Limoges, France, 87042                                                    |
| Public contact               | Dr Jean-Bernard AULIAC, Centre Hospitalier de Créteil, 33 0157022092, Jean-Bernard.auliac@chicreteil.fr |
| Scientific contact           | Dr Jean-Bernard AULIAC, Centre Hospitalier de Créteil, 33 0157022092, Jean-Bernard.auliac@chicreteil.fr |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                   |
|------------------------------------------------------|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 16 September 2020 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 16 September 2020 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

Efficacy of the the nintedanib- docetaxel combination in second-line treatment in patients with no squamous non small cell lung cancer refractory to first line chemotherapy

Protection of trial subjects:

The informed consent of a patient is obtained prior to any study related procedures as per Good Clinical Practices (GCP) as set forth in the ICH guidelines.

Documentation that informed consent occurred prior to the patient's entry into the study and of the informed consent process is recorded in the patient's source documents. In addition, if a protocol is amended and it impacts on the content of the informed consent, patients participating in the study are informed and re-consente is required.

Finally, a DSMB was set up to monitor the progress of the trial and the adverse effects.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 20 May 2015 |
| 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 | France: 53 |
| Worldwide total number of subjects   | 53         |
| EEA total number of subjects         | 53         |

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)                      | 14 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 39 |
| 85 years and over   | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 59 patients in 23 French centers were enrolled and followed from December 7, 2015 to December 24, 2019

### Pre-assignment

Screening details:

The key inclusion criteria : histologically confirmed non-squamous stage IV NSCLC; no activating EGFR mutation; no ALK translocation or unknown status; at least one measurable lesion (RECIST 1.1); refractory disease, PS0 or 1; no history of other malignancy within the last 5 years ; normal hepatic, renal function and hematological function.

### Period 1

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

### Arms

|                                        |                      |
|----------------------------------------|----------------------|
| Arm title                              | Nintedanib+Docetaxel |
| Arm description: -                     |                      |
| Arm type                               | Experimental         |
| Investigational medicinal product name | nintedanib           |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Tablet               |
| Routes of administration               | Oral use             |

Dosage and administration details:

200 mg X 2 /day from Day 2 to Day 21 until progression or unacceptable toxicity  
possible reduction of nintedanib to 300 mg/day or 200 mg/day

|                                        |                       |
|----------------------------------------|-----------------------|
| Investigational medicinal product name | Docetaxel             |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

75 mg/m<sup>2</sup> by intravenous infusion on Day 1  
Possible reduction in the dose of docetaxel to 60 mg/m<sup>2</sup>

|                                       |                      |
|---------------------------------------|----------------------|
| <b>Number of subjects in period 1</b> | Nintedanib+Docetaxel |
| Started                               | 53                   |
| Completed                             | 53                   |



## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                                | overall trial | Total |  |
|-------------------------------------------------------|---------------|-------|--|
| Number of subjects                                    | 53            | 53    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero                                              | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 14            | 14    |  |
| From 65-84 years                                      | 39            | 39    |  |
| 85 years and over                                     | 0             | 0     |  |
| Age continuous                                        |               |       |  |
| Units: years                                          |               |       |  |
| arithmetic mean                                       | 58.5          |       |  |
| standard deviation                                    | ± 8.5         | -     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female                                                | 14            | 14    |  |
| Male                                                  | 39            | 39    |  |

## End points

### End points reporting groups

|                                |                      |
|--------------------------------|----------------------|
| Reporting group title          | Nintedanib+Docetaxel |
| Reporting group description: - |                      |

### Primary: Rate of PFS at 12 weeks after inclusion

|                        |                                                        |
|------------------------|--------------------------------------------------------|
| End point title        | Rate of PFS at 12 weeks after inclusion <sup>[1]</sup> |
| End point description: |                                                        |

|                          |         |
|--------------------------|---------|
| End point type           | Primary |
| End point timeframe:     |         |
| 12 weeks after inclusion |         |

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: The primary analysis associated with main objectif was a description of the percentage of patients who did not progress up to 12 week.

The 95% confidence interval of this percentage was also estimated using the exact method

|                                  |                      |  |  |  |
|----------------------------------|----------------------|--|--|--|
| <b>End point values</b>          | Nintedanib+Docetaxel |  |  |  |
| Subject group type               | Reporting group      |  |  |  |
| Number of subjects analysed      | 53                   |  |  |  |
| Units: percent                   |                      |  |  |  |
| number (confidence interval 95%) | 39.6 (26.5 to 54)    |  |  |  |

|                                   |                                                              |
|-----------------------------------|--------------------------------------------------------------|
| <b>Attachments (see zip file)</b> | Efficacy results ("As treated" population)/Table 2. Efficacy |
|-----------------------------------|--------------------------------------------------------------|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression-free survival (PFS)

|                        |                                 |
|------------------------|---------------------------------|
| End point title        | Progression-free survival (PFS) |
| End point description: |                                 |

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| At one year          |           |

|                                  |                      |  |  |  |
|----------------------------------|----------------------|--|--|--|
| <b>End point values</b>          | Nintedanib+Docetaxel |  |  |  |
| Subject group type               | Reporting group      |  |  |  |
| Number of subjects analysed      | 53                   |  |  |  |
| Units: Month                     |                      |  |  |  |
| number (confidence interval 95%) | 11.8 (4.8 to 22.2)   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Median PFS

|                        |            |
|------------------------|------------|
| End point title        | Median PFS |
| End point description: |            |
| End point type         | Secondary  |
| End point timeframe:   |            |
| At one year            |            |

|                                  |                      |  |  |  |
|----------------------------------|----------------------|--|--|--|
| <b>End point values</b>          | Nintedanib+Docetaxel |  |  |  |
| Subject group type               | Reporting group      |  |  |  |
| Number of subjects analysed      | 53                   |  |  |  |
| Units: Month                     |                      |  |  |  |
| number (confidence interval 95%) | 2.7 (1.4 to 4.1)     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival

|                        |                  |
|------------------------|------------------|
| End point title        | Overall Survival |
| End point description: |                  |
| End point type         | Secondary        |
| End point timeframe:   |                  |
| At one year            |                  |



|                                  |                      |  |  |  |
|----------------------------------|----------------------|--|--|--|
| <b>End point values</b>          | Nintedanib+Docetaxel |  |  |  |
| Subject group type               | Reporting group      |  |  |  |
| Number of subjects analysed      | 53                   |  |  |  |
| Units: Percent                   |                      |  |  |  |
| number (confidence interval 95%) | 32.1 (19.8 to 45.0)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival

|                        |                  |
|------------------------|------------------|
| End point title        | Overall Survival |
| End point description: |                  |
| End point type         | Secondary        |
| End point timeframe:   |                  |
| At 18 months           |                  |

|                                  |                      |  |  |  |
|----------------------------------|----------------------|--|--|--|
| <b>End point values</b>          | Nintedanib+Docetaxel |  |  |  |
| Subject group type               | Reporting group      |  |  |  |
| Number of subjects analysed      | 53                   |  |  |  |
| Units: percent                   |                      |  |  |  |
| number (confidence interval 95%) | 27.6 (16.1 to 40.4)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Best Response

|                                                                                                                                   |               |
|-----------------------------------------------------------------------------------------------------------------------------------|---------------|
| End point title                                                                                                                   | Best Response |
| End point description:                                                                                                            |               |
| Best response to treatment observed according to the RECIST 1.1 criteria over the patient's period of participation, ie one year. |               |
| End point type                                                                                                                    | Secondary     |
| End point timeframe:                                                                                                              |               |
| At 12 months                                                                                                                      |               |

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| <b>End point values</b>     | Nintedanib+Docetaxel |  |  |  |
| Subject group type          | Reporting group      |  |  |  |
| Number of subjects analysed | 53                   |  |  |  |
| Units: Number of patients   | 10                   |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Are concerned patients who received at least one dose of experimental treatment (docetaxel or nintedanib). The adverse events are those occurring between the date of the first administration and the end of the patient's participation + 30 days.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                                              | Overall trial    |  |  |
|---------------------------------------------------------------------|------------------|--|--|
| Total subjects affected by serious adverse events                   |                  |  |  |
| subjects affected / exposed                                         | 29 / 53 (54.72%) |  |  |
| number of deaths (all causes)                                       | 11               |  |  |
| number of deaths resulting from adverse events                      | 9                |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |  |  |
| Metastases to meninges                                              |                  |  |  |
| subjects affected / exposed                                         | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 1            |  |  |
| General disorders and administration site conditions                |                  |  |  |
| Asthenia                                                            |                  |  |  |
| subjects affected / exposed                                         | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all                     | 1 / 1            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Diarrhoea                                                           |                  |  |  |
| subjects affected / exposed                                         | 2 / 53 (3.77%)   |  |  |
| occurrences causally related to treatment / all                     | 2 / 2            |  |  |
| deaths causally related to treatment / all                          | 0 / 0            |  |  |
| Disease progression                                                 |                  |  |  |

|                                                 |                 |  |  |
|-------------------------------------------------|-----------------|--|--|
| subjects affected / exposed                     | 1 / 53 (1.89%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| General physical health deterioration           |                 |  |  |
| subjects affected / exposed                     | 6 / 53 (11.32%) |  |  |
| occurrences causally related to treatment / all | 1 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 3           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Dyspnoea                                        |                 |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Haemoptysis                                     |                 |  |  |
| subjects affected / exposed                     | 2 / 53 (3.77%)  |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |
| Pulmonary embolism                              |                 |  |  |
| subjects affected / exposed                     | 2 / 53 (3.77%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Investigations                                  |                 |  |  |
| Weight decreased                                |                 |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Overdose                                        |                 |  |  |
| subjects affected / exposed                     | 2 / 53 (3.77%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Pericardial effusion                            |                 |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| <b>Nervous system disorders</b>                 |                |  |  |
| <b>Monoplegia</b>                               |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Neuralgia</b>                                |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| <b>Partial seizures</b>                         |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Seizure</b>                                  |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Blood and lymphatic system disorders</b>     |                |  |  |
| <b>Febrile bone marrow aplasia</b>              |                |  |  |
| subjects affected / exposed                     | 5 / 53 (9.43%) |  |  |
| occurrences causally related to treatment / all | 5 / 5          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Febrile neutropenia</b>                      |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Neutropenia</b>                              |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Gastrointestinal disorders</b>               |                |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| Vomiting                                        |                  |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all | 1 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Renal and urinary disorders                     |                  |  |  |
| Renal failure                                   |                  |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all | 1 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Endocrine disorders                             |                  |  |  |
| Adrenal insufficiency                           |                  |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all | 1 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Musculoskeletal and connective tissue disorders |                  |  |  |
| Back pain                                       |                  |  |  |
| subjects affected / exposed                     | 2 / 53 (3.77%)   |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Bone pain                                       |                  |  |  |
| subjects affected / exposed                     | 11 / 53 (20.75%) |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Infections and infestations                     |                  |  |  |
| Bronchitis                                      |                  |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Clostridium difficile colitis                   |                  |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%)   |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Device related infection                        |                  |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumocystis jirovecii pneumonia                |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Sepsis                                          |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diabetes mellitus inadequate control            |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Malnutrition                                    |                |  |  |
| subjects affected / exposed                     | 1 / 53 (1.89%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                     | Overall trial    |  |  |
|-------------------------------------------------------|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 52 / 53 (98.11%) |  |  |
| Investigations                                        |                  |  |  |
| Aspartate aminotransferase increased                  |                  |  |  |
| subjects affected / exposed                           | 4 / 53 (7.55%)   |  |  |
| occurrences (all)                                     | 10               |  |  |

|                                                                                                                                                                                                                                   |                                                                                   |  |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--|--|
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                            | 3 / 53 (5.66%)<br>10                                                              |  |  |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Fatigue<br>subjects affected / exposed<br>occurrences (all)                                        | 14 / 53 (26.42%)<br>18<br><br>8 / 53 (15.09%)<br>12                               |  |  |
| Blood and lymphatic system disorders<br>Neutropenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Anaemia<br>subjects affected / exposed<br>occurrences (all)                                                        | 20 / 53 (37.74%)<br>51<br><br>12 / 53 (22.64%)<br>12                              |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 24 / 53 (45.28%)<br>33<br><br>18 / 53 (33.96%)<br>21<br><br>9 / 53 (16.98%)<br>10 |  |  |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all)                                                                                                                            | 8 / 53 (15.09%)<br>8                                                              |  |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                                                                                                                      | 11 / 53 (20.75%)<br>13                                                            |  |  |



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported