



Clinical trial results:

An open-label trial of the long-term safety and tolerability of nintedanib per os, on top of standard of care, over at least 3 years, in children and adolescents with clinically significant fibrosing Interstitial Lung Disease (InPedILD-ON)

Summary

| | |
|--------------------------|---|
| EudraCT number | 2020-005554-23 |
| Trial protocol | CZ ES PL HU BE NL GR DE FR PT FI DK IT NO |
| Global end of trial date | 13 August 2025 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 28 February 2026 |
| First version publication date | 28 February 2026 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 1199-0378 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05285982 |
| WHO universal trial number (UTN) | U1111-1305-7514 |
| Other trial identifiers | CTIS: 2024-515743-27-00 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216 |
| Public contact | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 1 018002430127, clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 1 018002430127, clintriage.rdg@boehringer-ingelheim.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001006-PIP05-18 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 September 2025 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 August 2025 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 August 2025 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to assess the safety and tolerability of long-term treatment with nintedanib in paediatric patients with clinically significant fibrosing interstitial lung disease (ILD).

Protection of trial subjects:

The patient's legally accepted representative (and/or the patient, where applicable) were informed that they were free to withdraw their consent (or assent, where applicable) at any time during the trial without penalty or prejudice.

Whenever feasible and for roll-over patients only, the first visits (Visit 1 and 2) of trial 1199-0378 were to occur on the same day as the end-of-treatment (EoT) Visit of trial 1199-0337 to allow for continuous treatment. In this case, procedures performed at the EoT of trial 1199-0337 were not to be repeated as part of Visit 1 or 2 in trial 1199-0378. Nintedanib dose could be interrupted/reduced without interruption at discretion of investigator.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 06 April 2022 |
| 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 | Argentina: 3 |
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Brazil: 5 |
| Country: Number of subjects enrolled | Canada: 3 |
| Country: Number of subjects enrolled | Czechia: 3 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Germany: 2 |
| Country: Number of subjects enrolled | Greece: 1 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | Mexico: 5 |
| Country: Number of subjects enrolled | Norway: 5 |
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Portugal: 3 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | United States: 23 |
| Country: Number of subjects enrolled | Finland: 1 |

| | |
|------------------------------------|----|
| Worldwide total number of subjects | 70 |
| EEA total number of subjects | 30 |

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) | 20 |
| Adolescents (12-17 years) | 45 |
| Adults (18-64 years) | 5 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Pediatric patients with clinically significant fibrosing Interstitial Lung Disease who completed the parent trial 1199-0337 or new patients who were eligible to enter this trial.

Pre-assignment

Screening details:

Only subjects that met all study eligibility criteria were to be entered. They were free to withdraw at any time for any reason given. Close monitoring was adhered to throughout trial conduct.

Period 1

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

Arms

| | |
|-----------|------------|
| Arm title | Nintedanib |
|-----------|------------|

Arm description:

Pediatric patients with clinically significant fibrosing interstitial lung disease (ILD) who either completed the parent trial 1199-0337 or were new patients received nintedanib soft gelatine capsules. Nintedanib doses ranged from 50 milligrams (mg) bid (13.5 to < 23 kilograms (kg) bodyweight) to 150 mg bid (\geq 57.5 kg bodyweight).

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nintedanib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, soft |
| Routes of administration | Oral use |

Dosage and administration details:

Nintedanib doses ranged from 50 milligrams (mg) bid (13.5 to <23 kilograms (kg) bodyweight) to 150 mg bid (\geq 57.5 kg bodyweight).

| Number of subjects in period 1 ^[1] | Nintedanib |
|---|------------|
| Started | 54 |
| Completed | 30 |
| Not completed | 24 |
| Adverse event, serious fatal | 1 |
| Other treatment option available | 2 |
| Adverse event, non-fatal | 6 |
| Perceived lack of efficacy | 2 |
| Burden of trial procedures | 2 |
| Change of residence | 1 |
| Other than listed | 9 |
| No reason provided | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of the 70 subjects enrolled, 54 started the trial.

Baseline characteristics

Reporting groups

| | |
|--|------------|
| Reporting group title | Nintedanib |
| Reporting group description: | |
| Pediatric patients with clinically significant fibrosing interstitial lung disease (ILD) who either completed the parent trial 1199-0337 or were new patients received nintedanib soft gelatine capsules. Nintedanib doses ranged from 50 milligrams (mg) bid (13.5 to < 23 kilograms (kg) bodyweight) to 150 mg bid (>=57.5 kg bodyweight). | |

| Reporting group values | Nintedanib | Total | |
|---|------------|-------|--|
| Number of subjects | 54 | 54 | |
| Age categorical | | | |
| Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication. | | | |
| Units: Participants | | | |
| 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) | 14 | 14 | |
| Adolescents (12-17 years) | 35 | 35 | |
| Adults (18-64 years) | 5 | 5 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication. | | | |
| Units: years | | | |
| arithmetic mean | 13.6 | | |
| standard deviation | ± 3.3 | - | |
| Sex: Female, Male | | | |
| Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication. | | | |
| Units: Participants | | | |
| Female | 33 | 33 | |
| Male | 21 | 21 | |
| Race (NIH/OMB) | | | |
| Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 3 | 3 | |
| Asian | 2 | 2 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 6 | 6 | |
| White | 41 | 41 | |
| More than one race | 1 | 1 | |
| Unknown or Not Reported | 1 | 1 | |
| Ethnicity (NIH/OMB) | | | |
| Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 16 | 16 | |

| | | | |
|-------------------------|----|----|--|
| Not Hispanic or Latino | 37 | 37 | |
| Unknown or Not Reported | 1 | 1 | |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | Nintedanib |
| Reporting group description: Pediatric patients with clinically significant fibrosing interstitial lung disease (ILD) who either completed the parent trial 1199-0337 or were new patients received nintedanib soft gelatine capsules. Nintedanib doses ranged from 50 milligrams (mg) bid (13.5 to < 23 kilograms (kg) bodyweight) to 150 mg bid (\geq 57.5 kg bodyweight). | |

Primary: Number of patients with treatment-emergent adverse events (AEs) over the whole trial

| | |
|---|---|
| End point title | Number of patients with treatment-emergent adverse events (AEs) over the whole trial ^[1] |
| End point description: Number of patients with treatment-emergent adverse events (AEs) over the whole trial. | |
| Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication. | |
| End point type | Primary |
| End point timeframe: From first drug administration until end of residual effect period (REP) 28 days after the last dose of trial medication, up to 1127 days. | |
| 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 endpoint was only analysed descriptively. | |

| End point values | Nintedanib | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 54 | | | |
| Units: Participants | 53 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first drug administration until end of residual effect period (REP) 28 days after the last dose of trial medication, up to 1127 days.

Adverse event reporting additional description:

Treated Set (TS): The TS included all patients who were administered at least 1 dose of trial medication.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 28.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description: -

| Serious adverse events | Total | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 54 (44.44%) | | |
| number of deaths (all causes) | 3 | | |
| number of deaths resulting from adverse events | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Teratoma | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Transplant rejection | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|----------------|--|--|
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumothorax | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pulmonary cavitation | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural | | | |

| | | | |
|---|----------------|--|--|
| complications | | | |
| Post procedural complication | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Sickle cell anaemia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial thrombosis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Right ventricular failure | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Sickle cell anaemia with crisis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Optic atrophy | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric fistula | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophageal hypomotility | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tooth development disorder | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug-induced liver injury | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gallbladder rupture | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 54 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pelvic abscess | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|----------------|--|--|
| Skin infection | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 54 (1.85%) | | |
| 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 | Total | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 53 / 54 (98.15%) | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 8 / 54 (14.81%) | | |
| occurrences (all) | 11 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 5 / 54 (9.26%) | | |
| occurrences (all) | 7 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 3 / 54 (5.56%) | | |
| occurrences (all) | 7 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 54 (24.07%) | | |
| occurrences (all) | 24 | | |
| Dizziness | | | |
| subjects affected / exposed | 4 / 54 (7.41%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 54 (12.96%) | | |
| occurrences (all) | 12 | | |

| | | | |
|--|------------------------|--|--|
| Chest pain subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Fatigue subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 26 / 54 (48.15%) 63 | | |
| Nausea subjects affected / exposed occurrences (all) | 17 / 54 (31.48%) 32 | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 10 / 54 (18.52%) 17 | | |
| Vomiting subjects affected / exposed occurrences (all) | 21 / 54 (38.89%) 60 | | |
| Dental caries subjects affected / exposed occurrences (all) | 16 / 54 (29.63%) 33 | | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Constipation subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 5 | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 4 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|------------------------|--|--|
| Nasal congestion subjects affected / exposed occurrences (all) | 7 / 54 (12.96%) 10 | | |
| Cough subjects affected / exposed occurrences (all) | 16 / 54 (29.63%) 22 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 4 | | |
| Interstitial lung disease subjects affected / exposed occurrences (all) | 6 / 54 (11.11%) 6 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 6 / 54 (11.11%) 6 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 7 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 8 | | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Musculoskeletal and connective tissue disorders Back pain | | | |

| | | | |
|---|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | | |
| Arthralgia subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | | |
| Infections and infestations | | | |
| Viral infection subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 12 / 54 (22.22%) 22 | | |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 9 / 54 (16.67%) 17 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 11 / 54 (20.37%) 17 | | |
| COVID-19 subjects affected / exposed occurrences (all) | 7 / 54 (12.96%) 9 | | |
| Bronchitis subjects affected / exposed occurrences (all) | 7 / 54 (12.96%) 11 | | |
| Rhinitis subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 3 | | |
| Pneumonia subjects affected / exposed occurrences (all) | 3 / 54 (5.56%) 9 | | |
| Influenza subjects affected / exposed occurrences (all) | 6 / 54 (11.11%) 9 | | |
| Gastroenteritis viral subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 6 | | |

| | | | |
|---|---------------------|--|--|
| Gastroenteritis subjects affected / exposed occurrences (all) | 4 / 54 (7.41%) 4 | | |
|---|---------------------|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 05 August 2022 | <p>In addition to minor corrections and clarification, the following main changes were introduced:</p> <ul style="list-style-type: none">• The trial rationale was defined specifically for new and roll-over patients (instead of all patients combined).• Per protocol, a transition period of 8 weeks was allowed. In Protocol Amendment 1, it was clarified that patients from trial 1199-0337 who were eligible for roll-over but had a transition period of more than 12 weeks were considered as 'new patients' in this trial. Furthermore, it was specified which inclusion and exclusion criteria applied to this subcategory of new patients. Patients with a transition period of more than 8 weeks, but up to 12 weeks were still considered roll-over patients, but this deviation was to be documented as individual protocol deviation (iPD).• The minimum treatment duration for new patients was changed from 'a minimum of 2 years' to 'until the end of trial or until alternative treatment options become available' in order to reflect the staggered enrolment of new patients. The overall end of trial was defined accordingly and the second interim analysis was removed.• A time window of +7 days was added for the follow-up/End of Study (EoS) Visit.• The time windows for follow-up bone imaging, dental imaging, and dental examination were revised to allow for some flexibility without compromising patient safety.• After a previous switch to smaller capsules, it was permitted to switch back to larger capsules (i.e., from 25 milligram (mg) to 100 mg capsules).• It was clarified that female partners of male patients did not have to follow the contraceptive guidelines.• To support the overall safety assessment, the possibility of review of bone and dental images by an external expert was added. Furthermore, a mandatory review of all dental findings of stunted growth as well as an optional review of other dental findings by the Adjudication Committee (AC) was added. |
| 18 April 2023 | <p>In addition to minor corrections and clarifications, the following main changes were introduced:</p> <ul style="list-style-type: none">• The allowed time windows for follow-up bone imaging, dental imaging, and dental examination were further clarified. In addition, a one-time pre-or postponement of an assessment by 2 months was allowed to allow for alignment of bone imaging and dental imaging/examination with the regular trial site visits.• In order to limit the burden for a patient without compromising on patient safety, the number of follow-up bone and dental imaging assessments was limited to 1 after End of Treatment (EoT).• The further endpoints 'change from baseline in sitting height' and 'change from baseline in leg length' were removed due to inconsistencies in the measurements, which would impact data comparability. |

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| 29 November 2023 | <p>In addition to minor corrections and clarifications, the following main changes were introduced:</p> <ul style="list-style-type: none"> • As agreed with European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use (CHMP), trial 1199-0378 was extended by an additional year of treatment, i.e., maximum treatment duration for roll-over patients was changed from 2 to 3 years. Four additional clinical visits were added during this extra year and timepoints of trial assessments were adapted accordingly. • As nintedanib is available for adult patients outside of the trial, patients should complete the trial before their 22nd birthday. • The possibility to collect information on age of menarche (for female patients only) and nutritional support was added. • Clarified that bone imaging follow-up procedures for patients aged 19 and older were only required on an annual basis. • New patients were approached in a way that would increase the collection of long-term data until the end of trial. • Additional timepoints were added for selected further endpoints (i.e., incidence of treatment-emergent pathological findings of epiphyseal growth plate on imaging and dental examination or imaging, length of hospitalisation) due to prolongation of trial treatment. • The possibility to restart trial treatment after pregnancy was added. |
| 15 April 2024 | <p>This amendment was introduced to harmonise the Clinical Trial Protocol (CTP) for the transition to European Union (EU) Clinical Trials Regulation. The amendment included local amendments already approved in concerned countries (the first 3 bullets) as well as a new change (the last bullet):</p> <ul style="list-style-type: none"> • As requested by French Health Authority (ANSM), trial population in France was limited to adolescents 12 to 17 years old at Visit 2. This change was introduced to Local Amendment 1 France (dated 05 Jul 2021) and approved by the local regulatory body prior to the global protocol harmonisation. • As requested by Polish authorities and Norwegian Medicines Agency, the frequency of the pregnancy test for female patients in Poland and Norway was revised to every 4 weeks. This change was introduced to Local Amendment 1 Poland (dated 09 Jul 2021) and Local Amendment 1 Norway (dated 19 Feb 2022) and approved by the respective local regulatory bodies prior to the global protocol harmonisation. • As requested by Norwegian Medicines Agency, Visit 3a was also applicable for new patients in Norway and had to be performed at Week 6 (Day 43). This change was introduced to Local Amendment 1 Norway (dated 19 Feb 2022) and approved by the respective local regulatory body prior to the global protocol harmonisation. • Several trial conducts were allowed to limit the burden for patients, e.g., replacing the End of Study (EoS) Visit with a phone call if patients were not able to visit sites for medical reasons, allowing the follow-up visit to be skipped if the End of Treatment (EoT) Visit was delayed and performed 28 days or more after treatment discontinuation. |
| 27 November 2024 | <p>In addition to minor corrections and clarifications, the following main changes were introduced:</p> <ul style="list-style-type: none"> • Clarified that the overall end of trial was to take place approximately when last roll-over patient was expected to reach 3 years of treatment. • As requested by Italian Health Authority, the frequency of the pregnancy test was revised to every 4 weeks for female patients in all countries. • Shortened the follow-up duration for urine pregnancy test for female patients who continued visits off treatment to limit the burden for patients. • Following regulatory interactions, additional timepoints were added for selected further safety endpoints, i.e., change in height from baseline, change in height-for-age z-score (ΔHAZ), change in weight-for-age z-score (ΔWAZ), and change in body mass index-for-age z-score (ΔBAZ). |

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.

Some limitations due to the nature of the extension trial should be considered when interpreting the data (i.e. bias in the selection of the population and no comparative arm). All endpoints were considered exploratory only.

Notes: