# Clinical trial results:
# An open label, multi-center nilotinib roll-over protocol for patients who have completed a previous Novartis sponsored nilotinib study and are judged by the investigator to benefit from continued nilotinib treatment

## Summary

| | |
|---|---|
| EudraCT number | 2012-003902-28 |
| Trial protocol | AT IT ES HU NL GB SK SE FR |
| Global end of trial date | 07 July 2023 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 04 January 2024 |
| First version publication date | 04 January 2024 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | CAMN107A2409 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01735955 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | Novartis Campus, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 07 July 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 07 July 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Primary objective - To evaluate long-term safety data (Serious Adverse Events (SAEs) and Adverse Events (AEs))
Secondary objective - To evaluate clinical benefit as assessed by the investigator

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 29 March 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | Canada: 7 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Hong Kong: 3 |
| Country: Number of subjects enrolled | Hungary: 6 |
| Country: Number of subjects enrolled | Israel: 1 |
| Country: Number of subjects enrolled | Italy: 6 |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Russian Federation: 2 |
| Country: Number of subjects enrolled | Singapore: 11 |
| Country: Number of subjects enrolled | Slovakia: 1 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | United States: 3 |
| Worldwide total number of subjects | 57 |
| EEA total number of subjects | 21 |

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) | 4 |
| Adolescents (12-17 years) | 3 |
| Adults (18-64 years) | 30 |
| From 65 to 84 years | 19 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study had no screening period. 57 patients were enrolled and treated with nilotinib in this study. Pts were rolled over from 5 parent studies with the following indications: Chronic myelogenous leukemia (CML), Metastatic gastrointestinal stromal tumors (GIST), Acute lymphoblastic leukemia (ALL) & Receptor tyrosine kinase (KIT) mutated melanoma.

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | Nilotinib |

Arm description:

Adult patients: ≤ 800mg/day; Pediatric patients: 230mg/m2 twice daily (BID) and ≤ 800mg/day

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | nilotinib |
| Investigational medicinal product code | AMN107 |
| Other name | Tasigna |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Adult patients: ≤ 800mg/day; Pediatric patients:  230mg/m2 twice daily (BID) and ≤ 800mg/day

| **Number of subjects in period 1** | Nilotinib |
|---|---|
| Started | 57 |
| Completed | 20 |
| Not completed | 37 |
| Patient withdrew consent | 2 |
| Physician decision | 4 |
| Disease progression | 24 |
| Adverse event, non-fatal | 5 |
| Administrative problems | 1 |
| Patient/guardian decision | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Nilotinib |
| Reporting group description: | |
| Adult patients: ≤ 800mg/day; Pediatric patients: 230mg/m2 twice daily (BID) and ≤ 800mg/day | |

| Reporting group values | Nilotinib | Total | |
|---|---|---|---|
| Number of subjects | 57 | 57 | |
| Age Categorical<br>Units: Participants | | | |
| <=18 years | 7 | 7 | |
| Between 18 and 65 years | 30 | 30 | |
| >=65 years | 20 | 20 | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 53.02 | | |
| standard deviation | ± 19.278 | - | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 30 | 30 | |
| Male | 27 | 27 | |

## End points

### End points reporting groups

| Reporting group title | Nilotinib |
|---|---|

Reporting group description:

Adult patients: ≤ 800mg/day; Pediatric patients: 230mg/m2 twice daily (BID) and ≤ 800mg/day

### Primary: Number of participants with adverse events and serious adverse events

| End point title | Number of participants with adverse events and serious adverse events[1] |
|---|---|

End point description:

An Adverse Event (AE) is any untoward medical occurrence (eg any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of a medicinal (investigational) product.

Serious adverse event (SAE) case data were collected in the Safety Database. Adverse event (AE) data (both non-serious and serious) were collected in the Clinical database.

Max. = Maximum
Yrs = Years
Approx. = Approximately
eCRF = electronic Case Report Form
Time = timeframe

| End point type | Primary |
|---|---|

End point timeframe:

SAE case data were collected the entire study duration after first dose of study treatment up to a max. time of approx. 10 yrs. AEs (both non-serious and serious) were collected in the eCRF 3 yrs after study initiation up to a max. time of approx. 7 yrs.

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: Not applicable for single arm studies and not applicable for AE data also.

| End point values | Nilotinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 57 | | | |
| Units: Participants | | | | |
| Adverse Events - total | 29 | | | |
| Adverse Events - Treatment-related adverse events | 15 | | | |
| SAEs - total | 17 | | | |
| SAEs - Treatment-related SAEs | 2 | | | |
| AEs leading to discontinuation - total | 3 | | | |
| Treatment-related AEs leading to discontinuation | 3 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with clinical benefit from nilotinib

| End point title | Number of participants with clinical benefit from nilotinib |
|---|---|

End point description:

Number of participants with clinical benefit as assessed by investigator.

Clinical benefit data were collected 3 years after study initiation; hence, it is not available for the patients who already discontinued and was not complete for the patients who had been enrolled prior to that time.

The time point was calculated from the date of first drug intake.

Assess. = assessment

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

End point timeframe:

Clinical benefit data were first collected 3 years after study initiation and up to a maximum timeframe of approx. 7 years (up to Year 11).

| End point values | Nilotinib | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 57 | | | |
| Units: Participants | | | | |
| Pts who had at least 1 assess.for clinical benefit | 33 | | | |
| Patients with clinical benefit - Baseline | 15 | | | |
| Patients with clinical benefit - Week 24 | 11 | | | |
| Patients with clinical benefit - Week 48 | 17 | | | |
| Patients with clinical benefit - Week 72 | 11 | | | |
| Patients with clinical benefit - Week 96 | 19 | | | |
| Patients with clinical benefit - Year 3 | 23 | | | |
| Patients with clinical benefit - Year 4 | 26 | | | |
| Patients with clinical benefit - Year 5 | 20 | | | |
| Patients with clinical benefit - Year 6 | 9 | | | |
| Patients with clinical benefit - Year 7 | 9 | | | |
| Patients with clinical benefit - Year 8 | 7 | | | |
| Patients with clinical benefit - Year 9 | 6 | | | |
| Patients with clinical benefit - Year 10 | 6 | | | |
| Patients with clinical benefit - Year 11 | 4 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAE case data were collected the entire study duration after first dose of study treatment up to a max. time of approx. 10 yrs. AEs (both non-serious and serious) were collected in the eCRF 3 yrs after study initiation up to a max. time of approx. 7 yrs.

Adverse event reporting additional description:

Serious adverse event (SAE) case data were collected in the Safety Database. Adverse event (AE) data (both non-serious and serious) were collected in the Clinical database.

Max. = Maximum
Yrs = Years
Approx. = Approximately
eCRF = electronic Case Report Form
Time = timeframe

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 26.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Nilotinib |

Reporting group description:

Adult patients: ≤ 800mg/day; Pediatric patients: 230mg/m2 twice daily (BID) and ≤ 800mg/day

| Serious adverse events | Nilotinib | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 57 (29.82%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Gastrointestinal stromal tumour | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Peripheral artery occlusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Small intestinal resection | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Ischaemic stroke | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Melaena | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis acute | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| Cholelithiasis | | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| Hydronephrosis | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dengue fever | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Infection | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 57 (1.75%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Nilotinib | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 57 (35.09%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 57 (8.77%) | | |
| occurrences (all) | 5 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 3 / 57 (5.26%) | | |
| occurrences (all) | 4 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Fatigue<br>subjects affected / exposed<br>occurrences (all) | 3 / 57 (5.26%)<br>3 | | |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 3 / 57 (5.26%)<br>4 | | |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 3 / 57 (5.26%)<br>4 | | |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | 4 / 57 (7.02%)<br>4 | | |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 4 / 57 (7.02%)<br>4<br><br>3 / 57 (5.26%)<br>3 | | |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 4 / 57 (7.02%)<br>4<br><br>3 / 57 (5.26%)<br>3 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 September 2013 | Added monthly pregnancy tests for female patients of childbearing potential to reflect the<br>requirement of highly effective contraception for patients on nilotinib treatment.<br>Clarified that dose modifications were based on guidelines provided in the parent protocol, as<br>well as investigator's judgment.<br>Clarified that patients could have access to the same strengths as specified in the parent<br>protocol.<br>Clarified that patients who were pregnant, who withdrew consent or died were required to be<br>withdrawn from the study. |
| 24 June 2014 | Incorporated guidance for the management of serum cholesterol and blood glucose increases,<br>other cardiac risk factors, and ischemic vascular or ischemic cardiovascular events occurring<br>in patients treated with nilotinib.<br>Updated the exclusion criteria relating to male trial participant's use highly effective<br>contraception to be aligned with the current Investigator Brochure. |
| 07 April 2016 | Included the collection of all AEs (including non-serious and serious AEs) and an investigator<br>attestation of continued clinical benefit into the clinical database. Increased visit frequency<br>from annually to quarterly.<br>Included hepatitis B virus testing as one of the study procedures to identify study patients who<br>might have been at risk of hepatitis B reactivation.<br>Included collection of relevant medical history/current medical condition.<br>Included the study evaluation completion eCRF page. |
| 27 July 2016 | Corrected an error in the language regarding pregnancy outcome collection. Pregnancy<br>outcomes from female partners of any males who took study treatment was not collected in<br>this study as nilotinib is not genotoxic and no effects on sperm count, motility, or on fertility<br>were noted in animal studies. |
| 30 August 2018 | Provided further clarity to the end of study definition and trial timelines |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported