



Clinical trial results:

Phase 2 Clinical Trial with Ponatinib as a Second Line Therapy for Patients with Chronic Myeloid Leukemia in Chronic Phase Resistant or Intolerant to prior First Line Tyrosine Kinase Inhibitor Treatment

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-000618-30 |
| Trial protocol | DE |
| Global end of trial date | 22 June 2023 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 27 June 2024 |
| First version publication date | 27 June 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | 11272 |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03807479 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GWT-TUD GmbH |
| Sponsor organisation address | Freiberger Str. 33, Dresden, Germany, 01067 |
| Public contact | Fachbereich MEDIZIN, GWT-TUD GmbH, +49 35125933100, medical.consulting@g-wt.de |
| Scientific contact | Fachbereich MEDIZIN, GWT-TUD GmbH, +49 35125933100, medical.consulting@g-wt.de |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 December 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 June 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 June 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Major molecular response (MMR) by 12 months of treatment with second line Ponatinib treatment

Protection of trial subjects:

The conduct of this study was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also carried out in keeping with applicable local law(s) and regulation(s).

Patients who are treated within ponatinib may encounter ocular damage. Therefore, prior to study start, an ophthalmologist needs to confirm patients' suitability for the study. During the course of the trial, patients need to be asked for any changes on visual acuity. In case a change is observed, an ophthalmologist again needs to be consulted in order to confirm that patient is safe to continue on the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 01 August 2018 |
| 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 | Germany: 18 |
| Worldwide total number of subjects | 18 |
| EEA total number of subjects | 18 |

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) | 16 |
| From 65 to 84 years | 2 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

From 12 Dec 2018 until 25 Jan 2022, in total 22 patients were screened at 6 study sites in Germany.

Pre-assignment

Screening details:

18 received study medication and were included in the evaluation. Eleven patients were enrolled after failure and seven after intolerance to 1st line TKI treatment.

Period 1

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

Arms

| | |
|--|--------------------|
| Arm title | Treatment period |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Ponatinib |
| Investigational medicinal product code | |
| Other name | Iclusig |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Starting dose of 30 mg (2 tablets à 15 mg) once daily. Doses might have been increased in case of inappropriate response or reduced to manage drug-related adverse events with re-escalation once events resolved.

If a patient had reached a major molecular response (MMR), the dose reduction to 15 mg/day could have been considered. Patients remained on study until disease progression or unacceptable toxicity occurred.

| Number of subjects in period 1 | Treatment period |
|-----------------------------------|------------------|
| Started | 18 |
| Completed | 7 |
| Not completed | 11 |
| Physician decision | 1 |
| not defined | 1 |
| Adverse event, non-fatal | 5 |
| started additional cancer therapy | 2 |
| Lost to follow-up | 1 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description: -

| Reporting group values | Treatment | Total | |
|---|-----------|-------|--|
| Number of subjects | 18 | 18 | |
| 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) | 16 | 16 | |
| From 65-84 years | 2 | 2 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 4 | |
| Male | 14 | 14 | |

End points

End points reporting groups

| | |
|--------------------------------|------------------|
| Reporting group title | Treatment period |
| Reporting group description: - | |

Primary: major molecular response (MMR)

| | |
|------------------------|---|
| End point title | major molecular response (MMR) ^[1] |
| End point description: | |

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| 12 months | |

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: A maximum of 54 patients was planned to be treated. Based on historical data, the rate of MMR by 12 months in the 2nd line setting is approximately 0.3. The goal of therapy was to improve this to at least 0.5. With one-sided α -error rate of 0.025 and power of 0.8, z-test for binominal proportion with continuity adjustment was used.

| End point values | Treatment period | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: patients | | | | |
| number (confidence interval 95%) | 55.6 (29.8 to 81.3) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 months

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

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

Reporting group description: -

| Serious adverse events | Overall | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedematous pancreatitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Overall | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 18 (94.44%) | | |
| Investigations | | | |
| Blood glucose increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Amylase increased | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | | |
| occurrences (all) | 3 | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | | |
| occurrences (all) | 2 | | |
| Lipase increased | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | | |
| occurrences (all) | 4 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | | |
| occurrences (all) | 3 | | |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |

| | | | |
|--|----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Headache subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | | |
| Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Gastrointestinal disorders Gastritis subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Edematous pancreatitis subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 4 / 18 (22.22%) 4 | | |
| Nausea subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 | | |
| Pancreatitis acute subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Hepatobiliary disorders Liver disorder subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |

| | | | |
|--|--|--|--|
| <p>Skin and subcutaneous tissue disorders</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Acne</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 18 (11.11%)</p> <p>2</p> <p>1 / 18 (5.56%)</p> <p>1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bone pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 18 (11.11%)</p> <p>2</p> <p>1 / 18 (5.56%)</p> <p>1</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Hypertriglyceridemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypertriglyceridaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 18 (5.56%)</p> <p>1</p> <p>1 / 18 (5.56%)</p> <p>1</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 02 September 2021 | Protocol Version 4.0: Specification of inclusion/exclusion criteria, reduction of frequency of bone marrow and viral Hep B analysis, recruitment time extended from 30 to 42 months |

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.

Due to the low recruitment rate, the study was terminated prematurely after inclusion of 22 patients.

Notes: