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) Headache subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1 2 / 18 (11.11%) 2		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1 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) Edematous pancreatitis subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Pancreatitis acute subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 4 / 18 (22.22%) 4 2 / 18 (11.11%) 2 1 / 18 (5.56%) 1		
Hepatobiliary disorders Liver disorder subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		

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

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: