Clinical trial results:
Imatinib in combination with Cytarabine as compared to Imatinib alone in patients with first chronic phase Chronic Myeloid Leukemia.

A prospective randomized phase III study.

Summary

EudraCT number	2005-003839-41
Trial protocol	BE
Global end of trial date	08 September 2015

Results information

Result version number	v1 (current)
This version publication date	24 December 2022
First version publication date	24 December 2022

Trial information

Trial identification

Sponsor protocol code	HOVON 78 CML

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	HOVON Data Center, HOVON, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, hdc@erasmusmc.nl

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	13 April 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2012
Global end of trial reached?	Yes
Global end of trial date	08 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of the combination of imatinib with cytarabine as compared to imatinib alone in terms of the rate of molecular response at 12 months from randomization.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 May 2006
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	Belgium: 4
Country: Number of subjects enrolled	Netherlands: 107
Worldwide total number of subjects	111
EEA total number of subjects	111

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)	1
Adults (18-64 years)	108
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Imatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

800 mg (2x400 mg) p.o. daily.

Arm title	Arm B

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Imatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

800 mg (2x400 mg) p.o. daily in cycles I-II.
800 mg (2x400 mg) p.o. daily until progression.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Cytarabine 200 mg/m2/day i.v. on days 1-7 in cycles I-II.

Number of subjects in period 1	Arm A	Arm B
Started	55	56
Completed	0	0
Not completed	55	56
Adverse reactions	11	11
Other	41	43
Lack of efficacy	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	111	111	
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)	1	1	
Adults (18-64 years)	108	108	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
median	45		
full range (min-max)	17 to 65	-	
Gender categorical Units: Subjects			
Female	43	43	
Male	68	68	

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B
Reporting group description: -	

Primary: Primary Endpoint

End point title	Primary Endpoint[1]
End point description:	
End point type	Primary
End point timeframe:	
See publication.	

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: See attached chart/documents for results.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	55	54		
Units: Whole	55	54		

Attachments (see zip file)	Statistical data section from publication/HO78 Statistical data List of reported non-SAE's/nonsaedata78-6Dec2022.pdf List of reported SAE's/saedata78-6Dec2022.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE’s will be reported on the CRF. All adverse events of Grade 2 or higher, with the exception of progression of disease, occurring during the protocol treatment period will be reported.

Adverse event reporting additional description:

Adverse events occurring after that period should also be reported if considered related to protocol treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3

Reporting groups

Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B

Reporting group description: -

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 55 (16.36%)	24 / 54 (44.44%)	
number of deaths (all causes)	3	3	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm benign, malignant and unspecif. (inc. cysts/polyp)	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	3 / 54 (5.56%)	
occurrences causally related to treatment / all	0 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see SAE chart for details.		

subjects affected / exposed	0 / 55 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	0 / 55 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nervous system disorder	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	16 / 54 (29.63%)	
occurrences causally related to treatment / all	1 / 1	16 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Renal and urinary disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	3 / 55 (5.45%)	8 / 54 (14.81%)	
occurrences causally related to treatment / all	1 / 3	7 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	0 / 54 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 55 (90.91%)	54 / 54 (100.00%)	
Vascular disorders			
Vascular	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	1 / 54 (1.85%)	
occurrences (all)	4	1	
Surgical and medical procedures			
Surgery/intra-operative injury	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
General disorders and administration site conditions			

(prolonged) hospitalisation	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	1 / 54 (1.85%)	
occurrences (all)	2	1	
Death	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 55 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Life threatening	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 55 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	6	
Other	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	32 / 55 (58.18%)	29 / 54 (53.70%)	
occurrences (all)	58	63	
Pain	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	14 / 55 (25.45%)	19 / 54 (35.19%)	
occurrences (all)	24	39	
Secondary malignancy	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	0 / 54 (0.00%)	
occurrences (all)	2	0	
Severe/permanent disability	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Syndromes	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 55 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Sexual/reproductive function	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	5 / 54 (9.26%)	
occurrences (all)	2	5	
Respiratory, thoracic and mediastinal disorders			
Pulmonary/upper respiratory	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	7 / 55 (12.73%)	5 / 54 (9.26%)	
occurrences (all)	17	5	
Nervous system disorders			
Neurology	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 55 (5.45%)	11 / 54 (20.37%)	
occurrences (all)	3	13	

Blood and lymphatic system disorders			
Blood/bone marrow	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	12 / 55 (21.82%)	8 / 54 (14.81%)	
occurrences (all)	19	12	
Hemorrhage/bleeding	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	1 / 55 (1.82%)	12 / 54 (22.22%)	
occurrences (all)	1	17	
Lymphatics	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	13 / 55 (23.64%)	14 / 54 (25.93%)	
occurrences (all)	19	28	
Eye disorders			
Ocular/visual	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	13 / 55 (23.64%)	8 / 54 (14.81%)	
occurrences (all)	26	10	
Gastrointestinal disorders			
GI	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	26 / 55 (47.27%)	18 / 54 (33.33%)	
occurrences (all)	73	32	
Hepatobiliary disorders			
Hepatobiliary/pancreas	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 55 (5.45%)	0 / 54 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Dermatology/skin	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	14 / 55 (25.45%)	8 / 54 (14.81%)	
occurrences (all)	20	10	
Renal and urinary disorders			
Renal/genitourinary	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 55 (5.45%)	1 / 54 (1.85%)	
occurrences (all)	7	1	
Endocrine disorders			
Endocrine	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 55 (3.64%)	3 / 54 (5.56%)	
occurrences (all)	2	3	
Musculoskeletal and connective tissue disorders			
Musculoskeletal/soft tissue	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	19 / 55 (34.55%)	10 / 54 (18.52%)	
occurrences (all)	33	15	

Infections and infestations			
Infections	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	21 / 55 (38.18%)	35 / 54 (64.81%)	
occurrences (all)	39	58	
Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	4 / 55 (7.27%)	9 / 54 (16.67%)	
occurrences (all)	6	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported