



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
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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
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Arm title	Arm A
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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
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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
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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
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	3
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Reporting groups

Reporting group title	Arm A
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Reporting group description: -

Reporting group title	Arm B
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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	Additional description: All combined, see SAE chart for details.		
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	Additional description: All combined, see SAE chart for details.		
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	Additional description: All combined, see SAE chart for details.		
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	Additional description: All combined, see non-SAE chart for details.		
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	Additional description: All combined, see non-SAE chart for details.		
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 subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	2 / 55 (3.64%) 2	1 / 54 (1.85%) 1
Death subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	0 / 55 (0.00%) 0	2 / 54 (3.70%) 2
Life threatening subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	0 / 55 (0.00%) 0	3 / 54 (5.56%) 6
Other subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	32 / 55 (58.18%) 58	29 / 54 (53.70%) 63
Pain subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	14 / 55 (25.45%) 24	19 / 54 (35.19%) 39
Secondary malignancy subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	2 / 55 (3.64%) 2	0 / 54 (0.00%) 0
Severe/permanent disability subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	0 / 55 (0.00%) 0	1 / 54 (1.85%) 1
Syndromes subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	0 / 55 (0.00%) 0	1 / 54 (1.85%) 1
Reproductive system and breast disorders Sexual/reproductive function subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	2 / 55 (3.64%) 2	5 / 54 (9.26%) 5
Respiratory, thoracic and mediastinal disorders Pulmonary/upper respiratory subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	7 / 55 (12.73%) 17	5 / 54 (9.26%) 5
Nervous system disorders Neurology subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.	
	3 / 55 (5.45%) 3	11 / 54 (20.37%) 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 subjects affected / exposed occurrences (all)			
	Additional description: All combined, see non-SAE chart for details.		
	21 / 55 (38.18%) 39	35 / 54 (64.81%) 58	
Metabolism and nutrition disorders Metabolic/laboratory subjects affected / exposed occurrences (all)			
	Additional description: All combined, see non-SAE chart for details.		
	4 / 55 (7.27%) 6	9 / 54 (16.67%) 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