Clinical trial results:
A Phase II multicenter study to assess the tolerability and efficacy of the addition of Bevacizumab to standard induction therapy in AML and high risk MDS above 60 years.

Summary

EudraCT number	2006-001777-19
Trial protocol	NL BE
Global end of trial date	31 October 2017

Results information

Result version number	v1 (current)
This version publication date	28 December 2022
First version publication date	28 December 2022

Trial information

Trial identification

Sponsor protocol code	HOVON 81 AML

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	31 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2011
Global end of trial reached?	Yes
Global end of trial date	31 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To assess the safety and tolerability of bevacizumab added to standard induction chemotherapy for AML (frequency and severity of toxicities and the durations of neutropenia and thrombocytopenia)
2. To assess in a randomized comparison the effect of bevacizumab on the CR rate.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 March 2007
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	Netherlands: 138
Country: Number of subjects enrolled	Belgium: 40
Country: Number of subjects enrolled	Switzerland: 41
Worldwide total number of subjects	219
EEA total number of subjects	178

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)	75
From 65 to 84 years	144
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	Control Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Dauno
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Dauno 45mg/m2 3hrs infusion day 1,2,3

Investigational medicinal product name	Cytarabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Cytarabin 200 mg/m2 24hr cont. Infusion, day 1-7, cycle 1
Cytarabin 1000 mg/m2 6hr infusion q 12hr x 12 day 1-6 cycle 2

Arm title	Experimental Group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Dauno
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Dauno 45mg/m2 3hrs infusion day 1,2,3

Investigational medicinal product name	Cytarabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details: Cytarabin 200 mg/m2 24hr cont. Infusion, day 1-7, cycle 1 Cytarabin 1000 mg/m2 6hr infusion q 12hr x 12 day 1-6 cycle 2	
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details: 5 or 10mg/kg, 1,5hr infusion day 1, 15 cycle 1 and 2	

Number of subjects in period 1	Control Group	Experimental Group
Started	110	109
Completed	73	65
Not completed	37	44
Adverse reactions	5	12
Other	9	5
At patient's request	2	2
Lack of efficacy	21	25

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	219	219	
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)	75	75	
From 65-84 years	144	144	
85 years and over	0	0	
Age continuous Units: years			
median	66		
full range (min-max)	60 to 80	-	
Gender categorical Units: Subjects			
Female	104	104	
Male	115	115	

End points

End points reporting groups

Reporting group title	Control Group
Reporting group description: -	
Reporting group title	Experimental Group
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	Control Group	Experimental Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	86		
Units: Whole	85	86		

Attachments (see zip file)	Statistical data section from publication/HO81 Statistical data List of reported non-SAE's/nonsaedata81-7Dec2022.pdf List of reported SAE's/saedata81-7Dec2022.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs of Grade 2 or higher, with the exception of progression of disease, occurring during the protocol treatment period will be reported. 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	Control Group
Reporting group description: -	
Reporting group title	Experimental Group
Reporting group description: -	

Serious adverse events	Control Group	Experimental Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	37 / 109 (33.94%)	60 / 105 (57.14%)	
number of deaths (all causes)	97	97	
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	0 / 109 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Vascular disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	0 / 109 (0.00%)	3 / 105 (2.86%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
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 / 109 (1.83%)	3 / 105 (2.86%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 2	0 / 1	

Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	9 / 109 (8.26%)	7 / 105 (6.67%)	
occurrences causally related to treatment / all	7 / 9	4 / 7	
deaths causally related to treatment / all	3 / 4	1 / 2	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 109 (0.92%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	9 / 109 (8.26%)	14 / 105 (13.33%)	
occurrences causally related to treatment / all	3 / 9	11 / 16	
deaths causally related to treatment / all	0 / 3	2 / 3	
Nervous system disorders			
Nervous system disorder	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	4 / 109 (3.67%)	9 / 105 (8.57%)	
occurrences causally related to treatment / all	2 / 4	5 / 9	
deaths causally related to treatment / all	0 / 1	2 / 4	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	0 / 109 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 109 (1.83%)	9 / 105 (8.57%)	
occurrences causally related to treatment / all	2 / 2	8 / 9	
deaths causally related to treatment / all	1 / 1	3 / 3	
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All combined, see SAE chart for details.		

subjects affected / exposed	1 / 109 (0.92%)	3 / 105 (2.86%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 109 (1.83%)	3 / 105 (2.86%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	11 / 109 (10.09%)	23 / 105 (21.90%)	
occurrences causally related to treatment / all	6 / 11	16 / 23	
deaths causally related to treatment / all	4 / 8	10 / 12	
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	0 / 109 (0.00%)	2 / 105 (1.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Control Group	Experimental Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 109 (97.25%)	103 / 105 (98.10%)	
Vascular disorders			
Vascular	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	12 / 109 (11.01%)	10 / 105 (9.52%)	
occurrences (all)	12	12	
General disorders and administration site conditions			
Constitutional symptoms	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	22 / 109 (20.18%)	25 / 105 (23.81%)	
occurrences (all)	29	37	
Growth and development	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 109 (0.00%)	1 / 105 (0.95%)	
occurrences (all)	0	1	
Pain	Additional description: All combined, see non-SAE chart for details.		

subjects affected / exposed	24 / 109 (22.02%)	17 / 105 (16.19%)	
occurrences (all)	30	26	
Syndromes	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 109 (2.75%)	2 / 105 (1.90%)	
occurrences (all)	3	2	
Immune system disorders			
Allergy/immunology	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	14 / 109 (12.84%)	7 / 105 (6.67%)	
occurrences (all)	16	9	
Respiratory, thoracic and mediastinal disorders			
Pulmonary/upper respiratory	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	22 / 109 (20.18%)	28 / 105 (26.67%)	
occurrences (all)	25	41	
Cardiac disorders			
Cardiac arrythmia	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 109 (8.26%)	9 / 105 (8.57%)	
occurrences (all)	9	9	
Cardiac general	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	13 / 109 (11.93%)	29 / 105 (27.62%)	
occurrences (all)	14	37	
Nervous system disorders			
Neurology	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	20 / 109 (18.35%)	27 / 105 (25.71%)	
occurrences (all)	27	34	
Blood and lymphatic system disorders			
Blood/bone marrow	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	7 / 109 (6.42%)	3 / 105 (2.86%)	
occurrences (all)	7	3	
Coagulation	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 109 (8.26%)	4 / 105 (3.81%)	
occurrences (all)	10	4	
Hemorrhage/bleeding	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	15 / 109 (13.76%)	25 / 105 (23.81%)	
occurrences (all)	26	38	
Lymphatics	Additional description: All combined, see non-SAE chart for details.		

subjects affected / exposed	10 / 109 (9.17%)	7 / 105 (6.67%)	
occurrences (all)	14	7	
Ear and labyrinth disorders			
Auditory/ear	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 109 (2.75%)	2 / 105 (1.90%)	
occurrences (all)	4	2	
Eye disorders			
Ocular/visual	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	8 / 109 (7.34%)	8 / 105 (7.62%)	
occurrences (all)	8	8	
Gastrointestinal disorders			
Gastrointestinal	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	74 / 109 (67.89%)	75 / 105 (71.43%)	
occurrences (all)	152	170	
Hepatobiliary disorders			
Hepatobiliary/pancreas	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 109 (0.00%)	2 / 105 (1.90%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Dermatology/skin	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	66 / 109 (60.55%)	52 / 105 (49.52%)	
occurrences (all)	105	73	
Renal and urinary disorders			
Renal/genitourinary	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 109 (8.26%)	11 / 105 (10.48%)	
occurrences (all)	10	14	
Endocrine disorders			
Endocrine	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	0 / 109 (0.00%)	3 / 105 (2.86%)	
occurrences (all)	0	4	
Musculoskeletal and connective tissue disorders			
Musculoskeletal/soft tissue	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	5 / 109 (4.59%)	5 / 105 (4.76%)	
occurrences (all)	6	5	
Infections and infestations			
Infection	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	92 / 109 (84.40%)	95 / 105 (90.48%)	
occurrences (all)	260	285	

Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	45 / 109 (41.28%)	39 / 105 (37.14%)	
occurrences (all)	109	145	

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