



## Clinical trial results:

**Randomized maintenance therapy with Azacitidine (Vidaza) in older patients ( 60 years of age) with acute myeloid leukemia (AML) and refractory anemia with excess of blasts (RAEB, RAEB-t). A phase III study.**

### Summary

EudraCT number	2008-001290-15
Trial protocol	NL BE
Global end of trial date	31 December 2021

### Results information

Result version number	v1 (current)
This version publication date	26 January 2023
First version publication date	26 January 2023

### Trial information

#### Trial identification

Sponsor protocol code	HO97
-----------------------	------

#### 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, +31 (0)107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, +31 (0)107041560, 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	26 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 July 2018
Global end of trial reached?	Yes
Global end of trial date	31 December 2021
Was the trial ended prematurely?	Yes

Notes:

---

**General information about the trial**

---

Main objective of the trial:

To assess, in a randomized study the value of Azacitidine as post remission therapy (in comparison to observation) in elderly patients with AML, RAEB or RAEB-t with respect to the disease free survival.

Protection of trial subjects:

Monitoring and insurance.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

---

**Population of trial subjects**

---

**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 80
Country: Number of subjects enrolled	Belgium: 38
Worldwide total number of subjects	118
EEA total number of subjects	118

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)	5
From 65 to 84 years	113
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
<b>Arm title</b>	Arm A

Arm description: -

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Arm title</b>	Arm B
------------------	-------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	Vidaza
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

50 mg/m<sup>2</sup>, days 1,2,3,4,5 every 4 weeks until relapse for a maximum of 12 cycles.

Number of subjects in period 1	Arm A	Arm B
Started	60	58
Completed	23	35
Not completed	37	23
Adverse reactions	-	3
Other	3	6
Lack of efficacy	34	14

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	118	118	
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)	5	5	
From 65-84 years	113	113	
85 years and over	0	0	
Age continuous			
Units: years			
median	69		
full range (min-max)	60 to 81	-	
Gender categorical			
Units: Subjects			
Female	50	50	
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 <sup>[1]</sup>
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	60	56		
Units: Whole	60	56		

<b>Attachments (see zip file)</b>	Statistical data section from publication/HO85 Statistical data List of reported non-SAE's/nonsaedata85-10Jan2023.pdf List of reported SAE's/saedata85-10Jan2023.pdf
-----------------------------------	--

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All AEs of CTCAE grade 2 or higher have to be reported from the first study-related procedure until 30 days following the last protocol treatment or until the start of subsequent systemic therapy for the disease under study, if earlier.

Adverse event reporting additional description:

Adverse events occurring after 30 days should also be reported if considered related to study drug. Grade 3 or 4 adverse events considered related to study drug must be followed until recovery or until 6 months after the last protocol treatment, whichever comes first.

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	4 / 60 (6.67%)	14 / 55 (25.45%)	
number of deaths (all causes)	45	41	
number of deaths resulting from adverse events			
Investigations			
Investigations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
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 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
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	1 / 60 (1.67%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 60 (1.67%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
Blood and lymphatic disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
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 / 60 (3.33%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Skin and subcutaneous tissue disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
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		
subjects affected / exposed	0 / 60 (0.00%)	3 / 55 (5.45%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	2 / 55 (3.64%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
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	29 / 60 (48.33%)	39 / 55 (70.91%)	
Vascular disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 60 (3.33%)	1 / 55 (1.82%)	
occurrences (all)	2	1	
Surgical and medical procedures	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
General disorders and administration site conditions	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	0 / 60 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Constitutional symptoms	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 60 (5.00%)	9 / 55 (16.36%)	
occurrences (all)	3	11	
Death	Additional description: All combined, see non-SAE chart for details		



subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 55 (1.82%) 1	
Immune system disorders			
Allergy/immunology	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	3 / 55 (5.45%) 3	
Reproductive system and breast disorders			
Sexual/reproductive function	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	0 / 55 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary/upper respiratory	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 5	6 / 55 (10.91%) 8	
Cardiac disorders			
Cardiac arrhythmia	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 55 (1.82%) 2	
Cardiac general	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	2 / 55 (3.64%) 2	
Nervous system disorders			
Neurology	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	2 / 60 (3.33%) 3	4 / 55 (7.27%) 4	
Blood and lymphatic system disorders			
Blood/bone marrow	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 2	10 / 55 (18.18%) 21	
Hemorrhage/bleeding	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1	1 / 55 (1.82%) 1	
Lymphatics	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	2 / 55 (3.64%) 2	
Ear and labyrinth disorders			

Auditory/ear subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	1 / 60 (1.67%)	2 / 55 (3.64%)	
	1	3	
Eye disorders Ocular/visual subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	1 / 60 (1.67%)	1 / 55 (1.82%)	
	1	1	
Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all)  Pain subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	2 / 60 (3.33%)	12 / 55 (21.82%)	
	2	22	
	Additional description: All combined, see non-SAE chart for details		
	6 / 60 (10.00%)	5 / 55 (9.09%)	
	6	8	
Hepatobiliary disorders Hepatobiliary/pancreas subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	2 / 60 (3.33%)	3 / 55 (5.45%)	
	3	3	
Skin and subcutaneous tissue disorders Dermatology/skin subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	5 / 60 (8.33%)	8 / 55 (14.55%)	
	7	14	
Renal and urinary disorders Renal/genitourinary subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	1 / 60 (1.67%)	3 / 55 (5.45%)	
	1	3	
Endocrine disorders Endocrine subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	0 / 60 (0.00%)	1 / 55 (1.82%)	
	0	1	
Musculoskeletal and connective tissue disorders Musculoskeletal/soft tissue subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	3 / 60 (5.00%)	4 / 55 (7.27%)	
	3	4	
Infections and infestations Infection subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	11 / 60 (18.33%)	11 / 55 (20.00%)	
	14	19	

Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 60 (3.33%)	4 / 55 (7.27%)	
occurrences (all)	2	4	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2011	Page 1: Statistician Y. van Norden changed into Prof. Dr. Ir. C.A.G. van Montfort and Mw. Dr. Ir. D. Chitu Page 7, §3: End of recruitment I 2012 changed into IV 2013 Page 8, §4: Cytological and Immunophenotype Review M.B. van 't Veer changed into M. Jongen-Lavrencic Page 8, §4: Statistician Y. van Norden changed into Prof. Dr. Ir. C.A.G. van Montfort and Mw. Dr. Ir. D. Chitu Page 17(18), §11: Required investigations at entry X-thorax removed from table Page 17(18), §11.1: Evaluations prior to start treatment Chest X-ray removed Page 20(22), §13.2: hematological toxicities, abnormal laboratory values that have been recorded as being not clinically significant and progression of the disease under study and a pre-existing condition that does not increase in severity should be reported on the baseline concomitant diseases form added to adverse events that should not be reported Page 22(24), §13.3: Description of SUSAR evaluation and SUSAR reporting adjusted to the current procedure, agreement of reporting of SAE to EC added
29 October 2012	Page 8, §4: Principal Investigator, G. Huls, University Medical Center, Groningen changed into University Medical Center St. Radboud, Nijmegen Page 8, §4: Writing Committee, G. Huls, University Medical Center, Groningen changed into University Medical Center St. Radboud, Nijmegen

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported