Clinical trial results:
A phase I/II feasibility study of panoninostat alone and the combination of panobinostat and decitabine prior to donor lymphocyte infusion in recipients of allogeneic stem cell transplantation with poor and very poor risk AML

Summary

EudraCT number	2012-003344-74
Trial protocol	NL BE
Global end of trial date	02 August 2022

Results information

Result version number	v1 (current)
This version publication date	17 November 2023
First version publication date	17 November 2023

Trial information

Trial identification

Sponsor protocol code	HO116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	EC number: MEC-2013-310, Nederland Trila Register: NTR4269, CCMO dossier number: NL41789.078.13

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	17 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 August 2018
Global end of trial reached?	Yes
Global end of trial date	02 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

*Phase I part
- To asses the safety and feasibility of post-transplant panobinostat combined with decitabine to a regimen of T-cell replete RIC alloHSCT in patient with (very) poor-risk AML/RAEB, and select the recommended dose level for part II of the study
*Phase II part
- To assess the feasibility and efficacy of addition of post-transplant panobinostat combined with decitabine to a regimen of T-cell replete RIC alloHSCT and DLI in patients with (very) poor-risk AML/RAEB
*Phase III part
- To assess the feasibility and efficacy of post-transplant panobinostat monotherapy to a regimen of T-cell replete RIC alloHSCT and DLI in patients with (very) poor-risk AML

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 November 2013
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: 132
Country: Number of subjects enrolled	Belgium: 8
Worldwide total number of subjects	140
EEA total number of subjects	140

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)	103
From 65 to 84 years	37
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 period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Experimental group

Arm description: -

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

Dosage and administration details:

4 cycles of panobinostat (20 mg on days 1, 4, 8, 11). Cycle 1 and 2 after alloHSCT, cycle 3 and 4 after first DLI during part II of the study.

Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

4 cycles of decitabine as indicated by dose level (0-20 mg/m2 on days 1-3/5). Cycle 1 and 2 after alloHSCT, cycle 3 and 4 after first DLI during part II of the study.

Number of subjects in period 1	Experimental group
Started	140
Completed	48
Not completed	92
Adverse reactions	7
At patient's request	6
Lack of efficacy	7
not specified	72

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	140	140	
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)	103	103	
From 65-84 years	37	37	
85 years and over	0	0	
Age continuous Units: years			
median	59		
full range (min-max)	18 to 71	-	
Gender categorical Units: Subjects			
Female	59	59	
Male	81	81	

End points

End points reporting groups

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.

Attachments (see zip file)	Statistical data section from publication/HO116_Statistical data List of reported non-SAE's/nonsaedata116-19Apr2023.pdf List of reported SAE's/saedata116-19Apr2023.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be reported from the first study-related procedure until 30 days following the last dose of any drug from the protocol treatment schedule 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 at least possibly related to the investigational medicinal product by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Experimental group

Reporting group description: -

Serious adverse events	Experimental group		
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 110 (43.64%)		
number of deaths (all causes)	83		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Vascular disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General disorders and administrative site conditions	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	4 / 110 (3.64%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		

Immune system disorders			
Immune system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	11 / 110 (10.00%)		
occurrences causally related to treatment / all	5 / 11		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	7 / 110 (6.36%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	2 / 3		
Investigations			
Investigations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disoders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	3 / 110 (2.73%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	12 / 110 (10.91%)		
occurrences causally related to treatment / all	5 / 12		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	3 / 110 (2.73%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	21 / 110 (19.09%)		
occurrences causally related to treatment / all	8 / 23		
deaths causally related to treatment / all	1 / 2		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 110 (90.91%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences (all)	1		
Vascular disorders			
Vascular disorders	Additional description: All combined, see non-SAE chart for detail		
subjects affected / exposed	20 / 110 (18.18%)		
occurrences (all)	20		
General disorders and administration site conditions			

General disorders and administration site conditions	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	22 / 110 (20.00%)		
occurrences (all)	23		
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	11 / 110 (10.00%)		
occurrences (all)	11		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 110 (2.73%)		
occurrences (all)	3		
Investigations			
Investigations	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	47 / 110 (42.73%)		
occurrences (all)	91		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences (all)	2		
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	13 / 110 (11.82%)		
occurrences (all)	14		
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	16 / 110 (14.55%)		
occurrences (all)	18		
Blood and lymphatic system disorders			
Blood and lymphatic system disorder	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	36 / 110 (32.73%)		
occurrences (all)	41		

Ear and labyrinth disorders			
Ear and labyrinth disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 110 (0.91%)		
occurrences (all)	1		
Eye disorders			
Eye disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 110 (4.55%)		
occurrences (all)	5		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	29 / 110 (26.36%)		
occurrences (all)	48		
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	16 / 110 (14.55%)		
occurrences (all)	18		
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	15 / 110 (13.64%)		
occurrences (all)	15		
Endocrine disorders			
Endocrine disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 110 (1.82%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	4 / 110 (3.64%)		
occurrences (all)	5		
Infections and infestations			
Infections and infestations	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	54 / 110 (49.09%)		
occurrences (all)	85		
Metabolism and nutrition disorders			

Metabolism and nutrition disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	23 / 110 (20.91%)		
occurrences (all)	31		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2014	New protocol version (v6) and change of several local investigators. Submitted & approved in NL + BE.
23 June 2015	New protocol version (v7) and change of an independent physician in NL. Submitted & approved in NL + BE.
28 July 2016	New protocol version (v8), new ICF, and change of some investigators in NL. Submitted and approved in NL+BE.
13 March 2017	New protocol version (v9) due to changes in risk tables appendix C & D. Submitted and approved in NL+BE
16 December 2021	New protocol version (v10) and change of several local investigators. Submitted & approved in NL + BE.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32936907