



Clinical trial results:

A randomized phase II multicenter study with a safety run-in to assess the tolerability and efficacy of the addition of oral lenalidomide to standard induction therapy in AML and RAEB 66 years and very poor risk AML 18 years.

A study in the frame of the masterprotocol of parallel randomized phase II studies in elderly AML

Summary

EudraCT number	2009-013094-17
Trial protocol	NL BE NO
Global end of trial date	19 September 2024

Results information

Result version number	v1 (current)
This version publication date	28 December 2025
First version publication date	28 December 2025

Trial information

Trial identification

Sponsor protocol code	HOVON103AMLEN
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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	Dr. Molewaterplein 40, Rotterdam, Netherlands,
Public contact	HOVON Data Center, Erasmus MC, +31 107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, Erasmus MC, +31 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	29 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2023
Global end of trial reached?	Yes
Global end of trial date	19 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

For part A of the study (if applicable):

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

For part B:

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

Protection of trial subjects:

Insurance and monitoring

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2010
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: 205
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Belgium: 66
Country: Number of subjects enrolled	Switzerland: 65
Worldwide total number of subjects	337
EEA total number of subjects	272

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)	1
From 65 to 84 years	336
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	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Control group

Arm description:

Control with standard medication, no IMP:

Daunomycin Days 45mg/m2 3hr infusion on days 1,2,3

Cytarabine 200mg/m2 continuous infusion(24hrs) on days 1 thru 7

Arm type	Active comparator
Investigational medicinal product name	Daunomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Daunomycin Days 45mg/m2 3hr infusion on days 1,2,3

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cytarabine 200mg/m2 continuous infusion(24hrs) on days 1 thru 7

Arm title	Experimental
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Arm description:

Like control, this arm receives standard medication:

Daunomycin Days 45mg/m2 3hr infusion on days 1,2,3

Cytarabine 200mg/m2 continuous infusion(24hrs) on days 1 thru 7

Arm type	Experimental
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	CC-5013
Other name	REVLIMID®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Remission induction treatment Cycle I:

lenalidomide is started at a dose level of 10 mg orally day 1-21.

Remission induction treatment Cycle II:

Decisions regarding dose escalation to 15 and 20 mg day 1-21 of each cycle, continuation with dose level 10, 15 or 20mg or stopping is based on the incidence of DLT.

Cycle II will be given as soon as possible after cycle I but at least within 8 weeks after start of cycle I. If after cycle I the bone marrow shows persistence of leukemia it is recommended that patients proceed to cycle II immediately. Otherwise cycle II will be started as soon as there is evidence of haematological regeneration. No dose reduction is allowed.

Investigational medicinal product name	Daunomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Daunomycin Days 45mg/m² 3hr infusion on days 1,2,3

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cytarabine 200mg/m² continuous infusion(24hrs) on days 1 thru 7

Number of subjects in period 1	Control group	Experimental
Started	172	165
Completed	104	77
Not completed	68	88
Adverse reactions	16	28
Consent withdrawn by subject	4	9
Other	12	21
Lack of efficacy	36	30

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	337	337	
Age categorical			
Units: Subjects			
Adults (18-64 years)	1	1	
From 65-84 years	336	336	
Age continuous			
Units: years			
median	69		
full range (min-max)	64 to 84	-	
Gender categorical			
Units: Subjects			
Female	147	147	
Male	190	190	

End points

End points reporting groups

Reporting group title	Control group
Reporting group description: Control with standard medication, no IMP: Daunomycin Days 45mg/m2 3hr infusion on days 1,2,3 Cytarabine 200mg/m2 continuous infusion(24hrs) on days 1 thru 7	
Reporting group title	Experimental
Reporting group description: Like control, this arm receives standard medication: Daunomycin Days 45mg/m2 3hr infusion on days 1,2,3 Cytarabine 200mg/m2 continuous infusion(24hrs) on days 1 thru 7	

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		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	165		
Units: Whole	172	165		

Attachments (see zip file)	List of reported SAE's/Lena-saedata103-2Dec2025.pdf Statistical data section from List of reported non-SAE's/Lena-nonsaedata103-2Dec2025.pdf
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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 protocol treatment or until the start of subsequent systemic therapy for the disease under study, if earlier.

Adverse event reporting additional description:

All AEs of CTCAE grade 2 or higher have to be reported on the Adverse Events CRF, with the exception of alopecia, nausea/vomiting and progression of the disease under study, a pre-existing condition that does not increase in severity. Adverse events occurring after 30 days should also be reported if considered related to study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Control group
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Reporting group description: -

Reporting group title	Experimental group
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Reporting group description: -

Serious adverse events	Control group	Experimental group	
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 169 (40.24%)	82 / 159 (51.57%)	
number of deaths (all causes)	136	136	
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		
subjects affected / exposed	4 / 169 (2.37%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Vascular disorders	Additional description: All combined		
subjects affected / exposed	4 / 169 (2.37%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	2 / 4	1 / 1	
deaths causally related to treatment / all	2 / 3	0 / 0	
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined		

subjects affected / exposed	3 / 169 (1.78%)	14 / 159 (8.81%)	
occurrences causally related to treatment / all	3 / 3	7 / 14	
deaths causally related to treatment / all	2 / 2	3 / 9	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined		
subjects affected / exposed	8 / 169 (4.73%)	17 / 159 (10.69%)	
occurrences causally related to treatment / all	5 / 9	13 / 18	
deaths causally related to treatment / all	2 / 5	4 / 7	
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined		
subjects affected / exposed	0 / 169 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Investigations	Additional description: All combined		
subjects affected / exposed	0 / 169 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined		
subjects affected / exposed	2 / 169 (1.18%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorders	Additional description: All combined		
subjects affected / exposed	9 / 169 (5.33%)	9 / 159 (5.66%)	
occurrences causally related to treatment / all	3 / 9	7 / 9	
deaths causally related to treatment / all	1 / 6	2 / 2	
Nervous system disorders			
Nervous system disorders	Additional description: All combined		
subjects affected / exposed	6 / 169 (3.55%)	9 / 159 (5.66%)	
occurrences causally related to treatment / all	2 / 6	8 / 9	
deaths causally related to treatment / all	1 / 2	0 / 0	
Blood and lymphatic system disorders			

Blood and lymphatic system disorders	Additional description: All combined		
subjects affected / exposed	7 / 169 (4.14%)	10 / 159 (6.29%)	
occurrences causally related to treatment / all	7 / 7	10 / 11	
deaths causally related to treatment / all	2 / 2	0 / 0	
Gastrointestinal disorders	Additional description: All combined		
Gastrointestinal disorders	Additional description: All combined		
subjects affected / exposed	11 / 169 (6.51%)	11 / 159 (6.92%)	
occurrences causally related to treatment / all	10 / 11	10 / 11	
deaths causally related to treatment / all	4 / 4	1 / 1	
Hepatobiliary disorders	Additional description: All combined		
Hepatobiliary disorders	Additional description: All combined		
subjects affected / exposed	1 / 169 (0.59%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	1 / 1	0 / 1	
Skin and subcutaneous tissue disorders	Additional description: All combined		
Skin and subcutaneous tissue disorders	Additional description: All combined		
subjects affected / exposed	1 / 169 (0.59%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders	Additional description: All combined		
Renal and urinary disorders	Additional description: All combined		
subjects affected / exposed	1 / 169 (0.59%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations	Additional description: All combined		
Infections and infestations	Additional description: All combined		
subjects affected / exposed	22 / 169 (13.02%)	26 / 159 (16.35%)	
occurrences causally related to treatment / all	23 / 25	21 / 28	
deaths causally related to treatment / all	8 / 10	9 / 12	
Metabolism and nutrition disorders	Additional description: All combined		
Metabolism and nutrition disorders	Additional description: All combined		
subjects affected / exposed	4 / 169 (2.37%)	6 / 159 (3.77%)	
occurrences causally related to treatment / all	4 / 4	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	

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	166 / 169 (98.22%)	157 / 159 (98.74%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: All combined		
subjects affected / exposed	2 / 169 (1.18%)	0 / 159 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Vascular disorders	Additional description: All combined		
subjects affected / exposed	39 / 169 (23.08%)	50 / 159 (31.45%)	
occurrences (all)	54	71	
Surgical and medical procedures			
Surgical and medical procedures	Additional description: All combined		
subjects affected / exposed	1 / 169 (0.59%)	2 / 159 (1.26%)	
occurrences (all)	1	2	
Pregnancy, puerperium and perinatal conditions			
Pregnancy, puerperium and perinatal conditions	Additional description: All combined		
subjects affected / exposed	1 / 169 (0.59%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined		
subjects affected / exposed	47 / 169 (27.81%)	56 / 159 (35.22%)	
occurrences (all)	63	106	
Immune system disorders			
Immune system disorders	Additional description: All combined		
subjects affected / exposed	9 / 169 (5.33%)	12 / 159 (7.55%)	
occurrences (all)	9	15	
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined		
subjects affected / exposed	5 / 169 (2.96%)	2 / 159 (1.26%)	
occurrences (all)	5	2	
Respiratory, thoracic and mediastinal disorders			

Respiratory, thoracic and mediastinal disorders	Additional description: All combined		
subjects affected / exposed	42 / 169 (24.85%)	50 / 159 (31.45%)	
occurrences (all)	55	75	
Psychiatric disorders	Additional description: All combined		
Psychiatric disorders	Additional description: All combined		
subjects affected / exposed	24 / 169 (14.20%)	25 / 159 (15.72%)	
occurrences (all)	35	35	
Investigations	Additional description: All combined		
Investigations	Additional description: All combined		
subjects affected / exposed	61 / 169 (36.09%)	60 / 159 (37.74%)	
occurrences (all)	171	174	
Injury, poisoning and procedural complications	Additional description: All combined		
Injury, poisoning and procedural complications	Additional description: All combined		
subjects affected / exposed	3 / 169 (1.78%)	2 / 159 (1.26%)	
occurrences (all)	3	2	
Cardiac disorders	Additional description: All combined		
Cardiac disorders	Additional description: All combined		
subjects affected / exposed	27 / 169 (15.98%)	35 / 159 (22.01%)	
occurrences (all)	35	41	
Nervous system disorders	Additional description: All combined		
Nervous system disorders	Additional description: All combined		
subjects affected / exposed	23 / 169 (13.61%)	40 / 159 (25.16%)	
occurrences (all)	29	62	
Blood and lymphatic system disorders	Additional description: All combined		
Blood and lymphatic system disorders	Additional description: All combined		
subjects affected / exposed	98 / 169 (57.99%)	90 / 159 (56.60%)	
occurrences (all)	185	167	
Ear and labyrinth disorders	Additional description: All combined		
Ear and labyrinth disorders	Additional description: All combined		
subjects affected / exposed	1 / 169 (0.59%)	5 / 159 (3.14%)	
occurrences (all)	1	5	
Eye disorders	Additional description: All combined		
Eye disorders	Additional description: All combined		
subjects affected / exposed	17 / 169 (10.06%)	14 / 159 (8.81%)	
occurrences (all)	18	14	
Gastrointestinal disorders			

Gastrointestinal disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	111 / 169 (65.68%) 236	111 / 159 (69.81%) 216	
Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	4 / 169 (2.37%) 4	6 / 159 (3.77%) 8	
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	86 / 169 (50.89%) 120	97 / 159 (61.01%) 165	
Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	19 / 169 (11.24%) 30	28 / 159 (17.61%) 28	
Endocrine disorders Endocrine disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	3 / 169 (1.78%) 3	0 / 159 (0.00%) 0	
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	20 / 169 (11.83%) 24	14 / 159 (8.81%) 18	
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	Additional description: All combined		
	111 / 169 (65.68%) 228	109 / 159 (68.55%) 234	
Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	77 / 169 (45.56%) 209	83 / 159 (52.20%) 192	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2011	Amendment 1 The reason for this amendment is to add participating centers.
08 December 2011	Amendment 2 The reason for this amendment/addendum is the change in packaging and distribution of the IMP and the addition of the pregnancy prevention RMP. Brief description of amendment/addendum: Protocol update following the change in the ABR and EudraCT form regarding the packaging of the IMP lenalidomide (from capsules in bottles to capsules in blisters/wallets, capsules themselves remain unchanged) and the addition of the lenalidomide pregnancy prevention RMP. NB: The already supplied (QP-released) medication in bottles will be used up by the sites.
05 June 2012	Amendment 3 The reason for this amendment is to correct some errors regarding section D of the EudraCT form (splitting the IMP into 2 IMPs due to different strengths, authorities in section D9, country where marketing authorization has been granted), which prevents the distributor from releasing medication.
10 April 2013	Amendment 4 The reason for this amendment is to add participating centers and to change local investigators.

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/32020044>