



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 |
|-----------------------|---------------|

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 |
|------------------|--------------|

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/m ² 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/m ² 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 |
|-----------------------|----------------|

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 |
|-----------------------------------|--|

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 |
|-----------------|------------|

Dictionary used

| | |
|--------------------|-------|
| Dictionary name | CTCAE |
| Dictionary version | 4 |

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 | 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>