



Clinical trial results:

Imatinib in combination with Cytarabine as compared to Imatinib alone in patients with first chronic phase Chronic Myeloid Leukemia.

A prospective randomized phase III study.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2005-003839-41 |
| Trial protocol | BE |
| Global end of trial date | 08 September 2015 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 24 December 2022 |
| First version publication date | 24 December 2022 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | HOVON 78 CML |
|-----------------------|--------------|

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 | 13 April 2012 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 March 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 September 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of the combination of imatinib with cytarabine as compared to imatinib alone in terms of the rate of molecular response at 12 months from randomization.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 24 May 2006 |
| 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 | Belgium: 4 |
| Country: Number of subjects enrolled | Netherlands: 107 |
| Worldwide total number of subjects | 111 |
| EEA total number of subjects | 111 |

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) | 1 |
| Adults (18-64 years) | 108 |
| From 65 to 84 years | 2 |
| 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 | Arm A |

Arm description: -

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Imatinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

800 mg (2x400 mg) p.o. daily.

| | |
|------------------|-------|
| Arm title | Arm B |
|------------------|-------|

Arm description: -

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

Dosage and administration details:

800 mg (2x400 mg) p.o. daily in cycles I-II.

800 mg (2x400 mg) p.o. daily until progression.

| | |
|--|------------------------|
| Investigational medicinal product name | Cytarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cytarabine 200 mg/m²/day i.v. on days 1-7 in cycles I-II.

| Number of subjects in period 1 | Arm A | Arm B |
|---------------------------------------|-------|-------|
| Started | 55 | 56 |
| Completed | 0 | 0 |
| Not completed | 55 | 56 |
| Adverse reactions | 11 | 11 |
| Other | 41 | 43 |
| Lack of efficacy | 3 | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | Overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 111 | 111 | |
| 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) | 1 | 1 | |
| Adults (18-64 years) | 108 | 108 | |
| From 65-84 years | 2 | 2 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 45 | | |
| full range (min-max) | 17 to 65 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 43 | 43 | |
| 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 ^[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 | Arm A | Arm B | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 54 | | |
| Units: Whole | 55 | 54 | | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | Statistical data section from publication/HO78 Statistical data List of reported non-SAE's/nonsaedata78-6Dec2022.pdf List of reported SAE's/saedata78-6Dec2022.pdf |
|-----------------------------------|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE's will be reported on the CRF. All adverse events of Grade 2 or higher, with the exception of progression of disease, occurring during the protocol treatment period will be reported.

Adverse event reporting additional description:

Adverse events occurring after that period should also be reported if considered related to protocol treatment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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|-----------------|-------|
| 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 | 9 / 55 (16.36%) | 24 / 54 (44.44%) | |
| number of deaths (all causes) | 3 | 3 | |
| 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 | 1 / 55 (1.82%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| 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 / 55 (3.64%) | 3 / 54 (5.56%) | |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Reproductive system and breast disorders | Additional description: All combined, see SAE chart for details. | | |

| | | | |
|---|--|------------------|--|
| subjects affected / exposed | 0 / 55 (0.00%) | 2 / 54 (3.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Injury, poisoning and procedural complications | Additional description: All combined, see SAE chart for details. | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| 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 | 0 / 55 (0.00%) | 2 / 54 (3.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Nervous system disorder | Additional description: All combined, see SAE chart for details. | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Blood and lymphatic system disorders | Additional description: All combined, see SAE chart for details. | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 16 / 54 (29.63%) | |
| occurrences causally related to treatment / all | 1 / 1 | 16 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Eye disorders | Additional description: All combined, see SAE chart for details. | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 1 / 54 (1.85%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastrointestinal disorders | Additional description: All combined, see SAE chart for details. | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 54 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|--|--|-----------------|--|
| Renal and urinary disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details. | | |
| | 1 / 55 (1.82%) | 0 / 54 (0.00%) | |
| | 0 / 3 | 0 / 0 | |
| | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details. | | |
| | 0 / 55 (0.00%) | 1 / 54 (1.85%) | |
| | 0 / 0 | 1 / 1 | |
| | 0 / 0 | 0 / 0 | |
| Infections and infestations Infections and infestations subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details. | | |
| | 3 / 55 (5.45%) | 8 / 54 (14.81%) | |
| | 1 / 3 | 7 / 9 | |
| | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details. | | |
| | 1 / 55 (1.82%) | 0 / 54 (0.00%) | |
| | 1 / 2 | 0 / 0 | |
| | 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 | 50 / 55 (90.91%) | 54 / 54 (100.00%) | |
| Vascular disorders Vascular subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | | |
| | 2 / 55 (3.64%) | 1 / 54 (1.85%) | |
| | 4 | 1 | |
| Surgical and medical procedures Surgery/intra-operative injury subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | | |
| | 1 / 55 (1.82%) | 1 / 54 (1.85%) | |
| | 1 | 1 | |
| General disorders and administration site conditions | | | |

| | | |
|---|--|------------------------|
| (prolonged) hospitalisation subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 2 / 55 (3.64%) 2 | 1 / 54 (1.85%) 1 |
| Death subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 0 / 55 (0.00%) 0 | 2 / 54 (3.70%) 2 |
| Life threatening subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 0 / 55 (0.00%) 0 | 3 / 54 (5.56%) 6 |
| Other subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 32 / 55 (58.18%) 58 | 29 / 54 (53.70%) 63 |
| Pain subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 14 / 55 (25.45%) 24 | 19 / 54 (35.19%) 39 |
| Secondary malignancy subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 2 / 55 (3.64%) 2 | 0 / 54 (0.00%) 0 |
| Severe/permanent disability subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 0 / 55 (0.00%) 0 | 1 / 54 (1.85%) 1 |
| Syndromes subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 0 / 55 (0.00%) 0 | 1 / 54 (1.85%) 1 |
| Reproductive system and breast disorders Sexual/reproductive function subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 2 / 55 (3.64%) 2 | 5 / 54 (9.26%) 5 |
| Respiratory, thoracic and mediastinal disorders Pulmonary/upper respiratory subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 7 / 55 (12.73%) 17 | 5 / 54 (9.26%) 5 |
| Nervous system disorders Neurology subjects affected / exposed occurrences (all) | Additional description: All combined, see non-SAE chart for details. | |
| | 3 / 55 (5.45%) 3 | 11 / 54 (20.37%) 13 |

| | | | |
|---|--|------------------|--|
| Blood and lymphatic system disorders | | | |
| Blood/bone marrow | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 12 / 55 (21.82%) | 8 / 54 (14.81%) | |
| occurrences (all) | 19 | 12 | |
| Hemorrhage/bleeding | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 12 / 54 (22.22%) | |
| occurrences (all) | 1 | 17 | |
| Lymphatics | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 13 / 55 (23.64%) | 14 / 54 (25.93%) | |
| occurrences (all) | 19 | 28 | |
| Eye disorders | | | |
| Ocular/visual | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 13 / 55 (23.64%) | 8 / 54 (14.81%) | |
| occurrences (all) | 26 | 10 | |
| Gastrointestinal disorders | | | |
| GI | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 26 / 55 (47.27%) | 18 / 54 (33.33%) | |
| occurrences (all) | 73 | 32 | |
| Hepatobiliary disorders | | | |
| Hepatobiliary/pancreas | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 0 / 54 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatology/skin | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 14 / 55 (25.45%) | 8 / 54 (14.81%) | |
| occurrences (all) | 20 | 10 | |
| Renal and urinary disorders | | | |
| Renal/genitourinary | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 1 / 54 (1.85%) | |
| occurrences (all) | 7 | 1 | |
| Endocrine disorders | | | |
| Endocrine | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 3 / 54 (5.56%) | |
| occurrences (all) | 2 | 3 | |
| Musculoskeletal and connective tissue disorders | | | |
| Musculoskeletal/soft tissue | Additional description: All combined, see non-SAE chart for details. | | |
| subjects affected / exposed | 19 / 55 (34.55%) | 10 / 54 (18.52%) | |
| occurrences (all) | 33 | 15 | |

| | | | |
|---|-----------------------------------|-----------------------------------|--|
| <p>Infections and infestations</p> <p>Infections</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>21 / 55 (38.18%)</p> <p>39</p> | <p>35 / 54 (64.81%)</p> <p>58</p> | |
| <p>Additional description: All combined, see non-SAE chart for details.</p> | | | |
| <p>Metabolism and nutrition disorders</p> <p>Metabolic/laboratory</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 55 (7.27%)</p> <p>6</p> | <p>9 / 54 (16.67%)</p> <p>12</p> | |
| <p>Additional description: All combined, see non-SAE chart for details.</p> | | | |

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