



Clinical trial results:

Randomized phase II Trial comparing Lenalidomide with lowdose dexamethasone versus Lenalidomide in Second Line Multiple Myeloma (MM)

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2010-021857-38 |
| Trial protocol | SE DK |
| Global end of trial date | 20 November 2015 |

Results information

| | |
|-----------------------------------|-----------------------|
| Result version number | v1 (current) |
| This version publication date | 11 January 2020 |
| First version publication date | 11 January 2020 |
| Summary attachment (see zip file) | summary (summary.pdf) |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | PI-RV-MM-10-07 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Karolinska univ. hospital |
| Sponsor organisation address | 141 86, Stockholm, Sweden, |
| Public contact | Hareth Nahi, Karolinska universe. hospital, +46 737121465, hareth.nahi@sll.se |
| Scientific contact | Hareth Nahi, Karolinska Inst, +46 737121465, hareth.nahi@sll.se |

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 | 10 January 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 November 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 November 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy (TTP) of maintenance treatment with lenalidomide alone compared to a regimen with lenalidomide and low dose dexamethasone

Protection of trial subjects:

Subjects were be fully informed of the risks and requirements of the study and, during the study, subjects were given any new information that may affect their decision to continue participation. They were told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who were fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

Background therapy:

In order to achieve a response of best possible quality as soon as possible the combination of lenalidomide and dexamethasone works synergistically to reduce the tumor burden by several mechanisms adding up to a fast tumoricidal effect.

Evidence for comparator:

The mechanism of action of lenalidomide has a duality of effects: it directly leads to tumour cell death and improves the immune system to keep the tumour in remission (Chanan-Khan 2008). When combined with dexamethasone, lenalidomide therapy provides sustained control of multiple myeloma in relapsed/refractory patients who have received at least one prior therapy (San M 2009). Unlike chemotherapy, lenalidomide stimulates the immune response while also demonstrating tumoricidal activity (ChananKhan 2008, Schütt 2006). Additionally lenalidomide has a well-characterized safety profile, even with longer-term use (San Miguel JF et al. Haematologica. 2009)

| | |
|---|---------------|
| Actual start date of recruitment | 01 March 2011 |
| 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 | Norway: 9 |
| Country: Number of subjects enrolled | Sweden: 47 |
| Country: Number of subjects enrolled | Denmark: 6 |
| Worldwide total number of subjects | 62 |
| EEA total number of subjects | 62 |

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) | 52 |
| From 65 to 84 years | 8 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Patients who are in at least PR and have received lenalidomide as 2nd line treatment for MM will were recruited.

Pre-assignment

Screening details:

A written informed consent must be obtained before any study-specific screening procedures are performed.

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 | Len/dex |

Arm description:

treatment with Lenalidomide and dexamethasone

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

Dosage and administration details:

P.O. 25mg

| | |
|------------------|--------------|
| Arm title | Lenalidomide |
|------------------|--------------|

Arm description:

Treatment with Lenalidomide only

| | |
|---|-----------|
| Arm type | study arm |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | Len/dex | Lenalidomide |
|--------------------------------|---------|--------------|
| Started | 31 | 31 |
| Completed | 31 | 31 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Len/dex |
|-----------------------|---------|

Reporting group description:

treatment with Lenalidomide and dexamethasone

| | |
|-----------------------|--------------|
| Reporting group title | Lenalidomide |
|-----------------------|--------------|

Reporting group description:

Treatment with Lenalidomide only

| Reporting group values | Len/dex | Lenalidomide | Total |
|------------------------|---------|--------------|-------|
| Number of subjects | 31 | 31 | 62 |
| Age categorical | | | |
| Len | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 20 | 22 | 42 |
| From 65-84 years | 9 | 8 | 17 |
| 85 years and over | 2 | 1 | 3 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 17 | 16 | 33 |
| Male | 14 | 15 | 29 |

End points

End points reporting groups

| | |
|---|--------------|
| Reporting group title | Len/dex |
| Reporting group description: treatment with Lenalidomide and dexamethasone | |
| Reporting group title | Lenalidomide |
| Reporting group description: Treatment with Lenalidomide only | |

Primary: TTP

| | |
|--|---------|
| End point title | TTP |
| End point description: After 26 months' median follow-up, median TTP was 24.9 months (12.5-not calculable) versus not reached with Len versus Len+Dex | |
| End point type | Primary |
| End point timeframe: From randomisation until 24m from the last patient randomised | |

| End point values | Len/dex | Lenalidomide | | |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 31 ^[1] | 31 | | |
| Units: months | | | | |
| number (not applicable) | 30 | 25 | | |

Notes:

[1] - The actual value is not reached

Statistical analyses

| | |
|---|------------------------|
| Statistical analysis title | methods |
| Statistical analysis description: Graphs were generated and statistical analyses performed by GraphPad Prism (GraphPad Software Inc. La Jolla, CA, USA) and FlowJo X software (TreeStar Inc. OR, USA). | |
| Comparison groups | Lenalidomide v Len/dex |
| Number of subjects included in analysis | 62 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[2] |
| P-value | = 1 ^[3] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |

Notes:

[2] - comparison between len and len/dex

[3] - <0.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signed informed consent until end of the trial

Adverse event reporting additional description:

. The most common haematologic TEAEs during the observational study were thrombocytopenia (38%), anaemia (30%), and neutropenia (13%). Febrile neutropenia was reported in only 2% of the observational study population. Upper respiratory tract infection was the most common non-haematologic TEAE (15%). Thromboembolic events occurred in seven patients

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|---|
| Dictionary version | 2 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Fatigue |
|-----------------------|---------|

Reporting group description:

standard arm

| Serious adverse events | Fatigue | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Infections and infestations | | | |
| Pneumonia | Additional description: 1(3%) in the Len and 5(16%) in the len/dex | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Fatigue | | |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 31 (19.35%) | | |
| Psychiatric disorders | | | |
| Fatigue | Additional description: Was equal between the arms, 6 (19%) | | |
| subjects affected / exposed | 6 / 31 (19.35%) | | |
| occurrences (all) | 6 | | |

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