



Clinical trial results:

A randomized pre-surgical pharmacodynamics study to assess the biological activity of LEE011 plus letrozole versus single agent letrozole in primary breast cancer (MONALEESA-1)

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2013-002588-24 |
| Trial protocol | NL ES FR |
| Global end of trial date | 10 September 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 12 June 2016 |
| First version publication date | 12 June 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CLEE011A2201 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01919229 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

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 September 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 September 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To estimate the difference in anti-proliferative activity of ribociclib 600 mg once daily and ribociclib 400 mg once daily in combination with letrozole 2.5 mg once daily vs. single agent letrozole 2.5 mg once daily as measured by changes in levels of the proliferative marker Ki67 from Baseline to time of surgery (Day 15).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 10 October 2013 |
| 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 | Spain: 6 |
| Country: Number of subjects enrolled | United States: 8 |
| Worldwide total number of subjects | 14 |
| EEA total number of subjects | 6 |

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) | 7 |
| From 65 to 84 years | 7 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

20 patients were screened, of those 14 patients completed the Screening phase and were randomized. 6 patients discontinued during the Screening phase; 3 patients were considered screen failure and 3 patients discontinued due to patient's decision.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Letrozole |

Arm description:

Letrozole 2.5 mg alone once daily

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

Dosage and administration details:

Letrozole was supplied in 2.5mg tablets for oral use

| | |
|------------------|--------------------------|
| Arm title | LEE011 400mg + letrozole |
|------------------|--------------------------|

Arm description:

Letrozole 2.5 mg once daily and ribociclib 400 mg (2 capsules of 200 mg each) once daily.

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

Dosage and administration details:

Letrozole was supplied in 2.5mg tablets for oral use

| | |
|--|---------------|
| Investigational medicinal product name | Ribociclib |
| Investigational medicinal product code | LEE011 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Ribociclib was supplied in 200 mg hard gelatin capsules for oral use.

| | |
|------------------|--------------------------|
| Arm title | LEE011 600mg + letrozole |
|------------------|--------------------------|

Arm description:

Letrozole 2.5 mg once daily and ribociclib 600 mg (3 capsules of 200 mg each) once daily.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|---------------|
| Investigational medicinal product name | Ribociclib |
| Investigational medicinal product code | LEE011 |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Ribociclib was supplied in 200 mg hard gelatin capsules for oral use.

| | |
|--|-----------|
| Investigational medicinal product name | Letrozole |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Letrozole was supplied in 2.5mg tablets for oral use

| Number of subjects in period 1 | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole |
|---------------------------------------|-----------|-----------------------------|-----------------------------|
| Started | 4 | 6 | 4 |
| Completed | 4 | 6 | 3 |
| Not completed | 0 | 0 | 1 |
| Subject/guardian decision | - | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|--------------------------|
| Reporting group title | Letrozole |
| Reporting group description: Letrozole 2.5 mg alone once daily | |
| Reporting group title | LEE011 400mg + letrozole |
| Reporting group description: Letrozole 2.5 mg once daily and ribociclib 400 mg (2 capsules of 200 mg each) once daily. | |
| Reporting group title | LEE011 600mg + letrozole |
| Reporting group description: Letrozole 2.5 mg once daily and ribociclib 600 mg (3 capsules of 200 mg each) once daily. | |

| Reporting group values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole |
|--|-----------|-----------------------------|-----------------------------|
| Number of subjects | 4 | 6 | 4 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 4 | 3 | 0 |
| From 65-84 years | 0 | 3 | 4 |
| Age Continuous Units: years | | | |
| arithmetic mean | 57 | 64.2 | 70 |
| standard deviation | ± 5.48 | ± 9.91 | ± 4.24 |
| Gender, Male/Female Units: Participants | | | |
| Female | 4 | 6 | 4 |
| Male | 0 | 0 | 0 |

| Reporting group values | Total | | |
|--|-------|--|--|
| Number of subjects | 14 | | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 7 | | |
| From 65-84 years | 7 | | |
| Age Continuous Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender, Male/Female Units: Participants | | | |
| Female | 14 | | |
| Male | 0 | | |

End points

End points reporting groups

| | |
|------------------------------|---|
| Reporting group title | Letrozole |
| Reporting group description: | Letrozole 2.5 mg alone once daily |
| Reporting group title | LEE011 400mg + letrozole |
| Reporting group description: | Letrozole 2.5 mg once daily and ribociclib 400 mg (2 capsules of 200 mg each) once daily. |
| Reporting group title | LEE011 600mg + letrozole |
| Reporting group description: | Letrozole 2.5 mg once daily and ribociclib 600 mg (3 capsules of 200 mg each) once daily. |

Primary: Cell cycle response rate per cell proliferation marker Ki67

| | |
|------------------------|--|
| End point title | Cell cycle response rate per cell proliferation marker Ki67 ^[1] |
| End point description: | Cell cycle response rate is defined by percentage of patients with natural logarithm of Ki-67 levels (expressed as percentage of baseline values) of less than 1 at the time of surgery. Since the trial was prematurely terminated, no statistical analysis was done. |
| End point type | Primary |
| End point timeframe: | Day 1, Day15 |

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: Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|--|------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | 0 ^[4] | |
| Units: Percentage of positive cells for Ki67 | | | | |
| number (not applicable) | | | | |

Notes:

[2] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[3] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[4] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability of the combination

| | |
|------------------------|--|
| End point title | Safety and tolerability of the combination |
| End point description: | Occurrence, frequency and severity of adverse events (AEs), laboratory abnormalities |
| End point type | Secondary |

End point timeframe:
Up to 30 days after the last dose

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-----------------------------|-----------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 6 | 4 | |
| Units: patients | | | | |
| Adverse Events | 0 | 0 | 0 | |
| Serious Adverse Events | 0 | 0 | 0 | |
| Death | 0 | 0 | 0 | |
| Other Adverse Events | 2 | 5 | 4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in electrocardiogram (ECG) parameters

End point title Change from baseline in electrocardiogram (ECG) parameters

End point description:

End point type Secondary

End point timeframe:

Baseline, Day 14

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-------------------------------------|------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[5] | 0 ^[6] | 0 ^[7] | |
| Units: milliseconds | | | | |
| least squares mean (standard error) | () | () | () | |

Notes:

[5] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[6] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[7] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in expression of Retinoblastoma Protein (pRB)

End point title Change from baseline in expression of Retinoblastoma Protein (pRB)

End point description:

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Day 15 | |

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-----------------------------|------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | 0 ^[10] | |
| Units: g/dL | | | | |

Notes:

[8] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[9] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[10] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Secondary: PK (pharmacokinetics) parameters, including but not limited to, Cmax, Tmax, AUClast for LEE011 (and any relevant metabolites) and letrozole.

| | |
|-----------------|--|
| End point title | PK (pharmacokinetics) parameters, including but not limited to, Cmax, Tmax, AUClast for LEE011 (and any relevant metabolites) and letrozole. |
|-----------------|--|

End point description:

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Days 1, 8, 14 and 15 | |

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-----------------------------|-------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[11] | 0 ^[12] | 0 ^[13] | |
| Units: ng/mL | | | | |

Notes:

[11] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[12] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[13] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ECG morphology

| | |
|-----------------|--------------------------|
| End point title | Change in ECG morphology |
|-----------------|--------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 14

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-----------------------------|-------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | 0 ^[16] | |
| Units: milliseconds | | | | |

Notes:

[14] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[15] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[16] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation between PK concentrations and ECG changes

| | |
|-----------------|---|
| End point title | Correlation between PK concentrations and ECG changes |
|-----------------|---|

End point description:

Correlation between the QTc interval change from baseline and plasma concentrations of LEE011 and/or any relevant metabolites

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 14

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-----------------------------|-------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[17] | 0 ^[18] | 0 ^[19] | |
| Units: ratio | | | | |

Notes:

[17] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[18] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[19] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in expression of Cyclin-Dependent Kinase 1 (CDK1)

| | |
|-----------------|--|
| End point title | Change from baseline in expression of Cyclin-Dependent Kinase 1 (CDK1) |
|-----------------|--|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Day 15

| End point values | Letrozole | LEE011 400mg + letrozole | LEE011 600mg + letrozole | |
|-----------------------------|-------------------|-----------------------------|-----------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[20] | 0 ^[21] | 0 ^[22] | |
| Units: percentage | | | | |

Notes:

[20] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[21] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

[22] - Trial was terminated with only a few patients enrolled. Hence no statistical analysis was done

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Letrozole |
|-----------------------|-----------|

Reporting group description:

Letrozole 2.5 mg alone once daily

| | |
|-----------------------|--------------------------|
| Reporting group title | LEE011 600mg + letrozole |
|-----------------------|--------------------------|

Reporting group description:

Letrozole 2.5 mg once daily and ribociclib 600 mg (3 capsules of 200 mg each) once daily.

| | |
|-----------------------|--------------------------|
| Reporting group title | LEE011 400mg + letrozole |
|-----------------------|--------------------------|

Reporting group description:

Letrozole 2.5 mg once daily and ribociclib 400 mg (2 capsules of 200 mg each) once daily.

| Serious adverse events | Letrozole | LEE011 600mg + letrozole | LEE011 400mg + letrozole |
|---|---------------|--------------------------|--------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Letrozole | LEE011 600mg + letrozole | LEE011 400mg + letrozole |
|---|----------------|--------------------------|--------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 4 / 4 (100.00%) | 5 / 6 (83.33%) |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ELECTROCARDIOGRAM QT PROLONGED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SEROMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| HOT FLUSH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 1 | 2 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PYREXIA | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| Ear and labyrinth disorders VERTIGO subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| Immune system disorders HYPERSENSITIVITY subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Gastrointestinal disorders ABDOMINAL PAIN subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| DIARRHOEA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| DYSPEPSIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| NAUSEA subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 3 / 4 (75.00%) 3 | 0 / 6 (0.00%) 0 |
| STOMATITIS subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| VOMITING subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 2 / 4 (50.00%) 3 | 0 / 6 (0.00%) 0 |
| Reproductive system and breast disorders BREAST PAIN subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders DYSпноEA | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Skin and subcutaneous tissue disorders ERYTHEMA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| Infections and infestations HERPES ZOSTER subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| POST PROCEDURAL INFECTION subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Metabolism and nutrition disorders DECREASED APPETITE subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 2 / 4 (50.00%) 2 | 0 / 6 (0.00%) 0 |
| HYPOMAGNESAEMIA subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 06 March 2014 | The purpose of amendment 1 was to clarify some of the study assessments required in the protocol and to take into consideration differences in local practice at the study centers, based on consultation with the study steering committee and feedback received from participating centers' IRBs/IECs and Health Authorities. The amendment also included an update of nonclinical and clinical data for ribociclib alone and in combination with letrozole. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported