



Clinical trial results:

A Phase II Randomised, Double-Blind, Parallel Cohort Study of Neoadjuvant Letrozole + GDC-0032 versus Letrozole + Placebo in Post-Menopausal Women with ER+/HER2-Primary Breast Cancer

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2013-000568-28 |
| Trial protocol | BE DE AT CZ PT HU IT GB ES PL |
| Global end of trial date | 13 March 2017 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 22 March 2018 |
| First version publication date | 22 March 2018 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | GO28888 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02273973 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Acronym: LORELEI |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |

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 March 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 13 March 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of taselisib plus letrozole (taselisib+L) versus placebo plus letrozole (placebo+L) in women with ER + /HER2- early stage breast cancer.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 12 November 2014 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 1 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Australia: 13 |
| Country: Number of subjects enrolled | Austria: 33 |
| Country: Number of subjects enrolled | Belgium: 21 |
| Country: Number of subjects enrolled | Brazil: 9 |
| Country: Number of subjects enrolled | Chile: 3 |
| Country: Number of subjects enrolled | Czech Republic: 8 |
| Country: Number of subjects enrolled | El Salvador: 6 |
| Country: Number of subjects enrolled | France: 9 |
| Country: Number of subjects enrolled | Germany: 23 |
| Country: Number of subjects enrolled | Guatemala: 6 |
| Country: Number of subjects enrolled | Hungary: 29 |
| Country: Number of subjects enrolled | Italy: 21 |
| Country: Number of subjects enrolled | Mexico: 6 |
| Country: Number of subjects enrolled | Panama: 3 |
| Country: Number of subjects enrolled | Peru: 4 |
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Portugal: 10 |
| Country: Number of subjects enrolled | Korea, Republic of: 8 |
| Country: Number of subjects enrolled | Spain: 78 |
| Country: Number of subjects enrolled | Switzerland: 2 |

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | United States: 35 |
| Worldwide total number of subjects | 334 |
| EEA total number of subjects | 239 |

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) | 176 |
| From 65 to 84 years | 158 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study recruited post-menopausal subjects with breast cancer in 22 countries from November 2014 to March 2017.

Pre-assignment

Screening details:

A total of 334 subjects were randomised: 166 subjects to the taselisib+L arm and 168 subjects to the placebo+L arm. One subject was randomised to the placebo+L arm but received taselisib+L in safety population.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Experimental: Taselisib + Letrozole |

Arm description:

Subjects received 2.5 milligrams (mg) letrozole tablets orally once daily (QD) along with taselisib tablets at 4 mg (two 2 mg tablets) orally on a 5 days-on/2 days-off schedule for a total of 16 weeks.

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

Dosage and administration details:

Subjects received 2.5 milligrams (mg) letrozole tablets orally once daily (QD) along with taselisib tablets at 4 mg (two 2 mg tablets) orally on a 5 days-on/2 days-off schedule for a total of 16 weeks.

| | |
|------------------|---|
| Arm title | Placebo Comparator: Placebo + Letrozole |
|------------------|---|

Arm description:

Subjects received 2.5 mg letrozole tablets orally QD along with placebo on a 5-days-on/2-days-off schedule for a total of 16 weeks.

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

Dosage and administration details:

Subjects received 2.5 mg letrozole tablets orally QD along with placebo on a 5-days-on/2-days-off schedule for a total of 16 weeks.

| Number of subjects in period 1 | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole |
|---------------------------------------|--|--|
| Started | 166 | 168 |
| Completed | 157 | 160 |
| Not completed | 9 | 8 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 2 | 3 |
| Physician decision | - | 1 |
| Adverse event, non-fatal | 4 | - |
| Non-compliance | 1 | - |
| Progression of disease | - | 2 |
| Lost to follow-up | - | 1 |
| Reason not specified | - | 1 |
| Protocol deviation | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Experimental: Taselisib + Letrozole |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received 2.5 milligrams (mg) letrozole tablets orally once daily (QD) along with taselisib tablets at 4 mg (two 2 mg tablets) orally on a 5 days-on/2 days-off schedule for a total of 16 weeks.

| | |
|-----------------------|---|
| Reporting group title | Placebo Comparator: Placebo + Letrozole |
|-----------------------|---|

Reporting group description:

Subjects received 2.5 mg letrozole tablets orally QD along with placebo on a 5-days-on/2-days-off schedule for a total of 16 weeks.

| Reporting group values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | Total |
|------------------------|--|--|-------|
| Number of subjects | 166 | 168 | 334 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|-----------------------------------|-------|-------|-----|
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 64.6 | 64.7 | |
| standard deviation | ± 8.5 | ± 8.7 | - |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 166 | 168 | 334 |
| Male | 0 | 0 | 0 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White | 143 | 140 | 283 |
| American Indian or Alaskan Native | 11 | 11 | 22 |
| Asian | 6 | 6 | 12 |
| Black or African American | 1 | 5 | 6 |
| Multiple | 1 | 0 | 1 |
| Other | 3 | 6 | 9 |
| Missing | 1 | 0 | 1 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 36 | 48 | 84 |
| Not Hispanic or Latino | 114 | 109 | 223 |
| Not Reported | 13 | 10 | 23 |
| Unknown | 3 | 1 | 4 |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Experimental: Taselisib + Letrozole |
| Reporting group description: Subjects received 2.5 milligrams (mg) letrozole tablets orally once daily (QD) along with taselisib tablets at 4 mg (two 2 mg tablets) orally on a 5 days-on/2 days-off schedule for a total of 16 weeks. | |
| Reporting group title | Placebo Comparator: Placebo + Letrozole |
| Reporting group description: Subjects received 2.5 mg letrozole tablets orally QD along with placebo on a 5-days-on/2-days-off schedule for a total of 16 weeks. | |
| Subject analysis set title | Taselisib + Letrozole |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received 2.5 milligrams (mg) letrozole tablets orally once daily (QD) along with taselisib tablets at 4 mg (two 2 mg tablets) orally on a 5 days-on/2 days-off schedule for a total of 16 weeks. | |
| Subject analysis set title | Placebo + Letrozole |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received 2.5 mg letrozole tablets orally QD along with placebo on a 5-days-on/2-days-off schedule for a total of 16 weeks. | |

Primary: Percentage of Subjects With Objective Response (OR) by Centrally Assessed Breast Magnetic Resonance Imaging (MRI) via Modified Response Evaluation Criteria in Solid Tumors (mRECIST) Version 1.1

| | |
|---|---|
| End point title | Percentage of Subjects With Objective Response (OR) by Centrally Assessed Breast Magnetic Resonance Imaging (MRI) via Modified Response Evaluation Criteria in Solid Tumors (mRECIST) Version 1.1 |
| End point description: Objective response rate (ORR) was defined as proportion of subjects achieving complete response (CR) or partial response (PR). As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). | |
| End point type | Primary |
| End point timeframe: From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 168 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 50.0 | 39.3 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |
| Number of subjects included in analysis | 334 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.049 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 10.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.11 |
| upper limit | 21.32 |

Primary: Percentage of Subjects with Total Pathologic Complete Response (total pCR), Defined as Having pCR in Both Breast and Axilla, Using American Joint Committee on Cancer (AJCC) Staging System

| | |
|-----------------|---|
| End point title | Percentage of Subjects with Total Pathologic Complete Response (total pCR), Defined as Having pCR in Both Breast and Axilla, Using American Joint Committee on Cancer (AJCC) Staging System |
|-----------------|---|

End point description:

Total pCR was assessed by local pathology review on samples taken at surgery following completion of neoadjuvant therapy. tpCR was defined as the absence of any residual invasive cancer on hematoxylin and eosin evaluation of the resected breast specimen and all sampled ipsilateral lymph nodes (i.e., ypT0/Tis, ypN0 in the AJCC staging system, 7th edition). ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline to 16 weeks

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 168 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 1.8 | 0.6 | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 334 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3698 |
| Method | Fisher exact |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 1.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.12 |
| upper limit | 3.55 |

Primary: Percentage of Subjects With OR by Centrally Assessed Breast MRI via mRECIST Version 1.1 in Phosphatidylinositol-4,5-Bisphosphate 3-Kinase, Catalytic Subunit Alpha (PIK3CA) Mutant (MT) Subjects

| | |
|-----------------|--|
| End point title | Percentage of Subjects With OR by Centrally Assessed Breast MRI via mRECIST Version 1.1 in Phosphatidylinositol-4,5-Bisphosphate 3-Kinase, Catalytic Subunit Alpha (PIK3CA) Mutant (MT) Subjects |
|-----------------|--|

End point description:

ORR was defined as proportion of participants achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline to 16 weeks

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 79 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 56.2 | 38.0 | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0332 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 18.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.57 |
| upper limit | 33.81 |

Primary: Percentage of Subjects With Total pCR , Defined as Having pCR in Both Breast and Axilla, Using AJCC Staging System in PIK3CA MT Subjects

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Total pCR , Defined as Having pCR in Both Breast and Axilla, Using AJCC Staging System in PIK3CA MT Subjects |
|-----------------|--|

End point description:

Total pCR was assessed by local pathology review on samples taken at surgery following completion of neoadjuvant therapy. tpCR was defined as the absence of any residual invasive cancer on hematoxylin and eosin evaluation of the resected breast specimen and all sampled ipsilateral lymph nodes (i.e., ypT0/Tis, ypN0 in the AJCC staging system, 7th edition). ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline to 16 weeks

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 79 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 1.4 | 0 | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4803 |
| Method | Fisher exact |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 1.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 4.04 |

Secondary: Percentage of Subjects With OR by Centrally Assessed Breast MRI via mRECIST Version 1.1 in PIK3CA Wildtype (WT) Subjects

| | |
|-----------------|--|
| End point title | Percentage of Subjects With OR by Centrally Assessed Breast MRI via mRECIST Version 1.1 in PIK3CA Wildtype (WT) Subjects |
|-----------------|--|

End point description:

ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

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

End point timeframe:

From Baseline to 16 weeks

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 89 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 45.7 | 40.4 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5017 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 5.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.2 |
| upper limit | 19.61 |

Secondary: Percentage of Subjects With Total pCR Defined as Having pCR in Both Breast and Axilla, Using AJCC Staging System in PIK3CA WT Subjects

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Total pCR Defined as Having pCR in Both Breast and Axilla, Using AJCC Staging System in PIK3CA WT Subjects |
|-----------------|--|

End point description:

Total pCR was assessed by local pathology review on samples taken at surgery following completion of neoadjuvant therapy. tpCR was defined as the absence of any residual invasive cancer on hematoxylin and eosin evaluation of the resected breast specimen and all sampled ipsilateral lymph nodes (i.e., ypT0/Tis, ypN0 in the AJCC staging system, 7th edition). ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

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

End point timeframe:

From Baseline to 16 weeks

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 89 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 2.2 | 1.1 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 1 |
| Method | Fisher exact |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.65 |
| upper limit | 4.75 |

Secondary: Percentage of Subjects With OR by Breast Ultrasound via mRECIST Version 1.1 in PIK3CA MT Subjects

| | |
|---------------------------|--|
| End point title | Percentage of Subjects With OR by Breast Ultrasound via mRECIST Version 1.1 in PIK3CA MT Subjects |
| End point description: | ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 79 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 61.6 | 40.5 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0115 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 21.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.59 |
| upper limit | 36.68 |

Secondary: Percentage of Subjects With OR by Breast Ultrasound via mRECIST Version 1.1 in PIK3CA WT Subjects

| | |
|---------------------------|---|
| End point title | Percentage of Subjects With OR by Breast Ultrasound via mRECIST Version 1.1 in PIK3CA WT Subjects |
| End point description: | <p>ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).</p> |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 89 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 54.3 | 51.7 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.7928 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 2.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.88 |
| upper limit | 17.2 |

Secondary: Percentage of Subjects With OR by Mammography via mRECIST Version 1.1 in PIK3CA MT Subjects

| | |
|---------------------------|--|
| End point title | Percentage of Subjects With OR by Mammography via mRECIST Version 1.1 in PIK3CA MT Subjects |
| End point description: | ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 79 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 41.1 | 31.6 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2659 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 9.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.8 |
| upper limit | 24.7 |

Secondary: Percentage of Subjects With OR by Mammography via mRECIST Version 1.1 in PIK3CA WT Subjects

| | |
|---------------------------|--|
| End point title | Percentage of Subjects With OR by Mammography via mRECIST Version 1.1 in PIK3CA WT Subjects |
| End point description: | ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 89 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 40.2 | 32.6 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3299 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 7.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.34 |
| upper limit | 21.6 |

Secondary: Percentage of Subjects With OR by Clinical Breast Exam (Palpation) via mRECIST Version 1.1 in PIK3CA MT Subjects

| | |
|---------------------------|---|
| End point title | Percentage of Subjects With OR by Clinical Breast Exam (Palpation) via mRECIST Version 1.1 in PIK3CA MT Subjects |
| End point description: | <p>ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).</p> |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 73 | 79 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 74.0 | 63.3 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.1554 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 10.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.96 |
| upper limit | 25.32 |

Secondary: Percentage of Subjects With OR by Clinical Breast Exam (Palpation) via mRECIST Version 1.1 in PIK3CA WT Subjects

| | |
|---------------------------|---|
| End point title | Percentage of Subjects With OR by Clinical Breast Exam (Palpation) via mRECIST Version 1.1 in PIK3CA WT Subjects |
| End point description: | <p>ORR was defined as proportion of subjects achieving CR or PR. As per modified RECIST v1.1, CR: disappearance of all target lesions, PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).</p> |
| End point type | Secondary |
| End point timeframe: | |
| From Baseline to 16 weeks | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 92 | 89 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 62.0 | 59.6 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|------------------------------|
| Number of subjects included in analysis | 181 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.787 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 2.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.82 |
| upper limit | 16.63 |

Secondary: Central Assessments of Changes in Ki67 levels

| | |
|------------------------|---|
| End point title | Central Assessments of Changes in Ki67 levels |
| End point description: | Ki67 is a prognostic marker and is used to evaluate the proliferative activity of breast cancer. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). |
| End point type | Secondary |
| End point timeframe: | From Baseline to Week 3 and Surgery (Weeks 17-18); and Week 3 to Surgery (Weeks 17-18) |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 168 | | |
| Units: percentage | | | | |
| number (confidence interval 95%) | | | | |
| From Baseline to Week 3 | -83.81 (-86.73 to -80.23) | -80.44 (-83.93 to -76.19) | | |
| From Baseline to Surgery | -75.58 (-80.45 to -69.49) | -80.51 (-84.41 to -75.64) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Statistical analysis description: | Statistical analysis for changes in Ki67 levels from Baseline to Week 3. |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 334 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.117 |
| Method | Regression, Linear |
| Parameter estimate | Ratio of Least square mean |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 1.05 |

| | |
|---|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Statistical analysis description: | |
| Statistical analysis for changes in Ki67 levels from Baseline to Surgery. | |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |
| Number of subjects included in analysis | 334 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.105 |
| Method | Regression, Linear |
| Parameter estimate | Ratio of Least square mean |
| Point estimate | 1.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 1.65 |

| | |
|---|---|
| Secondary: Preoperative Endocrine Prognostic Index (PEPI) Score | |
| End point title | Preoperative Endocrine Prognostic Index (PEPI) Score |
| End point description: | |
| To obtain the PEPI score, risk points for relapse-free survival (RFS) and breast cancer-specific survival (BCSS) are assigned depending on the hazard ratio (HR) from the multivariable analysis. The total PEPI score assigned to each subject is the sum of the risk points derived from the primary tumor (pT) stage, regional lymph nodes (pN) stage, Ki67 level, and estrogen receptor status of the surgical specimen. A HR in the range of 1 to 2 receives one risk point; a HR in the 2 to 2.5 range, two risk points; a HR greater than 2.5, three risk points. The total risk point score for each participant is the sum of all the risk points accumulated from the four factors in the model, ranges from 0 (best possible outcome) to 12 (worst possible outcome). ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). Here, 99999 indicates that the centrally derived PEPI score was not interpretable; therefore, analysis was not performed. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 16 | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 155 | | |
| Units: score on a scale | | | | |
| number (not applicable) | 99999 | 99999 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Surgery in Enhancing Tumor Volume as Measured by Breast MRI

| | |
|--|---|
| End point title | Percent Change from Baseline to Surgery in Enhancing Tumor Volume as Measured by Breast MRI |
| End point description: ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo). | |
| End point type | Secondary |
| End point timeframe: From Baseline to Surgery (Weeks 17-18) | |

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 168 | | |
| Units: percent change | | | | |
| number (confidence interval 95%) | -70.60 (-77.53 to -63.66) | -57.28 (-64.21 to -50.35) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Taselisib + Letrozole vs Placebo + Letrozole |
| Comparison groups | Experimental: Taselisib + Letrozole v Placebo Comparator: Placebo + Letrozole |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 334 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.002 |
| Method | Regression, Linear |
| Parameter estimate | Least squares mean difference |
| Point estimate | -13.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.67 |
| upper limit | -4.96 |

Secondary: Mean Score for Health-Related Quality of Life Measured by the European Organization for Research C30 (EORTC QLQ-C30)

| | |
|-----------------|--|
| End point title | Mean Score for Health-Related Quality of Life Measured by the European Organization for Research C30 (EORTC QLQ-C30) |
|-----------------|--|

End point description:

EORTC QLQ-C30 includes 30 questions used to assess overall quality of life (QOL) in cancer subjects. The first 28 questions used a 4-point scale (1=not at all, 2=a little, 3=quite a bit, 4=very much) for evaluating 5 functional scales (physical, role, social, cognitive, emotional), 8 symptom scales/items (diarrhea, fatigue, dyspnea, appetite loss, insomnia, nausea and vomiting, constipation and pain) and a single item (financial [fin.] difficulties). The last 2 questions, the subject's assessment of overall health and quality of life, used a 7-point scale (1=very poor to 7=excellent). EORTC QLQ-C30 global scores were linearly transformed on scale of 0 to 100, with high score indicating better QOL. Negative change from Baseline values indicated deterioration in QOL or functioning and positive values indicated improvement. Here, Post surgery= PS. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

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

End point timeframe:

Weeks 1, 5, 9, 13, 16, 4-week Post-Surgery

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|--|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 168 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Appetite Loss: Baseline (n=157,165) | 6.2 (± 16.4) | 5.9 (± 14.2) | | |
| Appetite Loss: Change at Week 5 (n=155,160) | 3.0 (± 18.4) | 1.9 (± 18.8) | | |
| Appetite Loss: Change at Week 9 (n=152,158) | 5.3 (± 21.4) | 3.0 (± 17.8) | | |
| Appetite Loss: Change at Week 13 (n=152,157) | 5.5 (± 23.8) | 2.1 (± 16.3) | | |
| Appetite Loss: Change at Week 16 (n=146,151) | 6.8 (± 24.1) | 0.9 (± 16.3) | | |
| Appetite Loss: Change at PS Visit (n=140,146) | 5.0 (± 24.9) | 5.0 (± 23.3) | | |

| | | | | |
|--|---------------|---------------|--|--|
| Cognitive function: Baseline (n=158,163) | 90.8 (± 15.8) | 90.9 (± 16.6) | | |
| Cognitive function: Change at Week 5 (n=154,157) | 0.4 (± 12.8) | -2.5 (± 12.3) | | |
| Cognitive function: Change at Week 9 (n=151,157) | -1.1 (± 14.4) | -4.2 (± 14.7) | | |
| Cognitive function: Change at Week 13 (n=153,156) | -3.4 (± 15.8) | -5.1 (± 15.7) | | |
| Cognitive function: Change at Week 16 (n=147,147) | -4.2 (± 15.2) | -4.1 (± 17.5) | | |
| Cognitive function: Change at PS Visit (n=140,144) | -3.1 (± 18.9) | -5.4 (± 16.8) | | |
| Constipation: Baseline (n=158,164) | 6.8 (± 15.9) | 8.3 (± 18.2) | | |
| Constipation: Change at Week 5 (n=155,159) | 0.0 (± 16.1) | 3.1 (± 22.1) | | |
| Constipation: Change at Week 9 (n=151,158) | 0.2 (± 17.0) | 0.2 (± 18.6) | | |
| Constipation: Change at Week 13 (n=151,156) | -0.4 (± 18.5) | -0.6 (± 19.5) | | |
| Constipation: Change at Week 16 (n=146,148) | -1.1 (± 17.2) | 1.6 (± 20.3) | | |
| Constipation: Change at PS Visit (n=140,145) | 4.8 (± 23.2) | 1.1 (± 16.9) | | |
| Diarrhoea: Baseline (n=157,163) | 5.9 (± 14.9) | 4.3 (± 11.8) | | |
| Diarrhoea: Change at Week 5 (n=154,155) | 6.7 (± 21.7) | -0.2 (± 13.4) | | |
| Diarrhoea: Change at Week 9 (n=150,157) | 6.4 (± 24.3) | 0.8 (± 15.1) | | |
| Diarrhoea: Change at Week 13 (n=152,155) | 7.9 (± 22.3) | -0.4 (± 14.7) | | |
| Diarrhoea: Change at Week 16 (n=146,146) | 8.4 (± 23.1) | 0.2 (± 16.4) | | |
| Diarrhoea: Change at PS Visit (n=140,144) | 0.2 (± 17.7) | -0.9 (± 15.7) | | |
| Dyspnoea: Baseline (n=157,165) | 7.4 (± 15.8) | 8.5 (± 17.5) | | |
| Dyspnoea: Change at Week 5 (n=154,160) | -0.2 (± 14.0) | 0.6 (± 18.1) | | |
| Dyspnoea: Change at Week 9 (n=150,159) | 2.0 (± 17.4) | 1.9 (± 19.9) | | |
| Dyspnoea: Change at Week 13 (n=151,157) | 3.5 (± 21.1) | 1.7 (± 22.3) | | |
| Dyspnoea: Change at Week 16 (n=146,151) | 3.4 (± 20.2) | 2.6 (± 22.6) | | |
| Dyspnoea: Change at PS Visit (n=138,146) | 3.1 (± 24.8) | 2.1 (± 21.5) | | |
| Emotional function: Baseline (n=158,163) | 77.0 (± 20.4) | 78.2 (± 19.9) | | |
| Emotional function: Change at Week 5 (n=154,157) | 4.2 (± 15.2) | 2.4 (± 17.0) | | |
| Emotional function: Change at Week 9 (n=151,157) | 3.8 (± 14.7) | 1.3 (± 20.7) | | |
| Emotional function: Change at Week 13 (n=153,156) | 2.5 (± 15.2) | -1.4 (± 18.6) | | |
| Emotional function: Change at Week 16 (n=147,147) | 1.0 (± 17.0) | -3.5 (± 20.2) | | |
| Emotional function: Change at PS Visit (n=140,144) | -0.8 (± 19.0) | -3.6 (± 20.9) | | |
| Fatigue: Baseline (n=158,165) | 14.8 (± 18.7) | 15.6 (± 18.5) | | |
| Fatigue: Change at Week 5 (n=155,161) | 4.7 (± 13.9) | 4.9 (± 17.9) | | |

| | | | | |
|--|---------------|---------------|--|--|
| Fatigue: Change at Week 9 (n=152,159) | 5.0 (± 15.9) | 7.5 (± 20.3) | | |
| Fatigue: Change at Week 13 (n=151,158) | 7.9 (± 18.1) | 8.8 (± 21.4) | | |
| Fatigue: Change at Week 16 (n=146,151) | 6.8 (± 17.5) | 8.0 (± 20.4) | | |
| Fatigue: Change at PS Visit (n=140,146) | 12.3 (± 19.5) | 12.4 (± 22.6) | | |
| Fin. difficulties: Baseline (n=156,160) | 9.0 (± 20.9) | 10.0 (± 20.4) | | |
| Fin. difficulties: Change at Week 5 (n=152,154) | -2.6 (± 14.6) | -0.4 (± 20.2) | | |
| Fin. difficulties: Change at Week 9 (n=151,153) | -2.6 (± 17.9) | 0.7 (± 20.4) | | |
| Fin. difficulties: Change at Week 13 (n=150,152) | -1.1 (± 17.9) | 0.0 (± 19.9) | | |
| Fin. difficulties: Change at Week 16 (n=145,144) | -1.1 (± 15.9) | 2.1 (± 24.4) | | |
| Fin. difficulties: Change at PS Visit (n=138,141) | 1.9 (± 20.0) | 3.8 (± 23.6) | | |
| Global health status: Baseline (n=158,162) | 75.3 (± 19.7) | 74.6 (± 21.2) | | |
| Global health status: Change at Week 5 (n=153,156) | 1.5 (± 15.2) | -1.1 (± 18.5) | | |
| Global health status: Change at Week 9 (n=150,155) | -1.1 (± 15.9) | -3.2 (± 22.7) | | |
| Global health status: Change at Week 13 (n=152,155) | -2.4 (± 19.5) | -3.7 (± 20.7) | | |
| Global health status: Change at Week 16 (n=147,146) | -2.2 (± 18.4) | -2.9 (± 22.6) | | |
| Global health status: Change at PS Visit (n=139,143) | -5.9 (± 19.7) | -7.0 (± 22.2) | | |
| Insomnia: Baseline (n=158,165) | 23.0 (± 27.1) | 22.4 (± 28.1) | | |
| Insomnia: Change at Week 5 (n=155,161) | -2.4 (± 24.1) | -0.4 (± 27.6) | | |
| Insomnia: Change at Week 9 (n=151,159) | -1.8 (± 24.9) | -0.6 (± 26.9) | | |
| Insomnia: Change at Week 13 (n=153,158) | -1.1 (± 27.7) | 2.1 (± 29.5) | | |
| Insomnia: Change at Week 16 (n=146,149) | -0.7 (± 26.1) | -2.2 (± 27.6) | | |
| Insomnia: Change at PS Visit (n=140,146) | -1.4 (± 26.8) | 3.2 (± 34.4) | | |
| Nausea / vomiting: Baseline (n=158,165) | 1.9 (± 7.5) | 1.6 (± 6.2) | | |
| Nausea / vomiting: Change at Week 5 (n=155,161) | 3.7 (± 11.3) | 1.9 (± 9.9) | | |
| Nausea / vomiting: Change at Week 9 (n=152,159) | 3.4 (± 10.9) | 1.7 (± 10.3) | | |
| Nausea / vomiting: Change at Week 13 (n=153,158) | 3.7 (± 12.9) | 0.7 (± 8.5) | | |
| Nausea / vomiting: Change at Week 16 (n=146,151) | 2.5 (± 14.0) | 0.6 (± 8.0) | | |
| Nausea / vomiting: Change at PS Visit (n=140,146) | 2.1 (± 14.8) | 1.0 (± 8.6) | | |
| Pain: Baseline (n=157,165) | 13.1 (± 20.4) | 12.3 (± 19.6) | | |
| Pain: Change at Week 5 (n=155,161) | -0.6 (± 18.8) | 2.6 (± 17.5) | | |
| Pain: Change at Week 9 (n=152,159) | -1.8 (± 16.5) | 3.8 (± 22.9) | | |
| Pain: Change at Week 13 (n=152,158) | -1.4 (± 18.4) | 4.7 (± 23.4) | | |
| Pain: Change at Week 16 (n=147,151) | -0.9 (± 19.1) | 1.8 (± 22.0) | | |
| Pain: Change at PS Visit (n=140,146) | 11.1 (± 26.0) | 13.8 (± 26.6) | | |

| | | | | |
|---|----------------|----------------|--|--|
| Physical function: Baseline (n=158,165) | 89.6 (± 13.7) | 90.8 (± 13.4) | | |
| Physical function: Change at Week 5 (n=155,161) | 0.5 (± 9.6) | -1.2 (± 11.5) | | |
| Physical function: Change at Week 9 (n=152,157) | 0.2 (± 10.1) | -2.0 (± 13.1) | | |
| Physical function: Change at Week 13 (n=152,158) | -0.3 (± 12.4) | -1.9 (± 14.0) | | |
| Physical function: Change at Week 16 (n=146,150) | -0.5 (± 10.9) | -3.4 (± 15.1) | | |
| Physical function: Change at PS Visit (n=140,146) | -5.2 (± 16.0) | -7.5 (± 15.7) | | |
| Role function: Baseline (n=157,165) | 90.7 (± 20.1) | 93.1 (± 16.5) | | |
| Role function: Change at Week 5 (n=155,160) | 1.3 (± 14.3) | -2.5 (± 17.1) | | |
| Role function: Change at Week 9 (n=150,159) | -0.2 (± 12.8) | -4.9 (± 18.9) | | |
| Role function: Change at Week 13 (n=152,157) | -2.3 (± 17.4) | -5.6 (± 19.8) | | |
| Role function: Change at Week 16 (n=146,151) | -4.6 (± 16.3) | -4.4 (± 18.9) | | |
| Role function: Change at PS Visit (n=140,146) | -15.1 (± 24.7) | -20.1 (± 28.1) | | |
| Social function: Baseline (n=155,161) | 91.2 (± 17.6) | 94.9 (± 14.3) | | |
| Social function: Change at Week 5 (n=151,155) | 3.1 (± 12.8) | -2.0 (± 15.7) | | |
| Social function: Change at Week 9 (n=150,155) | 2.0 (± 13.4) | -4.0 (± 18.1) | | |
| Social function: Change at Week 13 (n=150,154) | 0.0 (± 13.7) | -4.0 (± 19.0) | | |
| Social function: Change at Week 16 (n=146,145) | -0.5 (± 13.7) | -3.1 (± 19.3) | | |
| Social function: Change at PS Visit (n=139,142) | -6.4 (± 20.3) | -10.1 (± 24.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Score for Treatment of Cancer Quality of Life Questionnaire BR23 (QLQ-BR23)

| | |
|-----------------|--|
| End point title | Mean Score for Treatment of Cancer Quality of Life Questionnaire BR23 (QLQ-BR23) |
|-----------------|--|

End point description:

EORTC-QLQ-BR23 is a 23-item breast cancer-specific companion module to the EORTC-QLQ-C30 and consists of four functional scales (body image, sexual enjoyment, sexual functioning, future perspective [FP]) and four symptom scales (systematic therapy side effects [SE], upset by hair loss, arm symptoms, breast symptoms). Questions used 4-point scale (1=not at all, 2=a little, 3=quite a bit, 4=very much). Scores were averaged and transformed to 0-100 scale. High score for functional scale indicated high/better level of functioning/healthy functioning. Negative change from Baseline indicated deterioration in QOL and positive change from Baseline indicated an improvement in QOL. Here, Post surgery= PS. ITT population includes all randomised subjects regardless of whether they received any study drug (taselisib or placebo).

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

End point timeframe:

Weeks 1, 5, 9, 13, 16, 4-week Post-Surgery

| End point values | Experimental: Taselisib + Letrozole | Placebo Comparator: Placebo + Letrozole | | |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 168 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Body image: Baseline (n=155,160) | 91.8 (± 15.7) | 94.0 (± 14.6) | | |
| Body image: Change at Week 5 (n=152,151) | 2.8 (± 8.8) | 0.6 (± 11.4) | | |
| Body image: Change at Week 9 (n=149,150) | 1.2 (± 9.8) | -0.2 (± 10.3) | | |
| Body image: Change at Week 13 (n=150,149) | 1.2 (± 11.6) | -1.6 (± 13.8) | | |
| Body image: Change at Week 16 (n=145,143) | 0.1 (± 10.8) | -1.2 (± 12.8) | | |
| Body image: Change at PS Visit (n=138,140) | -6.5 (± 22.3) | -8.3 (± 19.2) | | |
| Breast symptoms: Baseline (n=154,160) | 5.3 (± 9.8) | 6.9 (± 12.7) | | |
| Breast symptoms: Change at Week 5 (n=148,150) | 2.3 (± 14.6) | 1.0 (± 13.0) | | |
| Breast symptoms: Change at Week 9 (n=148,151) | 4.5 (± 15.1) | 1.8 (± 11.7) | | |
| Breast symptoms: Change at Week 13 (n=149,151) | 5.8 (± 16.0) | 2.3 (± 13.3) | | |
| Breast symptoms: Change at Week 16 (n=146,146) | 7.9 (± 18.6) | 3.9 (± 14.9) | | |
| Breast symptoms: Change at PS Visit (n=136,140) | 6.6 (± 17.9) | 4.3 (± 14.2) | | |
| Future perspective: Baseline (n=157,159) | 57.7 (± 31.0) | 58.7 (± 29.9) | | |
| Future perspective: Change at Week 5 (n=154,151) | 6.5 (± 26.7) | 9.3 (± 28.1) | | |
| Future perspective: Change at Week 9 (n=150,151) | 10.2 (± 25.0) | 9.7 (± 26.6) | | |
| Future perspective: Change at Week 13 (n=151,152) | 7.7 (± 28.4) | 4.4 (± 29.1) | | |
| Future perspective: Change at Week 16 (n=147,145) | 10.2 (± 26.1) | 5.1 (± 29.2) | | |
| Future perspective: Change at PS Visit (n=139,139) | 6.5 (± 29.7) | 3.4 (± 34.8) | | |
| Sexual enjoyment: Baseline (n=48,29) | 41.7 (± 22.3) | 47.1 (± 28.9) | | |
| Sexual enjoyment: Change at Week 5 (n=40,24) | 3.3 (± 18.2) | 11.1 (± 23.4) | | |
| Sexual enjoyment: Change at Week 9 (n=40,22) | 8.3 (± 23.6) | 10.6 (± 23.9) | | |
| Sexual enjoyment: Change at Week 13 (n=33,21) | 6.1 (± 19.5) | 1.6 (± 22.3) | | |
| Sexual enjoyment: Change at Week 16 (n=34,22) | 9.8 (± 19.3) | 7.6 (± 22.8) | | |
| Sexual enjoyment: Change at PS Visit (n=21,15) | 14.3 (± 27.0) | 2.2 (± 23.5) | | |
| Sexual functioning: Baseline (n=149,147) | 81.2 (± 23.4) | 85.1 (± 20.2) | | |

| | | | | |
|--|---------------|---------------|--|--|
| Sexual functioning: Change at Week 5 (n=144,133) | 1.2 (± 13.6) | 1.0 (± 15.0) | | |
| Sexual functioning: Change at Week 9 (n=136,131) | 1.3 (± 14.5) | 0.3 (± 16.5) | | |
| Sexual functioning: Change at Week 13 (n=129,126) | 4.1 (± 16.1) | 1.6 (± 17.7) | | |
| Sexual functioning: Change at Week 16 (n=128,124) | 4.8 (± 15.9) | 1.1 (± 18.1) | | |
| Sexual functioning: Change at PS Visit (n=120,121) | 9.6 (± 19.2) | 4.1 (± 21.8) | | |
| SE: Baseline (n=159,162) | 8.7 (± 10.8) | 9.5 (± 11.5) | | |
| SE: Change at Week 5 (n=156,153) | 4.3 (± 10.0) | 3.9 (± 10.5) | | |
| SE: Change at Week 9 (n=153,154) | 6.7 (± 10.8) | 5.9 (± 12.1) | | |
| SE: Change at Week 13 (n=154,155) | 7.3 (± 11.0) | 6.2 (± 13.1) | | |
| SE: Change at Week 16 (n=149,149) | 7.5 (± 12.9) | 7.1 (± 12.6) | | |
| SE: Change at PS Visit (n=141,142) | 7.0 (± 12.0) | 5.9 (± 12.1) | | |
| Upset by hair loss: Baseline (n=19,18) | 24.6 (± 26.9) | 35.2 (± 31.3) | | |
| Upset by hair loss: Change at Week 5 (n=12,10) | 11.1 (± 32.8) | -3.3 (± 18.9) | | |
| Upset by hair loss: Change at Week 9 (n=11,11) | 9.1 (± 44.9) | -9.1 (± 26.2) | | |
| Upset by hair loss: Change at Week 13 (n=10,11) | 16.7 (± 36.0) | -3.0 (± 34.8) | | |
| Upset by hair loss: Change at Week 16 (n=11,14) | 21.2 (± 34.2) | -7.1 (± 23.3) | | |
| Upset by hair loss: Change at PS Visit (n=13,13) | 30.8 (± 37.2) | -2.6 (± 34.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adverse Events

| End point title | Percentage of Subjects With Adverse Events |
|--|--|
| End point description: | |
| An adverse event (AE) is any untoward medical occurrence in a subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. The safety population includes all randomised subjects who received at least one dose of taselisib or placebo. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to 22 weeks | |

| End point values | Taselisib + Letrozole | Placebo + Letrozole | | |
|-------------------------------|-----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 167 | 167 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | 91.0 | 83.2 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 22 weeks

Adverse event reporting additional description:

The safety population includes all randomised subjects who received at least one dose of taselisib or placebo.

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

Dictionary used

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

| | |
|--------------------|----------|
| Dictionary version | 19, 19.1 |
|--------------------|----------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Placebo Comparator: Placebo + Letrozole |
|-----------------------|---|

Reporting group description:

Subjects received 2.5 mg letrozole tablets orally QD along with placebo on a 5-days-on/2-days-off schedule for a total of 16 weeks.

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Experimental: Taselisib + Letrozole |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received 2.5 milligrams (mg) letrozole tablets orally once daily (QD) along with taselisib tablets at 4 mg (two 2 mg tablets) orally on a 5 days-on/2 days-off schedule for a total of 16 weeks.

| Serious adverse events | Placebo Comparator: Placebo + Letrozole | Experimental: Taselisib + Letrozole | |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 167 (2.40%) | 20 / 167 (11.98%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | | | |
| Cardiac disorders | | | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Hypertensive encephalopathy | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Memory impairment | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 5 / 167 (2.99%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema multiforme | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma infection | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo Comparator: Placebo + Letrozole | Experimental: Taselisib + Letrozole | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 126 / 167 (75.45%) | 130 / 167 (77.84%) | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 167 (2.40%) 4 | 9 / 167 (5.39%) 9 | |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all) | 33 / 167 (19.76%) 33 11 / 167 (6.59%) 13 | 25 / 167 (14.97%) 25 10 / 167 (5.99%) 10 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) | 18 / 167 (10.78%) 19 9 / 167 (5.39%) 9 | 16 / 167 (9.58%) 18 9 / 167 (5.39%) 9 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all) | 40 / 167 (23.95%) 43 16 / 167 (9.58%) 18 | 33 / 167 (19.76%) 34 17 / 167 (10.18%) 20 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomatitis | 20 / 167 (11.98%) 25 19 / 167 (11.38%) 21 | 49 / 167 (29.34%) 68 35 / 167 (20.96%) 40 | |

| | | | |
|--|------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 5 / 167 (2.99%) 6 | 22 / 167 (13.17%) 26 | |
| Dry mouth subjects affected / exposed occurrences (all) | 14 / 167 (8.38%) 14 | 6 / 167 (3.59%) 6 | |
| Constipation subjects affected / exposed occurrences (all) | 7 / 167 (4.19%) 7 | 10 / 167 (5.99%) 10 | |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 167 (3.59%) 6 | 10 / 167 (5.99%) 10 | |
| Dyspepsia subjects affected / exposed occurrences (all) | 1 / 167 (0.60%) 1 | 9 / 167 (5.39%) 9 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 8 / 167 (4.79%) 8 | 9 / 167 (5.39%) 11 | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) | 8 / 167 (4.79%) 8 | 14 / 167 (8.38%) 14 | |
| Rash subjects affected / exposed occurrences (all) | 5 / 167 (2.99%) 6 | 15 / 167 (8.98%) 16 | |
| Pruritus subjects affected / exposed occurrences (all) | 9 / 167 (5.39%) 10 | 6 / 167 (3.59%) 6 | |
| Dry skin subjects affected / exposed occurrences (all) | 3 / 167 (1.80%) 3 | 10 / 167 (5.99%) 10 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 11 / 167 (6.59%) 11 | 6 / 167 (3.59%) 7 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| Arthralgia subjects affected / exposed occurrences (all) | 36 / 167 (21.56%) 39 | 19 / 167 (11.38%) 20 | |
| Back pain subjects affected / exposed occurrences (all) | 10 / 167 (5.99%) 10 | 6 / 167 (3.59%) 6 | |
| Infections and infestations Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 13 / 167 (7.78%) 13 | 6 / 167 (3.59%) 7 | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 9 / 167 (5.39%) 9 | 7 / 167 (4.19%) 7 | |
| Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) | 12 / 167 (7.19%) 12 | 26 / 167 (15.57%) 27 | |
| Decreased appetite subjects affected / exposed occurrences (all) | 6 / 167 (3.59%) 6 | 11 / 167 (6.59%) 12 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 09 April 2014 | <ul style="list-style-type: none">• To improve clarity: Language was added that the investigator had the sole responsibility to break the treatment code in emergency situations• To improve safety of subjects in respect to pneumonitis as a known taselisib toxicity: Additional screening and management of pulmonary function was added• To ensure enrollment of appropriate subjects: Exclusion criteria were added for subjects with immediate surgery indicated and chemotherapy judged to be the optimal neoadjuvant treatment• To improve safety of subjects in respect to letrozole being an estrogen-lowering agent: Additional assessments and adequate monitoring were added• Bisphosphonates were added as permitted concomitant therapy for osteoporosis• Potent CYP3A4 inducers were added as prohibited therapy |
| 22 May 2014 | <ul style="list-style-type: none">• Taselisib 2 mg tablet formulation information and information on relative bioavailability of taselisib capsules and tablets were added• Requirement for taking taselisib on an empty stomach was removed• Adverse event of special interest (AESI) management guidelines were updated |
| 27 July 2015 | <ul style="list-style-type: none">• To increase monitoring of diarrhea: AESI Grade ≥ 3 diarrhea was changed to Grade ≥ 2 diarrhea; Grade ≥ 1 diarrhea that persisted for more than 2 weeks despite antidiarrheals (e.g., loperamide) was added as an AESI; recommendation for management of Gastrointestinal (GI) toxicities that subjects experiencing Grade ≥ 1 diarrhea be contacted at least weekly was added; AE assessments at Weeks 7 and 11 by telephone were added• To enable correlation of response with biomarker analysis: Collection was added of an additional blood sample at 4-week post-surgical follow-up visit for Circulating Tumor Deoxyribonucleic Acid (ctDNA) and plasma protein biomarkers analysis |
| 27 July 2015 | <ul style="list-style-type: none">• To prevent subjects with potential predisposition to gastrointestinal side effects from being enrolled: Additional restriction was added to the following exclusion criterion: "History of prior or currently active small or large intestine inflammation (such as Crohn's disease or ulcerative colitis). Any subject with a baseline medical condition involving the GI tract or who may have a predisposition for GI toxicity requires prior approval from the Medical Monitor"• To improve clarity: Requirement was added for Target Lesion #2, if selected, to be ≥ 10 mm; "Investigational Agents" was added amongst prohibited concomitant therapies; specification that there was a 4-week "wash-out" period for any other investigational agent prior to initiation of taselisib treatment was added |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported