



Clinical trial results:

A Phase 1b/2 Study of GS-5829 in Combination with Fulvestrant or Exemestane in Subjects with Advanced Estrogen Receptor Positive, HER2 Negative Breast Cancer

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-002365-63 |
| Trial protocol | ES BE GB FR |
| Global end of trial date | 19 July 2018 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 31 July 2019 |
| First version publication date | 31 July 2019 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-350-1937 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02983604 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com |
| Scientific contact | Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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 | 19 July 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 19 July 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the Phase 1b Dose Escalation part of this study were to characterize the safety and tolerability of GS-5829 in combination with exemestane or fulvestrant and to determine the maximum tolerated dose (MTD) or the recommended Phase 2 dose of GS-5829 in combination with fulvestrant in women with advanced estrogen receptor positive, HER2-negative (ER+/HER2-) breast cancer.

The primary objective of the Randomized Phase 2 Dose Expansion portion of this study was to evaluate the efficacy of GS-5829 in combination with fulvestrant compared to fulvestrant alone in women with advanced ER+/HER2- breast cancer.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 10 January 2017 |
| 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 | United States: 14 |
| Worldwide total number of subjects | 14 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|----|
| wk | |
| 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) | 14 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States. The first participant was screened on 10 January 2017. The last study visit occurred on 19 July 2018.

Pre-assignment

Screening details:

17 participants were screened.

Period 1

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

Arms

| | |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | GS-5829 4 mg + Exemestane |

Arm description:

GS-5829 4 mg tablets once daily + exemestane 25 mg tablet once daily

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | GS-5829 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

4 mg once daily

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

Dosage and administration details:

25 mg once daily

| | |
|------------------|----------------------------|
| Arm title | GS-5829 4 mg + Fulvestrant |
|------------------|----------------------------|

Arm description:

GS-5829 4 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | GS-5829 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

4 mg once daily

| | |
|--|-------------|
| Investigational medicinal product name | Fulvestrant |
| Investigational medicinal product code | |
| Other name | Faslodex® |

| | |
|--------------------------------------|------------------------|
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| 500 mg every 28 days (\pm 3 days) | |

| | |
|------------------|----------------------------|
| Arm title | GS-5829 6 mg + Fulvestrant |
|------------------|----------------------------|

Arm description:

GS-5829 6 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | GS-5829 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

6 mg once daily

| | |
|--|------------------------|
| Investigational medicinal product name | Fulvestrant |
| Investigational medicinal product code | |
| Other name | Faslodex® |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

500 mg every 28 days (\pm 3 days)

| | |
|------------------|----------------------------|
| Arm title | GS-5829 9 mg + Fulvestrant |
|------------------|----------------------------|

Arm description:

GS-5829 9 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | GS-5829 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

9 mg once daily

| | |
|--|------------------------|
| Investigational medicinal product name | Fulvestrant |
| Investigational medicinal product code | |
| Other name | Faslodex® |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

500 mg every 28 days (\pm 3 days)

| Number of subjects in period 1 ^[1] | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant |
|--|------------------------------|-------------------------------|-------------------------------|
| | | | |
| Started | 4 | 3 | 3 |
| Completed | 4 | 3 | 3 |

| Number of subjects in period 1 ^[1] | GS-5829 9 mg + Fulvestrant |
|--|-------------------------------|
| | |
| Started | 3 |
| Completed | 3 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1 participant who was enrolled but not treated is not included in the subject disposition table.

Baseline characteristics

Reporting groups

| | |
|---|----------------------------|
| Reporting group title | GS-5829 4 mg + Exemestane |
| Reporting group description: GS-5829 4 mg tablets once daily + exemestane 25 mg tablet once daily | |
| Reporting group title | GS-5829 4 mg + Fulvestrant |
| Reporting group description: GS-5829 4 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling) | |
| Reporting group title | GS-5829 6 mg + Fulvestrant |
| Reporting group description: GS-5829 6 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling) | |
| Reporting group title | GS-5829 9 mg + Fulvestrant |
| Reporting group description: GS-5829 9 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling) | |

| Reporting group values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant |
|------------------------------------|---------------------------|----------------------------|----------------------------|
| Number of subjects | 4 | 3 | 3 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------|----------------|----------------|
| Age continuous Units: years arithmetic mean standard deviation | 59.3 ± 4.50 | 61.3 ± 7.51 | 63.0 ± 9.54 |
| Gender categorical Units: Subjects | | | |
| Female | 4 | 3 | 3 |
| Male | 0 | 0 | 0 |
| Ethnicity Units: Subjects | | | |
| Not Hispanic or Latino | 4 | 3 | 3 |
| Race Units: Subjects | | | |
| White | 3 | 3 | 3 |
| Other | 1 | 0 | 0 |

| Reporting group values | GS-5829 9 mg + Fulvestrant | Total | |
|------------------------------------|----------------------------|-------|--|
| Number of subjects | 3 | 13 | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----------------|---|--|
| Age continuous Units: years arithmetic mean standard deviation | 65.0 ± 12.29 | - | |
|---|-----------------|---|--|

| | | | |
|---------------------------------------|---|----|--|
| Gender categorical Units: Subjects | | | |
| Female | 3 | 13 | |
| Male | 0 | 0 | |
| Ethnicity Units: Subjects | | | |
| Not Hispanic or Latino | 3 | 13 | |
| Race Units: Subjects | | | |
| White | 3 | 12 | |
| Other | 0 | 1 | |

End points

End points reporting groups

| | |
|---|----------------------------|
| Reporting group title | GS-5829 4 mg + Exemestane |
| Reporting group description: GS-5829 4 mg tablets once daily + exemestane 25 mg tablet once daily | |
| Reporting group title | GS-5829 4 mg + Fulvestrant |
| Reporting group description: GS-5829 4 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling) | |
| Reporting group title | GS-5829 6 mg + Fulvestrant |
| Reporting group description: GS-5829 6 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling) | |
| Reporting group title | GS-5829 9 mg + Fulvestrant |
| Reporting group description: GS-5829 9 mg tablets once daily + fulvestrant 500 mg administered intramuscularly on Days 1, 15, and 29, and then every 28 days (or in accordance with locally approved labeling) | |

Primary: Phase 1b Dose Escalation: Number of Participants Experiencing Dose Limiting Toxicities (DLTs) Through Day 28 at Each Dose Level of GS-5829

| | |
|---|---|
| End point title | Phase 1b Dose Escalation: Number of Participants Experiencing Dose Limiting Toxicities (DLTs) Through Day 28 at Each Dose Level of GS-5829 ^[1] |
| End point description: A DLT was a toxicity defined as: • Grade ≥ 4 neutropenia, • Grade ≥ 3 neutropenia with fever, • Grade ≥ 3 thrombocytopenia, • Grade ≥ 2 bleeding, • Grade ≥ 3 or higher non-hematologic toxicity, except: 1) Grade 3 nausea or emesis with maximum duration of 48 hrs on adequate medical therapy, 2) Grade 3 diarrhea which persists for < 72 hrs in the absence of adequate medical therapy, • Grade ≥ 2 non-hematologic TEAE that in the opinion of the investigator is of potential clinical significance such that further dose escalation would expose participants to unacceptable risk, • Treatment interruption of ≥ 7 days due to unresolved toxicity, or • Grade 3 or Grade 4 elevation in aspartate transaminase or alanine transaminase associated with a Grade 2 elevation in bilirubin that is at least possibly related to study drug. DLT Analysis Set included participants who completed all treatment & safety procedures through Day 28, inclusive, or experienced a DLT prior to Day 28, exclusive. | |
| End point type | Primary |
| End point timeframe: Baseline up to 28 days | |

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: No statistical comparison was planned or performed.

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|-----------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 3 |
| Units: participants | 1 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Primary: Randomized Phase 2 Dose Expansion: Progression-Free Survival

| | |
|-----------------|---|
| End point title | Randomized Phase 2 Dose Expansion: Progression-Free Survival ^[2] |
|-----------------|---|

End point description:

Progression-Free Survival (PFS) was defined as the interval from date of randomization to the earlier of the first documented confirmed disease progression or death from any cause. As the study was terminated prior to the Phase 2 portion of the study, no participants were enrolled in the Phase 2 portion of the study and data was not collected for this endpoint.

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

End point timeframe:

Baseline up to 2 years

Notes:

[2] - 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: As the study was terminated prior to the Phase 2 portion of the study, no participants were enrolled in the Phase 2 portion of the study and data was not collected for this endpoint.

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|-----------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[3] | 0 ^[4] | 0 ^[5] | 0 ^[6] |
| Units: Not applicable | | | | |

Notes:

[3] - No participants were enrolled in the Phase 2 portion of the study.

[4] - No participants were enrolled in the Phase 2 portion of the study.

[5] - No participants were enrolled in the Phase 2 portion of the study.

[6] - No participants were enrolled in the Phase 2 portion of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: Pharmacokinetic (PK) Parameter: Cmax of GS-5829

| | |
|-----------------|---|
| End point title | Phase 1b Dose Escalation: Pharmacokinetic (PK) Parameter: Cmax of GS-5829 |
|-----------------|---|

End point description:

Cmax is defined as the maximum observed concentration of drug. The PK Analysis Set included all enrolled participants who received at least 1 dose of study drug and have at least 1 nonmissing postdose concentration value reported by the PK laboratory, excluding participants who received concomitant medications prohibited in this study. Only participants with available data were analyzed.

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

End point timeframe:

Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 hours postdose on Days 1 and 15

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|--------------------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 3 | 2 |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (N = 4, 3, 3, 2) | 318.25 (± 107.844) | 247.00 (± 3.464) | 244.00 (± 9.000) | 518.00 (± 60.811) |
| Day 15 (N = 3, 3, 3, 2) | 389.666 (± 105.6424) | 370.333 (± 52.5483) | 375.666 (± 67.0919) | 634.000 (± 46.6690) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b Dose Escalation: PK Parameter: AUCtau of GS-5829

| | |
|--|---|
| End point title | Phase 1b Dose Escalation: PK Parameter: AUCtau of GS-5829 |
| End point description: | |
| AUCtau is defined as concentration of drug over time (the area under the concentration verses time curve over the dosing interval). Participants in the PK Analysis Set with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Predose, 0.5, 1, 2, 3, 4, 6, 8, and 24 hours postdose on Day 15 | |

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|--------------------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 2 |
| Units: h*ng/mL | | | | |
| arithmetic mean (standard deviation) | 4989.809 (± 1655.8737) | 5218.820 (± 1326.2407) | 3937.709 (± 667.4396) | 7638.847 (± 938.3444) |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Phase 2 Dose Expansion: Overall Safety Profile as Assessed by the Percentage of Participants Experiencing Any Adverse Events (AEs), Grade 3 or 4 AEs, Treatment-Related AEs, or Abnormalities in Laboratory Tests or Electrocardiograms

| | |
|-----------------|--|
| End point title | Randomized Phase 2 Dose Expansion: Overall Safety Profile as Assessed by the Percentage of Participants Experiencing Any Adverse Events (AEs), Grade 3 or 4 AEs, Treatment-Related AEs, or Abnormalities in Laboratory Tests or Electrocardiograms |
|-----------------|--|

End point description:

As the study was terminated prior to the Phase 2 portion of the study, no participants were enrolled in the Phase 2 portion of the study and data was not collected for this endpoint.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to 2 years | |

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|-----------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[7] | 0 ^[8] | 0 ^[9] | 0 ^[10] |
| Units: Not applicable | | | | |

Notes:

[7] - No participants were enrolled in the Phase 2 portion of the study.

[8] - No participants were enrolled in the Phase 2 portion of the study.

[9] - No participants were enrolled in the Phase 2 portion of the study.

[10] - No participants were enrolled in the Phase 2 portion of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Phase 2 Dose Expansion: Overall Response Rate

| | |
|-----------------|--|
| End point title | Randomized Phase 2 Dose Expansion: Overall Response Rate |
|-----------------|--|

End point description:

Overall response rate (ORR) was defined as the proportion of participants who achieve complete response (CR) or partial response (PR), based on Response Evaluation Criteria in Solid Tumors (RECIST) v. 1.1 study progression criteria. As the study was terminated prior to the Phase 2 portion of the study, no participants were enrolled in the Phase 2 portion of the study and data was not collected for this endpoint.

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

End point timeframe:

Baseline up to 2 years

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|-----------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[11] | 0 ^[12] | 0 ^[13] | 0 ^[14] |
| Units: Not applicable | | | | |

Notes:

[11] - No participants were enrolled in the Phase 2 portion of the study.

[12] - No participants were enrolled in the Phase 2 portion of the study.

[13] - No participants were enrolled in the Phase 2 portion of the study.

[14] - No participants were enrolled in the Phase 2 portion of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Phase 2 Dose Expansion: Clinical Benefit Rate

| | |
|-----------------|--|
| End point title | Randomized Phase 2 Dose Expansion: Clinical Benefit Rate |
|-----------------|--|

End point description:

Clinical benefit rate (CBR) was defined as the proportion of participants who achieve CR, PR, or stable disease that lasts for > 24 weeks based on RECIST v. 1.1 study progression criteria. As the study was terminated prior to the Phase 2 portion of the study, no participants were enrolled in the Phase 2 portion of the study and data was not collected for this endpoint.

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

End point timeframe:

Baseline up to 2 years

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|-----------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[15] | 0 ^[16] | 0 ^[17] | 0 ^[18] |
| Units: Not applicable | | | | |

Notes:

[15] - No participants were enrolled in the Phase 2 portion of the study.

[16] - No participants were enrolled in the Phase 2 portion of the study.

[17] - No participants were enrolled in the Phase 2 portion of the study.

[18] - No participants were enrolled in the Phase 2 portion of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized Phase 2 Dose Expansion: Overall Survival

| | |
|-----------------|---|
| End point title | Randomized Phase 2 Dose Expansion: Overall Survival |
|-----------------|---|

End point description:

Overall survival was defined as the interval from date of randomization to date of death from any cause. As the study was terminated prior to the Phase 2 portion of the study, no participants were enrolled in the Phase 2 portion of the study and data was not collected for this endpoint.

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

End point timeframe:

Baseline up to 2 years

| End point values | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant | GS-5829 9 mg + Fulvestrant |
|-----------------------------|---------------------------|----------------------------|----------------------------|----------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[19] | 0 ^[20] | 0 ^[21] | 0 ^[22] |
| Units: Not applicable | | | | |

Notes:

[19] - No participants were enrolled in the Phase 2 portion of the study.

[20] - No participants were enrolled in the Phase 2 portion of the study.

[21] - No participants were enrolled in the Phase 2 portion of the study.

[22] - No participants were enrolled in the Phase 2 portion of the study.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose date to last dose date (average: 14.5 weeks; maximum: 53 weeks) plus 30 days

Adverse event reporting additional description:

Safety Analysis Set included all participants who were enrolled and received at least 1 dose of any study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | GS-5829 4 mg + Exemestane |
|-----------------------|---------------------------|

Reporting group description:

GS-5829 4 mg tablets once daily + exemestane 25 mg tablet once daily

| | |
|-----------------------|----------------------------|
| Reporting group title | GS-5829 4 mg + Fulvestrant |
|-----------------------|----------------------------|

Reporting group description:

GS-5829 4 mg tablets once daily + fulvestrant 500 mg administered intramuscularly every 28 days (\pm 3 days)

| | |
|-----------------------|----------------------------|
| Reporting group title | GS-5829 6 mg + Fulvestrant |
|-----------------------|----------------------------|

Reporting group description:

GS-5829 6 mg tablets once daily + fulvestrant 500 mg administered intramuscularly every 28 days (\pm 3 days)

| | |
|-----------------------|----------------------------|
| Reporting group title | GS-5829 9 mg + Fulvestrant |
|-----------------------|----------------------------|

Reporting group description:

GS-5829 9 mg tablets once daily + fulvestrant 500 mg administered intramuscularly every 28 days (\pm 3 days)

| Serious adverse events | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant |
|--|---------------------------|----------------------------|----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 2 / 3 (66.67%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Dysphagia | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|----------------------------|--|--|
| Serious adverse events | GS-5829 9 mg + Fulvestrant | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---------------|--|--|
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | GS-5829 4 mg + Exemestane | GS-5829 4 mg + Fulvestrant | GS-5829 6 mg + Fulvestrant |
|---|---------------------------|----------------------------|----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 3 / 3 (100.00%) | 3 / 3 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 3 (66.67%) | 1 / 3 (33.33%) |
| occurrences (all) | 2 | 2 | 1 |
| Asthenia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Breast haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 3 (66.67%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 3 (66.67%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |

| | | | |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Investigations | | | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Platelet count decreased subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 3 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Nervous system disorders | | | |
| Dysgeusia subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Balance disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 3 |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Anaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Neutropenia | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all) | 4 | 1 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 3 (66.67%) | 2 / 3 (66.67%) |
| occurrences (all) | 1 | 2 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 3 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal tenderness | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Salivary hypersecretion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 |
| Alopecia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Dermatitis acneiform subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 2 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 1 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 1 |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Flank pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Musculoskeletal discomfort subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Infections and infestations | | | |
| Cellulitis subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Fungal skin infection subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 |
| Gastroenteritis viral subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Herpes zoster subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 |
| Oral candidiasis subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Oral infection subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Pharyngitis subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Urinary tract infection | | | |

| | | | |
|------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 2 | 0 | 1 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|----------------------------|--|--|
| Non-serious adverse events | GS-5829 9 mg + Fulvestrant | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Gait disturbance | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Influenza like illness subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Injection site bruising subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Reproductive system and breast disorders Breast haemorrhage subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Investigations | | | |

| | | | |
|--|---------------------|--|--|
| Weight decreased subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Balance disorder subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) | 2 / 3 (66.67%) 3 | | |
| Anaemia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Neutropenia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Gastrointestinal disorders | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| Nausea | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | | |
| occurrences (all) | 3 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | | |
| occurrences (all) | 3 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal tenderness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|----------------|--|--|
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|---------------------|--|--|
| Musculoskeletal discomfort subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Infections and infestations | | | |
| Cellulitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Fungal skin infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Gastroenteritis viral subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Herpes zoster subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Oral candidiasis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Oral infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Pharyngitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |
| Viral infection | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | | |
| Dehydration | | | |
| subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|--|
| 10 August 2016 | <ul style="list-style-type: none">• Updated inclusion/exclusion criteria• Clarified contraception methods• Clarified prior therapies• Updated clinical experience with GS-5829• Updated statistical modeling of probability of DLT occurrence rate based on emerging safety data from Studies GS-US-350-1604 and GS-US-350-1599• Clarified pregnancy testing timing |
| 05 May 2017 | <ul style="list-style-type: none">• Updated study design: 1) Phase 1b Dose Escalation: Group A (GS-5829 + exemestane) no longer enrolled past the 4-mg safety assessment, 2) Phase 2 Dose Expansion: Removal of Group 1 (GS-5829+ exemestane and exemestane alone)• Added stratification to the Phase 2 Dose Expansion. Participants were to be stratified by prior CDK4/6 inhibitor plus AI status (naive vs. progressed). The target number of participants in each of the 2 strata was approximately 60 (40 subjects for GS-5829 + fulvestrant and 20 participants for fulvestrant alone).• Reduced the Phase 1b target number of participants from 60 to 30• Revised the inclusion/exclusion criteria for clarity and due to changing study design• Defined study drug initiation as Cycle 1 Day 1 throughout the inclusion/exclusion criteria |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|--|--------------|
| 19 July 2018 | Enrollment in Group A (GS-5829 + exemestane) was stopped following safety assessments of the 4-mg GS-5829 dose. Enrollment in Group B (GS-5829 + fulvestrant) was stopped following safety assessments of the 9-mg GS-5829 dose. The study was terminated prior to the initiation of the Phase 2 portion of the study. | - |

Notes:

Limitations and caveats

None reported