ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/15/2012

ClinicalTrials.gov ID: NCT00561795

## Study Identification

| | |
|---|---|
| Unique Protocol ID: | VEG110190 |
| Brief Title: | Feasibility Study of Pazopanib in Combination With Chemotherapy in Gynaecological Tumors |
| Official Title: | A Phase I/II, Open-Label, Multicenter, Two-Arm, Feasibility Study of Pazopanib, Carboplatin, and Paclitaxel in Women With Newly Diagnosed, Previously Untreated, Gynaecological Tumors |
| Secondary IDs: | |

## Study Status

| | |
|---|---|
| Record Verification: | March 2011 |
| Overall Status: | Completed |
| Study Start: | September 2007 |
| Primary Completion: | April 2008 [Actual] |
| Study Completion: | April 2008 [Actual] |

## Sponsor/Collaborators

| | |
|---|---|
| Sponsor: | GlaxoSmithKline |
| Responsible Party: | Sponsor |
| Collaborators: | |

## Oversight

| | |
|---|---|
| FDA Regulated?: | |
| IND/IDE Protocol?: | Yes |

| | |
|---|---|
| IND/IDE Information: | Grantor: CDER<br>IND/IDE Number: 65747<br>Serial Number: 0412<br>Has Expanded Access? No |
| Review Board: | Approval Status: Approved<br>Approval Number: 45/2007<br>Board Name: Ethik-Kommission bei der Landesaerztekammer Hessen<br>Board Affiliation: Im Vogelsgesang 3<br>Phone: 0049-69-97672-<br>Email: ethikkommission@laekh.de |
| Data Monitoring?: | No |
| Plan to Share Data?: | |
| Oversight Authorities: | Germany: Federal Institute for Drugs and Medical Devices<br>United States: Food and Drug Administration |

## Study Description

| | |
|---|---|
| Brief Summary: | This is an open-label, two-arm, multicenter feasibility study to evaluate the safety and tolerability of pazopanib in combination with carboplatin and paclitaxel in female subjects with newly diagnosed advanced gynaecological tumors. Subjects will have received no prior therapy for their disease. A minimum of 12 and a maximum of 46 subjects will be enrolled. Dose schemas for each study arm are described in the protocol. For each arm, six subjects will be evaluated in treatment cohorts, which will be expanded to 20 subjects if initial toxicity is acceptable. Overall safety and tolerability of the regimen will be based on dose limiting toxicities, adverse events, and percentage of subjects that complete 6 courses of study treatment. Antitumor activity will be assessed using RECIST criteria and cancer antigen 125 (CA-125) responses. |
| Detailed Description: | |

## Conditions

| | |
|---|---|
| Conditions: | Primary Peritoneal Carcinoma<br>Tumor<br>Epithelial Ovarian Cancer<br>Uterine Disease<br>Cervix Diseases<br>Neoplasms, Ovarian<br>Cancer |
| Keywords: | AGO<br>Advanced,<br>Gynaecologic cancer(s),<br>Genetics<br>GW786034, |

Genetics
Pazopanib,
GW786034,
Gynaecologic cancer(s),
AGO
Pazopanib,
Advanced,

## Study Design

| | |
|---|---|
| Study Type: | Interventional |
| Primary Purpose: | Treatment |
| Study Phase: | Phase 2 |
| Intervention Model: | Parallel Assignment |
| Number of Arms: | 2 |
| Masking: | Open Label |
| Allocation: | Non-Randomized |
| Endpoint Classification: | Safety/Efficacy Study |
| Enrollment: | 12 [Actual] |

## Arms and Interventions

| Arms | Assigned Interventions |
|---|---|
| Experimental: Arm A<br>Oral Pazopanib 800 mg once a day+ carboplatin area under the concentration-time curve (AUC) 5 intravenous (IV) over 1 hour every 3 weeks + paclitaxel 175 mg/m^2 IV over three hours day one q 3 weeks for six cycles | Drug: pazopanib (GW786034)<br>800 mg orally once a day for 6 cycles<br>Other Names:<br>• Pazopanib (GW786034)<br>Drug: pazopanib (GW786034)<br>800 mg orally once a day for 6 cycles<br>Other Names:<br>• Pazopanib (GW786034)<br>Drug: carboplatin<br>IV over one hour every 3 weeks of 6 cycles<br>Drug: carboplatin<br>IV over one hour every 3 weeks of 6 cycles<br>Drug: paclitaxel |

| Arms | Assigned Interventions |
|---|---|
| | IV 175 mg/m^2 given over 3 hours on day one of a 21 day cycle for six cycles<br>Drug: paclitaxel<br>IV 175 mg/m^2 given over 3 hours on day one of a 21 day cycle for six cycles |
| Experimental: Arm B<br>Oral Pazopanib 800 mg once a day+ carboplatin AUC 6 IV over 1 hour every 3 weeks + paclitaxel 175 mg/m^2 IV over three hours day one q 3 weeks for six cycles | Drug: pazopanib (GW786034)<br>800 mg orally once a day for 6 cycles<br>Other Names:<br>• Pazopanib (GW786034)<br>Drug: pazopanib (GW786034)<br>800 mg orally once a day for 6 cycles<br>Other Names:<br>• Pazopanib (GW786034)<br>Drug: carboplatin<br>IV over one hour every 3 weeks of 6 cycles<br>Drug: carboplatin<br>IV over one hour every 3 weeks of 6 cycles<br>Drug: paclitaxel<br>IV 175 mg/m^2 given over 3 hours on day one of a 21 day cycle for six cycles<br>Drug: paclitaxel<br>IV 175 mg/m^2 given over 3 hours on day one of a 21 day cycle for six cycles |

## Outcome Measures

[See Results Section.]

## Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion criteria:

- Inclusion Criteria
- A subject will be considered eligible for inclusion in this study only if all of the following criteria are met:

- Subjects must provide written informed consent prior to performance of study specific procedures or assessments, and must be willing to comply with treatment and follow up.
- Procedures conducted as a part of routine clinical management of the subject (e.g., blood count, imaging study) and obtained prior to signed informed consent may be utilized for Screening or Baseline purposes provided these tests are obtained as specified in the protocol).
- Female subjects ≥18 years of age with newly diagnosed advanced gynaecological malignancies for whom carboplatin and paclitaxel based chemotherapy is indicated. Patients may have surgery to debulk or resect disease but may not have received chemotherapy or radiotherapy.
- Histological confirmation of the following: epithelial ovarian cancer, endometrial carcinoma, uterine sarcoma, mixed Müllerian tumour, fallopian tube carcinoma, primary peritoneal carcinoma, cervical carcinoma or vulvar carcinoma.
- Performance status must be ECOG 0 1.
- Adequate organ system function as defined in Table 6
- Table 6 Definitions for Adequate Organ Function
- System (Laboratory Values)
- Hematologic:
- Absolute neutrophil count (ANC) (≥ 1.5 X 109/L)
- Hemoglobin1 (≥9 g/dL)
- Platelets (≥100 X 109/L)
- International normalized ratio (INR)(≤ 1.2 X upper limit of normal (ULN))
- Partial thromboplastin time (PTT) (≤1.2 X ULN)
- Hepatic:

p Total bilirubin (≤1.5 X upper limit of normal (ULN))

- AST and ALT (≤ 2.5 X ULN)
- Renal:
- Serum Creatinine (≤ 1.5 mg/dL)
- Or, if serum creatinine >1.5 mg/dL, (≥ 50 mL/min)
- Calculated creatinine clearance
- Urine Protein to Creatinine Ratio2 (<1)
- Patients may not have had a transfusion within 7 days of screening assessment.
- If UPC ≥1, then a 24-hour urine protein must be assessed. Patients must have a 24-hour urine protein value <1g to be eligible.
- Measurable or non-measurable disease.
- A female subject is eligible to enter and participate in the study if she is:
- Of non-childbearing potential (i.e., physiologically incapable of becoming pregnant) including any woman who:
- Has had a hysterectomy, or
- Has had a bilateral oophorectomy (ovariectomy), or
- Has had a bilateral tubal ligation, or
- Is post-menopausal
- Subjects not using hormone replacement therapy (HRT) must have experienced total cessation of menses for ≥ 1 year and be greater than 45 years in age, OR, in questionable cases, have a follicle stimulating hormone (FSH) value >40 mIU/mL and an estradiol value < 40pg/mL (<140 pmol/L).
- Subjects who are using hormone replacement therapy and whose menopausal status is in doubt will be required to use a highly effective method of contraception (as outlined in this inclusion criterion) if they wish to continue their HRT during the study. Otherwise, these subjects must discontinue HRT prior to study enrollment to allow confirmation of

post menopausal status. For most forms of HRT, at least 2-4 weeks must elapse between the cessation of HRT and determination of menopausal status; length of this interval depends on the type and dosage of HRT. Following confirmation of post menopausal status, these subjects can resume HRT during the study without use of contraception.
- Childbearing potential, including any female who has had a negative serum pregnancy test within 2 weeks prior to the first dose of study treatment, preferably as close to the first dose as possible, and agrees to use adequate contraception. GSK acceptable contraceptive methods, when used consistently and in accordance with both the product label and the instructions of the physician, are as follow:
- An intrauterine device with a documented failure rate of less than 1% per year.
- Vasectomized partner who is sterile prior to the female subject's entry and is the sole sexual partner for that female.
- Complete abstinence from sexual intercourse for 14 days before exposure to investigational product, through the dosing period, and for at least 21 days after the last dose of investigational product.
- Double-barrier contraception (condom with spermicidal jelly, foam suppository, or film; diaphragm with spermicide; or male condom and diaphragm with spermicide).

Note: Oral contraceptives are not reliable due to potential drug-drug interactions.

- Female subjects who are lactating should discontinue nursing prior to the first dose of study drug and should refrain from nursing throughout the treatment period and for 14 days following the last dose of study drug.
- Recovered from the effects of surgery.
- Prior radiotherapy is permissible, provided at least 4 weeks have elapsed since the last treatment to allow for full bone marrow recovery.

Exclusion Criteria

- A subject will not be eligible for inclusion in this study if any of the following criteria apply:
- Prior use of anticancer therapy (except cytoreductive surgery [debulking]) for their cancer.
- Presence of bulky, residual, squamous cell tumors.
- Is unable to discontinue prohibited medications, as listed in Section 8.2 for 14 days or five half-lives of a drug prior to Visit 1 and for the duration of the study.
- Clinically significant gastrointestinal abnormalities which might interfere with oral dosing, including but not limited to:
- Malabsorption syndrome
- Major resection of the stomach or small bowel that could affect the absorption of study drug
- Active peptic ulcer disease
- Inflammatory bowel disease
- Ulcerative colitis, or other gastrointestinal conditions with increased risk of perforation
- History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within 28 days prior to beginning study treatment.
- Any unstable or serious concurrent condition (e.g., active infection requiring systemic therapy).
- Inadequately controlled hypertension (systolic blood pressure [SBP] of ≥140 mmHg, or diastolic blood pressure [DBP] of ≥ 90 mmHg). Initiation or adjustment of blood pressure medication is permitted prior to study entry provided the subject has 2 consecutive blood pressure readings less than 140/90 mmHg, each separated by a minimum of 24 hours. These readings need to be collected prior to the first dose.
- Hemoptysis within four weeks prior to first dose of study drug.
- Prior major trauma within 14 days prior to first dose of study drug.
- Prior major surgery within 14 days prior to first dose of study drug and/or presence of any non-healing wound, fracture, or ulcer. In the case of surgery involving the bowel, subjects must be 28 days post-surgery to be eligible.

- Prolongation of corrected QT interval (QTc) > 480 msecs.
- History of any one of more of the following cardiovascular conditions within the past 6 months:
- Cardiac angioplasty or stenting
- Myocardial infarction
- Unstable angina
- Symptomatic peripheral vascular disease
- Class III or IV congestive heart failure as defined by the New York Heart Association (NYHA) [See History of cerebrovascular accident (CVA), pulmonary embolism or untreated deep venous thrombosis (DVT) within the past 6 months.
- Note: Subjects with recent DVT who have been treated with therapeutic anti-coagulant agents (excluding therapeutic warfarin) for at least 6 weeks are eligible.
- Metastatic disease to the brain or leptomeninges.

## Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director
GlaxoSmithKline

Locations: France
GSK Investigational Site
Strasbourg, France, 67085

Germany
GSK Investigational Site
Wiesbaden, Hessen, Germany, 65199

GSK Investigational Site
Marburg, Hessen, Germany, 35043

France
GSK Investigational Site
Lyon Cedex 08, France, 69373

Germany
GSK Investigational Site
Essen, Nordrhein-westfalen, Germany, 45122

## References

Citations:

Links:

Study Data/Documents:

# Study Results

## Participant Flow

| | |
|---|---|
| Recruitment Details | Enrollment was to occur in Arm B (Arm A6-1 or A6-2) if <2 subjects experienced dose-limiting toxicities (DLTs) while on Arm A5-1 or A5-2. After review of data (pre-specified in protocol) ≥2 subjects in Arms A5-1 and A5-2 experienced DLTs; the study was closed and no subjects were enrolled into Arm B. Three ongoing subjects were taken off regimen. |

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |
| A6-1 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A6-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Overall Study

| | A5-1 | A5-2 | A6-1 | A6-2 |
|---|---|---|---|---|
| Started | 6 | 6 | 0 | 0 |
| Completed | 2 | 0 | 0 | 0 |
| Not Completed | 4 | 6 | 0 | 0 |
| Adverse Event | 3 | 3 | 0 | 0 |
| Study Closed/Terminated | 0 | 3 | 0 | 0 |
| Physician Decision | 1 | 0 | 0 | 0 |

## Baseline Characteristics

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Baseline Measures

| | A5-1 | A5-2 | Total |
|---|---|---|---|
| Number of Participants | 6 | 6 | 12 |
| Age, Continuous<br>[units: years]<br>Mean (Standard Deviation) | 55.0 (9.84) | 52.3 (9.85) | 53.7 (9.49) |
| Gender, Male/Female<br>[units: participants] | | | |
| Female | 6 | 6 | 12 |
| Male | 0 | 0 | 0 |
| Race/Ethnicity, Customized<br>White - White/Caucasian/European Heritage [units: participants] | 6 | 6 | 12 |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Number of Participants Experiencing Serious Adverse Events and Non-serious Adverse Events |
| Measure Description | Safety and tolerability were measured by the number of participants with serious adverse events and non-serious adverse events. See the "Adverse Event" section of the results record for additional details and data. |
| Time Frame | Baseline to End of Study (up to a year) |
| Safety Issue? | No |

Analysis Population Description

[Not Specified]

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |
| A6-1 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A6-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Measured Values

| | A5-1 | A5-2 | A6-1 | A6-2 |
|---|---|---|---|---|
| Number of Participants Analyzed | 0 | 0 | 0 | 0 |

No data displayed because Outcome Measure has zero total participants analyzed.

2. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Overall Response |
| Measure Description | Although the study protocol specified several efficacy analyses, due to poor tolerability of the combination regimen and the consequent early withdrawal of most participants, which led to a small sample size, efficacy analyses were not performed. Overall response is defined as the number of participants with CR or PR per Response Evaluation Criteria In Solid Tumors (RECIST): CR, all detectable tumor has disappeared; PR, a >=30% decrease in the sum of the longest dimensions of the target lesions taking as a reference the baseline sum. |
| Time Frame | Baseline until either response or progression (up to 2 years) |
| Safety Issue? | No |

Analysis Population Description

[Not Specified]

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |

| | Description |
|---|---|
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |
| A6-1 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A6-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Measured Values

| | A5-1 | A5-2 | A6-1 | A6-2 |
|---|---|---|---|---|
| Number of Participants Analyzed | 0 | 0 | 0 | 0 |

No data displayed because Outcome Measure has zero total participants analyzed.

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Cancer Antigen (CA-125) Response |
| Measure Description | Defined as the number of participants who achieved a confirmed CA-125 response, which is defined as at least a 50% reduction in CA-125 levels from a pre-treatment sample. |
| Time Frame | Baseline until response (up to 2 years) |
| Safety Issue? | No |

Analysis Population Description

[Not Specified]

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |
| A6-1 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A6-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Measured Values

| | A5-1 | A5-2 | A6-1 | A6-2 |
|---|---|---|---|---|
| Number of Participants Analyzed | 0 | 0 | 0 | 0 |

No data displayed because Outcome Measure has zero total participants analyzed.

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | 18-week Progression Free Survival |
| Measure Description | Defined as the number participants who have not had radiological disease progression per RECIST, confirmed CA-125 progression, or death due to any cause by the end of 18 weeks. |
| Time Frame | Baseline to Week 18 |
| Safety Issue? | No |

Analysis Population Description

[Not Specified]

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |
| A6-1 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A6-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC6 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Measured Values

| | A5-1 | A5-2 | A6-1 | A6-2 |
|---|---|---|---|---|
| Number of Participants Analyzed | 0 | 0 | 0 | 0 |

No data displayed because Outcome Measure has zero total participants analyzed.

## Reported Adverse Events

| | |
|---|---|
| Time Frame | Enrollment to End of Study (up to a year) |
| Additional Description | [Not specified] |

Reporting Groups

| | Description |
|---|---|
| A5-1 | Paclitaxel 175 milligrams (mg)/square meter (m^2) plus carboplatin area under the concentration-time curve (AUC) 5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 800 mg/day orally starting on Day 1 for the duration of the study |
| A5-2 | Paclitaxel 175 mg/m^2 plus carboplatin AUC5 intravenously (IV) on Day 1 of a 21-day cycle for 6 cycles plus pazopanib 400 mg/day orally starting on Day 1 for the duration of the study |

Serious Adverse Events

| | A5-1 | A5-2 |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 6/6 (100%) | 2/6 (33.33%) |
| Blood and lymphatic system disorders | | |
| Febrile Neutropenia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Neutropenia [A] † | 5/6 (83.33%) | 2/6 (33.33%) |
| Thrombocytopenia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Gastrointestinal disorders | | |
| Abdominal Pain [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Ascites [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Ileal Perforation [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Intestinal Perforation [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Nausea [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Vomiting [A] † | 1/6 (16.67%) | 0/6 (0%) |
| General disorders | | |

| | A5-1 | A5-2 |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Fatigue [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Investigations | | |
| Haemoglobin Increase [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Skin and subcutaneous tissue disorders | | |
| Skin Necrosis [A] † | 0/6 (0%) | 1/6 (16.67%) |

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

| | A5-1 | A5-2 |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 5/6 (83.33%) | 4/6 (66.67%) |
| Blood and lymphatic system disorders | | |
| Anaemia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Leukopenia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Neutropenia [A] † | 4/6 (66.67%) | 2/6 (33.33%) |
| Thrombocytopenia [A] † | 3/6 (50%) | 1/6 (16.67%) |
| Ear and labyrinth disorders | | |
| Tinnitus [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Endocrine disorders | | |
| Hyperthyroidism [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Gastrointestinal disorders | | |
| Abdominal Pain [A] † | 2/6 (33.33%) | 2/6 (33.33%) |
| Abdominal Pain Upper [A] † | 1/6 (16.67%) | 0/6 (0%) |

| | A5-1 | A5-2 |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Constipation [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Diarrhoea [A] † | 2/6 (33.33%) | 2/6 (33.33%) |
| Gastric Disorder [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Intestinal Perforation [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Nausea [A] † | 3/6 (50%) | 3/6 (50%) |
| Paraesthesia Oral [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Stomatitis [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Tooth Disorder [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Vomiting [A] † | 2/6 (33.33%) | 1/6 (16.67%) |
| General disorders | | |
| Fatigue [A] † | 4/6 (66.67%) | 3/6 (50%) |
| Mucosal Inflammation [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Oedema Peripheral [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Pain [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Immune system disorders | | |
| Drug hypersensitivity [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Infections and infestations | | |
| Catheter Related Infection [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Cystitis [A] † | 0/6 (0%) | 2/6 (33.33%) |
| Nasopharyngitis [A] † | 3/6 (50%) | 0/6 (0%) |
| Urinary Tract Infection [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Investigations | | |
| C-Reactive Protein increased [A] † | 1/6 (16.67%) | 0/6 (0%) |

| | A5-1 | A5-2 |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Haemoglobin Decreased [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Weight Decreased [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Metabolism and nutrition disorders | | |
| Anorexia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Hyperglycaemia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Hypokalaemia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Musculoskeletal and connective tissue disorders | | |
| Arthralgia [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Back Pain [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Muscular Weakness [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Myalgia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Nervous system disorders | | |
| Dizziness [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Dysgeusia [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Headache [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Paraesthesia [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Peripheral Sensory Neuropathy [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Psychiatric disorders | | |
| Depression [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Nervousness [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Restlessness [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Sleep Disorder [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Respiratory, thoracic and mediastinal disorders | | |

| | A5-1 | A5-2 |
|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) |
| Cough [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Dyspnoea [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Epistaxis [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Nasal Dryness [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Oropharyngeal Pain [A] † | 2/6 (33.33%) | 0/6 (0%) |
| Skin and subcutaneous tissue disorders | | |
| Acne [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Alopecia [A] † | 4/6 (66.67%) | 3/6 (50%) |
| Erythema [A] † | 0/6 (0%) | 2/6 (33.33%) |
| Palmar-Plantar erythrodysaesthesia syndrome [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Pruritus [A] † | 1/6 (16.67%) | 0/6 (0%) |
| Rash [A] † | 1/6 (16.67%) | 1/6 (16.67%) |
| Skin Fissures [A] † | 0/6 (0%) | 1/6 (16.67%) |
| Vascular disorders | | |
| Hypertension [A] † | 1/6 (16.67%) | 0/6 (0%) |

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

## Limitations and Caveats

As defined in the protocol, a review of the safety data in Arm A showed that >=2 participants in each regimen of Arm A experienced dose-limiting toxicities. Thus the study was closed to further enrollment and no participants were enrolled into Arm B.

## More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

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