Title: Reporting and Analysis Plan of Final Analysis for AGO-OVAR16/VEG110655/PZP034C2301 - A Phase III Study to Evaluate the Efficacy and Safety of Pazopanib Monotherapy Versus Placebo in Women Who Have not Progressed after First Line Chemotherapy for Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

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Description: This document details the reporting and analysis plan for the final analysis for AGO-OVAR16/VEG110655, a randomized, double-blinded, placebo-controlled multi-center Phase III study to evaluate efficacy and safety of pazopanib compared to placebo in women who have not progressed after first line chemotherapy for epithelial ovarian, fallopian tube or primary peritoneal cancer.

Subject: Overall survival, Safety

Author’s Name, Title and Functional Area: Novartis Oncology
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## List of abbreviations

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<th>Definition</th>
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<tr>
<td>AE</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CTCAE</td>
<td>Common Terminology Criteria for Adverse Events</td>
</tr>
<tr>
<td>CR</td>
<td>Complete response</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>ECOG</td>
<td>Eastern Cooperative Oncology Group</td>
</tr>
<tr>
<td>eCRF</td>
<td>Electronic Case Report Form</td>
</tr>
<tr>
<td>EORTC QLQ-C30</td>
<td>EORTC quality of life questionnaire core 30</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>EuroQoL-5D</td>
</tr>
<tr>
<td>GSK</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>hr(s)</td>
<td>Hour(s)</td>
</tr>
<tr>
<td>HR</td>
<td>Hazard ratio</td>
</tr>
<tr>
<td>IDMC</td>
<td>Independent data monitoring committee</td>
</tr>
<tr>
<td>IDSL</td>
<td>Integrated data standards library</td>
</tr>
<tr>
<td>ITT</td>
<td>Intend-to-treat</td>
</tr>
<tr>
<td>MedDRA</td>
<td>Medical dictionary for regulatory activities</td>
</tr>
<tr>
<td>Min</td>
<td>Minute(s)</td>
</tr>
<tr>
<td>Mg</td>
<td>Milligram(s)</td>
</tr>
<tr>
<td>mL</td>
<td>Milliliter(s)</td>
</tr>
<tr>
<td>mmHg</td>
<td>Millimeters of mercury (BP)</td>
</tr>
<tr>
<td>mRCC</td>
<td>Metastatic renal cell carcinoma</td>
</tr>
<tr>
<td>Msec</td>
<td>Millisecond(s)</td>
</tr>
<tr>
<td>OS</td>
<td>Overall survival</td>
</tr>
<tr>
<td>PD</td>
<td>Progressive disease</td>
</tr>
<tr>
<td>PFS</td>
<td>Progression-free survival</td>
</tr>
<tr>
<td>PGx</td>
<td>Pharmacogenetics</td>
</tr>
<tr>
<td>PK</td>
<td>Pharmacokinetic</td>
</tr>
<tr>
<td>PR</td>
<td>Partial response</td>
</tr>
<tr>
<td>PT</td>
<td>preferred term</td>
</tr>
<tr>
<td>QTc</td>
<td>Heart rate-corrected Q-T interval</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of life</td>
</tr>
<tr>
<td>QTcB</td>
<td>Bazett’s corrected QT intervals</td>
</tr>
<tr>
<td>RAP</td>
<td>Report and analysis plan</td>
</tr>
<tr>
<td>RAMOS</td>
<td>Registration and Medication Ordering System</td>
</tr>
<tr>
<td>RECIST</td>
<td>Response Evaluation Criteria In Solid Tumors</td>
</tr>
<tr>
<td>RS</td>
<td>Raw score</td>
</tr>
<tr>
<td>SAE</td>
<td>Serious adverse event</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic blood pressure</td>
</tr>
<tr>
<td>SD</td>
<td>Stable disease</td>
</tr>
<tr>
<td>SI</td>
<td>System independent</td>
</tr>
<tr>
<td>SOC</td>
<td>System Organ Classes</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid-stimulating hormone</td>
</tr>
<tr>
<td>µg</td>
<td>Microgram(s)</td>
</tr>
<tr>
<td>ULN</td>
<td>Upper limit of normal</td>
</tr>
<tr>
<td>WBC</td>
<td>White blood cell(s)</td>
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# Trademark Information

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<th>Trademarks not owned by the GlaxoSmithKline group of companies</th>
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<td>VOTRIENT</td>
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1. **Introduction**

This reporting and analysis plan (RAP) details all planned final analyses for study AGO-OVAR16/VEG110655/PZP034C2301. This is a phase III study to evaluate the efficacy and safety of pazopanib (trademark: Votrient) compared to placebo using a randomized, double-blinded, placebo-controlled, and multi-center design in women with non-bulky, FIGO Stage II-IV epithelial ovarian, fallopian tube, or primary peritoneal cancer that has not progressed after first line chemotherapy.

For further information on the study design, see Protocol Amendment 9, dated May 09, 2016 (GlaxoSmithKline Document Number UM2008/00144/0).

2. **Study Objective(s) and Endpoint(s)**

2.1. **Study Objective(s)**

**Primary**

- To determine whether pazopanib (up to 24 months of pazopanib 800 mg daily) prolongs progression free survival (PFS by RECIST 1.0) compared to placebo in women with non-bulky, FIGO Stage II-IV epithelial ovarian, fallopian tube, or primary peritoneal cancer that has not progressed after first line chemotherapy.

**Secondary**

The principal secondary objective is:

- To compare overall survival (OS) of patients treated with up to 24 months of pazopanib 800 mg daily to those treated with placebo.
Other secondary objectives are:
To compare the effect of 24 months of pazopanib 800 mg daily versus placebo on
- Safety
- PFS by GCIG criteria
- 3-year PFS (by RECIST) rate
- Quality of life (measured using EORTC QLQ-C30 with the OV-28 module, and EuroQOL EQ-5D)

2.2. Study Endpoint(s)

Primary
- PFS is defined as the interval between the date of randomization and the earliest date of either radiological progression or death due to any cause. The primary analysis will be based on the radiological progression per RECIST as determined by the investigator.

Secondary
The principal secondary endpoint:
- OS is defined as the time from date of randomization until date of death due to any cause.

Other secondary endpoints:
- PFS by GCIG Criteria is defined as the time from randomization to the earliest date of either progression by GCIG criteria or death due to any cause.
- 3-year PFS is defined as the percentage of subjects who are alive and progression-free (progression defined as radiological progression per RECIST or death due to any cause) at 3 years from randomization.
- Safety will include evaluation of AEs and changes from baseline in vital signs, ECGs, and laboratory parameters
- Quality of life is measured using the EORTC QLQ-C30 with the OV-28 module, and EuroQOL EQ-5D.

2.3. Statistical Hypotheses

The primary objective of this study is to compare progression free survival (PFS) of pazopanib versus placebo each given for up to 24 months in women with non-bulky Stage II-IV epithelial ovarian (EOC), fallopian tube, or primary peritoneal cancer that has not progressed after first line chemotherapy. For the primary hypothesis, PFS is defined as the interval between the date of randomization and the earliest date of disease progression (as defined by the investigator based on RECIST criteria) or death due to any cause.

The study is designed to provide evidence with regard to PFS to support the null hypothesis $H_0: \lambda = 1$ or to reject it in favor of the alternative hypothesis $HA: \lambda \neq 1$, where $\lambda$ is the hazard ratio: pazopanib / placebo. While the primary endpoint of the study is PFS, the study will have 80% power to detect a 27% increase in median survival in subjects.
who receive pazopanib compared to subjects who receive placebo (49 months vs. 38.5 months).

The study will have more than 90% power to detect a 47% increase in median PFS in subjects who receive up to 24 months of pazopanib compared to subjects who receive placebo (19.8 months vs. 13.5 months) at the time of final PFS analysis.

Confidence intervals will be two-sided and will use 95% confidence levels unless otherwise specified. Two-sided hypotheses will be tested at the 5% significance level unless otherwise specified.

2.4. Pharmacokinetic (PK) and PK/Pharmacodynamic (PD) hypotheses

Not applicable

3. Study Design

For information on the study design, see Protocol (UM2008/00144/0).

4. Planned Analyses

The 3rd interim analysis for futility based on OS has occurred at 80% information fraction (at least 441 OS events). An overall conditional power of 20% served as the boundary for futility. Based on the estimated hazard ratio at the third interim analysis, the futility criteria was met, and the study will be closed (conditional power was <1%).

The main purpose of the final analyses is to report the updated OS results after all patients have completed the end of study visit.

5. Sample Size Considerations

For information on sample size considerations, see Protocol (UM2008/00144/0).

6. Analysis populations

The Intent-to-Treat (ITT) population will comprise all randomized subjects who are not screen failure, i.e. subjects who were screen failure but randomized by mistake and were not treated will not be included. The treatment group assignment will be based on the randomized treatment instead of the actual treatment received. The ITT population will be used for the analysis of efficacy data and summaries of study population.

The All Treated population will comprise all randomized subjects who receive at least one dose of investigational product, and will be based on the actual treatment received if this differs from that to which the subject was randomized. The All Treated population will be used for the analysis of safety data.

It is possible that during the course of the study a subject will only temporarily receive the incorrect treatment, which means the subject will receive incorrect treatment for some time, but not the whole treatment period. Pazopanib subjects who temporarily receive placebo will be treated similarly to subjects with drug interruptions. Placebo subjects who temporarily receive pazopanib will be included in the safety summaries for pazopanib arm.
7. Treatment comparisons

The single treatment comparison will be between pazopanib and placebo. Unless otherwise stated, all efficacy comparisons will be performed using the ITT population and all safety comparisons will be performed using the All Treated population (as defined in Section 6).

7.1. Data Display Treatment and Other Sub-group Descriptors

The following treatment descriptors will be used on all applicable tabulations:

- Pazopanib
- Placebo

8. general considerations for data analyses

8.1. Multicentre Studies

Data from all participating centers will be pooled prior to analysis. Since patient accrual is spread thinly across multiple centers, summaries of data by center would be unlikely to be informative and will not, therefore, be provided.

8.2. Other Strata and Covariates

Prior to randomization, eligible patients are stratified according to the following two stratification factors:

1. First-line treatment outcome:
   a) no evidence of disease [NED] after surgery (or, if unknown, FIGO stage II-IIIA at diagnosis) and NED after chemotherapy and normal Screening CA-125; versus,
   b) residual tumor after surgery (or, if unknown residual tumor after initial surgery, FIGO stage IIIB-IV at diagnosis) and NED after chemotherapy and normal Screening CA-125; versus,
   c) residual tumor after chemotherapy or elevated Screening CA 125 regardless of tumor status after surgery and FIGO stage at diagnosis

2. Geographic coverage of participating cooperative group: Europe vs Asia vs North America/Australia.

This represents a total of nine (9) sub-strata. Patients in each sub-stratum are then centrally randomized in a 1:1 ratio to receive either 800 mg pazopanib daily dosing or the matching placebo.

The OS analyses will include stratified log rank tests using the above listed stratification factors for a total of nine substrata. In such an analysis, these stratification factors will be adjusted for by including them as covariates in the model. If a sub-stratum is too small, it may be pooled with others. Significance tests will be conducted for the overall pooled analysis population.

The analyses will be performed based on the data collected in the CRF, not the actual assigned stratum at the time of randomization.
8.3. Multiple Comparisons and Multiplicity

No further statistical testing will be performed as this study is closed out due to futility.

9. Data handling conventions

9.1. Premature Withdrawal and Missing Data

Subjects are considered to have completed the study if death occurs. Subjects who withdraw from the study will be included in analyses up to the time of withdrawal, regardless of the duration of treatment.

As the length of treatment for any patient will depend on the efficacy and toxicity of the treatment, the duration of follow-up will vary among patients. Consequently, there will be no imputation for missing data. Where appropriate, available data will be summarized over specified intervals (e.g. from randomization until withdrawal from the study) using suitable summary statistics.

10. Disposition of Subjects

A summary of the number and percentage of subjects who completed the study as well as subjects who withdrew prematurely from the study will be displayed based on the ITT population. Reasons for premature withdrawal will be presented in the order they are displayed in the CRF, which include study closed/terminated, lost to follow-up, investigator discretion, and withdrew consent.

11. Efficacy Analyses

Unless otherwise specified, all the efficacy analyses will be based on the ITT population as defined in Section 6.

11.1. Overall Survival (OS)

OS is defined as the interval between the date of randomization and date of death due to any cause. The length of this interval (in days) is estimated as the date of death minus date of randomization plus 1 day. Subjects who have not died will be censored at the date of last contact (as recorded in the eCRF). Last date of contact will be defined as the maximum date of any visit date, survival follow-up date, or date of study withdrawal. Only patient contacts recorded in the eCRF can be used for the calculation of last date of contact.

OS will be summarized using Kaplan-Meier survival curves, and compared between treatment arms using a stratified log rank test based on the stratification factors defined in Section 8.2. For each Kaplan-Meier analysis the following estimates will also be provided:

The Pike estimator [Berry, 1991] of the treatment hazard ratio based on the corresponding stratified log-rank test statistic will be provided together with a naïve 95% confidence interval. For each treatment group, the Kaplan-Meier estimates for the median OS time, the first and third quartiles will be presented, along with approximate naïve 95% confidence intervals. Brookmeyer-Crowley method [Brookmeyer, 1982] will be used to calculate the confidence intervals.
11.1.1.1. **Subgroup analyses of OS**

The second interim OS analysis revealed a negative trend for Asian patients with HR: 1.71 (95% CI: 1.01 to 2.89; \( p=0.047 \)). To better understand whether the negative trend observed in the Asian subgroup at the first two OS interim analyses was due to a true negative treatment effect or it was rather secondary to random variation, a subgroup analysis by region (Asia vs. non-Asia) was performed at the time of third OS interim analysis. A numerical trend was also observed in this third analysis (HR=1.35, 95% CI: 0.87, 2.09 and \( p=0.181 \)), but not as strong as that in the second analysis. Updated results will be presented at the time of the final analyses. It is important to note that the study was not designed to make definitive conclusions in any of the subgroups including the Asia subgroup. The analysis of OS by the ethnicity subgroups should be considered exploratory in nature.

12. **Safety Analyses**

Unless otherwise specified, all the safety analyses will be based on the All Treated population. Given all patients were off treatment as of the primary analysis/first OS interim analysis, the only safety analyses to be conducted at the time of third OS interim analysis will be the summary of deaths.

All deaths occurring any time from the time of informed consent to the clinical cut-off date will be summarised based on the number and percentage of subjects. This summary
will classify subjects by time of death relative to the last dose of medication (>28 days or ≤28 days) and primary cause of death (disease under study, toxicity or other). The summary will also be provided in the following subgroups:

- Region: Asia vs. Non-Asia.

All deaths will be listed with subject level details. In addition, a listing of adverse events with onset date after the third interim analysis cutoff date (Jan 12th, 2017) will be provided.

13. REFERENCES


GlaxoSmithKline Document Number UM2008/00144/09, protocol, A Phase III Study to Evaluate the Efficacy and Safety of Pazopanib Monotherapy Versus Placebo in Women Who Have not Progressed after First Line Chemotherapy for Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer, Effective Date: 09-MAY-2016

14. Attachments

14.1. Table of Contents for Data Display Specifications

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<th>Note (output number in SAC reporting effort)</th>
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<td>7.1000</td>
<td>Statistical Analysis of Overall Survival</td>
<td>7.3000</td>
</tr>
<tr>
<td>7.1100</td>
<td>Statistical Analysis of Overall Survival (Asia)</td>
<td>7.3002</td>
</tr>
<tr>
<td>7.1200</td>
<td>Statistical Analysis of Overall Survival (Non-Asia)</td>
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<tr>
<td>7.3005</td>
<td>Sensitivity Analysis of Overall Survival</td>
<td>7.3000 (see the shells below)</td>
</tr>
</tbody>
</table>

<p>| Figure 7.1000 | Kaplan-Meier Curves of Overall Survival            | Figure 7.3000                              |
| Figure 7.1100 | Kaplan-Meier Curves of Overall Survival (Asia)     | Figure 7.3000                              |
| Figure 7.1200 | Kaplan-Meier Curves of Overall Survival            | Figure 7.3000                              |</p>
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<th>Description</th>
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<td>8.1100</td>
<td>Summary of Deaths (Asia)</td>
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<tr>
<td>8.1200</td>
<td>Summary of Deaths (Non-Asia)</td>
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<td>8.3001</td>
<td>On-treatment deaths and serious adverse events by system organ class and preferred term</td>
<td>8.3000 (see the shells below)</td>
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<td>8.4001</td>
<td>Non-serious adverse events (threshold = 5%) by system organ class and preferred term</td>
<td>8.4000 (see the shells below)</td>
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<td>Listing of Adverse Events with Onset Date after Third Interim Analysis Cutoff Date (Jan 12th, 2017)</td>
<td>15.8030</td>
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<tr>
<td>15.2000</td>
<td>Listing of Deaths</td>
<td>15.7180</td>
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### Table 7.3005  Sensitivity Analysis of Overall Survival

**Protocol:** AGO-OVAR16/VEG110655  
**Population:** Intent-to-Treat

Data as of:

<table>
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<tr>
<th></th>
<th>Placebo (N=50)</th>
<th>Pazopanib (N=50)</th>
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</thead>
<tbody>
<tr>
<td><strong>Number of Patients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died (event)</td>
<td>xx (xx%)</td>
<td>xx (xx%)</td>
</tr>
<tr>
<td>Censored, follow-up ended</td>
<td>xx (xx%)</td>
<td>xx (xx%)</td>
</tr>
<tr>
<td>Censored, follow-up ongoing</td>
<td>xx (xx%)</td>
<td>xx (xx%)</td>
</tr>
<tr>
<td><strong>Adjusted Hazard Ratio [1]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimate</td>
<td>xx</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>(xx,xx)</td>
<td></td>
</tr>
<tr>
<td><strong>Stratified Log-Rank P-Value [1]</strong></td>
<td></td>
<td>xx</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Estimates for overall survival(months) [2]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Quartile</td>
<td>xx</td>
<td>xx</td>
</tr>
<tr>
<td>95% CI</td>
<td>(xx,xx)</td>
<td>(xx,xx)</td>
</tr>
<tr>
<td>Median</td>
<td>xx</td>
<td>xx</td>
</tr>
<tr>
<td>95% CI</td>
<td>(xx,xx)</td>
<td>(xx,xx)</td>
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<tr>
<td>3rd Quartile</td>
<td>xx</td>
<td>xx</td>
</tr>
<tr>
<td>95% CI</td>
<td>(xx,xx)</td>
<td>(xx,xx)</td>
</tr>
</tbody>
</table>

[1] The Hazard ratio is estimated using a Pike estimator. A hazard ratio <1 indicates a lower risk with pazopanib compared with placebo. Hazard Ratio and P-value from stratified log-rank test are adjusted for the two stratification factors.

[2] Confidence intervals are estimated using the Brookmeyer-Crowley method.

[3] Patients who have missing death dates are treated as have died on the last contact date.
Table 8.3001  On-treatment deaths and serious adverse events by system organ class and preferred term

Protocol: AGO-OVAR16/VEG110655
Page 1 of n
Population: All Treated
Data as of:

<table>
<thead>
<tr>
<th>Primary system organ class</th>
<th>Preferred term</th>
<th>Placebo N=xxx</th>
<th>Pazopanib N=xxx</th>
<th>All patients N=xxx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of subjects affected</td>
<td>Subjects affected by serious adverse events / exposed (%)</td>
<td>xxx/xxx</td>
<td>xxx/xxx</td>
<td>xxx/xxx</td>
</tr>
<tr>
<td></td>
<td>Number of deaths (all causes)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
<tr>
<td></td>
<td>Number of deaths resulting from adverse events*</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

Infections and infestations

- **Pneumonia**
  - Subjects affected / exposed (%): xxx/xxx (xx.xx) (xx.xx)
  - Occurrences causally related to treatment/all: xx/xx (xx.xx)
  - Deaths causally related to treatment/all: xx/xx (xx.xx)

- **Sepsis**
  - Subjects affected / exposed (%): xxx/xxx (xx.xx) (xx.xx)
  - Occurrences causally related to treatment/all: xx/xx (xx.xx)
  - Deaths causally related to treatment/all: xx/xx (xx.xx)

Investigations

- **Platelet count decreased**
  - Subjects affected / exposed (%): xxx/xxx (xx.xx) (xx.xx)
  - Occurrences causally related to treatment/all: xx/xx (xx.xx)
  - Deaths causally related to treatment/all: xx/xx (xx.xx)

- **Weight decreased**
  - Subjects affected / exposed (%): xxx/xxx (xx.xx) (xx.xx)
  - Occurrences causally related to treatment/all: xx/xx (xx.xx)
  - Deaths causally related to treatment/all: xx/xx (xx.xx)

etc.

*Number of deaths resulting from adverse events corresponds to deaths resulting from serious AE causally related to treatment.
Occurrences causally related to treatment/all: all occurrences are all SAEs occurrences regardless of causality to treatment.
Deaths causally related to treatment/all: all deaths are all SAEs with fatal outcome regardless of causality to treatment.
On-treatment SAEs are included i.e. serious adverse events starting on or
after the day of the first intake of study treatment and no later than 28 days after the last treatment date.
MedDRA version 19.0.
Table 8.4001  Non-serious adverse events (threshold = 5%) by system organ class and preferred term
Protocol: AGO-OVAR16/VEG110655
Page 1 of n
Population: All Treated
Data as of:

Non-serious adverse events (threshold = 5%) by system organ class and preferred term

<table>
<thead>
<tr>
<th>Primary system organ class</th>
<th>Preferred term</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of subjects affected</td>
<td>Subjects affected by non-serious adverse events / exposed (%)</td>
<td>xxx/xxx (xx.xx)</td>
<td>xxx/xxx (xx.xx)</td>
<td>xxx/xxx (xx.xx)</td>
</tr>
</tbody>
</table>

**Blood and lymphatic system disorders**

Anemia

<table>
<thead>
<tr>
<th>Subjects affected / exposed (%)</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrences (all)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

Thrombocytopenia

<table>
<thead>
<tr>
<th>Subjects affected / exposed (%)</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrences (all)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

**Infections and infestations**

Pneumonia

<table>
<thead>
<tr>
<th>Subjects affected / exposed (%)</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrences (all)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

Sepsis

<table>
<thead>
<tr>
<th>Subjects affected / exposed (%)</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrences (all)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

**Investigations**

Platelet count decreased

<table>
<thead>
<tr>
<th>Subjects affected / exposed (%)</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrences (all)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

Weight decreased

<table>
<thead>
<tr>
<th>Subjects affected / exposed (%)</th>
<th>Placebo N=xxx (%)</th>
<th>Pazopanib N=xxx (%)</th>
<th>All Patients N=xxx (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurrences (all)</td>
<td>xx</td>
<td>xx</td>
<td>xx</td>
</tr>
</tbody>
</table>

*etc.*

Total number of subjects affected by non-serious AEs are those subjects who had at least one preferred term that met the threshold criteria.
Preferred terms with a frequency greater than 5% in any treatment arm were printed. On-treatment AEs are included i.e. adverse events starting on or after the day of the first intake of study treatment and no later than 28 days after the last treatment date. MedDRA version 19.0.