Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for FDC116114: Implementation of a screening tool for subjects with benign prostatic enlargement/obstruction to identify men ≥50 years presenting in General Practice with other co-morbidities who should be assessed for BPH
Compound Number	:	Not Applicable
Effective Date	:	20-APR-2017

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) for Protocol FDC116114. This document contains the RAP Amendment 01.

Author's Name and Functional Area:

Original	PPD Principal Biostatistician, Biostatistics, PAREXEL International Employee of PAREXEL on behalf of GSK	17-FEB-2017
Amendment 01	PPD Principal Biostatistician, Biostatistics, PAREXEL International Employee of PAREXEL on behalf of GSK	19-APR-2017

Approved by:

Original	PPD *(email approval dated 28-Feb-2017)* Director Statistics & Programming, GSK	28-FEB-2017
Amendment 01	PPD *(email approval dated 20-APR-2017)* Director Statistics & Programming, GSK	20-APR-2017

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this Reporting and Analysis Plan (RAP) is to describe the planned summaries and statistical analyses to be included in the Clinical Study Report (CSR) for Protocol FDC116114.
Protocol	• This RAP is based on protocol amendment 02 (Dated: 18/JAN/2016) of study FDC116114 (GSK Document No. :2012N140248_02] and eCRF Version 2.0.1. This document contains the RAP amendment 01. • The aim of the study is to evaluate the utility of the Benign Prostatic Enlargement (BPE)/Benign Prostatic Obstruction (BPO) screening tool in a general practice setting. The results of this screening tool may be used for further investigation.
Primary Objective	• The primary objective is to assess the utility of a BPE/BPO screening tool in conjunction with serum prostate specific antigen (PSA) in finding men confirmed to have benign prostatic hyperplasia (BPH) on full Urologist assessment of diagnostic test results.
Primary Endpoint	• The primary endpoint is the proportion of men that are confirmed to have BPH based on full Urologist assessment of diagnostic test results among men with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA≥2 ng/mL.
Study Design	• No investigational study drug is being administered during this study. • This is a non-randomized, interventional study utilizing a questionnaire-based assessment of men in general practice. Men who sign the informed consent form and meet the eligibility criteria will be enrolled and complete the Part I diagnostic tests at the General Practitioners (GP) clinic. If the GP determines that the subject has probable BPH, the subject proceeds to Part II and is scheduled for a Urologist assessment and diagnostic tests to confirm or refute a BPH diagnosis and to assess risk of progression of BPH. • Approximately 1,500 males ≥50 years presenting to a GP for a reason that is not related to this study will be screened for probable BPH to yield 500 subjects being referred to a Urologist. • The duration of the study will be 1 week (±4 days) and up to 6 weeks to allow for GP and Urologist visit scheduling.
Planned Analyses	• No investigational study drug is being administered during this study. • The primary endpoint is defined as the proportion of men confirmed to have BPH based on full Urologist diagnostic testing among men with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL. Primary endpoint summaries will be descriptively presented in terms of the calculated proportion, described below in the Primary Analyses Section, and 95% confidence interval on the proportion. Formal hypothesis testing will not be conducted.

Overview	Key Elements of the RAP
	• Secondary endpoints and other measures of interest are defined in terms of proportions for each: probable BPH diagnosis by GP, BPH diagnosis by Urologist, and BPH progression risk by Urologist along with use of 1) BPE/BPO screening tool and 2) International Prostate Symptom Score (IPSS) screening tool. The 95% confidence intervals for these proportions will be presented. • Additional summaries, proportions and related 95% confidence intervals, will be generated as outlined above, but in terms of a positive result for both the BPE/BPO and the IPSS screening tools, and separately for either the BPE/BPO or IPSS screening tools. • Another secondary endpoint of this study is to assess the level of agreement between the BPE/BPO and the IPSS screening tools for selecting men to investigate for BPH. The number and proportion of subjects with a positive or with a negative response to both the BPE/BPO and IPSS screening tools at screening will be summarized. Agreement of the BPE/BPO and the IPSS screening tools will be assessed using the kappa coefficient. The simple kappa coefficient along with the 95% confidence interval based on the asymptotic standard error will be generated using SAS. The associated null hypothesis is that the two measures (BPE/BPO and IPSS screening tools) are independent, i.e., kappa = 0. The alternative hypothesis is that the agreement of the two measures is better than one would expect by chance. If the 95% confidence interval does not contain the value zero (0), reject the hypothesis that kappa=0 (no agreement) for these data at the 0.05 level of significance. • The above defined kappa coefficient will be characterized as proposed by Landis and Koch (Landis, 1977) with <0 indicating no agreement, 0-0.20 as slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81 – 1 as almost perfect agreement. • The proportion of subjects who discontinued from the study before the GP was able to assess the presence of probable BPH will be summarized. The proportion of subjects who withdrew from the study before a Urologist visit, among subjects with a probable GP BPH diagnosis will be summarized. • The above described proportions, for both primary and secondary endpoints, will also be summarized by country, and separately by country and center.

<table>
<tr><th>Overview</th><th>Key Elements of the RAP</th></tr>
<tr><td>Analysis Populations</td><td>

No investigational study drug is being administered during this study.
Subjects are not randomized or dispensed study treatment.

<table>
<tr><th>Population</th><th>Definition / Criteria</th></tr>
<tr><td>Screened</td><td>Comprised of all subjects who are screened for eligibility.</td></tr>
<tr><td>Screened But Not Evaluable</td><td>Comprised of all subjects who are screened for eligibility, but do not qualify for the Evaluable Population.</td></tr>
<tr><td>Evaluable</td><td>Comprised of all subjects who meet the entry criteria, including a positive IPSS screening result (score ≥8) and/or a positive BPE/BPO screening result (score ≥3).</td></tr>
</table>
</td></tr>
<tr><td>Hypothesis</td><td>

The primary endpoint is defined as the proportion of men confirmed to have BPH based on full Urologist diagnostic testing in men with a positive result on the BPE/BPO screening tool (score ≥ 3) and a serum PSA ≥ 2 ng/mL. Formal hypothesis testing will not be conducted in terms of the primary and secondary endpoint proportions.

</td></tr>
<tr><td>Primary Analyses</td><td>

The primary endpoint is defined as the proportion of men confirmed to have BPH based on full Urologist diagnostic testing among men with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL.
Primary endpoint summaries will be descriptively presented in terms of the calculated proportion, described below, and 95% confidence interval on the proportion. Formal hypothesis testing will not be conducted.

<table>
<tr><th>Tool</th><th>Proportion</th><th>Numerator</th><th>Denominator</th></tr>
<tr><td>BPE/BPO</td><td>BPH diagnosis by Urologist based upon BPE/BPO screening tool result (score≥3) and serum PSA ≥2 ng/mL.</td><td>Number of subjects diagnosed with BPH based upon a BPH assessment by Urologist</td><td>Number of subjects with a positive result on the BPE/BPO screening tool (score≥3) and serum PSA ≥2 ng/mL and a BPH assessment by Urologist.</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Overview</th><th>Key Elements of the RAP</th></tr>
<tr><td>Secondary Analyses</td><td>

Secondary endpoints and other measures of interest are defined in terms of proportions for each: probable BPH diagnosis by GP, BPH diagnosis by Urologist, and BPH progression risk by Urologist along with use of 1) BPE/BPO screening tool and 2) IPSS screening tool. The 95% confidence intervals for these proportions will be presented.

<table>
<tr><th colspan="4">Secondary Endpoints: Proportions only in terms of the BPE/BPO tool</th></tr>
<tr><th>Tool</th><th>Proportion</th><th>Numerator</th><th>Denominator</th></tr>
<tr><td>BPE/ BPO</td><td>BPH Progression Risk by Urologist based upon BPE/BPO screening tool result (score ≥3) and serum PSA ≥2 ng/mL</td><td>Number of subjects diagnosed with BPH progression risk by Urologist</td><td>Number of subjects with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL and a BPH progression risk assessment by Urologist</td></tr>
<tr><td>BPE/ BPO</td><td>Probable BPH Diagnosis by GP based upon BPE/BPO screening tool result (score ≥3)</td><td>Number of subjects diagnosed with ‘probable BPH’ by GP</td><td>Number of subjects with a positive result on the BPE/BPO screening tool (score ≥3) and a BPH assessment by GP</td></tr>
</table>
<table>
<tr><th colspan="4">Secondary Endpoints: Proportions only in terms of the IPSS screening tool</th></tr>
<tr><th>Tool</th><th>Proportion</th><th>Numerator</th><th>Denominator</th></tr>
<tr><td>IPSS</td><td>BPH Diagnosis by Urologist based upon IPSS screening result (score ≥8) and serum PSA ≥2 ng/mL</td><td>Number of subjects diagnosed with BPH based on a BPH assessment by Urologist.</td><td>Number of subjects with a positive result on the IPSS (score ≥8) and serum PSA ≥2 ng/mL and a BPH assessment by Urologist</td></tr>
<tr><td>IPSS</td><td>BPH Progression Risk by Urologist based upon IPSS screening result (score ≥8) and serum PSA ≥2 ng/mL</td><td>Number of subjects diagnosed with BPH progression risk by Urologist</td><td>Number of subjects with a positive result on the IPSS (score ≥8) and serum PSA ≥2 ng/mL and a BPH progression risk assessment by Urologist</td></tr>
<tr><td>IPSS</td><td>Probable BPH Diagnosis by GP based upon IPSS screening result (score ≥8)</td><td>Number of subjects diagnosed with ‘probable BPH’ by GP</td><td>Number of subjects with a positive result on the IPSS (score ≥8) and a BPH assessment by GP</td></tr>
</table>

Additional summaries, proportions and related 95% confidence intervals, will be generated as outlined above, but in terms of a positive result for both the BPE/BPO and the IPSS screening tools and separately for either the BPE/BPO or IPSS screening tools.
Another secondary endpoint of this study is to assess the level of agreement between the BPE/BPO and IPSS screening tools for selecting men to

</td></tr>
</table>

Overview	Key Elements of the RAP
	investigate for BPH. The number and proportion of subjects with a positive or with a negative response to both the BPE/BPO and IPSS screening tools at screening will be summarized. • Agreement of the BPE/BPO and the IPSS screening tools will be assessed using the kappa coefficient. The simple kappa coefficient along with the 95% confidence interval based on the asymptotic standard error will be generated using SAS. The associated null hypothesis is that the two measures (BPE/BPO and IPSS screening tools) are independent, i.e., kappa = 0. The alternative hypothesis is that the agreement of the two measures is better than one would expect by chance. If the 95% confidence interval does not contain the value zero (0), reject the hypothesis that kappa=0 (no agreement) for these data at the 0.05 level of significance. • The above defined kappa coefficient will be characterized as proposed by Landis and Koch (Landis, 1977) with <0 indicating no agreement, 0-0.20 as slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81 – 1 as almost perfect agreement. • The proportion of subjects who discontinued from the study before the GP was able to assess the presence of probable BPH will be summarized. The proportion of subjects who withdrew from the study before a Urologist visit, among subjects with a probable GP BPH diagnosis will be summarized. • The above described proportions, for both primary and secondary endpoints, will also be summarized by country, and separately by country and center.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in Protocol Amendment 2 (Dated: 18/Jan/2016).

This document contains the RAP amendment 01 which is based on the protocol amendment 2 noted above. RAP amendment 01 revisions primarily include redefining the Screened But Not Enrolled and the Enrolled study populations. These study populations will now be defined as the Screened But Not Evaluable and Evaluable populations. This amendment 01 includes no major changes to the planned analyses. The summary of RAP amendment 01 changes is contained in Appendix 17.

2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the utility of a BPE/BPO screening tool in conjunction with serum prostate specific antigen (PSA) in finding men confirmed to have BPH on full Urologist assessment of diagnostic test results.	• Proportion of men that are confirmed to have BPH based on full Urologist assessment of diagnostic test results among men with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL.
Secondary Objectives	**Secondary Endpoints**
• To assess the utility of the BPE/BPO and IPSS screening tools in conjunction with serum PSA in finding men with risk of BPH Progression on full Urologist assessment of diagnostic test results.	• Proportion of men that are confirmed to be a risk for BPH progression based upon full Urologist assessment among men with a positive result on the BPE/BPO, IPSS, BPE/BPO and IPSS, and BPE/BPO or IPSS screening tools and serum PSA ≥2 ng/mL.
• To assess the utility of the BPE/BPO and IPSS screening tools in finding men diagnosed with probable BPH[1] as assessed by the GP.	• Proportion of men that are diagnosed with probable BPH[1] as assessed by the GP among men with a positive result on the BPE/BPO, IPSS, BPE/BPO and IPSS, and BPE/BPO or IPSS screening tools.
• To assess the utility of the IPSS screening tool in conjunction with serum PSA in finding men confirmed to have BPH on full Urologist assessment of diagnostic test results.	• Proportion of men that are confirmed to have BPH based on full Urologist assessment of diagnostic test results among men with a positive result on the IPSS screening tool (score ≥8) and serum PSA ≥2 ng/mL.
• Compare the utility of the BPE/BPO screening tool with the IPSS screening tool.	• Level of agreement (using Kappa statistic for categories) between the BPE/BPO and the IPSS screening tools for selecting men to investigate for BPH.
[1] Probable BPH is the presumptive diagnosis of urinary tract obstruction from an enlarged prostate based on clinical symptoms and findings where urinary symptoms are not apparently related to any other cause.	

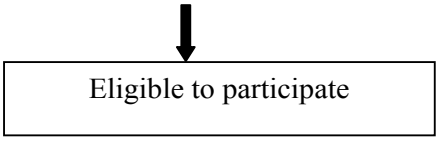
2.3. Study Design

Overview of Study Design and Key Features

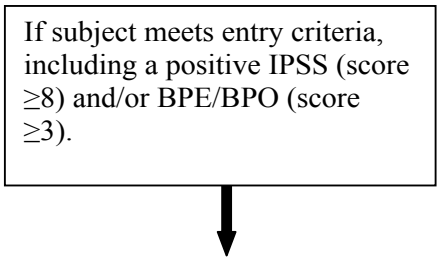
Description of Visits:

VISIT 1 (primary care clinic)

- Males ≥50 years visiting GP for reasons unrelated to the study
- Patient provides informed consent



- Inclusion/exclusion criteria confirmation
- Medical history and demography
- BPE/BPO and IPSS screening tools



ENROLLED: Subject is enrolled and proceeds to Part I (GP Assessment) of the study. If the GP diagnoses probable BPH, the subject will proceed to Part II (urologist assessment).

PART I: GP Assessment

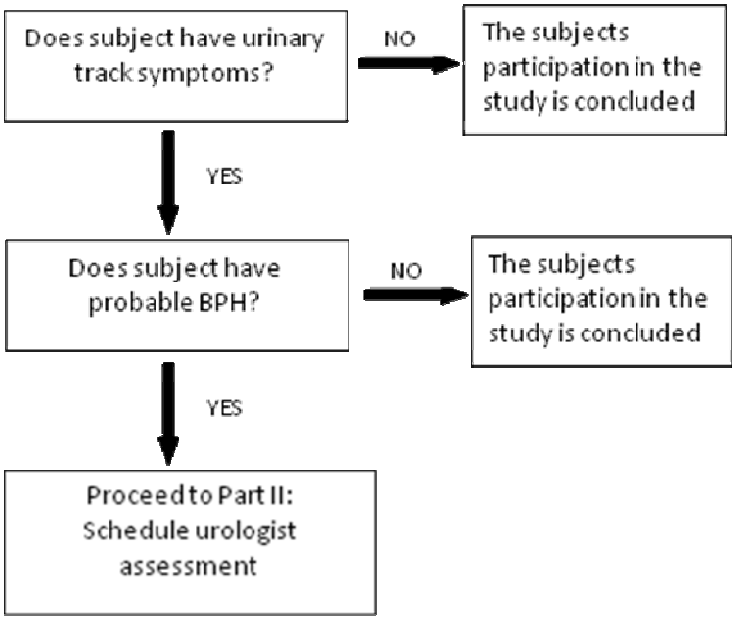
After being enrolled, complete the following at Visit 1:

- Urinalysis strip test.
    - If strip test is positive, send urine sample to local lab urinalysis.
- PSA blood test
- Additional testing may be performed as per standard of care to assist with a confirmatory diagnosis such as a DRE, however this is not required.

Overview of Study Design and Key Features

VISIT 2 (telephone call)

- GP reviews urinalysis and PSA lab results.
- Call subject: If lab results show NO probable BPH, then subject will not continue in the study. If PSA lab results show PROBABLE BPH (≥2 ng/mL), subject proceeds to Part II and Visit 3 is scheduled for the urologist assessment.



Overview of Study Design and Key Features

VISIT 3 (Part II – urologist clinic visit)

- Urologist reviews medical history and symptoms
- Brief physical examination
- DRE
- Review previous tests (BPE/BPO screening tool, IPSS screening tool, urinalysis, PSA)

Urologist provides:

- Confirmation of clinical diagnosis of BPH (or confirmation the subject does NOT have BPH).
- Estimate whether the patient is at risk of progression of BPH (PSA≥2.0ng/mL and other tests).

- NOTE: Urologist may need to perform additional diagnostic testing as per standard of care and as needed to assess the BPH diagnosis. This follow-up is not prescribed by this protocol, however, any data collected that is used for the final diagnosis will be entered in the study case report form (CRF). Advice or treatment post study will be discretion of the GP or Urologist.

Design Features	• No investigational study drug is being administered during this study. • This is a non-randomized, interventional study utilizing a questionnaire-based assessment of men in General Practice. Men who sign the informed consent form and meet the eligibility criteria will be enrolled and complete the Part I diagnostic tests at the GP clinic. If the GP determines that the subject has probable BPH, the subject proceeds to Part II and is scheduled for a Urologist assessment and diagnostic tests to confirm or refute a BPH diagnosis and to assess the risk of progression of BPH.

Overview of Study Design and Key Features	
Dosing	• No investigational study drug is being administered during this study.
Treatment Assignment	• Subjects are not randomized or dispensed study treatment. • Approximately 1,500 males presenting to a GP with a primary complaint other than LUTS will be screened for probable BPH to yield 500 subjects being referred to a Urologist.
Interim Analysis	• No interim analyses are planned for this study.

2.4. Statistical Hypotheses

The primary endpoint is defined as the proportion of men confirmed to have BPH based on full Urologist diagnostic testing in men with a positive result on the BPE/BPO screening tool and a probable BPH assessment by GP. Primary endpoint summaries will be descriptively presented in terms of the calculated proportion, described below, and a 95% confidence interval on the proportion. Formal hypothesis testing will not be conducted in terms of the primary and secondary endpoint proportions.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analyses are planned for this study.

3.2. Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All subjects have either completed, or withdrawn from, the study, as defined in the protocol.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.

The primary database freeze, using standard Data Management practices, will occur after the last subject completes Visit 3. Statistical analysis and reporting will be in terms of this primary database freeze and will be referred to as the 'Final Analysis' or primary 'Statistical Analysis Complete' (SAC).

4. ANALYSIS POPULATIONS

No investigational study drug is being administered during this study.

This is a non-randomized, interventional study utilizing a questionnaire-based assessment of men in general practice, therefore the populations are not defined in the traditional sense. The following populations will be used on this study.

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprised of all subjects who are screened for eligibility.	• Study Population • Efficacy (agreement between BPE/BPO and IPSS)
Screened But Not Evaluable	• Comprised of all subjects who are screened for eligibility, but do not qualify for the Evaluable Population.	• Study Population • Safety (Adverse Events Listing)
Evaluable	• Comprised of all subjects who meet the entry criteria, including a positive IPSS screening result (score ≥8) and/or a positive BPE/BPO screening result (score ≥3).	• Study Population • Efficacy • Safety

NOTES : Please refer to Appendix 15: List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarized and listed.

4.1.1. Inclusion / Exclusion Criteria Deviations

All inclusion / exclusion criteria deviations which are recorded on the inclusion / exclusion screens of the eCRF will be summarized. The tabular summaries will be in terms of number and percent of Screened But Not Evaluable Subjects violating any criterion and violating each criterion.

Listings of inclusion / exclusion criteria deviations will be produced for Screened But Not Evaluable subjects.

4.1.2. Important Protocol Deviations

Protocol deviations identified during the study will be tracked and reviewed by the study team in accordance with SOP-130050 and the FDC116114 Protocol Deviation Management Plan (PDMP). Prior to the final database lock and data analysis for the clinical study report (CSR), the FDC116114 Study team will determine whether any subjects will be excluded from the summary of important protocol deviations as specified in the reporting and analysis plan. Protocol deviation data entered into the eCRF (InForm) will be extracted and processed as a SAS dataset with identifiers for important protocol deviations. Subjects with important protocol deviations will be summarized and

discussed, and the CSR listings will include a list of important protocol deviations occurring in the study; listings of all protocol deviations will be available for regulators if requested.

- Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorized on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

Important Deviations will be summarized and listed for Evaluable subjects. The tabular summary will be in terms of number and percent of subjects with any Important Deviations and with each Important Deviation. Summaries will be output by the eCRF categories for the Evaluable subjects and by the following screening tool categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The eCRF categories are standardized for this study; examples are provided in the tabular summary shells.

Listings of important protocol deviations will be produced for Evaluable subjects.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions. A full set of appendices is provided in Section 11.

Table 1 Overview of Appendices

Section	Component
11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
11.2	Appendix 2: Time & Events
11.3	Appendix 3: Assessment Windows
11.4	Appendix 4: Treatment States and Phases
11.5	Appendix 5: Data Display Standards & Handling Conventions
11.6	Appendix 6: Derived and Transformed Data
11.7	Appendix 7: Premature Withdrawals & Handling of Missing Data
11.8	Appendix 8: Adverse Event Time Periods and Special Adverse Event Definitions
11.9	Appendix 9: Values of Potential Clinical Importance
11.10	Appendix 10: Multicenter Studies
11.11	Appendix 11: Examination of Covariates, Subgroups & Other Strata
11.12	Appendix 12: Multiple Comparisons & Multiplicity
11.13	Appendix 13: Model Checking and Diagnostics for Statistical Analyses.
11.14	Appendix 14: Abbreviations and Trademarks
11.15	Appendix 15: List of Data Displays
11.16	Appendix 16: Example Mock Shells for Data Displays
11.17	Appendix 17: Amendment 01 Revisions

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The study population analyses will be based on the Evaluable subjects, unless otherwise specified.

Table 2 provides an overview of the planned study population summaries and listings, with full details of planned data displays being presented in Appendix 15: List of Data Displays. All summaries will be presented by the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3, unless otherwise noted.

Formal hypothesis testing will not be performed in terms of the study population data.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Subject Accountability			
Numbers of Subjects, including Screened, Screened But Not Evaluable, and Evaluable	Y		
Number of Subjects, including: Evaluable, Evaluable with PSA Values (<2 or ≥2), GP Assessments, and Urologist Assessments	Y		Y
Subject Disposition			
Overall Disposition	Y		Y
Subject Withdrawals	Y		Y
Discontinuation by Visit	Y		
Inclusion / Exclusion Criteria Deviations (Screened But Not Evaluable Subjects)	Y		Y
Important Protocol Deviations	Y		Y
Demographic Characteristics			
Demographic Characteristics	Y		Y
Race	Y		Y
Medical Conditions and Concomitant Medications			
Medical Conditions by Body System	Y		Y
Surgical / Diagnostic Procedures	Y		Y
Concomitant Medications	Y		Y
Diagnostic Tests and Questionnaires			
PSA	Y		
IPSS and BPE/BPO	Y		

NOTES :

- Y = Yes display generated.
- There are no planned Study Population Figures.

6.2. Subject Accountability

Summaries for the following will be produced in terms of total number overall:

- All Screened Subjects
- All Evaluable Subjects

Evaluable subjects include those subjects who met all inclusion and exclusion criteria including a positive IPSS (score≥8) and/or BPE/BPO (score≥3). Summaries for the Screened and Evaluable subjects will also be presented by country, and separately by country and center.

A summary table will be produced for the screened subjects and will contain the following:

- Number of subjects who were sScreened but not Evaluable
- Number of subjects who were Evaluable

A summary of screened subjects by country, and separately by country and center will also be presented.

A summary table will be produced for the Evaluable subjects and will contain the following:

- All Evaluable Subjects (IPSS≥8 or BPE/BPO≥3)
- Evaluable Subjects with PSA<2.0ng/mL
- Evaluable Subjects with PSA≥2.0ng/mL
- Evaluable Subjects with Any GP Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes’’ and Urologist Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Any Urologist Risk Assessment of BPH Progression
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”No”

An overall summary and the data above will also be presented by country, and separately by country and center for the Evaluable subjects.

6.3. Subject Disposition

A subject may withdraw from the study at any time at the investigator's discretion or at the request of the subject.

The reason for study withdrawal is recorded in the eCRF for Evaluable subjects who prematurely withdrew from the study prior to completing Visits 1, 2, and 3. A tabular summary will be produced for number and percentage of subjects prematurely withdrawing from the study, overall and by reason. Additional tabular summaries will be produced by Visit (overall and by reason) for subjects withdrawing from the study. For these summaries, the percentages are calculated using the number of subjects in each of the categories (IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3) as the denominators.

Listings will be produced for subject disposition and reason for withdrawal and will include key accountability data including study status, completion or withdrawal date, all visit dates, and the primary reason for premature withdrawal.

6.4. Demographic Characteristics

The following demographic characteristics will be summarized for the Screened But Not Evaluable and Evaluable subjects; summaries for the Evaluable subjects will be repeated by country, and separately by country and center:

- Sex
- Age in years
- Age categories (years): <65, ≥65, <75, ≥75
- Race (Evaluable subjects only)

Listings will be produced for sex, age, and race (Evaluable subjects only). Race information will not be presented in tables or listings for subjects who were enrolled in the study in France.

6.5. Medical Conditions, Surgical Procedures, and Concomitant Medications

The following medical conditions and surgical procedures are GSK standardized data collections and/or are of interest in terms of the Evaluable subjects, and will be summarized in tabular and listing formats. The number and percentage of subjects reporting having each medical condition or surgical procedure will be included in the summary. Tabular summaries of surgical procedures will be presented for screening and post-screening visits.

Medical Conditions

- Cardiovascular Risk Factors
  - Angina Pectoris
  - Myocardial Infarction

  - Stroke
  - Diabetes
  - Hypertension
  - Hyperlipidemia

- Urinary Conditions
  - Incomplete Urination
  - Unable to Urinate
  - Urination Difficulty
  - Micturition Disorder
  - Increased Urinary Frequency
  - Recurrent Urinary Tract Infection
  - Hematuria
  - Urinary Incontinence Surgery
  - Urethral Stricture
  - Urine Flow Decreased
  - Post Void Dribbling
  - Nocturia
  - Urinary Calculus
  - Bladder Neoplasm/Tumor

Surgical Procedures

- Cystoscopy
- Transrectal Ultrasound
- Prostate Biopsy
- Ultrasound Abdomen
- Computerized Tomogram Abdomen
- Computerized Tomogram Pelvis
- Nuclear MRI Abdominal
- Pelvic MRI
- Renal Scan
- Bladder Scan
- Abdominal X-Ray
- Other

Concomitant medication data are collected on eCRF log forms and will be coded using the GSKDrug dictionary. Concomitant medications will be defined as any medication documented as such in the database, irrespective of start or stop dates or ongoing status.

A summary of concomitant medications will be provided. The number and percentage of subjects reporting the use of each concomitant medication will be summarized and will include ATC Level I and ingredient. A listing of the collected concomitant medications by country and center will be provided. A listing of the relationship between the ATC Level I, ingredient, and verbatim text for concomitant medications will also be provided.

6.6. Diagnostic Tests and Questionnaires

The IPSS screening tool is completed at the screening visit. The total IPSS score is the sum of the 7 individual questions. The total IPSS score will be summarized by N, Mean, Standard Deviation, Median, Minimum, and Maximum. The number and percentage of subjects with total IPSS scores will also be summarized categorically using the following categories: <8, 8 – 19, >19.

The BPE/BPO screening tool is completed at the screening visit. The total BPE/BPO score is the sum of the 3 individual questions. The total BPE/BPO score will be summarized by N, Mean, Standard Deviation, Median, Minimum, and Maximum. The number and percentage of subjects with total BPE/BPO scores will also be summarized categorically using the following categories: <3, 3 – 6, >6.

Serum PSA samples are scheduled at the screening visit after the subject is enrolled. Serum PSA will be summarized by N, Mean, Standard Deviation, Median, Minimum, and Maximum. The number and percentage of subjects with serum PSA data will also be summarized categorically using the following categories: <2, 2 – 9, >9.

The IPSS, BPE/BPO, and PSA data described above will also be summarized by country, and separately by country and center.

7. PRIMARY STATISTICAL ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Overview of Planned Primary Efficacy Analyses

The primary endpoint is defined as the proportion of men confirmed to have BPH based on full Urologist diagnostic testing among men with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL. The BPE/BPO questionnaire consists of three questions each with a score ranging from 0 to 5. This questionnaire is administered at the screening visit (Visit 1).

BPE/BPO (also called the BPE/BPO total score) is the sum of the three questions. BPE/BPO summaries will be in terms of the total (score); exceptions will be noted such as for supporting summaries of individual questions. For calculation of the BPE/BPO total, missing individual responses will not be imputed.

The primary efficacy analyses will be based on the Evaluable subjects, unless otherwise specified. Table 3 provides an overview of the planned BPE/BPO summaries and primary efficacy analyses, with full details of data displays being presented in Appendix 15: List of Data Displays.

Table 3 Overview of Planned Primary Efficacy Analyses

Endpoint	Stats Analysis			Absolute			
				Summary		Individual	
	T	F	L	T	F	F	L
Proportion of Men with BPH Based on full Urologist Diagnosis and BPE/BPO Score (≥3)							
Primary Analysis	Y[1]						
Supporting Data for Primary Endpoint							
BPE/BPO Individual and Total Scores at Visit 1				Y[2]			Y[2]
Summary of PSA Values				Y[3]			Y[3]

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Primary efficacy analyses are presented within this table; details of the analysis are in the following section.
2. Individual BPE/BPO question 1-3 responses and total scores support the primary analysis; total scores are also presented by country, and separately by country and center.
3. The PSA summary data supports the primary analysis; the PSA data Tables and Listings appear with the Safety Tables and Listings.

7.1.2. Planned Primary Efficacy Statistical Analyses

Primary Statistical Analyses

Endpoint(s)

- Proportion of men that are confirmed to have BPH based on full Urologist assessment of diagnostic test results among men with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL.
- Primary endpoint summaries will be descriptively presented in terms of the calculated proportion, described below, and 95% confidence interval on the proportion. Formal hypothesis testing will not be conducted.

Tool	Proportion	Numerator	Denominator
BPE/BPO	BPH diagnosis by Urologist based upon BPE/BPO screening tool (score≥3) and serum PSA ≥2 ng/mL.	Number of subjects diagnosed with BPH based upon a BPH assessment by Urologist.	Number of subjects with a positive result on the BPE/BPO screening tool (score≥3) and serum PSA ≥2 ng/mL and a BPH assessment by Urologist.

- Table 3 provides an overview of the planned summaries and primary efficacy analyses. A list of planned data displays is in Appendix 15: List of Data Displays.

Model Specification

- No models were used during the statistical analysis; proportions and confidence intervals were computed.

Model Checking & Diagnostics

- Not Applicable

Model Results Presentation

- Not Applicable

Sensitivity and Supportive Statistical Analyses

- Not Applicable

8. SECONDARY STATISTICAL ANALYSES

8.1. Secondary Efficacy Analyses

8.1.1. Overview of Planned Secondary Efficacy Analyses

The secondary efficacy analyses will be based on the Evaluable subjects, unless otherwise specified. Table 4 provides an overview of the planned secondary efficacy analyses, with further details of data displays being presented in Appendix 15: List of Data Displays.

Table 4 Overview of Planned Secondary Efficacy Analyses

Endpoint	Stats Analysis			Absolute			
				Summary		Individual	
	T	F	L	T	F	F	L
IPSS							
Total and individual scores at Visit 1				Y			Y
BPH-Related Health Status							
Scores at Visit 1				Y			Y
BPE/BPO							
Total and individual scores at Visit 1				Y			Y
Summary of BPH Diagnosis by Urologist[1], Summary of BPH Progression Risk by Urologist, and Summary of Probable BPH Diagnosis by GP							
Based upon BPE/BPO score (≥3)	Y						
Based upon IPSS score (≥8)	Y						
Based upon IPSS score (≥8) or BPE/BPO score (≥3)	Y						
Based upon IPSS score (≥8) and BPE/BPO score (≥3)	Y						
Summary of Subjects Who Discontinued From the Study Before the GP Was Able to Assess the Presence of Probable BPH and Summary of Subjects Who Withdrew from the Study Before a Urologist Visit, Among Subjects Who Were Eligible for Such a Visit							
Based upon BPE/BPO score (≥3)	Y						
Based upon IPSS score (≥8)	Y						
Based upon IPSS score (≥8) or BPE/BPO score (≥3)	Y						
Based upon IPSS score (≥8) and BPE/BPO score (≥3)	Y						

Endpoint	Stats Analysis			Absolute			
				Summary		Individual	
	T	F	L	T	F	F	L
BPE/BPO and IPSS							
Summary of agreement between screening tools (Kappa statistic)	Y						
Figures (All Evaluable Subjects)							
Plot of IPSS Scores versus BPE/BPO Scores at Visit 1					Y		
Plot of IPSS Scores versus PSA Values at Visit 1					Y		
Plot of BPE/BPO Scores versus PSA Values at Visit 1					Y		

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
    1. Summary of BPH diagnosis by the Urologist based upon the BPE/BPO screening tool (score ≥3) is a Primary Endpoint and is not included in the Secondary Endpoint analysis.

8.1.2. Planned Secondary Efficacy Statistical Analyses

Primary Statistical Analyses

Endpoint(s)

Secondary endpoints and other measures of interest are defined in terms of proportions for each: probable BPH diagnosis by GP, BPH diagnosis by Urologist, and BPH progression risk by Urologist along with use of 1) BPE/BPO screening tool and 2) IPSS screening tool. The 95% confidence intervals (calculated using the exact (Clopper-Pearson) method) for these proportions will be presented.

Secondary Endpoints: Proportions only in terms of the BPE/BPO tool			
Tool	**Proportion**	**Numerator**	**Denominator**
BPE/BPO	BPH Progression Risk by Urologist based upon BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL	Number of subjects diagnosed with BPH progression risk by Urologist	Number of subjects with a positive result on the BPE/BPO screening tool (score ≥3) and serum PSA ≥2 ng/mL and a BPH progression risk assessment by Urologist
BPE/BPO	Probable BPH Diagnosis by GP based upon BPE/BPO screening tool (score ≥3)	Number of subjects diagnosed with 'probable BPH' by GP	Number of subjects with a positive result on the BPE/BPO screening tool (score ≥3) and a BPH assessment by GP

Primary Statistical Analyses

Secondary Endpoints: Proportions only in terms of the IPSS screening tool			
Tool	**Proportion**	**Numerator**	**Denominator**
IPSS	BPH Diagnosis by Urologist based upon IPSS (score ≥8) and serum PSA ≥2 ng/mL	Number of subjects diagnosed with BPH based upon BPH assessment by Urologist.	Number of subjects with a positive result on the IPSS (score ≥8) and serum PSA ≥2 ng/mL and a BPH assessment by Urologist
IPSS	BPH Progression Risk by Urologist based upon IPSS (score ≥8) and serum PSA ≥2 ng/mL	Number of subjects diagnosed with BPH progression risk by Urologist	Number of subjects with a positive result on the IPSS (score ≥8) and serum PSA ≥2 ng/mL and a BPH progression risk assessment by Urologist
IPSS	Probable BPH Diagnosis by GP based upon IPSS (score ≥8)	Number of subjects diagnosed with 'probable BPH' by GP	Number of subjects with a positive result on the IPSS (score ≥8) and a BPH assessment by GP

- Additional summaries, proportions and related 95% confidence intervals, will be generated as outlined above, but in terms of a positive result for both the BPE/BPO and the IPSS screening tools and separately for either the BPE/BPO or IPSS screening tools.
- Another secondary endpoint of this study is to assess the level of agreement (via the kappa statistic) between the BPE/BPO and/or IPSS screening tools for selecting men to investigate for BPH. The number and proportion of subjects with a positive or with a negative response to both the BPE/BPO and IPSS screening tools at screening will be summarized.
- The kappa coefficient will be characterized as proposed by Landis and Koch (Landis, 1977) with <0 indicating no agreement, 0-0.20 as slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81 – 1 as almost perfect agreement.
- The proportion of subjects who discontinued from the study before the GP was able to assess the presence of probable BPH will be summarized. The proportion of subjects who withdrew from the study before a Urologist visit, among subjects with a probable GP BPH diagnosis will be summarized.

Model Specification

- No models were used during the statistical analysis; proportions and confidence intervals were computed.

Model Checking & Diagnostics

- Not Applicable

Model Results Presentation

- Not Applicable

Sensitivity and Supportive Statistical Analyses

- Not Applicable

8.1.2.1. IPSS Screening Tool

The IPSS screening tool is completed at the screening visit (Visit 1). The total IPSS score is the sum of the 7 individual questions. The total IPSS score will be summarized by N, Mean, Standard Deviation, Median, Minimum, and Maximum for each of the following:

- All Evaluable Subjects (IPSS≥8 or BPE/BPO≥3)
- Evaluable Subjects with PSA<2.0ng/mL
- Evaluable Subjects with PSA≥2.0ng/mL
- Evaluable Subjects with Any GP Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes’’ and Urologist Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Any Urologist Risk Assessment of BPH Progression
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”No”

The total IPSS score will be presented by the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The total IPSS score data will also be presented by country, and separately by country and center.

A listing of the IPSS individual and total scores will be presented.

8.1.2.2. BPH-Related Health Status

BPH-Related Health Status (BHS) is collected as Question 8 on the IPSS questionnaire and ranges from 0 to 6. The IPSS questionnaire is administered, and thus BHS is collected, at the screening visit (Visit 1). The total number, as well as the number and percentage of subjects experiencing quality of life symptoms, will be provided.

BPH-Related Health Status values will be presented by the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The BPH-Related Health Status data will also be presented by country, and separately by country and center.

A listing of the BPH-Related Health Status individual scores will be presented.

8.1.2.3. BPE/BPO Screening Tool

The BPE/BPO screening tool is completed at the screening visit (Visit 1). The total BPE/BPO score is the sum of the 3 individual questions. The total BPE/BPO score will be summarized by N, Mean, Standard Deviation, Median, Minimum, and Maximum for each of the following:

- All Evaluable Subjects (IPSS≥8 or BPE/BPO≥3)
- Evaluable Subjects with PSA<2.0ng/mL
- Evaluable Subjects with PSA≥2.0ng/mL
- Evaluable Subjects with Any GP Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes’’ and Urologist Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Any Urologist Risk Assessment of BPH Progression
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”No”

The total BPE/BPO score will be presented by the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The total BPE/BPO score data will also be presented by country, and separately by country and center.

A listing of the BPE/BPO individual and total scores will be presented.

8.2. Safety Analyses

8.2.1. Overview of Planned Analyses

Safety summaries and analyses are reported in terms of the following data classifications: adverse events, clinical laboratory assessments (urinalysis), total serum prostate specific antigen (PSA), and digital rectal examination (DRE).

All safety analyses will be performed using the Evaluable subjects unless otherwise specified in text or data display shells. Applicable safety analysis and reporting definitions and presentations within "Program Safety Analysis Plan (PSAP, 2016) for GI198745 (dutasteride) and GSK2285985 (fixed dose combination of dutasteride [GI198745] and tamsulosin [GI138525]" are utilized within this RAP, with any deviations noted.

Table 5 provides an overview of the planned adverse event tabular summaries. A list of planned data displays is in Appendix 15: List of Data Displays.

Reference Section 4 (Analysis Populations) and Appendix 6 (Derived and Transformed Data) for supporting definitions on all below subsections.

Table 5 Overview of Planned Safety Analyses

Adverse Event Types, High Level					
	Any	Non-Serious	Serious	Leading to W/D from Study	Fatal
By Type	----------3.1 (5 above categories, excluding Non-Serious)----------				
Overall	3.2	3.3	3.11 3.14	3.17 3.18	3.16
By Age (<65, ≥65, <75, ≥75)	3.4 3.5		3.12 3.13		
By Country; By Country and Center	3.6 3.7		3.14 3.15		
By Maximum Intensity	3.8				
Most Common	3.9	3.10			
Sexual and Breast Adverse Events of Special Interest					
MedDRA	----------3.19----------				
Prostate Cancer Adverse Event of Special Interest					
Prostate Cancer Overall	----------3.20----------				
Cardiovascular Adverse Events of Special Interest					
MedDRA	----------3.21----------				
Infrequent Tier 1 Adverse Events of Special Interest					
MedDRA	----------3.22----------				

NOTES :

- Summaries are in terms of 'starting on or after enrollment' (defined in Appendix 6) unless otherwise noted.

8.2.2. Adverse Events

Adverse events (AEs) will be coded using the MedDRA (Medical Dictionary for Regulatory Activities) coding dictionary. As specified in the protocol, disease related events will not be reported as AEs or serious adverse events (SAEs) unless the investigator assesses the event as more severe than expected for the subject's condition. A mapping of the MedDRA primary system organ class and preferred term to which each verbatim term has been coded will be provided in a listing.

Adverse events (AEs) are to be recorded on the electronic case report form (eCRF) from the time of enrollment until the end of the study period (completion of Visits 1, 2, and 3). Serious AEs (SAEs) are to be recorded from the time of informed consent. Any SAEs assessed as related to study participation or related to a GSK concomitant medication, will be recorded from the time a subject consents to participate in the study up to the completion of the subject's final visit. The investigator will monitor all AEs/SAEs that are ongoing until resolution or stabilization of the event, or until the subject is lost to follow-up. Adverse events summaries will include non-serious as well as serious AEs.

The number of post-enrollment adverse events, the number and the percentage of subjects reporting any post-enrollment AE will be summarized for the following:

- All AEs
- Serious AEs
- AEs leading to withdrawal from study
- Fatal AEs

Total number of adverse events reported in the study as well as the number and percentage of subjects reporting at least one AE will be provided. Total number of AEs as well as the number and percentage of subjects reporting each AE will be reported by primary system organ class and preferred term. Non-serious post-enrollment AEs will be summarized. A summary of post-enrollment AEs will be provided by age group (<65, ≥ 65, <75, ≥ 75 years), by country, and separately by country and center.

A summary of post-enrollment AEs will also be provided by maximum intensity. If the same AE occurs on multiple occasions in the same subject, the AE with the highest intensity will be presented. Intensity will be categorized as mild, moderate, or severe; a category for missing/not applicable intensity will be included.

The most common AEs (Tier 2 events) are defined as those preferred terms occurring in at least 5% of the subjects (non-rounded). The total number of events as well as the number and percentage of subjects reporting at least one most common AE preferred term starting post-enrollment will be provided. The total number of events as well as the number and percentage of subjects reporting at least one non-serious most common AE preferred term starting post-enrollment will also be provided. Individual subject listings of all adverse events for the Screened But Not Evaluable and for the Evaluable subjects will be presented.

8.2.3. Deaths and Serious Adverse Events

Total number of serious adverse events as well as the number and percentage of subjects reporting at least one serious AE will be provided. Total number of serious adverse events as well as the number and percentage of subjects reporting each serious AE will be reported by primary system organ class and preferred term. A summary of post-enrollment serious AEs will be provided by age group (<65, ≥65, <75, ≥75), by country, and separately by country and center. A summary of all post-enrollment fatal AEs will be provided.

Individual subject listings of all non-fatal serious AEs and a separate listing of all fatal AEs will be provided. The listing will indicate the timing of the serious AE with respect to enrollment date.

8.2.4. Adverse Events Leading to Withdrawal From the Study and Other Significant Adverse Events

8.2.4.1. Adverse Events Leading to Withdrawal from the Study

A summary of adverse events starting post-enrollment and leading to withdrawal from the study will be provided for the following categories:

- All AEs
- Serious AEs

Subject listings of AEs leading to withdrawal from the study will be provided. The listings will indicate the timing of the AE with respect to enrollment start date.

8.2.4.2. Adverse Events of Special Interest

Tier 1 adverse events of special interest are pre-specified adverse event preferred terms for which there are predefined hypotheses about the existence of a potential occurrence. These events include the following:

- Sexual and breast events
- Prostate cancer
- Cardiovascular events
- Infrequent events

Summaries for these events are specified in the following sections and will be based on post-enrollment AEs unless otherwise indicated. A mapping of the MedDRA primary system organ class and preferred term to which each verbatim term in the special interest AE categories has been coded will be provided in a listing.

8.2.4.3. Sexual and Breast Tier 1 Adverse Events of Special Interest

Altered (decreased) libido, impotence, ejaculation disorders, and breast disorders, will be defined as sexual and breast adverse events of special interest. Two subgroups of breast disorders (breast disorders: breast enlargement, and breast disorders: breast tenderness) are of special interest. MedDRA system organ class and preferred terms included in these special interest adverse events are defined in Appendix 8, Table A.

Total number of, as well as number and percentage of the subjects experiencing, sexual and breast adverse events of special interest will be provided.

Listings of sexual and breast adverse events of special interest will be provided.

8.2.4.4. Prostate Cancer Adverse Events of Special Interest

Prostate cancer will be defined as an adverse event of special interest. MedDRA preferred terms and codes included in this special interest adverse event are defined in Appendix 8, Table B. Prostate cancer events will be summarized separately following the same format done for sexual and breast special interest AEs described above.

Listings of prostate cancer adverse events of special interest will be provided.

8.2.4.5. Cardiovascular Adverse Events of Special Interest

Cardiovascular adverse events of special interest will be defined as those included in the following six categories: acute coronary syndrome, ischemic coronary artery disorders/atherosclerosis, ischemic cerebrovascular events, cardiac failure, cardiac arrhythmias, and peripheral vascular disease. MedDRA preferred terms and codes included in these special interest adverse events are defined in Appendix 8, Table C. Total number of cardiovascular events as well as the number and percentage of subjects experiencing cardiovascular events will be provided.

Listings of cardiovascular adverse events of special interest will be provided.

8.2.4.6. Infrequent Tier 1 Adverse Events of Special Interest

Infrequent Tier 1 adverse events of special interest will be defined as those included in the following categories:

- Breast cancer
- Potential for decreased male fertility due to effects on sperm/semen characteristics
- Interference with formation of external genitalia in a male fetus if a woman carrying a male fetus is exposed to dutasteride
- Hair changes
- Allergic reactions
- Depressed mood
- Testicular pain and swelling
- Intraoperative floppy iris syndrome
- Orthostasis
- Priapism
- Stevens-Johnson syndrome
- Atrial fibrillation, tachycardia, arrhythmias

MedDRA preferred terms and codes included in these special interest adverse events are defined in Appendix 8, Table D. Total number of infrequent Tier 1 events as well as the number and percentage of subjects with infrequent Tier 1 events will be provided.

Listings of infrequent Tier 1 adverse events of special interest will be provided.

8.2.5. Clinical Laboratory Assessments

A urine strip test (dipstick) will be performed at screening for all Evaluable subjects (Visit 1). If the dipstick is positive, the urine sample will be submitted to the local laboratory for urinalysis. The urine microscopy values assessed on the urine sample will include the following parameters:

- Urine Protein
- Urine Glucose
- Urine RBC
- Urine WBC

The overall number of subjects tested and the number and percentage of subjects with positive /negative results will be presented by the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The urinalysis data will also be presented by country, and separately by country and center.

A listing of the urinalysis data will be provided.

8.2.6. Serum PSA

Serum PSA samples are scheduled at the screening visit (Visit 1) after the subject is enrolled. Serum PSA will be summarized by N, Mean, Standard Deviation, Median, Minimum, and Maximum for each of the following:

- All Evaluable Subjects (IPSS≥8 or BPE/BPO≥3)
- Evaluable Subjects with PSA<2.0ng/mL
- Evaluable Subjects with PSA≥2.0ng/mL
- Evaluable Subjects with Any GP Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH
- Evaluable Subjects with GP Assessment of BPH=”Yes’’ and Urologist Assessment of BPH=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Assessment of BPH=”No”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Any Urologist Risk Assessment of BPH Progression
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”Yes”
- Evaluable Subjects with GP Assessment of BPH=”Yes” and Urologist Risk Assessment of BPH Progression=”No”

Serum PSA values will be presented by the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The serum PSA data will also be presented by country, and separately by country and center.

A listing of the serum PSA data will be provided.

8.2.7. Digital Rectal Examinations

A digital rectal examination (DRE) is scheduled to be performed at Visit 3 and may be performed at the screening visit (Visit 1). The results of normal versus focal abnormality, in addition to clinical significance, will be summarized for each visit using the following categories: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3. The digital rectal examination data will also be presented by country, and separately by country and center.

A listing of digital rectal examination data will be provided.

8.3. Pharmacokinetic Analyses

Pharmacokinetic (PK) samples were not collected. No PK analyses are planned for this study.

8.4. Pharmacodynamic (and / or Biomarker) Analyses

Pharmacodynamic and Biomarker samples were not collected. No pharmacodynamic or biomarker analyses are planned for this study.

8.5. Pharmacokinetic / Pharmacodynamic Analyses

Pharmacokinetic/pharmacodynamic samples were not collected. No pharmacokinetic/pharmacodynamic analyses are planned for this study.

9. OTHER STATISTICAL ANALYSES

No other statistical analyses are planned for this study.

10. REFERENCES

GlaxoSmithKline Document Number 2012N140248_02 Study ID FDC116114. Implementation of a screening tool for subjects with benign prostatic enlargement/obstruction to identify men ≥50 years presenting in General Practice with other co-morbidities who should be assessed for BPH. Effective Date 18Jan2016.

GlaxoSmithKline Document: Program Safety Analysis Plan (PSAP) for GI198745 (dutasteride) and GSK2285985 (fixed dose combination of dutasteride [GI198745] and tamsulosin [GI138525]); PSAP approval date 09Dec2016.

Landis, J.R.; Koch, G.G. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33 (1): 159-174

Stokes, Maura E., Charles S. Davis, and Gary G. Koch. 2000. *Categorical Data Analysis Using the SAS® System, Second Edition.* Cary, NC: SAS Institute Inc.

11. APPENDICES

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11.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

11.1.1. Exclusions from Per Protocol Population

No investigational study drug is being administered during this study.

This is a non-randomized, interventional study utilizing a questionnaire-based assessment of men in general practice, therefore the populations are not defined in the traditional sense; there will be no Per Protocol population for this study. The analysis population will be All Evaluable Subjects.

In accordance with SOP-130050 and the FDC116114 Protocol Deviation Management Plan (PDMP), a final review of the study deviations will be conducted by members of the internal and external Data Management team in advance of database freeze (DBF).

Below is a list of the deviations which are considered important as per the PDMP and will be summarized in a table by category; a supportive 'by subject' data listing will also be provided.

Deviation Category:

- Informed Consent
- Violation of Inclusion Criteria (Inclusion #)
- Violation of Exclusion Criteria (Exclusion #)
- Not Withdrawn After Developing Withdrawal Criteria
- Excluded Medication, Vaccine, or Device
- Assessment or Time Point Completion[1]
- Failure to Report Safety Events per Protocol

[1] Deviations pertaining to incomplete and out of window assessments will be reviewed in-stream and assigned importance status during protocol deviation review meetings. Deviations related to missed assessments affecting subject safety will be marked "IMP = Y," deviations not affecting subject safety will be marked "IMP=N."

11.2. Appendix 2: Time & Events

11.2.1. Protocol Defined Time & Events

Procedure	VISIT 1: Screening/ Enrollment at GP Clinic	Study Period (1 week ±4 days to 6 weeks)	
		VISIT 2 (phone call): GP	VISIT 3: Urologist[6] (up to 6 weeks after V1)
Informed consent	X		
Inclusion and exclusion criteria	X		
Demography	X		
Medical history	X		
Concomitant medications (all ongoing and within 30 days prior to Visit 1)	X		
IPSS screening tool	X		
BPE/BPO screening tool	X		
PROCEDURES AFTER SUBJECT IS ENROLLED[1]:			
Urine strip test[2]	X		
Urinalysis (only if urine strip test is positive)[2]	X		
PSA blood test[3]	X		
Results phone call to subject[4]		X	
Digital rectal exam (DRE)[5]	X		X
Brief physical examination			X
Enter prostate-related results in the CRF from non-protocol required procedures			X
AE/SAE review (related to study procedures and/or participation)	←==========→		
Concomitant medication review	←==========→		

1. Subject is enrolled after meeting eligibility requirements, which includes a positive BPE/BPO screening tool and/or positive IPSS screening tool.
2. Urinalysis sent to local laboratory only if urine strip test is positive.
3. PSA blood test sent to local lab. Local lab results and reference ranges are entered in the CRF.
4. For Visit 2, the GP calls the subject to report yes or no for probable BPH. If the subject has probable BPH, the GP schedules the subject for Visit 3 with the Urologist. If the subject does not have probable BPH, then the subject has completed the study.
5. DRE is performed by the Urologist. The GP may conduct a DRE at visit 1 however the DRE will be repeated by the Urologist to confirm the diagnosis and to rule out an abnormality suggesting prostate cancer.
6. Information collected during visit 3 will be entered into the eCRF by the Principal Investigator.

11.3. Appendix 3: Assessment Windows

No assessment windows for the statistical analysis are defined. If a subject is eligible for enrollment, diagnostic testing is performed at Visit 1.Visit 2 is a phone call from the GP to the subject within 1 week ± 4 days of Visit 1 detailing the diagnostic test results and a determination of probable BPH. Visit 3 is an Urologist assessment and should be completed within 6 weeks of Visit 1.

11.4. Appendix 4: Treatment States and Phases

There are no treatment states or phases for this study.

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Study Treatment & Sub-group Display Descriptors

There are no study treatments for this study. However, results for IPSS and BPE/BPO screening tests will be displayed using the following groupings: IPSS≥8, BPE/BPO≥3, IPSS≥8 and BPE/BPO≥3, and IPSS≥8 or BPE/BPO≥3.

11.5.2. Baseline Definition & Derivations

Baseline data are collected at Visit 1. No change from baseline values are calculated.

11.5.3. Reporting Process & Standards

Reporting Process	
Software	
• SAS software will be used for all analyses except when noted. It is anticipated that the SAS software version 9.3 will be in use at statistical analysis complete; use of a version other than 9.3 will be documented in IMMS Study File.	
Reporting Area *The following server and areas are identified as of RAP finalization. Revisions to these areas, for example due to platform / server relocation, will be documented in IMMS Study File.*	
HARP Server	US1SALX00259
HARP Area	The high level area is defined as: /arenv/arprod/gsk2285985/fdc116114/final.
QC Spreadsheet	QC process and documentation for analysis and reporting will be maintained as a text file on HARP server US1SALX00259 within above noted area.
Analysis Datasets	
• Analysis datasets will be created according to Legacy GSK A&R dataset	
Generation of RTF Files	
• RTF files will be generated for all tabular summaries with the reporting efforts described in the RAP unless clearly stated as not required by the assigned Scientific and Medical Writer(s).	

Reporting Standards
General
The current GSK Integrated Data Standards Library (IDSL) and GSK IDSL Statistical Principles will be applied for reporting, unless otherwise stated within RAP text or indicated in table, listing, figure shells: • 4.03 to 4.24: General Principles • 5.01 to 5.08: Principles Related to Data Listings • 6.01 to 6.11: Principles Related to Summary Tables • 7.01 to 7.13: Principles Related to Graphics From the above standards and principles as well as to be aligned with historical reporting for this

Reporting Standards	
indication, the key reporting standards to be applied are: • Within listings, numeric data will be reported at the precision collected in the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of decimal places. • Within tabular summaries, the minimum and maximum values are presented with the same number of decimal places as the raw data collected on the eCRF. The mean and percentiles (e.g. median, Q1, and Q3) are presented using one additional decimal place. The standard deviation and standard error are presented using two additional decimal places. • Continuous variables (e.g., age) will be summarized using the number of observations (n), mean, standard deviation (SD), median, minimum, and maximum. • Categorical variables will be summarized using the number of subjects (n) and percentage (%) in each category.	
Planned and Actual Time	
• Reporting for tables, figures, data listings, and formal statistical analyses: • No investigational study drug is being administered during this study, therefore, there are no protocol-defined time windows.	
Unscheduled Visits	
• There should be no unscheduled visits on this study.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

11.6. Appendix 6: Derived and Transformed Data

11.6.1. General

No investigational study drug is being administered during this study. No data are transformed.

Date of Enrollment
An Evaluable Subject is a subject that was not a screen failure and also met the IPSS and/or BPE/BPO entry criteria (IPSS ≥8 and/or BPE/BPO ≥3). The Date of Enrollment is the later of the Screening date and IPSS and BPE/BPO assessment completion dates. Study Day is calculated as the number of days from the Date of Enrollment: • Enrollment Date = Missing → Study Day = Missing • Reference Date < Enrollment Date → Study Day = Reference Date – Enrollment Date • Reference Date ≥ Enrollment Date → Study Day = Reference Date – (Enrollment Date) + 1

11.6.2. Study Population

Demographics
Age
Only year of birth is collected in the eCRF. For purposes of calculating age for a given subject, date of birth will be defined as June 30th of the corresponding year of birth. Age is calculated in terms of Screening (Visit 1) date and output as a truncated integer. Age categories include <65, ≥65, <75, ≥75 years.

Race

Race will be determined based on a subject's reported geographic ancestry as defined in the following table. Race information will not be presented for subjects who were enrolled in the study in France.

Race				
	Asian	**White**	**Other**	
Geographic Ancestry	Any combination of (restricted to the categories below only): -Asian – East Asian Heritage -Asian – Japanese Heritage -Asian – South East Asian Heritage -Asian – Central / South Asian Heritage	Any combination of (restricted to the below categories only) -White – Arabic/North African Heritage -White – White/Caucasian/European Heritage	African American/African Heritage American Indian or Alaskan Native Native Hawaiian or Other Pacific Islander	

Diagnostic Tests and Questionnaires

IPSS (total score)

IPSS (total score) = Sum of IPSS individual questions 1-7.

BPE/BPO (total score)

BPE/BPO (total score) = Sum of BPE/BPO individual questions 1-3.

11.7. Appendix 7: Premature Withdrawals & Handling of Missing Data

11.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completing Visits 1, 2, and 3. • Withdrawn subjects were not replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • Number and percent of Evaluable subjects completing the study and those withdrawing from the study, along with eCRF recorded reasons for premature withdrawals, will be summarized.

11.7.2. Handling of Missing Data

Element	Reporting Detail
General	• No investigational study drug is being administered during this study. • Subjects are not randomized or dispensed study treatment. As designed in the protocol, the number of subjects will decrease from the screening period to GP Assessment (Part I) and then again in the subsequent Urologist Assessment (Part II) either due to not qualifying for progression to the next part of the study or due to any withdrawal. • The decreases, along with planned multiple summary and analysis types, will impact and restrict the evaluable population for a given endpoint. Therefore, populations are not defined in the traditional sense. There are no ITT or Per Protocol populations in this study. The analysis population will be All Evaluable Subjects. • Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument : o These data will be indicated by the use of a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as “Not applicable” and “Not evaluable” or “Not Done” are not considered to be missing data and should be displayed as such. o Due to the design of the study and types of endpoints incorporated, ‘observed cases’ will be summarized. For the primary analyses, there will be no imputations for missing data, no imputations for missing responses within the BPE/BPO or IPSS screening tools, and no imputations for subjects withdrawing from the study or not qualifying for a subsequent part of the study.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

11.7.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of the study; in this case the study start date will be used. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of the study; in this case the study stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied.

11.7.2.2. Handling of Partial Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.
Adverse Events	• Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. o However, if this results in a date prior to Week 1 Day 1 and the event could possibly have occurred while on study from the partial information, then the Week 1 Day 1 date will be assumed to be the start date. o The AE will then be considered to start on-study (worst case). o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

11.8. Appendix 8: Adverse Event Time Periods and Special Adverse Event Definitions

Date-related derivations and transformations related to adverse events (AEs) are described below.

AE Onset Time since Enrollment
= AE Onset Date – Enrollment Date if Enrollment start date > AE onset date
= AE Onset Date – Enrollment Start Date +1 if Enrollment start date <= AE start date
= missing otherwise

AE Duration (in days) = AE Resolution Date – AE Onset Date + 1

If the AE onset date is partially missing, the timing is determined as follows:
1. If the non-missing parts of the date (either just year or year/month) are unambiguously before the start of enrollment, the AE is considered Pre-Enrollment.
2. If the non-missing parts of the date are unambiguously after Visit 3, the AE is considered post-study.
3. If #1 or #2 above cannot be assigned, then the AE is considered during the study.

For computing AE duration, partial AE start and end dates will be imputed as previously described, and events with completely unknown (missing) end dates will be censored at the latter of the following two dates: date of last clinic visit, latest AE start date. AE duration is the total number of non-overlapping days for all events per subject, and will be considered censored if any contributing event is censored.

Time to death is defined as (date of death – enrollment date +1). For subjects who do not experience death, time to death is censored at the date of last clinic visit (if missing, the subject will be censored at the enrollment start date).

Special interest adverse events, including MedDRA preferred terms (MedDRA Version 19.1) and codes, are presented below in Tables A-D:
Table A: Sexual and Breast Adverse Events of Special Interest

Table B: Prostate Cancer Adverse Events of Special Interest

Table C: Cardiovascular Adverse Events of Special Interest

Table D: Infrequent Tier 1 Adverse Events of Special Interest

Table A Sexual and Breast Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
Special Interest Event	**MedDRA Preferred Term**	**PT_Code**
Altered (Decreased) Libido	Sexual dysfunction	10040477
	Male sexual dysfunction	10057672
	Libido decreased	10024419
	Loss of libido	10024870
	Libido disorder	10061221
Impotence	Erectile dysfunction	10061461
	Organic erectile dysfunction	10052004
	Disturbance in sexual arousal	10058929
	Psychogenic erectile dysfunction	10052005
Ejaculation Disorders	Ejaculation delayed	10014325
	Ejaculation disorder	10014326
	Ejaculation failure	10014328
	Retrograde ejaculation	10038967
	Anorgasmia	10002652
	Orgasm abnormal	10031085
	Premature ejaculation	10036596
	Male orgasmic disorder	10025513
	Orgasmic sensation decreased	10052449
	Semen volume decreased	10039944
Breast Disorders	Breast hyperplasia	10006256
	Breast enlargement	10006242
	Gynaecomastia	10018800
	Nipple disorder	10029417
	Breast engorgement	10006240
	Breast swelling	10006312
	Breast pain	10006298
	Breast tenderness	10006313
	Nipple pain	10029421
	Nipple swelling	10058680
	Breast discomfort	10049872
Breast Disorders: Breast Enlargement	Breast hyperplasia	10006256
	Breast enlargement	10006242
	Gynaecomastia	10018800
	Nipple disorder	10029417
	Breast engorgement	10006240
	Breast swelling	10006312
Breast Disorders: Breast Tenderness	Breast pain	10006298
	Breast tenderness	10006313
	Nipple pain	10029421
	Nipple swelling	10058680
	Breast discomfort	10049872

Table B. Prostate Cancer Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
Special Interest Event	**MedDRA Preferred Term**	**PT_Code**
Prostate Cancer	Prostate cancer	10060862
	Prostate cancer stage 0	10036912
	Prostate cancer stage I	10036917
	Prostate cancer stage II	10036918
	Prostate cancer stage III	10036919
	Prostate cancer stage IV	10036920
	Prostate cancer recurrent	10036911
	Prostate cancer metastatic	10036909

Table C. Cardiovascular Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
Special Interest Event	**MedDRA Preferred Term**	**PT_Code**
Acute Coronary Syndrome	Acute myocardial infarction	10000891
	Myocardial infarction	10028596
	Silent myocardial infarction	10049768
	Sudden cardiac death	10049418
	Angina unstable	10002388
	Cardiac arrest	10007515
	Cardio-respiratory arrest	10007617
	Cardiac death	10049993
	Acute coronary syndrome	10051592
Ischemic Cerebrovascular Events	Cerebrovascular accident	10008190
	Transient ischemic attack	10044390
	Cerebral infarction	10008118
	Cerebrovascular disorder	10008196
	Cerebral artery embolism	10008088
	Cerebral artery occlusion	10008089
	Cerebral artery thrombosis	10008092
	Ischemic stroke	10061256
	Cerebral circulatory failure	10008097
	Cerebellar infarction	10008034
	Thalamic infarction	10064961
	Reversible ischemic neurologic deficit	10050496
	Thrombotic stroke	10043647
	Embolic stroke	10014498
	Vertebral artery occlusion	10048965
	Carotid arterial embolus	10007684
	Carotid artery occlusion	10048964
	Carotid artery stenosis	10007687
	Carotid artery thrombosis	10007688
	Thrombotic cerebral infarction	10067347
	Brain stem infarction	10006147
	Embolic cerebral infarction	10060839
	Lacunar infarction	10051078
	Brain stem stroke	10068644
	Stroke in evolution	10059613
	Ischaemic cerebral infarction	10060840

Table C Cardiovascular Adverse Events of Special Interest: MedDRA Preferred Terms and Codes (continued)		
Special Interest Event	**MedDRA Preferred Term**	**PT_Code**
Cardiac Failure	Cardiac failure congestive	10007559
	Cardiac failure	10007554
	Left ventricular failure	10024119
	Cardiac failure acute	10007556
	Cardiogenic shock	10007625
	Left ventricular failure acute	10063081
	Right ventricular failure	10039163
	Right ventricular failure acute	10063082
	Ventricular failure	10060953
	Cardiopulmonary failure	10051093
	Congestive cardiomyopathy	10056370
Ischemic Coronary Artery Disorders/ Atherosclerosis	Coronary artery embolism	10011084
	Coronary artery occlusion	10011086
	Coronary artery stenosis	10011089
	Coronary artery thrombosis	10011091
	Myocardial ischemia	10028600
	Coronary artery disease	10011078
	Arteriosclerosis coronary artery	10003211
Cardiac Arrhythmias	Ventricular extrasystoles	10047289
	Torsade de Pointes	10044066
	Ventricular fibrillation	10047290
	Cardiac Fibrillation	10061592
	Pulseless electrical activity	10058151
	Ventricular asystole	10047284
	Long QT syndrome	10024803
	Ventricular tachycardia	10047302
	Ventricular Arrhythmia	10047281
	Ventricular flutter	10047294
Peripheral Vascular Disease	Deep Vein Thrombosis	10051055

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
Special Interest Event	**MedDRA Preferred Term**	**PT_Code**
Relevant for dutasteride:		
Allergic reactions	Anaphylactic reaction	10002198
	Anaphylactic shock	10002199
	Anaphylactic transfusion reaction	10067113
	Anaphylactoid reaction	10002216
	Anaphylactoid shock	10063119
	Circulatory collapse	10009192
	Kounis syndrome	10069167
	Shock	10040560
	Type I hypersensitivity	10045240
	Allergic oedema	10060934
	Angioedema	10002424
	Circumoral oedema	10052250
	Conjunctival oedema	10010726
	Corneal oedema	10011033
	Epiglottic oedema	10015029
	Eye oedema	10052139
	Eye swelling	10015967
	Eyelid oedema	10015993
	Face oedema	10016029
	Gingival oedema	10049305
	Gingival swelling	10018291
	Gleich's syndrome	10066837
	Hereditary angioedema	10019860
	Idiopathic angioedema	10073257
	Idiopathic urticaria	10021247
	Laryngeal oedema	10023845
	Laryngotracheal oedema	10023893
	Limbal swelling	10070492
	Lip oedema	10024558
	Lip swelling	10024570
	Mouth Swelling	10075203
	Oculorespiratory syndrome	10067317
	Oedema mouth	10030110
	Oropharyngeal swelling	10031118
	Palatal oedema	10056998
	Palatal swelling	10074403
	Periorbital oedema	10034545
	Pharyngeal oedema	10034829
	Scleral oedema	10057431
	Swelling face	10042682
	Swollen tongue	10042727
	Tongue oedema	10043967
	Tracheal oedema	10044296
	Urticaria	10046735
	Urticaria cholinergic	10046740
	Urticaria chronic	10052568
	Urticaria papular	10046750
	Acquired epidermolysis bullosa	10056508
	Blister	10005191
	Blister rupture	10073385
	Bullous impetigo	10006563

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Conjunctivitis	10010741
	Corneal exfoliation	10064489
	Drug eruption	10013687
	Epidermolysis	10053177
	Epidermolysis bullosa	10014989
	Genital ulceration	10018180
	HLA-B*1502 assay positive	10074771
	HLA-B*5801 assay positive	10074774
	Lip exfoliation	10064482
	Mouth ulceration	10028034
	Mucocutaneous ulceration	10028084
	Mucosa vesicle	10028103
	Mucosal erosion	10061297
	Mucosal exfoliation	10064486
	Mucosal necrosis	10067993
	Mucosal ulceration	10028124
	Nikolsky's sign	10029415
	Noninfective conjunctivitis	10074701
	Oral mucosal blistering	10030995
	Oral mucosal exfoliation	10064487
	Oral papule	10031010
	Oropharyngeal blistering	10067950
	Pemphigoid	10034277
	Pemphigus	10034280
	Penile exfoliation	10064485
	Skin erosion	10040840
	Skin exfoliation	10040844
	Staphylococcal scalded skin syndrome	10041929
	Stomatitis	10042128
	Tongue exfoliation	10064488
	Vaginal exfoliation	10064483
	Vaginal ulceration	10046943
	Vulval ulceration	10047768
	Vulvovaginal rash	10071588
	Vulvovaginal ulceration	10050181
	Application site pruritus	10003053
	Aquagenic pruritus	10003071
	Injection site pruritus	10022093
	Pruritus	10037087
	Pruritus genital	10037093
	Rash pruritic	10037884
	Senile pruritus	10039986
	Itching scar	10050818
	Eyelids pruritus	10051627
	Catheter site pruritus	10052270
	Pruritus generalised	10052576
	Infusion site pruritus	10053664
	Vulvovaginal pruritus	10056530
	Incision site pruritus	10059386
	Uraemic pruritus	10060875
	Pruritus allergic	10063438
	Instillation site pruritus	10063763
	Implant site pruritus	10063785

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Cholestatic pruritus	10064190
	Polymorphic eruption of pregnancy	10066100
	Vessel puncture site pruritus	10067254
	Vaccination site pruritus	10068881
	Brachioradial pruritus	10071443
	Notalgia paraesthetica	10072643
Breast Cancer	Apocrine breast carcinoma	10066206
	Invasive breast carcinoma	10075713
	Triple negative breast cancer	10075566
	Breast cancer	10006187
	Breast cancer female	10057654
	Breast cancer in situ	10006189
	Breast cancer male	10061020
	Breast cancer metastatic	10055113
	Breast cancer recurrent	10006198
	Breast cancer stage I	10006199
	Breast cancer stage II	10006200
	Breast cancer stage III	10006201
	Breast cancer stage IV	10006202
	Breast sarcoma	10068582
	Breast sarcoma metastatic	10068583
	Breast sarcoma recurrent	10068584
	Electron radiation therapy to breast	10014437
	Extended radical mastectomy	10015721
	Gamma radiation therapy to breast	10017677
	HER-2 positive breast cancer	10065430
	Inflammatory carcinoma of breast recurrent	10021977
	Inflammatory carcinoma of breast stage III	10021978
	Inflammatory carcinoma of breast stage IV	10021979
	Inflammatory carcinoma of the breast	10021980
	Intraductal papillary breast neoplasm	10073540
	Intraductal proliferative breast lesion	10073094
	Invasive ductal breast carcinoma	10073095
	Invasive lobular breast carcinoma	10073096
	Invasive papillary breast carcinoma	10073098
	Lobular breast carcinoma in situ	10073099
	Malignant nipple neoplasm	10062051
	Malignant nipple neoplasm female	10053129
	Malignant nipple neoplasm male	10053128
	Mastectomy	10026878
	Medullary carcinoma of breast	10027095
	Metaplastic breast carcinoma	10073100
	Modified radical mastectomy	10027799
	Mucinous breast carcinoma	10073101
	Neuroendocrine breast tumour	10073103
	Oestrogen receptor assay positive	10054054
	Oestrogen receptor positive breast cancer	10070577
	Paget's disease of nipple	10033364

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Photon radiation therapy to breast	10034949
	Postmastectomy lymphoedema syndrome	10036390
	Progesterone receptor assay positive	10054057
	Radical mastectomy	10037773
	Radiotherapy to breast	10062090
	Simple mastectomy	10040700
	Tubular breast carcinoma	10073104
	X-ray therapy to breast	10048199
	Antioestrogen therapy	10002816
	Breast reconstruction	10006305
	Breast neoplasm	10006279
	Nipple neoplasm	10056286
	Phyllodes tumour	10071776
	Biopsy breast abnormal	10004745
	Breast calcifications	10048782
	Breast dysplasia	10006237
	Breast prosthesis implantation	10006303
	Computerised tomogram breast abnormal	10074534
Depressed mood	Activation syndrome	10066817
	Adjustment disorder with depressed mood	10001297
	Columbia suicide severity rating scale abnormal	10075616
	Adjustment disorder with mixed anxiety and depressed mood	10001299
	Agitated depression	10001496
	Anhedonia	10002511
	Antidepressant therapy	10054976
	Childhood depression	10068631
	Decreased interest	10011971
	Depressed mood	10012374
	Depression	10012378
	Depression postoperative	10012390
	Depressive symptom	10054089
	Dysphoria	10013954
	Electroconvulsive therapy	10014404
	Feeling guilty	10049708
	Feeling of despair	10016344
	Feelings of worthlessness	10016374
	Major depression	10057840
	Menopausal depression	10067371
	Post stroke depression	10070606
	Postictal depression	10071324
	Completed suicide	10010144
	Depression suicidal	10012397
	Intentional overdose	10022523
	Intentional self-injury	10022524
	Poisoning deliberate	10036000
	Self-injurious ideation	10051154
	Suicidal behaviour	10065604

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Suicidal ideation	10042458
	Suicide attempt	10042464
Hair changes	Alopecia	10001760
	Alopecia areata	10001761
	Alopecia scarring	10001764
	Alopecia syphilitic	10001765
	Alopecia totalis	10001766
	Alopecia universalis	10001767
	Hypotrichosis	10021126
	Progeria	10036794
	Madarosis	10051235
	Follicular mucinosis	10056506
	Application site alopecia	10059046
	Androgenetic alopecia	10068168
	Satoyoshi syndrome	10070579
	Radiation alopecia	10072045
	Diffuse alopecia	10073736
	Hypertrichosis	10020864
Interference with formation of external genitalia in a male fetus	Congenital vas deferens absence	10010670
	Cryptorchism	10011498
	Epispadias	10015088
	Hypospadias	10021093
	Reproductive tract hypoplasia, male	10057858
	Testicular dysplasia	10059271
	Congenital genital malformation male	10059492
	Penoscrotal fusion	10064951
	Sertoli-cell-only syndrome	10066833
	Buried penis syndrome	10067131
	Penoscrotal transposition	10067287
	Penile torsion	10070235
Potential for decreased male fertility	Infertility tests	10021931
	pH semen	10034784
	pH semen decreased	10034786
	pH semen increased	10034788
	pH semen normal	10034790
	Red blood cells semen	10038176
	Red blood cells semen negative	10038179
	Red blood cells semen positive	10038180
	Semen liquefaction	10039931
	Semen liquefaction normal	10039933
	Semen liquefaction prolonged	10039934
	Semen liquefaction shortened	10039935
	Semen viscosity	10039936
	Semen viscosity decreased	10039938
	Semen viscosity increased	10039940
	Semen viscosity normal	10039942
	Semen volume abnormal	10039943
	Semen volume decreased	10039944
	Semen volume increased	10039946
	Semen volume normal	10039948
	Sperm analysis	10041476
	Sperm analysis abnormal	10041477
	Sperm analysis normal	10041478

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Spermatozoa abnormal	10041498
	Spermatozoa morphology	10041501
	Spermatozoa morphology abnormal	10041502
	Spermatozoa morphology normal	10041503
	Spermatozoa progressive motility abnormal	10041504
	Spermatozoa progressive motility decreased	10041506
	Spermatozoa progressive motility normal	10041507
	White blood cells semen	10047956
	White blood cells semen negative	10047959
	White blood cells semen positive	10047960
	Fructose semen decreased	10052476
	Fructose semen increased	10052477
	Prostatic fluid leukocytes increased	10053866
	Infertility tests abnormal	10062020
	Infertility tests normal	10062021
	pH semen abnormal	10062074
	Semen liquefaction abnormal	10062159
	Semen viscosity abnormal	10062160
	Semen analysis normal	10062238
	Semen analysis	10068482
	Semen analysis abnormal	10068483
	Sperm concentration decreased	10070925
	Sperm concentration increased	10070926
	Sperm concentration abnormal	10070927
	Sperm concentration normal	10070928
	Sperm concentration	10070929
	Sperm concentration zero	10070930
	Total sperm count	10070931
	Total sperm count decreased	10070932
	Infertility	10021926
	Infertility male	10021929
Testicular pain and swelling	Anorchism	10002641
	Eunuchoidism	10015532
	Hypogonadism male	10021011
	Testicular atrophy	10043298
	Testicular disorder	10043306
	Testicular failure	10043315
	Testicular failure postoperative	10043317
	Testicular failure primary	10043318
	Testicular hyperfunction	10043334
	Testicular infarction	10043337
	Testicular pain	10043345
	Testicular retraction	10043348
	Testicular swelling	10043354
	Testicular torsion	10043356
	Testicular necrosis	10049572
	Spermatic cord mass	10049792
	Testicular appendage torsion	10050476
	Spermatic cord pain	10051221

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Testicular injury	10051872
	Testicular haemorrhage	10051877
	Epididymal calculus	10052321
	Epididymal enlargement	10052322
	Epididymal tenderness	10052323
	Testis discomfort	10052531
	Monorchidism	10055002
	Epididymal disorder	10055045
	Spermatic cord disorder	10056348
	Testicular mass	10058901
	Testotoxicosis	10063654
	Spermatic cord haemorrhage	10065742
	Spermatic cord obstruction	10065805
	Spermatic cord perforation	10065806
	Spermatic cord stenosis	10065807
	Testicular perforation	10065808
	Testicular hypertrophy	10066101
	Testicular oedema	10066769
	Sperm granuloma	10067802
	Testicular microlithiasis	10067829
	Congenital monorchidism	10069505
	Testicular autoimmunity	10071574
Relevant for tamsulosin:		
Atrial fibrillation, tachycardia, arrhythmias	Arrhythmia	10003119
	Heart alternation	10058155
	Heart rate irregular	10019304
	Pacemaker generated arrhythmia	10053486
	Pacemaker syndrome	10051994
	Paroxysmal arrhythmia	10050106
	Pulseless electrical activity	10058151
	Reperfusion arrhythmia	10058156
	Withdrawal arrhythmia	10047997
	Arrhythmia supraventricular	10003130
	Atrial fibrillation	10003658
	Atrial flutter	10003662
	Atrial parasystole	10071666
	Atrial tachycardia	10003668
	Junctional ectopic tachycardia	10074640
	Sinus tachycardia	10040752
	Supraventricular extrasystoles	10042602
	Supraventricular tachyarrhythmia	10065342
	Supraventricular tachycardia	10042604
	ECG P wave inverted	10057526
	Electrocardiogram P wave abnormal	10050384
	Retrograde p-waves	10071187
	Anomalous atrioventricular excitation	10002611
	Cardiac flutter	10052840
	Extrasystoles	10015856
	Tachyarrhythmia	10049447
	Accelerated idioventricular rhythm	10049003
	Cardiac fibrillation	10061592
	Parasystole	10033929
	Rhythm idioventricular	10039111

Table D. Infrequent Tier 1 Adverse Events of Special Interest: MedDRA Preferred Terms and Codes		
	Torsade de pointes	10044066
	Ventricular arrhythmia	10047281
	Ventricular extrasystoles	10047289
	Ventricular fibrillation	10047290
	Ventricular flutter	10047294
	Ventricular parasystole	10058184
	Ventricular pre-excitation	10049761
	Ventricular tachyarrhythmia	10065341
	Ventricular tachycardia	10047302
Floppy Iris Syndrome	Floppy iris syndrome	10066373
Orthostasis	Dizziness	10013573
	Dizziness postural	10013578
	Orthostatic hypotension	10031127
	Hypotension	10021097
	Syncope	10042772
	Presyncope	10036653
	Blood pressure orthostatic abnormal	10053354
	Blood pressure orthostatic decreased	10053356
Priapism	Priapism	10036661
Stevens-Johnson syndrome	Acute generalised exanthematous pustulosis	10048799
	Cutaneous vasculitis	10011686
	Dermatitis bullous	10012441
	Dermatitis exfoliative	10012455
	Dermatitis exfoliative generalised	10012456
	Drug reaction with eosinophilia and systemic symptoms	10073508
	Epidermal necrosis	10059284
	Erythema multiforme	10015218
	Exfoliative rash	10064579
	Oculomucocutaneous syndrome	10030081
	Skin necrosis	10040893
	Stevens-Johnson syndrome	10042033
	Toxic epidermal necrolysis	10044223
	Toxic skin eruption	10057970

11.9. Appendix 9: Values of Potential Clinical Importance

11.9.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (> x)**
Prostate Specific Antigen (PSA)	Ng/mL	NA	Not Applicable	9.9

Urinalysis			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
Urine Dipstick	NA	Pos / Neg	Not Applicable
Urine Glucose (dipstick)	NA	Pos / Neg	Not Applicable
Urine Microscopy – Red Blood Cells	NA	Pos / Neg	Not Applicable
Urine Leukocyte Esterase test for detecting WBC (dipstick)	NA	Pos / Neg	Not Applicable
Urine Protein (dipstick)	NA	Pos / Neg	Not Applicable

11.10. Appendix 10: Multicenter Studies

11.10.1. Methods for Handling Centers

- The countries participating in this trial include: Russia, Germany, Italy, France, and Spain.
- In this multicentre study, enrollment will be presented by country, and separately by country and center.

11.11. Appendix 11: Examination of Covariates, Subgroups & Other Strata

11.11.1. Subgroups

- Covariates and Other Strata will not be used to perform the analysis.
- The following subgroups may be used in descriptive summaries and statistical analyses:
  - Country
  - Center

11.12. Appendix 12: Multiple Comparisons & Multiplicity

11.12.1. Handling of Multiple Comparisons & Multiplicity

All pre-planned summary statistics results will be presented. There are no established controls for interpretation of the multiple outputs.

11.13. Appendix 13: Model Checking and Diagnostics for Statistical Analyses

No models were used during the statistical analysis; only proportions and confidence intervals were calculated.

11.14. Appendix 14: Abbreviations and Trademarks

11.14.1. Abbreviations

AE	Adverse Event
BPH	Benign prostatic hyperplasia
BPE	Benign prostatic enlargement
BPO	Benign prostatic obstruction
CSR	Clinical Study Report
eCRF	Electronic case report form
DRE	Digital rectal examination
GSK	GlaxoSmithKline
GP	General Practitioner
IPSS	International Prostate Symptom Score (Version 2), I-PSS2
MedDRA	Medical Dictionary for Regulatory Activities
PD	Pharmacodynamic
PK	Pharmacokinetic
PSA	Prostate specific antigen
RAP	Reporting and analysis plan
SAE	Serious adverse event

11.14.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS

11.15. Appendix 15: List of Data Displays

11.15.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.29	NA
Efficacy	2.1 to 2.54	2.1 to 2.3
Safety	3.1 to 3.31	NA
Section	**Listings**	
ICH Listings	1.3-1.7, 1.10-1.11, 2.1, 2.3, 3.2-3.9	
Other Listings	1.1-1.2, 1.8-1.9, 2.2, 3.1, 3.10-3.12	

11.15.2. Study Population Tables

Study Population Tables		
No	**Population**	**Title**
Population: All Screened Subjects		
1.1.	All Screened Subjects	Summary of Subject Accountability for Screened Subjects
1.2.	All Screened Subjects	Summary of Screened Subjects by Country
1.3.	All Screened Subjects	Summary of Screened Subjects by Country and Center
Population: Screened But Not Evaluable Subjects		
1.4.	Screened But Not Evaluable Subjects	Summary of Demographic Characteristics for Subjects Who Were Screened But Not Evaluable
1.5.	Screened But Not Evaluable Subjects	Summary of Inclusion/Exclusion Criteria Deviations for Subjects Who Were Screened But Not Evaluable
Population: All Evaluable Subjects		
1.6.	All Evaluable Subjects	Summary of Subject Accountability for Evaluable Subjects
1.7.	All Evaluable Subjects	Summary of Subject Accountability for Evaluable Subjects by Country
1.8.	All Evaluable Subjects	Summary of Subject Accountability for Evaluable Subjects by Country and Center
1.9.	All Evaluable Subjects	Summary of Evaluable Subjects by Country
1.10.	All Evaluable Subjects	Summary of Evaluable Subjects by Country and Center
1.11.	All Evaluable Subjects	Summary of Subject Disposition
1.12.	All Evaluable Subjects	Summary of Subject Discontinuation by Visit
1.13.	All Evaluable Subjects	Summary of Primary Reason for Study Withdrawal, by Period of Discontinuation
1.14.	All Evaluable Subjects	Summary of Important Protocol Deviations for Evaluable Subjects
1.15.	All Evaluable Subjects	Summary of Demographic Characteristics for Evaluable Subjects
1.16.	All Evaluable Subjects	Summary of Demographic Characteristics for Evaluable Subjects by Country
1.17.	All Evaluable Subjects	Summary of Demographic Characteristics for Evaluable Subjects by Country and Center
1.18.	All Evaluable Subjects	Summary of Race
1.19.	All Evaluable Subjects	Summary of Race by Country
1.20.	All Evaluable Subjects	Summary of Race by Country and Center
1.21.	All Evaluable Subjects	Summary of PSA Values at Visit 1
1.22.	All Evaluable Subjects	Summary of PSA Values at Visit 1 by Country
1.23.	All Evaluable Subjects	Summary of PSA Values at Visit 1 by Country and Center
1.24.	All Evaluable Subjects	Summary of BPE/BPO and IPSS at Visit 1
1.25.	All Evaluable Subjects	Summary of BPE/BPO and IPSS at Visit 1 by Country
1.26.	All Evaluable Subjects	Summary of BPE/BPO and IPSS at Visit 1 by Country and Center
1.27.	All Evaluable Subjects	Summary of Specific Medical Conditions at Screening

Study Population Tables		
No	**Population**	**Title**
1.28.	All Evaluable Subjects	Summary of Surgical/Diagnostic Procedures
1.29.	All Evaluable Subjects	Summary of Concomitant Medications

11.15.3. Efficacy Tables

Efficacy: Tables		
No	**Population**	**Title**
Population: All Screened Subjects		
2.1.	All Screened Subjects	Summary of Agreement Between BPE/BPO and IPSS Screening Tools
2.2.	All Screened Subjects	Summary of Agreement Between BPE/BPO and IPSS Screening Tools by Country
2.3.	All Screened Subjects	Summary of Agreement Between BPE/BPO and IPSS Screening Tools by Country and Center
Population: All Evaluable Subjects		
2.4.	All Evaluable Subjects	Summary of IPSS Scores at Visit 1 by Subgroup
2.5.	All Evaluable Subjects	Summary of IPSS Scores at Visit 1 by Country and Subgroup
2.6.	All Evaluable Subjects	Summary of IPSS Scores at Visit 1 by Country, Center, and Subgroup
2.7.	All Evaluable Subjects	Summary of BPH-Related Health Status at Visit 1 (IPSS Question 8)
2.8.	All Evaluable Subjects	Summary of BPH-Related Health Status at Visit 1 (IPSS Question 8) by Country
2.9.	All Evaluable Subjects	Summary of BPH-Related Health Status at Visit 1 (IPSS Question 8) by Country and Center
2.10.	All Evaluable Subjects	Summary of BPE/BPO Scores at Visit 1 by Subgroup
2.11.	All Evaluable Subjects	Summary of BPE/BPO Scores at Visit 1 by Country and Subgroup
2.12.	All Evaluable Subjects	Summary of BPE/BPO Scores at Visit 1 by Country, Center, and Subgroup
2.13.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon BPE/BPO Score (≥3)
2.14.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon BPE/BPO Score (≥3) by Country
2.15.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon BPE/BPO Score (≥3) by Country and Center
2.16.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8)
2.17.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) by Country
2.18.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) by Country and Center
2.19.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3)
2.20.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3) by Country
2.21.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3) by Country and Center
2.22.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3)

Efficacy: Tables		
No	**Population**	**Title**
2.23.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3) by Country
2.24.	All Evaluable Subjects	Summary of BPH Diagnosis by Urologist Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3) by Country and Center
2.25.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon BPE/BPO Score (≥3)
2.26.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon BPE/BPO Score (≥3) by Country
2.27.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon BPE/BPO Score (≥3) by Country and Center
2.28.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8)
2.29.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) by Country
2.30.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) by Country and Center
2.31.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3)
2.32.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3) by Country
2.33.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3) by Country and Center
2.34.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3)
2.35.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3) by Country
2.36.	All Evaluable Subjects	Summary of BPH Progression Risk by Urologist Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3) by Country and Center
2.37.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon BPE/BPO Score (≥3)
2.38.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon BPE/BPO Score (≥3) by Country
2.39.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon BPE/BPO Score (≥3) by Country and Center
2.40.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8)
2.41.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) by Country
2.42.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) by Country and Center
2.43.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3)

Efficacy: Tables		
No	**Population**	**Title**
2.44.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3) by Country
2.45.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) or BPE/BPO Score (≥3) by Country and Center
2.46.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3)
2.47.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3) by Country
2.48.	All Evaluable Subjects	Summary of Probable BPH Diagnosis by GP Based Upon IPSS Score (≥8) and BPE/BPO Score (≥3) by Country and Center
2.49.	All Evaluable Subjects	Summary of Subjects Who Discontinued From the Study Before the GP Was Able to Assess the Presence of Probable BPH
2.50.	All Evaluable Subjects	Summary of Subjects Who Discontinued From the Study Before the GP Was Able to Assess the Presence of Probable BPH by Country
2.51.	All Evaluable Subjects	Summary of Subjects Who Discontinued From the Study Before the GP Was Able to Assess the Presence of Probable BPH by Country and Center
2.52.	All Evaluable Subjects	Summary of Subjects Who Withdrew From the Study Before a Urologist Visit, Among Subjects Who Were Eligible for Such a Visit
2.53.	All Evaluable Subjects	Summary of Subjects Who Withdrew From the Study Before a Urologist Visit, Among Subjects Who Were Eligible for Such a Visit by Country
2.54.	All Evaluable Subjects	Summary of Subjects Who Withdrew From the Study Before a Urologist Visit, Among Subjects Who Were Eligible for Such a Visit by Country and Center

11.15.4. Efficacy Figures

Efficacy: Figures		
No	**Population**	**Title**
Population: All Evaluable Subjects		
2.1.	All Evaluable Subjects	Plot of IPSS Scores Versus BPE/BPO Scores at Visit 1 for All Evaluable Subjects
2.2.	All Evaluable Subjects	Plot of IPSS Scores Versus PSA Values at Visit 1 for All Evaluable Subjects
2.3.	All Evaluable Subjects	Plot of BPE/BPO Scores Versus PSA Values at Visit 1 for All Evaluable Subjects

11.15.5. Safety Tables

Safety : Tables		
No	**Population**	**Title**
Population: All Evaluable Subjects		
3.1.	All Evaluable Subjects	Summary of Adverse Events by Type Starting Post-Enrollment
3.2.	All Evaluable Subjects	Summary of Adverse Events Starting Post-Enrollment
3.3.	All Evaluable Subjects	Summary of Non-Serious Adverse Events Starting Post-Enrollment
3.4.	All Evaluable Subjects	Summary of Adverse Events Starting Post-Enrollment by Age Group (<65, ≥65)
3.5.	All Evaluable Subjects	Summary of Adverse Events Starting Post-Enrollment by Age Group (<75, ≥75)
3.6.	All Evaluable Subjects	Summary of Adverse Events Starting Post-Enrollment by Country
3.7.	All Evaluable Subjects	Summary of Adverse Events Starting Post-Enrollment by Country and Center
3.8.	All Evaluable Subjects	Summary of Adverse Events Starting post-Enrollment by Maximum Intensity
3.9.	All Evaluable Subjects	Summary of Most Common Adverse Events Starting Post-Enrollment
3.10.	All Evaluable Subjects	Summary of Most Common Non-Serious Adverse Events Starting Post-Enrollment
3.11.	All Evaluable Subjects	Summary of Serious Adverse Events Starting Post-Enrollment
3.12.	All Evaluable Subjects	Summary of Serious Adverse Events Starting Post-Enrollment by Age Group (<65, ≥65)
3.13.	All Evaluable Subjects	Summary of Serious Adverse Events Starting Post-Enrollment by Age Group (<75, ≥75)
3.14.	All Evaluable Subjects	Summary of Serious Adverse Events Starting Post-Enrollment by Country
3.15.	All Evaluable Subjects	Summary of Serious Adverse Events Starting Post-Enrollment by Country and Center
3.16.	All Evaluable Subjects	Summary of Fatal Adverse Events Starting Post-Enrollment
3.17.	All Evaluable Subjects	Summary of Adverse Events Starting Post-Enrollment Leading to Withdrawal From the Study
3.18.	All Evaluable Subjects	Summary of Serious Adverse Events Starting Post-Enrollment Leading to Withdrawal From the Study
3.19.	All Evaluable Subjects	Summary of Sexual and Breast Adverse Events of Special Interest Starting Post-Enrollment
3.20.	All Evaluable Subjects	Summary of Special Interest Adverse Events Starting Post-Enrollment: Prostate Cancer
3.21.	All Evaluable Subjects	Summary of Cardiovascular Adverse Events of Special Interest Starting Post-Enrollment
3.22.	All Evaluable Subjects	Summary of Infrequent Tier I Special Interest Adverse Events Starting Post-Enrollment
3.23.	All Evaluable Subjects	Summary of PSA (ng/mL) at Visit 1 by Subgroup

Safety : Tables		
No	**Population**	**Title**
3.24.	All Evaluable Subjects	Summary of PSA (ng/mL) at Visit 1 by Country and Subgroup
3.25.	All Evaluable Subjects	Summary of PSA (ng/mL) at Visit 1 by Country, Center, and Subgroup
3.26.	All Evaluable Subjects	Summary of Laboratory Data at Visit 1
3.27.	All Evaluable Subjects	Summary of Laboratory Data at Visit 1 by Country
3.28.	All Evaluable Subjects	Summary of Laboratory Data at Visit 1 by Country and Center
3.29.	All Evaluable Subjects	Summary of Digital Rectal Examination
3.30.	All Evaluable Subjects	Summary of Digital Rectal Examination by Country
3.31.	All Evaluable Subjects	Summary of Digital Rectal Examination by Country and Center

11.15.6. ICH Listings

The following categorizes data listings as ICH (International Conference on Harmonization) used to support critical analyses or non-ICH. The two classifications are assigned with consideration for general regulatory requirements across countries at point of RAP finalization. Changes to these classifications may occur at point of reporting as a result of specific country requirements or requests and will not result in a RAP revision.

ICH and Non-ICH Listings			
ICH	**Non-ICH**	**Study Population**	**Title**
	1.1	Screened But Not Evaluable	Listing of Demographic Characteristics for Subjects Who Were Screened But Not Evaluable
	1.2	Screened But Not Evaluable	Listing of Subjects With Inclusion/Exclusion Criteria Deviations Who Were Screened But Not Evaluable
1.3		All Evaluable Subjects	Listing of Subject Accountability
1.4		All Evaluable Subjects	Listing of Reasons for Study Withdrawal
1.5		All Evaluable Subjects	Listing of Important Protocol Deviations for Evaluable Subjects
1.6		All Evaluable Subjects	Listing of Demographic Characteristics for Evaluable Subjects
1.7		All Evaluable Subjects	Listing of Race Details
	1.8	All Evaluable Subjects	Listing of Specific Medical Conditions at Screening
	1.9	All Evaluable Subjects	Listing of Surgical/Diagnostic Procedures
1.10		All Evaluable Subjects	Listing of Concomitant Medications
1.11		All Evaluable Subjects	Listing of Relationship Between ATC Level 1, Ingredient, and Verbatim Text
2.1		All Evaluable Subjects	Listing of IPSS
	2.2	All Evaluable Subjects	Listing of BPH-Related Health Status
2.3		All Evaluable Subjects	Listing of BPE/BPO
	3.1	Screened But Not Evaluable Subjects	Listing of All Adverse Events for Screened But Not Evaluable Subjects
3.2		All Evaluable Subjects	Listing of All Adverse Events for Evaluable Subjects
3.3		All Evaluable Subjects	Listing of Relationship Between System Organ Class and Verbatim Text
3.4		All Evaluable Subjects	Listing of Subject Numbers for Specific Adverse Events
3.5		All Evaluable Subjects	Listing of Fatal Adverse Events
3.6		All Evaluable Subjects	Listing of Non-Fatal Serious Adverse Events
3.7		All Evaluable Subjects	Listing of Adverse Events Leading to Withdrawal From the Study
3.8		All Evaluable Subjects	Listing of Relationship Between Special Interest Adverse Events and Verbatim Text
3.9		All Evaluable Subjects	Listing of Adverse Events of Special Interest
	3.10	All Evaluable Subjects	Listing of PSA (ng/mL) Values
	3.11	All Evaluable Subjects	Listing of Urine Dipstick and Urinalysis Data
	3.12	All Evaluable Subjects	Listing of Digital Rectal Examination Data

11.16. Appendix 16: Example Mock Shells for Data Displays

Filed separately in IMMS.

11.17. Appendix 17: Amendment 01 Revision

Item	RAP Revision General Description	RAP Section
01	Indicate RAP "Amendment Number 01" with administrative details including revision number, copyright year, effective date, description, author, and approver.	-Cover page -Document header -Section 1: Key Elements of the RAP -Section 2.1: Changes to the Protocol Defined Statistical Analysis Plan
02	Redefine the Analysis Populations as follows: Previous: Screened But Not Enrolled Population – Comprised of all subjects who are screened for eligibility but who do not meet the entry criteria. Current: Screened But Not Evaluable Population - Comprised of all subjects who are screened for eligibility, but do not qualify for the Evaluable Population. Previous: Enrolled Population - Comprised of all subjects who meet the entry criteria, including a positive IPSS screening result (score ≥8) and/or a positive BPE/BPO screening result (score ≥3). Current: Evaluable Population - Comprised of all subjects who meet the entry criteria, including a positive IPSS screening result (score ≥8) and/or a positive BPE/BPO screening result (score ≥3). Note: the population definition did not change for the Enrolled/Evaluable Population.	-Section 1: Key Elements of the RAP -Analysis Populations -Section 4: Analysis Populations
03	Remove the following text: Number of subjects who were incorrectly enrolled with IPSS<8 and BPE/BPO<3. This bullet point is no longer needed in this section. This group of subjects will no longer need to appear on the Summary Table for Screened subjects since they will be included with the Number of Screened But Not Evaluable subjects.	-Section 6.2: Subject Accountability
04	Update the names of the study populations as follows: Screened But Not Enrolled Population is changed to the Screened But Not Evaluable Population Enrolled Population is changed to the Evaluable Population.	-Section 4.1.1: Inclusion / Exclusion Criteria Deviations -Section 4.1.2: Important Protocol Deviations -Section 6.1: Overview of Planned Analyses -Table 2: Overview of Planned Study Population analyses

		-Section 6.2: Subject Accountability -Section 6.3: Subject Disposition -Section 6.4: Demographic Characteristics -Section 6.5: Medical Conditions, Surgical procedures, and Concomitant Medications -Section 7.1.1: Overview of Planned primary Efficacy Analyses -Section 8.1.1 and Table 4: Overview of Planned Secondary Efficacy Analyses -Section 8.1.2.1: IPSS Screening Tool -Section 8.1.2.3: BPE/BPO Screening Tool -Section 8.2.1: Overview of Planned Analyses -Section 8.2.2: Adverse Events -Section 8.2.5: Clinical Laboratory Assessments -Section 8.2.6: Serum PSA -Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population -Section 11.1.1: Exclusions from Per Protocol Population -Appendix 6: Derived and Transformed Data -Section 11.6.1 General (Date of Enrollment) -Appendix 7: Premature Withdrawals and Handling of Missing Data -Section 11.7.1: Premature Withdrawals -Section 11.7.2 Handling of Missing Data -Appendix 15: List of Data Displays -Section 11.15.2: Study Population Tables -Section 11.15.3: Efficacy Tables -Section 11.15.4: Efficacy Figures -Section 11.15.5: Safety Tables -Section 11.15.6: ICH Listings
05	Revise title of Table 1.4 – Table 1.10, Table 1.14 – Table 1.17 Revise title of Figure 2.1 – Figure 2.3 Revise title of Listing 1.1 – Listing 1.2, Listing 1.5 –	-Appendix 15: List of Data Displays -Section 11.15.2: Study Population Tables -Section 11.15.4: Efficacy Figures -Section 11.15.6: ICH Listings

	Listing 1.6, Listing 3.1 – Listing 3.2 Screened But Not Enrolled Population is changed to the Screened But Not Evaluable Population Enrolled Population is changed to the Evaluable Population.	