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Statistical Analysis Plan

Zenith Epigenetics Ltd.

ZEN003694-002

A Phase 1b Safety and Tolerability Study of ZEN003694 in Combination with Enzalutamide or Abiraterone in Patients with Metastatic Castration-Resistant Prostate Cancer

Protocol Version: 05 November 2018 (Amendment 10)

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2.0	27 JAN 2020

Approval

Upon review of this document, including table, listing, and figure shells, the undersigned approves the Statistical Analysis Plan. The analysis methods and data presentation are acceptable.

Signature	Date
[redacted]	[redacted]
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LIST OF ABBREVIATIONS

ADaM	Analysis data model
AE	Adverse event
ARSI	Androgen receptor signaling inhibitor
ATC	Anatomical Therapeutic Chemical
$AUC_{0\text{-inf}}$	Area under the curve, from time zero to infinity with a quantifiable level of drug
$AUC_{0\text{-last}}$	Area under the curve, from time zero to last time point with a quantifiable level of drug
BET	Bromodomain and extra-terminal domain
BMI	Body mass index
C_{max}	Maximum plasma concentration
C_{min}	Minimum or trough concentration
CR	Complete response
CRF	Case report form
CSR	Clinical study report
Css	Concentration steady-state
CTC	Circulating tumor cell(s)
CTCAE	Common Terminology Criteria for Adverse Events
ctDNA	circulating tumor DNA
DC cohort	Dose confirmation group
DE cohort	Dose escalation group
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
ICH	International Council for Harmonisation
INR	International normalized ratio
mCRPC	Metastatic castration-resistant prostate cancer
MedDRA	Medical Dictionary for Regulatory Activities
mRNA	Messenger ribonucleic acid
MTD	Maximum tolerated dose
MUGA	Multigated acquisition (scan)
MYC	V-Myc avian myelocytomatosis viral oncogene homolog
NE	Not evaluable

OCT	Optical coherence tomography
PCWG2	Prostate Cancer Working Group 2
PD	Progressive disease
PFS	Progression-free survival
PK	Pharmacokinetic(s)
PR	Partial response
PSA	Prostate-specific antigen
QTc	Corrected QT interval
QTcF	Corrected QT interval according to Fridericia formula
RECIST	Response Evaluation Criteria in Solid tumors
rPFS	Radiographic progression-free survival
RTF	Rich text format
SAP	Statistical analysis plan
SD	Stable disease
$t_{1/2}$	Half-life
TEAE	Treatment-emergent adverse event
TLFs	Tables, listings, and figures
T_{max}	Time to reach maximum plasma concentration
WHO	World Health Organization

DEFINITIONS

Adverse Event	An adverse event (AE) is any reaction, side effect, or other untoward event, regardless of relationship to study drug, which occurs anytime during or after the patient's first exposure to study drug. For an event to be recorded as an AE, the onset must occur during or after the patient's first exposure to study drug and no later than 30 days after the last study drug dose.
PSA Evaluable Population	Patients who receive at least 1 dose of ZEN003694, have a non-missing baseline prostate-specific antigen (PSA), and have at least 1 nonmissing postbaseline PSA assessment or who discontinue study treatment due to disease progression or death.
Radiographic Evaluable Population	Patients who receive at least 1 dose of ZEN003694, have a nonmissing baseline and have at least 1 evaluable postbaseline radiographic assessment or who discontinue study treatment due to disease progression or death.
Safety Population	Patients who receive at least 1 dose of ZEN003694.
CTC Evaluable Population	Patients who receive at least 1 dose of ZEN003694, have a nonmissing baseline and at least 1 evaluable post-baseline circulating tumor cell (CTC) collection.
Serious AE	An AE occurring at any dose that results in death; is a life-threatening experience; requires inpatient hospitalization or prolongation of an existing hospitalization; results in a persistent or significant disability/incapacity; or is a congenital anomaly/birth defect in the offspring of a patient who received study drug; is any other important medical event; other AEs, based on appropriate medical judgment, that may jeopardize the patient and may require medical or surgical intervention to prevent a serious outcome.
Treatment-Emergent AE	AEs with an onset time after the initial dose of ZEN003694.

Tumor Burden	High tumor burden defined as 1 or more of: visceral metastases, sum of target lesions ≥30mm, ≥10 bone lesions. Low tumor burden is everyone else.

1. INTRODUCTION

This document outlines the statistical methods to be implemented during the analyses of data collected within the scope of Zenith Epigenetics Ltd. Protocol ZEN003694-002, "A Phase 1b Safety and Tolerability Study of ZEN003694 in Combination with Enzalutamide or Abiraterone in Patients with Metastatic Castration-Resistant Prostate Cancer." The purpose of this plan is to provide specific guidelines from which the statistical analyses will proceed. Any deviations from this plan will be documented in the clinical study report (CSR).

2. STUDY DOCUMENTS

The following study documents were used for the preparation of the statistical analysis plan (SAP):

- Protocol Version 10, 05NOV2018

  On 11APR2019, Zenith informed all study sites that they no longer plan to move forward with the abiraterone combination of the Zenith metastatic castration-resistant prostate cancer (mCRPC) study, ZEN003694-002, Part 2. Part 2 will be postponed indefinitely. Therefore, this SAP includes the statistical methods for Part 1 of the study only.
- Annotated electronic case report form (eCRF) version 12, 14MAY2019
- Data management plan version 1, 29APR2016

3. STUDY OBJECTIVES

3.1 Primary Objective

- To determine the safety, tolerability, and maximum tolerated dose (MTD) of ZEN03694 in combination with enzalutamide in patients with mCRPC who have progressed during prior treatment with enzalutamide or apalutamide (Cohort DE-A) or with abiraterone (Cohort DE-B) by Prostate Cancer Working Group 2 (PCWG2) criteria 2007 (Scher 2008) (dose escalation).
- To confirm the safety and tolerability of the MTD and recommended Phase 2 dose of ZEN003694 in combination with enzalutamide in the following two cohorts of patients with mCRPC (dose confirmation):
  - Cohort DC-A: Patients with prior progression on enzalutamide or apalutamide by PCWG2 criteria who are currently or will be receiving a stable dose of enzalutamide
  - Cohort DC-B: Patients who are enzalutamide-naïve and apalutamide-naïve with prior progression on abiraterone by PCWG2 criteria

3.2 Secondary Objective

- To determine the pharmacokinetics (PK) of ZEN003694 and the PK of enzalutamide along with their primary active metabolites when administered in combination
- To evaluate the preliminary clinical activity of ZEN003694 in combination with enzalutamide as applicable:
    - Prostate-specific antigen (PSA) response rate by PCWG2 criteria
    - Radiographic response rate by PCWG2 criteria
    - Median radiographic progression-free survival (rPFS) by PCWG2 criteria
    - Median progression-free survival (PFS) by PCWG2 criteria
    - Circulating tumor cell (CTC) response rate (dose confirmation only)

3.3 Exploratory Objectives

- To explore pharmacodynamics, prognostic and/or predictive biomarkers of ZEN003694 in combination with enzalutamide in whole blood, plasma and tumor samples in the dose escalation phase and/or dose confirmation phase as follows:
    - Possible relationship of baseline tumor abnormalities (such as mutations, translocations, messenger ribonucleic acid (mRNA), protein expression and localization), in circulating tumor DNA (ctDNA), CTC and tumor biopsies and/or on-treatment changes with any observed antitumor activity
- To explore the effects of ZEN003694 on immuno-oncology markers in tumor tissue and peripheral blood mononuclear cells

4. STUDY DESIGN AND PLAN

This study is an open-label, nonrandomized, Phase 1 dose-escalation/dose-confirmation study of ZEN003694 in combination with enzalutamide in patients with mCRPC.

A standard 3+3 cohort design will be utilized. Cohorts of up to 6 patients will be enrolled at each dose level, and each patient will participate in only 1 cohort. Each cycle will be 28 days in duration. Up to 10 sites in the United States will be used to enroll patients. Approximately 40 patients will be enrolled in the dose escalation phase and up to 40 patients will be enrolled in the dose confirmation phase for a total of 80 evaluable patients.

Dose Escalation

For patients who have progressed on abiraterone (Cohort DE-B), enzalutamide will be administered orally as a single agent daily for 14 days before the initiation of the combination therapy (Lead-in) to reach enzalutamide steady-state concentration (Css) during Cycle 1. After the Lead-in, if applicable, ZEN003694 will be administered orally in combination with daily

enzalutamide for 28-day cycles. Patients who are progressing on enzalutamide or apalutamide (Cohort DE-A, Sub-arm A1) and who are currently receiving a stable dose of enzalutamide will continue to receive enzalutamide in combination with ZEN003694, if eligibility criteria are met. Patients in Cohort DE-A who are currently receiving enzalutamide or apalutamide or are currently taking apalutamide (Cohort DE-A, Sub-arm A2) will be administered enzalutamide orally once daily for 14 days prior to the initiation of the combination therapy (Lead-in) to reach enzalutamide Css during Cycle 1.

After the Lead-in, ZEN003694 will be administered orally in combination with daily enzalutamide for 28-day cycles. The first patient at each dose level will be treated with ZEN003694 for one week before the second patient at the same dose level is allowed to receive their first dose of ZEN003694. Patients at each dose level will be treated (for 28 days) and observed through the end of the first cycle before treatment of patients at the next higher dose level can begin. In unusual circumstances, (e.g., if there is 1 slot remaining to fill a cohort and 2 prospective enrollees are being screened and qualify simultaneously) the sponsor may allow an extra subject to enter a cohort, although the same rules for determining MTD will apply.

ZEN003694-related adverse events (AEs) for determination of DLTs will be assessed for each patient during the 28 days of Cycle 1. The most common AEs for enzalutamide are well-known. As such, the Investigator should to the best of his/her ability assess the relatedness of an AE observed as attributable to enzalutamide or ZEN003694 alone, or if unable to do so, as attributable to the combination of enzalutamide and ZEN003694.

Dose escalation will continue after all patients enrolled within a cohort have completed the 28-day Cycle 1 DLT observation period with either 0 of 3 patients, or no more than 1 out of 6 patients in a cohort experiencing a DLT, with the proviso that dose escalation to MTD may be waived in Part 2. Dose escalation decisions will be made based on clinical safety and (when available) PK data (maximum or peak concentration [Cmax] and AUC) after review by the Cohort Review Committee (CRC), consisting of all Investigators and the Zenith Medical Monitor. If a DLT is observed in 1 of 3 patients in a cohort and confirmed by the CRC, 3 additional patients will be enrolled into that cohort. If 1 of 6 patients in a cohort experiences a DLT, then dose escalation may continue in the next cohort or the MTD of the combination can be declared. If ≥2 of 3 to 6 patients experience DLTs within a cohort, then the MTD will be considered to have been exceeded and further dose escalation will cease. In this case, if fewer than 6 patients have been enrolled at the previous dose level, that cohort will be expanded to 6 patients to confirm the MTD. Should the MTD of the combination be exceeded at Dose Level 1, a cohort may be explored with a reduced dose of ZEN003694 or enzalutamide at the discretion of the CRC. Cohort management is summarized below.

Dose-limiting Toxicity and Cohort Management

Number of Patients with Dose-limiting Toxicity	Action
1 of 1	Add 5 more patients
0 of 3	Proceed to next dose level

1 of 3	Add 3 more patients
1 of 6	Proceed to next dose level
≥2 of 3 or ≥2 of 6	Add 3 more patients in the next lower dose level if only 3 patients were treated in the next lower dose. If 6 patients were treated at the next lower dose level and no more than one patient had DLT, then the next lower

Enzalutamide is a strong inducer of CYP3A4. Treatment with enzalutamide reduces the Cmax and AUC of the sensitive CYP3A4 substrate midazolam approximately 7- and 4-fold, respectively. ZEN003694 is also a CYP3A4 substrate and therefore the levels of ZEN003694 may be substantially lower when administrated to patients treated with enzalutamide due to increased clearance of ZEN003694 compared to ZEN003694 treatment alone. Enrollment in this study with ZEN003694 in combination with enzalutamide will commence with 36 mg as the starting dose for ZEN003694 and 160 mg dose of enzalutamide (or at a lower stable dose for patients in DE-A or DC-A). The dose of enzalutamide will be held constant through Cycle 1 of the Dose Escalation. After Cycle 1, the dose of enzalutamide may be modified for toxicity per the XTANDI® Package Insert. Due to the possible higher clearance of ZEN003694 during co-administration with enzalutamide, higher doses of ZEN003694 may be needed to achieve sufficient ZEN003694 exposure with the combination treatment than with ZEN003694 alone. If enzalutamide dose is reduced at any time after Cycle 1, PK samples are to be obtained 28 Days (±7 Days) following dose modification. Dose escalation of ZEN003694 in this study will proceed as follows unless intervening toxicity is observed.

Dose Level	**ZEN003694 (mg)**	**Fold Increase from Prior Dose Level**
1	36	--
2	48	1.33
3	60	1.25
4	72	1.20
5	96	1.33*
Additional levels may be explored at the discretion of the CRC		

Dose escalation increments between cohorts will be determined by the CRC based on safety and available PK data (e.g., Cmax and AUC) based on the following schema:

- Dose escalation up to 2-fold is allowed in Dose Level 2 and 3 unless one drug-related Grade 2 event is observed in Dose Level 1 and 2, respectively
- Subsequent dose escalation up to 1.5-fold is allowed until a DLT is observed
- Subsequent dose escalation up to 1.33-fold is allowed until MTD is established, or, in Part 2, if MTD is waived and RP2D is declared

All dose escalations will be guided by the available PK data (e.g., Cmax and AUC) from both ZEN003694-001 and this study, ZEN003694-002, with respect to the combined AUC0-24 of ZEN003694 and its active metabolite ZEN003791. [redacted]

Intermediate doses and/or alternative dosing schedules may be evaluated to best determine the MTD and/or RP2D of ZEN003694 in combination with enzalutamide based on evaluation of clinical safety and available PK data (e.g., Cmax and AUC) and upon agreement of the CRC members. No intra-patient dose escalation is allowed during the first three cycles of therapy. If a patient has not experienced any Grade 2 or higher drug-related AEs after three cycles, dose escalation up to the highest dose currently declared tolerable by the CRC will be allowed and further intra-patient dose escalation(s) will be determined on a cycle-by-cycle basis at the discretion of the Investigator and with approval from the CRC.

DLT

Determination of DLT will be made during the first 28 days of treatment (i.e., Cycle 1) in the dose escalation phase. Toxicity will be graded and recorded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 4.03 (see Appendix 2). A DLT is defined as a clinically significant AE or laboratory abnormality that is considered possibly, probably or definitely related to ZEN003694 and which meets any of the following criteria:

- Grade 3 or greater non-hematologic clinical toxicity with the exception of Grade 3 nausea or Grade 3/4 vomiting and diarrhea persisting less than 72 hours in the absence of maximal medical therapy
- Grade 4 neutropenia lasting more than 5 days
- Grade 3 or greater febrile neutropenia (temperature ≥38.5ºC)
- Grade 4 thrombocytopenia or Grade 3 thrombocytopenia with clinically significant bleeding, or any requirement for platelet transfusion
- Any other Grade 3 or 4 laboratory abnormality that requires hospitalization
- An ALT >3 × ULN with concomitant total bilirubin >2 × ULN
- Any ZEN003694-related toxicity that results in more than 25% of missed doses during Cycle 1 of treatment
- In the situation where toxicity requires withholding ZEN003694 following the receipt of at least 75% of scheduled dosing during Cycle 1: Failure to begin Cycle 2 within 1 week of the scheduled start date due to ongoing toxicity

All patients experiencing a DLT must discontinue dosing with ZEN003694; patients must complete the Safety Follow-up visit prior to discontinuation from the study.

Determination of evaluability will be made during the first 28 days of ZEN003694 treatment (i.e., Cycle 1) in the dose escalation phase. Patients meeting one or more of the following will be considered unevaluable and will be replaced:

Patients who miss more than 25% of ZEN003694 and/or enzalutamide or abiraterone doses or fail to begin Cycle 2 within 1 week of the scheduled start date for reasons other than ZEN003694-related toxicity

- Patients who require enzalutamide or abiraterone dose hold or modification in Cycle 1, including during the 14-day Lead-in period for reasons other than ZEN003694-related toxicity
- If a patient is unable to tolerate enzalutamide for any reason at dose of 160 mg during the 14 day Lead-in prior to first dose of ZEN003694, then the patient should not receive ZEN003694, and be withdrawn from the study and replaced

Dose Confirmation

Once the MTD of ZEN003694 in combination with enzalutamide has been determined in the dose escalation portion of the study, up to 20 patients who meet the inclusion/exclusion criteria for Cohort DC-A and up to 20 patients who meet the inclusion/exclusion criteria for Cohort DC-B of the dose confirmation phase will be enrolled for further evaluation of safety, PK, pharmacodynamics, and preliminary clinical activity.

Enzalutamide-naive and apalutamide-naïve patients in Cohort DC-B will be administered enzalutamide (160 mg) orally once daily for 14 days prior to the initiation of the combination therapy (Lead-in) to reach enzalutamide Css during Cycle 1. After the Lead-in, ZEN003694 will be administered orally in combination with daily enzalutamide for 28-day cycles. Patients in Cohort DC-A who are currently receiving a stable dose of enzalutamide (Sub-arm A1) will continue to receive enzalutamide and will not participate in the Lead-in. Patients in Cohort DC-A who are not currently receiving enzalutamide or apalutamide or are currently taking apalutamide (Sub-arm A2) will be administered enzalutamide orally once daily for 14 days prior to the initiation of the combination therapy (Lead-in) to reach enzalutamide Css. After the Lead-in, ZEN003694 will be administered orally in combination with daily enzalutamide for 28-day cycles.

When the 6th patient in each cohort in the dose confirmation phase has completed one cycle of therapy, or earlier if clinically indicated, the CRC will review the safety data. If ≥2 patients have experienced drug-related SAEs or DLT-equivalent events, the CRC may recommend a modification in the dose or regimen of ZEN003694 in combination with enzalutamide for the dose confirmation phase.

5. DETERMINATION OF SAMPLE SIZE

The sample size for this study was not based on any formal statistical considerations.

6. GENERAL ANALYSIS CONSIDERATIONS

The statistical analyses will be reported using summary tables, listings, and figures (TLFs). The International Council for Harmonisation (ICH) numbering convention will be used for all TLFs.

Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums and valid cases.

Categorical variables will be summarized by counts and by percentage of patients in corresponding categories. Percentages for missing values are omitted and do not account for the percent calculation of other categories. Percentages are routinely based on the total category count excluding the missing category if not otherwise mentioned. Percentages showing a rate relative to the total number of patients in this group are given in special tables (e.g. adverse event [AE] tables). Footnotes will specify the percent basis. All summary tables will be presented by treatment group. Baseline summaries will also include a total summary column.

Individual patient data obtained from the case report forms (CRFs), local clinical lab, and any derived data will be presented by patient in data listings.

For AEs and concomitant medications, no imputation of partial or missing dates will be performed except for the determination for treatment emergence and prior and/or concomitant medications. The most conservative approach will be systematically considered for determining treatment emergence and prior and/or concomitant medications. If the AE onset date is missing or incomplete, it is assumed to have occurred during the study treatment phase (ie, considered a treatment-emergent adverse event [TEAE]) unless the partial onset date or other data, such as the stop date, indicates differently. Similarly, a medication with partial start and stop dates could be considered as both a prior and concomitant treatment.

The analyses described in this plan are considered a priori, in that they have been defined prior to database lock. Post-hoc analyses will be labeled as such on the output and identified in the CSR.

All analyses and tabulations will be performed using SAS® Version 9.4 or higher. Tables, listings, and figures will be presented in RTF format.

7. NOTATION OF TREATMENT GROUPS AND VISITS

The following notation of **treatment groups** will be used throughout the report:

Full notation (as used in the study protocol)	***Notation as used throughout all tables, listings and figures***
36 mg, Dose Escalation	DE-A, 36mg
36 mg, Dose Escalation	DE-B, 36mg
48 mg, Dose Escalation	DE-A, 48mg
48 mg, Dose Escalation	DE-B, 48mg
60 mg, Dose Escalation	DE-A, 60mg
60 mg, Dose Escalation	DE-B, 60mg
72 mg, Dose Escalation	DE-A, 72mg
72 mg, Dose Escalation	DE-B, 72mg
96 mg, Dose Escalation	DE-A, 96mg

96 mg, Dose Escalation	DE-B, 96mg
120 mg, Dose Escalation	DE-A, 120mg
144 mg, Dose Escalation	DE-A, 144mg
48 mg, Dose Confirmation	DC-A, 48mg
48 mg, Dose Confirmation	DC-B, 48mg
96 mg, Dose Confirmation	DC-A, 96mg
96 mg, Dose Confirmation	DC-B, 96mg

Note: The table shells are created based on all treatment groups used in the protocol. However, actual table programming may/may not necessarily include all of these doses if they were not included in the study.

The following **visit terminology** will be used throughout the report:

Visit	***Notation as used throughout all tables, listings and figures***
Screening	Screening
Cycle X Day X	CXDX, Baseline

8. ANALYSIS POPULATIONS

The following patient population will be used for demographic, baseline characteristics and primary endpoints:

- Safety population

The following patient populations may be used for primary and secondary endpoints:

- Safety population
- Safety population with radiographic progression or ongoing at study completion
- PSA Evaluable Population, which will be used for PSA related endpoints.
- Radiographic Evaluable Population, which will be used for overall tumor response rate.

The following patient population will be used for PK analyses:

- PK Population will include all patients who have adequate PK data. Pharmacokinetic analysis will be performed by an independent party and will be provided separately.

Note, for all analyses, treatment group will be based on the treatment the patient was assigned to when enrolled in the study.

9. STUDY POPULATION

9.1 Patient Disposition

Patient disposition information will be summarized for all patients by dose regimen. Summaries will include: the number of screened patients, the number of enrolled patients, the number of patients in each analysis population, the number of cycles a patient completed, and the primary reason for study completion/discontinuation.

Information for screen failures will be described separately in the CSR.

9.2 Protocol Deviations

All protocol deviations will be presented by patient in a data listing and summarized in the following categories:

- Major
    - Inclusion/exclusion criteria not met
    - Noncompliance with study protocol
- Minor

For major protocol deviations, noncompliance with study protocol includes any subject who met withdrawal criteria but was not withdrawn from the study treatment, received excluded or prohibited concomitant medication or treatment, and received the wrong study treatment or incorrect dose of study treatment.

9.3 Demographic and Baseline Characteristics

Demographic variables include: age, sex, ethnicity, race, height (cm), weight (kg), body mass index (BMI) (kg/m^2). Age will be calculated in years relative to the informed consent date. Baseline characteristics include Eastern Cooperative Oncology Group (ECOG) performance status, PSA (ng/mL), tumor burden, pain (from external data), opioid use, metastatic location, alkaline phosphatase, lactic acid dehydrogenase, albumin, hemoglobin, number of prior chemotherapies, duration of prior androgen receptor signaling inhibitor (ARSI) therapy, and reason for prior enzalutamide/abiraterone discontinuation.

Descriptive statistics will be presented for age, baseline age, height, weight, BMI, PSA, alkaline phosphatase, lactic acid dehydrogenase, albumin, hemoglobin, number of prior chemotherapies and duration prior ARSI therapy. Frequency counts and percentages will be presented for sex, ethnicity, race, medical history, opioid use, ECOG performance status, and reason for prior enzalutamide/abiraterone discontinuation. Demographic and baseline characteristics will be summarized for the Safety Population.

Prostate cancer history, PSA history and prior cancer therapy will be presented by patient in a data listing. Baseline medical history will be be summarized by primary system organ class and dictionary-derived term in a table.

9.4 Prior Cancer Therapy, Chemotherapy Treatment, Surgical Treatment, and Radiotherapy Treatment

Prior cancer therapy reported by prior systemic treatment (from the Prior Chemotherapy Treatment CRF page), prior surgical treatment and prior radiotherapy treatment are summarized by frequency counts by dose regimen. Prior chemotherapy treatment includes type of chemotherapy treatment (chemotherapy, biologic therapy, immunotherapy, hormonal therapy, or other), best overall response, route, and reason stopped. Prior surgical treatment includes intent (curative, palliative, and adjunctive). Prior radiotherapy treatment includes type of radiotherapy, site of treatment, total radiation dose (descriptive statistics), and best overall response.

9.5 Prior and Concomitant Medications

Prior and concomitant medication verbatim terms on CRFs will be mapped to Anatomical Therapeutic Chemical (ATC) class and preferred terms using the World Health Organization (WHO) Drug Dictionary Enhanced (version 01MAR2019).

Prior medications are those medications taken prior to the initial dose of ZEN003694. Concomitant medications are those medications taken after the initial dose of ZEN003694 or medications started prior to initial dose of ZEN003694 and continued during the treatment period. A medication can be classified as both prior and concomitant. If it cannot be determined whether the medication was a prior (or concomitant) medication due to a partial start or stop date, then it will be counted as both prior and concomitant.

Prior and concomitant medications will be summarized for each treatment by WHO ATC class and preferred name. These summaries will present the number and percentage of patients using each medication. Patients may have more than 1 medication per ATC class and preferred name. At each level of patient summarization, a patient is counted once if he/she reported 1 or more medications at that level. Each summary will be ordered by descending order of incidence of ATC class and preferred name within each ATC class.

10. CLINICAL ACTIVITY ANALYSES

10.1 Clinical Activity Variables

Tumor response, PSA response, and time-to-event analysis will be based on the Safety Population. The PK analysis will be based on the PK Population. The CTC response will be analyzed for CTC Population.

Secondary endpoints

- Plasma concentrations of ZEN003694, the active metabolite ZEN003791 and enzalutamide and the active metabolite des-methyl enzalutamide.* The following PK parameters, at a minimum, will be calculated as appropriate: area under the curve, from time zero to last time point with a quantifiable level of drug ($AUC_{0\text{-last}}$) and area under the curve, from time zero to infinity with a quantifiable level of drug ($AUC_{0\text{-inf}}$), maximum plasma concentration (C_{max}) and minimum or trough concentration (C_{min}), dosing interval, and time to reach maxium plasma concentration (T_{max}) and half-life ($t_{1/2}$)
- Overall response rate
- PSA response rate by PCWG2 criteria
- PFS by PCWG2 criteria
    - Overall PFS by PCWG2 criteria
    - rPFS by PCWG2 criteria
    - Time to PSA progression by PCWG2 criteria
- CTC response*

Exploratory endpoints*

- Baseline and change from baseline post-treatment in bromodomain and extra-terminal domain (*BET*) gene expression in whole blood
- Baseline and change from baseline post-treatment in quantification of androgen receptor splice variants in blood (dose confirmation) and post-treatment in tumor tissue and response (complete response [CR], partial response [PR], progressive disease [PD])
- Baseline and change from baseline post-treatment in V-Myc avian myelocytomatosis viral oncogene homolog (*MYC*) expression in tumor tissue and response (CR, PR, PD)
- Baseline and change from baseline post-treatment in glucocorticoid receptor expression in tumor tissue and response (CR, PR, PD)
- Possible relationship of baseline tumor abnormalities (such as mutations, translocations, mRNA, protein expression and localization), in ctDNA, CTC and tumor biopsies and/or on-treatment changes with any observed antitumor activity
- Baseline and change from baseline post-treatment in immune-oncology biomarkers, if observed
- Correlation between ZEN003694, ZEN003791, enzalutamide and des-methyl enzalutamide plasma exposure levels and PD responses
- Correlation between PSA and radiographic response (CR, PR, PD)

Note: *The analysis methodology for PK, exploratory endpoints and CTC response will be provided by the sponsor in a separate document. Further, the analyses will be performed by the sponsor and the analysis results will be provided in a separate document appended to the CSR.

10.2 Baseline Values

Unless otherwise noted, baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide. If the date is the same as first dose of ZEN003694 (DE-A and DC-A) or enzalutamide (DE-B or DC-B), it will be baseline unless a time is collected then we compare it with dosing time.

10.3 Adjustments for Covariates

No adjustments for covariates are planned for the clinical activity analyses.

10.4 Handling of Dropouts or Missing Data

No imputations will be made for missing values except as described for missing start and stop dates for AEs and medications. Summaries will be based on observed data only.

10.5 Interim Analysis and Data Monitoring

There are no planned interim analyses for this study.

10.6 Examination of Subgroups

No subgroup analyses are planned.

10.7 Multiple Comparison/Multiplicity

No adjustments for multiplicity will be made in this study.

10.8 Multicenter Studies

No analyses by site are planned.

11. DEFINITIONS OF CLINICAL ACTIVITY ENDPOINTS

11.1 Radiographic Tumor Response (Overall Response Rate) by PCWG2 Criteria

Tumor response will be evaluated using the PCWG2 criteria. Patients with measurable disease will be evaluated for clinical benefit as determined by tumor response using RECIST v1.1.

Patients with non-measurable bone disease will be evaluated for progression based on the presence of any new lesions by bone scans. Radiographic tumor evaluation will be performed at screening and every 3 cycles or more frequently as determined by the investigator. Evaluations include computed tomography of thorax, abdomen and pelvis, bone scan, or magnetic resonance imaging as indicated for assessment of measurable lesions. For each assessment, the overall tumor response to treatment will be one of the following: CR, PR, stable disease (SD), PD, symptomatic deterioration, and not evaluable (NE). Progressive disease and symptomatic deterioration are considered equivalent in terms of disease progression.

A status of PR or CR must be confirmed by repeat evaluation at least 4 weeks (28 days) after the criteria for response are first met.

Using the tumor response that is determined by the investigator, best overall response will be determined using RECIST v1.1. Best overall response is defined as the best response recorded from the start of treatment until disease progression or study exit. Each overall tumor response assessment collected at protocol-specified time points will be considered.

The best responses for pairs of time point responses (when confirmation of CR and PR are required) are determined as shown below in Table 3. Table 3 is an extended version of Table 3 in the RECIST v1.1 guidance (Eisenhauer 2009). The additional discussions provided here clarify how best responses for individual pairs of overall responses, i.e., paired by sequential time points, are determined by the investigator. All of these best responses, as determined by the investigator, are then used to determine the best overall response.

In the table below, the first and subsequent time points referenced in the column headers refer to an arbitrary pair of sequential time points. Also, as indicated in the table and in the table notes, special rules may apply when the first time point of the pair is the very first (post-treatment) assessment time point or when there is only 1 assessment.

Table 3: Best Response When Confirmation of CR and PR are Required

	Overall Response First Time Point	Overall Response Subsequent Time Point	Best Response for the Pair
1	CR	CR	**CR** (if minimum criteria for CR duration is met), otherwise **Best Response = NE.**
2	CR	PR	If the first time point is truly CR, any worsening at a subsequent time point—even disease meeting the PR criteria—makes the disease PD at that subsequent time point. Then **Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = PD**. However, sometimes 'CR' may still be claimed when subsequent scans suggest small lesions that were likely present and in fact the patient had PR, not CR, at the first time point. Under these

	Overall Response First Time Point	Overall Response Subsequent Time Point	Best Response for the Pair
			circumstances, the original CR should be changed to PR; see **Row 6 for Best Response criteria**.
3	CR	SD	**Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = PD**.
4	CR, PR, SD	PD	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = PD**.
5	CR, PR	NE	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = NE.**
6	PR	CR, PR	**Best Response = PR** provided minimum criteria for PR duration is met; otherwise, **Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = NE.**
7	PR	SD	**Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = NE.**
8	SD	SD, CR, PR	**Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = NE**.
9	SD	NE	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = NE**.
10	SD	PD	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response =PD.**
11	PD	CR, PR, SD, PD, NE	**Best Response = PD.**
12	NE	CR, PR, SD, NE	**Best Response = NE.**
13	NE	PD	**Best Response = PD.**
14	CR, PR, SD	No 2nd visit	**Best Response = SD** provided minimum criteria for SD duration is met at first time point; otherwise **Best Response = NE.**
15	PD	No 2nd visit	**Best Response = PD.**
16	NE	No 2nd visit	**Best Response = NE.**

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, NE = not evaluable.

Note: If response = SD, CR, or PR at the initial post-treatment assessment then, in meeting the minimum criteria for SD duration (only SD, not CR or PR), duration is measured from the treatment start date rather than the date of the assessment.

Note: In some situations, it may be necessary to check across more than two sequential time points in order to determine whether or not a minimum duration criteria has been met. The same logic as used for the pairs of time points should be applied. For example, for the triplet SD CR SD, duration is calculated

from the first assessment date (or from the treatment start date if these are the initial assessments) to the third assessment date, if needed, to determine whether the minimum criteria for SD duration has been met.

Per the RECIST v1.1 guidance and as indicated in the first table note, for patients with SD at the first time point: in determining whether the minimum criteria for SD duration is met, duration is measured from the treatment start date to that first assessment date. Then, if the duration meets the minimum interval requirement for SD, **Best Response = SD**, otherwise **Best Response = NE**. Further, as indicated in the note, this same rule is also applied to patients with a response better than SD at the first time point.

In some situations, it may be necessary to check across more than two sequential time points in order to determine whether or not a minimum duration criteria has been met. The same logic used for the pairs of time points should be applied. For example, note the following examples.

- For the triplet SD CR SD, duration is calculated from the first assessment date (or from the treatment start date if these are the initial assessments) to the third assessment date, if needed, to determine whether the minimum criteria for SD duration has been met. If it is met, then **Best Response = SD**. Otherwise, **Best Response = NE.**
- For the triplet CR NE CR, if the minimum criteria for CR duration is met for the interval between the two CR assessments, then **Best Response = CR**. Otherwise **Best Response = NE**.
- For the triplet PR NE PR, if the minimum interval criteria for PR is met for the interval between the two PR assessments, then **Best Response = PR**. Otherwise **Best Response = NE**.
- For the triplet SD NE SD, **Best Response = NE**.

The minimum interval of CR and PR to be considered for assessment of the best overall response is is 4 weeks (28 days). The minimum interval of SD to be considered for assessment of the best overall response is 12 weeks (84 days).

A best response is determined by the investigator for each sequential pair of post-treatment time points (and in some cases, triplets of sequential time points) as indicated in the previous section. Then, the best overall response (when confirmation of CR and PR are required) for a patient equals the best of these best responses.

Using the best overall response, overall response rate is defined as the proportion of patients with CR or PR. The start of the response is the date the patient first meets the criteria for CR or PR to the time of disease progression.

11.2 PSA Response Rate by PCWG2 Criteria

The PSA response rate will be evaluated using PCWG2 criteria and defined as the proportion of patients with a PSA decline of at least 50% in a table. Three categories of PSA decline will be

summarized - less than 30% decline, at least a 30% decline, and at least a 50% decline in PSA from baseline to study exit. Any change from baseline is confirmed by a second measurement at least 3 weeks later. Subjects can be included in both the ≥30% and ≥50% response categories

PSA Response Rate will be evaluated using PCWG2 criteria and defined as following in figures

- Percentage change from baseline in PSA to 12 weeks post ZEN-003694 dose. Only evaluate for patients with at least 12 weeks of treatment, the PSA assessment at 12 weeks (84 days +/–3 days) will be used.
- Maximum percent decrease in PSA from baseline that occurs at any point after treatment. Evalubale for all patients with post-baseline PSA.

Note that safety follow-up PSA is 30 days after end of treatment and patient off treatment for significant time, therefore safety follow-up collection will not be used for PSA response rate calculation.

Individual PSA response will be presented in a patient listing.

11.3 Progression-Free Survival by PCWG2 Criteria

Progression-free survival includes 3 separate analyses for median overall progression-free survival, median radiographic progression-free survival, and median time to PSA progression. Doses will be combined for patients in both the Dose Escaltion (DE) and Dose Confirmation (DC) groups. Kaplan-Meier Plots will be repeated for 3 patient groups: enzalutamide progressor in DE and DC, abiraterone progressor in DE and DC, and all patients.

11.3.1 Overall Progression-Free Survival by PCWG2 Criteria

Overall PFS is determined using the PCWG2 criteria. Overall progressive disease includes disease progression determined by radiographic assessments and clinical deterioration (development of an indication for radiotherapy while on treatment and global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression).

Overall PFS is measured from baseline until the time that disease progression (radiographic progressive disease or clinical deterioration) or death is documented, whichever occurs first. Disease progression is documented in the tumor assessment CRF and study exit status CRF. If a patient has no reported disease progression from a tumor assessment but disease progression is reported in the study exit status CRF (i.e., clinical progression by PCWG2, radiographic progression by PCWG2, PSA progression with clinical progression by PCWG2, or PSA progression with radiographic progression by PCWG2 is marked as the primary reason for study completion/discontinuation), then the patient is considered to have progressed. Radiographic progression is measured from baseline to the date of the first scan that shows the change. If radiographic disease progression is identified at the first on-treatment radiographic assessment at

Cycle 3 Day 1 (8 weeks), radiographic progression must be confirmed by a second assessment 6 or more weeks later. Clinical progression is measured from baseline to date of last dose of ZEN003694.

Patients who did not progress overall or did not die prior to study exit are censored on the date of their last dose of ZEN003694.

11.3.2 Radiographic Progression-Free Survival by PCWG2 Criteria

Radiographic progression-free survival (rPFS) is determined using the PCWG2 criteria to assess both soft-tissue and bone assessments.

The rPFS is measured from the baseline until the time that disease progression based on radiographic assessments or death is documented. Radiographic disease progression is documented in the tumor assessment CRF and study exit status CRF. If a patient has no reported disease progression from a tumor assessment but disease progression is reported in the study exit status CRF (i.e., radiographic progression by PCWG2 or PSA progression with radiographic progression by PCWG2 is marked as the primary reason for study completion/discontinuation), then the patient is considered to have progressed. rPFS is measured from baseline to the date of the first scan that shows the change. rPFS is also measured from date of screening scan to the date of the first scan that shows the change. If radiographic disease progression is identified at the first on-treatment radiographic assessment at Cycle 3 Day 1 (8 weeks), radiographic progression must be confirmed by a second assessment 6 or more weeks later.

Patients who do not progress radiographically or did not die prior to study exit are censored on the date of their last dose of ZEN003694.

11.3.3 Time to PSA Progression by PCWG2 Criteria

Time to PSA progression is determined using the PCWG2 criteria. Only subjects with at least 12 weeks of treatment with ZEN003694 are evaluable for PSA progression. PSA progression occurs when the PSA has increased 25% or greater above nadir and an absolute increase of 2 ng/mL or more from the nadir is documented. When no decline is observed, PSA progression occurs when a 25% increase from baseline value along with an increase in absolute value of 2 ng/mL or more. Progression is confirmed by a second assessment 3 or more weeks after the initial documented PSA increase that meets the progression criteria. Time to PSA progression is measured from the start of treatment with ZEN003694 until the time that the PSA progression is first documented. PSA progression is documented in the serum PSA CRF and study exit status CRF. If a patient has no reported PSA progression from a serum PSA assessment but PSA progression is reported in the study exit status CRF (i.e., PSA progression with clinical progression by PCWG2 or PSA progression with radiographic progression by PCWG2 is marked as the primary reason for study completion/discontinuation), then the patient is considered to have progressed.

Patients who do not progress or who die are censored on the date of their last PSA assessment or, if they die, on their date of death.

11.4 CTC Response

As described in Section 10.1, the analysis methodology and results for CTC Response will be provided by the sponsor in a separate document appended to the CSR.

11.5 Exploratory Analysis

As described in Section 10.1, exploratory analyses include pharmacodynamic analysis (including *BET* inhibitor gene expression profiles, and exploratory biomarkers), and immuno-oncology biomarker analysis will be provided by the sponsor in a separate document appended to the CSR.

12. METHODS OF CLINICAL ACTIVITY ANALYSES

12.1 Response Rate Endpoints

The response rate endpoints include overall response rate and PSA response rate. Each response rate, along with its exact binomial 95% confidence interval, will be summarized by dose regimen.

The best overall response and PSA response at each protocol-defined time point will also be summarized descriptively by dose regimen.

Individual tumor and PSA response will be presented in patient listings.

12.2 Time to Event Endpoints

Time to event endpoints include overall PFS, rPFS, and time to PSA progression. Each endpoint will be summarized in a tabular summary that will include the number and percent of patients that progressed or died and the number and percent of patients that did not progress and are alive. Progression and timing of events is described in a previous section (Section 11.3). For all patients and non-censored patients, the minimum and maximum number of months a patient was progression-free will be included. The Kaplan-Meier quartile estimates for number of progression-free months and corresponding 95% confidence intervals will be reported (25th percentile, median, and 75th percentile) along with the Kaplan-Meier product limit estimates and number of patients at risk at 3 month intervals. Time to event endpoints will also be summarized by dose levels and progressor groups in Kaplan-Meier plots.

Individual time to endpoints will be presented in patient listings.

13. PHARMACOKINETIC AND PHARMACODYNAMIC ANALYSES

PK analyses will be described in a separate plan and performed by the sponsor. Pharmacodynamic analyses are outlined in Section 10.1.

14. SAFETY ANALYSES

All safety analyses will be based on the Safety population.

14.1 Extent of Exposure

Study drug exposure will be summarized for each ZEN003694 dose level using the actual number of doses taken, number of cycles, duration of treatment (days) and compliance.

Study drug compliance over the study will be calculated as follows:

$$\text{Compliance [\%]} = \frac{\text{Actual Number of Doses}}{\text{Duration of Study Treatment (days)}} \times 100\%$$

All in-clinic study drug administration is reported on the ZEN003694 Administration – Single Dose CRF and all out-clinic study drug administration is reported on the ZEN003694 Administration Log CRF.

In order to calculate the actual number of doses used, the number of administration days will be determined by adding each administration day from the ZEN003694 Single Dose CRF and the number of days of administration reported in the ZEN003694 Administration Log CRF. The number of days the dose was held or missed reported on the ZEN003694 Administration Log CRF will not be included in the calculation of actual number of doses used. Since the dose is taken once daily, it is assumed that 1 day is equal to 1 dose.

Duration of study treatment is defined as the last dose date minus the first dose date plus 1.

Individual enzalutamide exposure data will be presented in patient listings.

14.2 Adverse Events

All AE summaries will be restricted to TEAEs, which are defined as those AEs that occurred after dosing and those existing AEs that worsened during the study. In this study, only events that started after administration of study drug until 30 days after the last dose of study drug are considered AEs and recorded. Those that started before study drug administration were to be recorded on the Medical History CRF. If it cannot be determined whether the AE is treatment emergent due to a partial onset date then it will be counted as treatment emergent. Verbatim terms on CRFs will be mapped to preferred terms and system organ classes using the Medical Dictionary for Regulatory Activities (MedDRA) (version 19.0).

Each AE summary will be displayed by treatment group. Summaries that are displayed by system organ class and preferred terms will be ordered by descending order of patient incidence

of system organ class and preferred term within each system organ class. Summaries of the following types will be presented:

Overall summary of TEAEs which contain an overview of each item below.

- Patient incidence of TEAEs and total number of unique TEAEs by MedDRA system organ class and preferred term.
- Patient incidence of TEAEs by MedDRA system organ class, preferred term, and highest severity. At each level of patient summarization a patient is classified according to the highest severity if the patient reported 1 or more events. AEs with missing severity will be considered severe for this summary.
- Patient incidence of TEAEs by MedDRA system organ class, preferred term, and closest relationship to study drug (Related/Not Related). Related AEs are those reported as "Related" and unrelated AEs are those reported as "Not Related." At each level of patient summarization, a patient is classified according to the closest relationship if the patient reported 1 or more events. Adverse events with a missing relationship will be considered related for this summary.
- Patient incidence of serious TEAEs and total number of unique serious TEAEs by MedDRA system organ class and preferred term.
- Patient incidence of serious TEAEs by MedDRA system organ class, preferred term, and highest severity. At each level of patient summarization a patient is classified according to the highest severity if the patient reported 1 or more events. AEs with missing severity will be considered severe for this summary.
- Patient incidence of serious TEAEs by MedDRA system organ class, preferred term, and closest relationship to study drug (Related/Not Related). Related AEs are those reported as "Related" and unrelated AEs are those reported as "Not Related." At each level of patient summarization a patient is classified according to the closest relationship if the patient reported 1 or more events. Adverse events with a missing relationship will be considered related for this summary.
- Patient incidence of TEAEs leading to death as an outcome by MedDRA system organ class and preferred term
- Patient incidence of TEAEs leading to study discontinuation by MedDRA system organ class and preferred term.

14.3 Clinical Laboratory Evaluation

Laboratory parameters (serum chemistry, hematology, coagulation tests [international normalized ratio, prothrombin time, and partial thromboplastin time], serum troponin [troponin T and/or I proteins, based on local laboratory procedure], PSA, and urinalysis) will be collected at protocol-defined time points. Parameters will be summarized using descriptive statistics at baseline and at each post-baseline time point. Changes from baseline will also be summarized.

Serum troponin will be provided in the same listing as the 12-lead electrocardiogram (ECG) data. PSA values will be listed separately from other clinical assessments for the PCWG2 Evaluable Population and for the Safety Population (if that population is different from the efficacy population). Serum testosterone (collected on the first day of each cycle will be included in the serum chemistry listing. The incidence of clinically significant laboratory results will be summarized by number of unique subjects per parameter at any post-baseline time point.

In addition, shift tables (i.e., low-normal-high at baseline versus low-normal-high at follow-up in a 3-by-3 contingency table) will be provided to assess changes in laboratory values from baseline to follow-up.

Select laboratory parameters will be graded according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v4.03 as specified in Appendix D. Select laboratory parameters include platelet counts, neutrophils, lymphocyte, white blood cells), creatinine, alanine aminotransferase, aspartate aminotransferase, total bilirubin, and glucose. Shift tables assessing changes from baseline in CTCAE grade will be presented.

Urinalysis results will not be summarized but will be provided in a data listing.

14.4 Vital Signs

Vital signs will be summarized using descriptive statistics at baseline and at each post-baseline time point. Changes from baseline will also be summarized. Vital signs parameters include temperature, systolic and diastolic blood pressure, and heart rate. The position of the patient will also be reported. Height is only measured at screening while weight is measured at specific time points specified in the protocol.

Vital signs will be reported in a patient data listing as well.

14.5 Physical Examination

Physical examination results will be included in data listings only.

14.6 Echocardiogram or Multigated Acquisition (MUGA) Scan

An echocardiogram or multigated acquisition (MUGA) scan with left ventricular ejection fraction will be obtained during the Screening period. Results will be included in patient data listings only.

14.7 Electrocardiogram

A triplicate 12-lead ECG will be performed at protocol-defined time points. Electrocardiogram parameters collected include interpretation and clinical significance, ventricular rate (bpm), RR interval (msec), PR interval (msec), QRS duration (msec), QT interval (msec), corrected QT interval according to Fridericia formula (QTcF) (msec), and average QTcF (msec).

The ECG data analysis will be conducted based on methodology recommended in the ICH E14 Guidance, "The clinical evaluation of QT/corrected QT interval (QTc) interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs." Descriptive statistics at baseline and at each post-baseline time point as well as changes from baseline will be summarized for each ECG parameter using the average result. Each individual QTcF measurement will be re-derived using the following equation:

$$QTcF\ (msec)=QT/(RR^{0.33})$$

In addition, categorical summaries of abnormal average QTcF values will be presented as follows:

- Number of patients with QTcF values at each time point (>450 msec to <480 msec, >480 msec to <500 msec, and >500 msec)
- Number of patients with change from baseline values in QTcF at each post-baseline time point (>30 msec to <60 msec, >60 msec)

14.8 Eastern Cooperative Oncology Group (ECOG) Performance Status

ECOG performance status is classified on a 6-point (0 to 5) rating scale.

- 0 = Fully active, able to carry on all pre-disease performance without restriction.
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of light or sedentary nature, e.g., light house work, office work.
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.
- 3 = Capable of only limited self-care , confined to bed or chair more than 50% of waking hours.
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.
- 5 = Dead.

ECOG performance status will be summarized in a shift from baseline table and presented in a patient listing.

14.9 Ophthalmology Assessments

Ophthalmology assessments include: a detailed ophthalmic history, Snellen best corrected visual acuity (including refraction, if needed), color vision testing (using standard HRR pseudoisochromatic plates), pupillometry, confrontational visual field testing, intraocular pressure (using Goldmann tonometry or TonoPen tonometry), external eye and ocular motility exam and slit lamp biomicroscopy, indirect ophthalmoscopy, optical coherence tomography

(OCT) optic nerve and macula tests, fundus photography, and other exams are clinically indicated.

Any clinically significant changes from baseline for each parameter (best-corrected visual acuity, color vision plates, relative afferent pupillary deficit, pupil diameter in bright light, pupil diameter in dim light, velocity of pupillary constriction, intraocular pressure, slit lamp exam, dilated fundoscopic exam, OCT of optic nerve, macular OCT, and fundus photographs of the posterior pole) will be summarized in a table for on-study examinations and presented in a listing by patient.

Baseline and in-clinic qualitative exploration of visual symptoms will be summarized in a table and presented in a patient listing. In the tabular summary, all categorical parameters will be summarized using frequency counts and percentages while all continuous parameters will be summarized using descriptive statistics. Only known times for duration since dosing and start of symptoms will be summarized. For unknown times, the number of unknown times and reported time ranges will be displayed.

15. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

The primary purpose of this section is to modify and/or clarify items specified in the protocol (Version 05NOV2018 Amendment 10) as noted below:

- On 11APR2019, Zenith informed all study sites that they no longer plan to move forward with the abiraterone combination of the Zenith mCRPC study, ZEN003694-002, Part 2. Part 2 will be postponed indefinitely.
- A DLT Population was specified in the protocol as an analysis population but no analyses are planned that are specific to this population. Thus, this patient population is not defined in the SAP. Adverse events that qualify as a DLT will be marked as such in an AE listing.
- A PK population was not explicitly defined in the protocol. In order to clarify the PK analyses, a definition of PK Population has been added to this SAP.
- Patients in the Radiographic Evaluable Population are included in the tumor response, Overall PFS, and rPFS analyses. Patients in the PSA Evaluable Population are included in the PSA response rate and time to PSA progression endpoint analyses.
- In order to capture all meaningful endpoints in PCWG2 criteria, 3 separate analyses are included in the SAP: median overall PFS, radiographic PFS, and median time to PSA progression. Only median PFS by PCWG2 criteria was pre-specified in the protocol.

17. REFERENCES

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US Department of Health and Human Services (DHHS), Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Guidance for industry. E14 The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-antiarrhythmic Drugs. October 2005.

18. APPENDICES

Appendix A: Presentation of Data and Programming Specifications

General

- Specialized text styles, such as bold, italics, borders, shading, superscripted and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters are to be used in tables and data listings.
- Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used on a table, figure, or data listing.
- Hexadecimal character representations are allowed (e.g., μ, a, ß).
- All footnotes will be left justified and at the bottom of a page. Footnotes should be used sparingly and must add value to the table, figure, or data listing.

Tables

- Formal organization of tabulations may be changed during programming if appropriate, e.g., tables for the different variables may be combined into a single table, or tables with more than 1 variable may be split into several tables.
- Means and medians will be presented to 1 more decimal place than the raw data. Standard deviations will be presented to two more decimal places than the raw data. Minimums and maximums will be reported with the same number of decimal places as the raw data.
- Percentages will be presented to the tenths place.
- For frequency counts of categorical variables, categories whose counts are zero will be displayed for the sake of completeness. For example, if none of the subjects discontinue due to "lost to follow-up," this reason will be included in the table with a count of 0. Categories with zero counts will not have zero percentages displayed.
- Lower and upper confidence interval values should be presented to 1 decimal place more than the raw/derived data (i.e., to the same number of decimal places as the mean).
- Percentiles (e.g., 25%, 75%) should be presented to 1 decimal place more than the raw/derived data.
- For all inferential analyses, p-values will be rounded to four decimal places (or at the highest level of precision) with a leading zero (0.0001). P-values less than 0.0001 will be presented as "<0.0001".
- The last footnotes will be
  - "Source: xxx", where xxx indicates the source table number(s) if applicable (in case aggregated results like mean or median are plotted) or the source listing(s) (in case individual responses are plotted) and/or source datatset(s) (eg, analysis data model [ADaM]).

Figures

- Legends will be used for all figures with more than 1 variable or item displayed. Dose regimen group sizes (n=xx) will be included, as appropriate.
- Figures will be in black and white but can be in color to add value to the clarity and readability of a figure. Lines should be wide enough to see the line after being copied.
- The last footnotes will be
  - "Source: xxx", where xxx indicates the source listing number(s) and/or source datatset(s) (eg, ADaM).
  - "PROGRAM SOURCE: ...\\xx.sas, DATA CUT OFF DATE: DDMMMYYYY, RUN DATE: DDMMYY hh:mm".
  where extraxt date is the datestamp of the data snapshot used.

Listings

- Formal organization of the listing may be changed during programming if appropriate, e.g., additional variables may be included, change in the column order, or the listing may be split into multiple parts due to space constraints, etc.
- If not otherwise specified, all data listings will be sorted by sequence/treatment, center, patient number, visit, and date/time as appropriate.
- All date values will be presented in a SAS date (e.g., 29AUG2001) format.
- All observed time values will be presented using a 24-hour clock HH:MM:SS format (e.g., 01:35:45 or 11:26). Seconds will only be reported if they were measured as part of the study.
- The last footnote will be
  - "PROGRAM SOURCE: ...\\xx.sas, DATA CUT OFF DATE: DDMMMYYYY, RUN DATE: DDMMYY hh:mm".

where extract date is the datestamp of the data snapshot used.

Missing or incomplete dates (i.e., AEs and concomitant medications)

The most conservative approach will be systematically considered. If the AE onset date is missing / incomplete, it is assumed to have occurred during the study treatment phase (i.e., considered a TEAE) except if the partial onset date or other data such as the stop date, indicates differently. Similarly, a medication with partial start and stop dates could be considered as both a prior and concomitant treatment.

The following algorithms will be applied to missing and incomplete start and stop dates:

Start Dates

- If the day portion of the start date is missing, then the start date will be estimated to be equal to the date of first dose of study drug, provided the start month and year are the

same as the first dose of study drug and the stop date is either after the first dose of study drug or completely missing. Otherwise, the missing day portion will be estimated as '01'.

- If both the day and month portions of the start date are missing, then the start date will be estimated to be equal to the date of first dose of study drug, provided the start year is the same as the first dose of study drug and the stop date is either after the first dose of study drug or completely missing. Otherwise, the event will be assumed to start on the first day of the given year (e.g., ??-???-2013 is estimated as 01-JAN-2013).
- If the start date is completely missing and the stop date is either after the dose of study drug or completely missing, the start date will be estimated to be the day of study drug dosing. Otherwise, the start date will be estimated to be the first day of the same year as the stop date. All other non-AE and non-concomitant medication day calculations where only partial dates are available will be handled as follows: the first day of the month will be used in the calculations if the day part of a start date is missing while January 1 will be employed if both the month and day parts of a start date are missing.

Stop Dates

- If only the day of resolution is unknown, the day will be assumed to the last of the month (e.g., ??-JAN-2013 will be treated as 31-JAN-2013).
- If both the day and month of resolution are unknown, the event will be assumed to have ceased on the last day of the year (e.g., ??-???-2013 will be treated as 31-DEC-2013).
- If the stop date is completely missing or the event is continuing, the event will be assumed to be after first dose of study drug and will be imputed using the last known date on the study.

Standard Calculations

Variables requiring calculation will be derived using the following formulas:

- **Days** – A duration expressed in days between 1 date (*date1*) and another later date (*date2*) is calculated using the formulas noted below:

  duration in days = date2 – date1 + 1, where date1 ≥first dose date

  duration in days = date2 – date1, where date1 <first dose date
- **Months** – A duration expressed in months is calculated as the number days divided by 365.25/12 (~30.4).
- **Years** – A duration expressed in years between 1 date (*date1*) and another later date (*date2*) is calculated using the formula noted below:
  duration in years = (date2-date1+1)/365.25
- **Age** –Age is calculated as the number of years from the date of birth (*DOB*) to the date of informed consent (*DOIC*). If the month of DOIC <month of DOB or the month of DOIC=DOB and the day of DOIC <day of DOB, then the following formula is used:

age (years) = year of DOIC – year of DOB – 1.

Otherwise, the following formula is used:

age (years) = year of DOIC – year of DOB.

- **Height** – Height entries made in inches (in) are converted to centimeters (cm) using the following formula:
  height (cm) = height (in) * 2.54
- **Weight** – Weight entries made in pounds (lb) are converted to kilograms (kg) using the following formula:
  weight (kg) = weight (lb) / 2.2046
- **Temperature** – Temperature entries in degrees Fahrenheit are converted to degrees centigrade using the following formula:
  temp (degrees centigrade) = 5/9 * [temp (degrees Fahrenheit) - 32]
- **Body Mass Index (BMI)** – BMI is calculated using height (cm) and weight (kg) using the following formula:
  BMI (kg/m^2) = weight (kg) / $[[height\ (cm)/100]^2]$
- **Change from baseline** – Change from baseline will be calculated as:
  Change = post baseline value – baseline value
- **Percent change from baseline** – Change from baseline will be calculated as:
  Percent change from baseline = post baseline value – baseline value / baseline value × 100

Appendix B: SAS programming QC requirements

SDTM/TDM:

1. **Program Review**
   - **1.1.** **Program name** follows standard naming conventions and is consistent with other study program names.
   - **1.2.** **Program header** uses standard template with all relevant information completed. This includes the SDTMIG Version and SDTM controlled terminology version (i.e., date).
   - **1.3.** **Program flow** is logical (i.e., header → initialization code → macro variable definitions → format definitions → main body).
   - **1.4.** **Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.
   - **1.5.** **Hard coding,** if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.
   - **1.6.** **SAP Derivation** rules, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.
   - **1.7.** **Permanent intermediate datasets** utilized as source data have either been fully validated elsewhere or are fully validated within the scope of this QC.
   - **1.8.** **Program runs** properly and output dataset is generated as intended.

2. **SAS Log Review**
   - **2.1.** **Scan of entire log** confirming that each data step and procedure completed properly.
   - **2.2.** **Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.
   - **2.3.** **Other messages** such as “PUT” or “INFO” messages (e.g., overwritten variables following merge) are handled appropriately, if they are found in log.

3. **Dataset Structure**
   - **3.1.** **Output dataset name** follows standard naming conventions and is consistent with other study dataset file names.
   - **3.2.** **Number of records** is as expected (e.g., all expected records from source data are kept).
   - **3.3.** **Dataset label** is assigned according to specifications/SDTMIG.
   - **3.4.** **Variable attributes** meet the specifications/SDTMIG as defined (e.g., name, length, and label).
   - **3.5.** **Variable lengths** are appropriate and are not arbitrarily set to a large value and do not exceed 200 characters.
   - **3.6.** **Sorting order** is based on the defined sort key variables and creates unique records.

3.7. **All SDTMIG "Required" variables** have been created and are populated following SDTMIG requirements.
3.8. **All SDTMIG "Expected" variables** have been created and are populated, where source data content allows, following SDTMIG requirements.
3.9. **All SDTMIG "Permissible" variables** that may be needed based on the source data content and/or analysis needs, have been created following SDTMIG requirements.
3.10. **SDTMIG labels** have been used. User-defined labels follow the SDTMIG and are 40 characters or less in length.
3.11. **SDTMIG variable names** have been used. User-defined variable names follow the SDTMIG and are 8 characters or less in length.
3.12. **No formats or informats** are attached to variables.
3.13. **Supplemental datasets** are created, if source data warrants, following SDTMIG guidelines.
3.14. **Dataset size** is no larger than 1 gb.
3.15. **OpenCDISC validator** is run. Any findings that result are updated or explained.

4. Verification of Data

4.1. TDM Programmer

- Each TDM is opened and data are reviewed for consistency with the protocol, SAP, and/or CRF (no programming is necessary).

4.2. TDM Validator

- Full validation is performed against the protocol, SAP, and/or CRF without utilizing the dataset specifications document. This may be done programmatically or through a manual review. The Trial Summary (TS) domain should be validated by the Study Statistician or Biostatistics Project Lead, and may require input from the sponsor or a Clinical Operations team member.

4.3. SDTM Programmer

- All data fields are spot-checked for at least 3 subjects.

4.4. **SDTM Validator** uses one of the following methods. The choice of QC method must be approved by the Biostatistics Project Lead.

- Independent program to confirm all content from all data fields.
- Independent program to confirm all content from derived data fields and a spot-check of source data against the output dataset is performed on at least 3 subjects for non-derived fields.
- Study specific alternative method (if applicable) that is agreed upon by the sponsor and defined prospectively in a study specific document (e.g., Validation Plan, SAP or a modified QC requirement template TMP-SOP-0205-003).

5. Documentation

5.1. The Programmer and Validator must document completion of QC (e.g., date of QC and method used) in **TMP-SOP-0205-002 Program Status Document**.

5.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.

5.3. The following must be retained electronically within the study folder by the Programmer as supporting documentation for SDTM and TDM datasets:

- OpenCDISC report generated at time of QC including comments explaining findings.

5.4. The following must be retained electronically within the study folder by the Validator as supporting documentation:

- PROC CONTENTS of permanent dataset.
- Confirmatory output (See Section 4.4).
- If a spot-check of subject data is performed, output that clearly identifies the subjects that are checked (See Section 4.4).
- OpenCDISC report generated at time of QC including comments explaining findings.

ADaM:

1. **Program Review**
   - **1.1.** **Program name** follows standard naming conventions and is consistent with other study program names.
   - **1.2.** **Program header** uses standard template with all relevant information completed. This includes the ADaMIG Version and ADaM controlled terminology version (i.e., date).
   - **1.3.** **Program flow** is logical (i.e., header → initialization code → macro variable definitions → format definitions → main body).
   - **1.4.** **Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.
   - **1.5.** **Hard coding,** if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.
   - **1.6.** **SAP Derivation** rules, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.
   - **1.7.** **Permanent intermediate datasets** utilized as source data have either been fully validated elsewhere or are fully validated within the scope of this QC.
   - **1.8.** **Program runs** properly and output dataset is generated as intended.

2. **SAS Log Review**
   - **2.1.** **Scan of entire log** confirming that each data step and procedure completed properly.
   - **2.2.** **Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.

2.3. **Other messages** such as "PUT" or "INFO" messages (e.g., overwritten variables following merge) are handled appropriately, if they are found in log.

3. **ADaM and ADaM-Like Dataset Structure**
   - 3.1. **Output dataset name** follows standard naming conventions and is consistent with other study dataset file names.
   - 3.2. **Number of records** is as expected (e.g., all records for non-screen failures).
   - 3.3. **Dataset label** is assigned according to specifications.
   - 3.4. **Variable attributes** meet the specifications as defined (e.g., name, length, and label).
   - 3.5. **Variable lengths** are appropriate and are not arbitrarily set to a large value and do not exceed 200 characters.
   - 3.6. **Sorting order** is based on the defined sort key variables and creates unique records.

4. **ADaM Requirements**
   - 4.1. **Appropriate ADaM structure** is followed as specified in the ADaMIG and supplemental documents (e.g., ADSL, Basic Data Structure, ADAE, etc.).
   - 4.2. **All ADaMIG "Required" variables** have been created and are populated following ADaMIG requirements.
   - 4.3. **All ADaMIG "Conditional" variables** that are needed based on the trial design and/or analysis have been created and are populated following ADaMIG requirements.
   - 4.4. **All ADaMIG "Permissible" variables** that may be needed based on the analysis needs have been created and are populated following ADaMIG requirements.
   - 4.5. **Core variables,** as specified in ADSL, are included in non-ADSL datasets.
   - 4.6. **Variables from SDTM** keeping the same name are unchanged (i.e., have the same values, meaning, and attributes as found in the source SDTM domain).
   - 4.7. **No further derivations** are required to generate analysis (e.g., manipulation of AVAL). Separate procedures for different sections of an output (e.g., numerators and denominators) are expected.
   - 4.8. **ADaM IG variable names** are used for ADaM-defined variables. User-defined variable names are 8 characters or less in length.
   - 4.9. **ADaM IG labels** have been used for ADaM-defined variables. User-defined variable labels are 40 characters or less in length.
   - 4.10. **No formats or informats** are attached to variables except for date, time and date/time variables.
   - 4.11. **ADSL source data** are SDTM datasets.
   - 4.12. **ADaM dataset source data** are ADSL, other ADaM datasets and SDTM datasets. No circular logic is used.
   - 4.13. **OpenCDISC validator** is run. Any findings that result are updated or explained.

5. **Verification of Data**
   - 5.1. **Validator** uses one of the following methods. The choice of QC method must be approved by the Biostatistics Project Lead.
     - Independent program to confirm all content from all data fields.
     - Independent program to confirm all content from derived data fields and a spot-check of source data against the output dataset is performed on at least 3 subjects for non-derived fields.
     - Study specific alternative method (if applicable) that is agreed upon by the sponsor and defined prospectively in a study specific document (e.g., Validation Plan, SAP or a modified QC requirement template TMP-SOP-0205-003).

6. **Documentation**
   - 6.1. The Programmer and Validator must document completion of QC (e.g. date of QC and method used) in **TMP-SOP-0205-002 Program Status Document.**
   - 6.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.
   - 6.3. The following must be retained electronically within the study folder by the Programmer as supporting documentation
     - If following ADaM standards, OpenCDISC report generated at time of QC including comments explaining findings.
   - 6.4. The following must be retained electronically within the study folder by the Validator as supporting documentation
     - PROC CONTENTS of permanent dataset.
     - Confirmatory output that displays results of programmatic dataset comparison (e.g., PROC COMPARE output) (See Section 5.1).
     - If a spot-check of subject data is performed, output that clearly identifies the subjects that are checked (See Section 5.1).
     - If following ADaM standards, OpenCDISC report generated at time of QC including comments explaining findings.

Tables:

1. **Program Review**
   - 1.1. **Program name** follows standard naming conventions and is consistent with other study program names.
   - 1.2. **Program header** uses standard template with all relevant information completed.
   - 1.3. **Program flow** is logical (i.e., header → initialization code → macro variable definitions → format definitions → main body).

1.4. **Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.
1.5. **Hard coding,** if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.
1.6. **SAP Derivation** rules, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.
1.7. **Endpoints** are generally derived in source datasets and not within the program itself.
1.8. **Program runs** properly and output file is generated as intended.

2. **SAS Log Review**
2.1. **Scan of entire log** confirming that each data step and procedure completed properly.
2.2. **Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.
2.3. **Other messages** such as "PUT" or "INFO" messages (e.g., overwritten variables following merge) are handled appropriately, if they are found in log.

3. **Output Review**
3.1. **Output file name** follows standard naming conventions and is consistent with other study output file names.
3.2. **Titles and footnotes** are verified against mock table (if available). Discrepancies, including footnotes added for clarification, are noted and verified.
3.3. **Column/row header text** is verified against mock table and/or CRF.
3.4. **Format and sorting order** are correct relative to mock table and/or CRF.
3.5. **Pages breaks** are as intended throughout the document.
3.6. **Significant digits** are appropriate for summary results (e.g., mean is 1 more digit than collected on the CRF, etc.).
3.7. **Analysis population totals** are verified as correct based on SAP definitions and are consistent with other tables using the same population(s).
3.8. **Inappropriate data:** checked for outliers, invalid numbers, missing results, etc.

4. **Verification/Review of Results**

Results are either verified as described in Section 4.1 or are reviewed as described in Section 4.2. A study specific alternative method may also be used if agreed upon by the sponsor and defined prospectively in a study specific document (e.g., Validation Plan, SAP or a modified QC requirement template TMP-SOP-0205-003). An abbreviated review of results (Section 4.2) is only allowed when the program uses standard validated macros to produce summary statistics and generate the output. Verification of results (Section 4.1) is required for primary efficacy analysis output regardless of the

method used to produce the output. The choice of QC method must be approved by the Biostatistics Project Lead.

4.1. **Verification of results** can be performed using one of the following methods

4.1.1. Independent confirmatory program is written to match output results.

4.1.2. Manual calculations (if feasible based on small Ns or frequency counts).

4.2. **Abbreviated review** - Please see Section 5.2 of "QC Requirements #08: Abbreviated QC Requirements".

5. Documentation

5.1. The Programmer and Validator must document completion of QC (e.g., date of QC completion and method used) in **TMP-SOP-0205-002 Program Status Document**.

5.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.

5.3. The following must be retained electronically within the study folder by the Validator to document the method of QC performed:

- Table output generated at time of QC completion.
- If independent confirmatory program is created, a portion of the resulting output that verifies results (Section 4.1.1).
- If manual calculations are performed, insert a comment into the output file to indicate verification of results (Section 4.1.2).

Listings:

1. Program Review

1.1. **Program name** follows standard naming conventions and is consistent with other study program names.

1.2. **Program header** uses standard template with all relevant information completed.

1.3. **Program flow** is logical (i.e., header → initialization code → macro variable definitions → format definitions → main body).

1.4. **Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.

1.5. **Hard coding,** if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.

1.6. **SAP Derivation** rules, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.

1.7. **Endpoints** are generally derived in source datasets and not within the program itself.

1.8. **Program runs** properly and output file is generated as intended.

2. SAS Log Review

2.1. **Scan of entire log** confirming that each data step and procedure completed properly.
2.2. **Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.
2.3. **Other messages** such as "PUT" or "INFO" messages (e.g., overwritten variables following merge) are handled appropriately, if they are found in log.
2.4. **Number of records** is as expected based on source data.

3. Output Review

3.1. **Output file name** follows standard naming conventions and is consistent with other study output file names.
3.2. **Titles and footnotes** are verified against mock listing (if available) or SAP list of listings. Discrepancies, including footnotes added for clarification or to match corresponding table, are noted and verified.
3.3. **Column header text** is verified against mock listing and/or CRF. Verify that all corresponding CRF fields are included or document reason why a field is excluded.
3.4. **Format and sorting order** of rows and columns are correct relative to mock listing and/or CRF.
3.5. **Pages breaks** are as intended throughout the document.
3.6. **Inappropriate data:** checked for outliers, invalid numbers, missing results, etc.

4. Verification/Review of Results

4.1. **Listing content** is as expected (e.g., listing includes all enrolled subjects, all expected visits, etc.)
4.2. **Variables directly from source dataset** are spot-checked for accuracy and completeness.
4.3. **Derived or calculated variables** are confirmed through independent confirmatory program or compared to corresponding source data for at least 3 subjects.
4.4. **Study specific alternative method** (if applicable) that is agreed upon by the sponsor and defined prospectively in a study specific document (e.g., Validation Plan, SAP or a modified QC requirement template TMP-SOP-0205-003).

5. Documentation

5.1. The Programmer and Validator must document completion of QC (e.g., date of QC completion and method used) in **TMP-SOP-0205-002 Program Status Document**.
5.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.
5.3. The following must be retained electronically within the study folder by the Validator to document the method of QC performed:

- Listing output generated at time of QC completion.
- If independent confirmatory program is created, a portion of the resulting output that verifies results (Section 4.3).

If a spot-check of subject data is performed, output that clearly identifies the subjects that are checked (Section 4.3).

Figures:

1. **Program Review**
   - **1.1. Program name** follows standard naming conventions and is consistent with other study program names.
   - **1.2. Program header** uses standard template with all relevant information completed.
   - **1.3. Program flow** is logical (i.e., header → initialization code → macro variable definitions → format definitions → main body).
   - **1.4. Programmer comments** are included throughout program to describe purpose of individual sections or macros and provide understanding of specific code, if necessary. All comments are clear and up-to-date.
   - **1.5. Hard coding,** if any, is implemented correctly and documented in program header with: date, reason, and reference to sponsor approval. A comment is also inserted at the location of the hard coding.
   - **1.6. SAP Derivation** rules, if any, are followed. Significant deviations from mock table or SAP text are documented in the SAS Program Header.
   - **1.7. Endpoints** are generally derived in source datasets and not within the program itself.
   - **1.8. Program runs** properly and output file is generated as intended.

2. **SAS Log Review**
   - **2.1. Scan of entire log** confirming that each data step and procedure completed properly.
   - **2.2. Critical messages** such as: errors, warnings, merge notes, or uninitialized variables are not found in log. Unavoidable critical messages are verified to not adversely affect the output and the reasons why they are unavoidable are documented.
   - **2.3. Other messages** such as "PUT" or "INFO" messages (e.g., overwritten variables following merge) are handled appropriately, if they are found in log.

3. **Output Review**
   - **3.1. Output file name** follows standard naming conventions and is consistent with other study output file names.
   - **3.2. Titles and footnotes** are verified against mock figure (if available), corresponding table and/or SAP list of figures. Discrepancies, including footnotes added for clarification or to match corresponding table, are noted and verified.
   - **3.3. Axis/legend labels** are verified against mock figure and/or corresponding table.
   - **3.4. Axis ranges** capture all available data and, if required, are consistent across other figures. Tick marks are spaced appropriately.
   - **3.5. Pages breaks** are as intended throughout the document.
   - **3.6. Inappropriate data:** checked for outliers, invalid numbers, missing results, etc.

4. Verification of Results

Verification of results may be performed using one of the following methods. The choice of QC method must be approved by the Biostatistics Project Lead.

4.1. Manual comparison to the corresponding table, where the table is validated and all data points on the figure are compared to the corresponding value on the table.

4.2. Independent confirmatory program is written to match output results.

4.3. Manual calculations (if feasible based on small Ns or frequency counts).

4.4. Manual comparison and program review, where the related table, if produced, is validated and a subset of data points are compared to the table. Program code and logs are reviewed to confirm the intended data is used appropriately throughout the program.

4.5. Study specific alternative method (if applicable) that is agreed upon by the sponsor and defined prospectively in a study specific document (e.g., Validation Plan, SAP or a modified QC requirement template TMP-SOP-0205-003).

5 Documentation

5.1. The Programmer and Validator must document completion of QC (e.g., date of QC completion and method used) in **TMP-SOP-0205-002 Program Status Document**.

5.2. Validator findings and/or comments may be tracked in the Program Status Document along with a description of how the finding was resolved and resolution date.

5.3. The following must be retained electronically within the study folder by the Validator to document the method of QC performed:

- Figure output generated at time of QC completion.
- If comparison to corresponding validated table is performed, the corresponding table output that verifies results (Section 4.1).
- If independent confirmatory program is created, a portion of the resulting output that verifies results (Section 4.2).
- If manual calculations are performed, insert a comment into the output file to indicate verification of results (Section 4.3).

Senior Level Review:

1. Output Package

1.1. **All analysis tables, listings and figures**, as outlined in the SAP are contained in the package. If any are missing, the reason is documented appropriately.

1.2. **Dates and times of electronic output files** are consistent with each other and with the corresponding dates of the source data sets.

1.3. **Output files are sorted in a user-friendly format** such as by table, listing, and figure number. Table of Contents document is included to decode file names, or TLF number is included in the filename itself.

2. **Database and Documentation**
   - **2.1.** **File dates of datasets** within the clinical database, SDTM datasets, and analysis datasets are consistent. All clinical database datasets were updated together at the appropriate time, SDTM datasets (if any) were updated following the update of the clinical database, and analysis datasets were updated following the update of the clinical source datasets and SDTM datasets (if any).
   - **2.2.** **QC of all programs** has been completed by both the Programmer and Validator, as confirmed by **TMP-SOP-0205-002 Program Status Document**.
   - **2.3.** **All datasets, SAS programs, and SAS program logs** have been saved and are ready for archival.
   - **2.4.** **The randomization assignments** have been verified to be accurate in all datasets at the time of the final batch run of programs**.**

3. **Output Review**
   - **3.1.** **Titles are appropriate** and match the corresponding mocks and Table of Contents (if available). Title format and numbering is consistent across all TLFs.
   - **3.2.** **Footnotes are appropriate** and match the corresponding mocks and Table of Contents (if available). Reference numbers are consistent in format and correspond to the body of the output. Version of output is represented accordingly (e.g., DRAFT designation is removed, if final).
   - **3.3.** **Formatting is consistent** across all analysis tables, listings, and figures (i.e., case/punctuation in column and row headers, underlining of column headers, page breaks, etc.).
   - **3.4.** **Invalid data** such as blatant data point errors, outliers, missing data are scanned for in the outputs.
   - **3.5.** **Population denominators** are consistent across summary tables and figures.
   - **3.6.** **Potential discrepancies**, if any, found during review have been corrected and/or handled appropriately.

4. **Statistical Review**
   - **4.1.** **The primary efficacy analysis** and any key secondary efficacy or safety analyses are carefully reviewed for consistency and plausibility. Any potential issues are investigated and discussed with the Programmer and/or Biostatistician.

Appendix C: Prostate Cancer Working Group 2 (PCWG2) Criteria

The PCWG2 criteria establishes disease progression as the following:

Soft-tissue Lesions
Objective response criteria for target, non-target, and new lesions follow RECIST v1.1 criteria:

Target Lesions

Response	Definition
Complete Response (CR)	Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.
Partial Response (PR)	At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
Progressive Disease (PD)	At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of 1 or more new lesions is also considered progression.
Stable Disease (SD)	Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum diameters while on study.

Non-Target Lesions

Response	Definition
Complete Response (CR)	Disappearance of all non-target lesions and normalization of tumour marker level. All lymph nodes must be non-pathological in size (<10 mm short axis).
Non-CR/Non-Progressive Disease (Non-PD)	Persistence of 1 or more non-target lesion(s) and/or maintenance of tumour marker level above the normal limits.
Progressive Disease (PD)	Unequivocal progression of existing non-target lesions. The appearance of 1 or more new lesions is also considered progression.

New Lesions

The unequivocal appearance of new malignant lesions denotes disease progression.

Additional PCWG2 criteria for evaluation of objective response:

- Only changes in lymph nodes that were ≥2 cm in diameter at baseline should be reported
- Favorable change is confirmed with a second scan
- Progression at first assessment must be confirmed by a second scan 6 or more weeks later

Bone Lesions

Response criteria for bone lesions are reported as new lesions or no new lesions. If new lesions are observed, a confirmatory scan 6 or more weeks later is required. If new lesions are observed in the subsequent reassessment, then it is considered progression. For progression, the appearance of ≥2 new lesions, and, for the first reassessment only, a confirmatory scan performed 6 or more weeks later that shows a minimum of 2 or more additional new lesions. The date of progression is the date of the first scan that shows the change.

PSA

PCWG2 criteria recognizes that effects on PSA may be delayed for 12 weeks or more and early rises (prior to 2 weeks) should be ignored in determining PSA response. Percent change from baseline at 12 weeks and the maximal change at any time should be reported.

PSA progression is defined as the date that a 25% or greater increase and an absolute increase of 2 ng/mL or more from the nadir is documented, which is confirmed by a second value obtained 3 or more weeks later. Where no decline from baseline is documented, PCWG2 defines PSA progression as a 25% increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks of treatments.

Appendix D: NCI CTCAE v4.03 Toxicity Grades for Clinical Laboratory Abnormalities

Laboratory Category	Analyte	SI Unit	Directional Change	CTCAE Toxicity Grades
Hematology	Platelet Count	10^9/L	Decrease	Grade 1: < LLN to 75.0 x 10^9/L Grade 2: < 75.0 to 50.0 x 10^9/L Grade 3: <50.0 to 25.0 x 10^9/L Grade 4: < 25.0 x 10^9/L Grade 5: Not defined
	Neutrophils	10^9/L	Decrease	Grade 1: < LLN to 1.5 x 10^9/L Grade 2: < 1.5 to 1.0 x 10^9/L Grade 3: < 1.0 to 0.5 x 10^9/L Grade 4: < 0.5 x 10^9/L Grade 5: Not defined
	Lymphocytes	10^9/L	Decrease	Grade 1: < LLN to 0.8 x 10^9/L Grade 2: < 0.8 to 0.5 x 10^9/L Grade 3: < 0.5 to 0.2 x 10^9/L Grade 4: < 0.2 x 10^9/L Grade 5: Not defined
	White Blood Cells (WBC)	10^9/L	Decrease	Grade 1: < LLN to 3.0 x 10^9/L Grade 2: < 3.0 to 2.0 x 10^9/L Grade 3: < 2.0 to 1.0 x 10^9/L Grade 4: < 1.0 x 10^9/L Grade 5: Not defined
Serum Chemistry	Creatinine	umol/L	Increase	Grade 1: > 1 to 1.5 x baseline or > ULN to 1.5 x ULN Grade 2: > 1.5 to 3 x baseline or 1>1.5 to 3.0 x ULN Grade 3: > 3.0 x baseline or > 3.0 to 6.0 x ULN Grade 4: > 6.0 x ULN Grade 5: Not defined
	Bilirubin (total)	umol/L	Increase	Grade 1: > ULN to 1.5 x ULN Grade 2: > 1.5 to 3.0 x ULN Grade 3: > 3.0 to to 10.0 x ULN Grade 4: > 10.0 x ULN Grade 5: Not defined
	AST (SGOT)	U/L	Increase	Grade 1: > ULN to 3.0 x ULN Grade 2: > 3.0 to 5.0 x ULN Grade 3: > 5.0 to to 20.0 x ULN Grade 4: > 20.0 x ULN Grade 5: Not defined

NCI CTCAE v4.03 Toxicity Grades for Clinical Laboratory Abnormalities (continued)

Laboratory Category	**Analyte**	**Standard Unit**	**Directional Change**	**CTCAE Toxicity Grades**
Serum Chemistry	ALT (SGPT)	U/L	Increase	Grade 1: > ULN to 3.0 x ULN Grade 2: > 3.0 to 5.0 x ULN Grade 3: > 5.0 to to 20.0 x ULN Grade 4: > 20.0 x ULN Grade 5: Not defined
	Glucose	mmol/L	Decrease	Grade 1: < LLN to 3.0 mmol/L Grade 2: < 3.0 to 2.2 mmol/L Grade 3: < 2.2 to 1.7 mmol/L Grade 4: < 1.7 mmol/L Grade 5: Not defined
	Glucose	mmol/L	Increase	Grade 1: > ULN to 8.9 mmol/L Grade 2: > 8.9-13.9 mmol/L Grade 3: > 13.9-27.8 mmol/L Grade 4: > 27.8 mmol/L Grade 5: Not defined

Appendix E: List of Tables, Figures, and Listings

The following TLF numbering is completed according to ICH guidelines. The ICH heading number and description are in **bold**. Minor changes from this planned index do not need to be amended in the SAP.

Formal organization of tabulations may be changed during programming if appropriate, e.g., tables for the different variables may be combined into a single table, or tables with more than 1 variable may be split into several tables.

List of Tables

	Table Number	Table Title
	14	**TABLES, FIGURES, AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT**
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	14.1.1	Patient Disposition
	14.1.2	Protocol Deviations
	14.1.3.1	Demographic (Safety Population)
	14.1.3.2	Baseline Characteristics (Safety Population)
	14.1.4	Medical History at Baseline (Safety Population)
	14.1.5	Prior Cancer Therapy (Safety Population)
	14.1.6	Prior and Concomitant Medications (Safety Population)
	14.2	**EFFICACY DATA**
	14.2.1.1	Overall Response Rate (Radiographic Evaluable Population)
	14.2.1.2	Overall Response Rate (Safety Population)
	14.2.2	PSA Response Rate by PCWG2 Criteria (PSA Evaluable Population)
	14.2.3.1	Serum PSA Change from Baseline (PSA Evaluable Population)

	Table Number	Table Title
	14.2.4	Overall Progression-Free Survival by PCWG2 Criteria (Safety Population)
	14.2.5.1	Radiographic Progression-Free Survival by PCWG2 Criteria – Measured from Baseline (Safety Population)
	14.2.5.2	Radiographic Progression-Free Survival by PCWG2 Criteria – Measured from Baseline (Safety Population with Radiographic Progression or Ongoing at Study Completion)
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14.3		**SAFETY DATA**
	14.3.1	Study Drug Exposure (Safety Population)
14.3.1		**Displays of Adverse Events**
	14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events (Safety Population)
	14.3.1.2	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)
	14.3.1.3	Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Safety Population)
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	14.3.1.5	Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (Safety Population)
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	14.3.4.2	Hematology - Shift from Baseline (Safety Population)
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	14.3.4.9	Serum Troponin (Safety Population)
	14.3.4.10	Incidence of Clinically Significant Laboratory Abnormalities (Safety Population)
	14.3.4.11	ECOG Performance Status – Shift from Baseline (Safety Population)
	14.3.4.12	Vital Signs (Safety Population)
	14.3.4.13	12-Lead Electrocardiogram (Safety Population)
	14.3.4.14	12-Lead Electrocardiogram QTcF Abnormalities (Safety Population)
	14.3.4.15	Ophthalmology Assessments (On-Study Examination) – Clinically Significant Changes from Baseline (Safety Population)

	Table Number	Table Title
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	14.2.2.1	Kaplan-Meier Plot for Overall Progression-Free Survival (Safety Population by Dose Level)
	14.2.2.2	Kaplan-Meier Plot for Overall Progression-Free Survival (Safety Population by Progressor)
	14.2.3.1	Kaplan-Meier Plot for Radiographic Progression-Free Survival (Safety Population by Dose Level)
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List of Data Listings

ICH Heading	Listing Number	Listing Description
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16.2.2		**Protocol deviations**
	16.2.2.1	Protocol Deviations
	16.2.2.2	Informed Consent and Inclusion/Exclusion Criteria
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	16.2.4.4	Prostate-Specific Antigen History
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	16.2.4.6	Prior and Concomitant Medications
16.2.5		**Compliance and/or drug concentration data**
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	16.2.5.2	ZEN003694 Administration – Single Dose
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16.2.6		**Individual efficacy response data**
	16.2.6.1	Tumor Evaluation – Target Lesions
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ICH Heading	Listing Number	Listing Description
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	16.2.8.10	Eastern Cooperative Oncology Group (ECOG) Performance Status
	16.2.8.11	Ophthalmology Examination (Baseline and On-Study) (Safety Population)
	16.2.8.12	Qualitative Exploration of Visual Symptoms (Baseline and In-Clinic) (Safety Population)

Appendix F: Table Layouts

General Table Format Display

Below header applies to all safety analysis tables

	Dose Escalation												Dose Confirmation				
	DE-A							DE-B					DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)

Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.

Below header applies to all efficacy analysis tables (14.2.1.1–14.2.6)

	Enzalutamide Progressor								Abiraterone Progressor					
	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)

Note: 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.

Programmer note: All tables should follow the same column/format display. Tables may/may not necessarily include all of these doses if they were not included in the study. Even if the table shell shows a different structure this general table format display takes precedence. If table cannot fit in one page, please separate to Part 1, Par 2, etc..

Table 14.1.1
Patient Disposition
All Patients

	Dose Escalation												Dose Confirmation				
	DE-A							DE-B					DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Patients Enrolled	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
Safety Population [1]	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Radiographic Evaluable Population [2]	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
PSA Evaluable Population [3]	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
PSA Evaluable Population with at least 12 weeks of treatment	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number of Cycles Completed																	
≤ 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
≤ 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
≤ 6	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
≤ 12	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
> 12	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Primary Reason for Study Completion/Discontinuation																	
Completed study	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Clinical progression by PCWG2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Radiographic progression by PCWG2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
PSA progression with clinical progression by PCWG2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

PSA progression with radiographic progression by PCWG2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Adverse Event	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Treatment with or need for prohibited concomitant medication	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Withdrawal by Subject	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Withdrawal by Physician	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Non-Compliance, Specify	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Lost to Follow-up	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Death	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Termination of study by sponsor	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Other, Specify	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Patients who received any least one dose of ZEN003694.
[2] Patients who receive at least one dose of ZEN003694, have a non-missing baseline and at least one evaluable post-baseline radiographic assessment or discontinues study treatment due to disease progression or death.
[3] Patients who receive at least one dose of ZEN003694, have a non-missing baseline PSA and at least one non-missing post-baseline PSA assessment or discontinues study treatment due to disease progression or death.

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Programmer note: Include all applicable dose escalation and dose confirmation cohorts.

Table 14.1.2
Protocol Deviation

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Number of Protocol Deviations	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Major Protocol Deviations [1]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Inclusion/Exclusion Criteria Not Met	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Non-Compliance with Study Protocol [2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Minor Protocol Deviations	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentage is calculated by dividing the number of protocol deviations (n) by the total number of protocol deviations per cohort. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Patients may be included in more than one protocol deviation category.
[2] Non-compliance with study protocol includes any subject who met withdrawal criteria but was not withdrawn from the study treatment, received excluded or prohibited concomitant medication or treatment, and received the wrong study treatment or incorrect dose of study treatment.

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Table 14.1.3.1
Demographics
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Age (years) [1]														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Sex														
Male	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Ethnicity														
Hispanic or Latino	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not Hispanic or Latino	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Race														
American Indian or Alaska Native	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Asian	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Black or African American	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Native Hawaiian or Other Pacific Islander	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
White	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Multiple Races Checked [2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Height (in)														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Weight (kg)														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
BMI (kg/m^2)														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Source: xxx
Note: Percentages are based on the N of each dose regimen. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Relative to informed consent date.
[2] Subjects with multiple races may not add to the total number of each treatment.

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Table 14.1.3.2
Baseline[1] Characteristics
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
PSA (ng/mL)														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Tumor Burden														
High	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Low	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ECOG Performance Status														
0	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pain	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Opioid Use	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Metastatic Location														
Bone +/- other sites	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Bone only	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Lymphatic +/- other sites	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Visceral	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Soft tissue	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Baseline ALP														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)

Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline LDH														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline Albumin														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Baseline Hemoglobin														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Number of Prior Chemotherapies														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Duration prior ARSI therapy [2]														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Reason for Prior Enzalutamide/Abiraterone Discontinuation														
rPD	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

rPD + PSA	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
cPD + PSA	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
PSA	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.
[2] Prior ARSI therapy includes prior Enzalutamide, prior Apalutamide, prior Abiraterone and prior Ena + Abiraterone if used both.

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Table 14.1.4
Medical History at Baseline
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
Primary System Organ Class / Dictionary-Derived Term	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Resolved Medical History at Baseline														
Primary System Organ Class #1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Primary System Organ Class #2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Ongoing Medical History at Baseline														
Primary System Organ Class #1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Primary System Organ Class #2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dictionary-Derived Term 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. At each level of summation (overall, primary system organ class, dictionary-derived term), patients reporting more than one event are counted only once. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.

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Table 14.1.5
Prior Cancer Therapy
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Prior Systemic Treatment														
Treatment Type														
Chemotherapy	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Biologic Therapy	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Immunotherapy	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Hormonal Therapy	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Other	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Best Overall Response														
CR	n	n	…	n	n	n	n	…	n	n	n	n	n	n
PR	n	n	…	n	n	n	n	…	n	n	n	n	n	n
SD	n	n	…	n	n	n	n	…	n	n	n	n	n	n
PD	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Unknown	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Not Applicable	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Route														
IV	n	n	…	n	n	n	n	…	n	n	n	n	n	n
PO	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Topical	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Other	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Reason Stopped														
Completed Scheduled Regimen	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Progressive Disease	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Toxicity	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Achieved Disease Control	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Other	n	n	…	n	n	n	n	…	n	n	n	n	n	n

Table 14.1.5
Prior Cancer Therapy (continued)
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Prior Surgical Treatment														
Intent														
Curative	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Palliative	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Adjunctive	n	n	…	n	n	n	n	…	n	n	n	n	n	n
								…						
Prior Radiotherapy Treatment														
Type of Radiotherapy														
Internal	n	n	…	n	n	n	n	…	n	n	n	n	n	n
External	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Site of Treatment														
Adrenal Glands	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Bladder	n	n	…	n	n	n	n	…	n	n	n	n	n	n
.														
.														
Other Organ	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Total Radiation Dose (cGY)														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	xx x (xx xx)	xx x (xx xx)		xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)		xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)
Median	xx x	xx x	…	xx x	xx x	xx x	xx x	…	xx x	xx.x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	…	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Best Overall Response														
CR	n	n	…	n	n	n	n	…	n	n	n	n	n	n
PR	n	n	…	n	n	n	n	…	n	n	n	n	n	n
SD	n	n	…	n	n	n	n	…	n	n	n	n	n	n

PD	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Unknown	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Not Applicable	n	n	…	n	n	n	n	…	n	n	n	n	n	n

Source: xxx
Note: CR=Complete Response; PR=Partial Response; SD=Stable Disease; PD=Progressive Disease.
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.

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Table 14.1.6
Prior and Concomitant Medications
Safety Population
Part 1 of 2

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
ATC Class / Preferred Name	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Patients Receiving any Prior Medications [1]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ATC Class 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ATC Class 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.1.6
Prior and Concomitant Medications
Safety Population
Part 2 of 2

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
ATC Class / Preferred Name	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Patients Receiving any Concomitant Medications [2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ATC Class 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ATC Class 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Name 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Preferred Name 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. At each level of summation (overall, ATC class, preferred name), patients reporting more than one medication are counted only once. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Prior medications are those medications taken within 21 days prior to enrollment in the study.
[2] Concomitant medications are those medications taken after the initial dose of ZEN003694.

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Table 14.2.1.1
Overall Response Rate
Radiographic Evaluable Population

	Enzalutamide Progressor								Abiraterone Progressor					
	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)
Best Overall Response (confirmed)														
Complete Response (CR)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Partial Response (PR)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Stable Disease (SD)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Progressive Disease (PD)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not Evaluable (NE)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Overall Response Rate [95% Confidence Interval] [1]														
Confirmed CR + PR	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx.x %]	n (%) [xx.x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx.x %]	n (%) [xx x %, xx x %]	n (%) [xx.x %, xx x %]	n (%) [xx.x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx.x %]

Source: xxx
Note: Percentages are based on the N of each dose regimen. 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.
[1] Binomial exact 95% confidence interval.

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Programmer note: repeat for table 14.2.1.2 Overall Response Rate (Safety Population)

Table 14.2.2
PSA Response Rate by PCWG2 Criteria
PSA Evaluable Population

	Enzalutamide Progressor								Abiraterone Progressor					
	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)
PSA Decline														
< 30% Decline	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
>= 30% Decline	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
>= 50% Decline	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
PSA Response Rate [95% Confidence Interval] [1]														
>= 50% Decline	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx.x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx.x %]	n (%) [xx.x %, xx x %]	n (%) [xx x %, xx.x %]	n (%) [xx.x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx.x %]	n (%) [xx x %, xx x %]	n (%) [xx x %, xx x %]

Source: xxx
Note: Percentages are based on the N of each dose regimen. 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.
[1] Binomial exact 95% confidence interval.

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Programming note: safety follow-up PSA is 30 days after end of treatment and patient off treatment for significant time, therefore this SFU collection should not be used for PSA response rate calculations

Table 14.2.3.1
Serum PSA Change from Baseline
PSA Evaluable Population

	Enzalutamide Progressor								Abiraterone Progressor					
	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)
Baseline [1] (ng/mL)														
n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
Mean (SD)	x x (x xx)	x.x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)	x.x (x.xx)	x.x (x xx)	x.x (x.xx)	x x (x.xx)	x x (x xx)	x.x (x.xx)	x x (x xx)	x x (x xx)
Median	x x	x.x	x x	x.x	x x	x x	x.x	x.x	x x	x x	x x	x x	x x	x x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
Cycle 2 Day 1 (ng/mL)														
n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
Mean (SD)	x x (x xx)	x.x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)	x.x (x.xx)	x.x (x xx)	x.x (x.xx)	x x (x.xx)	x x (x xx)	x.x (x.xx)	x x (x xx)	x x (x xx)
Median	x x	x.x	x x	x.x	x x	x x	x.x	x.x	x x	x x	x x	x x	x x	x x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
Change from Baseline to Cycle 2 Day 1														
n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
Mean (SD)	x x (x xx)	x.x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)	x.x (x.xx)	x.x (x xx)	x.x (x.xx)	x x (x.xx)	x x (x xx)	x.x (x.xx)	x x (x xx)	x x (x xx)
Median	x x	x.x	x x	x.x	x x	x x	x.x	x.x	x x	x x	x x	x x	x x	x x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
Percent Change from Baseline to Cycle 2 Day 1														
n	n	n	n	n	n	n	n	n	n	n	n	n	n	n
Mean (SD)	x x (x xx)	x.x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)	x.x (x.xx)	x.x (x xx)	x.x (x.xx)	x x (x.xx)	x x (x xx)	x.x (x.xx)	x x (x xx)	x x (x xx)
Median	x x	x.x	x x	x.x	x x	x x	x.x	x.x	x x	x x	x x	x x	x x	x x
Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x

…

Source: xxx
Note: 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.
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Table 14.2.4
Overall Progression-Free Survival by PCWG2 Criteria
Safety Population

	Enzalutamide Progressor								Abiraterone Progressor					
Survival Estimates	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)
Number (%) of Patients that Progressed or Died	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number (%) of Patients that Did Not Progress and are Alive	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Min, Max (months patient was progression-free for all patients)	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Min, Max for Non-Censored Patients (months patient was progression-free for patients that progressed or died)	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Kaplan-Meier Quartile Estimates [95% CI] (months progression-free)														
25th Percentile	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
Median	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
75th Percentile	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
Kaplan-Meier Product Limit Estimates (# of patients at risk)														
3 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
6 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
9 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
12 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)

18 Months	x xxx	x xxx	x.xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x.xxx	x.xxx
	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)
24 Months	x xxx	x xxx	x.xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x.xxx	x.xxx
	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)

Source: xxx
Note: Percentages are based on the N of each dose regimen. For patients who progressed (radiographic progression or clinical deterioration) or died, their time to event is calculated as [(date of progression or death) – (treatment start date +1)]/30.44. Patients who did not progress are censored on the date of their last tumor assessment. Their time to event is calculated as [(date of last tumor assessment) – (treatment start date +1)]/30.44.
Note: 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.

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Table 14.2.5.1
Radiographic Progression-Free Survival by PCWG2 Criteria
– Measured from Baseline
Safety Population

	Enzalutamide Progressor								Abiraterone Progressor					
Survival Estimates	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)
Number (%) of Patients that Progressed or Died	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number (%) of Patients that Did Not Progress and are Alive	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Min, Max (months patient was progression-free for all patients)	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Min, Max for Non-Censored Patients (months patient was progression-free for patients that progressed or died)	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Kaplan-Meier Quartile Estimates [95% CI] (months progression-free)														
25th Percentile	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
Median	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
75th Percentile	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
Kaplan-Meier Product Limit Estimates (# of patients at risk)														
3 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
6 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
9 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
12 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)

18 Months	x xxx	x xxx	x.xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x.xxx	x.xxx
	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)
24 Months	x xxx	x xxx	x.xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x.xxx	x.xxx
	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)

Source: xxx
Note: Percentages are based on the N of each dose regimen. For patients who progressed or died, their time to event is calculated as [(date of progression or death) – (treatment start date +1)]/30.44. Patients who did not progress are censored on the date of their last tumor assessment. Their time to event is calculated as [(date of last tumor assessment) – (treatment start date +1)]/30.44.
Note: 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.

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Programmer note: Repeat for table 14.2.5.2 Radiographic Progression-Free Survival by PCWG2 Criteria – Measured from Baseline (Safety Population with Radiographic Progression or Ongoing at Study Completion)

Programmer note: Repeat for table 14.2.5.3 Radiographic Progression-Free Survival by PCWG2 Criteria – Measured from Screening Scan (Safety Population)
Update Note: Percentages are based on the N of each dose regimen. For patients who progressed or died, their time to event is calculated as [(date of progression or death) – (date of screening scan +1)]/30.44. Patients who did not progress are censored on the date of their last tumor assessment. Their time to event is calculated as [(date of last tumor assessment) – (date of screening scan +1)]/30.44.

Table 14.2.6
Time to PSA Progression by PCWG2 Criteria
PSA Evaluable Population with at least 12 weeks of treatment

	Enzalutamide Progressor								Abiraterone Progressor					
Survival Estimates	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	120 mg (N=)	144 mg (N=)	Total (N=)	36 mg (N=)	48 mg (N=)	60 mg (N=)	72 mg (N=)	96 mg (N=)	Total (N=)
Number (%) of Patients with PSA Progression	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Number (%) of Patients that Did Not Progress or Died	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Min, Max (months patient was progression-free for all patients)	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Min, Max for Non-Censored Patients (months patient was progression-free for patients that progressed)	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Kaplan-Meier Quartile Estimates [95% CI] (months progression-free)														
25th Percentile	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
Median	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
75th Percentile	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]	xx [xx, xx]
Kaplan-Meier Product Limit Estimates (# of patients at risk)														
3 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
6 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
9 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)
12 Months	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x xxx (xxx)	x.xxx (xxx)	x.xxx (xxx)

18 Months	x xxx	x xxx	x.xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x.xxx	x.xxx
	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)
24 Months	x xxx	x xxx	x.xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x xxx	x.xxx	x.xxx
	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)	(xxx)

Source: xxx
Note: Percentages are based on the N of each dose regimen. For patients with PSA progression, their time to event is calculated as [(date of PSA progression) – (treatment start date +1)]/30.44. Patients who did not progress or died at time of study exit are censored on the date of their last PSA assessment or date of death. Their time to event is calculated as [(date of last PSA assessment or death) – (treatment start date +1)]/30.44.
Note: 48mg and 96mg dose levels are pooled from Dose Escalation and Dose Comfirmation.

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Table 14.3.1
Study Drug Exposure
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Total Number of Doses Taken														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	x.x (x xx)	x x (x xx)	…	x x (x.xx)	x x (x xx)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)
Median	x x	x x	…	x x	x x	x x	x x	…	x x	x x	x x	x.x	x x	x x
Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x	x, x	x, x	x, x	x, x	x, x
Number of Cycles														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	x.x (x xx)	x x (x xx)	…	x x (x.xx)	x x (x xx)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)
Median	x x	x x	…	x x	x x	x x	x x	…	x x	x x	x x	x.x	x x	x x
Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x	x, x	x, x	x, x	x, x	x, x
Duration of Treatment (weeks) [1]														
n	n	n	…	n	n	n	n	…	n	n	n	n	n	n
Mean (SD)	x.x (x xx)	x x (x xx)	…	x x (x.xx)	x x (x xx)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x xx)	x x (x xx)	x.x (x xx)	x x (x xx)	x x (x xx)
Median	x x	x x	…	x x	x x	x x	x x	…	x x	x x	x x	x.x	x x	x x
Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x	x, x	x, x	x, x	x, x	x, x
Compliance [2]														
>100%	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
>90 – 100%	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
>80 – 90%	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
>70 – 80%	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
<70%	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Duration of treatment is defined as the last dose date minus the first dose date plus 1 divided by 7.
[2] Compliance is calculated using the following equation: Compliance (%)=(Actual number of used doses in total)/(Number of days from treatment start date to treatment end) ×100%.

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Programmer Note: Compliance can be further broken down by visits as appropriate.

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Patients Reporting at Least One TEAE	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One TEAE Related to ZEN003694[2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One TEAE Related to Enzalutamide[2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One Serious TEAE	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One Serious TEAE Related to ZEN003694[2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One Serious TEAE Related to Enzalutamide[2]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One TEAE Leading to Death	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients Reporting at Least One TEAE Leading to Study Discontinuation	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Maximum Severity of TEAEs by CTCAE Grade[1]														
Grade 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 3	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 4	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 5	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Maximum Severity of Serious TEAEs by CTCAE Grade[1]														

Grade 1	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 2	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 3	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 4	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 5	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Closest Relationship to ZEN003694 [2]														
Related[3]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not Related[4]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Closest Relationship to Enzalutamide[2]														
Related[3]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not Related[4]	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	…	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Patients reporting more than one adverse event are counted only once using the highest severity.
[2] Patients reporting more than one adverse event are counted only once using the closest relationship to study drug.
[3] Includes all events reported as "Related" or missing relationship to study drug.
[4] Includes all events reported as "Not Related" relationship to study drug.

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Table 14.3.1.2
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population
Part 1 of 3

	Dose Escalation							
	DE-A							
	36 mg (N=)		48 mg (N=)		…	120 mg (N=)		144mg (N=)	
System Organ Class / Preferred Term	Patients [1]	Events	Patients [1]	Events		Patients [1]	Events	Patients [1]	Events
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n	n		n (%)	n	n (%)	n
System Organ Class 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n		n (%)	n	n (%)	n
.									
.									
System Organ Class 2	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n		n (%)	n	n (%)	n

Table 14.3.1.2
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population
Part 2 of 3

	Dose Escalation							
	DE-B							
	36 mg (N=)		48 mg (N=)		…	72 mg (N=)		96mg (N=)	
System Organ Class / Preferred Term	Patients [1]	Events	Patients [1]	Events		Patients [1]	Events	Patients [1]	Events
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n	n		n (%)	n	n (%)	n
System Organ Class 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n

Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n
.								
.								
System Organ Class 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n

Table 14.3.1.2
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population
Part 3 of 3

	Dose Confirmation									
	DC-A				DC-B					
System Organ Class / Preferred Term	36 mg (N=)		48 mg (N=)		72 mg (N=)		96mg (N=)		Total (N=)	
	Patients [1]	Events	Patients [1]	Events	Patients [1]	Events	Patients [1]	Events	Patients [1]	Events
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
System Organ Class 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
.										
.										
System Organ Class 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n

Source: xxx
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Percentages are based on the N of each dose regimen. At each level of summation (overall, system organ class, preferred term), patients reporting more than one adverse event are counted only once.

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Repeat format for the following tables:

14.3.1.5 "Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term (Safety Population)" *Update first row label to "Patients Reporting at Least One Serious Adverse Event"*

14.3.1.8 "Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term (Safety Population)" *Update first row label to "Patients Reporting at Least One Adverse Event Leading to Death"*

14.3.1.9 "Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term (Safety Population)" *Update first row label to "Patients Reporting at Least One Adverse Event Leading to Study Discontinuation"*

Table 14.3.1.3
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population
Part 1 of 4

	Dose Escalation									
	DE-A									
	36 mg (N=)					…	144 mg (N=)				
System Organ Class / Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
System Organ Class 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
.											
.											
System Organ Class 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.3.1.3
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population
Part 2 of 4

	Dose Escalation									
	DE-B									
	36 mg (N=)					…	96 mg (N=)				
System Organ Class / Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)

System Organ Class 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.										
.										
System Organ Class 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.3.1.3
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population
Part 3 of 4

	Dose Confirmation									
	DC-A									
	36 mg (N=)					96 mg (N=)				
System Organ Class / Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
System Organ Class 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.										
.										
System Organ Class 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.3.1.3
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity
Safety Population
Part 4 of 4

System Organ Class / Preferred Term	Dose Confirmation DC-A 36 mg (N=)					Dose Confirmation DC-A 96 mg (N=)					Total (N=)				
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Patients Reporting at Least One Adverse Event	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
System Organ Class 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.															
.															
System Organ Class 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Preferred Term 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the N of each dose regimen. At each level of summation (overall, system organ class, preferred term), patients reporting more than one adverse event are counted only once using the highest severity. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.

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Repeat format for the following tables:
14.3.1.6 "Serious Treatment-Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Safety Population)" *Update first row label to "Patients Reporting at Least One Serious Adverse Event"*

Table 14.3.1.4
Treatment-Emergent Related[1] Adverse Events by System Organ Class and Preferred Term
Safety Population
Part 1 of 3

System Organ Class / Preferred Term	Dose Escalation DE-A 36 mg (N=) Patients [2]	Events	48 mg (N=) Patients [2]	Events	…	120 mg (N=) Patients [2]	Events	144mg (N=) Patients [2]	Events
Patients Reporting at Least One Related [1] Adverse Event	n (%)	n (%)	n	n		n (%)	n	n (%)	n
System Organ Class 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n		n (%)	n	n (%)	n
.									
.									
System Organ Class 2	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n		n (%)	n	n (%)	n

Table 14.3.1.4
Treatment-Emergent Related[1] Adverse Events by System Organ Class and Preferred Term
Safety Population
Part 2 of 3

System Organ Class / Preferred Term	Dose Escalation DE-B 36 mg (N=) Patients [2]	Events	48 mg (N=) Patients [2]	Events	…	72 mg (N=) Patients [2]	Events	96mg (N=) Patients [2]	Events
Patients Reporting at Least One Related [1] Adverse Event	n (%)	n (%)	n	n		n (%)	n	n (%)	n
System Organ Class 1	n (%)	n (%)	n	n		n (%)	n	n (%)	n

Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n
.								
.								
System Organ Class 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n

Table 14.3.1.4
Treatment-Emergent Related[1] Adverse Events by System Organ Class and Preferred Term
Safety Population
Part 3 of 3

	Dose Confirmation									
	DC-A				DC-B					
	36 mg (N=)		48 mg (N=)		72 mg (N=)		96mg (N=)		Total (N=)	
System Organ Class / Preferred Term	Patients [2]	Events	Patients [2]	Events	Patients [2]	Events	Patients [2]	Events	Patients [2]	Events
Patients Reporting at Least One Related [1] Adverse Event	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
System Organ Class 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
.										
.										
System Organ Class 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 1	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n
Preferred Term 2	n (%)	n (%)	n	n	n (%)	n	n (%)	n	n (%)	n

Source: xxx
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Includes all events reported as "Related" or missing relationship to ZEN003694.
[2] Percentages are based on the N of each dose regimen. At each level of summation (overall, system organ class, preferred term), patients reporting more than one related adverse event are counted only once.

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Repeat format for the following tables:
14.3.1.7 "Treatment-Emergent Related[1] Serious Adverse Events by System Organ Class and Preferred Term (Safety Population)" *Update first row label to "Patients Reporting at Least One Serious Related[1] Adverse Event"*

Table 14.3.2.1
Serious Adverse Events

Dose Regimen	Cohort	Subject ID	AE #	Verbatim Term// MedDRA Preferred Term// System Organ Class	Onset Date (Study Day)	End Date (Study Day)	Severity (CTCAE Toxicity Grade)	DLT	Relationship to ZEN003694	Relationship to Enzalutamide	Action Taken with ZEN003694	Action Taken with Enzalutamide	Treatment of Event	Final Outcome
xx mg, Dose Escalation	1	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/NA	relationship	relationship	action taken	action taken	treatment	outcome
.														
xx mg, Dose Confirmation	x	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/NA	relationship	relationship	action taken	action taken	treatment	outcome

Note: NA=Not Applicable.
* indicates onset of Adverse Event was prior to first Dose.

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Programmer note: sort by onset date and resolution date within each patient

Table 14.3.2.2
Treatment-Emergent Adverse Events Leading to Study Discontinuation

Dose Regimen	Cohort	Subject ID	AE #	Verbatim Term// MedDRA Preferred Term// System Organ Class	Onset Date (Study Day)	End Date (Study Day)	Severity (CTCAE Toxicity Grade)	DLT	Serious	Relationship to ZEN003694	Relationship to Enzalutamide	Action Taken with ZEN003694	Action Taken with Enzalutamide	Treatment of Event	Final Outcome
xx mg, Dose Escalation	1	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/NA	Yes/No	relationship	relationship	action taken	action taken	treatment	outcome
.															
xx mg, Dose Confirmation	x	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/NA	Yes/No	relationship	relationship	action taken	action taken	treatment	outcome

Note: NA=Not Applicable.

path\l_program.sas date time

Programmer note: sort by onset date and resolution date within each patient

Table 14.3.2.3
Treatment-Emergent Adverse Events Leading to Death
Safety Population

Dose Regimen	Cohort	Subject ID	AE #	Verbatim Term// MedDRA Preferred Term// System Organ Class	Onset Date (Study Day)	End Date (Study Day)	Severity (CTCAE Toxicity Grade)	DLT	Serious	Relationship to ZEN003694	Relationship to Enzalutamide	Action Taken with ZEN003694	Action Taken with Enzalutamide	Treatment of Event	Final Outcome
xx mg, Dose Escalation	1	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/NA	Yes/No	relationship	relationship	action taken	action taken	treatment	outcome
.															
xx mg, Dose Confirmation	x	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/NA	Yes/No	relationship	relationship	action taken	action taken	treatment	outcome

Note: NA=Not Applicable.

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Programmer note: sort by onset date and resolution date within each patient

Table 14.3.2.4
Death Details

Dose Regimen	Cohort	Subject ID	Date of Death	Cause of Death	Comments
xx mg, Dose Escalation	1	xxx-xxx	date9.	Progressive Disease/Unknown/ Other, specify	comments
.					
xx mg, Dose Confirmation	x	xxx-xxx	date9.	Progressive Disease/Unknown/ Other, specify	comments

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Table 14.3.4.1
Hematology
Safety Population
Part 1 of 2

		Dose Escalation								
		DE-A					DE-B			
Laboratory Parameter	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
WBC (10^9/L)	Baseline [1]									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Cycle 1 Day 8									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Change from Baseline to C1D8									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	.									
	.									
Neutrophils (10^9/L)										
.										
.										

Table 14.3.4.1
Hematology
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
Laboratory Parameter	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
WBC (10^9/L)	Baseline [1]					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Cycle 1 Day 8					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Change from Baseline to C1D8					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	.					
	.					
Neutrophils (10^9/L)						
.						

Source: xxx
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.
path\t_program.sas date time
Programmer note: Table will include the following hematology parameters: WBC (10^9/L), Neutrophils (10^9/L), Lymphocytes (10^9/L), etc.

Table 14.3.4.2
Hematology – Shift from Baseline
Safety Population
Part 1 of 3

		Dose Escalation								
		DE-A								
		36 mg (N=)			…	120 mg (N=)			144 mg (N=)	
		Baseline [1]				Baseline [1]			Baseline [1]	
Laboratory Parameter	Time Point	Low	Normal	High		Low	Normal	High	Low	Normal	High
WBC	Cycle 1 Day 8		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Cycle 1 Day 15		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	.										
Neutrophils											
.											
.											

Table 14.3.4.2
Hematology – Shift from Baseline
Safety Population
Part 2 of 3

	Dose Escalation				
	DE-B				
	36 mg (N=)		…	72 mg (N=)	96 mg (N=)
	Baseline [1]			Baseline [1]	Baseline [1]

Laboratory Parameter	Time Point	Low	Normal	High	Low	Normal	High	Low	Normal	High
WBC	Cycle 1 Day 8		(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Cycle 1 Day 15		(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.									
	.									
Neutrophils										
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Table 14.3.4.2
Hematology – Shift from Baseline
Safety Population
Part 3 of 3

		Dose Confirmation														
		DC-A						DC-B								
		48 mg (N=) Baseline [1]			96 mg (N=) Baseline [1]			48 mg (N=) Baseline [1]			48 mg (N=) Baseline [1]			Total (N=)		
Laboratory Parameter	Time Point	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High
WBC	Cycle 1 Day 8		(n =)			(n =)			(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Cycle 1 Day 15		(n =)			(n =)			(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.															

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Neutrophils
.
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Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Programmer note: Table will include the following hematology parameters: WBC, Neutrophils, Lymphocyte, etc.

Table 14.3.4.3
Select Hematology Parameters – CTCAE Shift from Baseline
Safety Population
Part 1 of 4

Laboratory Parameter	Time Point	Dose Escalation									
		DE-A									
		36 mg (N=)				…	144 mg (N=)				
		Baseline [1]					Baseline [1]				
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Platelets	Cycle 1 Day 8			(n =)					(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	Cycle 1 Day 15			(n =)					(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	…										
…											

Table 14.3.4.3
Select Hematology Parameters – CTCAE Shift from Baseline
Safety Population
Part 2 of 4

		Dose Escalation

Laboratory Parameter	Time Point	DE-B 36 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	…	DE-B 96 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Platelets	Cycle 1 Day 8			(n =)						(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	.											
	Cycle 1 Day 15			(n =)						(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	…											
…												

Table 14.3.4.3
Select Hematology Parameters – CTCAE Shift from Baseline
Safety Population
Part 3 of 4

Laboratory Parameter	Time Point	Dose Confirmation DC-A 36 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	DC-A 96 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Platelets	Cycle 1 Day 8			(n =)					(n =)		

Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.										
Cycle 1 Day 15			(n =)					(n =)		
Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

…

…

Table 14.3.4.3
Select Hematology Parameters – CTCAE Shift from Baseline
Safety Population
Part 4 of 4

		Dose Confirmation														
		DC-A														
		36 mg (N=)					96 mg (N=)					Total (N=)				
Laboratory Parameter	Time Point	Baseline [1]					Baseline [1]					Baseline [1]				
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Platelets	Cycle 1 Day 8			(n =)					(n =)					(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.															
	Cycle 1 Day 15			(n =)					(n =)					(n =)		

Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

…

…

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

path\t_program.sas date time

Programmer note: Table will include the following hematology parameters: Platelets, WBC, Neutrophils, and Lymphocyte.

Table 14.3.4.4
Coagulation
Safety Population
Part 1 of 2

		Dose Escalation								
		DE-A					DE-B			
Laboratory Parameter	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
PT (sec)	Baseline [1]									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Cycle 1 Day 15									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Change from Baseline to C1D15									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	.									
	.									
INR										
.										

Table 14.3.4.4
Coagulation
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
Laboratory Parameter	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
PT (sec)	Baseline [1]					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Cycle 1 Day 15					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Change from Baseline to C1D15					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	.					
	.					
INR						
.						

Source: xxx
Note: PT=Prothrombin Time; INR=International Normalized Ratio; PTT= Partial Thromboplastin Time. Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

path\t_program.sas date time
Programmer note: Table will include the following coagulation parameters: PT (sec), INR, and PTT (sec)

Table 14.3.4.5
Coagulation – Shift from Baseline
Safety Population
Part 1 of 3

		Dose Escalation								
		DE-A								
		36 mg (N=) Baseline [1]			…	120 mg (N=) Baseline [1]			144 mg (N=) Baseline [1]	
Laboratory Parameter	Time Point	Low	Normal	High		Low	Normal	High	Low	Normal	High
PTT	Cycle 1 Day 15		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Cycle 2 Day 1		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	.										
INR											
.											
.											

Table 14.3.4.5
Coagulation – Shift from Baseline
Safety Population
Part 2 of 3

	Dose Escalation
	DE-B

Laboratory Parameter	Time Point	36 mg (N=) Baseline [1] Low	Normal	High	…	72 mg (N=) Baseline [1] Low	Normal	High	96 mg (N=) Baseline [1] Low	Normal	High
PTT	Cycle 1 Day 15		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Cycle 2 Day 1		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	.										
INR											
.											
.											

Table 14.3.4.5
Coagulation – Shift from Baseline
Safety Population
Part 3 of 3

		Dose Confirmation														
		DC-A						DC-B								
		48 mg (N=) Baseline [1]			96 mg (N=) Baseline [1]			48 mg (N=) Baseline [1]			48 mg (N=) Baseline [1]			Total (N=)		
Laboratory Parameter	Time Point	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High
PTT	Cycle 1 Day 15		(n =)			(n =)			(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Cycle 2 Day 1		(n =)			(n =)			(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

.
.

INR
.
.

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

path\t_program.sas date time

Programmer note: Table will include the following coagulation parameters: PT, INR, and PTT.

Table 14.3.4.6
Serum Chemistry
Safety Population
Part 1 of 2

		Dose Escalation								
		DE-A					DE-B			
Laboratory Parameter	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
ALT (SGPT) (U/L)	Baseline [1]									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Post-Baseline 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Change from Baseline to PB 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	.									
	.									
AST (SGOT) (U/L)										
.										
.										

Table 14.3.4.6
Serum Chemistry
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
Laboratory Parameter	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
ALT (SGPT) (U/L)	Baseline [1]					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Post-Baseline 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Change from Baseline to PB 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	.					
	.					
AST (SGOT) (U/L)						
.						

Source: xxx
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

path\t_program.sas date time
Programmer note: Table will include the following serum chemistry parameters: ALT (SGPT) (U/L), AST (SGOT) (U/L), Alkaline Phosphatase (U/L), Amylase (U/L), Albumin (g/L), Total Bilirubin (umol/L), Blood Urea Nitrogen (BUN) (mmol/L), Creatinine (umol/L), Sodium (mmol/L), Potassium (mmol/L), Chloride (mmol/L), Bicarbonate (mmol/L), Phosphorous (mmol/L), Calcium (mmol/L), Glucose (mmol/L), Magnesium (mmol/L), LDH (U/L), Lipase (U/L), and Serum Testosterone (nmol/L).

Table 14.3.4.7
Serum Chemistry – Shift from Baseline
Safety Population
Part 1 of 3

		Dose Escalation								
		DE-A								
		36 mg (N=) Baseline [1]			…	120 mg (N=) Baseline [1]			144 mg (N=) Baseline [1]	
Laboratory Parameter	Time Point	Low	Normal	High		Low	Normal	High	Low	Normal	High
ALT (SGPT)	Post-Baseline 1		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Post-Baseline 2		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	.										
AST (SGOT)											
.											
.											

Table 14.3.4.7
Serum Chemistry – Shift from Baseline
Safety Population
Part 2 of 3

	Dose Escalation
	DE-B

Laboratory Parameter	Time Point	36 mg (N=) Baseline [1]			…	72 mg (N=) Baseline [1]			96 mg (N=) Baseline [1]		
		Low	Normal	High		Low	Normal	High	Low	Normal	High
ALT (SGPT)	Post-Baseline 1		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Post-Baseline 2		(n =)				(n =)			(n =)	
	Low	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	.										
AST (SGOT)											
.											
.											

Table 14.3.4.7
Serum Chemistry – Shift from Baseline
Safety Population
Part 3 of 3

		Dose Confirmation														
		DC-A						DC-B								
		48 mg (N=) Baseline [1]			96 mg (N=) Baseline [1]			48 mg (N=) Baseline [1]			48 mg (N=) Baseline [1]			Total (N=)		
Laboratory Parameter	Time Point	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High
ALT (SGPT)	Post-Baseline 1		(n =)			(n =)			(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Post-Baseline 2		(n =)			(n =)			(n =)			(n =)			(n =)	
	Low	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Normal	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
High	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

.
.

AST (SGOT)
.
.

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

path\t_program.sas date time

Programmer note: Table will include the following serum chemistry parameters: ALT (SGPT), AST (SGOT), Alkaline Phosphatase, etc.

Table 14.3.4.8
Select Serum Chemistry Parameters– CTCAE Shift from Baseline
Safety Population
Part 1 of 4

Laboratory Parameter	Time Point	Dose Escalation									
		DE-A									
		36 mg (N=)				…	144 mg (N=)				
		Baseline [1]					Baseline [1]				
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
ALT (SGPT)	Cycle 1 Day 8			(n =)					(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	Cycle 1 Day 15			(n =)					(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	…										
…											

Table 14.3.4.8
Select Serum Chemistry Parameters– CTCAE Shift from Baseline
Safety Population
Part 2 of 4

Laboratory Parameter	Time Point	Dose Escalation DE-B 36 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	…	Dose Escalation DE-B 96 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
ALT (SGPT)	Cycle 1 Day 8			(n =)						(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	.											
	Cycle 1 Day 15			(n =)						(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)
	…											
…												

Table 14.3.4.8
Select Serum Chemistry Parameters– CTCAE Shift from Baseline
Safety Population
Part 3 of 4

Laboratory Parameter	Time Point	Dose Confirmation DC-A 36 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Dose Confirmation DC-A 96 mg (N=) Baseline [1] Grade 1	Grade 2	Grade 3	Grade 4	Grade 5

ALT (SGPT)	Cycle 1 Day 8			(n =)				(n =)			
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.										
	Cycle 1 Day 15			(n =)				(n =)			
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	…										
…											

Table 14.3.4.8
Select Serum Chemistry Parameters– CTCAE Shift from Baseline
Safety Population
Part 4 of 4

		Dose Confirmation														
		DC-A														
		36 mg (N=)					96 mg (N=)					Total (N=)				
Laboratory Parameter	Time Point	Baseline [1]					Baseline [1]					Baseline [1]				
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
ALT (SGPT)	Cycle 1 Day 8			(n =)					(n =)					(n =)		
	Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	.															

Cycle 1 Day 15			(n =)					(n =)					(n =)			
Grade 0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Grade 4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

…

…

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Programmer note: Table will include the following serum chemistry parameters: ALT (SGPT), AST (SGOT), Total Bilirubin, Creatinine, and Glucose

Table 14.3.4.9
Serum Troponin
Safety Population
Part 1 of 2

		Dose Escalation								
		DE-A					DE-B			
Laboratory Parameter	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
Troponin I (ng/mL)	Baseline [1]									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Post-Baseline 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Change from Baseline to PB 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x

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Table 14.3.4.9
Serum Troponin
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
Laboratory Parameter	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Troponin I (ng/mL)	Baseline [1]					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Post-Baseline 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Change from Baseline to PB 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	.					
.						

Source: xxx
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

path\t_program.sas date time *Programmer note: Table will include all applicable dose escalation cohorts, and time points. If Troponin T records are available, add Troponin T summaries by visit as well.*

Table 14.3.4.10
Incidence of Clinically Significant Laboratory Abnormalities
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
Any Post-Baseline Clinically Significant Abnormalities?	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Hematology														
WBC	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Neutrophils	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.														
.														
Serum Chemistry														
ALT (SGPT)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
AST (SGOT)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.														
.														

Source: xxx
Note: Percentages are based on the N of each dose regimen. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.

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Table 14.3.4.11
Eastern Cooperative Oncology Group (ECOG) Performance Status – Shift from Baseline
Safety Population
Part 1 of 4

	Dose Escalation																	
	DE-A																	
	36 mg (N=)						48 mg (N=)						…	144 mg (N=)				
	Baseline[1]						Baseline[1]							Baseline[1]				
Time Point	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5
Cycle 1 Day 8			(n =)						(n =)							(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cycle 1 Day 15			(n =)						(n =)							(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.3.4.11
Eastern Cooperative Oncology Group (ECOG) Performance Status – Shift from Baseline
Safety Population
Part 2 of 4

	Dose Escalation
	DE-B

	36 mg (N=) Baseline[1]						48 mg (N=) Baseline[1]						…	96 mg (N=) Baseline[1]					
Time Point	0	1	2	3	4	5	0	1	2	3	4	5		0	1	2	3	4	5
Cycle 1 Day 8			(n =)						(n =)							(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cycle 1 Day 15			(n =)						(n =)							(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.3.4.11
Eastern Cooperative Oncology Group (ECOG) Performance Status – Shift from Baseline
Safety Population
Part 3 of 4

	Dose Confirmation DC-A											
	48 mg (N=) Baseline[1]						96 mg (N=) Baseline[1]					
Time Point	0	1	2	3	4	5	0	1	2	3	4	5
Cycle 1 Day 8			(n =)						(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cycle 1 Day 15			(n =)						(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Table 14.3.4.11
Eastern Cooperative Oncology Group (ECOG) Performance Status – Shift from Baseline
Safety Population
Part 4 of 4

	Dose Confirmation																	
	DC-B																	
	48 mg (N=)						96 mg (N=)						Total (N=)					
	Baseline[1]						Baseline[1]						Baseline[1]					
Time Point	0	1	2	3	4	5	0	1	2	3	4	5	0	1	2	3	4	5
Cycle 1 Day 8			(n =)						(n =)						(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cycle 1 Day 15			(n =)						(n =)						(n =)			
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Programmer note: Table will include all applicable dose escalation cohorts, and time points.

Table 14.3.4.12
Vital Signs
Safety Population
Part 1 of 2

		Dose Escalation								
		DE-A					DE-B			
Vital Sign	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
Systolic Blood Pressure (mmHg)	Baseline [1]									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Post-Baseline 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Change from Baseline to PB 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	.									
Diastolic Blood Pressure (mmHg)										
.										

Table 14.3.4.12
Vital Signs
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
Vital Sign	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Systolic Blood Pressure (mmHg)	Baseline [1]					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Post-Baseline 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Change from Baseline to PB 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	.					
Diastolic Blood Pressure (mmHg)						
.						

Source: xxx
Note: DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Programmer note: Table will include the following vital signs: systolic BP (mmHg), diastolic BP (mmHg), etc.

Table 14.3.4.13
12-Lead Electrocardiogram
Safety Population
Part 1 of 2

		Dose Escalation								
		DE-A					DE-B			
ECG Parameter	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
Ventricular Rate (bpm)	Baseline [1]									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Post-Baseline 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	Change from Baseline to PB 1									
	n	n	n	…	n	n	n	n	…	n
	Mean (SD)	x x (x xx)	x x (x.xx)	…	x x (x.xx)	x x (x.xx)	x.x (x xx)	x.x (x xx)	…	x.x (x xx)
	Median	x x	x x	…	x x	x x	x.x	x.x	…	x.x
	Min, Max	x, x	x, x		x, x	x, x	x, x	x, x		x, x
	.									
	.									
RR Interval (msec)										
.										
.										

Table 14.3.4.13
12-Lead Electrocardiogram
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
ECG Parameter	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Ventricular Rate (bpm)	Baseline [1]					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Post-Baseline 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Change from Baseline to PB 1					
	n	n	n	n	n	n
	Mean (SD)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)	x x (x xx)
	Median	x x	x x	x x	x x	x x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	.					
RR Interval (msec)						
.						

Source: xxx
Note: All descriptive statistics for each ECG parameters are based on the averaged triplicate measurements at each time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Programmer note: Table will include the following ECG parameters: Ventricular rate (bpm RR Interval (msec), PR Interval (msec), QRS Duration (msec), QT Interval (msec), and QTcF (Fridericia's Method) (msec).

Table 14.3.4.14
12-Lead Electrocardiogram – QTc Abnormalities
Safety Population
Part 1 of 2

		Dose Escalation							
		DE-A				DE-B			
ECG Parameter	Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)
QTcF (Fridericia's Method)	Baseline [1]	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)
	> 450 msec and ≤ 480 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 480 msec and ≤ 500 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 500 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	Any Post-Baseline									
	> 450 msec and ≤ 480 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 480 msec and ≤ 500 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 500 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	Change from Baseline to Any PB									
	> 30 msec and ≤ 60 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 60 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	Post-Baseline 1	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)
	> 450 msec and ≤ 480 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 480 msec and ≤ 500 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 500 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	Change from Baseline to PB 1	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)
	> 30 msec and ≤ 60 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	> 60 msec	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)
	.									
	.									

Table 14.3.4.14
12-Lead Electrocardiogram – QTc Abnormalities
Safety Population
Part 2 of 2

		Dose Confirmation				
		DC-A		DC-B		
ECG Parameter	Time Point	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
QTcF (Fridericia's Method)	Baseline [1]	(n =)	(n =)	(n =)	(n =)	(n =)
	> 450 msec and ≤ 480 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 480 msec and ≤ 500 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 500 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	Any Post-Baseline					
	> 450 msec and ≤ 480 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 480 msec and ≤ 500 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 500 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	Change from Baseline to Any PB					
	> 30 msec and ≤ 60 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 60 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	Post-Baseline 1	(n =)	(n =)	(n =)	(n =)	(n =)
	> 450 msec and ≤ 480 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 480 msec and ≤ 500 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 500 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	Change from Baseline to PB 1	(n =)	(n =)	(n =)	(n =)	(n =)
	> 30 msec and ≤ 60 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	> 60 msec	n (%)	n (%)	n (%)	n (%)	n (%)
	.					
	.					

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Table 14.3.4.15
Ophthalmology Assessments (On-Study Examination) – Clinically Significant Changes from Baseline
Safety Population

		Dose Escalation									Dose Confirmation				
		DE-A					DE-B				DC-A		DC-B		
Time Point	Eye	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Cycle 2 Day 1	Left/Right	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)	(n =)	(n =)
New clinically significant changes from baseline		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Consistent with Drug Effect		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not Consistent with Drug Effect		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Unknown		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
BCVA		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Color Vision Plates		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
RAPD		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pupil diameter in bright light		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pupil diameter in dim light		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Velocity of pupillary constriction		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Intraocular Pressure		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Slip lamp exam		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dilated fundoscopic exam		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
OCT of the optic nerve		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Macular OCT		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Fundus photographs of the posterior pole		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cycle 6 Day 1	Left/Right	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)	(n =)	(n =)
.		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
.		n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.

path\t_program.sas date time
Programmer note: Table will include all applicable dose escalation cohorts and time points.

Table 14.3.4.16
Ophthalmology Assessments (Qualitative Exploration of Visual Symptoms)
Safety Population

	Dose Escalation									Dose Confirmation				
	DE-A					DE-B				DC-A		DC-B		
Time Point	36 mg (N=)	48 mg (N=)	…	120 mg (N=)	144 mg (N=)	36 mg (N=)	48 mg (N=)	…	96 mg (N=)	48 mg (N=)	96 mg (N=)	48 mg (N=)	96 mg (N=)	Total (N=)
Baseline [1]	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)	(n =)	(n =)
Abnormal color vision	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Perception of light appearing brighter than normal	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pain or discomfort when in bright environments or looking at bright lights	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Perception of flashing lights	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Trouble navigating or seeing in dimly lit environments	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cycle 2 Day 1	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)		(n =)	(n =)	(n =)	(n =)	(n =)	(n =)
Abnormal color vision	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Perception of light appearing brighter than normal	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pain or discomfort when in bright environments or looking at bright lights	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Perception of flashing lights	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Trouble navigating or seeing in dimly lit environments	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Frequency of Symptoms														
After every dose	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1-2 days/week	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3-4 days/week	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5-7 days/week	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Time after Dosing to Onset of Symptoms (mins)												
n	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx.x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)
Median	xx x	xx x	xx x	xx x	xx x	xx.x	xx x	xx x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Unknown	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Time Until Resolution of Symptoms (mins)												
n	x	x	x	x	x	x	x	x	x	x	x	x
Mean (SD)	xx x (xx xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx.x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx.xx)	xx x (xx.xx)	xx x (xx xx)	xx x (xx.xx)
Median	xx x	xx x	xx x	xx x	xx x	xx.x	xx x	xx x	xx x	xx x	xx x	xx x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Unknown	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Symptoms Constant	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Behaviors that lessen visual symptoms	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Change of symptoms over time while on study	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)	(n =)
Yes, they are lessening	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Yes, they are worsening	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
No, they remain about the same	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Not clear, the symptoms fluctuate too much to tell	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)

Source: xxx
Note: Percentages are based on the n of each dose regimen by time point. DE-A and DC-A indicate enzalutamide progressor. DE-B and DC-B indicate abiraterone progressor.
[1] Baseline is defined as the last non-missing value recorded prior to the first dose of ZEN003694 for patients in Cohorts DE-A and DC-A. For patients in Cohorts DE-B and DC-B, baseline is defined as the last non-missing value recorded prior to the first dose of enzalutamide.

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Programmer note: Table will include all applicable dose escalation cohorts and time points.

Appendix G: Figure Layouts

Appendix H: Listing Layouts

Listing 16.2.1.1
Patient Disposition

Dose Regimen	Cohort	Subject ID	Safety Population [1]	PSA Evaluable Population [2]	PSA Evaluable Population (12 Weeks of Treatment)	Radiographic Evaluable Population [3]	Date of First Dose	Date of Last Dose	Date of Study Exit	Primary Reason for Study Completion/Discontinuation
xx mg, Dose Escalation	1	xxx-xxx	Yes/No	Yes/No	Yes/No	Yes/No	date9.	date9.	date9.	reason
.										
xx mg, Dose Confirmation	x	xxx-xxx	Yes/No	Yes/No	Yes/No	Yes/No	date9.	date9.	date9.	reason

[1] Patients who receive at least one dose of ZEN003694.
[2] Patients who receive at least one dose of ZEN003694, have a non-missing baseline prostate-specific antigen (PSA), and have at least one non-missing postbaseline PSA assessment or who discontinue study treatment due to disease progression or death.
[3] Patients who receive at least one dose of ZEN003694, have a non-missing baseline and have at least one evaluable postbaseline radiographic assessment or who discontinue study treatment due to disease progression or death.

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Listing 16.2.2.1
Protocol Deviations

Dose Regimen	Cohort	Subject ID	Deviation Type	Protocol Deviation Category	Description of Protocol Deviation
xx mg, Dose Escalation	1	xxx-xxx	Major/Minor	category	description
.					
xx mg, Dose Confirmation	x	xxx-xxx	Major/Minor	category	description

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Listing 16.2.2.2
Informed Consent and Inclusion/Exclusion Criteria

Dose Regimen	Cohort	Subject ID	Date Informed Consent Signed	Protocol Version	Did the subject meet all eligibility criteria?	Criterion NOT Met	Criterion No.	Waiver requested?	If requested, Zenith Epigenetics Ltd. approved?	Date Waiver Approved	Re-consent in subsequent protocol?	Protocol Version of Re-Consent	Date of Re-Consent
xx mg, Dose Escalation	1	xxx-xxx	date9.	Ax	Yes/No	INCLXX	EXCLXX	Yes/No	Yes/No	date9.	Yes/No	Ax	date9.
.													
xx mg, Dose Confirmation	x	xxx-xxx	date9.	Ax	Yes/No	INCLXX	EXCLXX	Yes/No	Yes/No	date9.	Yes/No	Ax	date9.

Note: Protocol version dates are as follows: A1=22JAN2016, A2=19SEP2016, A3=20JAN2017, A4=30JUN2017, A5=21JUL2017, A8=09JAN2018, A9=23MAR2018, and A10=05NOV2018.

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Listing 16.2.4.1
Demographics and Baseline Characteristics

Dose Regimen	Cohort	Subject ID	Date Informed Consent Signed	Birth Date	Age on Consent Date (Years)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m^2)	ECOG Score	PSA (ng/mL)
xx mg, Dose Escalation	1	xxx-xxx	date9.	date9.	xx	Male/Female	xxxxx	Hispanic or Latino / Not Hispanic or Latino	xx x	xx x	xx x	x	xx xxx
.													
xx mg, Dose Confirmation	x	xxx-xxx	date9.	date9.	xx	Male/Female	xxxxx	Hispanic or Latino / Not Hispanic or Latino	xx.x	xx x	xx.x	x	xx xxx

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Listing 16.2.4.2
Medical History

Dose Regimen	Cohort	Subject ID	Primary System Organ Class	Condition // Dictionary-Derived Term	Onset Date	Ongoing/ Resolved?	Resolution Date
xx mg, Dose Escalation	1	xxx-xxx	Primary System Organ Class	condition // Dictionary-Derived Term	date9./ Unknown	Ongoing/ Resolved	date9./ Unknown
.							
xx mg, Dose Confirmation	x	xxx-xxx	Primary System Organ Class	condition // Dictionary-Derived Term	date9./ Unknown	Ongoing/ Resolved	date9./ Unknown

Note: A blank onset or resolution date indicates the date is unknown.

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Programmer note: sort by onset date within each patient.

Listing 16.2.4.3
Prostate Cancer History
Part 1 of 4

			Initial Diagnosis					Metastatic Disease		
Dose Regimen	Cohort	Subject ID	Date	Method	Result	Stage	Date of Initial Metastatic Diagnosis	Status	Current Stage	Current Metastatic Sites
xx mg, Dose Escalation	1	xxx-xxx	date9.	method	Adenocarcinoma/ Other, specify	stage	date9.	Histologically Confirmed/Not Histologically Confirmed	stage	sites
.										
xx mg, Dose Confirmation	x	xxx-xxx	date9.	method	Adenocarcinoma/ Other, specify	stage	date9.	Histologically Confirmed/Not Histologically Confirmed	stage	sites

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Listing 16.2.4.3
Prostate Cancer History
Part 2 of 4

							If yes, mark all that apply		
Dose Regimen	Cohort	Subject ID	Last Date of Anti-androgen Therapy	Date of Progression Relative to Anti-androgen Therapy	Disease Progression?[1]	If Yes, Date of Qualifying Event	20% increase in sum of diameter[2]	Growth of existing bone lesions	Growth of existing visceral lesions
xx mg, Dose Escalation	1	xxx-xxx	date9.	date9.	Yes/No/NA	stage	Yes/No	Yes/No	Yes/No
.									
xx mg, Dose Confirmation	x	xxx-xxx	date9.	date9.	Yes/No/NA	stage	Yes/No	Yes/No	Yes/No

Note: NA=Not Applicable
[1] Protocol-defined disease progression per RECIST criteria in a subject with “measureable disease”?
[2] At least 20% increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum longest diameter recorded since the treatment started.
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Listing 16.2.4.3
Prostate Cancer History
Part 3 of 4

				If yes, mark all that apply			If yes, mark all that apply				
Dose Regimen	Cohort	Subject ID	New non-bone scan lesions or 2+ bone scan lesions?[3]	New bone lesions	New visceral lesions	Was there clinical progression?	Unconfirmed new bone lesions	Unconfirmed new visceral lesions	Unconfirmed growth of existing bone lesions	Unconfirmed growth of existing visceral lesions	Clinical status/deterioration
xx mg, Dose Escalation	1	xxx-xxx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
.											
xx mg, Dose Confirmation	x	xxx-xxx	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No

Note: NA=Not Applicable
[3] The appearance of one or more new non-bone scan lesions or two or more bone scan lesions.

Listing 16.2.4.3
Prostate Cancer History
Part 4 of 4

				Reference PSA		Qualifying PSA		Most Recent PSA (Qualifying PSA #2)	
Dose Regimen	Cohort	Subject ID	PSA progression?[4]	Date	Result (ng/mL)	Date	Result (ng/mL)	Date	Result (ng/mL)
xx mg, Dose Escalation	1	xxx-xxx	Yes/No/NA	date9.	xx xxx	date9.	xx xxx	date9.	xx.xxx
.									
xx mg, Dose Confirmation	x	xxx-xxx	Yes/No/NA	date9.	xx xxx	date9.	xx xxx	date9.	xx.xxx

Note: NA=Not Applicable
[4] Protocol-specific PSA progression in a subject with “non-measurable disease”?

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Listing 16.2.4.4
Prostate-Specific Antigen History

Dose Regimen	Cohort	Subject ID	AR Inhibitor Therapy	Result Number	PSA Date of Collection	PSA result (ng/mL)
xx mg, Dose Escalation	1	xxx-xxx	Abiraterone/ Enzalutamide	xxx	date9.	xxx
.						
xx mg, Dose Confirmation	x	xxx-xxx	Abiraterone/ Enzalutamide	xxx	date9.	xxx

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Listing 16.2.4.5
Prior Cancer Therapy
Part 1 of 3 – Prior Chemotherapy Treatment

Dose Regimen	Cohort	Subject ID	Regimen	Treatment Type	Best Overall Response	Drug Name	Start Date	End Date	Route	Reason Stopped	Subject progress following treatment?[1]	Date of Disease Progression[2]	Any additional regimen?[3]
xx mg, Dose Escalation	1	xxx-xxx	regimen	type	CR/PR/SD/PD/ Unknown/NA	drug name	date9.	date9.	route	reason	Yes/No	date9.	Yes/No
xx mg, Dose Confirmation	x	xxx-xxx	regimen	type	CR/PR/SD/PD/ Unknown/NA	drug name	date9.	date9.	route	reason	Yes/No	date9.	Yes/No

Note: NA=Not Applicable; CR=Complete Response; PR=Partial Response; SD=Stable Disease; PD=Progressive Disease.
Note: Listing only includes subjects with reported prior chemotherapy treatment.
[1] Did the subject progress following treatment regimen?
[2] If Yes, Date of Disease Progression following Treatment Regimen.
[3] Are there any additional regimen(s) to be reported?

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Listing 16.2.4.5
Prior Cancer Therapy
Part 2 of 3 – Prior Surgical Treatment

Dose Regimen	Cohort	Subject ID	Procedure	Date of Procedure	Intent
xx mg, Dose Escalation	1	xxx-xxx	procedure	date9.	intent
xx mg, Dose Confirmation	x	xxx-xxx	procedure	date9.	intent

Note: Listing only includes subjects with reported prior surgical treatment.

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Listing 16.2.4.5
Prior Cancer Therapy
Part 3 of 3 – Prior Radiotherapy Treatment

Dose Regimen	Cohort	Subject ID	Type of Radiotherapy	Site Treatment	Total cGY	Best Overall Response	Start Date	End Date
xx mg, Dose Escalation	1	xxx-xxx	Internal/External	site	xxx/Unknown	CR/PR/SD/PD/ Unknown/NA	date9.	xx xxx
.								
xx mg, Dose Confirmation	x	xxx-xxx	Internal/External	site	xxx/Unknown	CR/PR/SD/PD/ Unknown/NA	date9.	xx xxx

Note: NA=Not Applicable; CR=Complete Response; PR=Partial Response; SD=Stable Disease; PD=Progressive Disease.
Note: Listing only includes subjects with reported prior radiotherapy treatment.

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Listing 16.2.4.6
Prior and Concomitant Medications

Dose Regimen	Cohort	Subject ID	CM #	Verbatim Term // Preferred Name	Start Date (Study Day)	Stop Date (Study Day)	Dose (Units)	Form	Route	Frequency	Indication
xx mg, Dose Escalation	1	xxx-xxx	xx	Verbatim term // Preferred Name	date9. (xx)	date9. (xx)/ Ongoing	dose (units)	form	route	frequency	MH: term / AE: term1, term2, term3 / Other: specify
.											
xx mg, Dose Confirmation	x	xxx-xxx	xx	Verbatim term // Preferred Name	date9. (xx)	date9. (xx)/ Ongoing	dose (units)	form	route	frequency	MH: term / AE: term1, term2, term3 / Other: specify

Note: "*" indicates that a medication is a prior medication.

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Programmer note: sort by start date and stop date within each patient.

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Listing 16.2.5.1
Study Drug Compliance

Dose Regimen	Cohort	Subject ID	Date of First Dose	Start Time	Date of Last Dose	# of Doses Taken	Number of Cycles	Duration of Treatment (weeks)	Compliance(%)[1]
xx mg, Dose Escalation	1	xxx-xxx	date9.	time5.	date9.	xx	xx	xx	xx x
.									
xx mg, Dose Confirmation	x	xxx-xxx	date9.	time5.	date9.	xx	xx	xx	xx x

[1] Compliance is calculated using the following equation: Compliance (%)=(Actual number of used doses in total)/(Number of days from treatment start date to treatment end date) ×100%.

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Listing 16.2.5.2
ZEN003694 Administration - Single Dose

Dose Regimen	Cohort	Subject ID	Visit	Was dose taken?	If No, Reason Dose Not Taken	Primary AE [1]	Strength of Dose Taken (mg)	Treatment Date (Study Day)	Treatment Time	Prior after Eating [2]	If No, Estimate Time Subject Ate	Was dose modified since last visit?	Reason for Dose Modification[3]	Primary AE[3]
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes, with no Issue/Yes, with Issues/No	xxxxx	xx	xx	date9.	time5.	Yes/No	time5./ Unknown	Yes, dose increased/Yes, dose decreased/No	xxxxx	xx
.														
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes, with no Issue/Yes, with Issues/No	xxxxx	xx	xx	date9.	time5.	Yes/No	time5./ Unknown	Yes, dose increased/Yes, dose decreased/No	xxxxx	xx

[1] If dose was not taken due to an Adverse Event, provide primary Adverse Event.
[2] Did the subject take their dose at least 1 hour prior to the morning meal or at least 2 hours after eating?
[3] If dose was modified since last visit, specify reason for dose modification. If dose was modified due to an Adverse Event, provide primary Adverse Event.

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Listing 16.2.5.3
ZEN003694 Administration Log

							Dose Taken					Dose Not Taken			
Dose Regimen	Cohort	Subject ID	Start Date (Study Day)	End Date (Study Day)	Frequency	Dose Taken [1]	Specify Dose (mg)	Dose Modified, Specify Reason[2]	Dose Modified, Specify Primary AE[3]	Dose Taken in the Morning[4]	If No, Number of Dose Not Taken in the Morning[5]	Dose Held or Missed[6]	If Dose Was Held, Specify Reason	If Dose Was Missed, Specify Reason	Primary AE[7]
xx mg, Dose Escalation	1	xxx-xxx	date9. (xx)	date9. (xx)	xx	xx	xx	xx	xx	Yes/No/ Unknown	xx	xx	xx	xx	xx
.															
xx mg, Dose Confirmation	x	xxx-xxx	date9. (xx)	date9. (xx)	xx	xx	xx	xx	xx	Yes/No/ Unknown	xx	xx	xx	xx	xx

[1] Was dose/were all doses taken in this time period?
[2] If dose was modified since last entry, specify reason:
[3] If dose was modified due to an Adverse Event, specify Primary AE:
[4] Were all doses in this time period taken in the morning?
[5] If No, how many doses were not taken in the morning based on the dosing diary and accountability?
[6] Was dose held or missed at the time of the Start Date in this time period?
[7] If dose was held or missed due to an Adverse Event, provide primary Adverse Event.

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Listing 16.2.5.4
Enzalautamide Administration - Single Dose

Dose Regimen	Cohort	Subject ID	Visit	Was dose taken?	If No, Reason Dose Not Taken	Primary AE [1]	Strength of Dose Taken (mg)	Treatment Date (Study Day)	Treatment Time	Was dose modified since last visit?	Reason for Dose Modification[2]	Primary AE[2]
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes, with no Issues/Yes, with Issues/No	xxxxx	xx	xx	date9.	time5.	Yes, dose increased/Yes, dose decreased/No	xxxxx	xx
.												
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes, with no Issues/Yes, with Issues/No	xxxxx	xx	xx	date9.	time5.	Yes, dose increased/Yes, dose decreased/No	xxxxx	xx

[1] If dose was not taken due to an Adverse Event, provide primary Adverse Event.
[2] If dose was modified since last visit, specify reason for dose modification. If dose was modified due to an Adverse Event, provide primary Adverse Event.

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Listing 16.2.5.5
Enzalutamide Administration Log

							Dose Taken					Dose Not Taken			
Dose Regimen	Cohort	Subject ID	Start Date (Study Day)	End Date (Study Day)	Frequency	Dose Taken [1]	Specify Dose (mg)	Dose Modified, Specify Reason[2]	Dose Modified, Specify Primary AE[3]	Dose Taken in the Morning[4]	If No, Number of Dose Not Taken in the Morning[5]	Dose Held or Missed[6]	If Dose Was Held, Specify Reason	If Dose Was Missed, Specify Reason	Primary AE[7]
xx mg, Dose Escalation	1	xxx-xxx	date9. (xx)	date9. (xx)	xx	xx	xx	xx	xx	Yes/No/ Unknown	xx	xx	xx	xx	xx
.															
xx mg, Dose Confirmation	x	xxx-xxx	date9. (xx)	date9. (xx)	xx	xx	xx	xx	xx	Yes/No/ Unknown	xx	xx	xx	xx	xx

[1] Was dose/were all doses taken in this time period?
[2] If dose was modified since last entry, specify reason:
[3] If dose was modified due to an Adverse Event, specify Primary AE:
[4] Were all doses in this time period taken in the morning?
[5] If No, how many doses were not taken in the morning based on the dosing diary and accountability?
[6] Was dose held or missed at the time of the Start Date in this time period?
[7] If dose was held or missed due to an Adverse Event, provide primary Adverse Event.

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Listing 16.2.6.1
Tumor Evaluation – Target Lesions

Dose Regimen	Cohort	Subject ID	Visit	Was Radiographic Evaluation performed?	Assessment Date	Lesion #	Location	Technique Used	Longest Diameter (mm)	Sum of Longest Diameters (mm)	Target Lesion Response to Treatment
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes/No/No Target Lesions	date9.	xx	xxx	xxx	xx x/ UNM	xx x	CR/PR/SD/PD/NE
.											
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes/No/No Target Lesions	date9.	xx	xxx	xxx	xx x/ UNM	xx x	CR/PR/SD/PD/NE

Note: UNM=Unable to Measure; NA=Not Applicable.
Note: CR=Complete Response; PR=Partial Response; SD=Stable Disease; PD=Progressive Disease; NE=Not Evaluable.

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Listing 16.2.6.2
Tumor Evaluation – Non-Target Lesions

Dose Regimen	Cohort	Subject ID	Visit	Was Radiographic Evaluation performed?	Assessment Date	Lesion #	Location	Technique Used	Non-Target Lesion Status	Measurement (mm)	Non-Target Lesion Response to Treatment
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes/No/No Non-Target Lesions	date9.	xx	xxx	xxx	xxxx	xx x	CR/IR/SD/PD/NE
.											
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes/No/No Non-Target Lesions	date9.	xx	xxx	xxx	xx.x	xx x	CR/IR/SD/PD/NE

Note: UP=Unequivocally Progressed; UNE=Unable to Evaluate.
Note: CR=Complete Response; IR/SD=Incomplete Response/Stable Disease; PD=Progressive Disease; NE=Not Evaluable.

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Listing 16.2.6.3
Tumor Evaluation – New Lesions

Dose Regimen	Cohort	Subject ID	Visit	Are there any new lesions for this subject?	Assessment Date	Lesion #	Location	Technique Used	Longest Diameter (mm)
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes/No	date9.	xx	xxx	xxx	xx x/ UNM
.									
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes/No	date9.	xx	xxx	xxx	xx x/ UNM

Note: UNM=Unable to Measure.

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Listing 16.2.6.4
Overall Tumor Response Assessment

Dose Regimen	Cohort	Subject ID	Visit	Was the Overall Tumor Response Assessment performed?	Assessment Date	Overall Tumor Response to Treatment
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes/No	date9.	CR/PR/SD/PD/SYMD/NE
.						
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes/No	date9.	CR/PR/SD/PD/SYMD/NE

Note: CR=Complete Response; PR=Partial Response; SD= Stable Disease; PD=Progressive Disease; SYMD=Symptomatic Deterioration; NE=Not Evaluable.

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Listing 16.2.6.5
Derived Clinical Activity Data

Dose Regimen	Cohort	Subject ID	Best Overall Tumor Response[1]	PSA Response[2]	Overall Progression-Free Survival[2][3]		Radiographic Progression-Free Survival[2 [4]		Time to PSA Progression[2][5]	
					Months	Censor	Months	Censor	Months	Censor
xx mg, Dose Escalation	1	xxx-xxx	CR/PR/SD/PD/NE	<30% Decline;30% Decline/50% Decline	xx x	Yes/No	xx x	Yes/No	xx.x	Yes/No
.										
xx mg, Dose Confirmation	x	xxx-xxx	CR/PR/SD/PD/NE	<30% Decline;30% Decline/50% Decline	xx x	Yes/No	xx x	Yes/No	xx.x	Yes/No

Note: CR=Complete Response; PR=Partial Response; SD= Stable Disease; PD=Progressive Disease; NE=Not Evaluable; N/A=Not Applicable.
[1] Best overall tumor response is derived using RECIST 1.1 criteria.
[2] PSA response, radiographic progression-free survival, and time to PSA progression are derived using the PCWG2 criteria.
[3] Overall progression-free survival is measured from the start of treatment with ZEN003694 until the time that disease progression (radiographic disease progression or clinical deterioration) or death is documented. Patients who did not progress overall or did not die prior to study exit are censored on the date of their last tumor assessment.
[4] Radiographic progression-free survival is measured from the start of treatment with ZEN003694 until the time that disease progression based on radiographic assessments or death is documented. Patients who did not progress or did not die prior to study exit are censored on the date of their last radiographic assessment.
[5] PSA Progression occurs when the PSA has increased 25% or greater above nadir and an absolute increase of 2 ng/mL or more from the nadir is documented. When no decline is observed, PSA progression occurs when a 25% increase from baseline value along with an increase in absolute value of 2 ng/mL or more. Time to PSA Progression is measured from the start of treatment with ZEN003694 until the time that the PSA progression is first documented. Patients who did not progress or died prior to study exit are censored on the date of their last PSA assessment or date of death.

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Listing 16.2.6.6
Fresh and Archival Tumor Tissue Collection

Dose Regimen	Cohort	Subject ID	Visit	Was a tissue sample collected?	Type of Biopsy	Sample Collection Date	Sample Collection Time	Stage of Disease when the Tissue was Taken	# Tissue Cores Collected	Tissue Anatomical Location	Detailed Description of Tissue Location
xx mg, Dose Escalation	1	xxx-xxx	visit	Yes/No: reason not done	Archival Tumor Tissue/Fresh Tumor Tissue	date9.	time5./ Unknown	stage	xx	xxxxx	xxxxxx
.											
xx mg, Dose Confirmation	x	xxx-xxx	visit	Yes/No: reason not done	Archival Tumor Tissue/Fresh Tumor Tissue	date9.	time5./ Unknown	stage	xx	xxxxx	xxxxxx

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Note: If Type of Biopsy is blank, the tumor tissue was collected on the Fresh Tumor Tissue Collection CRF.

Programmer note: sort by date, visit, and type of biopsy. Both an archival and fresh tumor tissue sample can be collected at the same time. In these cases, make sure to output both sample information for that visit.

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Listing 16.2.7.1
Adverse Events

Dose Regimen	Cohort	Subject ID	AE #	Verbatim Term// MedDRA Preferred Term// System Organ Class	Onset Date (Study Day)	Resolution Date (Study Day)	Severity (CTCAE Toxicity Grade)	DLT	Severity	Relationship to ZEN003694	Action Taken Relationship to Enzalutamide / Abiraterone	Action Taken with ZEN003694	Action Taken with Enzalutamide / Abiraterone	Treatment of Event	Outcome
xx mg, Dose Escalation	1	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/ NA	Yes/No	relationship	relationship	action taken	action taken	treatment	outcome
.															
xx mg, Dose Confirmation	1	xxx-xxx	xx	xxxxxx	date9.	date9.	grade	Yes/No/ NA	Yes/No	relationship	relationship	action taken	action taken	treatment	outcome

Note: NA=Not Applicable.
Note: * indicates onset of Adverse Event was prior to first dose.

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Programmer note: sort by onset date and resolution date within each patient

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Listing 16.2.8.1
Hematology
Safety Population
Part 1 of 2

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	WBC (10^9/L)	Absolute Neutrophils (10^9/L)	Absolute Lymphocytes (10^9/L)	Absolute Monocytes (10^9/L)	Absolute Eosinophils (10^9/L)	Absolute Basophils (10^9/L)
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx
.											
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx

Listing 16.2.8.1
Hematology
Safety Population
Part 2 of 2

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	RBC (10^{12}/L)	Platelets (10^9/L)	Hemoglobin (g/L)	Hematocrit	MCV (fL)
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xx.xx	xx xx	xx xx	xx xx	xx.xx
.										
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xx.xx	xx xx	xx xx	xx xx	xx.xx

Note: L=Low and H=High with respect to laboratory reference ranges. CS=Clinically Significant, NCS=Not Clinically Significant. CTCAE V4.03 grades are in brackets, where applicable.

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Listing 16.2.8.2
Coagulation
Safety Population

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	PT (sec)	INR	PTT (sec)
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xx.xx	xx xx	xx xx
.								
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xx.xx	xx xx	xx xx

Note: L=Low and H=High with respect to laboratory reference ranges. CS=Clinically Significant, NCS=Not Clinically Significant.

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Listing 16.2.8.3
Serum Chemistry
Safety Population
Part 1 of 3

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	ALT (SGPT) (U/L)	AST (SGOT) (U/L)	Alkaline Phosphatase (U/L)	Amylase (U/L)	Albumin (g/L)	Total Bilirubin (umol/L)	Blood Urea Nitrogen (BUN) (mmol/L)	Creatinine (umol/L)
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx.xx	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx
.													
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx.xx	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx

Listing 16.2.8.3
Serum Chemistry
Safety Population
Part 2 of 3

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Bicarbonate (mmol/L)	Phosphorus (mmol/L)	Calcium (mmol/L)	Glucose (mmol/L)
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx
.												
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx	xx xx

Listing 16.2.8.3
Serum Chemistry
Safety Population
Part 3 of 3

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	Magnesium (mmol/L)	LDH (U/L)	Lipase (U/L)	Serum Testosterone (nmol/L)
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx xx	xx xx	xx xx
.									
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xx xx	xx xx	xx xx	xx xx

Note: L=Low and H=High with respect to laboratory reference ranges. CS=Clinically Significant, NCS=Not Clinically Significant. CTCAE V4.03 grades are in brackets, where applicable.

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Listing 16.2.8.4
Urinalysis
Safety Population
Part 1 of 2

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	Appearance	Color	Protein	Glucose	Ketones	Occult Blood	Bilirubin
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	xxxx	xxxx	xxxx	xxx	xxx	xxx	xxx
.												
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xxxx	xxxx	xxxx	xxx	xxx	xxx	xxx

Listing 16.2.8.4
Urinalysis
Safety Population
Part 2 of 2

Dose Regimen	Cohort	Subject ID	Visit	Collection Date (Study Day)	Collection Time	Was a microscopic exam performed?	Bacteria	Casts	Crystals	RBC (/HPF)	WBC (/HPF)	pH	Specific Gravity
xx mg, Dose Escalation	1	xxx-xxx	xxxx	date9. (xx)	time5.	Yes/No	xxxx	xxxx	xxx	xx.xx	xx xx	xx xx	xx.xx
.													
xx mg, Dose Confirmation	x	xxx-xxx	xxxx	date9. (xx)	time5.	xxxx	xxxx	xxxx	xxx	xx.xx	xx xx	xx xx	xx.xx

Note: L=Low and H=High with respect to laboratory reference ranges. CS=Clinically Significant, NCS=Not Clinically Significant. CTCAE V4.0 grades are in brackets, where applicable.

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Programmer note: "Other" urinalysis test is collected on the CRF. Is other urinalysis test is collected, add a column for this test after Crystals. Column header will be "Other Test Name (unit)".

Listing 16.2.8.5
Serum PSA
Safety Population

Dose Regimen	Cohort	Subject ID	Was a Serum PSA sample collected?	Visit	Collection Date (Study Day)	Collection Time	PSA (ug/L)	Has the subject completed 12 weeks of treatment?	If Yes, has the PSA result increased >25% and at least 2 ng/mL above nadir or baseline, per PCWG2 criteria?
xx mg, Dose Escalation	1	xxx-xxx	Yes/No	xxxx	date9. (xx)	time5.	xx xx	Yes/No	Yes/No
.									
xx mg, Dose Confirmation	x	xxx-xxx	Yes/No	xxxx	date9. (xx)	time5.	xx xx	Yes/No	Yes/No

Note: L=Low and H=High with respect to laboratory reference ranges. CS=Clinically Significant; NCS=Not Clinically Significant.

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Listing 16.2.8.6
Physical Examination

Dose Regimen	Cohort	Subject ID	Visit	Date of Examination	Were there any abnormal findings on the physical examination?
xx mg, Dose Escalation	1	xxx-xxx	visit	date9./Not Done	Yes/No
.					
xx mg, Dose Confirmation	x	xxx-xxx	visit	date9./Not Done	Yes/No

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Listing 16.2.8.7
Echocardiogram or MUGA Scan

Dose Regimen	Cohort	Subject ID	Visit	Was an echocardiogram or MUGA scan performed?	Date of Assessment	Type	LVEF (%)	If abnormal, specify:
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/No	date9.	Echocardiogram/ MUGA Scan	xxx	xxxx
.								
xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/No	date9.	Echocardiogram/ MUGA Scan	xxx	xxxx

Note: LVEF=Left Ventricular Ejection Fraction.

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Listing 16.2.8.8
Vital Signs

Dose Regimen	Cohort	Subject ID	Visit	Were vital signs collected?	Date of Measurements	Time of Measurements	Height (cm)	Weight (kg)	Temperature (°F)	Heart Rate (bpm)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Position of Subject
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/No	date9.	time5.	xx x	xx x	xx x	xxx	xxx	xxx	position
.													
xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/No	date9.	time5.	xx x	xx x	xx x	xxx	xxx	xxx	position

Note: ND=Not Done.

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Listing 16.2.8.9
12-Lead Electrocardiogram
Part 1 of 2 – Interpretation and Clinically Significant Findings

Dose Regimen	Cohort	Subject ID	Visit	Was ECG performed?	Visit Date	Reading No.	Time	Interpretation	Comments Regarding Clinically Significant Findings
xx mg, Dose Escalation	1	xxx-xxx	xxx	Yes/No	date9.	1	Time5./ND	Normal/Abnormal NCS/Abnormal CS	comments
						2	Time5./ND	Normal/Abnormal NCS/Abnormal CS	comments
						3	Time5./ND	Normal/Abnormal NCS/Abnormal CS	comments
						Average[1]	.	.	
.									
xx mg, Dose Confirmation	x	xxx-xxx	xxx	Yes/No	date9.	1	Time5./ND	Normal/Abnormal NCS/Abnormal CS	comments
						2	Time5./ND	Normal/Abnormal NCS/Abnormal CS	comments
						3	Time5./ND	Normal/Abnormal NCS/Abnormal CS	comments
						Average[1	.	.	

Note: ND=Not Done; NCS=Not Clinically Significant; CS=Clinically Significant.

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Listing 16.2.8.9
12-Lead Electrocardiogram
Part 2 of 2 – Quantitative Results

Dose Regimen	Cohort	Subject ID	Visit	Was ECG performed?	Visit Date	Reading No.	Time	Ventricular Rate (bpm)	RR Interval (msec)	PR Interval (msec)	QRS Duration (msec)	QT Interval (msec)	QTc Interval Fridericia (msec) [2]	Serum Troponin (ug/L)
xx mg, Dose Escalation	1	xxx-xxx	xxx	Yes/No	date9.	1	Time5./ ND	xxx	xxx	xxx	xxx	xxx	xxx	xxx
						2	Time5./ ND	xxx	xxx	xxx	xxx	xxx	xxx	xxx
						3	Time5./ ND	xxx	xxx	xxx	xxx	xxx	xxx	xxx
						Average[1]	.	xxx	xxx	xxx	xxx	xxx	xxx	xxx
.														
xx mg, Dose Confirmation	x	xxx-xxx	xxx	Yes/No	date9.	1	Time5./ ND	xxx	xxx	xxx	xxx	xxx	xxx	xxx
						2	Time5./ ND	xxx	xxx	xxx	xxx	xxx	xxx	xxx
						3	Time5./ ND	xxx	xxx	xxx	xxx	xxx	xxx	xxx
						Average[1	.	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Note: ND=Not Done; NCS=Not Clinically Significant; CS=Clinically Significant.
Note: '*' indicates that the Serum Troponin assay used was Troponin T.
[1] Average readings are derived by taking the average measurement of the triplicate measurements (i.e., readings 1-3).
[2] Each individual QTcF result is re-calculated using the following equation: QTcF (msec)=QT/(RR^0.33). The average QTcF result re-derived using the re-calculated individual QTcF results.

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Listing 16.2.8.10
Eastern Cooperative Oncology Group (ECOG) Performance Status

Dose Regimen	Cohort	Subject ID	Visit	Was ECOG assessment performed?	Date of Assessment	Score
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/No	date9.	X - Full score description
.						
xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/No	date9.	X - Full score description

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Programmer note: Display full score description as shown on the actual CRF –

0 – Fully active, able to carry on all pre-disease performance without restriction.
1 – Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work).
2 – Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours.
3 – Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4 – Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.
5 – Dead.

Listing 16.2.8.11
Ophthalmology Examination (Baseline and On-Study)
Safety Population
Part 1 of 2

Dose Regimen	Cohort	Subject ID	Visit	Was eye exam performed?	Date of Exam	Eye	BCVA worse than 20/400?	Color Vision Plates	RAPD present?	Pupil diameter in bright light (mm)	Pupil diameter in dim light (mm)	Velocity of pupillary constriction	Intraocular Pressure (mmHg)
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Left/ Right	Yes: xx/ No: xx	xx/xx	Yes/No	xx xx	xx xx	xxxx	xx xx
.													
xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Left/ Right	Yes: xx/ No: xx	xx/xx	Yes/No	xx xx	xx xx	xxxx	xx xx

Note: BCVA=Best-corrected Visual Acuity. CF=Count Fingers, HM=Hand Motions, LP=Light Perception, and NLP=No Light Perception. RAPD=Relative Afferent Pupillary Deficit.
Note: '*' indicates a clinically significant change from baseline.

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Programmer note: For "Best-Corrected Visual Acuity worse than 20/400?" column, if result is No, include reported Best-corrected visual acuity in Snellen Notation (e.g., 20/20, 20/40, etc.). If result is yes, include level of visual function present (e.g., CF, HM, LP, NLP).

Listing 16.2.8.11
Ophthalmology Examination (Baseline and On-Study)
Safety Population
Part 2 of 2

						Clinically significant abnormalities on:						
Dose Regimen	Cohort	Subject ID	Visit	Was eye exam performed?	Date of Exam	Slight Lamp Exam?	Dilated Funduscopic Exam?	OCT of the optic nerve?	Macular OCT?	Fundus photographs of the posterior pole?	Any new clinically significant changes since baseline?	If changes were detected, were changes consistent with drug effect?
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Yes/No	Yes/No	Yes/No/ ND	Yes/No/ ND	Yes/No/ ND	Yes/No	Yes/No/Unknown
.												
xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Yes/No	Yes/No	Yes/No/ ND	Yes/No/ ND	Yes/No/ ND	Yes/No	Yes/No/Unknown

Note: ND=Not Done.
Note: '*' indicates a clinically significant change from baseline.

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Listing 16.2.8.12
Qualitative Exploration of Visual Symptoms (Baseline and In-Clinic)
Safety Population
Part 1 of 2

							Have you had any of the following symptoms?				
Dose Regimen	Cohort	Subject ID	Visit	Was visual symptom assessment performed?	Date of Exam	Have you experienced any visual symptoms of concern in the past?	Abnormal color vision	Perception of light appearing brighter than normal	Pain or discomfort when in bright environments or looking at bright lights	Perception of flashing lights	Trouble navigating or seeing in dimly lit environments
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
.											
xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No

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Listing 16.2.8.12
Qualitative Exploration of Visual Symptoms (Baseline and In-Clinic)
Safety Population
Part 2 of 2

Dose Regimen	Cohort	Subject ID	Visit	Was visual symptom assessment performed?	Date of Exam	Symptoms occur after ever dose?	How long after dosing do these symptoms start? (mins)	Are symptoms constant?	If no, how long after the symptoms start does it take for them to resolve? (mins)	Are there certain behaviors that lessen these visual symptoms?	Are visual symptoms changing over the time that you have been on the study?
xx mg, Dose Escalation	1	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Yes/No: frequency	xx or range	Yes/No	xx or range	Yes/No	xxx

.

xx mg, Dose Confirmation	x	xxx-xxx	xxxxx	Yes/ No: reason	date9.	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	xxxx

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