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CLINICAL STUDY REPORT

PROCADE: A Multinational, Phase 3, Randomized, Double-Blind, Non-Inferiority, Efficacy, and Safety Study of Oral HC-1119 Versus Enzalutamide in Metastatic Castration-Resistant Prostate Cancer (mCRPC)

STUDY NUMBER: HC1119-CS-03

Name of Test Product:	**HC-1119**
Indication:	Metastatic castration-resistant prostate cancer
Regulatory Agency Identification Number:	EudraCT Number: 2019-001144-22 ClinicalTrials.gov Identifier: NCT03850795
Drug Development Phase:	Phase 3
Sponsor:	Hinova Pharmaceuticals (USA) Inc. 5405 Morehouse Drive, Suite 320 San Diego, CA 92121
Sponsor Signatory:	Xinghai Li, MD, PhD Chief Scientific Officer xhli@hinovapharma.com
Study Initiation Date:	First patient first visit: 15 Mar 2021
Study Completion Date:	Last patient last visit: 28 Jun 2024
Medical Officer:	Frank Perabo, MD, PhD Chief Medical Officer Hinova Pharmaceuticals (USA) Inc.
Date of Report:	**Document Version** / **Date** Original Version 1 / 11 Apr 2025

The study was conducted according to the International Council for Harmonisation harmonized tripartite guideline E6(R2): Good Clinical Practice.

CONFIDENTIAL

Synopsis

Title of Study: PROCADE: A Multinational, Phase 3, Randomized, Double-Blind, Non-Inferiority, Efficacy, and Safety Study of Oral HC-1119 Versus Enzalutamide in Metastatic Castration-Resistant Prostate Cancer (mCRPC)

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Study Phase: Phase 3

Name of Test Product: HC-1119

Sponsor: Hinova Pharmaceuticals (USA) Inc.
5405 Morehouse Drive, Suite 320
San Diego, CA 92121

Study Sites: There was a total of 61 sites including 3 sites in APAC, 46 sites in EMEA, and 12 sites in North America.

Publication(s) (Reference): None

Study Period (Years): 15 Mar 2021 (First patient first visit) to 28 Jun 2024 (Last patient last visit)

Background and Rationale: Prostate cancer remains a significant health concern and is a leading cause of cancer-related deaths among men worldwide. The activity of the androgen receptor (AR) is crucial for the development and progression of prostate cancer, making androgen signaling a key therapeutic target in both localized and advanced stages of the disease. Enzalutamide is a mainstay treatment for mCRPC. However, it is associated with significant central nervous system (CNS) adverse events (AEs), such as severe fatigue, falls, and seizures, due to its ability to penetrate the brain. Deuteration technology, used in drug discovery, is believed to have minimal effects on the chemophysical properties and biochemical activities of a compound but typically alters the drug's pharmacokinetic (PK) characteristics. Deuterium-containing drugs often have significantly lower rates of metabolism, resulting in a longer half-life. Thus, they have the potential to improve drug efficacy through increased circulation time or enhance safety by allowing decreased dose levels without losing efficacy.

HC-1119, a deuterated form of enzalutamide, features a distinct PK profile characterized by slower metabolism and reduced metabolite production due to the kinetic isotope effect. This

results in active substance exposure including HC-1119+M2 in the brain, which is lower than that of enzalutamide, while maintaining similar plasma levels, compared to enzalutamide, potentially leading to fewer CNS effects. Preclinical studies investigating efficacy, toxicology and genotoxicity have been conducted and showed favorable results.

Phase 1 Study Results: Multiple Phase 1 studies evaluating dose escalation, dose expansion, and comparisons with enzalutamide have been conducted in China. Results demonstrated that HC-1119, at doses ranging from 40 mg to 200 mg, showed approximately dose-proportional increases in pharmacokinetics. Additionally, HC-1119 at 80 mg was well-tolerated and showed a favorable safety profile.

In conclusion, preclinical data and Phase 1 study results support further investigation of HC-1119 at 80 mg as a promising therapeutic agent for mCRPC.

Study Objectives and Endpoints:

Objectives	Endpoints
Primary	
• To determine the efficacy of HC-1119 as compared to enzalutamide as assessed by overall response rate (ORR) by Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 until 24 weeks	• Proportion of patients (%) who achieved a confirmed complete or partial response per RECIST 1.1 criteria within 24 weeks after start of treatment
Key Secondary	
• To determine the efficacy of HC-1119 as compared to enzalutamide as assessed by prostate-specific antigen (PSA_{50}) (decline of ≥50% from baseline) at 24 weeks	• Proportion of patients showing a PSA decline of ≥50% from baseline at Week 24
Other Secondary	
• To determine the efficacy of HC-1119 as compared to enzalutamide as assessed by radiologic progression-free survival (rPFS)	• Proportion of patients showing objective evidence or radiologic progression (PD) at Week 24
• To determine the efficacy of HC-1119 as compared to enzalutamide as assessed by overall survival (OS)	• Proportion of patients who are still alive at the time of preplanned primary endpoint analysis
• To determine the efficacy of HC-1119 as compared to enzalutamide as assessed by duration of response (DOR)	• Duration between initial response and first objective evidence or radiologic progression or death
• To determine the efficacy of HC-1119 as compared to enzalutamide as assessed by time to PSA progression	• Time from randomization to first observation of PSA progression

Objectives	Endpoints
• To determine the safety and tolerability of orally administrated HC-1119 as compared to enzalutamide	• Occurrence of AEs and SAEs, clinical laboratory results, physical examinations, vital signs, electrocardiogram (ECG), and concomitant medications
Exploratory	
• To determine the effect of HC-1119 as compared to enzalutamide on first skeletal-related event	• Time to first skeletal-related event, defined as radiation therapy or surgery to bone, pathologic bone fracture, spinal cord compression, or change of antineoplastic therapy to treat bone pain
• To evaluate the effect of HC-1119 as compared to enzalutamide as assessed by PSA response ≥90%	• Confirmed PSA responses were defined as ≥90% reductions in PSA from baseline to lowest postbaseline PSA result
• To evaluate the effect of HC-1119 as compared to enzalutamide on the quality of life using the Functional Assessment of Cancer Therapy-Prostate (FACT-P)	• FACT-P Quality of life questionnaire (assessment of prostate-related symptoms)
• To evaluate the effect of HC-1119 as compared to enzalutamide using the European Quality of Life 5-Domain Scale (EQ-5D) instruments	• EQ-5D Scale answers
• To evaluate the effect of HC-1119 on the Brief Fatigue Inventory (BFI) as compared to enzalutamide	• BFI
• To evaluate the effect of HC-1119 on electrocardiogram (ECG) changes as compared to enzalutamide	• Correlation between changes from baseline in QTcF and plasma concentrations of study drugs and major metabolites
• To collect plasma concentration data of HC-1119, enzalutamide and related metabolite(s)	• Plasma concentrations of studies drug and metabolites
• To construct a population PK model of HC-1119 and related metabolite(s)	• Population pharmacokinetic modelling
• To determine the PK profile of HC-1119, enzalutamide, and related metabolites in a subset of Caucasian (non-Chinese) patients	• Individual PK NCA analysis
• To explore the possible relationship between PK (ie, HC-1119 and related metabolite[s] concentrations) and PD (safety [eg, QT/QTc] and efficacy-related parameter[s])	• Exposure-response analysis for ORR, PSA_{50}, QTcF, and other highly correlated covariates

Methodology:

This was a multinational Phase 3, randomized, double-blind, noninferiority, efficacy, and safety study of oral HC-1119 (80 mg/day) versus enzalutamide (160 mg/day) in asymptomatic or mildly symptomatic patients with progressive mCRPC who have failed androgen deprivation

therapy (ADT). Patients must not had been previously treated with next-generation AR-inhibitors or androgen biosynthesis inhibitors or prior cytotoxic chemotherapy for prostate cancer. Assuming a dropout rate of 10%, approximately 430 patients were planned to be enrolled to have at least 388 evaluable patients, with approximately 60 (ie, ~15%) of the total enrolled patients from China. The study was centrally randomized. The patients were randomly assigned to receive HC-1119 or enzalutamide in a 1:1 ratio. Randomization was stratified by geographic region of the investigative sites (North America, EMEA/Australia, China) as well as by the Eastern Cooperative Oncology Group (ECOG) performance status (ECOG Grades 0 and 1).

Study drug was not to be discontinued unless there was evidence of confirmed radiographic disease progression. Rising PSA alone without evidence radiographic progression was not a reason to discontinue study drug during the first 12 weeks of therapy and was discouraged as a criterion to start a new systemic antineoplastic therapy throughout the study. Radiation therapy and initiation of bisphosphonates or other approved bone targeting agents, with the exception of Radium-223, were allowed and had not to be resulted in discontinuation of study drug therapy. Study drug had to be discontinued prior to initiation of an investigational agent or cytotoxic chemotherapy, whichever occurred first.

Radiographic disease progression was defined by the RECIST 1.1 for soft tissue disease, or the appearance of 2 or more new bone lesions on bone scan as per Prostate Cancer Working Group 3 (PCWG3). Disease progression requires a confirmatory scan. The DOR of HC-1119 was defined as the time between the initial partial or complete response and first objective evidence of radiographic progression (assessed by independent review) or date of death on study due to any cause, whichever occurs first.

The following assessments of prostate cancer status were performed during the trial: soft tissue disease on computed tomography (CT) scan or on magnetic resonance imaging (MRI), bone disease on radionuclide bone scans, FACT-P and EQ-5D, Brief Fatigue Inventory, and PSA.

Study films (CT/MRI and bone scan) were to be read on site and submitted in digital format for an independent central radiology review. Ideally, each site was designated the same radiologist to evaluate the images for any 1 patient for the duration of the trial. Imaging for assessment of radiographic progression was no longer required once radiographic progression was determined (with the exception of confirmatory scans for the first observed progression).

Throughout the study, safety and tolerability was assessed by the recording of AEs, monitoring of vital signs and physical examinations, safety laboratory evaluations, and 12-lead ECGs. Blood samples for population PK for HC-1119 and enzalutamide and related metabolites were collected prior to dosing in Weeks 1, 5, 9, 13, and 25. Blood sample for calculating a full PK profile of

HC-1119 and enzalutamide and related metabolites was collected in 1 patient on Day 1 and in Week 9 or Week 13.

A 25-week ECG sub-study consisting of 8 patients was included to assess safety of HC-1119. Triplicate 12-lead ECGs were taken prior to dosing on Days 1, 8 (Week 2), 15 (Week 3), 22 (Week 4), 29 (Week 5), 57 (Week 9), 85 (Week 13), and 169 (Week 25). ECG recordings were read by a central laboratory only for patients in the ECG sub-study and ECG recordings were read locally for patients who did not participate in the sub-study.

Patients were to have a safety follow-up visit 30 days after last dose of study drug or prior to initiation of any new therapy, or an investigational agent or cytotoxic chemotherapy, whichever occurs first. The end of trial was defined as last patient last visit (LPLV).

Diagnosis and Main Criteria for Inclusion and Exclusion:

The study enrolled patients aged 18 years and above with asymptomatic or mildly symptomatic progressive mCRPC who had failed ADT. Patients with histologically or cytologically confirmed adenocarcinoma of the prostate without significant or relevant neuroendocrine differentiation or small cell features, per the investigator's judgment, were included. Patients who were receiving ADT with a gonadotrophin releasing hormone analogue, antagonist or bilateral orchiectomy (ie, surgical or medical castration) were included. Patients with serum testosterone level <1.7 nmol/L (50 ng/dL) at the screening visit were included. Patients with progressive disease at study entry was defined as 1 or more of the following criteria that occurred while the patient was on ADT:

a. PSA progression defined by a minimum of 2 rising PSA levels with an interval of ≥1 week between each determination. Patients who received an antiandrogen agent were supposed to have progression after withdrawal (≥4 weeks since last flutamide or ≥6 weeks since last bicalutamide or nilutamide). The PSA value at the screening visit had to be ≥2 µg/L (2 ng/mL); and/or
b. Soft tissue disease progression defined by RECIST 1.1; and/or
c. Bone disease progression defined by PCWG3 with ≥2 new lesions on bone scan.

Patients with estimated life expectancy of ≥6 months and with no prior cytotoxic chemotherapy were included.

Patients who either had prior use of or had participated in a clinical study, of an agent that blocks androgen synthesis (eg, abiraterone) or blocks the AR were excluded. Patients with severe concurrent disease, infection, or comorbidity that, in the judgment of the investigator, would have made the patient inappropriate for enrollment; patients with known suspected brain metastasis or active leptomeningeal disease or history of another malignancy within the previous

2 years other than curatively treated nonmelanomatous skin cancer or history of seizure or any condition that might have predisposed a patient to seizure were also excluded. Patients were also excluded if they had received treatment with flutamide, 5-α reductase inhibitors (finasteride, dutasteride), estrogens, systemic biologic therapy for prostate cancer (other than the approved bone targeted agents); or used an investigational agent; received radionuclide therapy; or had undergone major surgery within 4 weeks of enrollment (Day 1 visit).

Study Drug, Dose, and Mode of Administration:

Test Product: HC-1119 was provided as 40 mg soft gelatin capsules to be taken orally 80 mg once per day on a continuous dosing schedule with or without food.

Comparator: The active comparator was enzalutamide and was given daily at 160 mg once per day. Enzalutamide was a marketed product available as 40 mg soft gelatin capsules. For blinding purposes, both HC-1119 and enzalutamide were overencapsulated.

Duration of Study: The total duration of study was 75 months (1 Jan 2019 to 31 Mar 2025).

Patients experiencing clinical effect (as determined by the investigator in consultation with the physician responsible for treating the patient's prostate cancer) continued to receive blinded treatment until the preplanned primary endpoint analysis (24 weeks beyond LPI). Treatment assignment blinding was maintained until the study was unblinded after database lock. The patients continued to receive the same study drug until any discontinuation criterion occurs. All patients were planned to be followed for OS.

Statistical Methods: Assuming a dropout rate of 10%, approximately 430 patients were to be enrolled to have at least 388 evaluable patients. Efficacy was assessed through ORR, PSA decline, rPFS, OS, DOR, time to PSA progression, FACT-P, EQ-5D, and BFI. The efficacy analyses were conducted using a Per-protocol (PP) and an Intent-to-treat (ITT) analysis sets. Safety was assessed through summaries of AEs, laboratory evaluations, vital signs, physical examinations, and ECGs. The safety analyses were conducted using Safety (SAF) analysis set. Drug exposure was summarized by descriptive statistics. The interim analysis was planned but not conducted due to slow enrollment of study patients. An independent data safety monitoring board was planned to be implemented to assess safety on an ongoing basis.

Summary of Results:

***Patient Disposition*:**

A total of 135 patients were screened for the study, of which 31 patients failed screening, mostly as they did not meet the study eligibility criteria.

Of the 135 screened patients, 104 patients were randomly assigned to study drug, with 52 patients in the HC-1119 group and 52 patients in the enzalutamide group. All 104 patients were treated with their assigned treatment, but none completed the study drug due to the reasons listed below.

The most common reasons for discontinuation of study drug were similar between the treatment groups and included: study termination by the sponsor (45 [43.3%] patients of total patients); and progressive disease (42 [40.4%] patients of total patients). AEs leading to study drug discontinuation were reported in 4 [3.8%] patients, all in the HC-1119 group (Note: In some cases, investigators reported 'PSA increased' as a TEAE leading to study or study drug discontinuation in the context of overall clinical disease progression. However, PSA increased is typically not an adverse event, but related to progression, and is therefore not included/counted). Three (5.8%) patients in the HC-1119 group and 2 (3.8%) patients in the enzalutamide group died before treatment completion.

Data Sets Analyzed

All 104 patients who received the study drug were included in both the ITT and SAF sets. Of the 104 patients in the ITT set, 74 (71.2%) patients were included in the PP set.

The most common reasons (>10% of patients overall) for exclusion from the PP set were the absence of postbaseline data for the primary efficacy endpoint (23 [22.1%] patients; 14 [26.9%] patients in HC-1119 group including 11 patients in EMEA region and 3 patients in NA region; and 9 [17.3%] patients in enzalutamide group, all in EMEA region) [Note: This was due to either baseline imaging not showing measurable disease or due to inadequate follow-up imaging (missing contrast, lesions could not be visualized, etc.). It was investigated and as per the local reads, the patients were evaluable], and noncompliance with the inclusion or exclusion criteria (11 [10.6%] patients). Other reasons for exclusion included intake of forbidden medication and noncompliance with the randomization procedure (each in 3 [2.9%] patients); and noncompliance with the study drug (2 [1.9%] patients).

Protocol Deviations

The most frequently reported (>5% of patients overall) major protocol deviation was related to inclusion criteria (10 [9.6%] patients). Other major protocol deviations included concomitant

medication (2 [1.9%] patients); accidental blinding and exclusion criteria (each in 1 [1.0%] patient).

***Demography and Other Baseline Characteristics*:**

Majority of the patients (82 [78.8%]) in the ITT set were >65 years of age with a median age of 72 years (range: 51 years to 86 years). The median body mass index was 28.4 kg/m^2 (range: 18.7 kg/m^2 to 46.7 kg/m^2).

Most patients were White (94 [90.4%] patients), not Hispanic or Latino (98 [94.2%] patients) and from the EMEA/Australia (90 [86.5%] patients) region. None of the patients were enrolled from China region.

All patients had an ECOG performance status of 0 or 1 at randomization. The mean (SD) PSA level at baseline was 93.882 (206.6603) ng/mL.

Overall, demographics and baseline characteristics were as expected in the enrolled population and were comparable between the treatment groups.

Exposure and Compliance:

Exposure

The median duration of study drug was longer in the enzalutamide group compared to the HC-1119 group (500 days vs 404.5 days). Subsequently, the overall median number of capsules taken by patients was higher in the enzalutamide group than in the HC-1119 group (2996.5 vs 2461.0).

Overall, the mean number of days with a dose held was 2 days in both treatment groups. The mean number of days with a missed dose was slightly higher in the HC-1119 group than in the enzalutamide group (9.4 days vs 3.2 days).

Compliance

In the ITT set, the overall median treatment compliance was 99.740% in the HC-1119 group and 100% in the enzalutamide group. In the HC-1119 group, 50 (96.2%) patients had good treatment compliance (defined as >80% of scheduled intake), while all 52 (100%) patients in the enzalutamide group had good treatment compliance.

Similar results were observed in the PP set where the overall median treatment compliance was 99.945% in the HC-1119 group and 100% in the enzalutamide group. In both treatment groups, all patients in the PP set had good treatment compliance.

Efficacy :

The PP dataset was used for primary analyses of the primary and secondary efficacy endpoints, while the ITT dataset was used for secondary analyses of the primary and secondary efficacy endpoints.

Primary Efficacy Endpoint:

- Objective Response Rate Until Week 24

  - There was no statistically significant difference in the proportion of patients achieving an ORR until Week 24 between the 2 treatment groups (44.4% patients in the HC-1119 group vs 52.6% patients in the enzalutamide group, *P*=0.6452). The HC-1119's efficacy, in terms of ORR, did not differ significantly from enzalutamide. However, due to the early termination of the study and only small sample size, no meaningful noninferiority comparison could be made. The results for the primary endpoint observed in the ITT set were similar to those observed in the PP set.

  - The results of the primary endpoint based on the 2 different stratification variables (geographic region and ECOG performance status) were consistent with that of the overall group.

Key Secondary Efficacy Endpoint:

- Proportion of Patients Showing Prostate-Specific Antigen Decline of ≥50% From Baseline at Week 24

  - There was no statistically significant difference in the proportion of patients showing a PSA decline of ≥50% from baseline at Week 24 (55.6% patients in the HC-1119 group vs 65.8% patients in the enzalutamide group, 95% CI: 0.605, 1.274, *P*=0.4909). The results for the key secondary endpoint observed in the ITT set were similar to those observed in the PP set.

Other Secondary Efficacy Endpoint:

- Radiographic Progression-Free Survival

  - The median time to rPFS was 422 days in the HC-1119 group and 468 days in the enzalutamide group, with no statistically significant difference between the 2 treatment groups (*P*=0.7497).

- At Week 24, 10 (27.8%) patients experienced radiologic progression in the HC-1119 group, compared to 7 (18.4%) patients in the enzalutamide group, as assessed by an independent central radiology review. There was no statistically significant difference in the risk of radiologic progression between the 2 treatment groups. Similar results observed in the objective evidence of radiologic progression at Week 24, as assessed by investigator.

➢ Overall Survival:

- The median OS time could not be estimated in either treatment group (12 [33.3%] patients in the HC-1119 group and 8 [21.2%] patients in the enzalutamide group, hazard ratio HC-1119 vs enzalutamide: 1.448, 95% CI: 0.580, 3.614, P=0.4252).

➢ Duration of Response:

- The median DOR for patients treated with HC-1119 was 286 days (range: 98 days to 789 days) and for those treated with enzalutamide was 314 days (range: 83 days to 590 days).

➢ Time to Prostate-Specific Antigen Progression

- The median time to PSA progression could not be estimated for either treatment group, number of events (PSA progression): 4 (11.1%) patients in the HC-1119 vs 6 (15.8%) patients in the enzalutamide group). There was no statistically significant difference between the 2 treatment groups in the time to PSA progression (*P*=0.8770).

The results for the other secondary efficacy endpoints in the ITT set were similar to those observed in the PP set.

<u>Exploratory Efficacy Endpoint:</u>

➢ Prostate-Specific Antigen Response ≥90%

- Proportion of patients with PSA response ≥90% was similar between the HC-1119 group (22 [42.3%] patients) and enzalutamide group (21 [40.4%] patients).

➢ Functional Assessment of Cancer Therapy-Prostate

- The baseline FACT-G total and its subscale scores, prostate cancer subscale score, FACT-P trial outcome index, and subsequently, the FACT-P total score was comparable in both treatment groups. Over time, up to Week 85, all scores showed only small changes from baseline in both treatment groups. After Week 85, the FACT-P scores for its component

variables were available in only few patients in both treatment groups, and no valid conclusions could be made.

- European Quality of Life 5-Domain Scale

  - The mean EQ-5D VAS score at baseline was similar between the 2 treatment groups (71.5 in the HC-1119 group and 71.3 in the enzalutamide group) and showed minimum change from baseline through Week 85 and ranged from –3.5 to 2.5 in the HC-1119 group and –5.6 to 0.8 in the enzalutamide group.

- Brief Fatigue Inventory

  - The BFI fatigue items (fatigue now, fatigue usual level [during past 24 hours], and fatigue worst level [during past 24 hours]) as well as the BFI interference items (general activity, mood, walking ability, normal work, relations with other people, and enjoyment of life) showed minimum change over time from baseline to Week 25.

No apparent treatment-related trends were observed, and no clinically relevant changes in FACT-P score, EQ-5D score, and Brief Fatigue Inventory score were seen in either treatment group.

Safety Results:

- A total of 435 treatment-emergent adverse events (TEAEs) were reported in 88 (84.6%) patients overall, with 45 (86.5%) patients in the HC-1119 group, and 43 (82.7%) patients in the enzalutamide group. The most common TEAEs (>5% of patients in any treatment group) by preferred term (PT) included asthenia, fatigue, hot flush, constipation, coronavirus disease (COVID-19), arthralgia, weight decreased, headache, anemia, edema peripheral, nausea, nasopharyngitis, back pain, diarrhea, decreased appetite, insomnia, neck pain, hypertension, hypotension, fall, and pelvic pain.

  - A total of 36 (34.6%) patients reported Grade 3 or higher TEAEs; 20 (38.5%) patients in the HC-1119 group and 16 (30.8%) patients in the enzalutamide group.

- A total of 38 (36.5%) patients reported TEAEs considered related to study drug:17 (32.7%) patients in HC-1119 group and 21 (40.4%) patients in the enzalutamide group. The most common (>5% of patients in any treatment group) study drug related TEAEs by PT included asthenia, fatigue, hot flush, and nausea. No seizures were observed in any treatment group.

- Three (2.9%) patients experienced AEs that led to death, with 2 (3.8%) patients in the HC-1119 group and 1 (1.9%) patient in the enzalutamide group.

- A total of 34 treatment-emergent serious adverse events (TESAEs) were reported by 22 (21.2%) patients: 22 TESAEs in the HC-1119 group (12 [23.1%] patients) and 12 TESAEs in the enzalutamide group (10 [19.2%] patients). None of the TESAEs by PT were reported in >1 patient in either treatment group, except COVID-19, which was reported in 2 (3.8%) patients in the enzalutamide group and none in the HC-1119 group. One (1.9%) patient, in the enzalutamide group, had a study drug related TESAE of epistaxis.

- A total of 12 TEAEs were reported in 10 (9.6%) patients, which led to study drug discontinuation. This included 7 TEAEs in the HC-1119 group (7 [13.5%] patients) and 5 TEAEs in the enzalutamide group (3 [5.8%] patients). TEAEs by PT leading to HC-1119 discontinuation included weight decreased, COVID-19 pneumonia, anemia, joint range of motion decreased, chronic lymphocytic leukemia, hemorrhage intracranial, and end stage renal disease. TEAEs by PT leading to enzalutamide discontinuation included alanine aminotransferase increased, aspartate aminotransferase increased, COVID-19, peripheral swelling, and scrotal edema.

- Ten TEAEs leading to study discontinuation were reported in 8 (7.7%) patients, with 7 TEAEs in the HC-1119 group (6 [11.5%] patients) and 3 TEAEs in the enzalutamide group (2 [3.8%] patients). TEAEs by PT leading to study discontinuation in the HC-1119 group included weight decreased, joint range of motion decreased, muscular weakness, anemia, road traffic accident, hemorrhage intracranial, and end stage renal disease. TEAEs by PT leading to study discontinuation in the enzalutamide group included peripheral swelling, COVID-19, and scrotal edema.

- No apparent treatment-related trend and no clinically relevant changes were seen in the hematology, clinical chemistry, and urinalysis parameters.

- No apparent treatment-related trend and no clinically relevant changes were seen in the vital sign parameters, ECG measurements, and physical examination parameters.

Pharmacokinetic Results (if applicable):

The population PK report will be provided separately.

Conclusions:

In terms of efficacy, no statistically significant differences were observed between the HC-1119 and enzalutamide across the primary and secondary endpoints acknowledging the very small sample size for analysis. Both treatments demonstrated similar numerical outcomes in terms of ORR, PSA decline of ≥50%, rPFS, and time to PSA progression. Additionally, no significant differences were observed in median OS, DOR, and patient reported outcomes. Although due to the early termination of the study and small sample size, noninferiority comparison could not be made, the observed outcomes suggest that HC-1119 is comparable to enzalutamide in efficacy, with a level of uncertainty due to the relatively small sample sizes in both treatment groups.

In terms of safety, the safety profile of HC-1119 was generally comparable to that of enzalutamide in this study. Both treatments were safe and well-tolerated, with the majority of TEAEs being Grade <3. The overall incidence of TEAEs was similar between the HC-1119 group and the enzalutamide group, with the most common events being asthenia, fatigue, hot flush, constipation, and nausea. No seizures were observed in any group. There were no clinically relevant changes in laboratory tests, vital signs, ECG measurements, and physical examination parameters in either treatment group. Furthermore, no significant treatment-related trends were observed in the overall safety data.

Overall, due to the small sample size of the study, meaningful noninferiority comparison could not be made. Both HC-1119 and enzalutamide showed similar efficacy and safety profiles. The early termination due to the challenges with enrollment of the study limits the ability to definitively assess the full potential of HC-1119 as compared to enzalutamide.

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