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Clinical Trial Protocol

A Phase II, randomized, open-label, multi-center study of JSB462 (luxdegalutamide) in combination with abiraterone in adult male patients with metastatic hormone-sensitive prostate cancer (mHSPC)

Clinical Trial Protocol Number: CJSB462C12201

Version Number: Amended Protocol Version v01 (Clean)

Compound: JSB462

Brief Title: An open-label study of JSB462 (luxdegalutamide) in combination with abiraterone in adult male patients with metastatic hormone-sensitive prostate cancer (mHSPC)

Study Phase: II

Regulatory Agency Identifier Number(s): EU CT number: 2024-520156-22

Sponsor name: Novartis Pharma AG or its affiliates outside of the EEA (where applicable)

Sponsor address: Novartis Pharma AG, Lichtstrasse 35, 4056 Basel, Switzerland

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Clinical Trial Protocol Template Version 9.0 dated, effective 14-Oct-2024

The comparator treatment is abiraterone 1000 mg QD or enzalutamide 160 mg QD.

Treatment Groups:

Participants will be randomized in a 1:1:1 ratio to one of the following arms:

- **Arm 1:** JSB462 100 mg combined with abiraterone 1000 mg QD (arm 1)
- **Arm 2:** JSB462 300 mg combined with abiraterone 1000 mg QD (arm 2) or
- **Arm 3:** ARPI (abiraterone 1000 mg QD or enzalutamide 160 mg QD based on investigator's choice, arm 3)

Number of Participants:

The study will randomize approximately 150 participants.

Key Inclusion Criteria:

1. An Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) ≤2
2. Histologically confirmed adenocarcinoma of the prostate. Participants with mixed histology (neuroendocrine) are not eligible
3. High-volume mHSPC, defined by the presence of ≥1 metastatic visceral non-nodal lesion and/or ≥4 metastatic bone lesions (with at least one lesion outside the vertebral column and/or pelvis) in imaging exams (CT/MRI or bone scan) according to local radiology assessment by the investigator obtained ≤28 days prior to randomization
4. Participants must have a castrate level of serum/plasma testosterone (<50 ng/dL or <1.7 nmol/L). Ongoing ADT (as defined by prior orchiectomy and/or ongoing GnRH analog/antagonist) for ≤90 days is allowed prior to randomization, provided that PSA zero (PSA level <0.2 ng/ml according to local laboratory as assessed by the investigator) is not achieved prior to randomization.

Key Exclusion Criteria:

1. Prior exposure to a second generation ARPI (such as enzalutamide/darolutamide/apalutamide and/or abiraterone) for the treatment of advanced/metastatic disease is not allowed. Prior exposure to an ARPI, to taxane chemotherapy (up to 6 cycles) or to RLT in the context of (neo)adjuvant treatment for localized prostate cancer is allowed, if the last dose of this treatment was administered >12 months from randomization. Prior use of a first generation ARPI (such as bicalutamide) in the context of ADT initiation with a GnRH analog is allowed, provided the first generation ARPI was administered for ≤14 days and last dose was administered ≥7 days from randomization
2. Participants with biochemical recurrence only or those without evidence of metastatic disease by radiological imaging (CT/MRI or bone scan) are not eligible

Data Monitoring/Other Committee:

iDMC and Steering Committee