Apalutamide Plus Intermittent Versus Continuous Androgen Deprivation Therapy in Participants With Metastatic Hormone-Sensitive Prostate Cancer: LIBERTAS Phase 3 Study Design

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STUDY STATUS

- LIBERTAS is the first phase 3 study evaluating intermittent versus continuous ADT in mHSPC and the first degendered and transgender-inclusive prostate cancer study
- The study start date was August 31, 2023
- Approximately 333 participants will be enrolled over 2 years at 86 sites across 9 countries (Australia, Brazil, Canada, China, France, Germany, Mexico, Poland, and United States)
- Total time: ≈5.6 years (22 months accrual plus 45 months of treatment)

ADT, androgen deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer.

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INTRODUCTION

- Apalutamide (APA) is an androgen receptor pathway inhibitor approved for treatment of metastatic hormone-sensitive prostate cancer (mHSPC) and nonmetastatic castration-resistant prostate cancer with ongoing treatment with androgen deprivation therapy (ADT)[1]
- In the phase 3 TITAN study of participants with mHSPC treated with APA + ADT, a deep prostate-specific antigen (PSA) decline (≥90% PSA decline from baseline, undetectable PSA [≤0.2 ng/mL], or both) achieved at 3, 6, and 12 months of APA treatment was associated with improved clinical outcomes, including overall survival (OS) and radiographic progression-free survival (rPFS)[2]
- ADT is associated with adverse events and decreased quality of life (QoL) in individuals with advanced prostate cancer.[3] However, treatment recommendations on the use of intermittent ADT as an ADT-sparing approach are limited
- LIBERTAS is the first phase 3 study evaluating APA + intermittent versus continuous ADT in individuals with mHSPC
- Moreover, LIBERTAS is the first degendered and transgender-inclusive prostate cancer study, serving as a foundational guide for future clinical study protocols
- Broad eligibility criteria are used to achieve greater inclusiveness of underserved and under-represented populations and allow for increased diversity in race, ethnicity, gender identity, and physical disability of study participants

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OBJECTIVE

- The objective of the LIBERTAS study is to evaluate whether APA + intermittent ADT in participants with mHSPC who achieved PSA <0.2 ng/mL after 6 months of initial therapy with APA + ADT provides noninferior rPFS and reduces hot flash burden compared with APA + continuous ADT

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METHODS (1/4)

- LIBERTAS is an international, open-label, randomized study enrolling participants with mHSPC, inclusive of all gender identities (Figure 1)
- Approximately 333 participants will be enrolled over 2 years at 86 sites across 9 countries
- A degendered and trans-inclusive protocol is used to encourage recruitment and enrollment of participants in sexual and gender minority populations that are underserved and under-represented in clinical trials
- Subjective patient-reported outcomes (PROs) will be complemented with objective data from digital health tools (ActiGraph watch[4] and CANTAB® neurocognitive assessments[5]) to better characterize QoL in the intermittent and continuous ADT arms
- An independent data monitoring committee will conduct an interim analysis for futility for the primary end point and periodic review of safety data

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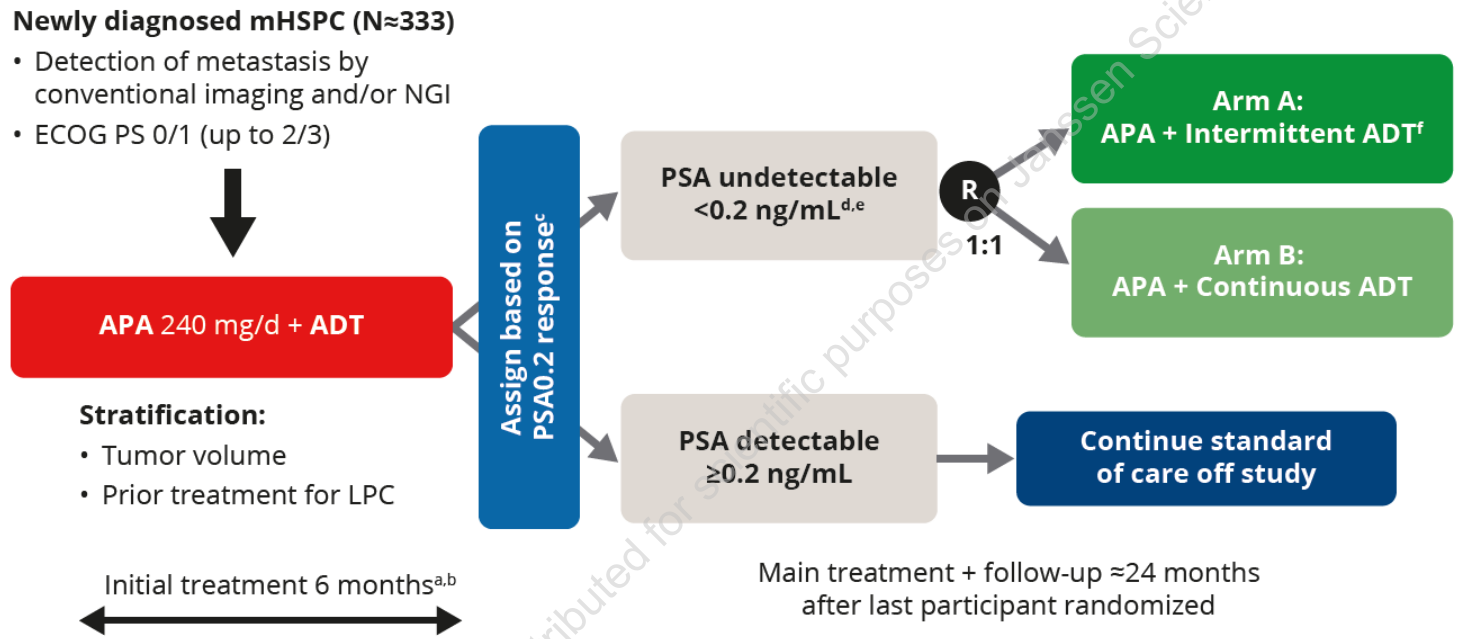
METHODS (2/4)

FIGURE 1: LIBERTAS study design



ECOG PS, Eastern Cooperative Oncology Group performance status; GnRHa, gonadotropin-releasing hormone agonist/antagonist; LPC, localized prostate cancer; NGI, next-generation imaging. [a]Participants receive APA 240 mg/d + ADT during the initial 6-month treatment phase. [b]The choice of the GnRHa (agonist or antagonist) will be at the discretion of the investigator. [c]PSA0.2 response refers to whether PSA is <0.2 or ≥0.2 ng/mL. [d]Participants with confirmed PSA <0.2 ng/mL at the end of the initial 6-month treatment phase enter the main treatment phase and are randomized 1:1 to APA (240 mg/d) + intermittent ADT or APA + continuous ADT. [e]Participants with PSA <0.2 ng/mL undergoing gender-affirming care will be evaluated as a separate cohort. These participants will not be randomized for the main treatment phase and will be treated similarly to Arm A participants. [f]ADT can be restarted in the APA + intermittent ADT group for participants with new or worsening cancer symptoms, PSA increase to >10 ng/mL (or return to baseline level when PSA was <10 ng/mL before start of ADT), or PSA doubling time <6 months.

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METHODS (3/4)

FIGURE 1: LIBERTAS study design (cont)

Coprimary end points
rPFS at 18 months from randomization • Radiographic progression assessed using conventional imaging[g]
Hot flash severity score and hot flash frequency at 18 months from randomization • Hot flashes will be evaluated using the Hot Flash Related Daily Interference Scale PRO questionnaire[6]

Key secondary end points
Mean daily changes in hot flash severity score from baseline to all postrandomization visits
PFS2
OS and cancer-specific survival
PSA outcomes
Duration of time on ADT
Duration of time with testosterone <50 ng/dL
Time to recovery of testosterone >50 ng/dL
Time to mCRPC
Safety
PROs, QoL, hot flash–related QoL[h]
Clinical (wearable) and neurocognitive insights[h]

mCRPC, metastatic castration-resistant prostate cancer; PFS2, progression-free survival on subsequent therapy.
[g]Conventional imaging (CT/MRI and ^{99m}Tc bone scans) will be used for the assessment of the primary and secondary end points. [h]Findings from digital health tools measure sleep, activity and neurocognitive function, and PROs, including physical and mental wellbeing.

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METHODS (4/4)

FIGURE 1: LIBERTAS study design (cont)

Key inclusion criteria

- Metastatic prostate cancer (≥2 distinct extraprostatic sites of metastasis) documented by conventional imaging (CT, MRI, or bone scan) and/or NGI
- Testosterone >50 ng/dL at screening, except in those who received ADT prior to screening
- ≤3 months of ADT prior to enrollment except for participants receiving ADT as part of their gender-affirming care
- ECOG PS 0 or 1; participants with ECOG PS 2 or 3 are eligible if their score is related to stable physical disabilities (eg, spinal cord injury or blindness) and not to prostate cancer or associated therapy

Key exclusion criteria

- Pelvic lymph nodes as only site of metastasis
- Prior treatment for metastatic prostate cancer, ≤3 months of ADT combined with focal radiation to an oligometastatic site since the diagnosis of mHSPC is permitted
- For LPC or LAPC, participants must have received ≤3 years total of ADT and all other forms of prior systemic therapies for prostate cancer and all such therapies completed ≥1 year prior to the first dose of APA (except for participants who receive gender-affirming hormonal therapy)
- Surgical intervention for the treatment of prostate cancer within 28 days of study drug initiation
- History of seizure or known condition determined to significantly predispose to seizure per investigator
- Any of the following within 6 months prior to screening: severe or unstable angina, myocardial infarction, symptomatic congestive heart failure, uncontrolled hypertension, clinically significant arterial or venous thromboembolic events

CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; LPC, localized prostate cancer; LAPC, locally advanced prostate cancer; MRI, magnetic resonance imaging; NGI, next-generation imaging.

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TRIAL REGISTRATION:

ClinicalTrials.gov Identifier: NCT05884398

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DISCLOSURES:

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