Deep Prostate-Specific Antigen Decline Among Early Participants in LIBERTAS, a Phase 3 Study of Apalutamide Plus Continuous Versus Intermittent Androgen Deprivation Therapy in Metastatic Castration-Sensitive Prostate Cancer

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[1]Peter MacCallum Cancer Centre, Melbourne, Australia; [2]Hospital Aranda de la Parra, Guanajuato, Mexico; [3]West China Hospital of Sichuan University, Sichuan, China; [4]Dana-Farber Cancer Institute, Boston, MA, USA; [5]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [6]New York-Presbyterian/Columbia University Medical Center, New York, NY, USA; [7]University of Texas, Southwestern Medical Center, Dallas, TX, USA; [8]University of Calgary, Calgary, Alberta, Canada; [9]University Hospital Schleswig-Holstein, Lübeck, Germany; [10]Johnson & Johnson, Raritan, NJ, USA; [11]Johnson & Johnson, Titusville, NJ, USA; [12]University of Utah Health Hospitals and Clinics, Salt Lake City, UT, USA

Presenting author

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KEY TAKEAWAY

Initial findings from LIBERTAS show that 70% of participants had a rapid and deep PSA decline at 6 months of APA + ADT, consistent with results from the pivotal TITAN phase 3 and real-world study observations

ADT, Androgen deprivation therapy; APA, Apalutamide ; PSA, Prostate-specific antigen.

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CONCLUSIONS

- In this prospective study, 70.6% and 79.0% of participants who completed the 6-month initial treatment phase with APA + ADT achieved PSA <0.2 ng/mL and ≥90% PSA decline from baseline, respectively
- No new safety signals were observed for APA + ADT; its safety profile remains consistent with prior findings
- LIBERTAS remains on track for successful completion of expected randomization for the standard APA + ADT versus APA + ADT de-escalation; enrollment is ongoing for participants undergoing gender-affirming care

ADT, Androgen deprivation therapy; APA, Apalutamide ; PSA, Prostate-specific antigen.

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INTRODUCTION

- LIBERTAS is the first phase 3 study that explores the use of APA in combination with intermittent ADT as an ADT de-escalation strategy for participants with mCSPC who achieved PSA <0.2 ng/mL after 6 months of initial treatment with APA + ADT
- ADT de-escalation in combination with an androgen receptor pathway inhibitor is highly desirable to reduce the ADT side effect burden without loss of efficacy
  - However, treatment recommendations on the use of an ADT de-escalation approach are limited
- Treatment of patients with mCSPC with the combination of APA + ADT led to a rapid and deep decline in PSA levels. In the TITAN phase 3 study, 54% (263/490) of patients with mCSPC treated with APA + ADT achieved undetectable PSA levels (≤0.2 ng/mL) at 3 months.[1] Patients reaching even lower PSA levels (ultralow at ≤0.02 ng/mL vs PSA >0.2 ng/mL) experienced incrementally longer survival and longer maintenance of health-related quality of life.[2,3] Consistent results of rapid and deep PSA decline with APA have been shown in real-world studies[4-6]
- The overall objective of the LIBERTAS study is to evaluate whether APA + intermittent ADT in participants with mCSPC 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
- Here, we present initial findings of participants enrolled early in LIBERTAS

1. Chowdhury S, et al. Ann Oncol. 2023;34:477-485. 2. Merseburger A, et al. BJU Int. 2024;134:982-991. 3. Small E, et al. Eur Urol Oncol. 2024;7:844-852. 4. Lowentritt B, et al. Urol Oncol. 2023:41:253e1-253e9. 5.López-Abad A, et al. J Clin Med. 2024;13:6221. 6. Wenzel M, et al. Eur Urol Oncol. 2024 Aug 31 [Epub ahead of print].

ADT, Androgen deprivation therapy; APA, Apalutamide; mCSP, Metastatic castration-sensitive prostate cancer; PSA, Prostate-specific antigen; rPFS, radiographic progression-free survival

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METHODS

- LIBERTAS uses eligibility criteria similar to those of TITAN and allows inclusion of individuals previously under-represented in clinical trials, including Black and African American participants, transgender, nonbinary, and gender-diverse participants, and participants with disabilities, as well as those showing metastases on PSMA-PET scan only
- Participants undergoing GAC are eligible for enrollment as a separate cohort with or without evidence of metastasis by conventional imaging or NGI
- In the initial 6-month treatment phase, all participants receive APA 240 mg/d + ADT. In the main treatment phase, participants with confirmed PSA <0.2 ng/mL after the initial treatment phase will be randomized 1:1 to APA 240 mg/d + intermittent or continuous ADT
- Primary endpoints are rPFS and reduction of hot flash burden, measured by the severity-adjusted hot flash score. Secondary end points and eligibility criteria are available at https://clinicaltrials.gov/study/NCT05884398

APA, Apalutamide; ADT, Androgen deprivation therapy; GAC, Gender-affirming care; NGI, Next-generation imaging; PSA, Prostate- specific antigen; PSMA, Prostate-specific membrane antigen positron emission tomography; rPFS, Radiographic progression-free survival

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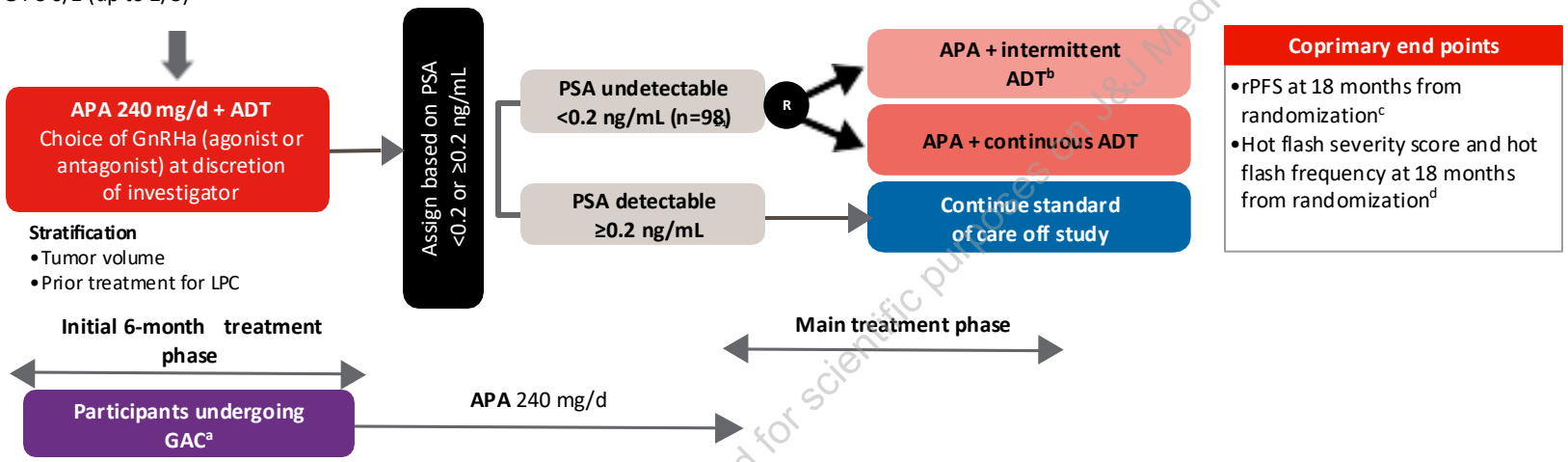
Figure 1: Early enrolment in LIBERTAS

N=420 participants enrolled early
- Newly diagnosed mCSPC
- Metastatic prostate cancer documented by conventional imaging and/or regional lymph node metastases by NGI
- ECOG PS 0/1 (up to 2/3)



Coprimary end points
- rPFS at 18 months from randomization[c]
- Hot flash severity score and hot flash frequency at 18 months from randomization[d]

[a]Participants undergoing GAC or with a variation in physical development who receive exogenous hormones will be evaluated as a separate cohort with regard to their outcomes in a descriptive manner. These participants will not be randomized for the main treatment phase and will be treated with APA continuously from study initiation until disease progression.
[b]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.
[c]Radiographic progression assessed using conventional imaging.
[d]Hot flashes will be evaluated using the Hot Flash Related Daily Interference Scale Patient-Reported Outcome questionnaire.

GnRHa, Gonadotropin-releasing hormone agonist or antagonist; LPC, Localized prostate cancer.

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RESULTS

- As of September 20, 2024, 420 participants at 73 sites in 9 countries have enrolled in the initial treatment phase, completing the LIBERTAS enrollment goal ahead of schedule.
- Data shown here are based on participants in the initial 6-month treatment phase
- Enrolled participants were 70.5% White, 9.5% Asian, and 8.6% Black or African American; at baseline, median age was 70 years, and median PSA was 7.32 ng/mL (Table 1). Enrollment for participants undergoing GAC is still open; none from this cohort have enrolled yet. The baseline clinical profile of LIBERTAS was similar to that of TITAN
- Among 143 participants who completed the initial 6-month treatment phase, 101 (70.6%) achieved PSA <0.2 ng/mL. Thus far, 98 of these participants have been randomized to the main treatment phase
- Demographics of the randomized participants were similar to those of the enrolled population

Table 1: Baseline demographics and disease characteristics

	Enrolled N=420	Randomized[a] N=98
Median (range) age, years	70 (48-88)	72 (51-86)
Gender identity, n (%)		
Man	235 (56.0)	70 (71.4)
Not reported or declined to answer	185 (44.0)	28 (28.6)
Race, n (%)		
White	296 (70.5)	76 (77.6)
Asian	40 (9.5)	10 (10.2)
Black or African American	36 (8.6)	10 (10.2)
Other or multiple	33 (7.9)	2 (2.0)
Not reported or unknown	13 (3.1)	0
American Indian or Alaska Native	2 (0.5)	0
Region, n (%)		
North America	189 (45.0)	55 (56.1)
Europe	63 (15.0)	19 (19.4)
Rest of world	168 (40.0)	24 (24.5)
Median (range) time from diagnosis to randomization, months	10.25 (6.1-271.1)	10.25 (6.1-271.1)
ECOG PS, n (%)		
0	311 (74.0)	80 (81.6)
1	106 (25.2)	17 (17.3)
2	3 (0.7)	1 (1.0)
Gleason score at initial diagnosis, n (%)		
≤7	139 (33.1)	34 (34.7)
>7	269 (64.0)	61 (62.2)
Missing	12 (2.9)	3 (3.1)
Metastasis stage at diagnosis, n (%)		
M0 or MX	145 (34.5)	38 (38.8)
M1	274 (65.2)	60 (61.2)
Missing	1 (0.2)	0
Visceral metastases at study entry, n (%)	61 (14.5)	13 (13.3)
Liver metastases	8 (1.9)	1 (1.0)
Median (range) baseline PSA, ng/mL	7.32 (0.0-4433.0)	3.36 (0.0-1030.0)

[a]As of November 4, 2024.
ECOG PS, Eastern Cooperative Oncology Group performance status; PSA, Prostate-specific antigen.

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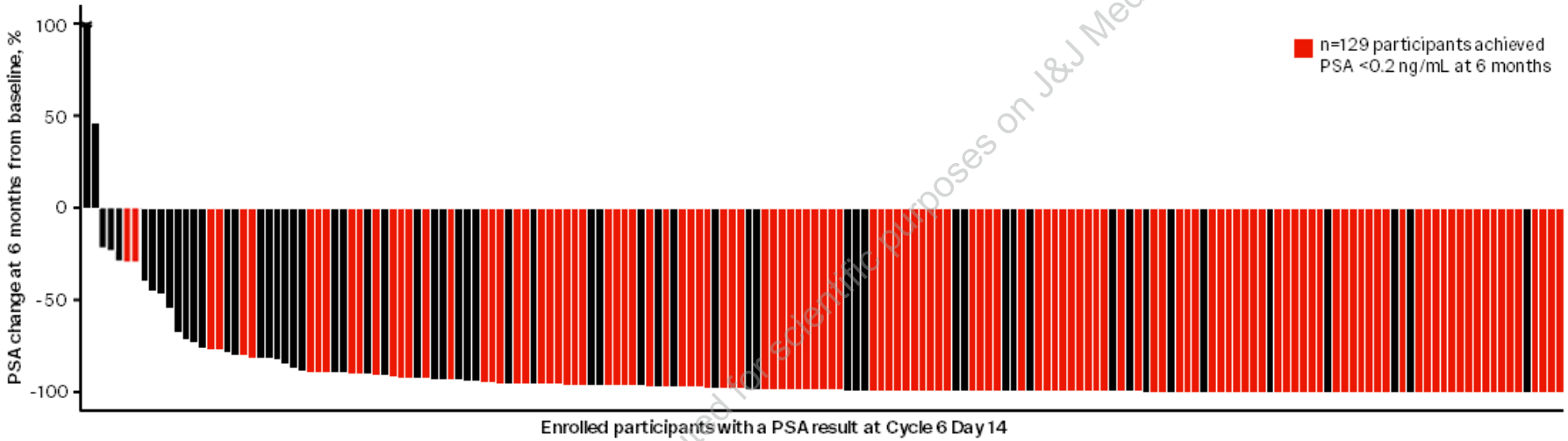
RESULTS

- APA + ADT led to rapid and deep PSA decline in a majority of participants (Table 2 and Figure 2)

Figure 2: Confirmed PSA change (%) at 6 months from baseline among enrolled participants with PSA data at 6 months (n=179)



Participants with a percentage change from baseline exceeding 100% (1 instance noted) are capped at 100%. Confirmed PSA obtained by 2 laboratory measurements: 1 from a central laboratory and a second confirmatory PSA sample done locally on a different day. Central PSA tests use ultrasensitive assays that detect PSA levels of 0.01 ng/mL.
ADT, Androgen deprivation therapy; APA, Apalutamide ; PSA, Prostate-specific antigen.

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RESULTS

- PSA decline ≥50% and ≥90% from baseline and PSA <0.2 ng/mL was achieved by 3 months of treatment by 90.7%, 61.7%, and 41.4% of participants, respectively (Table 2)

Table 2: Confirmed PSA decline after 3 months of treatment with APA + ADT in participants during initial treatment phase

Confirmed PSA decline	Enrolled participants N=420
PSA decline after 3 months, n (%)	
PSA decline ≥50%	381 (90.7)
PSA decline ≥90%	259 (61.7)
PSA <0.2 ng/mL	174 (41.4)
Median (range) time to achieve confirmed PSA decline, months	
PSA decline ≥50%	1.87 (1.0-5.3)
PSA decline ≥90%	1.87 (1.1-5.6)
PSA <0.2 ng/mL	2.76 (1.5-5.7)

PSA declines ≥50% and ≥90% are declines from baseline PSA level.
ADT, Androgen deprivation therapy; APA, Apalutamide ; PSA, Prostate-specific antigen.

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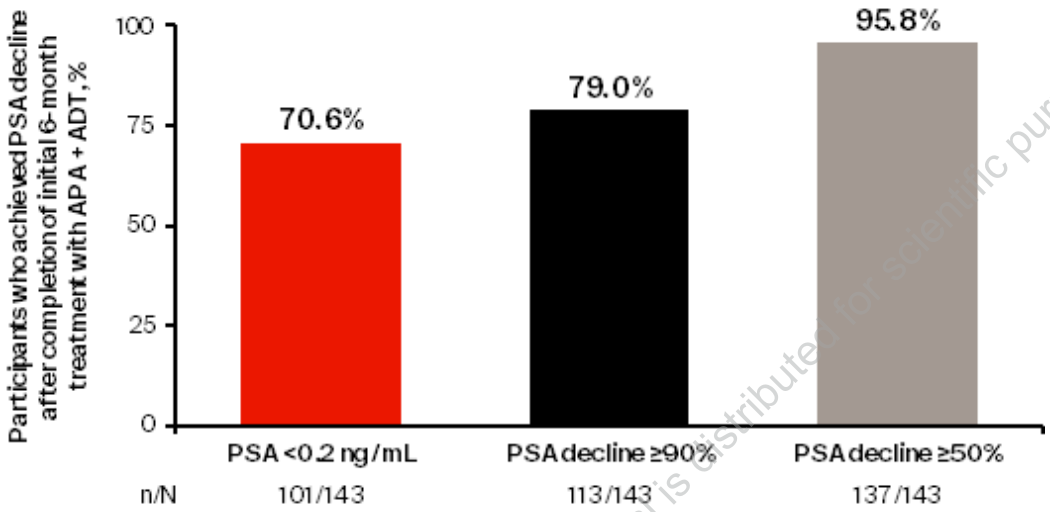
RESULTS

- Among the participants who completed the initial 6-month treatment phase, 95.8% and 79.0% achieved PSA decline ≥50% or ≥90% from baseline, respectively; 70.6% achieved PSA <0.2 ng/mL (Figure 3)
- The compliance rate for the completion of hot flash diary data consistently exceeded 80% across all visits
- With systematic close monitoring of hot flashes using a daily diary, the hot flash incidence in general appeared to be higher than previously reported. The details will be reported in the future with more mature data

Figure 3: Confirmed PSA decline among participants who completed the initial 6-month treatment phase with APA + ADT



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DISCLOSURES

Arun Azad reports relationships/financial interest in/relative to as follows: Aculeus Therapeutics, Amgen, Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Daiichi Sankyo, Ipsen, Johnson & Johnson, Merck Serono, Merck Sharp & Dohme, Novartis, Noxopharm, Pfizer, Sanofi, Telix Pharmaceuticals, Tolm.

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