The effect of prior docetaxel treatment on efficacy and safety of apalutamide plus androgen deprivation therapy in patients with metastatic castration-sensitive prostate cancer from TITAN

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INTRODUCTION

- TITAN, a placebo-controlled phase 3 study, showed that the androgen signaling inhibitor apalutamide (APA) added to androgen deprivation therapy (ADT) improved overall survival (OS) and other clinical outcomes in metastatic castration-sensitive prostate cancer (mCSPC).[1,2]
  - At first interim analysis for radiographic progression-free survival (rPFS) with 23 months' median follow-up, APA + ADT significantly improved rPFS (HR, 0.48 [95% CI, 0.39-0.60]; p < 0.001) and OS compared with placebo (PBO) + ADT.[1]
  - At final analysis with 44 months' median follow-up, APA + ADT significantly reduced the risk of death (HR, 0.65 [95% CI, 0.53-0.79]; p < 0.0001) and prostate-specific antigen (PSA) progression (HR, 0.27 [95% CI, 0.22-0.33] ; p < 0.0001) compared with PBO + ADT.[2] rPFS was not updated at the final analysis.
- It is not known whether the use of docetaxel (DOC) prior to androgen receptor signaling inhibitor in combination with ADT improves outcomes in mCSPC.

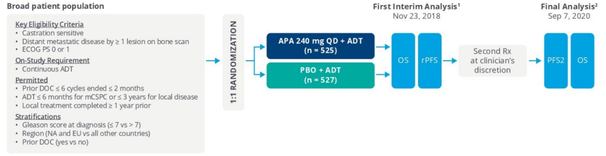
OBJECTIVE

- Post hoc analysis of TITAN to assess outcomes in patients who had received DOC prior to treatment with APA + ADT versus outcomes in those who did not.

METHODS

- In TITAN, 1052 patients were randomized 1:1 to APA (240 mg QD) or PBO added to ongoing ADT (Figure 1).
- ≤ 6 cycles of prior DOC must have ended ≤ 2 months prior to randomization, with no evidence of progression during DOC treatment or before randomization.
- We assessed rPFS at first interim analysis and OS, time to PSA progression, and achievement of PSA ≤ 0.2 ng/mL at final analysis in patients receiving APA plus ADT with or without prior DOC in:
  - the overall APA treatment group (n = 524), or
  - APA-treated patients with high- or low-volume of disease at randomization (baseline [BL]) per adapted CHAARTED criteria,[3] or
  - APA-treated patients with matched BL characteristics (Yes DOC:No DOC at 1:3), including:
    - BL PSA
    - time from initial diagnosis to randomization
    - time from metastatic diagnosis to randomization
    - tumor stage at diagnosis
    - lymph node stage at diagnosis
    - metastasis stage at diagnosis
    - number of bone lesions at study entry
    - high- or low-volume disease status at BL
- A Cox proportional hazards model was used to derive HRs and p values.

Figure 1: TITAN study design



ECOG PS, Eastern Cooperative Oncology Group performance status; PFS2, second progression-free survival; Tx, treatment.

PROSTATE CANCER

RESULTS

- TITAN patients from the APA + ADT group who received prior DOC had higher disease burden at BL (Table 1).
- A total of 58/525 (11%) patients from the APA + ADT group had received DOC prior to randomization.

TABLE 1: Clinical baseline patient and disease characteristics in APA-treated patients

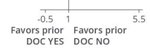
	Patients with prior DOC n = 58	Patients without prior DOC n = 467
Median age (range), years	65 (45-83)	69 (46-94)
Gleason score at initial diagnosis, n (%)		
≤ 7	7 (12.1)	167 (35.8)
≥ 8	51 (87.9)	300 (64.2)
ECOG PS score, n (%)		
0	38 (65.5)	290 (62.1)
> 1	20 (34.5)	177 (37.9)
Disease volume, n (%)		
Low	14 (24.1)	186 (39.8)
High	44 (75.9)	281 (60.2)
Metastases, n (%)		
Bone only	36 (62.1)	253 (54.2)
Visceral	9 (15.5)	47 (10.1)
> 10 bone lesions	34 (58.6)	173 (37.0)
Previous ADT for localized disease, n (%)	2 (3.4)	29 (6.2)
Median PSA (range), µg/mL	0.93 (0.0-194.9)	6.91 (0-2682.0)
Metastatic stage at initial diagnosis, n (%)		
M0	5 (8.6)	80 (17.1)
M1	51 (87.9)	360 (77.1)
MX	2 (3.4)	27 (5.8)

- In the overall APA-treated population and in the subset of patients with high-volume disease, rPFS, OS, time to PSA progression, and ≤ 0.2 ng/mL PSA response were similar in those who received prior DOC and those who did not (Figures 2 and 3).
- Patients with low-volume disease also had similar results for OS (Figure 2B) and other outcomes, although the number of patients was small.
- Clinical outcomes in patients with matched BL characteristics were similar regardless of prior use of DOC.

FIGURE 2: Outcomes in APA-treated patients by prior DOC

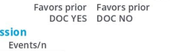
A. rPFS

Population	Events/n Prior DOC NO	Events/n Prior DOC YES	HR (95% CI)	p Value
Overall, n = 524[a]	124/466	10/58	0.78 (0.41-1.49)	0.454
High volume, n = 325	100/281	9/44	0.67 (0.34-1.33)	0.257
Overall, case-matched, n = 232	47/174	10/58	0.77 (0.39-1.54)	0.465



B. Overall survival

Population	Events/n Prior DOC NO	Events/n Prior DOC YES	HR (95% CI)	p Value
Overall, n = 524[a]	149/466	21/58	1.20 (0.76-1.90)	0.425
High volume, n = 325	116/281	18/44	1.04 (0.63-1.71)	0.883
Low volume, n = 199	33/185	3/14	1.20 (0.37-3.93)	0.759
Overall, case-matched, n = 232	60/174	21/58	1.13 (0.69-1.86)	0.634

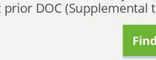


C. Time to PSA progression

Population	Events/n Prior DOC NO	Events/n Prior DOC YES	HR (95% CI)	p Value
Overall, n = 524[a]	120/466	18/58	1.31 (0.80-2.15)	0.289
High volume, n = 325	98/281	16/44	1.11 (0.65-1.88)	0.707
Overall, case-matched, n = 232	51/174	18/58	1.14 (0.66-1.95)	0.641

D. Confirmed PSA ≤ 0.2 ng/mL[b]

Population	Events/n Prior DOC NO	Events/n Prior DOC YES	HR (95% CI)	p Value
Overall, n = 524[a]	318/466	38/58	1.09 (0.76-1.55)	0.648
High volume, n = 325	163/281	26/44	1.23 (0.80-1.89)	0.349
Overall, case-matched, n = 232	110/174	38/58	1.18 (0.80-1.75)	0.399



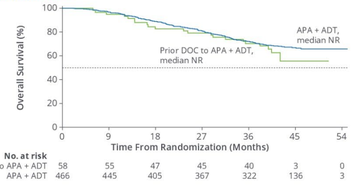
[a]Includes patients who received study treatment. [b]Achieved at any time during the study and confirmed on a subsequent measurement ≥ 4 weeks later.

- The safety profile of APA was not substantially different between patients with or without prior DOC (Supplemental tables).

Find out more

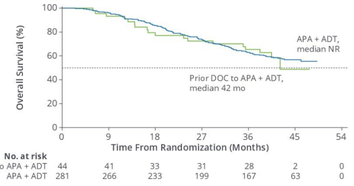
FIGURE 3: OS by prior DOC in overall, high-volume, and case-matched overall populations treated with APA + ADT

A. Overall population



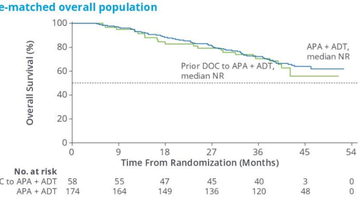
No. at risk							
Prior DOC to APA + ADT	58	55	47	45	40	3	0
APA + ADT	466	445	405	367	322	136	3

B. High-volume population



No. at risk							
Prior DOC to APA + ADT	44	41	33	31	28	2	0
APA + ADT	281	266	233	199	167	63	0

C. Case-matched overall population



No. at risk							
Prior DOC to APA + ADT	58	55	47	45	40	3	0
APA + ADT	174	164	149	136	120	48	0

NR, not reached.

LIMITATIONS

- Limitations of this post hoc analysis include lack of data on tumor volume and other disease characteristics at the initiation of prior DOC treatment.
- Interpretation was based on a limited number of patients with prior DOC (only 11% of TITAN patients).

KEY TAKEAWAYS

- In the overall APA-treated TITAN population, with or without matched baseline disease characteristics, or with high- or low-volume disease, clinical outcomes with APA + ADT were similar regardless of prior DOC, suggesting that use of DOC did not add to them.
- Use of DOC did not affect the safety profile of APA.

CONCLUSIONS

- This post hoc analysis of TITAN showed that prior use of DOC in patients with mCSPC did not further improve rPFS, OS, time to PSA progression, or achievement of deep PSA response ≤ 0.2 ng/mL following initiation of treatment with APA + ADT.
- Prospective studies are required to fully elucidate the effect of chemotherapy on the efficacy of APA + ADT.

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Additional information can be viewed by accessing this link: https://www.congresshub.com/oncology/gu2022/apalutamide/chi

REFERENCES

1. Chi KN, et al. *N Engl J Med*. 2019;381:13-24. 2. Chi KN, et al. *J Clin Oncol*. 2021;39:2294-2303. 3. Kyriakopoulos CE, et al. *J Clin Oncol*. 2018;36:1080-1087.

Poster presented at ASCO Genitourinary Cancers Symposium, February 17-19, 2022, San Francisco, CA, and online. Supported by funding from Janssen Research & Development

ACKNOWLEDGMENTS

This study is funded by Janssen Research & Development. Writing assistance was provided by Larissa Belova, PhD, of Parexel, and was funded by Janssen Global Services, LLC.

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