Survival Outcomes of APA as a Starting treatment: Impact in real-world patients with mCSPC (OASIS)

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KEY TAKEAWAYS

Compared to other treatments, use of APA+ADT in first-line mCSPC was associated with:

- Significantly longer overall survival
- Longer time to castration resistance
- Faster and deeper PSA response

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CONCLUSIONS

- 15% of patients were not treated with intensified therapies, despite their increased effectiveness as life prolonging therapies.
- Use of APA+ADT as starting treatment for mCSPC demonstrated significantly better clinical outcomes than other ARSIs or ADT alone in real-world clinical practice in the US.

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INTRODUCTION

- Prostate cancer is the second most common cancer in men.[1] The 5-year survival rate is 34.1% when distant metastases are present at diagnosis.[2]
- The treatment landscape for mCSPC has been evolving rapidly. Physicians now have a range of life-prolonging treatment options for use as starting therapy, including androgen receptor signaling inhibitors (ARSIs – apalutamide [APA], enzalutamide [ENZ], abiraterone acetate plus prednisone [AAP], darolutamide triple therapy). However, data are lacking to guide optimal treatment selection to maximize patient outcomes.
- We conducted a retrospective observational cohort study to examine the impact of the first-line of treatment of short- and long-term outcomes in mCSPC in real-world clinical practice in the United States.

1WHO. International Agency for Research on Cancer. GLOBOCAN 2020
2National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Prostate. SEER Relative Survival Rates by Time Since Diagnosis, 2000-2019

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METHODS

- This was a retrospective observational cohort study using ConcertAI.

  ConcertAI integrates data from electronic health records for >4 million patients from medical oncology clinics across the US. ConcertAI Patient 360 captures staging, PSA values, and castration resistance status.

- All patients ≥18 years with a diagnosis of mCSPC from 01 Jan 2018 until 30 Sept 2022 who started treatment with any ARSI, docetaxel (DTX), or ADT alone were included. Treatment groups were defined hierarchically with priority given to patients who started treatment with APA+ADT, ENZ+ADT, AAP+ADT, DTX+ADT, and ADT alone.
- Patients were followed up for at least 6 months, death, loss to follow-up, or March 31, 2023 for overall survival (OS), time to castration resistance (TTCR), time to ≥50% decline (PSA50) and ≥90% decline (PSA90) in PSA from baseline, and time to undetectable PSA (≤0.2 ng/mL).
- Kaplan–Meier method was used to estimate OS, PSA reduction, and castration resistance rates.
- Adjusted hazard ratios (aHR) of risk of death was estimated using Inverse Probability of Treatment Weighted (IPTW) multivariate Cox proportional hazard models adjusted for age, comorbidities, BMI, and baseline PSA.

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RESULTS

- There were 4,626 patients with mCSPC who had received relevant treatment and were enrolled.
- 165 patients with mCSPC started treatment with APA+ADT, 643 with ENZ+ADT, 1064 with AAP+ADT, 293 with DTX+ADT, and 543 with ADT alone.

FIGURE 1: Patient flow

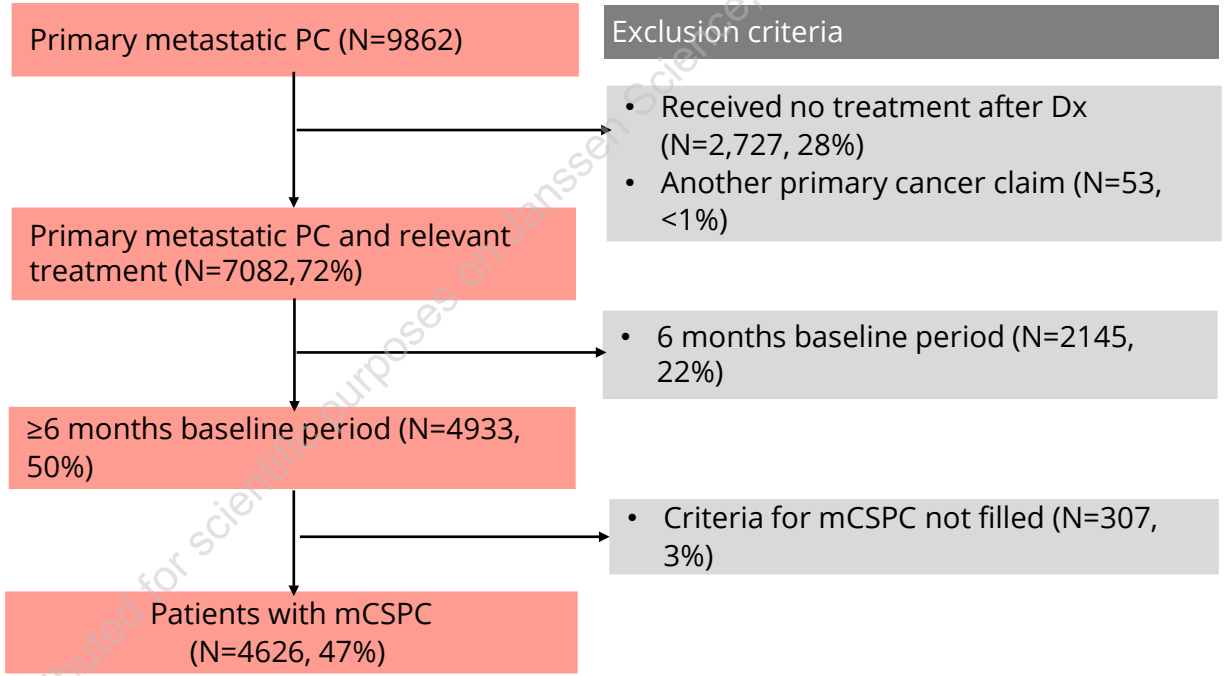

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Table 1. Baseline clinical features of patients with mCSPC

	APA+ADT N=165	ENZ+ADT N=643	AAP+ADT N=1064	DTX+ADT N=293	ADT alone N=543
Age, median (Q1, Q3)	74 (66, 80)	75 (68, 82)	73 (67, 81)	68 (63, 74)	74 (67, 82)
CCI, mean (SD)	0.57 (0.98)	0.69 (1.29)	0.71 (1.27)	0.66 (1.08)	0.77 (1.41)
Site of metastases, n (%)					
Bone	88 (84.6)	406 (84.8)	644 (84.6)	176 (76.9)	314 (80.1)
Visceral	11 (10.6)	32 (6.7)	62 (8.1)	23 (10.0)	36 (9.2)
Nodal	5 (4.8)	41 (8.6)	55 (7.2)	30 (13.1)	42 (10.7)
Unknown	61 (37.0)	164 (25.5)	303 (28.5)	64 (21.8)	151 (27.8)
Baseline PSA*, median (Q1, Q3) (ng/mL)	9.3 (1.7, 46.5)	14.5 (3.3, 66.8)	13.4 (2.5, 67.8)	26.9 (3.9, 128.0)	5.1 (0.5, 33.9)
Baseline Testosterone, Median (Q1, Q3) (ng/dL)	17.9 (10.0, 140.8)	15.0 (8.0, 32.0)	19.9 (8.0, 217.7)	19.9 (7.2, 272.0)	14.2 (7.0, 46.5)
Comorbidities, n (%)					
Cerebrovascular disease	6 (3.6)	25 (3.9)	45 (4.2)	8 (2.7)	36 (4.8)
COPD	7 (4.2)	31 (4.8)	78 (7.3)	19 (6.5)	38 (7.0)
Congestive heart failure	11 (6.7)	40 (6.2)	91 (8.6)	13 (4.4)	40 (7.4)
Diabetes	23 (13.9)	72 (11.2)	105 (9.9)	42 (14.3)	68 (12.5)
Peripheral vascular disease	7 (4.2)	32 (5.0)	64 (6.0)	22 (7.5)	38 (7.0)
Renal disease	8 (4.8)	52 (8.1)	74 (7.0)	18 (6.1)	51 (9.4)
Duration of the treatments (month), median (Q1, Q3)	11.5 (7.2, 20.4)	11.1 (4.9, 20.9)	13.3 (6.3, 23.0)	7.4 (4.0, 14.4)	10.1 (3.8, 19.2)

AAP, abiraterone acetate plus prednisone; ADT, androgen deprivation therapy; APA, apalutamide; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; DTX, docetaxel; ENZ, enzalutamide; SD, standard deviation; Q1, Q3, first and third quartiles.
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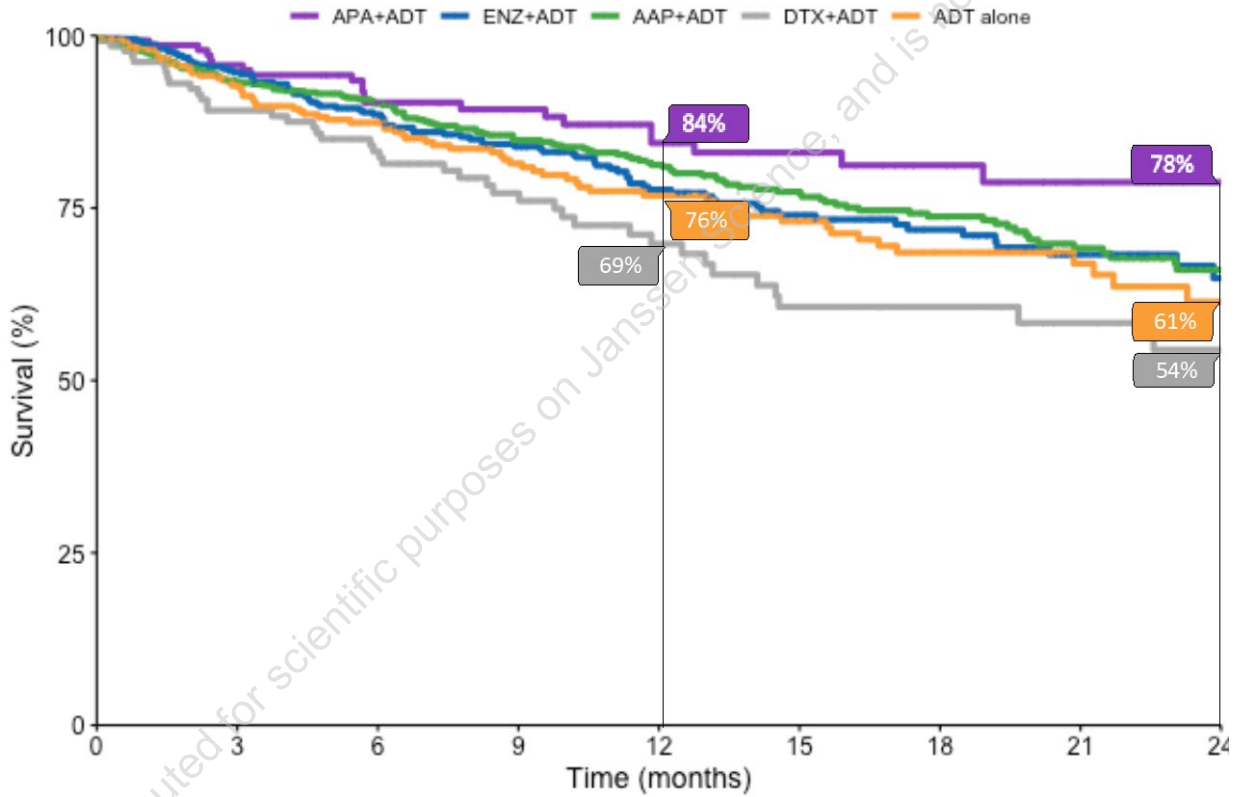
FIGURE 2: Overall survival using the Kaplan–Meier method

OS (p<0.01) was significantly longer in patients starting with APA+ADT compared with ADT alone.



N at Risk	0	3m	6m	9m	12m	15m	18m	21m	24m
APA+ADT	144	132	107	85	63	51	37	23	12
ENZ+ADT	394	342	283	225	169	120	93	56	35
AAP+ADT	555	490	429	351	270	206	153	102	70
DTX+ADT	131	113	93	69	50	39	32	20	12
ADT alone	308	252	198	150	113	86	65	41	27

AAP, abiraterone acetate plus prednisone
ADT, androgen deprivation therapy
APA, apalutamide
DTX, docetaxel
ENZ, enzalutamide

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FIGURE 3: Time to castration resistance using the Kaplan–Meier method

Time to castration resistance (p<0.001) was significantly longer in patients starting with APA+ADT compared with ADT alone.

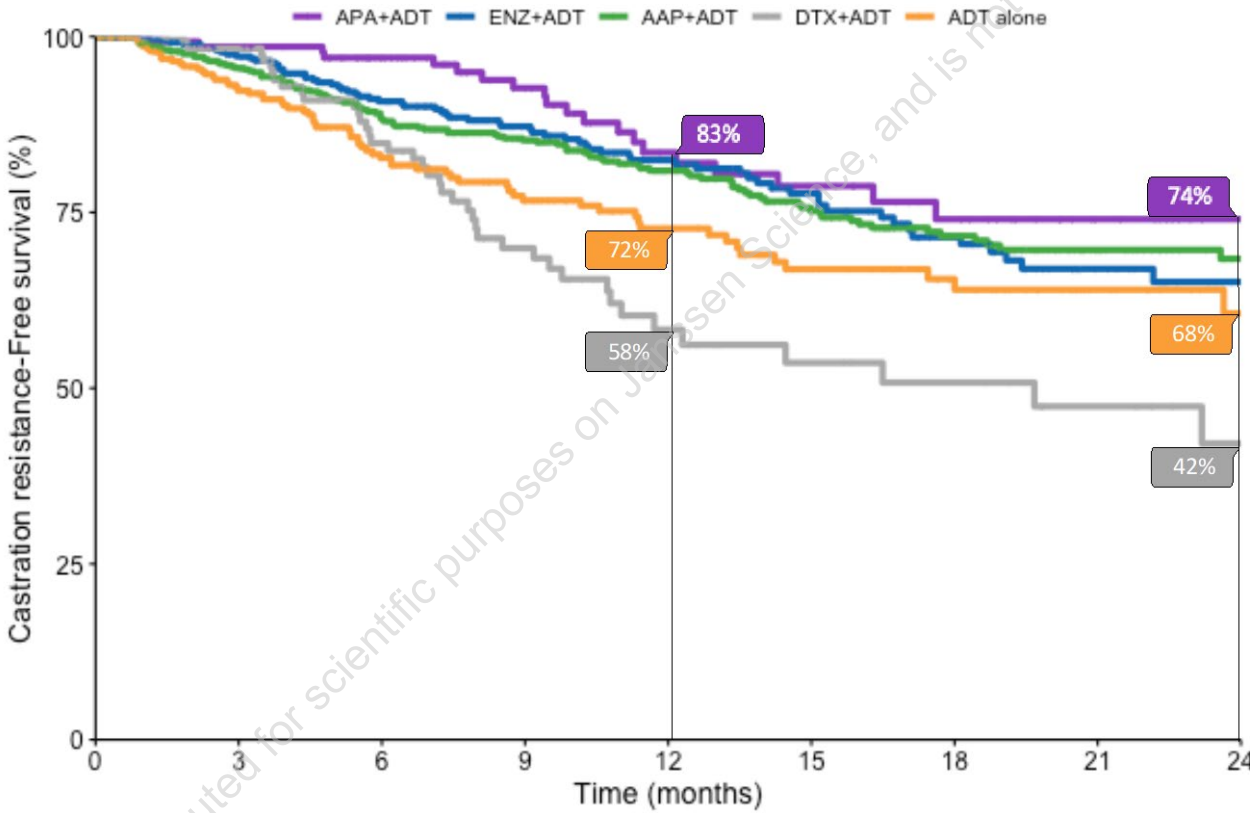

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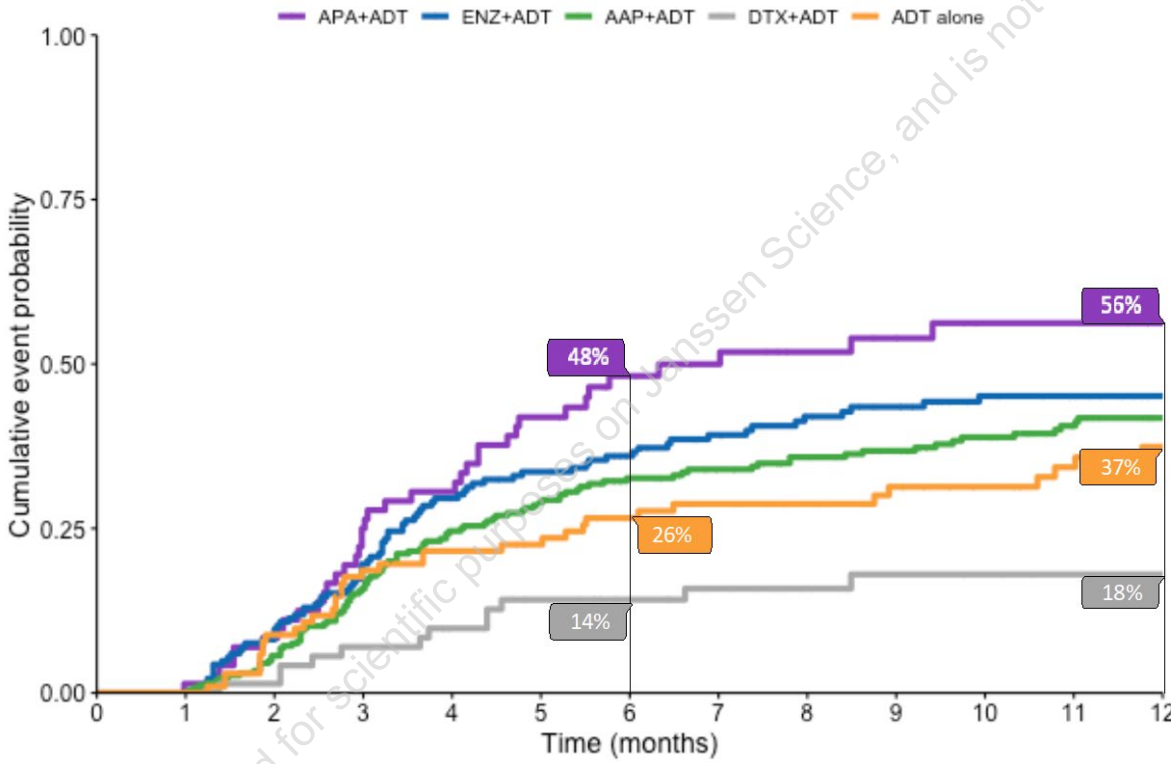
FIGURE 4: Time to undetectable PSA (≤0.2 ng/ml) using the Kaplan–Meier method

In patients with regular PSA assessment, a higher % starting with APA+ADT achieved undetectable PSA (p<0.0001) at 3 months compared with ADT alone.



N at risk	0	1m	2m	3m	4m	5m	6m	7m	8m	9m	10m	11m	12m
APA+ADT	72	71	66	54	49	40	31	27	23	21	17	17	15
ENZ+ADT	185	185	170	145	124	114	102	91	80	74	63	60	53
AAP+ADT	266	266	251	222	196	179	156	146	136	129	115	99	87
DTX+ADT	72	72	71	66	62	57	53	48	42	38	37	34	29
ADT alone	102	102	93	83	80	77	69	63	58	52	48	44	38

AAP, abiraterone acetate plus prednisone
ADT, androgen deprivation therapy
APA, apalutamide
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Table 2. Multivariate Cox regression (IPTW method) of risk of death in patients with mCSPC by starting treatment

Comparison between Treatments	aHR	95%CI	P-value
APA+ADT vs ENZ+ADT	0.5	(0.28, 0.92)	< 0.05
APA+ADT vs AAP+ADT	0.51	(0.29, 0.9)	< 0.05
APA+ADT vs DTX+ADT	0.52	(0.16, 0.75)	< 0.01
APA+ADT vs ADT Alone	0.38	(0.21, 0.7)	< 0.01

Starting treatment with APA+ADT was associated with a statistically significantly lower risk of death compared with ENZ+ADT or AAP+ADT:

- 50% reduction in risk of death in comparison with ENZ+ADT ($p<0.05$)
- 49% compared with AAP+ADT ($p<0.05$).

IPTW, Inverse Probability of Treatment Weighted multivariate Cox proportional hazard models adjusted for age, comorbidities, BMI, and baseline PSA.
AAP, abiraterone acetate plus prednisone; ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; DTX, docetaxel; ENZ, enzalutamide

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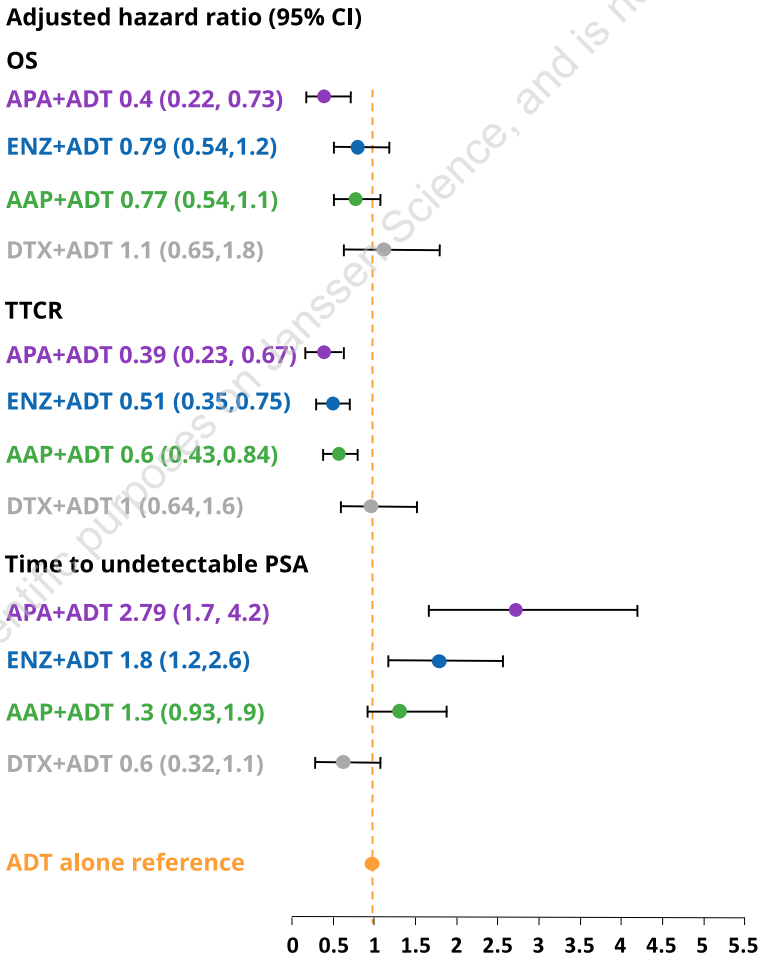
FIGURE 5: Forest plot of adjusted hazard ratios by initial treatment compared to ADT alone

- All ARSIs improved OS, TTCR and time to undetectable PSA compared to ADT alone.
- However, only APA+ADT showed statistically significant improvements for all outcomes.



AAP, abiraterone acetate plus prednisone
ADT, androgen deprivation therapy
APA, apalutamide
DTX, docetaxel
ENZ, enzalutamide
.OS, overall survival
TTCR, time to castration resistance

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LIMITATIONS

- Residual confounding cannot be excluded.
- Patients with mCSPC may have been excluded if there was not sufficient information to confidently assess their hormone sensitivity status.
- Available data did not allow adjustment for disease volume.
- We were unable to identify patients with confounding factors, eg CHAARTED high vs low volume disease or with known high-risk genomic factors.
- Number of patients treated with triple therapy was too small for analysis.

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DISCLOSURES:

Lawrence Karsh owns stock in Swan Valley Medical, has received honoraria from Astellas, Astra-Zeneca, Abbvie, Bayer, Dendreon, Janssen, Merck, Myovant, Pfizer, and Sanofi, has received financial compensation as a paid consultant/advisor to Astellas, Astra-Zeneca, Abbvie, Bayer, Bristol Myers Squibb, Bayer, Ferring, Dendreon, Janssen, Merck, Myovant, Pfizer, and Sanofi, and has received financial compensation to participate in speakers bureaus for Astellas, Astra-Zeneca, Bayer, Dendreon, Janssen, Merck, Myovant, and Pfizer. He has received institutional funding from Janssen, Bayer, Bristol Myers Squibb, Dendreon, Epizyme, Astellas, Pfizer, Astra Zeneca, BioExcel, Vaxiion, Kdx, OncoCell, Neuspera, Myovant, and FKD.

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Yanfang Liu, Suneel Mundle, Xiayi Wang, Mehregan Nematian-Samani, and Shawn Du are employees of Johnson & Johnson LLC. Yanfang Liu, Shawn Du, and Suneel Mundle hold stock/shares in Johnson & Johnson LLC.

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