Poster #618P

Apalutamide for Advanced Prostate Cancer in Older Patients: Combined Analysis of TITAN and SPARTAN

John Shen,[1] Simon Chowdhury,[2] Neeraj Agarwal,[3] Lawrence I. Karsh,[4] Stéphane Oudard,[5] Benjamin A. Gartrell,[6] Susan Feyerabend,[7] Fred Saad,[8] Christopher M. Pieczonka,[9] Kim N. Chi,[10] Sabine D. Brookman-May,[11,12] Brendan Rooney,[13] Amitabha Bhaumik,[14] Anil Londhe,[14] Sharon A. McCarthy,[15] Katherine B. Bevans,[16] Suneel D. Mundle,[15] Eric J. Small,[17] Matthew R. Smith,[18] Julie N. Graff[19]

[1]Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, USA; [2]Guy's, King's, and St. Thomas' Hospitals, and Sarah Cannon Research Institute, London, UK; [3]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [4]The Urology Center of Colorado, Denver, CO, USA; [5]Georges Pompidou Hospital, University of Paris, Paris, France; [6]Montefiore Medical Center, Bronx, NY, USA; [7]Studienpraxis Urologie, Nürtingen, Germany; [8]Centre Hospitalier de l'Université de Montréal, Université de Montréal, Montréal, QC, Canada; [9]Associated Medical Professionals of NY, Syracuse, NY, USA; [10]BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada; [11]Ludwig-Maximilians-University (LMU), Munich, Germany; [12]Janssen Research & Development, Los Angeles, CA, USA; [13]Janssen Research & Development, High Wycombe, UK; [14]Janssen Research & Development, Titusville, NJ, USA; [15]Janssen Research & Development, Raritan, NJ, USA; [16]Janssen Research & Development, Horsham, PA, USA; [17]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA; [18]Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA, USA; [19]VA Portland Health Care System, Portland, and Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA

Key Findings Statements

- **Regardless of age, APA provided clinical benefit in patients enrolled in TITAN and SPARTAN.**
- **Patients from all age groups reported that APA or PBO added to ADT was tolerable.**
- **The benefit/risk ratio with APA should be taken into consideration as there was an age-related increase in AEs in patients with mCSPC and nmCRPC.**

Conclusions

- Patients with mCSPC and nmCRPC derived clinical benefit and maintained HRQoL from APA plus ADT regardless of age.
- Despite increased AE rates with age, patients did not report greater side effect bother with addition of APA to ADT.
- Age-related benefit/risk assessments should be taken into consideration in patients with advanced disease.

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Additional information can be viewed by scanning the QR code or accessing this link: https://www.oncologysciencehub.com/esmo2021apalutamide/shen/.
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Introduction

- In the placebo (PBO)-controlled TITAN and SPARTAN studies, apalutamide (APA) added to continuous androgen deprivation therapy (ADT) improved
  - Radiographic progression-free survival (rPFS),[1] a co-primary end point of TITAN
  - Metastasis-free survival (MFS),[2] the primary end point of SPARTAN
  - Long-term outcomes, such as overall survival (OS),[3,4] despite crossover from PBO to APA after the studies were unblinded[3,4]
- The objective of this analysis was to assess the efficacy and safety of APA in the TITAN and SPARTAN studies by patient age.

Methods

- In this post hoc analysis, patients with metastatic castration-sensitive prostate cancer (mCSPC) and nonmetastatic castration-resistant prostate cancer (nmCRPC) were stratified by age: < 65, 65-79, and ≥ 80 years.
- rPFS and MFS were analyzed at first interim analysis (median follow-up of 22.7 months [TITAN] and 20.3 months [SPARTAN]).[1,2]
- Confirmed prostrate-specific androgen (PSA) decline, OS, health-related quality of life (HRQoL) per Functional Assessment of Cancer Therapy-Prostate (FACT-P), and safety were analyzed at final analysis (median follow-up of 44 months [TITAN] and 52 months [SPARTAN]).[3,4]
- Time-to-event end points were analyzed by Kaplan-Meier and Cox proportional hazards methods, and FACT-P was analyzed by repeated measures mixed effect modeling.

Results

- Patient disease characteristics were similar in TITAN and SPARTAN across age groups.
- Older patients had shorter median treatment duration (Table 1).
- The use of bone-sparing agents was low across treatment and age groups.
- Addition of APA improved PSA decline in all age groups of TITAN and SPARTAN patients (Table 2).

Table 1. Treatment Duration in TITAN and SPARTAN Stratified by Age

	TITAN (N = 1052)			SPARTAN (N = 1207)		
	< 65 y (n = 331)	65-79 y (n = 628)	≥ 80 y (n = 93)	< 65 y (n = 149)	65-79 y (n = 741)	≥ 80 y (n = 317)
Number of patients treated with APA, n (%)	148 (45)	324 (52)	52 (56)	106 (71)	491 (66)	206 (65)
Median APA duration, mo (range)	39.8 (1-53)	39.8 (0-56)	23.6 (2-48)	46.2 (0.5-70)	33.4 (0.3-75)	20.6 (0.1-73)

Table 2. APA Improved Confirmed PSA Decline in All Age Groups of TITAN and SPARTAN

	TITAN (N = 1052)						SPARTAN (N = 1207)					
	< 65 y		65-79 y		≥ 80 y		< 65		65-79 y		≥ 80 y	
	APA	PBO	APA	PBO	APA	PBO	APA	PBO	APA	PBO	APA	PBO
n[a]	148	182	324	304	52	41	106	43	488	246	205	106
Median PSA nadir, ng/mL	0.04[b]	0.9[c]	0.02[d]	0.7[e]	0.04	0.7	0.2	7	0.3	7	0.8	9
PSA decline ≥ 50% from BL,[f] %	89	47	90	59	94	59	93	2	92	2	84	3
PSA ≤ 0.2 ng/mL,[f] %	60	29	71	33	67	32	48	0	40	0	26	0
Median time to PSA ≤ 0.2 ng/mL, mo	2	1	2	3	2	5	3	NA	3	NA	3	NA

BL, baseline; NA, not available because of lack of response.
[a]Patients with available PSA data. [b]n = 148. [c]n = 181. [d]n = 321. [e]n = 303. [f]Confirmed on a subsequent measurement ≥ 4 weeks later.

References

1. Chi KN, et al. *N Engl J Med.* 2019;381:13-24.
2. Smith MR, et al. *N Engl J Med.* 2018;378:1408-1418.
3. Chi KN, et al. *J Clin Oncol.* 2021;39:2294-2303.
4. Smith MR, et al. *Eur Urol.* 2021;79:150-158.

Results (continued)

TITAN and SPARTAN Patients Derived Benefit With APA Regardless of Age

rPFS and MFS (Figure 1)

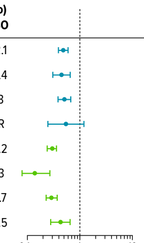
- Hazard ratios for rPFS favored APA in all age groups in TITAN, with pronounced benefit in patients aged < 65 and 65-79 years.
- MFS was improved with APA in SPARTAN patients of all ages.

Overall Survival (Figure 2 and Supplementary Figure via QR code)

- Hazard ratios for OS favored APA across all age groups, with pronounced benefit in
  - < 65 and 65-79 year age groups in TITAN
  - < 65 year age group in SPARTAN

Figure 1. rPFS and MFS by Age of TITAN and SPARTAN Patients

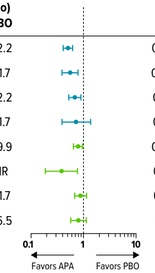
	Subgroup	Median (mo) APA	Median (mo) PBO	HR (95% CI)	Events/N APA	Events/N PBO
TITAN: rPFS 22.7 mo median follow-up	All patients	All	NR	22.1	0.49 (0.40-0.61)	134/525	231/527
	Age category (y)	< 65	NR	18.4	0.45 (0.31-0.66)	40/149	85/182
		65-79	NR	23	0.51 (0.39-0.68)	83/324	132/304
		≥ 80	NR	NR	0.55 (0.25-1.21)	11/52	14/41
SPARTAN: MFS 20.3 mo median follow-up	All patients	All	40.5	16.2	0.30 (0.24-0.36)	184/806	194/401
	Age category (y)	< 65	NR	7.3	0.14 (0.08-0.27)	19/106	25/43
		65-79	40.5	14.7	0.29 (0.23-0.37)	123/492	127/249
		≥ 80	NR	18.5	0.43 (0.28-0.65)	42/208	42/109



NR, not reached.

Figure 2. Long-Term Survival by Age of TITAN and SPARTAN Patients

	Subgroup	Median (mo) APA	Median (mo) PBO	HR (95% CI)	Events/N APA	Events/N PBO
TITAN: OS 44 mo median follow-up	All patients	All	NR	52.2	0.65 (0.53-0.79)	170/525	235/527
	Age category (y)	< 65	NR	41.7	0.57 (0.40-0.80)	49/149	90/182
		65-79	NR	52.2	0.70 (0.54-0.91)	102/324	125/304
		≥ 80	NR	41.7	0.74 (0.40-1.39)	19/52	20/41
SPARTAN: OS 52 mo median follow-up	All patients	All	73.9	59.9	0.79 (0.65-0.96)	274/806	154/401
	Age category (y)	< 65	NR	NR	0.39 (0.19-0.78)	18/106	14/43
		65-79	66.1	61.7	0.89 (0.69-1.16)	169/492	88/249
		≥ 80	53.7	46.5	0.81 (0.58-1.15)	87/208	52/109



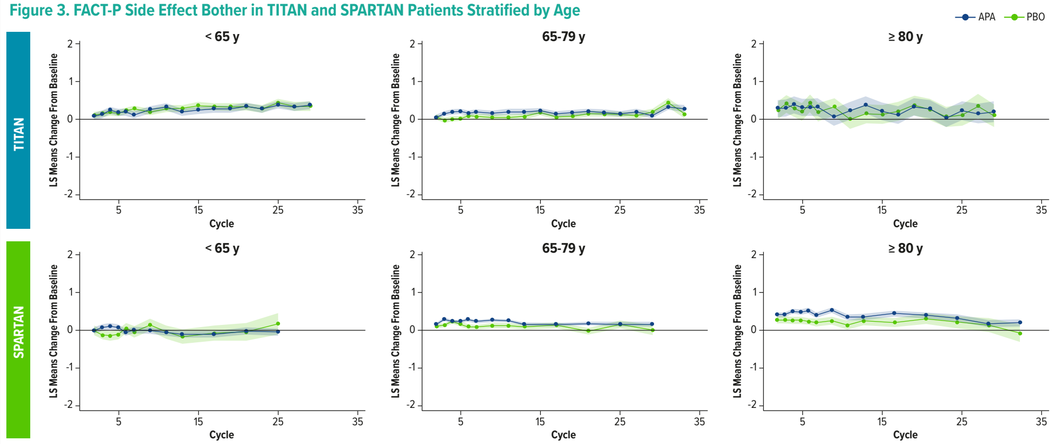
Older Patients Had More Adverse Events

- In TITAN and SPARTAN, exposure-adjusted rates of adverse events leading to treatment discontinuation, falls, and ischemic heart disease were increased with age regardless of treatment, and rates of skin rash were increased with age in the APA group (see Supplementary Table via QR code).

Self-Reported HRQoL and Tolerability Were Maintained in Patients Regardless of Age

- HRQoL, assessed by total FACT-P score, and side effect bother, assessed by item GP5 on FACT-P (Figure 3), did not worsen with the addition of APA to ADT in any age groups in TITAN and SPARTAN.

Figure 3. FACT-P Side Effect Bother in TITAN and SPARTAN Patients Stratified by Age



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