

Prostate-Specific Antigen Kinetics in Patients With Advanced Prostate Cancer Treated With Apalutamide: Results from the TITAN and SPARTAN Studies

Kim N. Chi*, Vancouver, Canada, Fred Saad, Montréal, Canada, Simon Chowdhury, London, United Kingdom, Julie N. Graff, Portland, OR, Neeraj Agarwal, Salt Lake City, UT, Stéphane Oudard, Paris, France, Gang Li, Raritan, NJ, Angela Lopez-Gitlitz, Julie S. Larsen, Los Angeles, CA, Sharon A. McCarthy, Suneel D. Mundle, Raritan, NJ, Matthew R. Smith, Boston, MA, Eric J. Small, San Francisco, CA

INTRODUCTION AND OBJECTIVE: The phase 3 TITAN and SPARTAN studies demonstrated improved outcomes with the addition of apalutamide (APA) to androgen deprivation therapy (ADT); outcomes included prolonging overall survival and radiographic progression-free survival (rPFS) in metastatic castration-sensitive prostate cancer (mCSPC) in TITAN, and metastasis-free survival (MFS) in nonmetastatic castration-resistant PC (nmCRPC) in SPARTAN. A post hoc analysis of prostate-specific antigen kinetics (PSA) kinetics in patients (pts) from both studies is reported.

METHODS: Baseline PSA at randomization, time to PSA nadir, and proportion of pts achieving a PSA decline of $\geq 90\%$ (PSA90) and of pts achieving a PSA ≤ 0.2 ng/mL at 3 and 12 months and at any time after treatment in the APA arms of the TITAN and SPARTAN studies were evaluated. Within each study, rPFS/MFS were compared between pts achieving a PSA90 or PSA ≤ 0.2 ng/mL response vs not.

RESULTS: 525 TITAN pts and 806 SPARTAN pts treated with APA were included in the analysis. Median baseline PSA, time to PSA nadir, median PSA nadir, and maximum percentage changes from baseline PSA are shown in the table. PSA90 and confirmed PSA ≤ 0.2 ng/mL were evident as early as 3 months in both TITAN and SPARTAN, and percentage of confirmed response continued to increase at 12 months. Pts treated with APA who achieved PSA90 were at lower risk of rPFS events in TITAN and of MFS events in SPARTAN, with a hazard ratio (95% confidence interval) of 0.46 (0.321-0.653) and 0.36 (0.271-0.489) in each respective study (both $p < 0.0001$), compared with APA pts who did not achieve PSA90. Pts with confirmed PSA ≤ 0.2 ng/mL had similar rPFS and MFS benefits.

CONCLUSIONS: Pts with advanced PC, whether mCSPC or nmCRPC, treated with APA + ADT demonstrated rapid PSA declines that continued over time. There was a high rate of pts with PSA90 and with PSA ≤ 0.2 ng/mL responses, with a majority of pts reaching PSA90 by 12 months. Pts achieving PSA90 and/or PSA nadir of ≤ 0.2 ng/mL had a prolonged rPFS and MFS in TITAN and SPARTAN, respectively.

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Table. PSA Kinetics in TITAN and SPARTAN		
	TITAN (mCSPC) N = 525	SPARTAN (nmCRPC) N = 806
Median baseline PSA, ng/mL	5.97	7.78
Time to PSA nadir (median), mo	5.55	7.36
Median PSA nadir, ng/mL	0.03	0.37
Maximum decrease from baseline (median), %	98	94
90% PSA rate, %		
3 mo	58	46
12 mo	71	61
Overall	72	62
Confirmed PSA ≤ 0.2 ng/mL, %		
3 mo	51	21
12 mo	64	35
Overall	67	38