Abstract# 165 Poster Bd #E4

Efficacy and safety of apalutamide in metastatic castration sensitive prostate cancer patients with a prior history of cardiovascular or metabolic risk factors – a post-hoc analysis of the TITAN study.

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Conclusions

- A large majority (~70%) of patients enrolled in TITAN reflected a patient population with a considerable CV and metabolic risk profile and were receiving concomitant meds for these conditions, in line with that commonly seen in the real world
- Addition of apalutamide to ADT resulted in a significant improvement in both rPFS and OS and achievement of PSA90 or PSA<0.2ng/ml regardless of prior CV and metabolic baseline risk or use of associated concomitant medications for these conditions
- TEAE's of any grade and Gr/3/4 were similar between subjects with and without CV and metabolic risk. Incidence of falls, IHD and Ischemic CV disorders and TEAE's associated with long term use of ADT were relatively infrequent, rates were higher in patients with history of CV and metabolic risk in both the APA and PBO arms possibly due to skewed higher age of this cohort.

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Supplementary material

https://www.congresshub.com/Oncology/GU2025/Apalutamide/Azad-Efficacy

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Disclosures
Please refer to ASCO website for relevant author disclosures: https://meetings.asco.org/abstracts-presentations/242386

Introduction

- TITAN, a phase III, randomized, placebo- controlled study, demonstrated improved radiographic progression-free survival (rPFS) at 22.7-month follow-up and OS at 22.7-month and long-term 44.0-month follow-ups with apalutamide (APA) added to ADT in a patient population with mCSPC versus ADT + placebo (PBO). [1, 2, 3]
- Patients with cardiovascular issues (CV), such as myocardial infarction, symptomatic congestive heart failure, or thromboembolic events occurring ≤6 months of randomization were excluded from the TITAN trial. However, patients with events occurring > 6 months prior or non-excluded CV conditions like ischemic heart disease without myocardial infarction were allowed to enroll.
- Considering the demographics of prostate cancer and given prolonged ADT use may worsen existing co-morbid conditions, we conducted a post-hoc analysis to assess the efficacy and safety of APA+ADT vs PBO+ADT in patients with or without ≥ 1 risk factor or a history of CV or metabolic risk factors at baseline.
- Given polypharmacy and concern for potential drug-drug interactions on the efficacy and safety with ARPI's in patients with advanced prostate cancer[4] , an additional analysis was performed in patients who were receiving associated concomitant medications for CV and metabolic conditions or risk factors at baseline.

Methods

- CV and metabolic risk factors were categorized using MeDRA terminology and included CV ischemia, CV failure, CV arrhythmia, diabetes, hyperlipidemia, HT and obesity.
- Use of associated concomitant medications (con meds) were identified at study entry.
- rPFS was assessed using first interim analysis cutoff that was prespecified to be final (median f/u 22.7 mo). OS and other clinical end-points were assessed at the final analysis (median f/u 44 mo). PBO arm included those patients who crossed over to receive APA after the I.A.
- The proportion of patients who achieved a decline in PSA level >90% (PSA90) or PSA nadir of < 0.2ng/ml from baseline was assessed according to Prostate Cancer Working Group 2 (PCWG2) recommendations
- TEAEs, TEAE's of Special Interest and TEAE's associated with long term use of ADT were also analysed in patients across these three cohorts

Results

Demographics

- In TITAN, 72% and 69% patients in the APA and PBO arms had a prior history of CV or metabolic risk factors. See supplementary materials.
- Patients with CV/metabolic risk had a median age 3-4 years higher and there was a higher percentage of patients aged over 75 in both APA and PBO arms.
- The median weight of patients with CV/metabolic risk factors was 8kg higher than those without these risk factors in both arms.
- Most patients with prior CV / metabolic risk were also receiving associated con meds for these conditions.

Table 1: Patient Demographics - 70% of patients had history of CV and metabolic risk factors

	With history of CV/metabolic risk		with history of CV/metabolic risk and con meds		No history of CV /metabolic risk	
	APA+ADT	PBO+ADT	APA+ADT	PBO+ADT	APA+ADT	PBO+ADT
Sub-group prevelance n (% of ITT population)	378 (72)	364 (69)	358 (68)	347 (66)	146 (28)	163 (31)
Median (Q1-Q3) Age in Years	69 (65-75)	70 (63-74)	69 (65-75)	70 (63-74)	66 (61-73)	66 (60-71)
<65 n (%)	94 (25)	109 (30)	89 (25)	103 (30)	55 (37)	73 (45)
>=75 n (%)	103 (27)	88 (24)	99 (27)	85 (24)	30 (20)	25 (15)
Median Baseline Weight (Q1-Q3) in kg	79.1(70-90)	80.3 (70-92)	80 (71-91)	81.2 (70-92)	72.8 (65-80)	70 (62-79)
Patients receiving ACE inhibitors and angiotensin ii antagonists	226 (59.8)	210 (57.7)	226 (63.1))	209 (60.2)	12 (8.2)	14 (8.6)
Patients receiving Statins n (%)	125 (33.1)	92 (25.3)	123 (34.4)	90 (25.9)	11 (7.5)	8 (4.9)
Patients receiving direct factor Xa inhibitors n(%)	22 (5.8)	18 (4.9)	22 (6.1)	18 (5.2)	2 (1.4)	3 (1.8)
Median Time from initial diagnosis to randomization in months (Q1-Q3)	4.29 (2.4-9.0)	4.04 (2.4-7.1)	4.4 (2.4 - 9.0)	4.07 (2.4-7.3)	3.78 (2.1-6.7)	3.94 (2.3 - 5.9)
Gleason score at initial diagnosis						
N	378	364	358	347	147	163
<8	138 (37)	123 (34)	130 (36)	118 (34)	36 (24)	46 (28)
≥8	240 (63)	241 (66)	228 (64)	229 (66)	111 (76)	117 (72)
ECOG Performance Status n(%)						
0	240 (64)	230 (63)	227 (63)	219 (63)	88 (60)	118 (72)
1	138 (37)	133 (37)	131 (37)	127 (37)	59 (40)	45 (28)
Metastasis stage at diagnosis n (%)						
M0	73 (19)	49 (14)	73 (20)	48 (14)	12 (8)	10 (6)
M1	287 (76)	294 (81)	269 (75)	278 (80)	124 (84)	147 (90)
MX	18 (5)	21 (6)	16 (5)	21 (6)	11 (8)	6 (4)
Volume of disease n (%)						
High volume	221 (59)	229 (63)	206 (58)	220 (63)	104 (71)	106 (65)
Low volume	157 (41)	135 (37)	152 (42)	127 (37)	43 (29)	57 (35)
Median Baseline PSA ng/L (Q1-Q3)	5.7 (1.2-22.9)	4.2 (0.9-28.7)	5.4 (1.1 - 21.9)	4.3 (1.1- 27.0)	8.3 (1.1 - 51.1)	2.9 (0.7-23.3)

Figure 1: Percentage of patients achieving PSA90 or PSA<0.2ng/ml was similar in those with and without baseline CV or metabolic risk factors or conmeds and approximately double in the APA vs PBO group

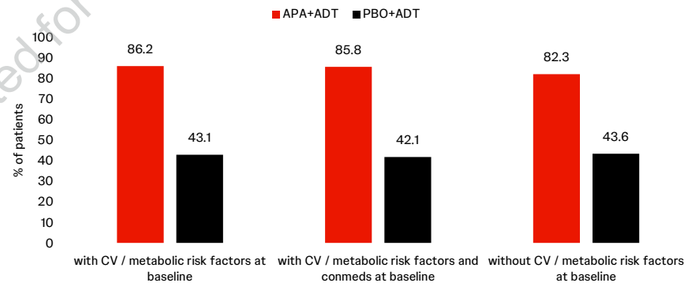
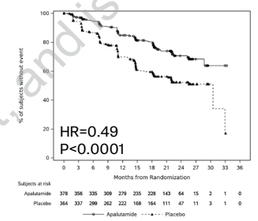
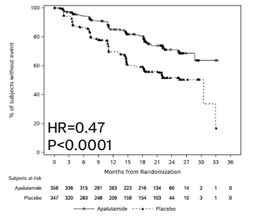


Figure 2 – Treatment effect of APA on rPFS was similar in those with and without baseline CV or metabolic risk factors +/- conmeds

a) With history of CV/metabolic risk factors



b) With history of CV/metabolic risk and con meds



c) no history of CV/metabolic risk

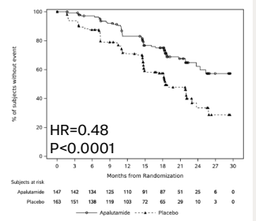


Figure 3 – Treatment effect of APA on OS was similar in those with and without baseline CV or metabolic risk factors +/- conmeds

a) With history of CV/metabolic risk factors

b) With history of CV/metabolic risk and con meds

c) no history of CV/metabolic risk

Table 2: Incidence of TEAEs were similar regardless of CV/metabolic risk. Rates of some TEAE of S.I or TEAE associated with LT ADT use were higher in patients with a history of these risk factors in both the APA and PBO arms. Cognitive deficits were infrequent.

	With history of CV / metabolic risk factors		With history CV/metabolic risk factors + associated con meds		without history of CV / metabolic risk factors	
	APA+ADT n (%)	PBO+ADT n (%)	APA+ADT n (%)	PBO+ADT n (%)	APA+ADT n (%)	PBO+ADT n (%)
n	378	364	358	347	146	163
Number of subjects with TEAEs	368 (97.4)	353 (97.0)	350 (97.8)	337 (97.1)	142 (97.3)	157 (96.3)
Number of subjects with Grade 3-4 TEAEs	183 (48.4)	165 (45.3)	177 (49.4)	161 (46.4)	76 (52.1)	55 (33.7)
Number of subjects with SAEs[b]	117 (31.0)	81 (22.3)	115 (32.1)	80 (23.1)	36 (24.7)	34 (20.9)
Number of subjects with TEAEs leading to treatment discontinuation	48 (12.7)	21 (5.8)	48 (13.4)	20 (5.8)	14 (9.6)	9 (5.5)
Number of subjects with TEAEs leading to death	15 (4.0)	11 (3.0)	15 (4.2)	11 (3.2)	5 (3.4)	6 (3.7)
TEAE of Special Interest - by category n (%)						
Skin Rash						
All grades	113 (29.9)	37 (10.2)	104 (29.1)	37 (10.7)	40 (27.4)	12 (7.4)
≥Gr 3	22 (5.8)	5 (1.4)	22 (6.1)	5 (1.4)	11 (7.5)	0
Fall						
All grades	38 (10.1)	30 (8.2)	37 (10.2)	29 (8.4)	11 (7.5)	7 (4.3)
≥Gr 3	6 (1.6)	3 (0.8)	6 (1.7)	3 (0.9)	1 (0.7)	2 (1.2)
Fracture						
All grades	38 (10.1)	17 (4.7)	38 (10.6)	16 (4.6)	16 (11)	9 (5.5)
≥Gr 3	10 (2.6)	4 (1.1)	10 (2.8)	4 (1.2)	8 (5.5)	0
Ischemic Heart Disease						
All grades	26 (6.9)	10 (2.7)	25 (7.0)	5 (1.4)	5 (3.4)	1 (0.6)
≥Gr 3	14 (3.7)	4 (1.0)	14 (4.1)	4 (1.0)	2 (1.4)	0
Ischaemic cerebrovascular disorders						
All grades	13 (3.4)	5 (1.4)	13 (3.6)	5 (1.4)	0	3 (1.8)
≥Gr 3	8 (2.1)	1 (0.3)	8 (2.2)	1 (0.3)	0	0
Seizure						
All grades	1 (0.3)	2 (0.5)	1 (0.3)	2 (0.5)	2 (1.4)	0
≥Gr 3	0	0	0	0	1 (0.7)	0
TEAEs associated with long-term use of ADT By Grouped terms n (%)						
Diabetes						
All grades	32 (8.5)	19 (5.2)	31 (8.7)	19 (5.5)	4 (2.7)	0
≥Gr 3	9 (2.4)	6 (1.6)	9 (2.5)	6 (1.7)	0	0
Arrhythmia & Cardiac Disorders						
All grades	23 (6.1)	15 (4.1)	22 (6.1)	15 (4.3)	7 (4.8)	2 (1.2)
≥Gr 3	9 (2.4)	6 (1.6)	8 (2.2)	6 (1.8)	4 (2.8)	0
Cardiac Failure						
All grades	14 (3.7)	9 (2.5)	14 (3.9)	9 (2.6)	1 (0.7)	1 (0.6)
≥Gr 3	8 (2.1)	3 (0.8)	8 (2.2)	3 (0.9)	0	0
Cognitive Deficits						
All grades	13 (3.4)	6 (1.6)	13 (3.6)	6 (1.7)	3 (2.1)	4 (2.5)
≥Gr 3	1 (0.3)	0	1 (0.3)	0	1 (0.7)	0

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