60-year-old man with low-risk metastatic castration sensitive prostate cancer

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Managing apalutamide-associated skin rash AE

Case courtesy of Dr Kohei HASHIMOTO, Sapporo Medical University School of Medicine

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Case courtesy of Dr Kohei HASHIMOTO, Sapporo Medical University School of Medicine

CLINICAL PRESENTATION

Photo by Alief Priyanto on Unsplash

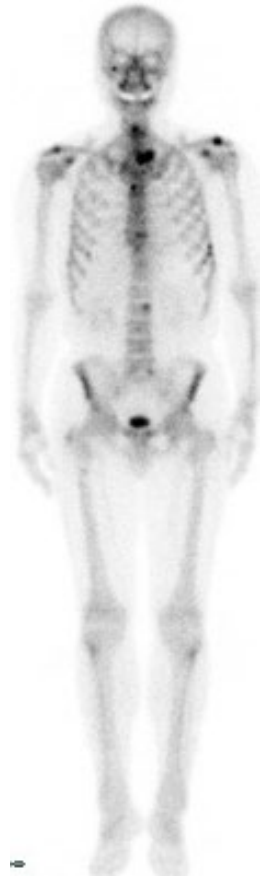
60-year-old man with low-risk metastatic castration sensitive prostate cancer

Age: 60
T2aN0M0
iPSA 10.13 ng/ml
Gleason score 5+4
Adenocarcinoma

IMRT 78Gy+ADT

PSA recurrence

PSA 2.85
Multiple bone metastasis



Low risk mCSPC

- **GS5+4**
- **Bone metastasis:2**

ADT, androgen deprivation therapy; GS, Gleason score; IMRT, intensity-modulated radiotherapy; mCSPC, metastatic castration sensitive prostate cancer; PSA, prostate specific antigen.

Case courtesy of Dr Kohei HASHIMOTO, Sapporo Medical University School of Medicine

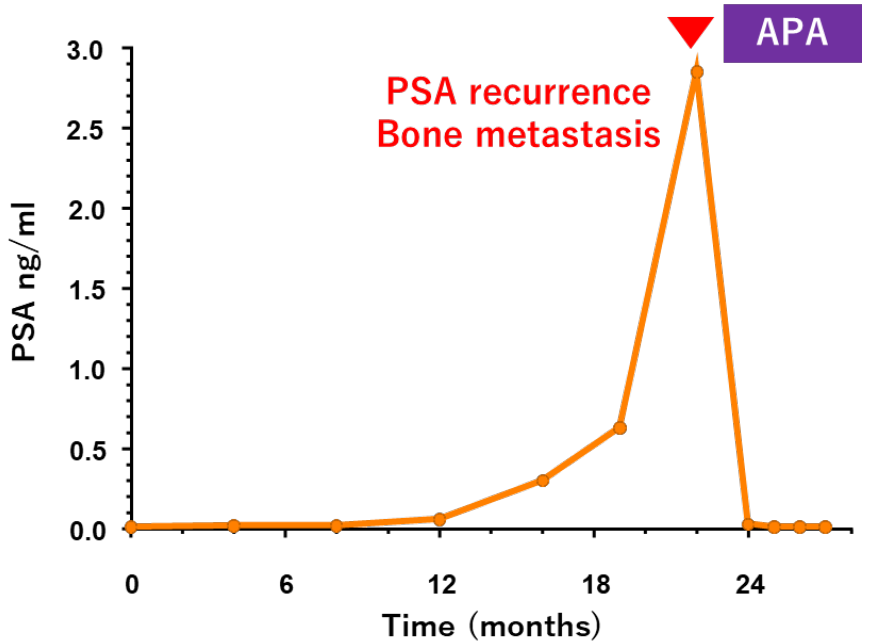
PsA levels following apalutamide

Age: 60
T2aN0M0
iPSA 10.13 ng/ml
Gleason score 5+4
Adenocarcinoma

IMRT 78Gy+ADT

PSA recurrence

PSA 2.85
Multiple bone metastasis



ADT, androgen deprivation therapy; APA, apalutamide; IMRT, intensity-modulated radiotherapy; mCSPC, metastatic castration sensitive prostate cancer; PSA, prostate specific antigen.

Case courtesy of Dr Kohei HASHIMOTO, Sapporo Medical University School of Medicine

Apalutamide-associated skin rash

Age: 60
T2aN0M0
iPSA 10.13 ng/ml
Gleason score 5+4
Adenocarcinoma

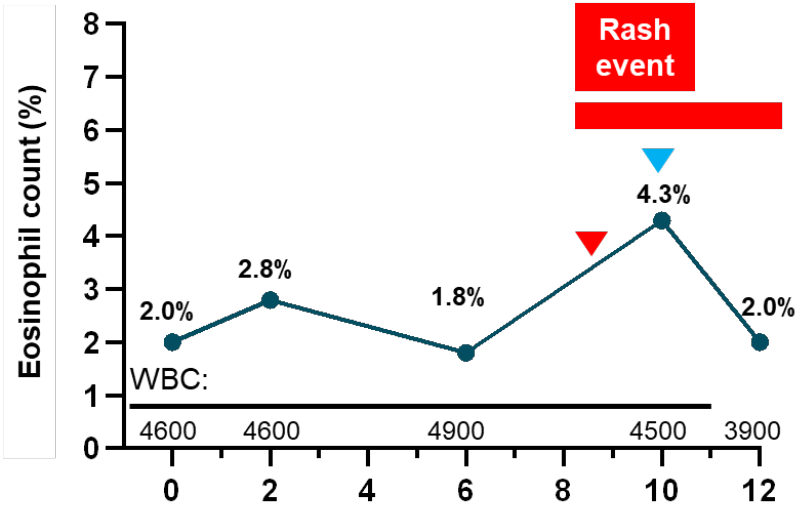
IMRT 78Gy+ADT

PSA recurrence

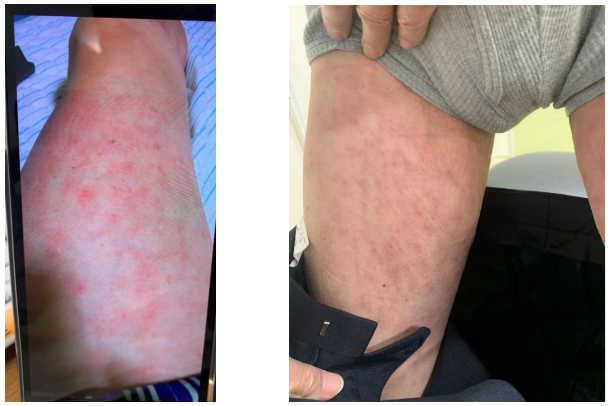
PSA 2.85
Multiple bone metastasis

ADT + apalutamide

240mg → **180mg**



Levocetirizine 5mg
(a second-generation antihistamine)



Wheal-like, papular rash Grade2
24 days

ADT, androgen deprivation therapy; IMRT, intensity-modulated radiotherapy; mCSPC, metastatic castration sensitive prostate cancer; PSA, prostate specific antigen.

MANAGING APALUTAMIDE-ASSOCIATED SKIN RASH AE

TITAN: Safety profile of APA plus ADT

Skin rash following administration of APA in Japanese patients

Relationship between rash and plasma exposure to APA

TITAN study: Adverse events

Safety Profile of APA Plus ADT Remained Consistent With Primary Analysis

Adverse Event, n(%)[a]	APA + ADT (n=524)		PBO + ADT (n=527)		Crossover (PBO to APA) + ADT (n=208)	
Any TEAE[b]	510 (97.3)		510 (96.8)		174 (83.7)	
Grade 3 to 4 TEAE	259 (49.4)		220 (41.7)		57 (27.4)	
Any serious TEAE[b]	153 (29.2)		115 (21.8)		29 (13.9)	
Any TEAE leading to treatment discontinuation	62 (11.8)		30 (5.7)		16 (7.7)	
TEAE leading to death	20 (3.8)		17 (3.2)		7 (3.4)	
Any COVID-19 AE	0		0		3 (1.4)	
Adverse Event of Interest by Group Term Grades, n (%)						
	All Grades	**Grade ≥ 3**	**All Grades**	**Grade ≥ 3**	**All Grades**	**Grade ≥ 3**
Skin rash	153 (29.2)	33 (6.3)	49 (9.3)	5 (0.9)	45 (21.6)	8 (3.8)
Fracture	54 (10.3)	18 (3.4)	26 (4.9)	4 (0.8)	5 (2.4)	0
Fall	49 (9.4)	7 (1.3)	37 (7.0)	5 (0.9)	8 (3.8)	0
Ischemic heart disease	31 (5.9)	16 (3.1)	11 (2.1)	4 (0.8)	1 (0.5)	1 (0.5)
Ischemic cerebrovascular disorder	13 (2.5)	8 (1.6)	8 (1.5)	1 (0.2)	5 (2.4)	5 (2.4)
Seizure	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0

Note: No new signals were observed after the primary analysis.
[a]Shown are adverse events (AEs) of any cause that occurred from the time of the first dose of the trial intervention through 30 days after the last dose. For each category, patients with multiple events were counted only once. AEs were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.3. One patient who was assigned to the APA group withdrew consent before treatment. [b]Excludes grade 5 events.
TEAE, treatment-emergent AE.

ADT, androgen deprivation therapy; APA, apalutamide; TEAE, treatment-emergent adverse event; PBO, placebo.

1. Chi KN, et al. Genitourinary Cancers Symposium 2021 Abstract #11.

Japanese patients: Adverse events

RESEARCH ARTICLE Open Access

Skin rash following Administration of Apalutamide in Japanese patients with Advanced Prostate Cancer: an integrated analysis of the phase 3 SPARTAN and TITAN studies and a phase 1 open-label study

Hiroji Uemura[1], Yosuke Koroki[2*], Yuki Iwaki[3], Keiichiro Imanaka[4], Takeshi Kambara[5], Angela Lopez-Gitlitz[6], Andressa Smith[6] and Hirotsugu Uemura[7]

types of rash in Apalutamide-treated

Analysis Set (N = 68)	Total n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)
Rash	35 (51.47)	9 (13.23)	16 (23.52)	10 (14.70)
Rash	13 (19.11)	8 (11.76)	4 (5.88)	1 (1.47)
Rash maculo-papular	11 (16.17)	2 (2.94)	6 (8.2)	3 (4.41)
Rash generalised	11 (16.17)	1 (1.47)	7 (10.29)	3 (4.41)
Erythema multiforme	3 (4.41)	0	1 (1.47)	2 (2.94)
Stomatitis	3 (4.41)	1 (1.47)	2 (2.94)	0
Urticaria	2 (2.94)	2 (2.94)	0	0
Blister	1 (1.47)	1 (1.47)	0	0
Drug eruption	1 (1.47)	0	0	1 (1.47)
Rash macular	1 (1.47)	0	0	1 (1.47)
Skin erosion	1 (1.47)	1 (1.47)	0	0
Skin exfoliation	1 (1.47)	1 (1.47)	0	0

Management of rash

1.0 month (IQR: 0.36–1.81)

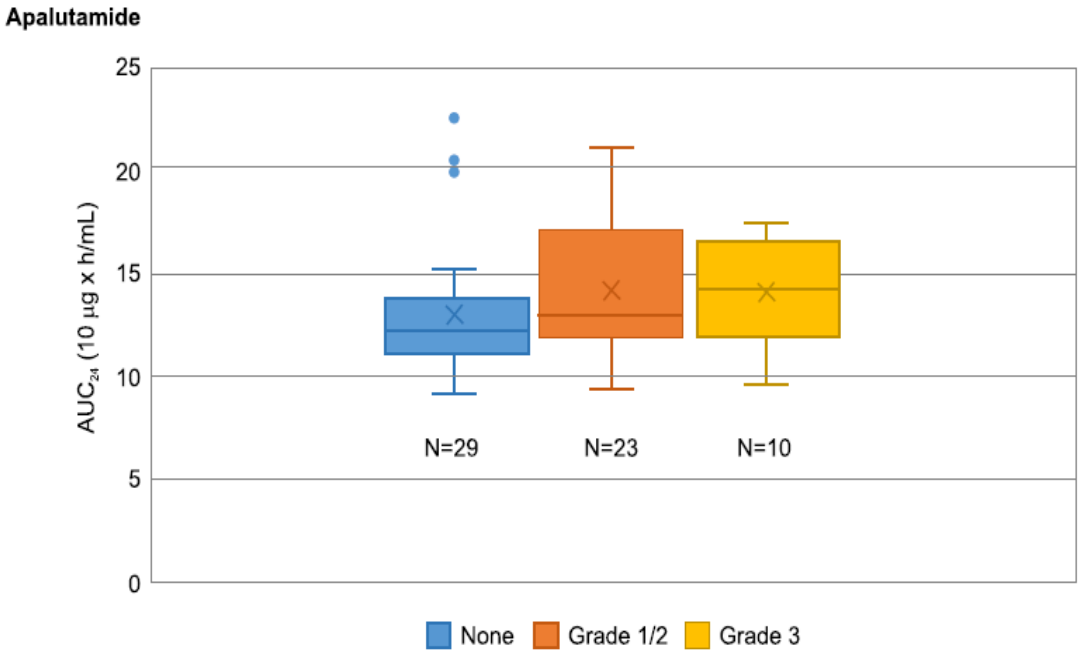
Analysis Set (N = 68)	SPARTAN	TITAN
Number of patients in safety analysis set, n	34	28
Rash, n (%)	19 (55.88)	14 (50.00)
Patients who received supportive care for rash, n (%)		
Oral antihistamine	11 (57.89)	6 (42.86)
Systemic corticosteroid	0 (0.00)	3 (21.43)
Topical corticosteroid	13 (68.42)	13 (92.86)
Drug interruption	11 (57.89)	6 (42.86)
Dose reduction	4 (21.05)	3 (21.43)
Drug discontinuation	3 (15.79)	2 (14.29)
Other	2 (10.53)	1 (7.14)

Uemura et al. BMC Urology 2020

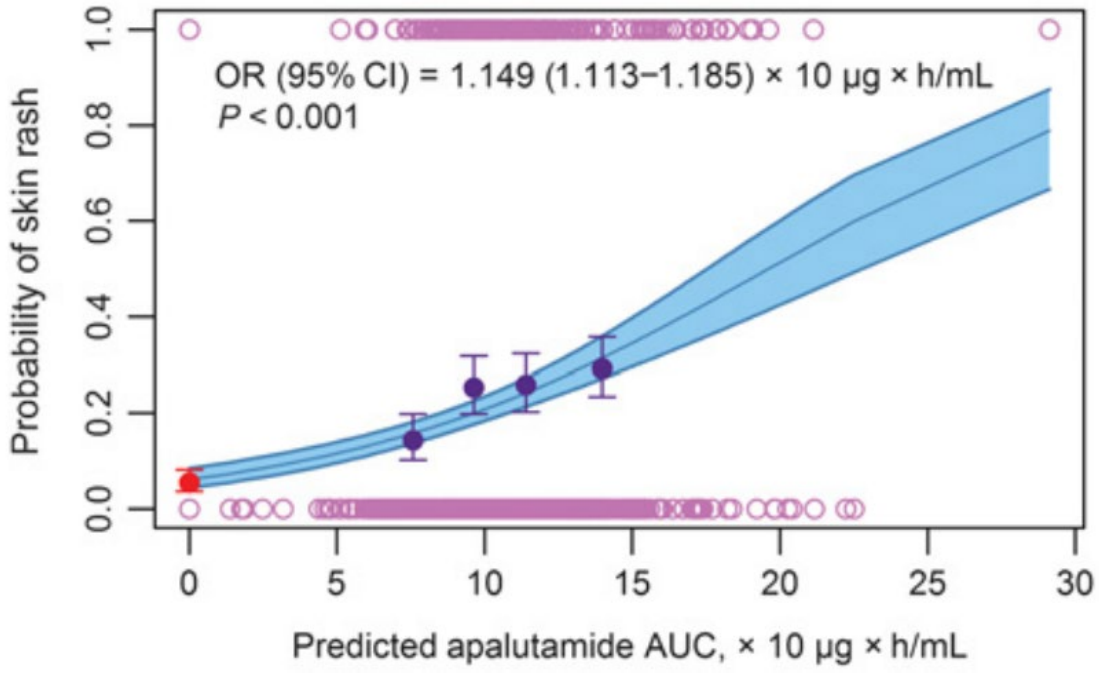
IQR, interquartile range.

1. Uemura H, et al. BMC Urology 2020; 20:139

Relationship between incidence of rash and plasma exposure (AUC0-24) to apalutamide



(Uemura et al. 2020)[1]



(Perez-Ruixo C 2021)[2]

AUC, area under curve; CI, confidence interval; OR, odds ratio.

1. Uemura H, et al. BMC Urology 2020; 20:139; 2. Perez-Ruixo C, et al. Clin Cancer Res 2020; 26(17):4460-4467.

CONCLUSION

- The incidence of apalutamide-related skin rash was higher in Japanese patients compared to patients from the rest of the world
  - Clinicians should look out for skin rashes as patients often do not self report
- There is a potential correlation between incidence of skin rash and plasma exposure to apalutamide
  - Eosinophil levels may be an important indication of whether patients will develop skin rashes

- **Management:**
  - Dose reductions/interruptions
  - Treatment with oral antihistamines and topical/systemic corticosteroids led to resolution of the majority of skin rashes observed in Japanese patients within 30 days

Photo by Alief Priyanto on Unsplash