



Dermatology Reports

<https://www.pagepress.org/journals/index.php/dr/index>

eISSN 2036-7406



SIDCO

Società Italiana di Dermatologia
Chirurgica, Oncologica, Correttiva ed Estetica

Publisher's Disclaimer. E-publishing ahead of print is increasingly important for the rapid dissemination of science. **Dermatology Reports** is, therefore, E-publishing PDF files of an early version of manuscripts that undergone a regular peer review and have been accepted for publication, but have not been through the copyediting, typesetting, pagination and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear on a regular issue of the journal. E-publishing of this PDF file has been approved by the authors.

Please cite this article as: Ciolfi C, Lunardon A, Cassalia F, Alaibac M. Apalutamide-induced ichthyosiform eruption. Dermatol Rep 2023 [Epub Ahead of Print] doi: 10.4081/dr.2023.9734



© the Author(s), 2023
Licensee PAGEPress, Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Apalutamide-induced ichthyosiform eruption

Christian Ciolfi, Anna Lunardon, Fortunato Cassalia, Mauro Alaibac

Dermatology Unit, Department of Medicine (DIMED), University of Padua, Padua, Italy

Corresponding Author:

Mauro Alaibac, M.D.

Dermatology Unit, Department of Medicine (DIMED)

University of Padua, Padua, Italy

Tel: +39 3293716018

E-mail: mauro.alaibac@unipd.it

Keywords: apalutamide, drug-induced, acquired ichthyosis, skin reaction, prostate cancer

Conflicts of interest: None

Acknowledgements: None

Fundings: None

Author Contributions: All authors contributed to designing and conducting the work, drafting and revising the manuscript and approved the final version for submission.

Dear Editor,

Skin eruptions are commonly observed in patients undergoing anticancer therapy, and with the introduction of new drugs in the antitumor treatment landscape evidence regarding their potential cutaneous adverse effects is still building.

We herein report the case of an acquired ichthyosiform reaction induced by apalutamide.

A 69-year-old man came to our attention for a one-month-history of a pruritic, scaly, thickened rash involving trunk, limbs and scalp.

His medical history revealed a metastatic castration-sensitive prostate cancer (Gleason score of $5 + 4 = 9$), with metastasis involving adrenal glands, external iliac lymph nodes and pelvic bones. He also suffered from arterial hypertension and atrial fibrillation, which were treated with irbesartan, amlodipine, and dabigatran.

The patient had been started treatment with gonadotrophin-releasing hormone antagonist degarelix, with subsequent introduction of androgen receptor selective inhibitor apalutamide (240 mg daily), with good response on primary tumor and metastasis. After about two months from the introduction of apalutamide, the pruritic rash occurred.

Skin examination revealed diffuse, dry, rough skin with prominent, polygonal scaling, with more severe involvement of lower legs, forearms and scalp (Figure 1).

No personal or family history of ichthyosis or atopy was reported. No other drugs were added or introduced except for apalutamide. The Naranjo Adverse Drug Reaction Probability Scale score for apalutamide was 5, while the score for the other medications the patient had been taken for years was 0. A diagnosis of apalutamide-induced acquired ichthyosis was then suspected and the patient was prescribed with topical emollients and keratolytics. He had moderate improvement in skin lesions with topical therapy and was able to continue anticancer therapy.

Apalutamide is an oral, non-steroidal, second-generation antiandrogen drug, which binds to the androgen receptor, preventing its translocation to the nucleus and subsequent DNA binding¹.

In the phase III, randomized, placebo-controlled TITAN study, the drug significantly improved the overall survival in patients with metastatic castration-sensitive prostate cancer receiving ongoing androgen deprivation therapy when compared to placebo²; moreover, in the phase III, randomized, double-blind, placebo-controlled SPARTAN study, the drug significantly increased the overall survival in patients with nonmetastatic castration-resistant prostate cancer receiving ongoing androgen deprivation therapy when compared to placebo³.

In both studies, skin rash was more common in the apalutamide group compared to placebo. In particular, cases of maculopapular rash, papular rash, generalized rash, butterfly rash, pustular rash, erythema multiforme, lichenoid drug eruptions, stomatitis, and urticaria have been reported during apalutamide treatment^{2,3}. Interestingly, Japanese patients were found to be more prone to develop cutaneous adverse events than the global population, still the reasons for this high incidence are poorly understood. In most cases, the skin rash occurred within four months of apalutamide treatment and was easily managed with topical/systemic corticosteroids or oral antihistamine, with or without dose adjustment⁴.

Furthermore, Miyagawa et al. reported the first case of a psoriasiform eruption occurring after apalutamide treatment, highlighting that sex hormone imbalances may be a trigger of psoriasis⁵.

To the best of our knowledge, this is the first report of an acquired ichthyosiform reaction induced by apalutamide. Nonetheless, the casual connection and the underlying pathogenetic mechanisms should be confirmed and strengthened by new case series and studies.

REFERENCES

1. Clegg NJ, Wongvipat J, Joseph JD et al. ARN-509: a novel antiandrogen for prostate cancer treatment. *Cancer Res.* 2012;72(6):1494-1503.
2. Chi KN, Agarwal N, Bjartell A et al. Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer. *N Engl J Med.* 2019;381(1):13-24.
3. Smith MR, Saad F, Chowdhury S et al. Apalutamide and Overall Survival in Prostate Cancer. *Eur Urol.* 2021;79(1):150-158.
4. Uemura H, Koroki Y, Iwaki Y et al. 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. *BMC Urol.* 2020;20(1):139.
5. Miyagawa F, Akioka N, Yoshida N et al. Psoriatic Skin Lesions after Apalutamide Treatment. *Acta Derm Venereol.* 2022;102:adv00659.

Figure 1. Diffuse, prominent, polygonal scaling is evident on lower legs (A, B), forearms (C) and scalp (D).

