General dermatology & dermatology in primary health care

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Funding sources: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of interest: None to declare.

Data availability: No data generated.

Ethics statement: Not applicable.

Case
A 24-year-old female patient with a background history of psoriasis, psoriatic arthritis, and hidradenitis suppurativa (HS) returned to the dermatology outpatient clinic complaining of a five-month history of excessive wrinkling of the palmar skin on contact with water. This was associated with a burning sensation and pruritus. For her psoriasis, psoriatic arthritis, and HS the patient had been stable on a regime of Methotrexate 5mg once weekly and Adalimumab 40mg every two weeks since 2019. In October 2022 she had a flare of HS and was commenced on Doxycycline 100mg once daily, shortly thereafter she noted the new symptoms. On review in clinic, time taken to develop symptoms was measured. A burning sensation was experienced at approximately 1 minute followed by skin changes including the development of papules and excessive oedematous wrinkling at approximately 2 minutes (Clinical Image 1.0).

Question
This condition is associated with which gene mutation?

(a) ABCC6
(b) ATP2A2
(c) CFTR
(d) FLCN
(e) TSC1/TSC2

Answer
(c) CFTR – up to 80% of patients with AWP have CF, while up to a further 20% are CFTR gene mutation carriers.

Explanations
(a) ABCC6 gene mutation is associated with pseudoxanthoma elasticum
ATP2A2 gene mutation is associated with Darier disease, a hereditary acantholytic dermatosis characterised by persistent scaly papules.

(c) CFTR – up to 80% of patients with AWP have CF, while up to a further 20% are CFTR gene mutation carriers.

(d) FLCN gene mutation is associated with Birt-Hogg-Dubé syndrome and the development of fibrofolliculomas.

(e) TSC1/TSC2 associated with tuberous sclerosis characterised by multiple hamartomas in the skin, brain, eyes, kidneys and heart

Discussion

Aquagenic wrinkling of the palms (AWP), also known as aquagenic palmoplantar keratoderma and aquagenic syringeal acrokeratoderma, was first described in 1996 by English and McCollough and is characterised by the appearance of transient translucent papules and wrinkling of the palms following contact with water. This “hand-in-bucket” sign is pathognomonic of AWP. Normal palmer wrinkling occurs following prolonged water submersion, however in AWP this can occur in as little as 3 minutes with increasing temperatures being known to precipitate the appearance. Associated symptoms, such as pruritus and burning, can last up to one hour following exposure. There is much to be uncovered regarding the epidemiology and pathogenesis of AWP. There is a strong association between AWP and patients with cystic fibrosis (CF) as well as gene mutation carriers, with signs generally taking longer to appear in those who are mutation carriers. Although there are many case reports detailing the association between AWP and CF, it should be noted that not all patients with CF display AWP symptoms. It is also widely accepted that AWP has a female predominance. Other associated conditions include hyperhidrosis, Raynauds phenomenon, marasmus and atopic dermatitis. In addition, there have been several case reports of drug induced AWP associated with COX inhibitors, aminoglycoside antibiotics, spironolactone, and gabapentin, all of which have full or partial response to withdrawal of the offending drug. It is hypothesised that mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene results in the production of hypertonic saline which through osmosis results in water flow into the eccrine gland ducts resulting in papules and wrinkling. In addition, it is proposed that certain drugs can induce dysregulation of skin aquaporins resulting in a similar clinical appearance. Histopathological findings in AWP include clear cell change, vacuolization, orthokeratotic hyperkeratosis and dilation of eccrine ducts. Multiple treatment options have been reported in the literature with varying results including topical tacrolimus, topical aluminium hydroxychloride, iontophoresis and botulinum toxin injections. In this case, doxycycline was withdrawn, and the patient was treated with topical Aluminium Chloride (20%) and Tacrolimus Ointment (0.1%) with some improvement in symptoms. Importantly the patient was referred to the National Department of Clinical Genetics for CF carrier testing.

References


5. Bouwman K, Menichino S, Kruithof I, Aalfs AS. Two new cases of aquagenic wrinkling of the palms and literature review on drug interactions. Dermatology online journal. 2020;26(11).

**Figure legend**

Figure 1. Translucent papules and wrinkling on the palmer surface following submersion in water.
CHANGING THE LANDSCAPE OF ORAL PSORIASIS TREATMENT\(^1-4\)

SOTYKTU is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy\(^1\)

DURABLE EFFICACY

Demonstrated superior PASI 75 response rates, and rates of clear or almost clear skin (sPGA 0/1), vs. placebo at Week 16 (co-primary endpoints)\(^2,3\)*

PASI 75 response rates were observed at Week 24 and maintained at Week 52\(^4\)*

ONCE DAILY, ORAL DOSING

Once-daily, oral treatment that can be taken with or without food, with no routine blood monitoring requirements after initiation and no identified DDIs\(^1\)

SOTYKTU is a novel, efficacious oral treatment that is generally well-tolerated\(^1-4\)*

GENERALLY WELL-TOLERATED

The most commonly reported adverse reaction is upper respiratory infections (18.9%)\(^1\)

Less than 3% of patients discontinued treatment due to AEs between Weeks 0–16\(^1-4\)

Adverse events should be reported. Reporting forms and information can be found at: UK – via the yellow card scheme at: www.mhra.gov.uk/yellowcard, or search for MHRA Yellow Card in the Google Play or Apple App Store. Ireland – via HPRA Pharmacovigilance at www.hpra.ie. Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (UK); 1 800 749 749 (Ireland)

Abbreviations: AE, adverse event; DDI, drug–drug interaction; PASI, Psoriasis Area and Severity Index; sPGA, static Physician’s Global Assessment; TYK2, tyrosine kinase 2.

References:

1. SOTYKTU. Summary of Product Characteristics.

\(^*\)SOTYKTU was studied in two global, Phase 3, randomised, multi-arm clinical studies: POETYK PSO-1 and PSO-2. PASI 75 and sPGA 0/1 vs. placebo at Week 16 were co-primary endpoints. PASI 75 was defined as ≥75% reduction from baseline in the Psoriasis Area and Severity Index. sPGA was defined as sPGA score of 0 or 1 with ≥2-point improvement from baseline. N numbers: PSO-1: SOTYKTU (n=332); apremilast (n=168), placebo (n=166); PSO-2: SOTYKTU (n=511); apremilast (n=254), placebo (n=255). SOTYKTU delivered superior PASI 75 response rates vs placebo (PSO-1: 58.4% vs. 12.7%, p<0.0001; PSO-2: 53.0% vs. 9.4%, p<0.0001) at Week 16, and superior results achieving clear or almost clear skin (sPGA 0/1) vs. placebo (PSO-1: 53.6% vs. 7.2%, p<0.0001; PSO-2: 49.5% vs. 8.6%, p<0.0001) at Week 16 (co-primary endpoints)\(^2,3\).

\(^1\)Via enzyme inhibition, enzyme induction, or transporter inhibition.

Learn more at sotyktu.co.uk

Bristol Myers Squibb
GENERALLY WELL-TOLERATED
The most commonly reported adverse reaction is upper respiratory infections (18.9%). Less ... should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (Great Britain).

PRESENTATION:
Film-coated tablet containing 6 mg of deucravacitinib.

INDICATION: Treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

PROTOCOL STUDIES:
Dosage: Treatment should be initiated under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis. Posology: 6 mg orally once daily. Special population: Elderly: No dose adjustment is required in elderly patients aged 65 years and older. Clinical experience in patients 75 years is very limited and deucravacitinib should be used with caution in this group of patients. Renal Impairment: No dose adjustment is required in patients with renal impairment, including end stage renal disease (ESRD) patients. Hepatic Impairment: No dose adjustment is required in patients with mild or moderate hepatic impairment. Deucravacitinib is not recommended to be used in patients with severe hepatic impairment. Paediatric population: The safety and efficacy of deucravacitinib in children and adolescents below the age of 18 years have not yet been established. No data are available. Method of administration: Oral. For oral use. Tablets can be swallowed whole and should not be chewed, cut, or chewed.

CONTRAINDICATIONS: Hypersensitivity to the active substance or any of the excipients (see SmPC). Clinically important adverse infections (e.g. active tuberculosis).

WARNING AND INSTRUCTIONS: Infectious: Treatment should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Contact the prescriber before treatment is started in patients with a chronic infection or a history of recurrent infection. Patients treated with deucravacitinib should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. Pneumocystis jirovecii pneumonia (PJP): If a patient is not on prophylaxis and is not responding to standard therapy, monitor carefully and deucravacitinib should not be given until the infection resolves. Pre-treatment evaluation for tuberculosis (TB): Prior to initiating treatment with deucravacitinib, patients should be evaluated for TB infection. Deucravacitinib should not be given to patients with active TB. Treatment of latent TB should be initiated prior to administering deucravacitinib. Anti-TB therapy should be continued prior to initiation of deucravacitinib in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving deucravacitinib should be monitored for signs and symptoms of active TB. Malignancies: Malignancies, including lymphomas and non-melanoma skin cancer (NMSC), were observed in clinical studies and post-approval data are available to assess the potential relationship of exposure to deucravacitinib and the development of malignancies. Long-term safety evaluations are ongoing. The risks and benefits of deucravacitinib treatment should be considered prior to initiating patients**. Major adverse cardiovascular events (MACE), deep venous thrombosis (DVT) and pulmonary embolism (PE): An increased risk was not observed in clinical trials with deucravacitinib. In a large randomised active-controlled study of a JAK inhibitor in rheumatoid arthritis (RA) patients 50 years and older, a higher rate of malignancies (particularly lung cancer, lymphoma and NMSC), a higher rate of MACE (defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke), and a higher rate of venous thromboembolism (including DVT and PE) were observed with a JAK inhibitor compared to TNF inhibitors.

INTERACTIONS: Deucravacitinib does not have any known interactions with other drugs.

PREGNANCY AND LACTATION: Pregnancy: There is a limited amount of data on the use of deucravacitinib in pregnant women. As a precautionary measure, it is preferable to avoid the use of deucravacitinib in women of childbearing potential. It is not known whether deucravacitinib/metabolites are excreted in human milk. As a precautionary measure, breastfeeding should be avoided. Excipients: Contains lactose.

ADVERSE REACTIONS:
Common (≥1/100 to < 1/10): Headache, nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, pharyngitis, sinusitis, acute sinusitis, rhinitis, rhinopharyngitis, aphthous ulcer, mouth ulceration, tongue ulceration, and stomatitis, Acneform rash (including acne, dermatis acneiform, rash, erythema, papule, pustule, plaque, and papulopustular), Folliculitis and Blood creatine phosphokinase increased. Uncommon (≤1/1000 to < 1/100): Herpes zoster***. Refer to SmPC for full details on adverse reactions.

***Serious adverse drug reaction

LEGAL CATEGORY: POM

MARKETING AUTHORIZATION NUMBER and BASIC NHS PRICE:
PLGB 15015/0719: Carton of 28 film-coated tablets 6 mg NHS price: £690.00; Carton of 84 film-coated tablets 6 mg NHS price: £2070.00.

MARKETING AUTHORIZATION HOLDER: Bristol-Myers Squibb Pharma EIEG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, Ireland.

FOR FURTHER INFORMATION CONTACT:
medical.information@bms.com or 0800 731 1736 (Great Britain).

DATE OF PREPARATION: May 2023

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 1787-GB-230000

SOTYKTU\textregistered (deucravacitinib) PRESCRIBING INFORMATION

Northern Ireland / Ireland

Consult Summary of Product Characteristics (SmPC) before prescribing. This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information

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DATE OF PREPARATION: June 2023

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

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