Commentary: anti-interleukin-17A for pityriasis rubra pilaris: catching the psoriasis biologic wave

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Pityriasis rubra pilaris (PRP) is a rare skin disease belonging to the spectrum of psoriasiform dermatoses.[1] Initially, PRP was considered a psoriasis variant until it achieved status as a distinct disease by the end of the 19th century.[2] However, PRP is now considered a group of related diseases known for their extensive phenotypic heterogeneity – classified into six subtypes – as well as being notoriously recalcitrant to therapy.[2,3] In the absence of approved therapies and high-level evidence, patients with PRP are trialled with conventional treatments.[3] Considering the clinical–histopathological overlap with psoriasis and the efficacious targeted therapies available for psoriasis, off-label treatment with psoriasis-approved biologics has been applied for challenging cases of PRP.[4] These include biologics targeting tumour necrosis factor-α and the interleukin (IL)-23–helper T cell 17 pathway.[4–6]

In this issue of the *BJD*, Boudreaux and colleagues report findings from a single-centre, open-label clinical trial that assessed the anti-IL-17A biologic secukinumab in PRP.[7] The study included 12 patients with PRP who had not responded to prior topical corticosteroids and at least one systemic agent – most often systemic corticosteroids (67%), acitretin (42%) and methotrexate (33%). Patients received secukinumab according to the psoriasis dosing regimen: 300 mg once weekly for the first 4 weeks, followed by once every 4 weeks. The primary endpoint of ≥ 75% reduction in Psoriasis Area and Severity Index (PASI 75) at week 28 was met by six of 11 patients (55%). Three patients (27%) achieved PASI 90, and there was a statistically significant reduction in mean Dermatology Life Quality Index. Another important finding was a 97% improvement in overall gene expression profiles in lesional skin after 2 weeks of treatment. Significant enrichment of innate immune pathways was noted in patients who did not respond to secukinumab.

This trial is relevant and timely given the need for effective therapies for PRP. It adds to mounting evidence in support of targeting IL-17 in PRP.[8] However, several limitations need consideration. The trial's lack of a placebo arm may have introduced bias, given that PRP is associated with spontaneous remission. Inclusion of a control arm would have enabled a double-blind design, increasing the strength of evidence tremendously. Dose ranging and refinement of the dosing regimen should be investigated as these might not be directly translatable from one dermatological disease to another.

Furthermore, the primary outcome measure PASI, borrowed from the 'cousin' psoriasis, is not validated for PRP and might not fully capture PRP manifestations. Development and agreement on PRP-specific outcome measures in a minimal clinical dataset – ideally a core outcome set – would allow harmonization of data collection across centres.[9] Multicentre collaboration is crucial given the rarity of PRP.[6]

Finally, the baseline transcriptomic analyses demonstrated extensive heterogeneity, which could explain the variable clinical responses to targeted therapy in PRP.[9] The way forward would be to utilize multi-omics technology to profile patients on a genetic, transcriptomic or proteomic level and to identify biomarkers to guide optimal drug selection.

In conclusion, building on the lessons learned from the 'tsunami' in psoriasis-targeted therapies, this trial is an important step forward to improving outcomes for a rare, high-burden skin disease. Further steps would benefit from dermatological drug development approaches, which also apply for drug repurposing.[10]

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