Prurigo nodularis: New treatments on the horizon

Gil Yosipovitch, MD
Miami, Florida

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Prurigo nodularis (PN) is one of the most challenging chronic itchy conditions dermatologists encounter.[1] The pathogenesis of PN is largely unknown. The condition has been associated with multiple dermatologic and nondermatologic diseases. There is a significant component of neural structural changes in this disease, as demonstrated by thickened nerves in the dermis and reduced innervation density in the epidermis on histopathology. Lesional skin nerves have a higher expression of substance P. Another mediator for itch overexpressed in PN is the T-cell helper 2–derived cytokine interleukin 31.[1]

Numerous treatments, such as corticosteroids, calcineurin inhibitors, methotrexate, cyclosporine, as well as drugs that target nerve fibers, such as capsaicin, gabapentinoids, naltrexone, thalidomide, and phototherapy have been used to treat this challenging and intractable condition. Most of these treatments have not been subjected to randomized controlled studies, and only 3 randomized studies with small sample sizes were performed thus far.[2] There is a lack of any targeted pharmacologic treatments.

The study by Stander et al[3] opens a new era of targeted treatments for this burdensome and difficult to treat disease. The authors performed the largest randomized controlled study so far using 128 patients with PN of >6 weeks who were refractory to previous treatments. The patients received a neurokinin 1 (NK-1)–inhibitor serlopitant 5 mg or placebo orally once daily for 8 weeks. NK-1 is the receptor of substance P and, as mentioned above, is overexpressed in nerves in PN.

Reductions in pruritus from baseline were observed as early as week 2 with serlopitant versus placebo, and a clinically meaningful itch reduction was achieved at week 8, the primary endpoint of this study.

Previously this drug showed efficacy in a randomized controlled study of different types of chronic severe itch, suggesting that the substance P–NK-1 pathway is an important target for treating chronic itch.[4] The adverse effects noted in this study and in previous studies were minimal. Of note, no central nervous effects, such as drowsiness, insomnia, and dizziness, common in other drugs used to treat PN and chronic itch (ie, gabapentinoids, thalidomide, naltrexone, and sedating antihistamines) were reported. This is extremely important in treating older age patients with PN.

There are multiple other promising drugs undergoing clinical trials for PN. Nalbuphine targets the neural system and is a mixed kappa agonist and mu antagonist. These types of drugs have already shown antipruritic effects in uremic and cholestatic pruritus, as well as for intractable chronic itch.[5] In several trials, biologic treatments are being used that target the neuroimmune system by inhibiting interleukin 31 receptors. Interleukin 31 is an important mediator of different chronic types of itch.[5] Dupilumab, an interleukin 4 receptor alpha antibody, has recently been reported in a case series to significantly improve PN and reduce itch.

From the Dr Phillip Frost Department of Dermatology and Cutaneous Surgery and Itch Center Miller School of Medicine, University of Miami.

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Correspondence to: Gil Yosipovitch, MD, University of Miami School of Medicine, 1600 NW 10th Ave, RMSB 2067, Miami, FL 33136. E-mail: yosipog@gmail.com.

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Our hope is that these types of drugs and other future targeted treatments tested in clinical trials will be approved and end the misery of severe itch in PN patients.

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