Title: Gabapentinoids for immune checkpoint-inhibitor associated pruritus: a retrospective cohort study

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Background: Pruritus is among the most common cutaneous immune-related adverse events (cirAEs) associated with immune checkpoint inhibitor (ICI) therapy, impairing quality of life and, in refractory cases, prompting ICI interruption or discontinuation. This is particularly relevant given the association between cirAEs and improved response to ICI therapy. Gabapentin and pregabalin are used off-label for refractory pruritus and appear as options in ASCO and NCCN irAE guidelines; however, evidence characterizing their use, tolerability, and role among other itch-directed therapies in the ICI population remains limited.

Methods: We performed a single-center retrospective chart review of patients who received ICI therapy and were concurrently prescribed gabapentin or pregabalin. Candidates were identified through an electronic health record query searching for concomitant ICI and gabapentin/pregabalin orders for encounters between 9/11/2011, and 8/28/2026, yielding 144 patients. Patients were excluded if pruritus was not attributable to ICI therapy, if gabapentinoid use did not temporally overlap with the pruritus episode, or if documentation was insufficient to determine whether the gabapentinoid affected the patient's itch, resulting in a final cohort of 30 patients. Abstracted variables included demographics, ICI regimen, concomitant systemic cancer therapy, gabapentinoid agent and dosing, concomitant itch-directed therapies, concomitant cirAE, dermatology referral, ICI hold status, and gabapentinoid-related adverse effects. Response was based on chart documentation indicating whether the gabapentinoid improved pruritus.

Results: Of 30 patients, 17 (57%) were male. Most (80%) were started on a gabapentinoid specifically for ICI-associated pruritus; 3 (10%) had an existing dose increased at itch onset, and 6 (20%) were already taking a gabapentinoid for an unrelated indication, with itch response documented only incidentally. Gabapentin was used in 22 patients (73%), pregabalin in 5 (17%), and both were trialed sequentially in 3 (10%). Concomitant itch-directed therapies were common: topical corticosteroids (73%), oral antihistamines (70%), topical antipruritics/emollients (43%), systemic corticosteroids (33%), and biologics/immunomodulators (20%). Among the biologics/immunomodulators, dupilumab was most common (n=3), with tocilizumab, naltrexone, and hydroxychloroquine each used once. Underlying concomitant cirAEs included lichenoid reactions (27%), eczematous dermatitis (23%), and nonspecific rash (10%), while 20% had no documented cutaneous findings; notably one patient had both lichenoid and eczematous features. Dermatology was consulted in 21 patients (70%). Subjective itch improvement was documented in 16 patients (53%) and no improvement in 13 (43%); response was not assessed in 1 patient who discontinued secondary to somnolence before response could be evaluated. The ICI was held for pruritus in 5 patients (17%). Gabapentinoid-

related adverse effects occurred in 5 patients (17%), predominantly sedation, and prompted discontinuation in 2 (7%).

Conclusions: Gabapentin and pregabalin were well tolerated in patients with ICI-associated pruritus, with few treatment-limiting adverse effects, and approximately half (53%) of patients reported itch improvement. Gabapentinoids may therefore be a reasonable treatment option for multimodal management of ICI-associated pruritus, consistent with ASCO and NCCN irAE guidance. Prospective, controlled studies are needed to define response rates, optimal dosing, and comparative efficacy against other itch-directed therapies, using validated itch outcome measures, such as the peak pruritus NRS and the Dermatology Life Quality Index.