To the Editor: Vitiligo is an acquired depigmenting skin disorder due to the absence of functional melanocytes affecting up to 1% of the general population.1 Initial treatment typically involves topical corticosteroids, topical calcineurin inhibitors, and phototherapy; however, topical Janus kinase inhibitors (JAKi) are being explored as a potential treatment option. This systematic review examines the efficacy and safety of topical JAKi therapies in vitiligo.

Following the PRISMA guidelines, MEDLINE and Embase Ovid searches were conducted, using variations and synonyms of keywords “Vitiligo” and “JAK inhibitor” (Supplementary File 1, available via Mendeley at https://data.mendeley.com/datasets/ngwr9gns95). After independent screening of 240 articles by 2 reviewers with no exclusion based on study type, 12 studies involving 213 patients were included. (Fig 1; Supplementary File 2, available via Mendeley at https://data.mendeley.com/datasets/ngwr9gns95). The mean age was 48.5 years (range: 4-73 years), with 108 males (50.7%) and 105 females (49.3%).

Ruxolitinib (84%) was the most common therapy followed by tofacitinib (15%) and delgocitinib (1%). Treatment duration was described in 212 instances (mean: 44.9 weeks; range: 4.6-52 weeks). Facial Vitiligo Area and Severity Index (F-VASI) scores were measured in 159 cases, with 64.8%, 53.5%, and 29.6% of cases achieving ≥50% (VASI50), ≥75% (VASI75), and ≥90% (VASI90) reductions from baseline VASI, respectively. Total VASI (T-VASI) scores were measured in 83.6% of cases, with 33.5%, 11.2%, and 6.7% of cases achieving ≥50% (T-VASI50), ≥75% (T-VASI75), and ≥90% (T-VASI90) reductions from baseline T-VASI, respectively. Concurrent treatment with non-JAKi therapies was noted in 39 cases, with phototherapy and topical corticosteroids accounting for 23 and 6 of the concurrent treatments, respectively (Supplementary File 2). Adverse events were reported in 113 cases using JAKi, with pruritis (12.2%), upper respiratory tract infections (10.8%), and acne (8.5%) being the most documented adverse events.

The appeal of topical JAKi is the potential to provide adequate response in patients no longer responding to older topical agents and to reduce adverse events of interest (eg, infections) that may present through oral JAKi administration. Ruxolitinib was the most studied topical JAKi treatment for vitiligo, with 49.7% and 29.6% of cases achieving F-VASI50/T-VASI50, respectively. In a phase 2 randomized controlled trial of topical ruxolitinib for vitiligo, 45% and 30% of cases achieving F-VASI50/T-VASI50, respectively. Ruxolitinib’s mechanism of action involves JAK mediated inhibition of IFNγ (interferon gamma) signaling. The IFNγ induced expression of C-X-C motif chemokine 10 in keratinocytes is an important mediator of depigmentation in vitiligo. Topical tofacitinib resulted in 46.9% and 53.1% of cases achieving F-VASI50/T-VASI50, respectively. Tofacitinib works in a similar fashion to ruxolitinib, with any differences in efficacy owing to targeting of JAK1/3 as opposed to JAK1/2 with ruxolitinib. Ruxolitinib is currently the only topical JAKi to receive FDA approval for vitiligo treatment.

Study limitations included lack of follow-up data and potential selection bias for cases with improved outcomes. Given the lack of standardized outcome measures and data heterogeneity, a meta-analysis could not be performed. Despite this, we highlight evidence for the effectiveness and safety of topical JAKi therapies, specifically ruxolitinib and tofacitinib, for treating vitiligo. Further long-term studies are warranted to establish practical clinical applications of topical JAK inhibitors.

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Conflicts of interest
Dr Yeung has been an advisor, consultant, speaker, and/or investigator for AbbVie, Allergan, Amgen, Astellas, Boehringer Ingelheim, Celgene, Centocor, Coherus, Dermira, Eli Lilly, Forward, Galderma, GSK, Janssen, LEO Pharma, Medimmune, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, Takeda, UCB, Valeant, and Xenon. Abduelmula, Mufti, Chong, Sood, and Sachdeva have no conflicts of interest to declare.

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