3. Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: a study of 90 patients. *J Am Acad Dermatol*. 2017;76:22-28.
4. Jerjen R, Meah N, Trindade de Carvalho L, Wall D, Eisman S, Sinclair R. Treatment of alopecia areata in pre-adolescent children with oral tofacitinib: a retrospective study. *Pediatr Dermatol*. 2021;38(1):103-108.
5. McKenzie PL, Maltenfort M, Bruckner AL, et al. Evaluation of the prevalence and incidence of pediatric alopecia areata using electronic health record data. *JAMA Dermatol*. 2022;158:547-551.
6. Yu DA, Kim YE, Kwon O, Park H. Treatment outcome of oral tofacitinib and ruxolitinib in patients with alopecia areata: a systematic review and meta-analysis. *Indian J Dermatol Venereol Leprol*. 2021;87:621-627.
7. Huang J, Li T, Tan Z, et al. Effectiveness of tofacitinib in pre-adolescent alopecia areata: a retrospective case series and literature review. *Acta Derm Venereol*. 2023;103: adv13418.
8. Bhokare A. Recovery of resistant alopecia areata treated with tofacitinib: an 8-year-old child's case report. *Int J Trichol*. 2022;14:135.
9. Swetha Sri S, Premkumar M, Thomas J. Successful management of alopecia areata in children with oral tofacitinib. *Specialusis Ugdymas*. 2022;1:516-522.

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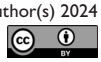

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Association of Proton Pump Inhibitors on Psoriasis Treatment and Development: A Systematic Review

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To the Editor,

Proton pump inhibitors (PPIs) are well-established for treatment of gastroesophageal reflux disease and peptic ulcer.[1] While novel, use of these therapies for psoriasis patients has been reported with additional studies evaluating development of psoriasis on PPI therapy.[1-3] This systematic review aims to examine evidence regarding these associations.

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to search Embase and MEDLINE databases using specific keywords (Supplemental Table 1). Quality of evidence was assessed using Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. After independent screening by 2 reviewers, 10 articles (publication date: 2000-2021) reflecting 3092

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patients were included (Supplemental Figure 1; Supplemental Table 2). The mean age was 50.4 years (range: 28-59 years) with sex reported in 2991 (96.7%) patients (male: 59.7%, 1787/2991; female: 40.2%, 1204/2991). Types of psoriasis documented were plaque (97.7%, 376/385), guttate (1%, 4/385), pustular (0.8%, 3/385), and palmoplantar (0.5%, 2/385). *Helicobacter pylori* infection was confirmed in 478 (15.5%) patients.

Outcomes were classified into the following categories: *de novo* psoriasis (93.5%, 2890/3092), improvement of psoriasis (6%, 192/3092), and no effect of PPI treatment on psoriasis (2.6%, 10/3092). The specific PPIs utilized were reported in 2533 (81.9%) instances, most commonly being lansoprazole (35.5%, 900/2533), omeprazole (29.4%, 745/2533), and esomeprazole (26.5%, 670/2533; Supplemental Table 3). Across 2 (20%) studies that reported on *de novo* psoriasis, odds ratios (ORs) were between 1.52 and 1.54 (highest incidence with lansoprazole; OR 1.25) and the highest adjusted hazard ratio was 2.6 ($P < .01$; Supplemental Table 2).[1,2] Among 8 (80%) studies reflecting 202 patients with reported outcomes of PPI use for psoriasis, complete clearance and partial resolution were achieved in 2 (1%) and 190 (94%) of cases, respectively (mean treatment duration: 15 days; 202/3092). Of these, a lack of resolution was observed in 10 (5%) patients with omeprazole use. The mean percent improvement from baseline in Psoriasis Area and Severity Index (PASI) was 58.9% [reported in 171/3092 (5.5%) of cases], with 63.6% (6/11) of reported patients achieving PASI 90 (Supplemental Table 3). Concurrent systemic medications and/or phototherapy for psoriasis were used in 153 (79.7%) of PPI-treated cases, majority being apremilast (26%, 50/192; Supplemental Table 2).

While the relationship between psoriasis and PPI use remains unclear, neutrophilic infiltrates along with glandular mucosal changes have been identified in patients with psoriasis.[4] Furthermore, it has been postulated that certain gut microbiota may induce the Th17 immune pathway.[5] As PPIs can mediate gastrointestinal inflammation and alter the microbiome balance, this may be a mechanism by which psoriasis may occur or improve with therapy. A population-based study in Taiwan identified an adjusted OR of 1.54 (95% confidence interval) for risk of psoriasis with PPI exposure.[1] Nonetheless, in certain subsets of patients, psoriasis may improve with PPI use as in the case of a prospective pilot study demonstrating a mean PASI improvement of 83.9% with esomeprazole monotherapy for a 90 day period.[3]

Study limitations include concomitant medication use and incomplete follow-up. Regardless, we highlight evidence demonstrating that in certain patient subsets, PPI use can induce and/or ameliorate psoriasis. Additional research is warranted regarding this relationship and appropriate monitoring.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

References

1. Li CY, Dai YX, Chang YT, et al. Proton pump inhibitors are associated with increased risk of psoriasis: a nationwide nested case-control study. *Dermatology*. 2021;237(6):884-890. doi:10.1159/000517515
2. Lin SH, Chang YS, Lin TM, et al. Proton pump inhibitors increase the risk of autoimmune diseases: a nationwide cohort study. *Front Immunol*. 2021;12:736036. doi:10.3389/fimmu.2021.736036
3. Bafutto M, Oliveira EC, Zaterka S. Evaluation of psoriasis treatment with esomeprazole—a pilot study. *Arq Gastroenterol*. 2019;56(3):261-263. doi:10.1590/S0004-2803.201900000-49
4. Scarpa R, Manguso F, D'Arienzo A, et al. Microscopic inflammatory changes in colon of patients with both active psoriasis and psoriatic arthritis without bowel symptoms. *J Rheumatol*. 2000;27(5):1241-1246.
5. Wilck N, Matus MG, Kearney SM, et al. Salt-responsive gut commensal modulates TH17 axis and disease. *Nature*. 2017;551(7682):585-589. doi:10.1038/nature24628