ORIGINAL ARTICLE

Inflammatory bowel disease among patients with psoriasis treated with ixekizumab: A presentation of adjudicated data from an integrated database of 7 randomized controlled and uncontrolled trials

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Background: Inflammatory bowel disease (IBD) occurs more frequently in patients with psoriasis. The 2 diseases have significant genetic overlap, but the pathogenesis underlying their co-occurrence is unknown.

Objective: We sought to report adjudicated IBD cases (Crohn's disease [CD] and ulcerative colitis [UC]) in patients exposed to ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin-17A.

Methods: Adverse events (AEs) integrated from 7 randomized controlled and uncontrolled trials were analyzed for the controlled induction period, controlled maintenance period, and all ixekizumab-treated patients. Suspected IBD cases were reviewed by blinded external experts using internationally recognized criteria (Registre Epidemiologique des Maladies de l'Appareil Digestif registry).

Results: In all, 4209 patients (6480 patient-exposure years) were exposed to ixekizumab. Suspected CD (N = 12) or UC (N = 17) AEs were reported; 19 were adjudicated as definite/probable IBD (CD, N = 7, incidence rate = 1.1/1000 patient-exposure years; UC, N = 12, incidence rate = 1.9/1000 patient-exposure years). Among these, 3 occurred during induction (CD, N = 1; UC, N = 2) and 7 during maintenance (CD, N = 4; UC, N = 3). Twelve of 16 patients with reported IBD history have not had an IBD treatment-emergent AE/serious AE to date.

Limitations: Clinical review (adjudication) was not prespecified. AE data collected post-hoc may have been limited by length of time from occurrence.

Conclusion: From an integrated database of 7 ixekizumab psoriasis trials, CD and UC cases were uncommon (<1%). (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.10.027.)

Key words: biologic therapy; Crohn's disease; inflammatory bowel disease; interleukin-17 antagonists; ixekizumab; psoriasis; ulcerative colitis.

CAPSULE SUMMARY

- Patients with psoriasis have an increased incidence of inflammatory bowel disease; the 2 diseases have significant genetic overlap.
- Animal and human studies suggest a potential role of interleukin-17 in inflammatory bowel disease.
- From an integrated database of 7 ixekizumab psoriasis trials, cases of Crohn's disease and ulcerative colitis were uncommon (<1%).

Plaque psoriasis is an immune-mediated inflammatory skin disease with increased risks for other inflammatory conditions such as inflammatory bowel disease (IBD). Although the exact pathogenesis underlying co-occurrence of psoriasis and certain comorbidities is unknown, similarities in genetic risk and shared inflammatory cytokines have been highlighted as potential risk factors. Crohn's disease (CD) and ulcerative colitis (UC) are the 2 most common forms of IBD and are characterized by chronic and recurrent intestinal inflammation. Several studies have demonstrated increased CD and UC prevalence among patients with psoriasis.[1-4] In 1 epidemiologic study, patients with psoriasis were 2.5 times more likely to have CD and 1.6 times more likely to have UC.[5]

Psoriasis and IBD share several characteristics in their inflammatory pathways. Cytokines, such as interleukin (IL)-23 and tumor necrosis factor, and T-helper 17 cells may be involved in both conditions.[6,7] Earlier research in animal models suggested IL-17 involvement in the pathogenesis of CD,[6] whereas IL-17 was protective against IBD in murine models,[8] and a human study showed IL-17 overexpression in intestinal tissue from patients with active CD.[9] In clinical trials of CD, both brodalumab (IL-17R antagonist) and secukinumab (IL-17A antagonist) failed to achieve the primary efficacy end point and in some cases CD worsened versus placebo while higher adverse event (AE) rates were also observed.[10,11]

In this context, during ongoing phase-III trials in patients receiving ixekizumab, a monoclonal antibody selectively targeting IL-17A, an independent external committee was established to adjudicate all potential AEs of IBD reported in an integrated database of 7 ixekizumab clinical trials in 4209 patients with moderate to severe psoriasis.

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