Incidence of Inflammatory Bowel Disease Events in Adalimumab Clinical Trials Across Indications

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BACKGROUND

• Adalimumab (ADA) is approved for the treatment of Crohn's disease (CD) and ulcerative colitis (UC); therefore, it is postulated that new onset or flare of inflammatory bowel disease (IBD) is a rare occurrence in ADA clinical trials for non-IBD indications.

OBJECTIVE

• The purpose of this analysis was to determine the rates of IBD adverse events (AEs) in ADA clinical trials, particularly in spondyloarthropathies (SpA) patients who are at a higher risk of IBD as a feature of SpA

METHODS

CLINICAL TRIALS

• The rates of IBD AEs in 73 phase 2–4 interventional ADA clinical trials (64 IBD clinical trials and 9 non-IBD, polyarthritis, juvenile idiopathic arthritis [JIA], psoriatic arthritis, and psoriasis prevention trials) were calculated separately for placebo (PBO)- and ADA-treated patients (Table 1). In ADA trials including both pre-existing and incident patients, the overall rate of IBD was 0.5/100 patient-years (PYs) (95% CI 0.3–0.8), while the rates in pre-existing patients were 0.2/100 PYs (95% CI 0.1–0.5) and in incident patients 1.5/100 PYs (95% CI 0.9–2.2) (Table 2). These rates were lower than the rates observed in non-IBD trials of ADAs (0.9–2.2/100 PYs) and in non-IBD ADA clinical trials of other TNF inhibitors (1.3–2.0/100 PYs) (95% CI 0.2–4.8). In patients at risk for IBD who require biologic therapy, ADA is a reasonable therapeutic option based on the observed low IBD event rates in ADA clinical trials and its demonstrated efficacy in treating UC and CD patients.

• The risk of an IBD event occurring over a 1-year period in all interventional ADA trials was 0.1/100 PYs (Table 4).

• The 1-year risk of an IBD event was 0.0 in PBO and Ps trials.

• The 1-year risk of an IBD event in PsA, Hidradenitis suppurativa, and Ps trials, was 0.0 and was reported in 1 patient treated with ADA.

• The 1-year risk of an IBD event in IBD clinical trials was 0.0 in PBO and Ps trials, 1.0 in Ps in ADA-controlled periods, and 0.0 in Ps in PBO-controlled periods.

• The risk of an IBD event over a 1-year period of ADA treatment was 0.1/100 PYs in PsA, non-PsA peripheral spondyloarthropathies (psSpA), inflammatory bowel disease (IBD) and pJIA patients.

• There were no reports of IBD events in patients without CD, UC, or IBD.

• Adalimumab is approved for the treatment of Crohn's disease (CD) and ulcerative colitis (UC); therefore, it is postulated that new onset or flare of inflammatory bowel disease (IBD) is a rare occurrence in ADA clinical trials for non-IBD indications.

• ADA was administered to 23,735 patients, representing 36,406.6 PYs of exposure.

• Incidence rates for IBD events during the PBO-controlled period of ADA interventional trials were 0.0/100 PYs for both ADA- and PBO-treated patients (Table 2).

• In adalimumab (ADA)-treated patients during PBO-controlled period were 0.2/100 PYs and 1.1/100 PYs, respectively (Table 2).

• In 1 IBD event reported in a patient on ADA treatment (in an AS patient) and 1 IBD event reported in patients treated with PBO (in a non-axSpA patient).

• Overall, the incidence rate for IBD events in ADA-treated patients during PBO-controlled periods and open-label extensions across all interventional clinical trials of ADA was 0.1/100 PYs (Table 3).

• The rates of IBD events varied across therapeutic indications from 0.1 to 0.8/100 PYs.

• In SpA, the overall rate of IBD was 0.5/100 PYs, while the rates were 0.0, 0.5, and 0.7/100 PYs in PsA, non-PsA psSpA, and psJIA, respectively (Table 3).

• 2266 patients with adalimumab (ADA; 1965, in adalimumab 196; 92 in adalimumab and AIA, respectively (Table 3).

• In adalimumab-treated patients during PBO-controlled period were 0.2/100 PYs and 1.1/100 PYs, respectively (Table 2).

• 3218 (3919.9) 19 0.5 (0.3–0.8)

• 196 (51.5) 1 0.0 366 (85.8) 0 0.0

• 3218 (1711.4) 8 0.5 (0.2–0.9)

• In PsA, the overall rate of IBD was 0.5/100 PYs.

• There were no reports of IBD events in non-IBD ADA clinical trials (Table 1).