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Vasculitis

Objectives: The aim of this multi-center (7 university-related hospitals), retrospective study is to clarify retention rates and reasons for discontinuation of 7 bDMARDs and tocilizumab (TOF), one of the JAKi, in both bDMARDs-naïve and bDMARDs-switched cases.

Methods: This study assessed 3,897 patients and 4,415 treatment courses of with bDMARDs and TOF from 2001 to 2019 (2,737 bDMARDs-naïve patients and 1,678 bDMARDs-switched patients [59.5% switched to their second agent], female 82.3%, baseline age 57 years, disease duration 8 years; rheumatoid factor positivity 78.4%, DAS28-ESR 4.3; concomitant prednisolone [PSL] 1 mg/day [42.4%] and methotrexate [MTX] 8.5 mg/week [80.9%].) Treatment courses included abatacept (ABT; n=663), adalimumab (ADA; n=536), certolizumab pegol (CZP; n=226), etanercept (ETN; n=856), golimumab (GLM; n=458), infliximab (IFX; n=724), tocilizumab (TCZ; n=851), and TOF (n=101 only bDMARDs-switched cases). Reasons for discontinuation were classified into four categories by each attending physician: 1) lack of effectiveness; 2) toxic adverse events; 3) non-toxic reasons; and 4) remission. Retention rates of each discontinuation reason were estimated at 36 months using the Kaplan-Meier method and adjusted for potential clinical confounders (age, sex, disease duration, concomitant PSL and MTX, starting date and number of switched bDMARDs) using Cox proportional hazards modeling.

Results: Adjusted drug retention rates for each discontinuation reason were as follows: lack of effectiveness in the bDMARDs-naïve group (from 70.8% [CZP] to 85.1% [ABT]; P<0.001 between agents) and the bDMARDs-switched group (from 52.8% [CZP] to 78.7% [TCZ]; P<0.001 between agents). Toxic adverse events in the bDMARDs-naïve group (from 86.9% [IFX] to 96.3% [ABT]; P<0.001 between agents) and the bDMARDs-switched group (from 81.1% [ADA] to 95.4% [ETN]; P=0.001 between agents). Finally, overall retention rates excluding discontinuation for non-toxic reasons or remission ranged from 62.4% [IFX] to 82.0% [ABT] (P<0.001 between agents) in the bDMARDs-naïve group (figure a) and from 44.2% (ADA) to 66.8% (IFX) (P<0.001 between agents) in the bDMARDs-switched group (figure b).

Conclusion: Remarkable differences were observed in drug retention of 7 bDMARDs and TOF between bDMARDs-naïve and bDMARDs-switched cases.
glucocorticoid induction regimen, or relapse severity) had a significant differential effect on the primary outcome. By 24 months after entry, 20 months after randomization, 11/85 (13%) patients in the RTX group had experienced a relapse compared to 32/85 (38%) patients in the AZA group. 19/85 (22%) patients in the RTX group and 31/85 (36%) patients in the AZA group experienced at least one severe adverse event (SAE), 25/85 (29%) and 42/85 (49%) patients in the RTX group developed hypogammaglobulinemia (IgG <5g/l) and non-severe infections respectively, compared to 21/85 (25%) and 41/85 (48%) in the AZA group.

Methods: At the end of part 1, patients entered open-label part 2, in which GCA therapy (including initiation/termination of open-label TCZ and/or GCs) was given at the investigator’s discretion according to disease status. Time to first GCA flare during the 3-year study period was assessed using Kaplan-Meier analysis for patients in the intention-to-treat population according to disease onset status at baseline (new-onset/relapsing) based on their originally assigned treatment groups: TCZ QW, TCZ Q2W, or pooled PBO. Kaplan-Meier analyses showed a clear separation between the AZA group and the pooled PBO groups over 3 years for patients with new-onset and relapsing GCA. Median time to first flare over 3 years was longer for patients assigned to TCZ treatment in part 1 than for patients assigned to PBO. Kaplan-Meier analysis showed a clear separation between the TCZ QW and the pooled PBO groups over 3 years for patients with new-onset and relapsing GCA (Figure 1A). Separation between the TCZ QW and TCZ Q2W groups was also observed over 3 years in patients with new-onset and relapsing GCA, although this was more evident in patients with relapsing GCA (Figure 1B). Higher proportions of patients in the TCZ Q2W group (new-onset, 49%; relapsing, 47%) than the pooled PBO group (new-onset, 28%; relapsing, 31%) and the TCZ Q2W group (new-onset, 27%; relapsing, 35%) remained flare-free during their entire treatment period. Cumulative prednisone dose over 3 years was lower for patients originally assigned to TCZ QW versus those originally assigned to PBO for patients with new-onset GCA and those with relapsing GCA at baseline (Figure 2).

Conclusion: In this 3-year analysis of GIACTA parts 1 and 2, time to first flare favored TCZ QW over TCZ Q2W in patients with new-onset and relapsing GCA. TCZ Q2W delayed time to first flare and resulted in lower cumulative GC exposure compared with PBO in patients with new-onset and relapsing GCA, supporting TCZ Q2W dosing in patients with GCA regardless of disease onset.

References:

Figure 1. Time to first GCA flare (primary endpoint) by treatment group, and time to first flare by new-onset or relapsing GCA

Figure 2. Cumulative prednisone dose over 3 years by treatment group

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OP0028 EFFICACY OF APREMILAST FOR THE PAIN OF ORAL ULCERS ASSOCIATED WITH ACTIVE BehÇûtÇ’s SYNDROME: 12-WEEK RESULTS FROM THE RANDOMIZED, PHASE III RELIEF STUDY

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Background: BehÇûtÇ’s syndrome (BS) is a chronic autoimmune inflammatory disease that affects the skin, joints, and mucous membranes. Oral ulcers associated with active BS are a common clinical manifestation of the disease. Apremilast is a selective phosphodiesterase 4 (PDE4) inhibitor that has been approved for the treatment of moderate to severe plaque psoriasis and psoriatic arthritis. The efficacy of apremilast in the treatment of oral ulcers associated with active BS has not been previously studied.

Objectives: The primary objective of this study was to evaluate the efficacy of apremilast compared to placebo (PBO) in reducing the mean pain score of oral ulcers associated with active BS at Week 12. The secondary objectives were to evaluate the efficacy of apremilast compared to PBO in reducing the mean number of oral ulcers, the proportion of patients achieving a 90% improvement from baseline in mean pain score and mean number of oral ulcers, and the proportion of patients achieving a 90% improvement from baseline in mean dis ease activity score (DAS) at Week 12.

Methods: This was a randomized, double-blind, placebo-controlled, parallel-group study conducted in 8 countries. Patients were randomized 1:1 to receive apremilast 30 mg twice daily or PBO for 12 weeks. The primary endpoint was the change from baseline in mean pain score of oral ulcers at Week 12. Secondary endpoints included the change from baseline in mean number of oral ulcers at Week 12, proportion of patients achieving a 90% improvement from baseline in mean pain score and mean number of oral ulcers at Week 12, and proportion of patients achieving a 90% improvement from baseline in mean DAS at Week 12.

Results: A total of 242 patients were enrolled and randomized to apremilast (n=121) or PBO (n=121). Baseline characteristics were similar between the two groups. The primary and secondary endpoints were met. Apremilast significantly reduced the mean pain score of oral ulcers compared to PBO at Week 12 (p<0.001). Apremilast also significantly reduced the mean number of oral ulcers compared to PBO at Week 12 (p<0.001). The proportion of patients achieving a 90% improvement from baseline in mean pain score and mean number of oral ulcers was significantly higher in the apremilast group compared to the PBO group at Week 12 (p<0.001). The proportion of patients achieving a 90% improvement from baseline in mean DAS was significantly higher in the apremilast group compared to the PBO group at Week 12 (p<0.001).

Conclusion: Apremilast significantly reduced the mean pain score, mean number of oral ulcers, and DAS compared to PBO at Week 12 in patients with active BS and oral ulcers. Apremilast was well tolerated in this study.

References: