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 tofacitinib (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 57.4 years, disease duration 8.5 years; rheumatoid factor positivity 78.4%; DAS28-ESR 4.3; concomitant prednisolone [PSL] 6.1 mg/day [42.4%] and methotrexate [MTX] 8.5 mg/week [60.9%]). 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]; $P=0.01$ between agents). Finally, overall retention rates excluding discontinuation for non-toxic reasons or remission ranged from 64.2% (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% (TCZ) ($P<0.001$ 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.

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Vasculitis

OP0026

A RANDOMIZED, CONTROLLED TRIAL OF RITUXIMAB VERSUS AZATHIOPRINE AFTER INDUCTION OF REMISSION WITH RITUXIMAB FOR PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND RELAPSING DISEASE

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Background: Rituximab (RTX) is an effective therapy for induction of remission in ANCA-associated vasculitis (AAV). However, the effect of RTX is not sustained, and subsequent relapse rates are high, especially in patients with a history of relapse.

Objectives: The RITAZAREM trial is an international, multi-center, open-labelled, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with RTX, of two relapse-prevention strategies: repeat dosing of RTX or daily oral azathioprine (AZA).

Methods: Patients with AAV were recruited at the time of relapse and received induction therapy with RTX and glucocorticoids. If remission was achieved by month 4, patients were randomized in a 1:1 ratio to receive either RTX (1000mg every 4 months for 5 doses) or AZA (2mg/kg/day) as maintenance therapy. Patients were followed for a minimum of 36 months, with the primary outcome being time to disease relapse.

Results: 190 patients were enrolled and 170 randomized at 4 months (85 to RTX; 85 to AZA). The data are complete on all patients up to at least month 24. Median age was 59 years (range 19-89), with a prior disease duration of 5.3 years (0.4-38.5). 123/170 (72%) patients had a history of testing positive for anti-proteinase 3 ANCA; 47/170 (28%) for myeloperoxidase ANCA; 104/170 (61%) were enrolled having suffered a major relapse, and 48/170 (28%) received a pre-specified higher dose glucocorticoid induction regimen (Table 1).

Table 1. Baseline characteristics of patients enrolled in RITAZAREM trial

	Rituximab (N=85)	Azathioprine (N=85)	Total (N=170)
Age, years: median (range)	57 (18-89)	61 (27-83)	59 (18-89)
Female, number (%)	42 (49.4%)	44 (51.8%)	86 (50.6%)
Disease duration, years: median (range)	5.8 (0.4-38.5)	4.9 (0.4-25.8)	5.3 (0.4-38.5)
Prior cyclophosphamide therapy			
Number of patients (%)	67/85 (78.8%)	66/85 (77.6%)	133/170 (78.2%)
Cumulative dose, grams (g): median (range)	7.1 g (0.2-301)	12 g (1.0-146)	10 g (0.2-301)
Prior rituximab therapy			
Number (%) patient	33/85 (38.8%)	27/85 (31.8%)	60/170 (35.3%)
Cumulative dose, grams (g): median (range)	3.2 g (2.0-16.0)	5.4 g (1.5-14.0)	3.9 g (1.5-16.0)
Glucocorticoid induction regimen			
1mg/kg/day starting dose	24/85 (28.2%)	24/85 (28.2%)	48/170 (28.2%)
0.5mg/kg/day starting dose	61/85 (71.8%)	61/85 (71.8%)	122/170 (71.8%)
ANCA type			
Anti-proteinase 3	61/85 (71.8%)	62/85 (72.9%)	123/170 (72.4%)
Anti-myeloperoxidase	24/85 (28.2%)	23/85 (27.1%)	47/170 (27.6%)
Relapse type upon entry into trial			
Severe	52/85 (61.2%)	52/85 (61.2%)	104/170 (61.2%)
Non-severe	33/85 (38.8%)	33/85 (38.8%)	66/170 (38.8%)

RTX was superior to AZA in preventing disease relapse with a preliminary overall hazard ratio (HR) estimate of 0.36 (95% CI 0.23-0.57, $p<0.001$) and a during-treatment HR estimate of 0.30 (95% CI 0.15-0.60, $p<0.001$) (Figure 1). After adjustment, none of the randomization stratification covariates (ANCA type,

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 hypogammaglobulinaemia (IgG <5g/l) and non-severe infections respectively, compared to 21/85 (25%) and 41/85 (48%) in the AZA group.

Figure 1. Relapse-free survival in RITAZAREM trial: rituximab versus azathioprine

Conclusion: In the RITAZAREM trial, following induction of remission with RTX, RTX was superior to AZA for preventing disease relapse in patients with AAV with a prior history of relapse. There were no new major safety signals for use of these medications in this population.

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OP0027

TIME TO FLARE AND GLUCOCORTICOID EXPOSURE IN PATIENTS WITH NEW-ONSET VERSUS RELAPSING GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB OR PLACEBO PLUS PREDNISONE TAPERING: 3-YEAR RESULTS FROM A RANDOMIZED CONTROLLED PHASE 3 TRIAL

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Background: In part 1 of the 52-week, double-blind GiACTA trial, tocilizumab (TCZ) every week (QW) or every other week (Q2W) + prednisone tapering reduced the risk for flare versus placebo (PBO) + 26-week prednisone tapering among patients with new-onset giant cell arteritis (GCA) at baseline. Among patients with relapsing GCA, TCZ QW but not Q2W + prednisone reduced the risk for flare versus both PBO groups, and there was separation in the time to flare between the TCZ QW and Q2W groups.¹

Objectives: To report time to first flare and potential cumulative glucocorticoid (GC) sparing over 3 years of the GiACTA trial (part 1 + 2-year open-label part 2) among patients with new-onset or relapsing GCA.

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 (PBO+26-week and PBO+52-week prednisone taper).

Results: Among patients randomly assigned in part 1, 47 of 100 (47%) in the TCZ QW group, 26 of 49 (53%) in the TCZ Q2W group, and 46 of 101 (46%) in the pooled PBO group had new-onset GCA at baseline; the rest had 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 QW 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 QW 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 QW dosing in patients with GCA regardless of disease onset.

References:

[1] Stone JH et al. N Engl J Med 2017;377:317-28.

Figure 2. Cumulative Prednisone Dose Over 3 Years: TCZ QW Versus PBO groups

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OP0028

EFFICACY OF APREMILAST FOR THE PAIN OF ORAL ULCERS ASSOCIATED WITH ACTIVE BEHÇET'S SYNDROME: 12-WEEK RESULTS FROM THE RANDOMIZED, PHASE III RELIEF STUDY

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