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Background: Oral ulcers (OU) associated with Behçet’s syndrome are often painful, may interfere with the ability to eat and can negatively affect quality of life.1 Apremilast (APR), an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in the treatment of OU associated with Behçet’s syndrome in a phase III, multicenter, randomized, double-blind, placebo (PBO)-controlled study (RELIEF; BCT-002).3

Objectives: To describe the efficacy of APR treatment in improving OU pain associated with Behçet’s syndrome in RELIEF.

Methods: Patients were randomized (1:1) to APR 30 mg twice daily (APR 30 BID) or PBO twice daily for a 12-week PBO-controlled phase, followed by a 52-week active treatment extension. Eligible patients were ≥18 years of age and had active Behçet’s syndrome with ≥3 OU at randomization or ≥2 OU at screening and randomization and without active major organ involvement. Clinical improvement in OU was evaluated by the area under the curve for the number of OU through Week 12 (AUCWk0-12; primary efficacy endpoint) and by assessments of OU number. Patient-reported OU pain was evaluated by the 100-mm visual analogue scale (VAS). The statistical tests were 2-sided (α=0.05). The proportions of patients achieving the minimal clinically important difference (MCID) and higher rates of improvement, defined as ≥10-mm, ≥30-mm (3-fold MCID), ≥50-mm (5-fold MCID) improvements in OU pain VAS scores, respectively, were analyzed through Week 12. An ANCOVA model was used to analyze the primary endpoint and assessments of OU number and OU pain (VAS). The proportion of patients achieving improvement in OU pain VAS scores at Week 12 were summarized descriptively.

Results: A total of 207 patients were randomized and received ≥1 dose of study medication (APR: n=104; PBO: n=103). Baseline, the mean (SD) number of OU was 4.2 (3.7) in the APR 30 BID group and 3.9 (2.7) in the PBO group, and the mean (SD) OU pain VAS scores were 61.2 (27.6) and 60.8 (28.9), respectively. At Week 12, significantly greater improvements were observed with APR 30 BID vs. PBO in AUCWk0-12 (least-squares [LS] mean [SE]: 129.5 [15.9] vs. 222.1 [15.9]; P<0.0001), number of OU (LS mean [SE]: 1.1 [0.2] vs. 2.0 [0.3]; P=0.0003) and OU pain VAS scores (LS mean [SE] change from baseline: −40.7 [3.3] vs. −15.9 [3.3]; P<0.0001). The proportion of patients who achieved the MCID of ≥10-mm improvement in OU pain VAS scores at Week 12 was greater with APR 30 BID vs. PBO; this pattern was also observed for the higher 3- and 5-fold improvements in MCID (Figure 1). Greater proportions of APR 30 BID vs. PBO patients achieved ≥10-mm and ≥30-mm improvements in OU pain VAS scores over 12 weeks. Notably, greater achievement of ≥50-mm improvement in OU pain VAS scores was observed with APR 30 BID vs. PBO as early as Week 1 and maintained up to Week 12 (Figure 2).

Conclusion: For patients with active Behçet’s syndrome, APR 30 BID provided significantly greater improvements vs. PBO in OU number and OU pain at Week 12, including the greater proportion of patients achieving MCID and 3- and 5-fold MCID of OU pain in the APR 30 BID group vs. the PBO group. These results indicate a clinically meaningful treatment effect of APR 30 BID on the OU associated with Behçet’s syndrome.

References:

Disclosure of Interests: Gulen Hatemi Grant/research support from: BMS, Celgene Corporation, Silk Road Therapeutics – grant/research support, Consultant of: Bayer, Eli Lilly – consultant, Speakers bureau: AbbVie, Mustafa Nevzat, Novartis, UCB – speaker, Alfred Mahr Consultant of: Celgene, Speakers bureau: Roche, Chugai, Mitsubishi Tanabe speakers bureau: Eli, Tanabe-Mitsubishi – speaker; Celgene Corporation – advisory board, Doyoung Kim: None declared, Melike Melkoc: None declared, Sue Chan-Faye Speakers bureau: GSK, Inc. – employment; Celgene Corporation – employment at the time of study conduct, Shannon McCue Employee of: Amgen Inc. – employment; Celgene Corporation – employment at the time of study conduct, Sven Richter Employee of: Amgen Inc. – employment; Celgene Corporation – participation at the time of study conduct, Michele Brunori Employee of: Amgen Inc. – employment; Celgene Corporation – employment at the time of study conduct, Maria Paris Employee of: Amgen Inc. – employment; Celgene Corporation – employment at the time of study conduct, Yusuf Yazici Consultant of: BMS, Celgene Corporation, Genentech, Sanofi – consultant, Consultant of: BMS, Celgene Corporation, Genentech, Sanofi – consultant DOI: 10.1136/annrheumdis-2020-eular.2908
without active disease and 19% still experiencing active disease. 32% were still receiving GCs - 22% of them receiving > 5mg/day. There was no negative impact on functional status with 14% reducing working hours, 13% restricted social life, 6% leaving employment, 6% registered as disabled and 2% leaving full time education.

Conclusion: The start of maintenance treatment in AAV is variably defined but typically at 6 months after start of remission induction therapy. Achieving full remission and preventing relapse are still clinical problems and many patients require ongoing GC therapy to maintain remission. Infectious complications and adverse events are common and there is significant negative impact on patient functional status over time. Disclosure of Interests: Peter Rutherford Shareholder of: Vifor Pharma. Employee of: Vifor Pharma, Baxter Healthcare, Dieter Götte Shareholder of: Vifor Pharma, Employee of: Vifor Pharma DOI: 10.1136/annrheumdis-2020-eular.844

GRANULOMATOSIS WITH POLYANGIITIS SUSTAINED REMISSION-OFF-THERAPY: DATA FROM THE FRENCH VASCULITIS STUDY GROUP REGISTRY

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Background: Data on granulomatosis with polyangiitis (GPA) sustained remission-off-therapy (SROT) is limited and it is unknown whether disease characteristics or treatment regimens may affect it.

Objectives: This study aimed to assess SROT of GPA patients from the French Vasculitis Study Group registry, and identify factors associated with its occurrence and duration during follow-up.

Methods: GPA had to satisfy the 1990 ACR classification criteria, and PASER definition. Patients who were never on GC were compared to those of registry GPA patients with available data at 3 years but not in SROT (controls), and 3-year SROT achieving 5-year SROT vs those who relapsed between 3-5 years. Patients with 3-year GPA SROT follow-up +7 years were analyzed according to maintained SROT or not.

Results: Among 756 database patients with new-onset GPA, 259 achieved at least 1 SROT at some time during their disease, after a median (IQR) of 36 [28-63] months post-diagnosis. The first SROT lasted a median of 14 [8-32] months. Among 202 of those patients who had follow-up, 73 (36%) remained in SROT for a median follow-up of 34 [14-45] months post-SROT. Among 443 (54%) patients followed for ≥2 years post-diagnosis, 82% had received GC and cyclophosphamide induction therapy. At 3 years post-diagnosis, 92 (21%) patients in SROT were compared to those of registry GPA patients with available data at 3 years but not in SROT (controls), and 3-year SROT achieving 5-year SROT vs those who relapsed between 3-5 years. Patients with 3-year GPA SROT follow-up +7 years were analyzed according to maintained SROT or not.

Conclusion: Only 3% of GPA patients achieved 10-year SROT after conventional induction and maintenance therapies. No baseline clinical or biological characteristics helped distinguish patients achieving or maintaining SROT and those who relapsed. However, patients achieving 3-year SROT had received more intensive induction therapy than those who relapsed or were still on GC or IS at 3 years.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1827

AN INCREASE IN SERUM CALPROTECTIN LEVEL IN ANCA-ASSOCIATED VASCULITIDES PATIENTS DURING MAINTENANCE TREATMENT IS ASSOCIATED WITH MORE RELAPSE AND ACCELERATED RENAL FUNCTION DECLINE

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Background: Calprotectin (S100A8/A9), a protein secreted by activated neutrophils and monocytes in inflammatory conditions, is upregulated in active ANCA-associated vasculitides. Serum calprotectin level variation during induction therapy is associated with disease relapse in PR3-ANCA-associated vasculitides (1). However, the place of this biomarker during maintenance therapy is unknown.

Objectives: To demonstrate whether variation in serum calprotectin level during maintenance therapy could be used as a biomarker predicting subsequent relapse in ANCA-associated vasculitides.

Methods: Patients with ANCA-associated vasculitides in complete remission (BVAS=0) after induction therapy with cyclophosphamide and included in the MAINRISTAN trial (2) were analyzed. Patients were randomized to receive rituximab or azathioprine as maintenance therapy. Relapse was defined as the re-occurrence or new onset of disease attributable to active vasculitides. Accelerated decline renal function (estimated Glomerular Filtration Rate (eGFR) assessed using the MDRD Equation) was defined in concordance with NICE 2015 guideline (3) as a decrease in eGFR of 25% or more and a change in GFR category or a sustained decrease in eGFR of 15 ml/m²/min over 12 months; Calprotectin was assessed in the serum at inclusion and 6 months by ELISA (IDK® Calprotectin ELISA kit, Immunodagnostik). We defined an increase in serum levels of calprotectin a positive variation of calprotectin level at M6 compared to baseline.

Results: Of all, 96 patients (female 45.8%, mean age 55.3±13, 69.8% PR3+, 62.5% ANCA positive at inclusion) had at least a calprotectin dosage (86 at baseline, 86 at M6 and 76 at patients this at 2 time-point). Calprotectin level at baseline or 6 months was not significantly different between relapsing patients and those without relapse after 18 months of follow-up, whereas the calprotectin variation at M6 compared to baseline was higher in relapsing patients (n=10) (mean (SD) 17991 (±28972) ng/ml) than in patients not experiencing any relapse (n=86) (9419 (±5002) ng/ml; p=0.03). An increase in serum calprotectin level at 6 months was significantly associated with an increased risk of relapse in PR3-ANCA patients (OR=5.6 (95%CI, 1.0-31.3; p=0.049) but not in the whole study group (OR=3.3 (95%CI, 0.8-14.1; p=0.1), and identified patients with accelerated renal function decline (all cohort: OR=10.6 (65%CI, 2.9-39.6; p=0.002; PR3+ patients: OR=5.909 (95%CI, 2.9-39.6; p=0.001)), whereas calprotectin level did not correlate with glomerular filtration rate (r = -0.07, p=0.35).

Conclusion: An increase in serum calprotectin during the first 6 months of maintenance therapy in ANCA-associated vasculitides is a useful biomarker predicting vasculitis relapse and accelerated renal function deterioration in the following 12 months.

References:

Acknowledgments: Supported by a grant from the Programme Hospitalier de Recherche Clinique, French Ministry of Health (2008-002846-51).

Disclosure of Interests: Xavier Romand Consultant of: Xavier ROMAND has declared, Athan Baillet Consultant of: Athan BAILLET has received honorarium fees from Abbvie for his participation as the coordinator of the systematic literature review on September 17, 2023 by guest. Protected by copyright.http://ard.bmj.com/ Ann Rheum Dis: first published as 10.1136/annrheumdis-2020-eular.844 on 2 June 2020. Downloaded from ...