Background: Reports of rheumatic immune-related adverse events (irAEs) in patients receiving immune checkpoint inhibitors (ICPi) have recently attracted new attention to the complex interrelations of malignancies and *rheumatic and musculoskeletal diseases (RMDs)*. Since those two entities represent two sides of a dysregulated immune response, further research on rheumatic irAEs and mechanisms underlying the better tumor response rates in irAE-affected patients may contribute to a better understanding of the different pathophysiology characterizing tumor and rheumatic disease.
Objectives: Given the heterogeneity of the patient population with rheumatic irAEs, a registry-based study has been conducted to provide first evidence regarding characteristics of rheumatic irAEs and further insights into the optimal diagnostic and therapeutic management of rheumatic irAEs.
Methods: The TRheuMa registry is a long-term, open-end observational study of a patient cohort suffering from rheumatic symptoms as a result of ICPi or other cancer therapies. The TRheuMa registry is one of the three subregistries of the MalheuR project, a registry-based study initiated in July 2018 at the at the university hospital Heidelberg to explore interrelations of malignancies and RMDs.
Results: Over 18 months, 52 of 63 patients in the TRheuMa registry were recruited with a rheumatic irAE under ICPi treatment (pembrolizumab n=21, nivolumab n=28, ipilimumab n=11, durvalumab n=1, atezolizumab n=2, avelumab n=1, history of >1 ICPi n=11). Of the 52 patients, 22 (42.3%) had non-small cell lung cancer and 23 (44.2%) had a melanoma. Eight (15.3%) patients experienced a flare of a preexisting RMD under ICPi treatment. The remaining 44 patients with *de novo* irAEs were characterized by rheumatoid arthritis-like (20.5%) or polymyalgia rheumatica-like (18.1%) and psoriatic or other spondyloarthritis-like phenotypes (50.0%). However, laboratory findings differed from classical RMDs with elevated CRP-levels in 73.1% particularly in psoriatic arthritis-like, but not necessarily in polymyalgia rheumatica-like irAEs. On the contrary, autoantibody positivity was very rare. The majority of patients (78.8%) showed signs of inflammation upon ultrasound examination.
Based on the severity of signs and symptoms as well as treatment response, we developed a therapeutic algorithm for rheumatic irAEs: non-steroidal anti-inflammatory drugs and/or low dosed glucocorticoids (≤10mg prednisone equivalent) as first treatment step were sufficient for 75% patients, whereas 17.3% required higher dosed glucocorticoids and 11.5% patients required further treatment with a cs- or bDMARD. In two cases ICPi-treatment was discontinued on patients' request due to the pain and functional impairment caused by the rheumatic irAE, although a satisfactory symptom control was reached in the further course.
Complete remission of cancer was observed in 43.5% of melanoma patients, 66.7% experienced additional severe irAEs in other organ systems.
Conclusion: Overall, data from the TRheuMa-registry show that rheumatic irAEs mostly resemble classical RMDs, however show distinct characteristics. Our diagnostic and therapeutic management of rheumatic irAEs demonstrated efficacy in the majority of patients. These findings contribute to the further understanding of rheumatic irAEs and malignancies. Future research agenda includes a correlation of irAE severity with tumor response.
Disclosure of Interests: Karolina Benesova Grant/research support from: Study grants for SCREENED study by Abbvie, Novartis and Rheumaliga Baden-Württemberg, Consultant of: One-time participation in Novartis advisory board., Leonore Diekmann: None declared, Hanns-Martin Lorenz Grant/research support from: Consultancy and/or speaker fees and/or travel reimbursements: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly. Scientific support and/or educational seminars and/or clinical studies: Abbvie, MSD, BMS, Pfizer, Celgene, Medac, GSK, Roche, Chugai, Novartis, UCB, Janssen-Cilag, Astra-Zeneca, Lilly, Baxter, SOBI, Biogen, Actelion, Bayer Vital, Shire, Octapharm, Sanofi, Hexal, Mundipharm, Thermo Fisher., Consultant of: see above, Karin Jordan Consultant of: Consultancy and/or speaker fees: MSD, Merck, Amgen, Hexal, Riemser, Helsinn, Tesaro, Kreussler, Voluntis, Pfizer, Pomme-med., Jan Leipe Grant/research support from: Consultancy and speaker fees: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. Scientific support: Novartis, Pfizer., Consultant of: Consultancy and speaker fees: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB. Scientific support: Novartis, Pfizer., Speakers bureau: Abbvie, AstraZeneca, BMS, Celgene, Hospira, Janssen-Cilag, LEO Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, UCB
DOI: 10.1136/annrheumdis-2020-eular.3790

OP0271 REAL-WORLD CLINICAL BURDEN AND GLUCOCORTICOID USE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

R. Punekar[1], P. Lafontaine[2], J. H. Stone[3]. [1]*Sanofi, Cambridge, United States of America;* [2]*Sanofi, Bridgewater, United States of America;* [3]*Harvard Medical School, Boston, United States of America*

Background: Polymyalgia rheumatica (PMR) is a chronic inflammatory condition characterized by aching and morning stiffness in the neck, shoulders and pelvic girdle. It is a common inflammatory rheumatic disease in patients age >50 years, particularly women. While giant cell arteritis (GCA) is present in 9–21% of PMR cases, many PMR patients have symptoms independent of GCA. Current treatment options are limited to long-term glucocorticoid (GC), however, with risks of GC-related complications, including cardiovascular disease, osteoporosis, and diabetes mellitus.
Objectives: To compare GC use and subsequent GC-related complications in patients with PMR vs a general population (GnP) cohort.
Methods: This retrospective, observational cohort study was based on Optum's de-identified Clinformatics® Data Mart Database (study period 01Jan2006-30June2018). The PMR cohort included patients with ≥1 inpatient or ≥2 outpatient claims ≥30 days apart with PMR related diagnosis codes (ICD-9: 725.xx or ICD-10: M35.3x) between 01Jan2006–30June2017 (patient identification period) during which first occurrence of a PMR-related medical claim was set as the index date (ID). Patients with ≥1 medical claim related to rheumatoid arthritis (RA) or GCA during the study period were excluded. The GnP cohort included patients without any RA, GCA or PMR diagnosis codes during the study period, with their ID set as 12 months from the start of continuous health plan enrollment. Patients in both cohorts were required to be age ≥50 years (on ID) with continuous health plan enrollment ≥12 months pre- and post-ID. Cohorts were 1:1 propensity score matched. GC use and incidence of GC-related complications were assessed from GC initiation, starting from the baseline period (12-months pre-ID) through to the end of GC use during the post-index period (i.e. the end of data availability, end of the study period or death [whichever occurred first]). Mean, standard deviation (SD) and median values for continuous variables, and frequency (n and %) for categorical variables were compared between the matched cohorts. Wilcoxon sum rank tests and *t*-tests on continuous variables and Chi-square tests or Fisher's exact tests on categorical variables between matched cohorts were conducted. Duration of GC use was analyzed using the Kaplan-Meier method and compared between matched cohorts using log-rank tests.
Results: In each of the PMR and GnP cohorts, 16,865 patients were included. In both matched cohorts, median age was 76 years, median Elixhauser comorbidity index score was 2.0, and the majority (~65%) were women. The median follow-up duration was 45 months and 51 months in the PMR and GnP cohorts, respectively. A higher proportion of patients in the PMR cohort than the matched GnP cohort (90.4% vs 62.8%; $p<0.001$) used GC. The mean (SD) duration of GC therapy was significantly longer in the PMR cohort than in the matched GnP cohort (242.1 [±317.2] days vs 35.5 [±124.6] days; $p<0.001$). Although patients in the PMR cohort had a lower average daily dose of GC (prednisone equivalent) vs the GnP cohort (mean [SD] mg 16.3 [± 21.9] vs 27.8 [±24.5], respectively [$p<0.0001$)], the cumulative GC dose was significantly higher in the PMR cohort than the GnP cohort (2125.4 [±3689.5] mg vs 476.6 [±1450.9] mg; $p<0.001$). This indicates PMR patients used chronic low dose GC while the GnP patients utilized higher dose GC burst therapy less frequently. The number of incident complications associated with GC use were significantly greater in the PMR cohort, and included hypertension, diabetes, skin toxicity, infections, neuropsychiatric effects, endocrine abnormalities, renal dysfunction/ failure, ocular effects, and cardiovascular disease ($p<0.05$).
Conclusion: The overall GC burden in patients with PMR is high. With a higher incidence of GC-related comorbidities among PMR patients, early onset of these complications may be a significant contributor to long-term healthcare costs in these patients.
Acknowledgments: This study was funded by Sanofi, Inc. Medical writing, under the direction of authors, was provided by Gauri Saal, MA Economics, Prime, Knutsford, UK, and funded by Sanofi.
Disclosure of Interests: Rajeshwari Punekar Shareholder of: Sanofi, Employee of: Sanofi, Patrick LaFontaine Shareholder of: Sanofi, Employee of: Sanofi, John H. Stone Grant/research support from: Roche, Consultant of: Roche
DOI: 10.1136/annrheumdis-2020-eular.4285

OP0272 LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FAMILIAL MEDITERRANEAN FEVER: RESULTS FROM THE RANDOMISED PHASE 3 CLUSTER TRIAL

S. Özen[1], E. Ben-Chetrit[2], I. Foeldvari[3], G. Amarilyo[4], H. Ozdogan[5], S. Vanderschueren[6], K. Marzan[7], J. M. Kahlenberg[8], E. Dekker[9], F. De Benedetti[10], I. Koné-Paut[11]. [1]*Hacettepe University, Department of Pediatric Rheumatology, Ankara, Turkey;* [2]*Hadassah-Hebrew University Medical Center, Rheumatology Unit, Jerusalem, Israel;* [3]*Hamburg Centre for Pediatric and Adolescent Rheumatology, An der Schön Klinik, Hamburg, Germany;* [4]*Schneider Children's Medical Center of Israel, Tel Aviv, Israel;* [5]*University of Istanbul-Cerrahpaşa, Department of Medicine, Istanbul, Turkey;* [6]*University Hospitals Leuven, Leuven, Belgium;* [7]*Children's Hospital Los Angeles, Los Angeles, United States of America;* [8]*University of Michigan, Department of*

Internal Medicine, Ann Arbor, United States of America; [9]Novartis Pharma AG, Basel, Switzerland; [10]Ospedale Pediatrico Bambino Gesù, Division of Rheumatology, Rome, Italy; [11]Department of Pediatric Rheumatology CHU de Bicêtre, CEREMAIA, Le Kremlin Bicêtre, France

Background: Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease associated with mutations in the *MEFV* gene. Colchicine is the cornerstone of current therapy for FMF; however, a subset of patients are resistant or intolerant to it. Previously published results from the CLUSTER trial [NCT02059291] demonstrated that canakinumab, a fully human anti-interleukin-1β monoclonal antibody, was effective in controlling and preventing flares in patients with colchicine-resistant familial Mediterranean fever (crFMF).[1]
Objectives: To evaluate the long-term efficacy and safety of canakinumab to treat patients with crFMF during Epoch 4 of the CLUSTER study.
Methods: Patients with active crFMF (baseline flare) were enrolled in the CLUSTER study. During Epoch 4 (weeks 40 to 113), patients received open-label canakinumab 150 or 300 mg, every 4 or 8 weeks (q4w or q8w). Patients started Epoch 4 on the same regimen that they were receiving at the end of Epoch 3, and stepwise up-titration of canakinumab was allowed in patients who experienced a flare, to a maximum dose of 300 mg q4w. We evaluated disease activity every 8 weeks using the physician global assessment of disease activity (PGA), counting the number of flares (defined as PGA ≥2 and CRP >30 mg/L), and measuring serum concentrations of C reactive protein (CRP) and serum amyloid A (SAA). Safety was assessed by the determination and classification of adverse events (AEs). We analysed safety and efficacy separately in two subgroups of patients receiving a cumulative dose of canakinumab lower than 2700 mg, or equal or higher than 2700 mg.
Results: Of the 61 patients with active crFMF who started the CLUSTER study, 60 entered Epoch 4 and 57 completed it. During the 72-week period, 35/60 (58.3%) patients experienced no flares, and 23/60 (38.3%) had one single flare, as compared with a median of 17.5 flares per year reported at baseline. The incidence of flares was similar in the two cumulative dose groups. PGA scores indicated no disease activity for the majority of patients throughout the study, in both cumulative dose groups. 23/57 (40%) of patients remained in the lower dosing group (150 mg q8w) until study end, whereas 9/57 (16%) required the highest dose allowed (300 mg q4w). Patients with higher body weight had an increased probability to require up-titration of canakinumab to control disease activity. Median CRP concentrations were lower than 10 mg/L at every time point in both cumulative dose groups, while median SAA concentrations remained in the 16-70 mg/L range, and were higher in the group receiving ≥2700 mg canakinumab (Figure 1). No opportunistic infections, renal disease caused by amyloidosis, new or unexpected AEs were reported.

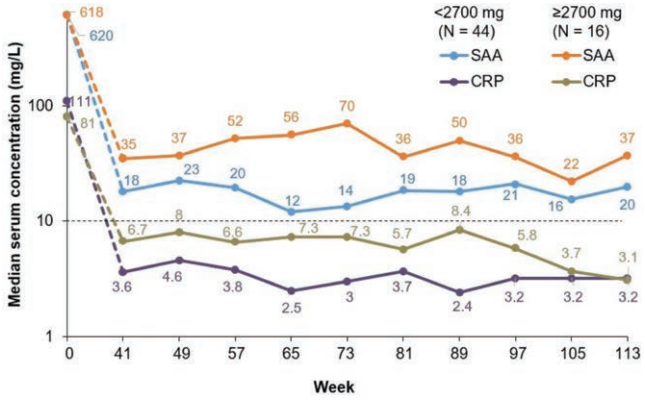

Figure 1. SAA and CRP blood levels in Epoch 4 of the CLUSTER study, in two subgroups of patients treated with a cumulative dose of canakinumab <2700 mg or ≥2700 mg

Conclusion: Patients with crFMF treated with canakinumab during 72 weeks experienced a minimal incidence of flares and good control of clinical disease activity, with no new safety signals reported.
References:
[1] De Benedetti F et al. *N Engl J Med* 2018;378:1908–19.
Disclosure of Interests: Seza Özen Consultant of: Novartis, Pfizer, Speakers bureau: SOBI, Novartis, Eldad Ben-Chetrit Speakers bureau: Novartis, Ivan Foeldvari Consultant of: Novartis, Gil Amarilyo Grant/research support from: Novartis, Speakers bureau: Novartis, Huri Ozdogan: None declared, Steven Vanderschueren: None declared, Katherine Marzan Grant/research support from: Novartis, J Michelle Kahlenberg Grant/research support from: Celgene, BMS, Consultant of: Eli Lilly, AstraZeneca, BMS, Boehringer Ingleheim, Elise Dekker Employee of: Novartis, Fabrizio De Benedetti Grant/research support from: AbbVie, Pfizer, Novartis, Novimmune, Sobi, Sanofi, Roche, Speakers bureau: AbbVie, Novartis, Roche, Sobi, Isabelle Koné-Paut Consultant of: Novartis, Chugai, Pfizer, LFB, AbbVie, Novimmune, SOBI
DOI: 10.1136/annrheumdis-2020-eular.522

OP0273 ADHERENCE TO COLCHICINE TREATMENT AND COLCHICINE RESISTANCE IN A MULTICENTRIC FMF NATIONAL COHORT

R. Gallizzi[1], M. Bustaffa[1], F. Mazza[1], D. Sutera[1], G. Fabio[1], L. Obici[1], M. Alessio[1], D. Rigante[1], L. Cantarini[1], A. Insalaco[1], M. Cattalini[1], M. C. Maggio[1], G. Simonini[1], A. N. Olivieri[1], S. Pastore[1], M. Lancieri[1], N. Ruperto[1], M. Gattorno[1]. [1]*on the behalf of the FMF Italian Study Group, Genova, Italy*

Background: Colchicine is the standard treatment for Familiar Mediterranean Fever (FMF), however about 5% of patients experience colchicine resistance. There is no standard definition of colchicine resistance. Recently a panel of experts elaborated a new definition based on a Delphi consensus approach.
Objectives: We aim to describe main features of the disease and clinical outcome of a cohort of FMF patients with particular interest on the colchicine resistance and tolerability according to the definitions proposed by the recent consensus.
Methods: Since November 2009, 425 Italian pediatric and adult FMF patients (pts) from 13 centers were enrolled in a national longitudinal cohort study, using the international EUROFEVER registry. Demographic, genetic and clinical data, including response to treatment, were analyzed. Supplementary information on health related quality of life and treatment adherence was also collected by a specific questionnaire.
Results: Complete information were available in 341 pts (189 M and 152 F, 211 children and 120 adults). The median age at disease onset was 5.0 years (1 m-59 y); the mean diagnostic delay was 8.7 y (range 0-61 y). The median age at enrollment was 12.1 y (range 3 m - 82 y). The MEFV genotype was the following: 103 (30.2%) pts carried biallelic pathogenic variants; 59 (17.3%) one pathogenic variants and one VOUS /LB variant; 27 (7.9%) had biallelic VOUS/LB variants; 97 (28.45%) were heterozygous for pathogenic variants; 30 (8.8%) were heterozygous for VOUS/LB, 25 (7.33%) were genetically negative.
Colchicine treatment was used in 280 pts; during treatment, biologic treatment (anti-IL1) in 22 pts. 61 pts received NSAID or steroid on demand.
We analyzed the behavior of the pts treated with colchicine according to the statements on colchicine resistance/intolerance defined by Ozen et al (1) (Table 1).

Table 1.

Adherence	62% displayed a total adherence (> 90% of prescription); 10.8% a good adherence (50-89% of prescriptions); 1.9% poor adherence (< 50% of prescriptions); 0.9% no adherence
Dose adjustment criteria/ Recommended maximum colchicine dose	Mean colchicine dose: Pts <5 years: 0.57mg/de (std. dev. 0.18) 5-10 year: 0.77mg/die (std. dev. 0.23) 10-18 years: 1.1mg/die (std. dev. 0.39) Adults: 1.16 mg/die (std. dev. 0.37) Pts with a dose inferior to the minimum recommended dose 5-10 years: 2.5% 10-18 years: 15% Adults: 4%
Resistance to Colchicine	Resistance was be defined as persistence of fever attacks, despite optimal treatment. 41.6% pts had a complete disease control 32.8% Pts had < 1 episode/month for 3 months 25.5% had ≥1 episode/month for 3 months
Inclusion of secondary amyloidosis in the definition of colchicine resistance	5 adult pts (1.5%) displayed amyloidosis
Colchicine intolerance	11 pts (3.2%) withdraw colchicine because of drug intolerance
Patient quality of life and patient-reported outcomes	20.7% of pts experience fatigue or chronic pain, 16.9% limitations in daily activities, and 16.9% have lost school/ work days.

Conclusion: Almost 58% of FMF pts display disease activity despite colchicine treatment. The treatment is generally under-dosed, especially in children. The adherence and the compliance to the treatment is generally good.
References:
[1] Ozen S et all. Recommendation on colchicine dosing and definition of colchicine resistance/intolerance in the management of FMF. Pediatric Rheumatology, 2019.
Acknowledgments: This research was financial supported by Novartis AG
Disclosure of Interests: Romina Gallizzi: None declared, Marta Bustaffa: None declared, Francesca Mazza: None declared, Diana Sutera: None declared,