Methods: An observational cohort study design was used. The population included adults in England with new diagnoses of inflammatory arthritis between May 2018 and March 2021 who enrolled in NEIAA. The outcomes were hospitalisation due to COVID-19 (primary admission reason or nosocomial acquisition) and death due to COVID-19 (COVID-19 stated on a death certificate), identified via linkage with secondary care records. Hazard ratios were calculated using Cox proportional hazards models, with adjustment for patient factors (age, gender, smoking status, and comorbidity) and disease factors (seropositivity, 28-joint disease activity score, patient-reported disability (HAQ), and functional impact (MSK-HQ)) recorded at baseline. Individuals were considered at risk from the date of diagnosis or February 2020 (whichever was later) and censored at a COVID-19 event, death or May 2021 (whichever was sooner).

Results: 14,127 patients were included. The mean age was 57 years; 62% were female; 19% were current smokers, while 29% were ex-smokers. The frequency of comorbidities at baseline were: hypertension (19%), diabetes mellitus (9%), and lung disease (9%). Overall, 20% had two or more comorbidities. Rheumatoid factor or CCP antibodies were positive in 56%. At presentation, mean scores for DAS28 were 4.6 (+/- 1.5), 1.1 (+/- 0.7) for HAQ, and 25 (+/- 11) for MSK-HQ. Initial DMARD therapy was known for 13,682/14,127 patients: methotrexate was the most common (54%), followed by hydroxychloroquine (23%), and sulfasalazine (11%).

There were 143 COVID-19 hospital admissions and 47 deaths, corresponding to incidence rates per 100 person-years for hospitalisation: 0.94 [95% CI: 0.79-1.10] and death: 0.31 [95% CI: 0.23-0.41]. Increasing age, male gender, diabetes, hypertension, lung disease and smoking status all predicted COVID-19 hospitalisation and death. Higher baseline DAS28 predicted COVID-19 hospitalisation (HR 1.24 [95% CI: 1.10-1.39]) and mortality (HR 1.33 [95% CI: 1.09-1.63]). Higher HAQ predicted both COVID-19 hospitalisation and death. Seropositivity was not a significant predictor of any COVID-19 event, nor was MSK-HQ. In unadjusted models, corticosteroids associated with COVID-19 death (HR 2.29 [95% CI: 1.02-5.13], and sulfasalazine monotherapy associated with COVID-19 hospitalisation (HR 1.93 [95% CI: 1.04-3.56]. In adjusted models, associations for corticosteroids and sulfasalazine were no longer significant. Only age, smoking status, and comorbidities independently predicted COVID-19 events.

Conclusion: The burden of COVID-19 amongst early arthritis patients was substantial during the pandemic, with concerns about the use of csDMARDs and corticosteroids.[1,2] Patient characteristics and rheumatoid disease severity at diagnosis appear to be the more important predictors of COVID-19 events than initial treatment strategy. An important limitation is that we have not looked at treatment changes over time, and must acknowledge that many patients, especially those recruited in 2019, may have changed therapy prior to the pandemic.

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OP0254 FACTORS ASSOCIATED WITH THE SEVERITY OF COVID-19 INFECTION IN PATIENTS WITH SPONDYLOARTHRITIS: RESULTS OF THE FRENCH RMD COVID-19 COHORT

L. Perrot[1], L. Boyer[2], R. M. Flipo[3], H. Marotte[4], E. Pertuiset[5], C. Miceli Richard[6], T. Thomas[4], R. Seror[7], P. Chazerain[8], R. Nicolas[9], C. Richez[10], T. Pham[1]. *[1]Aix Marseille University, APHM, Rheumatology, Marseille, France*; *[2]Aix Marseille University, APHM, Health Service Research and Quality of life Center, Marseille, France*; *[3]Univ-Lille, CHU Lille, Rheumatology, Lille, France*; *[4]CHU Saint-Etienne, Rheumatology, Saint-Etienne, France*; *[5]Centre Hospitalier René-Dubos, Rheumatology, Pontoise, France*; *[6]CHU Cochin, Rheumatology, Paris, France*; *[7]CHU Le Kremlin-Bicetre, Rheumatology, Marseille, France*; *[8]Groupe Hospitalier Diaconesses-Croix Saint-Simon, Rheumatology, Paris, France*; *[9]Hôpital Robert Schuman, Rheumatology, Metz, France*; *[10]CHU Pellegrin, Rheumatology, Bordeaux, France*

Background: To our knowledge, no published work has described precisely the severity and evolution of SARS-CoV-2 infection in patients with spondyloarthritis (SpA). Data on COVID-19 from cohorts of patients with immune-mediated inflammatory diseases concern small samples of SpA.

Objectives: Our objective was to describe the severity and course of COVID-19 in a large cohort of patients with SpA, including axial SpA (axSpA) and psoriatic arthritis (PsA), and to identify factors associated with severe forms.

Methods: Patients: individuals with Spondyloarthritis (SpA) from the French RMD COVID-19 cohort (observational, national, multicenter cohort) with a diagnosis of COVID-19 (clinical, PCR, CT or serology) were included.

Data collected: demographics, type of SpA, comorbidities, treatments, severity of COVID-19. Severity of COVID-19 was graded according to care needed: mild = outpatient care; moderate = non-intensive hospital treatment; severe = intensive care unit admission or death; severe = moderate or severe.

Statistical analyses: Logistic regression models were used to identify factors associated with these severe forms. All variables with p <0.20 in the univariate analysis were proposed in the multivariate model. Treatment variables (non-steroidal anti-inflammatory drugs (NSAIDs), methotrexate (MTX), sulfasalazine (SLZ), TNF inhibitors (TNFi), IL-17 inhibitors (IL-17i) and IL-23p19/p40 inhibitors (IL-23p19/p40i)) were included in the models, even if p≥0.20.

Results: Between March 2020 and April 2021, 626 SpAs reported COVID-19 with a mild course in 508 cases (81.1%), moderate in 93 cases (14.8%), and severe in 25 cases (3.9%), including 6 deaths.

The cohort analyzed included 349 women (55.8%), mean age 49.3 ± 14.1 years, mean BMI 27.1 ± 5.4 with 403 axSpA (64.4%), 187 PsA (29.9%) and 36 other SpA, duration of disease 11.3 ± 9.8 years; 352 (56.2%) had at least one comorbidity, of which obesity (23.6%), hypertension (15.5%), and smoking (10.4%) were the most frequent. Among them, 104 were treated with NSAIDs (16.6%), 186 with conventional synthetic disease-modifying antirheumatic drugs (DMARDs) including 156 MTX, and 460 (73.5%) with biological DMARDs (379 TNFi, 57 IL-17i, 15 IL-23p19/p40i, 9 others).

The following variables were associated with severe COVID-19 outcomes: age, body mass index, chronic obstructive lung disease, cardiovascular disease, diabetes, hypertension, interstitial lung disease, renal failure, and corticosteroids intake.

The factors independently associated with severe COVID-19 outcomes were corticosteroid intake (3.15 [CI95%: 1.46-6.76], p 0.004), and age (OR=1.06 [CI95%: 1.04-1.08], p <0.001] while anti-TNF (OR=0.26 [CI95%: 0.09-0.78], p=0.01]) was protective. NSAIDs intake (OR=0.97 [CI95%: 0.48-1.98]), SLZ (OR=7.9 [CI95%: 0.60-103]), or anti-IL17 (OR=0.37 [CI95%: 0.10-1.31]) was not associated with infection severity.

Conclusion: The course of COVID-19 was mild for the majority of SpA patients (81.1%). Corticosteroid intake was associated with more severe COVID-19 outcomes, whereas TNFi were found to be protective.

Disclosure of Interests: None declared

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Emerging treatment strategies in PsA

OP0255 BIMEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: 16-WEEK EFFICACY & SAFETY FROM BE COMPLETE, A PHASE 3, MULTICENTRE, RANDOMISED PLACEBO-CONTROLLED STUDY

J. F. Merola[1], I. McInnes[2], C. T. Ritchlin[3], P. J. Mease[4], R. B. M. Landewé[5,6], A. Asahina[7], Y. Tanaka[8], R. B. Warren[9], L. Gossec[10], D. D. Gladman[11,12], F. Behrens[13], B. Ink[14], D. Assudani[14], R. Bajracharya[14], J. Coarse[15], L. Coates[16,17]. *[1]Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America*; *[2]University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom*; *[3]University of Rochester, Department of Medicine, Rochester, United States of America*; *[4]University of Washington, Swedish Medical Center and Providence St. Joseph Health, Seattle, United States of America*; *[5]Amsterdam Rheumatology & Clinical Immunology Center, Department of Clinical Immunology & Rheumatology, Amsterdam, Netherlands*; *[6]Zuyderland MC, N/A, Heerlen, Netherlands*; *[7]The Jikei University School of Medicine, Department of Dermatology, Tokyo, Japan*; *[8]University of Occupational and Environmental Health, The First Department of Internal Medicine, Kitakyushu, Japan*; *[9]The University of Manchester, Manchester NIHR Biomedical Research Centre, Manchester, United Kingdom*; *[10]Sorbonne Université, Pitié Salpêtrière Hospital, Paris, France*; *[11]University of Toronto, Krembil Research Institute, Toronto, Canada*; *[12]University of Toronto, Schroeder Arthritis Institute, Toronto, Canada*; *[13]Goethe University, Rheumatology University Hospital and Fraunhofer Institute for Translational Medicine & Pharmacology ITMP, Frankfurt am Main, Germany*; *[14]UCB Pharma, N/A, Slough, United Kingdom*; *[15]UCB Pharma, N/A, Raleigh, United States of America*; *[16]University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Diseases, Oxford, United Kingdom*; *[17]Oxford University*

Hospitals NHS Trust, Oxford Biomedical Research Centre, Oxford, United Kingdom

Background: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A. BKZ has shown sustained efficacy and tolerability up to 152 wks in a phase 2b study in patients (pts) with active psoriatic arthritis (PsA).[1,2]

Objectives: To assess efficacy and safety of BKZ vs placebo (PBO) in pts with active PsA and prior inadequate tumour necrosis factor inhibitor (TNFi) response in the 16-wk pivotal phase 3 study, BE COMPLETE.

Methods: BE COMPLETE (NCT03896581) comprises a 16-wk double-blind, PBO-controlled period. Pts were aged ≥18 yrs, had a diagnosis of adult-onset, active PsA with ≥3 tender joints and ≥3 swollen joints, and inadequate response or intolerance to treatment with 1 or 2 TNFi. Pts were randomised 2:1 to BKZ 160 mg Q4W or PBO. From Wk 16, pts were eligible to enter an open-label extension, receiving BKZ 160 mg Q4W. The primary endpoint was a ≥50% improvement in American College of Rheumatology response criteria (ACR50) at Wk 16. Primary and ranked secondary efficacy endpoints were assessed at Wk 16.

Results: Of 400 randomised pts (BKZ: 267; PBO: 133), 388 (97.0%) completed Wk 16 (BKZ: 263 [98.5%]; PBO: 125 [94.0%]). Baseline characteristics were comparable between groups: mean age 50.5 yrs, weight 86.0 kg, BMI 29.8 kg/m^2, time since diagnosis 9.5 yrs; 47.5% pts were male.

At Wk 16, the primary endpoint (ACR50: 43.4% BKZ vs 6.8% PBO; p<0.001; Figure 1) and all ranked secondary endpoints (HAQ-DI CfB, PASI90, SF-36 PCS CfB and MDA response) were met (all p<0.001; Table 1). The ACR50 response was rapid with separation from PBO observed from Wk 4 (nominal p<0.001). Additional outcomes, including ACR20/70, TJC and SJC CfB, and PASI75/100, demonstrated numerical improvement with BKZ compared to PBO at Wk 16 (all nominal p<0.001; Table 1).

Table 1. Disease characteristics at baseline and efficacy at Wk 16

		PBO N=133	BKZ 160 mg Q4W N=267	p value
Baseline characteristics	**TJC** mean (SD)	19.3 (14.2)	18.4 (13.5)	-
	SJC mean (SD)	10.3 (8.2)	9.7 (7.5)	-
	PtGA-PsA mean (SD)	63.0 (22.0)	60.5 (22.5)	-
	PtAAP mean (SD)	61.7 (24.6)	58.3 (24.2)	-
	Psoriasis BSA n (%)			
	<3%	45 (33.8)	91 (34.1)	-
	≥3 to ≤10%	63 (47.4)	109 (40.8)	-
	>10%	25 (18.8)	67 (25.1)	-
	PASI[a] mean (SD)	8.5 (6.6)[b]	10.1 (9.1)[c]	-
	Prior TNFi n (%)			
	Inadequate response to 1 TNFi	103 (77.4)	204 (76.4)	-
	Inadequate response to 2 TNFi	15 (11.3)	29 (10.9)	-
	Intolerance to TNFi	15 (11.3)	34 (12.7)	-
	Current cDMARDs n (%)	63 (47.4)	139 (52.1)	-
Ranked endpoints in hierarchical order	**ACR50*** [NRI] n (%)	9 (6.8)	116 (43.4)	<0.001
	HAQ-DI CfB† [RBMI] mean (SE)	–0.1 (0.0)	–0.4 (0.0)	<0.001
	PASI90†[a] [NRI]n (%)	6 (6.8)[b]	121 (68.8)[c]	<0.001
	SF-36 PCS CfB† [RBMI]mean (SE)	1.4 (0.7)	7.3 (0.5)	<0.001
	MDA Response† [NRI]n (%)	8 (6.0)	118 (44.2)	<0.001
Other endpoints	**ACR20**† [NRI]n (%)	21 (15.8)	179 (67.0)	<0.001‡
	ACR70† [NRI] n (%)	1 (0.8)	71 (26.6)	<0.001‡
	TJC CfB [MI] mean (SE)	–2.4 (0.9)	–10.9 (0.8)	<0.001‡
	SJC CfB [MI] mean (SE)	–2.0 (0.5)	–7.0 (0.4)	<0.001‡
	PASI75[a] [NRI]n (%)	9 (10.2)[b]	145 (82.4)[c]	<0.001‡
	PASI100[a] [NRI]n (%)	4 (4.5)[b]	103 (58.5)[c]	<0.001‡

Randomised set (N=400). *Primary endpoint; †Secondary endpoint; ‡Nominal p value. [a]In patients with ≥3% BSA with PSO at BL; [b]n=88; [c]n=176.

Over 16 wks, 107/267 (40.1%) pts on BKZ had ≥1 TEAE vs 44/132 (33.3%) pts on PBO; the three most frequent TEAEs on BKZ were nasopharyngitis (BKZ: 3.7%; PBO: 0.8%), oral candidiasis (BKZ: 2.6%; PBO: 0%) and upper respiratory tract infection (BKZ: 2.2%; PBO: 1.5%). Incidence of SAEs was low (BKZ: 1.9%; PBO: 0%); none led to discontinuation. 2 pts on BKZ discontinued due to a TEAE (BKZ: 0.7%; PBO: 0%). No systemic candidiasis, cases of IBD, MACE, uveitis, VTE or deaths were reported.

Conclusion: Dual inhibition of IL-17A and IL-17F with BKZ in pts with active PsA and prior inadequate TNFi response resulted in rapid, clinically relevant and statistically significant improvements in efficacy outcomes vs PBO. No new safety signals were observed.[1,2]

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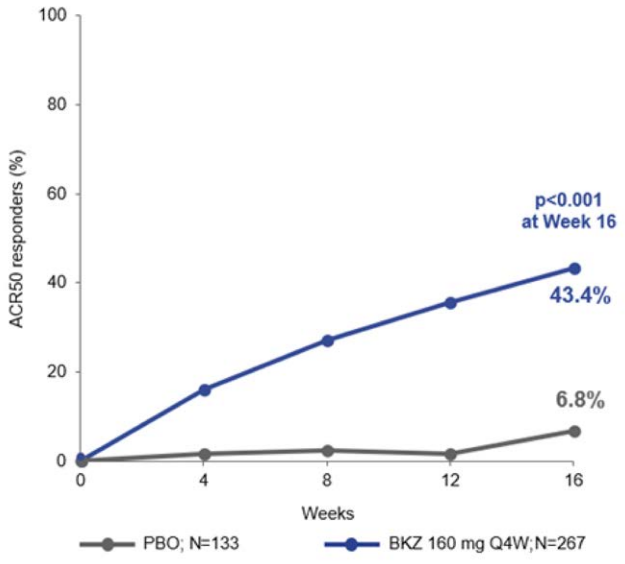
Figure. ACR50 responder rate over time to Wk 16



Randomised set (N=400). Data reported as NRI.

Abbreviations: ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology criteria; BKZ: bimekizumab; BL: baseline; BMI: body mass index; BSA: body surface area; CfB: change from baseline; cDMARD: conventional disease-modifying antirheumatic drug; HAQ-DI: health assessment questionnaire disability index; IBD: inflammatory bowel disease; IL: interleukin; MACE: major adverse cardiovascular events; MDA: minimal disease activity; MI: multiple imputation; NRI: non-responder imputation; PASI: psoriasis area and severity index; PASI75/90/100: ≥75/90/100% improvement in the psoriasis area and severity index; PBO: placebo; PsA: psoriatic arthritis; Pt: patient; PtAAP: patient's assessment of arthritis pain; PtGA: patient global assessment; PtGA-PsA: patient's global assessment of psoriatic arthritis; RBMI: reference-based multiple imputation; SF-36 PCS: 36-item short form survey physical component score; SAE: serious adverse event; SJC: swollen joint count; TEAE: treatment-emergent adverse event; TJC: tender joint count; TNFi: tumour necrosis factor inhibitor; VTE: venous thromboembolism; Wk: week; Yr: year.

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OP0256 FIBROBLAST ACTIVATION PROTEIN (FAP) PET-CT IMAGING ALLOWS TO DEPICT INFLAMMATORY JOINT REMODELING IN PATIENTS WITH PSORIATIC ARTHRITIS

C. Schmidkonz[1], S. Rauber[2], M. G. Raimondo[2], H. Labinsky[2], A. Atzinger[1], C. Treutlein[3], J. Knitza[2], S. Maschauer[1], F. Roemer[3], O. Prante[1], T. Kuwert[1], J. D. D. Cañete[4], G. Schett[2], A. Ramming[2]. *[1]Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and University Hospital Erlangen, Department of Nuclear Medicine, Erlangen, Germany*; *[2]Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and University Hospital Erlangen, Department of Internal Medicine 3, Rheumatology & Immunology, Erlangen, Germany*; *[3]Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and University Hospital Erlangen, Institute of Radiology, Erlangen, Germany*; *[4]Hospital Clinic and IDIBAPS, Arthritis Unit, Rheumatology Department, Barcelona, Germany*

Background: Psoriatic arthritis (PsA) is characterized by substantial mesenchymal tissue activation in the context of inflammation leading to structural damage. Measuring mesenchymal tissue activation in humans in vivo is challenging but may represent a possibility to detect regions at risk for structural damage. Recently, theranostic ligands have been developed that selectively bind Fibroblast Activation Protein (FAP) and allow recognition of activated mesenchymal cells in vivo. Accumulation of such FAP-based tracers can be visualized by positron-emission tomography (PET) (1).

Objectives: In this study, we analyzed whether FAP tracer-based PET-CT can detect mesenchymal tissue activation in patients with PsA and whether this signal is associated with joint damage.

Methods: 120 consecutive PsA patients fulfilling CASPAR criteria and 100 healthy controls without musculoskeletal disease received full-body PET-CT investigation using a ^{68}Ga-labelled FAP inhibitor (^{68}Ga-FAPI-04) tracer, specifically binding FAP. For all visually identified pathological tracer-positive lesions the mean and maximum standardized uptake value (SUV mean, SUV max) was assessed. Tracer uptake was quantified in peripheral and axial joints and correlated to various composite scores of PsA. Hand MRI scans were performed in parallel to assess inflammation and structural lesions. Follow-up ^{68}Ga-FAPI-04 PET-CT scans were obtained in a subset of patients treated with cytokine inhibitors (follow-up between 3-6 months) to assess joint damage over time. In addition, FAP related tissue responses in synovial biopsy samples were evaluated on a molecular level by high-resolution slide RNA-sequencing in a subset of patients.

Results: ^{68}Ga-FAPI-04 accumulated at synovial and enthesial sites in patients with PsA compared to healthy controls ($p < 0.0001$). Active pain in peripheral as well as axial joints as measured on a visual analogue scale highly correlated with an increased ^{68}Ga-FAPI-04 uptake (peripheral pain: $R = 0.718$, $p < 0.0001$; back pain: $R = 0.875$, $p < 0.0001$). Disease Activity in PSoriatic Arthritis (DAPSA) score also correlated with the SUV mean and SUV max of FAP expression ($R = 0.774$; $p = 0.0001$). Increased ^{68}Ga-FAPI-04 uptake at baseline was associated with progression of joint damage 3-6 months later as assessed by PsAMRIS score ($R = 0.778$, $p < 0.0001$). Treatment with cytokine inhibitors partially reduced FAP expression which was associated with arrest of joint damage in MRI. In contrast, persistent FAP expression was associated with a rapid progression of joint damage in MRI. Molecular analysis of synovial biopsy samples from FAP+ lesions revealed interactions between FAP+ fibroblasts and T cells, innate lymphoid cells and macrophages, which was correlated to a strong upregulation of NF-kB related pathways fostering cartilage and bone destruction.

Conclusion: Our study presents the first in-human evidence that fibroblast activation correlates with disease progression and joint damage in patients with PsA. FAP related imaging might therefore improve the risk assessment of rapidly emerging joint damage in PsA and open new options of treat-to-target strategies in PsA.

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OP0257 RISK OF HAEMATOLOGICAL MALIGNANCY IN PATIENTS WITH PSORIATIC ARTHRITIS, OVERALL AND IN RELATION TO TNF INHIBITORS - A NORDIC COHORT STUDY

R. Cordtz[1], J. Askling[2], B. Delcoigne[3], K. Ekström Smedby[3,4], E. Baecklund[5], C. Ballegaard[1,6], P. Isomäki[7], K. Aaltonen[8], B. Gudbjornsson[9], T. Love[10], S. A. Provan[11], B. Michelsen[11,12], J. Sexton[11], L. Dreyer[13], K. Hellgren[3]. *[1]Aalborg University Hospital, Aalborg University, Department of Rheumatology, Aalborg, Denmark*; *[2]Karolinska Institutet, Clinical Epidemiology Division and Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden*; *[3]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden*; *[4]Karolinska University Hospital, Department of Haematology, Solna, Stockholm, Sweden*; *[5]Uppsala University, Department of Medical Sciences, Uppsala, Sweden*; *[6]Copenhagen University, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark*; *[7]Tampere University Hospital and Tampere University, Centre for Rheumatology and Faculty of Medicine and Health Technology, Tampere, Finland*; *[8]Ministry of Social Affairs and Health, ROB-FIN, Pharmaceuticals Pricing Board, Helsinki, Finland*; *[9]University of Iceland, Centre for Rheumatology Research, Landspitali University Hospital, and Faculty of Medicine, Reykjavik, Iceland*; *[10]University of Iceland, Department of Science, Landspitali University Hospital of Iceland, and Faculty of Medicine, Reykjavik, Iceland*; *[11]Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway*; *[12]Hospital of Southern Norway, Division of Rheumatology, Department of Medicine, Trust, Norway*; *[13]Aalborg University Hospital, Aalborg University, DANBIO Registry and Department of Rheumatology, Aalborg, Denmark*

Background: Several autoimmune inflammatory diseases, including rheumatoid arthritis (RA), are associated with increased risk of malignant lymphomas. There is also a longstanding concern of lymphoma development with tumour necrosis factor inhibitor (TNFi) treatment, but most studies in RA to date do not indicate an additionally increased risk. Corresponding studies in psoriatic arthritis (PsA), both with respect to the underlying risks, and risks in relation to treatment with TNFi, are limited. Data on myeloid malignancies in PsA are scarce.

Objectives: To estimate the risk of haematological malignancy overall and by lymphoid and myeloid types in TNFi treated versus (vs.) biologics-naïve patients with PsA across the five Nordic countries. Additionally, we investigated the underlying risk of haematological malignancies in PsA as compared to the general population.

Methods: We identified patients with PsA starting a first ever TNFi from the clinical rheumatology registers (CRR) in Sweden (SE), Denmark (DK), Norway (NO), Finland (FI), and Iceland (ICE) from 2006 through 2019 (n=10 621). We identified biologics-naïve patients with PsA from a) the CRR (n=18 705, all countries) and b) the national patient registers (NPR, n=27 286, SE and DK only). To estimate the underlying risk of haematological malignancy in PsA, we randomly sampled general population comparators in SE and DK matched on year of birth, sex, and calendar year at start of follow-up, to the patients with PsA.

Through linkage to the mandatory national cancer registers in all five countries, we collected information on haematological malignancy overall, and categorised into lymphoid or myeloid types. By applying a modified Poisson regression, we estimated pooled incidence rate ratio (IRR) with 95% confidence intervals (CI) for TNFi treated vs. biologics-naïve PsA and for PsA vs. the general population, adjusted for age (18-55, 56-65, 66-70, >70 years), sex, calendar period (2006-2010, 2011-2019) and country, and using robust standard errors.

Results: We observed 40 events of haematological malignancies (during 59 827 person-years) among TNFi treated PsA, resulting in a crude incidence rate (IR) of 67 per 100 000 person-years. The corresponding IR was 91 (63 events) for biologics-naïve PsA from the CRR, and 118 (172 events) for biologics-naïve PsA from NPR. This resulted in a pooled IRR of 0.97 (0.69 to 1.37) for TNFi-treated vs. biologics-naïve PsA patients from the CRR, and 0.84 (0.64 to 1.10) vs. biologics-naïve PsA patients from the NPR. The pooled IRR of haematological malignancies in PsA overall vs. the general population was 1.35 (1.17 to 1.55). Throughout, the estimates were largely similar for lymphoid and myeloid malignancies (Figure 1). The crude IR of haematological malignancies were substantially akin across different TNFi agents.