RHEUMATOLOGY

Rheumatology 2020;59:2455–2461
doi:10.1093/rheumatology/kez656
Advance Access publication 20 January 2020

Concise report

Impact of discordance between patient's and evaluator's global assessment on treatment outcomes in 14 868 patients with spondyloarthritis

Brigitte Michelsen [1,2,3], Lykke Midtbøll Ørnbjerg[1,4], Tore K. Kvien[3], Karel Pavelka[5], Michael J. Nissen[6], Dan Nordström[7], Maria José Santos [8], Suleyman Serdar Koca[9], Johan Askling[10], Ziga Rotar[11], Bjorn Gudbjornsson[12], Catalin Codreanu[13], Anne Gitte Loft[4,14], Eirik Klami Kristianslund[4], Herman F. Mann[5], Adrian Ciurea [15], Kari K. Eklund[16], Elsa Vieira-Sousa[8], Ayten Yazici[17], Lennart Jacobsson[18], Matija Tomšič[11], Thorvardur Jón Löve[19], Ruxandra Ionescu[13], I. E. van der Horst-Bruinsma[20], Florenzo Iannone [21], Manuel Pombo-Suarez[22], Gareth T. Jones [23], Lise Hejl Hyldstrup[1], Niels Steen Krogh[24], Merete Lund Hetland[1,25,*] and Mikkel Østergaard[1,25,*]

Abstract

Objectives. To assess the impact of 'patient's minus evaluator's global assessment of disease activity' (ΔPEG) at treatment initiation on retention and remission rates of TNF inhibitors (TNFi) in psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) patients across Europe.

Methods. Real-life data from PsA and axSpA patients starting their first TNFi from 11 countries in the European Spondyloarthritis Research Collaboration Network were pooled. Retention rates were compared by Kaplan–Meier analyses with log-rank test and by Cox regression, and remission rates by χ^2 test and by logistic regression across quartiles of baseline ΔPEG, separately in female and male PsA and axSpA patients.

Results. We included 14 868 spondyloarthritis (5855 PsA, 9013 axSpA) patients. Baseline ΔPEG was negatively associated with 6/12/24-months' TNFi retention rates in female and male PsA and axSpA patients ($P < 0.001$), with 6/12/24-months' BASDAI < 2 ($P \leq 0.002$) and ASDAS < 1.3 ($P \leq 0.005$) in axSpA patients, and with DAS28CRP(4)< 2.6 ($P \leq 0.04$) and DAPSA28 ≤ 4 ($P \leq 0.01$), but not DAS28CRP(3)< 2.6 ($P \geq 0.13$) in PsA patients, with few exceptions on remission rates. Retention and remission rates were overall lower in female than male patients.

[1]EuroSpA Coordinating Center, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet, Glostrup, Denmark, [2]Division of Rheumatology, Department of Medicine, Hospital of Southern Norway Trust, Kristiansand, [3]Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway, [4]DANBIO Registry, Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet, Glostrup, Denmark, [5]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [6]Department of Rheumatology, Geneva University Hospital, Geneva, Switzerland, [7]ROB-FIN Registry, Helsinki University and Helsinki University Hospital, Helsinki, Finland, [8]Reuma.pt Registry and Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Portugal, [9]TURKBIO Registry and Division of Rheumatology, School of Medicine, Firat University, Elazig, Turkey, [10]Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden, [11]BioRx.si and the Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia, [12]Centre for Rheumatology Research (ICEBIO), University Hospital and Faculty of Medicine, University of Iceland, Reykjavik, Iceland, [13]Center of Rheumatic Diseases, University of Medicine and Pharmacy 'Carol Davila', Bucharest, Romania, [14]Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark, [15]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, [16]Inflammation Center, Department of Rheumatology, Helsinki University Hospital, Helsinki, Finland, [17]TURKBIO Registry and Division of Rheumatology, School of Medicine, Kocaeli University, Izmit, Turkey, [18]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [19]University of Iceland, Faculty of Medicine, Landspitali University Hospital, Reykjavik, Iceland, [20]Department Rheumatology & Immunology Center (ARC), Amsterdam University Medical Centres, Location VU University Medical Centre, Amsterdam, the Netherlands, [21]GISEA Registry, Rheumatology Unit – DETO, University of Bari, Italy, [22]Rheumatology Service, Hospital Clinico Universitario, Santiago de Compostela, Spain, [23]Epidemiology Group, School of Medicine, Medical Science and Nutrition, University of Aberdeen, Aberdeen, UK, [24]Zitelab Aps and [25]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

Submitted 13 August 2019; accepted 6 December 2019

*Merete Lund Hetland and Mikkel Østergaard contributed equally to this work.

Correspondence to: Brigitte Michelsen, EuroSpA Coordinating Center, Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Rigshospitalet, Valdemar Hansens Vej 17, 2600 Glostrup, Denmark.
E-mail: brigitte.michelsen@regionh.dk

CLINICAL SCIENCE

Conclusion. High baseline patient's compared with evaluator's global assessment was associated with lower 6/12/24-months' remission as well as retention rates of first TNFi in both PsA and axSpA patients. These results highlight the importance of discordance between patient's and evaluator's perspective on disease outcomes.

Key words: axial spondyloarthritis, psoriatic arthritis, TNF inhibitors, treatment outcomes

Rheumatology key messages

- Discordance between patient's and evaluator's global assessment negatively impacts retention and remission of TNFi in SpA.
- Remission criteria that objectively reflect disease activity should be included in patients with high discordance.
- TNFi retention and remission rates are overall lower for female than male patients with SpA.

Introduction

Discordance between patient's global assessment and physician's/evaluator's global assessment of disease activity at baseline is common [1, 2] and may reduce the likelihood of remission following tumour necrosis factor inhibitor (TNFi) treatment in patients with psoriatic arthritis (PsA) [2]. However, to our knowledge, the impact of such discordance on retention rates of TNFi treatment in PsA patients and on TNFi retention and remission rates in axial spondyloarthritis (axSpA) patients remains unexplored. Furthermore, it remains unknown whether the impact of such discordance on retention and remission rates may be influenced by gender in patients with spondyloarthritis.

In this study we aimed to assess the impact of baseline 'patient's minus evaluator's global assessment of disease activity' (ΔPEG), on retention and remission rates of first-time TNFi separately in female and male patients with PsA and axSpA across Europe.

Patients and methods

Patients

Anonymized data from PsA and axSpA patients who started their first TNFi between 2000 and 2017 were pooled from 11 registries participating in the European Spondyloarthritis Research Collaboration Network (EuroSpA) [3]: DANBIO (Denmark), NOR-DMARD (Norway), ATTRA (Czech Republic), SCQM (Switzerland), ROB-FIN (Finland), Reuma.pt (Portugal), TURKBIO (Turkey), ARTIS (Sweden), biorx.si (Slovenia), ICEBIO (Iceland) and RRBR (Romania). The study was approved by the respective national Data Protection Agencies and Research Ethical Committees according to legal regulatory requirements in the participating countries and was performed in accordance with the Declaration of Helsinki.

Assessments

Assessments included demographics, time since diagnosis, start and stop dates of first TNFi, visual analogue scales (0–100) of patient's and evaluator's global assessments (except for SCQM, biorx.si and RRBR using a 0–10 Numeric Rating Scale) and CRP. Furthermore, in PsA patients, assessments at baseline (pre-treatment), 6, 12 and 24 months included 28 tender and swollen joint counts, 28-joint Disease Activity Score *with* CRP and patient's global assessment (DAS28CRP(4)) [4], DAS28CRP *without* patients' global assessment (DAS28CRP(3)) [4] as well as 28-joint Disease Activity Index for Psoriatic Arthritis (DAPSA28) [5], and in axSpA patients BASDAI [6] and Ankylosing Spondylitis Disease Activity Score (ASDAS) [7].

Statistics

All analyses were conducted separately for female and male PsA and axSpA patients. Retention rates after 6-, 12- and 24-months' treatment with first TNFi were assessed by Kaplan–Meier analyses, with comparison between baseline ΔPEG quartiles by log-rank test. The impact of baseline ΔPEG quartiles on 6-, 12- and 24-months' retention rates was also explored with Cox regression analyses, adjusted for age, time since diagnosis and current smoking (yes/no). Proportions of axSpA patients achieving BASDAI remission (defined in two ways, either as <2, or as <2 with CRP <7mg/l [8]) and ASDAS inactive disease (<1.3) [9], as well as proportions of PsA patients in DAS28CRP(4) remission (<2.6) [10], DAS28CRP(3) remission (<2.6) [4] and DAPSA28 remission (≤ 4) [5] after 6-, 12- and 24-months' treatment were compared across ΔPEG quartiles by χ^2 test. The impact of baseline ΔPEG quartiles on 6-, 12- and 24-months' remission rates was also explored in logistic regression models adjusted for age, time since diagnosis and current smoking (yes/no). Statistical analyses were performed with R version 3.4.3 and SPSS version 25. All analyses were available case analyses. No data imputation was performed.

Results

A total of 14 868 spondyloarthritis patients were included, thereof 5855 PsA and 9013 axSpA patients. For PsA patients, mean (S.D.) age of women ($n = 2988$) and men ($n = 2867$) were 49.3 (12.5) and 47.4 (11.7)

years, respectively, time since diagnosis was 6.6 (7.3) and 6.7 (7.2) years and median (25–75 percentiles) baseline ΔPEG 17 (0–38) and 10 (0–30), respectively, and for axSpA patients mean (S.D.) age of women ($n = 3639$) and men ($n = 5374$) was 42.7 (12.0) and 41.7 (12.0) years, respectively, and time since diagnosis was 5.1 (7.4) and 6.9 (8.7) years and median (25–75 percentiles) baseline ΔPEG 20 (3–42) and 15 (0–37).

Impact of baseline ΔPEG on TNFi retention

TNFi retention rates at 6-, 12- and 24-months' follow-up were significantly lower for higher quartiles of ΔPEG both in female and male PsA and axSpA patients (Table 1, Fig. 1).

Adjustment of the analyses for age, time since diagnosis and smoking consistently showed lower TNFi retention rates for higher quartiles of ΔPEG ($P \leq 0.01$). Findings for third and fourth ΔPEG quartiles in axSpA patients were similar (Supplementary Fig. S1, available at *Rheumatology* online).

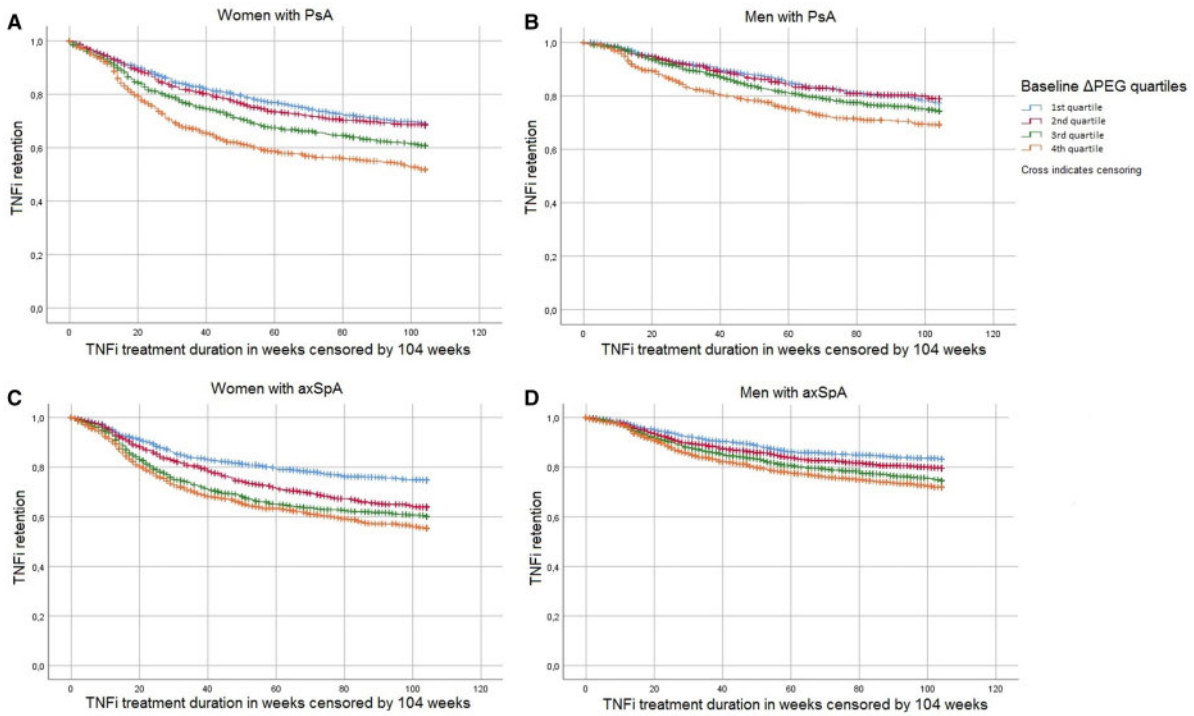
Impact of baseline ΔPEG on achievement of remission

Proportions of PsA patients achieving DAPSA28 and DAS28(4)CRP—but not DAS28(3)CRP remission—and axSpA patients achieving BASDAI remission and ASDAS inactive disease were significantly lower for higher quartiles of baseline ΔPEG both in women and men after 6-, 12- and 24-months' follow-up, except for 12-months' DAS28(4)CRP remission in men and 24-months' DAS28(3)CRP remission in women (Table 1). Adjustment for age, time since diagnosis and smoking in a logistic regression model did not change the significance of the above-mentioned patterns, with the following exceptions: 6- and 12-months' ASDAS inactive disease in female and 6-months' ASDAS inactive disease in male axSpA patients showed consistently lower point estimates for higher ΔPEG quartiles, but did not reach statistical significance (Supplementary Tables S1a and S1b, available at *Rheumatology* online).

Discussion

This longitudinal observational study including data from 11 European registries highlights the negative consequences of high baseline discordance between patient's and evaluator's global assessment (i.e. high baseline patient's compared with evaluator's global assessment, ΔPEG) for TNFi treatment outcomes in patients with PsA and axSpA. The higher the baseline ΔPEG, the lower were 6-, 12- and 24-months' TNFi drug retention as well as remission rates in both male and female PsA and axSpA patients, with few exceptions regarding remission rates. The study also highlights the importance of choice of remission criteria; baseline ΔPEG was negatively associated with achievement of 6-, 12- and 24-months' DAS28CRP(4) remission, which includes patient's global, but not with DAS28CRP(3) remission, which excludes patient's global. This is to our knowledge the first study

Fig. 1 TNFi retention rates across ΔPEG quartiles, censored by 104 weeks



(**A**) Women with PsA; (**B**) men with PsA; (**C**) women with axSpA; (**D**) men with axSpA.

Table 1 Retention and remission rates of first TNFi in psoriatic arthritis and axial spondyloarthritis patients

	Psoriatic arthritis patients (n = 5855)									
	Women (n = 2988)					Men (n = 2867)				
TNFi retention rates	Retention rates (%, 95% CI) of first TNFi compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 0) (n=815)	2nd ΔPEG quartile (1 to 17) (n=694)	3rd ΔPEG quartile (18 to 38) (n =739)	4td ΔPEG quartile (39 to 100) (n=740)	P-value	1st ΔPEG quartile (−100 to −1) (n=648)	2nd ΔPEG quartile (0 to 9) (n=683)	3rd ΔPEG quartile (10 to 30) (n=865)	4td ΔPEG quartile (31 to 100) (n=671)	P-value
6 months	87% (85, 90%) n=815	85% (82, 88%) n=694	81% (78, 84%) n=739	74% (71, 77%) n=740	<0.001	93% (91, 95%) n=648	93% (91, 95%) n=683	92% (90, 93%) n=865	86% (83, 89%) n=671	<0.001
12 months	79% (76, 82%) n=815	76% (73, 79%) n=694	70% (67, 74%) n=739	61% (57, 65%) n=740	<0.001	88% (85, 90%) n=648	86% (84, 89%) n=683	83% (80, 85%) n=865	78% (75, 81%) n=671	<0.001
24 months	69% (66, 72%) n=815	69% (65, 72%) n=694	61% (57, 65%) n=739	52% (48, 56%) n=740	<0.001	77% (74, 81%) n=648	79% (76, 82%) n=683	74% (71, 78%) n=865	69% (66, 73%) n=671	<0.001
DAPSA28 remission (≤4)	Proportions, % (95%CI), of patients achieving DAPSA28 remission compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 0)	2nd ΔPEG quartile (1 to 17)	3rd ΔPEG quartile (18 to 38)	4th ΔPEG quartile (39 to 100)	P-value	1st ΔPEG quartile (−100 to −1)	2nd ΔPEG quartile (0 to 9)	3rd ΔPEG quartile (10 to 30)	4th ΔPEG quartile (31 to 100)	P-value
6 months	21% (17, 25%) n=420	24% (19, 28%) n=413	12% (9, 15%) n=432	12% (9, 15%) n=457	<0.001	42% (37, 47%) n=339	38% (33, 42%) n=399	30% (26, 34%) n=465	27% (23, 32%) n=412	<0.001
12 months	23% (18, 27%) n=391	27% (22, 32%) n=352	16% (13, 20%) n=393	14% (11, 17%) n=400	<0.001	41% (36, 46%) n=333	40% (35, 45%) n=359	34% (29, 38%) n=455	29% (25, 34%) n=383	0.002
24 months	27% (23, 32%) n=325	27% (22, 32%) n=290	19% (15, 23%) n=328	13% (9, 17%) n=329	<0.001	46% (40, 51%) n=295	42% (36, 48%) n=300	33% (28, 37%) n=382	28% (23, 33%) n=309	<0.001
DAS28(4)CRP remission (<2.6)	Proportions, % (95%CI), of patients achieving DAS28(4)CRP remission compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 0)	2nd ΔPEG quartile (1 to 17)	3rd ΔPEG quartile (18 to 38)	4th ΔPEG quartile (39 to 100)	P-value	1st ΔPEG quartile (−100 to −1)	2nd ΔPEG quartile (0 to 9)	3rd ΔPEG quartile (10 to 30)	4th ΔPEG quartile (31 to 100)	P-value
6 months	51% (47, 56%) n=492	48% (44, 53%) n=464	39% (34, 43%) n=460	36% (32, 41%) n=465	<0.001	63% (58, 68%) n=378	67% (63, 71%) n=458	59% (55, 63%) n=506	59% (54, 63%) n=419	0.04
12 months	53% (48, 57%) n=449	53% (48, 58%) n=397	43% (38, 47%) n=419	38% (33, 43%) n=409	<0.001	68% (58, 68%) n=370	69% (63, 71%) n=404	63% (55, 63%) n=492	65% (54, 63%) n=389	0.21
24 months	58% (53, 63%) n=358	58% (52, 63%) n=323	47% (42, 53%) n=349	37% (32, 43%) n=337	<0.001	69% (64, 74%) n=324	72% (67, 77%) n=330	64% (59, 69%) n=408	60% (55, 66%) n=316	0.007
DAS28(3)CRP remission (<2.6)	Proportions, % (95%CI), of patients achieving DAS28(3)CRP remission compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 0)	2nd ΔPEG quartile (1 to 17)	3rd ΔPEG quartile (18 to 38)	4th ΔPEG quartile (39 to 100)	P-value	1st ΔPEG quartile (−100 to −1)	2nd ΔPEG quartile (0 to 9)	3rd ΔPEG quartile (10 to 30)	4th ΔPEG quartile (31 to 100)	P-value
6 months	52% (48, 57%) n=507	53% (48, 57%) n=469	47% (43, 52%) n=469	48% (43, 52%) n=472	0.19	65% (60, 70%) n=386	69% (64, 73%) n=467	64% (60, 68%) n=517	68% (64, 73%) n=426	0.28
12 months	54% (50, 59%) n=471	57% (52, 61%) n=409	53% (48, 57%) n=435	50% (45, 55%) n=420	0.30	70% (66, 75%) n=381	72% (67, 76%) n=411	69% (65, 73%) n=503	72% (68, 76%) n=396	0.77
24 months	61% (56, 66%) n=374	60% (55, 65%) n=336	55% (50, 60%) n=367	52% (46, 57%) n=347	0.04	74% (69, 79%) n=331	76% (71, 80%) n=341	70% (66, 74%) n=425	73% (69, 78%) n=323	0.32

(continued)

Table 1 Continued

	Axial spondyloarthritis patients (n=9013)									
	Women (n = 3639)					Men (n = 5374)				
TNFi retention rates	Retention rates of first TNFi (%, 95%CI) compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 2) (n=908)	2nd ΔPEG quartile (3 to 20) (n=915)	3rd ΔPEG quartile (21 to 42) (n=907)	4th ΔPEG quartile (43 to 100) (n=909)	P-value	1st ΔPEG quartile (−100 to -1) (n=1220)	2nd ΔPEG quartile (0 to 15) (n=1487)	3rd ΔPEG quartile (16 to 37) (n=1338)	4th ΔPEG quartile (38 to 100) (n=1329)	P-value
6 months	88% (86, 90%) n=908	84% (82, 87%) n=915	78% (75, 81%) n=907	76% (73, 79%) n=909	<0.001	94% (92, 95%) n=1220	91% (89, 92%) n=1487	89% (88, 91%) n=1338	87% (85, 89%) n=1329	<0.001
12 months	81% (78, 84%) n=908	74% (71, 77%) n=915	67% (64, 70%) n=907	64% (61, 68%) n=909	<0.001	88% (86, 90%) n=1220	86% (84, 88%) n=1487	83% (81, 85%) n=1338	79% (77, 82%) n=1329	<0.001
24 months	75% (72, 78%) n=908	64% (61, 67%) n=915	60% (57, 64%) n=907	55% (52, 59%) n=909	<0.001	83% (81, 86%) n=1220	80% (77, 82%) n=1487	75% (72, 77%) n=1338	72% (69, 75%) n=1329	<0.001
ASDAS<1.3	Proportions, % (95%CI), of patients achieving ASDAS<1.3 compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 2)	2nd ΔPEG quartile (3 to 20)	3rd ΔPEG quartile (21 to 42)	4th ΔPEG quartile (43 to 100)	P-value	1st ΔPEG quartile (−100 to −1)	2nd ΔPEG quartile (0 to 15)	3rd ΔPEG quartile (16 to 37)	4th ΔPEG quartile (38 to 100)	P-value
6 months	28% (23, 33%) n=313	24% (19, 28%) n=293	23% (18, 27%) n=289	17% (14, 21%) n=449	0.005	40% (36, 45%) n=507	41% (36, 45%) n=527	34% (30, 38%) n=446	31% (27, 35%) n=625	0.001
12 months	27% (22, 33%) n=266	23% (18, 29%) n=221	23% (18, 29%) n=233	15% (12, 19%) n=370	0.002	41% (37, 46%) n=427	41% (37, 46%) n=458	33% (28, 37%) n=403	31% (27, 35%) n=508	0.001
24 months	29% (23, 35%) n=225	24% 18, 30%) n=197	27% (21, 33%) n=205	16% (11, 20%) n=284	0.002	45% (40, 50%) n=369	41% (36, 45%) n=406	39% (33, 44%) n=335	31% (27, 35%) n=444	0.001
BASDAI<2	Proportions, % (95%CI), of patients achieving BASDAI<2 compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 2)	2nd ΔPEG quartile (3 to 20)	3rd ΔPEG quartile (21 to 42)	4th ΔPEG quartile (43 to 100)	P-value	1st ΔPEG quartile (−100 to −1)	2nd ΔPEG quartile (0 to 15)	3rd ΔPEG quartile (16 to 37)	4th ΔPEG quartile (38 to 100)	P-value
6 months	44% (39, 89%) n=517	31% (28, 35%) n=525	27% (23, 31%) n=535	26% (22, 29%) n=625	<0.001	57% (54, 61%) n=796	50% (47, 53%) n=955	44% (41, 47%) n=866	40% (37, 43%) n=921	<0.001
12 months	45% (41, 50%) n=487	32% (27, 36%) n=479	29% (24, 33%) n=471	24% (21, 28%) n=522	<0.001	59% (55, 62%) n=734	51% (48, 55%) n=892	44% (40, 47%) n=812	41% (38, 44%) n=833	<0.001
24 months	48% (43, 53%) n=385	33% (28, 38%) n=395	30% (25, 34%) n=386	21% (17, 25%) n=406	<0.001	60% (56, 63%) n=621	54% (50, 57%) n=759	44% (40, 47%) n=665	40% (37, 44%) n=686	<0.001
BASDAI<2 and CRP<7mg/l	Proportions, % (95%CI), of patients achieving BASDAI<2 and CRP<7mg/l compared across baseline ΔPEG quartiles									
	1st ΔPEG quartile (−100 to 2)	2nd ΔPEG quartile (3 to 20)	3rd ΔPEG quartile (21 to 42)	4th ΔPEG quartile (43 to 100)	P-value	1st ΔPEG quartile (−100 to −1)	2nd ΔPEG quartile (0 to 15)	3rd ΔPEG quartile (16 to 37)	4th ΔPEG quartile (38 to 100)	P-value
6 months	33% (29, 37%) n=527	23% (20, 27%) n=541	21% (18, 24%) n=557	20% (17, 23%) n=641	<0.001	43% (40, 47%) n=822	40% (37, 44%) n=973	33% (30, 36%) n=885	32% (29, 35%) n=927	<0.001
12 months	31% (26, 35%) n=496	21% (18, 25%) n=500	21% (17, 24%) n=488	17% (14, 20%) n=529	<0.001	45% (42, 49%) n=752	39% (36, 43%) n=905	35% (32, 38%) n=824	31% (28, 34%) n=828	<0.001
24 months	32% (28, 37%) n=404	23% (19, 27%) n=408	24% (19, 28%) n=394	16% (13, 20%) n=415	<0.001	46% (42, 50%) n=626	41% (38, 44%) n=772	33% (29, 36%) n=672	31% (28, 35%) n=681	<0.001

P-values retention rates: Kaplan–Meier analyses with log-rank test; P-values remission rates: χ^2 test.
n: numbers available; ASDAS: Ankylosing Spondylitis Disease Activity Score; DAS28(3)CRP: 28-joint disease activity score with CRP and three variables (excluding patient's global); DAS28(4)CRP: 28-joint disease activity score with CRP and four variables (including patient's global); ΔPEG: patient's minus evaluator's global assessment; TNFi: TNF inhibitor.

to identify ΔPEG as an independent predictor of TNFi retention in PsA and axSpA patients. Adjustment for age, time since diagnosis and smoking did not change these findings.

We found higher ΔPEG in female than male PsA and axSpA patients, which is in accordance with previous findings in PsA [1, 2]. Retention and remission rates were overall lower for female than male patients. In RA patients, high ΔPEG has been found associated with depression, fibromyalgia and polysymptomatic distress, but not with elevated joint inflammation, as evaluated by ultrasonography [11]. In a recent cross-sectional study on PsA patients ΔPEG was found to be independently associated with higher fatigue, lower self-perceived coping and impaired social participation [12]. Importantly, patients with elevated ΔPEG who do not achieve remission or who have had short treatment adherence to several TNFi may benefit from being identified and offered additional treatment approaches, e.g. social mapping, evaluation of depression and anxiety, and instruction in coping strategies and stress-management [12, 13].

Our study underscores that choice of remission criteria in PsA patients with high ΔPEG may have great impact on evaluation of treatment response. DAS28CRP(4) is more commonly used than DAS28CRP(3) in RA as well as PsA. However, in patients with high ΔPEG, DAS28CRP(3), which does not include patient's global assessment, may be a more suitable alternative.

Our study is in accordance with a smaller study on PsA patients where ΔPEG was found to be a negative predictor for achievement of 3- and 6-months' DAS28ESR(4) and 32-joint DAPSA remission. In that study, however, 12- and 24-months' outcomes, DAS28CRP(3) and retention rates were not evaluated [2].

Limitations of our study include lack of data regarding extra-articular manifestations in PsA patients (e.g. enthesitis, dactylitis and skin involvement) and the use of 28 and not 66/68 joint counts. This may have led to overestimation of remission rates in the PsA patients. Furthermore, DAS28 was developed for RA and not PsA, but has been validated in PsA patients in a clinical trial [14]. Also, there is no consensus as yet on the best cut-off for BASDAI remission in axSpA. Consequently, the two BASDAI remission cut-offs used in this study have not been validated, although one of them was recently used in another study [8]. However, the consistent findings for both these remission definitions as well as for ASDAS inactive disease support the validity and robustness of the results.

The major strength of this study is the longitudinal observational design including >14 000 patients with spondyloarthritis from 11 European countries. To our knowledge, this is the first study to assess the impact of baseline ΔPEG on TNFi retention rates in PsA and axSpA patients. It is also the first study to assess the impact of baseline ΔPEG for achievement of remission in axSpA patients as well as for achievement of 12- and 24-months' remission in patients with PsA.

In conclusion, high baseline patient's compared with evaluator's global assessment was associated with lower 6-, 12- and 24-months' retention and remission rates of first TNFi in female and male PsA and axSpA patients, except for DAS28CRP(3) remission in PsA. The study highlights the negative impact of high baseline ΔPEG on treatment outcomes in PsA and axSpA patients as well as the importance of including remission criteria that objectively reflect disease activity, particularly in the evaluation of PsA patients with high baseline ΔPEG.

Acknowledgements

Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

Funding: This work was supported by Novartis. Novartis had no influence on the data collection, statistical analyses, manuscript preparation or decision to submit.

Disclosure statement: B.M.: Novartis; L.M.Ø.: Novartis; T.K.K. has received fees for speaking and/or consulting from AbbVie, Biogen, BMS, Celltrion, Egis, Eli Lilly, MSD, Mylan, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, Sanofi and UCB; K.P.: AbbVie, Roche, Pfizer, Amgen, Sanofi, Egis, BMS, UCB, MSD, Eli Lilly; M.J.N.: Abbvie, Lilly, Pfizer, Novartis; D.N.: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, Sandoz, UCB; M.J.S.: Abbvie, Biogen, Roche, Lilly, Pfizer, Novartis; S.S.K.: None; J.A. has entered into agreements with Abbvie, BMS, Lilly, Merck, Pfizer, Roche, Samsung Bioepis, and UCB, mainly for safety monitoring via the Swedish ARTIS system, and received a travel reimbursement from Novartis. Karolinska Institutet has received remuneration for J.A.'s participation in meetings arranged by Pfizer and by Lilly; Z.R.: speaker or consulting fees from Abbvie, Amgen, Biogen, CellGen, Eli-Lilly, Jansen, Medis, MSD, Novartis, Pfizer, and Roche. BioRx.si has received funding for clinical research paid to Društvo za razvoj revmatologije from AbbVie, Celgene, Celtrion, Eli Lilly, Johnson & Johnson, Medis, MSD, Novartis, Pfizer and Roche; B.G.: Amgen, Novartis, Pfizer; C.C.: AbbVie, Amgen, Angellini, Astra Zeneca, BMS, Egis, MSD, Pfizer, Richter, Roche, Sanofi, Servier, Teva, UCB, Zentiva; A.G.L.: Novartis, AbbVie, MSD, Lilly, Roche; E.K.K.: None; H.F.M.: AbbVie, MSD, Novartis, Pfizer, Sanofi; A.C.: AbbVie, Celgene, Eli Lilly, Janssen-Cilag, MSD, Novartis, Pfizer and UCB; K.K.E.: None; E.V.-S.: None; A.Y.: None; L.J.: None; M.T.: Abbvie, Amgen, Biogen, CellGen, Eli-Lilly, Jansen, Medis, MSD, Novartis, Pfizer, and Roche; T.J.L.: None; R.I.: None; I.E.vdH.-B.: AbbVie, MSD, Novartis, Pfizer, Lilly, UCB; F.I.: BMS, Pfizer, Abbvie, UCB, Roche, Celgene, Eli-Lilly, Hospira, Janssen, Merck; M.P.-S.: consultant on Advisory Boards for Abbvie, Gilead, Sanofi. He has received lecture fees from BMS, Gilead, Janssen and Janssen, Lilly, Sanofi. He has received grants from MSD; G.T.J.: None; L.H.H.: Novartis; N.S.K.: None; M.L.H.: Abbvie, Biogen, BMS, CellTrion, MSD, Novartis, Orion, Pfizer, Samsung, UCB; M.Ø.: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-

Lilly, Hospira, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, UCB.

Supplementary data

Supplementary data are available at *Rheumatology* online.

References

1 Lindstrom Egholm C, Krogh NS, Pincus T *et al*. Discordance of global assessments by patient and physician is higher in female than in male patients regardless of the physician's sex: data on patients with rheumatoid arthritis, axial spondyloarthritis, and psoriatic arthritis from the DANBIO Registry. J Rheumatol 2015; 42:1781–5.

2 Michelsen B, Kristianslund EK, Hammer HB *et al*. Discordance between tender and swollen joint count as well as patient's and evaluator's global assessment may reduce likelihood of remission in patients with rheumatoid arthritis and psoriatic arthritis: data from the prospective multicentre NOR-DMARD study. Ann Rheum Dis 2016;76:708–11.

3 Ørnbjerg LM, Brahe CH, Askling J *et al*. Treatment response and drug retention rates in 24, 195 biologic-naïve patients with axial spondyloarthritis initiating TNFi treatment – routine care data from 12 registries in the EuroSpA collaboration. Ann Rheum Dis 2019;78: 1536–44.

4 van Riel PL. The development of the disease activity score (DAS) and the disease activity score using 28 joint counts (DAS28). Clin Exp Rheumatol 2014;32:S-65–74.

5 Michelsen B, Sexton J, Smolen JS, Aletaha D *et al*. Can disease activity in patients with psoriatic arthritis be adequately assessed by a modified Disease Activity index for PSoriatic Arthritis (DAPSA) based on 28 joints? Ann Rheum Dis 2018;77:1736–41.

6 Garrett S, Jenkinson T, Kennedy LG *et al*. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286–91.

7 Lukas C, Landewe R, Sieper J *et al*. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:18–24.

8 van der Heijde D, Dougados M, Landewe R *et al*. Sustained efficacy, safety and patient-reported outcomes of certolizumab pegol in axial spondyloarthritis: 4-year outcomes from RAPID-axSpA. Rheumatology 2017;56:1498–509.

9 Machado PM, Landewé R, Heijde DV, Assessment of SpondyloArthritis International Society (ASAS). Ankylosing Spondylitis Disease Activity Score (ASDAS): 2018 update of the nomenclature for disease activity states. Ann Rheum Dis 2018;77:1539–40.

10 Saber TP, Ng CT, Renard G *et al*. Remission in psoriatic arthritis: is it possible and how can it be predicted? Arthritis Res Ther 2010;12:R94.

11 Challa DN, Kvrgic Z, Cheville AL *et al*. Patient-provider discordance between global assessments of disease activity in rheumatoid arthritis: a comprehensive clinical evaluation. Arthritis Res Ther 2017;19:212.

12 Desthieux C, Granger B, Balanescu AR *et al*. Determinants of patient-physician discordance in global assessment in psoriatic arthritis: a Multicenter European Study. Arthritis Care Res 2017;69:1606–11.

13 Howells L, Chisholm A, Cotterill S *et al*. Impact of disease severity, illness beliefs, and coping strategies on outcomes in psoriatic arthritis. Arthritis Care Res 2018; 70:295–302.

14 Vander Cruyssen B, De Keyser F, Kruithof E, Mielants H, Van den Bosch F. Comparison of different outcome measures for psoriatic arthritis in patients treated with infliximab or placebo. Ann Rheum Dis 2006;66: 138–40.