



Original article

Four-year secukinumab treatment outcomes in European real-world patients with axial spondyloarthritis and psoriatic arthritis

Marion Pons^a, Stylianos Georgiadis^a, Mikkel Østergaard^{a,c}, Zohra Faizy Ahmadzay^{a,c}, Bente Glintborg^{a,b,c}, Jette Heberg^a, Sara Nysom Christensen^a, Simon Rasmussen^a, Anne Gitte Loft^{d,e}, Isabel Castrejón^{f,g}, Fernando Sánchez-Alonso^h, Florenzo Iannoneⁱ, Dan Nordström^j, Anna-Mari Hokkanen^j, Adrian Ciurea^k, Michael J. Nissen^l, Jakub Závada^{m,n}, Karel Pavelka^{m,n}, Ziga Rotar^{o,p}, Katja Perdan Pirkmajer^{o,p}, Brigitte Michelsen^{a,q,r}, Pawel Mielnik^s, Miguel Bernardes^t, Nikita Khmelinskii^{u,v}, Karin Laas^w, Sigrid Vorobjov^x, Catalin Codreanu^y, Gary J. Macfarlane^z, Gareth T. Jones^z, Bjorn Gudbjornsson^{aa,ab}, Olafur Pálsson^{ab,ac}, Johan K. Wallman^{ac}, Irene van der Horst-Bruinsma^{ad}, Fatos Onen^{ae}, Merete Lund Hetland^{a,c}, Lykke Midtbøll Ørnbjerg^{a,*}



^a Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre for Head and Orthopedics, Rigshospitalet, Glostrup, Denmark

^b DANBIO and Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark

^c Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

^d Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark

^e Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

^f Department of Rheumatology, Hospital General, Universitario Gregorio Marañón, Madrid, Spain

^g Faculty of Medicine, Complutense University of Madrid, Madrid, Spain

^h Research Unit, Spanish Society of Rheumatology, Madrid, Spain

ⁱ Rheumatology Unit, DiMePreJ, University of Bari, Bari, Italy

^j Departments of Medicine and Rheumatology, Helsinki University Hospital, Helsinki, Finland

^k Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

^l Department of Rheumatology, Geneva University Hospital, Geneva, Switzerland

^m Institute of Rheumatology, Prague, Czech Republic

ⁿ Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic

^o Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia

^p Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

^q Center for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Diakonhjemmet Hospital, Oslo, Norway

^r Research Unit, Sørlandet Hospital, Kristiansand, Norway

^s Section for Rheumatology, Department for Neurology, Rheumatology and Physical Medicine, Helse Førde, Førde, Norway

^t Department of Medicine, Faculty of Medicine, University of Porto, Rheumatology Department, Centro Hospitalar e Universitário de São João, Porto, Portugal

^u Department of Rheumatology, Unidade Local de Saúde Santa Maria, Lisbon, Portugal

^v Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon Academic Medical Centre, Lisbon, Portugal

^w Department of Rheumatology, East-Tallinn Central Hospital, Tallinn, Estonia

^x National Institute for Health Development, Tallinn, Estonia

^y Center for Rheumatic Diseases, University of Medicine and Pharmacy, Bucharest, Romania

^z Aberdeen Centre for Arthritis and Musculoskeletal Health (Epidemiology Group), University of Aberdeen, Aberdeen, UK

^{aa} Centre for Rheumatology Research, Landspítali University Hospital, Reykjavik, Iceland

^{ab} Faculty of Medicine, University of Iceland, Reykjavik, Iceland

^{ac} Department of Clinical Sciences Lund, Rheumatology, Skåne University Hospital, Lund University, Lund, Sweden

^{ad} Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands

^{ae} Division of Rheumatology, Department of Internal Medicine, Dokuz Eylül University School of Medicine, Izmir, Turkey

I N F O A R T I C L E

A B S T R A C T

Historique de l'article :

Accepté le 4 novembre 2024

Disponible sur Internet le 26 novembre 2024

Objectives. – In axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) patients initiating secukinumab, we aimed to assess retention rates and proportions of patients achieving remission and low disease activity (LDA), according to disease activity measures and patient-reported outcomes at 24 and 48 months.

* Corresponding author. 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.

Adresse e-mail : lykke.midtbøll.ørnbjerg@regionh.dk (L.M. Ørnbjerg).

<https://doi.org/10.1016/j.jbspin.2024.105824>

1297-319X/© 2024 The Author(s). Published by Elsevier Masson SAS on behalf of Société Française de Rhumatologie. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

Keywords :
Spondyloarthritis
Epidemiology
bDMARD

Patients and methods. – Data on patients with axSpA and PsA who initiated secukinumab treatment were pooled from 13 European registries. Analyses were performed overall and stratified according to the number of previous biologic/targeted synthetic Disease-Modifying Antirheumatic Drugs (b/tsDMARDs, 0/1/≥ 2). Kaplan-Meier plots and Cox regression analyses were performed to assess and compare secukinumab retention rates. Comparisons of remission and LDA rates were performed by logistic regression analyses.

Results. – The overall 24-/48-month secukinumab retention rates were 61%/51% in 767 axSpA patients, and 64%/49% in 975 PsA patients, respectively. Compared to b/tsDMARD naïve patients, a higher risk of withdrawal from secukinumab was found for those with ≥ 2 prior b/tsDMARDs in axSpA and PsA, and 1 prior b/tsDMARD in axSpA. Generally, remission and LDA rates were numerically higher in b/tsDMARD naïve patients. After adjustment for confounders, statistically significantly higher remission and LDA rates were found for b/tsDMARD naïve patients compared to patients with ≥ 2 prior b/tsDMARDs at 24 months in axSpA and PsA.

Conclusion. – This large European real-world study demonstrates that 4-year secukinumab retention rates were approximately 50% in both axSpA and PsA. b/tsDMARD naïve patients had higher retention, remission and LDA rates than patients with prior b/tsDMARD exposure.

© 2024 Les Auteurs. Publié par Elsevier Masson SAS au nom de Société Française de Rhumatologie. Cet article est publié en Open Access sous licence CC BY (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) are chronic, inflammatory rheumatic diseases within the spondyloarthritis (SpA) spectrum. AxSpA mainly affects the axial skeleton, i.e., the sacroiliac joints (SIJ) and spine [1], and the most common presenting symptoms are chronic back pain with inflammatory pattern and spinal stiffness, although peripheral and non-musculoskeletal (i.e., uveitis, inflammatory bowel disease (IBD), and psoriasis) manifestations also occur frequently. PsA is associated with psoriasis and characterized by peripheral arthritis, dactylitis and enthesitis, but axial involvement and non-musculoskeletal manifestations are also seen [2].

Secukinumab is a fully human IgG1 monoclonal antibody targeting interleukin-17A (IL-17A) and represents another approach in the treatment of SpA [3,4] as compared to tumor necrosis factor inhibitors (TNFi) [5]. Over the last years, secukinumab has demonstrated sustained improvements in signs and symptoms of both axSpA and PsA in randomized controlled trials (RCTs) [6,7], as well as in 12-month observational follow-up studies [8,9]. This has made secukinumab an alternative to TNFi, also as a first-line biologic disease-modifying antirheumatic drug (bDMARD) [10,11].

RCTs are considered the gold standard for the evaluation of efficacy. However, long-term follow-up trials are too expensive, and RCTs are not necessarily representative of patients treated in routine care, who constitute a heterogeneous population with a broad spectrum of various comorbidities and concomitant medications. There is currently no real-world evidence on long-term observational follow-up of patients treated with secukinumab, as well as on the impact of the number of previous biologic/targeted synthetic (b/ts) DMARDs on secukinumab effectiveness in SpA patients.

We, therefore, aimed to assess the following at 24 and 48 months, in separate cohorts of axSpA and PsA patients treated with secukinumab in routine care:

- retention rates;
- proportions of patients achieving remission and low disease activity (LDA) according to disease activity measures and patient-reported outcomes (PROs).

These aims were assessed both overall and stratified according to the number of previous b/tsDMARDs (0/1/≥ 2).

2. Methods

2.1. European Spondyloarthritis Research Collaboration Network

This study was conducted within the European Spondyloarthritis (EuroSpA) Research Collaboration Network [12]. The EuroSpA collaboration, initiated in 2016, aims to explore research questions by secondary use of prospectively collected real-world data in patients with SpA [9]. Based on a predefined study protocol, pseudonymized data were securely uploaded by individual registries onto the EuroSpA server. Subsequently, data were harmonized, quality checked and datasets from all registries were pooled before statistical analyses were conducted.

2.2. Patients

For this study, pseudonymized data from 13 registries were uploaded and pooled: ATTRA (Czech Republic), BIOBADASER (Spain), biorx.si (Slovenia), BSRBR-AS (United Kingdom, axSpA only), DANBIO (Denmark), ESRBTR (Estonia), GISEA (Italy), ICEBIO (Iceland), NOR-DMARD (Norway), Reuma.pt (Portugal), ROB-FIN (Finland), RRBR (Romania) and SCQM (Switzerland).

Patients eligible for inclusion had a diagnosis of axSpA or PsA as registered by the treating rheumatologist and were aged ≥ 18 years at the time of diagnosis. Patients were required to have a registered start date of their first secukinumab treatment course between January 1st 2015, when secukinumab was first marketed in Europe, and March 31st 2018 to ensure a minimum of 4 years follow-up.

2.3. Visits

The clinical visits were defined according to the following time windows: from 30 days prior to 30 days after secukinumab initiation (baseline), 549–913 days (24-month of follow-up), and 1279–1643 days (48-month of follow-up) in patients still treated. For the baseline visit, priority was given to visits at treatment start or before treatment start. If no visit was available, a visit after treatment start was selected. Visit data collected outside of the predefined windows were not included in the dataset.

3. Variables

The following baseline variables were extracted from each registry (when available): demographics (age, sex), disease duration (years), body mass index (BMI, kg/m²), smoking status (current/never or past smokers), radiographic status (radiographic/non-radiographic, according to the Modified New York criteria for ankylosing spondylitis [13], axSpA only), Human Leukocyte Antigen (HLA)-B27 status (axSpA only), presence of comorbidities during the disease course (cardiovascular disease, diabetes, kidney disease [ever/never]), presence of non-musculoskeletal manifestations during the disease course (uveitis, IBD, psoriasis [ever/never]), enthesitis (ever/never), dactylitis (ever/never), tender and/or swollen joint counts, secukinumab dose, concomitant conventional synthetic (cs)DMARD (methotrexate, leflunomide, sulfasalazine, other [yes/no]), Bath Ankylosing Spondylitis Functional Index (BASFI, 0–100 scale) [14], number of previous b/tsDMARDs (0/1/≥ 2).

The following variables were assessed at baseline, 24 and 48 months, in patients with axSpA and PsA: C-reactive protein (CRP mg/L), Physician Global Assessment (PhGA), pain, fatigue, Patient Global Assessment (PGA), Health Assessment Questionnaire (HAQ, 0–3 scale); in axSpA patients only: Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP [15], Bath Ankylosing Spondylitis Disease Activity Index (BASDAI, 0–100 scale) [15]; in PsA patients only: Disease Activity index for Psoriatic Arthritis (DAPSA, in 68 joints) [16], DAPSA28 (in 28 joints) [17]. Pain, fatigue, PGA and PhGA were scored on a 0–100 scale.

For each secukinumab treatment, start and, if relevant, stop dates of the treatment, reason for discontinuation (adverse events, lack of effectiveness, remission, other), and time since diagnosis (years) were identified.

Data on secukinumab dosage adjustments and skin manifestations during treatment were not available.

3.1. Remission and LDA outcomes

The following remission and LDA rates were calculated at 24-, and 48-month follow-up in patients with axSpA: BASDAI < 20 (inactive disease [ID]) [18], BASDAI < 40 (LDA) [10], ASDAS-CRP < 1.3 (ID) [19], ASDAS-CRP < 2.1 (LDA) [19].

The following remission and LDA rates were calculated at 24-, and 48-month follow-up in PsA patients: DAPSA28 ≤ 4 (remission) [17], DAPSA28 ≤ 14 (LDA) [17], DAPSA ≤ 4 (remission) [20], DAPSA ≤ 14 (LDA) [20].

For both axSpA and PsA, CRP < 10 mg/L and PROs (pain, fatigue, PGA and HAQ) remission rates were calculated at 24-, and 48-month follow-up. To date, there is no international consensus regarding the cut-off values for PRO remission neither in axSpA nor in PsA. Based on the ASAS definition for partial remission in axSpA [21] and the minimal disease activity (MDA) criteria in PsA [22], we have previously defined the following PRO remission rates: pain remission ≤ 20, PGA ≤ 20, fatigue ≤ 20 and HAQ ≤ 0.5 [23] for both axSpA and PsA to make comparisons feasible, although this is less stringent than the MDA criteria regarding pain remission in PsA [24].

4. Ethics

All patient data were collected in accordance with national legal and regulatory requirements in the different countries. The study was approved by the respective national Data Protection Agencies and Ethical Committees according to legal regulatory requirements in the participating countries, performed in accordance with the

Declaration of Helsinki, and followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [25].

5. Statistical analyses

Statistical analyses were performed according to a predefined statistical analysis plan. Descriptive statistics were assessed by median (interquartile range) for continuous variables and percentages for categorical variables. All analyses were performed in separate diagnosis groups (i.e., axSpA and PsA), and stratified according to number of previous b/tsDMARDs (0/1/≥ 2). Descriptive statistics were not presented if data on fewer than 20 patients were available.

Drug retention rates over the 48-month follow-up were estimated using Kaplan-Meier survival analyses, with baseline defined as the secukinumab treatment start date. Observations were censored at date of data extraction, date of death or end of registry follow-up, whichever came first. Comparisons of retention rates across patients with different numbers of previous b/tsDMARDs and determination of factors associated with drug discontinuation were performed by Cox regression models, adjusted for age, sex, Gross Domestic Product (GDP) per capita (USD 1000), time since diagnosis and disease activity at baseline. The latter was estimated by the ASDAS-CRP for axSpA, and the DAPSA28 for PsA.

Crude LDA and remission rates were calculated at 24-, and 48-month follow-up for patients still treated with secukinumab [26]. Comparison of remission rates stratified according to the number of previous b/tsDMARDs in patients still treated at 24-, and 48-month follow-up and determination of factors associated with LDA were performed by logistic regression analyses, adjusted analogously to the above-mentioned Cox regression models.

5.1. Missing values

Multiple imputation by chained equations (MICE) was used to impute all missing baseline covariates included in Cox and logistic regression models regardless of the extent of missingness, separately for axSpA and PsA (10 imputed datasets) [27].

A significance level of 0.05 was used. Statistical analyses and graphs were performed with R version 4.2.2 (R Core Team. R: A Language and Environment for Statistical Computing, Vienna, Austria: R Foundation for Statistical Computing; 2022).

6. Results

In total, 767 axSpA patients from 13 registries, and 975 PsA patients from 12 registries were included.

6.1. Baseline characteristics

AxSpA patients had a median (IQR) age of 47 (38–55) years, were predominantly male (60%), HLA-B27 positive (79%) and with radiographic disease (75%). The disease activity was high (median [IQR] ASDAS-CRP 3.6 [2.9–4.2]), and patients predominantly received secukinumab at a dose of 150 mg/month (79%). A total of 184, 182 and 401 patients had received 0, 1 and ≥ 2 previous b/tsDMARDs, respectively (Table 1).

PsA patients had a median (IQR) age of 52 (44–59) years, were predominantly female (56%), had moderate disease activity (median [IQR] DAPSA28 25.4 [16.7–37.4]), and received mainly secukinumab 300 mg/month (64%). A total of 238, 210 and 527 patients had received 0, 1 and ≥ 2 previous b/tsDMARDs, respectively (Table 2).

Baseline characteristics of axSpA and PsA patients according to the number of previous b/tsDMARDs are presented in

Table 1
Baseline characteristics of patients with axSpA, stratified by the number of previous b/tsDMARDs.

Baseline characteristics ^a	Overall	n = 767	b/tsDMARD naïve	n = 184	1 prior b/tsDMARD	n = 182	≥ 2 prior b/tsDMARDs	n = 401
	Value	n available	Value	n available	Value	n available	Value	n available
Demography, diagnosis and lifestyle								
Age at drug initiation (years)	47 (38–55)	767	43 (36–54)	184	46 (37–55)	182	48 (39–56)	401
Sex (male)	460 (60%)	767	131 (71%)	184	112 (62)	182	217 (54%)	401
Years since diagnosis (years)	7 (3–14)	751	3 (1–9)	178	5 (2–14)	180	9 (5–16)	393
BMI (kg/m ²)	26.9 (23.7–30.4)	568	26.6 (23.4–29.4)	154	27.2 (24.6–30.4)	132	26.9 (23.7–31.0)	282
Current smoker	206 (33%)	625	41 (28%)	148	42 (29)	143	123 (37%)	334
Radiographic status								
r-axSpA	211 (75%)	283	81 (83%)	98	46 (75%)	61	84 (68%)	124
nr-axSpA	72 (25%)	283	17 (17%)	98	15 (25%)	61	40 (32%)	124
Clinical measures								
HLA-B27 positive	419 (79%)	532	113 (80%)	142	105 (81%)	129	201 (77%)	261
Comorbidities^b								
Cardiovascular disease	146 (25%)	585	34 (22%)	154	31 (21%)	145	81 (28%)	286
Diabetes	45 (8%)	559	9 (6%)	154	13 (9%)	137	23 (9%)	268
Kidney disease	12 (2%)	553	4 (3%)	153	3 (2%)	135	5 (2%)	265
Non-musculoskeletal manifestations^b								
Uveitis	73 (14%)	528	14 (10%)	147	21 (16%)	133	38 (15%)	248
IBD	78 (17%)	449	11 (9%)	116	18 (18%)	99	49 (21%)	234
Psoriasis	67 (16%)	424	12 (12%)	104	20 (20%)	99	35 (16%)	221
History of enthesitis	110 (40%)	273	16 (18%)	90	31 (47%)	66	63 (54%)	117
History of dactylitis	36 (13%)	281	5 (6%)	83	7 (10%)	67	24 (18%)	131
CRP (mg/L)	7.0 (2.4–20.0)	538	11.0 (4.0–25.0)	133	5.8 (2.0–17.1)	118	5.6 (2.0–18.2)	287
CRP < 10 mg/L	319 (59%)	538	62 (47%)	133	74 (63%)	118	183 (64%)	287
ASDAS-CRP	3.6 (2.9–4.2)	418	4.0 (3.0–4.6)	101	3.5 (2.7–4.1)	86	3.5 (2.9–4.1)	231
PhGA (0–100)	48 (25–70)	344	64 (46–70)	68	49 (24–70)	71	40 (22–60)	205
28 swollen joint count (0–28)	0 (0–1)	266	0 (0–1)	59	0 (0–0)	49	0 (0–1)	158
28 tender joint count (0–28)	0 (0–2)	225	0 (0–2)	53	0 (0–3)	42	0 (0–2)	130
Treatment								
Secukinumab dose								
150 mg/month, n (%)	525 (79%)	662	156 (90%)	174	126 (79%)	160	243 (74%)	328
300 mg/month, n (%)	111 (17%)	662	14 (8%)	174	24 (15%)	160	73 (22%)	328
Unknown dose, n (%)	26 (4%)	662	4 (2%)	174	10 (6%)	160	12 (4%)	328
Concomitant csDMARDs								
1 or more csDMARDs	163 (37%)	439	38 (32%)	120	28 (33%)	86	97 (42%)	233
Methotrexate	105 (24%)	431	15 (13%)	112	17 (20%)	84	73 (31%)	235
Sulfasalazine	72 (17%)	420	23 (21%)	112	18 (22%)	83	31 (14%)	225
Leflunomide	11 (3%)	401	3 (3%)	108	2 (3%)	75	6 (3%)	218
Others	2 (0%)	454	0 (0%)	122	0 (0%)	94	2 (1%)	238
PROs								
Pain (0–100)	70 (50–80)	417	70 (50–80)	85	68 (50–80)	86	70 (50–80)	246
Fatigue (0–100)	70 (50–87)	220	69 (50–81)	48	69 (50–85)	41	72 (50–90)	131
PGA (0–100)	70 (50–83)	459	70 (50–80)	110	66 (48–80)	96	70 (50–87)	253
HAQ (0–3)	1.1 (0.6–1.6)	330	1.1 (0.8–1.6)	73	0.9 (0.5–1.5)	63	1.1 (0.8–1.5)	194
BASDAI (0–100)	62.0 (45.0–75.8)	623	62.5 (46.2–76.0)	154	55.9 (40.0–73.0)	145	63.8 (47.3–76.0)	324
BASFI (0–100)	57.5 (31.8–74.8)	359	57.5 (29.6–75.3)	77	46.0 (24.7–68.2)	79	61.0 (33.1–76.0)	203

ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Function Index; b/tsDMARD: biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; BMI: body mass index; CRP: C-reactive protein; csDMARD: conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; HAQ: Health Assessment Questionnaire; HLA-B27: Human Leukocyte Antigen-B27; IBD: inflammatory bowel disease; nr-axSpA: non-radiographic axial spondyloarthritis; PGA: Patient Global Assessment; PhGA: Physician Global Assessment; PROs: patient-reported outcomes; r-axSpA: radiographic axial spondyloarthritis. Pain, fatigue, PGA and PhGA are scored on a 0–100 scale. HAQ is scored on a 0–3 scale.

^a Values are presented as median (IQR) and n (%) for continuous and categorical variables, respectively.

^b Comorbidities and non-musculoskeletal manifestations were defined as ever or never present during the disease course.

Table 2
Baseline characteristics of patients with PsA, stratified by the number of previous b/tsDMARDs.

Baseline characteristics ^a	Overall	<i>n</i> = 975	b/tsDMARD naïve	<i>n</i> = 238	1 prior b/tsDMARD	<i>n</i> = 210	≥ 2 prior b/tsDMARDs	<i>n</i> = 527
	Value	<i>n</i> available	Value	<i>n</i> available	Value	<i>n</i> available	Value	<i>n</i> available
Demography, and lifestyle								
Age at drug initiation (years)	52 (44–59)	975	50 (41–57)	238	52 (44–58)	210	53 (45–60)	527
Sex (male)	426 (44%)	975	118 (50%)	238	97 (46%)	210	211 (40%)	527
Years since diagnosis (years)	7 (3–13)	922	3 (1–9)	222	6 (2–12)	198	9 (5–15)	502
BMI (kg/m ²)	27.4 (24.4–30.8)	713	27.4 (23.8–30.7)	175	27.5 (24.7–30.8)	153	27.3 (24.5–30.9)	385
Current smoker	177 (25%)	710	40 (25%)	163	49 (33%)	148	88 (22%)	399
Clinical measures								
Comorbidities^b								
Cardiovascular disease	206 (29%)	704	55 (31%)	176	47 (30%)	156	104 (28%)	372
Diabetes	86 (13%)	679	17 (10%)	173	19 (13%)	148	50 (14%)	358
Kidney disease	15 (2%)	688	4 (2%)	169	4 (3%)	149	7 (2%)	370
Non-musculoskeletal manifestations^b								
Uveitis	17 (3%)	658	5 (3%)	174	3 (2%)	149	9 (3%)	335
IBD	28 (5%)	575	2 (1%)	146	7 (5%)	133	19 (6%)	296
Psoriasis	415 (81%)	512	113 (88%)	128	96 (82%)	117	206 (77%)	67
History of enthesitis	93 (53%)	176	19 (33%)	57	21 (64%)	33	53 (62%)	86
History of dactylitis	99 (29%)	347	20 (19%)	107	24 (32%)	75	55 (33%)	165
CRP (mg/L)	5.0 (1.8–13.0)	742	7.0 (2.0–21.2)	176	3.0 (1.0–8.2)	142	4.8 (2.0–12.6)	424
CRP < 10 mg/L	507 (68%)	742	103 (59%)	176	111 (78%)	142	293 (69%)	424
DAPSA	25.2 (16.3–36.0)	283	28.5 (19.1–43.5)	83	20.0 (12.0–27.9)	53	25.9 (16.2–36.0)	147
DAPSA28	25.4 (16.7–37.4)	499	29.7 (19.4–42.3)	112	20.6 (11.4–32.6)	97	26.1 (17.2–37.5)	290
PhGA (0–100)	39 (20–60)	555	50 (27–70)	133	30 (15–50)	109	35 (18–51)	313
28 swollen joint count (0–28)	1 (0–4)	715	2 (0–4)	163	1 (0–3)	139	1 (0–4)	413
28 tender joint count (0–28)	4 (1–8)	725	4 (1–10)	165	3 (1–7)	142	4 (1–8)	418
Treatment								
Secukinumab dose								
150 mg/month, <i>n</i> (%)	263 (30%)	863	116 (52%)	222	41 (23%)	176	106 (23%)	465
300 mg/month, <i>n</i> (%)	554 (64%)	863	98 (44%)	222	124 (70%)	176	332 (71%)	465
Unknown dose, <i>n</i> (%)	46 (5%)	863	8 (4%)	222	11 (6%)	176	27 (6%)	465
Concomitant csDMARDs								
1 or more csDMARDs	400 (76%)	526	104 (78%)	133	59 (64%)	92	237 (79%)	301
Methotrexate	302 (59%)	509	82 (66%)	125	43 (47%)	92	177 (61%)	292
Sulfasalazine	65 (15%)	445	19 (19%)	100	12 (14%)	87	34 (13%)	258
Leflunomide	94 (20%)	464	30 (27%)	111	11 (13%)	85	53 (20%)	268
Others	17 (3%)	498	4 (4%)	110	2 (2%)	88	11 (4%)	300
PROs								
Pain (0–100)	69 (47–80)	602	70 (52–80)	143	58 (36–79)	120	70 (50–82)	339
Fatigue (0–100)	71 (51–87)	308	64 (46–75)	61	55 (28–78)	55	80 (57–91)	192
PGA (0–100)	70 (50–83)	708	70 (52–85)	171	65 (40–80)	137	70 (50–88)	400
HAQ (0–3)	1.0 (0.6–1.6)	574	1.0 (0.6–1.5)	131	0.9 (0.5–1.4)	116 (55%)	1.2 (0.8–1.8)	327

b/tsDMARD: biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; BMI: body mass index; CRP: C-reactive protein; csDMARD: conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; DAPSA: Disease Activity index for Psoriatic Arthritis; DAPSA28: Disease Activity index for Psoriatic Arthritis in 28 joints; HAQ: Health Assessment Questionnaire; IBD: inflammatory bowel disease; PGA: Patient Global Assessment; PhGA: Physician Global Assessment; PROs: patient-reported outcomes; PsA: psoriatic arthritis. Pain, fatigue, PGA and PhGA are scored on a 0–100 scale. HAQ is scored on a 0–3 scale.

^a Values are presented as median (IQR) and *n* (%) for continuous and categorical variables, respectively.

^b Comorbidities and non-musculoskeletal manifestations were defined as ever or never present during the disease course.

Tables 1 and 2, respectively. Variations in baseline characteristics were observed across registries (Table S1 for patients with axSpA and Table S2 for patients with PsA).

For all analyses, the number of patients available was higher in the ≥ 2 prior b/tsDMARDs group than in those with 0 or 1 prior b/tsDMARD (Table S3). In subgroups of patients with available data on disease activity (i.e., ASDAS-CRP for axSpA and DAPSA28 for PsA), pain and fatigue at both 24 and 48 months, crude response rates were overall similar to the main analysis (Table S4).

6.2. Secukinumab retention rates

The overall 24- and 48-month secukinumab retention rates were 61.4% and 50.5%, respectively, in axSpA patients, and 63.5% and 48.8%, respectively, in PsA patients.

In axSpA, the 48-month secukinumab retention rates were 66.0%, 44.8% and 46.0% in patients who previously received 0, 1 and ≥ 2 b/tsDMARDs, respectively. At 48 months, the probability for having withdrawn secukinumab was significantly higher in patients who had received 1 and ≥ 2 b/tsDMARDs than in b/tsDMARD naïve patients (HR [95% CI] = 2.04 [1.42–2.94], $P < 0.001$ and HR [95% CI] = 1.86 [1.33–2.62], $P < 0.001$, respectively; Figs. 1 and 2).

In PsA, the 48-month secukinumab retention rates were 53.2%, 53.6% and 44.9% in patients who previously received 0, 1 and ≥ 2 b/tsDMARDs, respectively. At 48 months, the probability for having withdrawn secukinumab was significantly higher in patients who received ≥ 2 b/tsDMARDs than b/tsDMARD naïve patients (HR [95% CI] = 1.40 [1.08–1.83], $P < 0.05$), whereas no difference was found between bio-naïve patients and those who had received 1 prior b/tsDMARD (Figs. 1 and 2).

Retention rates and HRs for withdrawing according to the number of previous b/tsDMARDs at 24 months are presented in Figs. 1 and 2, for both axSpA and PsA patients.

For all treatment lines, lack of effectiveness was the most frequent reason for discontinuation reported in both axSpA and PsA patients (approximately 60–70%), followed by adverse events (Table S5).

Baseline factors associated with secukinumab discontinuation at 24 and 48 months are presented in Table S6.

6.3. Median values in PROs and disease activity measures

In general, physician-reported and composite disease activity measures (i.e., CRP and PhGA in both axSpA and PsA, ASDAS-CRP in axSpA, DAPSA and DAPSA28 in PsA) were higher at baseline in b/tsDMARD naïve patients than in the groups with 1 or ≥ 2 prior b/tsDMARDs. A marked decrease was observed during follow-up in all groups and levels tended to be numerically similar between patients with 0, 1 or ≥ 2 prior b/tsDMARDs at 48 months (Table 3, Fig. S1).

In contrast, PRO values (i.e., pain, fatigue, PGA and HAQ in both axSpA and PsA, and BASDAI in axSpA), were overall similar at baseline between patients who previously received 0, 1 or ≥ 2 b/tsDMARDs. A decrease was observed in all groups during follow-up, but this tended to be numerically smaller in patients with ≥ 2 prior b/tsDMARDs (Table 3).

6.4. Remission and LDA rates

In axSpA, crude rates for ASDAS-CRP ID, ASDAS-CRP LDA, BASDAI ID, BASDAI LDA, pain remission and PGA remission at 24 and 48 months were numerically higher in b/tsDMARD naïve patients than in those who previously received 1 or ≥ 2 prior b/tsDMARDs. In the adjusted analyses, a statistically significant difference was found

between b/tsDMARD naïve and ≥ 2 prior b/tsDMARDs patients at 24 months (Table 4).

In PsA, crude rates for DAPSA remission, DAPSA LDA, DAPSA28 remission, DAPSA28 LDA, pain remission, PGA remission and HAQ remission at 24 and 48 months were numerically higher in b/tsDMARD naïve patients than in those who previously received 1 or ≥ 2 prior b/tsDMARDs. However, after adjustment for confounders, statistically significant differences between b/tsDMARD naïve and ≥ 2 prior b/tsDMARDs patients were only found at 24 months for most of the outcomes. At 48 months, a statistically significant difference between b/tsDMARD naïve and ≥ 2 prior b/tsDMARDs patients was only observed for HAQ remission (Table 4).

Baseline factors associated with ASDAS-CRP LDA (for patients with axSpA) and DAPSA28 LDA (for patients with PsA) at 24 and 48 months are presented in Table S6.

7. Discussion

In this large real-world study of patients with axSpA and PsA initiating secukinumab, we, for the first time, report 48-month retention rates as well as rates of remission and LDA. In more than 1500 patients from 13 European countries, we demonstrated that secukinumab retention rates after four years were approximately 50% in both axSpA and PsA patients. Importantly, b/tsDMARD naïve patients demonstrated higher retention, remission and LDA rates than patients with prior b/tsDMARDs exposure, particularly in axSpA.

Short-term real-world secukinumab effectiveness in spondyloarthritis has previously been reported, with an overall 12-month retention rate of 72% in axSpA [9], 76% in PsA [8] and 76% in a mixed cohort of radiographic axSpA/PsA patients [28]. Interestingly, the overall 24- and 48-month secukinumab retention rates reported in the present study are similar to the 24- and 48-month TNFi retention rates reported in prior European studies of spondyloarthritis. In a retrospective Italian study, Favalli et al. reported 2-year TNFi retention rates of 80% and 75% in b/tsDMARD naïve axSpA and PsA patients respectively, which is comparable to the 2-year secukinumab retention rates in our cohort of b/tsDMARD naïve patients (79% and 71% in axSpA and PsA patients, respectively) [29]. Lie et al., reported a 4-year TNFi retention rate of around 50% in undifferentiated SpA and 55% in ankylosing spondylitis [30]. In a cohort of patients with axSpA, Nissen et al. reported a 4-year TNFi retention rate of around 45% for patients receiving co-medication with csDMARDs and around 40% for patients without csDMARDs [31].

The retention of a first TNFi has been reported to be higher than a second or third TNFi in both axSpA and PsA [32,33]. Similar findings are reported regarding 12-, and 24-month secukinumab retention rates in both axSpA and PsA [8,9,24]. Also, two recent French studies report that prior exposure to TNFi was identified as a risk factor for secukinumab discontinuation in patients with axSpA after one year of treatment [34,35]. After 48 months of follow-up, this pattern was still present in our study, with a significantly higher risk of having withdrawn secukinumab in patients having received one or more previous b/tsDMARDs compared to b/tsDMARD naïve patients. This suggests that patients treated with secukinumab who have previously failed a b/tsDMARD constitute a more treatment resistant patient group.

We observed that the most frequent reason for discontinuation of secukinumab in both axSpA and PsA was lack of effectiveness. Unfortunately, our data is not sufficiently detailed to differentiate between primary or secondary lack of effectiveness. Misdiagnosis in SpA cannot be excluded, particularly in non-radiographic axSpA, as patients may have other reasons for back pain (e.g., degenerative spinal disease or fibromyalgia [36–38]), which may be misinterpreted as SpA disease activity. As highlighted in the recent ASAS-EULAR recommendations for the management of axSpA, reassessment of a

Table 3

Disease activity measures and PROs at 24 and 48 months in patients with axSpA and PsA remaining on secukinumab, stratified by the number of previous b/tsDMARDs.

Patients with axSpA <i>n</i> = 767					Patients with PsA <i>n</i> = 975				
Median values for PROs and disease activity measures ^a	No. of previous b/tsDMARDs	Baseline	24 months	48 months	Median values for PROs and disease activity measures ^a	No. of previous b/tsDMARDs	Baseline	24 months	48 months
CRP	0	11.0 (4.0–25.0)	5.0 (2.0–11.0)	5.0 (1.0–9.3)	CRP	0	7.0 (2.0–21.2)	2.8 (1.0–7.3)	2.9 (2.0–6.1)
	1	5.8 (2.0–17.1)	4.0 (2.0–7.0)	4.5 (1.5–8.0)		1	3.0 (1.0–8.2)	3.0 (1.5–5.1)	3.0 (1.8–6.3)
	≥ 2	5.6 (2.0–18.2)	5.0 (2.3–9.1)	3.1 (1.0–8.0)		≥ 2	4.8 (2.0–12.6)	3.0 (1.6–6.8)	3.0 (1.3–5.0)
ASDAS-CRP	0	4.0 (3.0–4.6)	1.9 (1.2–2.5)	1.6 (1.3–2.5)	DAPSA	0	28.5 (19.1–43.5)	8.1 (2.8–12.4)	9.2 (5.2–15.2)
	1	3.5 (2.7–4.1)	2.0 (1.5–2.6)	2.2 (1.5–2.7)		1	20.0 (12.0–27.9)	10.3 (6.8–15.1)	9.6 (5.6–15.5)
	≥ 2	3.5 (2.9–4.1)	2.8 (2.1–3.4)	2.3 (1.8–3.5)		≥ 2	25.9 (16.2–36.0)	13.8 (7.7–17.5)	10.8 (7.3–16.9)
BASDAI	0	62.5 (46.2–76.0)	21.0 (13.4–38.0)	19.1 (9.0–28.5)	DAPSA28	0	29.7 (19.4–42.3)	7.3 (2.8–13.5)	9.0 (4.6–13.4)
	1	55.9 (40.0–73.0)	26.0 (16.0–49.0)	24.5 (16.5–42.7)		1	20.6 (11.4–32.6)	11.7 (6.6–16.8)	10.4 (6.8–15.5)
	≥ 2	63.8 (47.3–76.0)	46.0 (22.9–64.0)	37.0 (25.0–57.0)		≥ 2	26.1 (17.2–37.5)	14.2 (10.0–20.2)	13.3 (7.3–18.6)
PhGA	0	64 (46–70)	12 (6–20)	12 (7–20)	PhGA	0	50 (27–70)	10 (2–20)	10 (5–20)
	1	49 (24–70)	10 (2–30)	<20 patients		1	30 (15–50)	10 (5–20)	10 (2–21)
	≥ 2	40 (22–60)	15 (5–25)	10 (6–30)		≥ 2	35 (18–51)	11 (6–24)	10 (5–22)
Pain	0	70 (50–80)	26 (10–38)	20 (10–35)	Pain	0	70 (52–80)	28 (12–45)	31 (20–48)
	1	68 (50–80)	42 (20–52)	<20 patients		1	58 (36–79)	40 (20–60)	40 (21–64)
	≥ 2	70 (50–80)	50 (25–71)	50 (26–70)		≥ 2	70 (50–82)	50 (30–70)	50 (24–72)
Fatigue	0	69 (50–81)	30 (15–41)	<20 patients	Fatigue	0	64 (46–75)	40 (15–64)	38 (10–54)
	1	69 (50–85)	<20 patients	<20 patients		1	55 (28–78)	37 (13–74)	<20 patients
	≥ 2	72 (50–90)	55 (30–77)	<20 patients		≥ 2	80 (57–91)	60 (36–79)	64 (35–78)
PGA	0	70 (50–80)	20 (10–30)	20 (10–38)	PGA	0	70 (52–85)	30 (11–50)	35 (19–50)
	1	66 (48–80)	30 (10–50)	30 (15–41)		1	65 (40–80)	34 (20–58)	40 (20–60)
	≥ 2	70 (50–87)	40 (20–67)	42 (20–70)		≥ 2	70 (50–88)	43 (28–70)	50 (20–72)
HAQ	0	1.1 (0.8–1.6)	0.6 (0.0–1.0)	0.2 (0.0–0.9)	HAQ	0	1.0 (0.6–1.5)	0.5 (0.0–0.9)	0.4 (0.1–1.1)
	1	0.9 (0.5–1.5)	0.4 (0.1–1.1)	<20 patients		1	0.9 (0.5–1.4)	0.8 (0.2–1.2)	0.6 (0.2–1.1)
	≥ 2	1.1 (0.8–1.5)	1.0 (0.4–1.4)	0.8 (0.2–1.3)		≥ 2	1.2 (0.8–1.8)	0.9 (0.5–1.5)	0.9 (0.4–1.2)

axSpA: axial spondyloarthritis; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score using C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; b/tsDMARD: biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; CRP: C-reactive protein; DAPSA: Disease Activity index for Psoriatic Arthritis; DAPSA28: Disease Activity index for Psoriatic Arthritis in 28 joints; HAQ: Health Assessment Questionnaire; PGA: Patient Global Assessment; PhGA: Physician Global Assessment; PROs: patient-reported outcomes; PsA: psoriatic arthritis. Pain, fatigue, PGA, PhGA and BASDAI are scored on a 0–100 scale. HAQ is scored on a 0–3 scale. <20 patients: values are presented if more than 20 patients had available data.

^a Values are presented as median (IQR).

Table 4

Remission and LDA rates at 24 and 48 months in patients with axSpA and PsA remaining on secukinumab, stratified by the number of previous b/tsDMARDs. Results of adjusted logistic regression analysis.

Patients with axSpA <i>n</i> = 767						Patients with PsA <i>n</i> = 975					
Remission and LDA rates	No. of previous b/tsDMARDs	24 months		48 months		Remission and LDA rates	No. of previous b/tsDMARDs	24 months		48 months	
		Crude rates (%)	Fully adjusted ^c OR [95% CI]	Crude rates <i>n</i> (%)	Fully adjusted ^c OR [95% CI]			Crude rates <i>n</i> (%)	Fully adjusted ^d OR [95% CI]	Crude rates (%)	Fully adjusted ^d OR [95% CI]
ASDAS-CRP ID (<1.3)	0	30	< 5 EPV	24	< 5 EPV	DAPSA remission (≤ 4)	0	30	< 5 EPV	17	< 5 EPV
	1	19		< 20 patients			1	11		19	
	≥ 2	5		7			≥ 2	11		14	
ASDAS-CRP LDA (<2.1)	0	59	Reference	59	NC	DAPSA LDA (≤ 14)	0	81	NC	60	NC
	1	52	0.87 [0.37–2.06], <i>P</i> = 0.75	39			1	69		67	
	≥ 2	27	0.40 [0.18–0.87]^a	38			≥ 2	52		66	
BASDAI ID (<20)	0	48	Reference	57	NC	DAPSA28 remission (≤ 4)	0	29	Reference	19	< 5 EPV
	1	39	0.70 [0.35–1.39], <i>P</i> = 0.30	35			1	15	0.36 [0.15–0.88]^a	14	
	≥ 2	22	0.34 [0.18–0.64]^a	20			≥ 2	8	0.18 [0.08–0.42]^b	11	
BASDAI LDA (<40)	0	79	Reference	82	NC	DAPSA28 LDA (≤ 14)	0	79	Reference	76	Reference
	1	66	0.53 [0.24–1.14], <i>P</i> = 0.10	73			1	61	0.39 [0.18–0.83]^a	68	0.70 [0.22–2.23], <i>P</i> = 0.55
	≥ 2	43	0.24 [0.12–0.47]^b	52			≥ 2	48	0.29 [0.15–0.57]^b	52	0.56 [0.21–21.54], <i>P</i> = 0.26
CRP < 10 mg/L	0	74	Reference	75		CRP < 10 mg/L	0	83	Reference	88	< 5 EPV
	1	84	1.54 [0.60–4.21], <i>P</i> = 0.35	83	NC		1	87	1.23 [0.54–2.80]	89	
	≥ 2	76	1.11 [0.50–2.45]	78			≥ 2	83	1.04 [0.53–2.05]	87	

Table 4 (Continued)

Patients with axSpA <i>n</i> = 767						Patients with PsA <i>n</i> = 975					
Remission and LDA rates	No. of previous b/tsDMARDs	24 months Crude rates (%)	Fully adjusted ^c OR [95% CI]	48 months Crude rates <i>n</i> (%)	Fully adjusted ^c OR [95% CI]	Remission and LDA rates	No. of previous b/tsDMARDs	24 months Crude rates <i>n</i> (%)	Fully adjusted ^d OR [95% CI]	48 months Crude rates (%)	Fully adjusted ^d OR [95% CI]
Pain remission (≤ 20)	0	43	Reference	55	NC	Pain remission (≤ 20)	0	45	Reference	37	< 5 EPV
	1	26	0.48 [0.19–1.23]	< 20 patients			1	36	0.71 [0.37–1.37]	26	
	≥ 2	19	0.33 [0.14–0.75]^a	16			≥ 2	20	0.34 [0.19–0.62]^b	21	
Fatigue remission (≤ 20)	0	37	< 5 EPV	50	NC	Fatigue remission (≤ 20)	0	32	NC	33	NC
	1	12		< 20 patients			1	32		< 20 patients	
	≥ 2	19		8			≥ 2	14		17	
PGA remission (≤ 20)	0	55	Reference	60	NC	PGA Remission (≤ 20)	0	41	Reference	31	< 5 EPV
	1	34	0.46 [0.20–1.08]	43			1	31	0.68 [0.36–1.26], <i>P</i> = 0.22	27	
	≥ 2	32	0.51 [0.25–1.03]	28			≥ 2	20	0.40 [0.23–0.69]^a	28	
HAQ remission (≤ 0.5)	0	47	NC	59	NC	HAQ Remission (≤ 0.5)	0	57	Reference	58	Reference
	1	59		< 20 patients			40	0.48 [0.24–0.94]^a	45	0.55 [0.20–1.53], <i>P</i> = 0.25	
	≥ 2	30		38			≥ 2	28	0.34 [0.19–0.60]^b	0.39 [0.16–0.96], <i>P</i> = 0.04	

ASAS: Assessment of SpondyloArthritis International Society; axSpA: axial spondyloarthritis; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score using C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; b/tsDMARD: biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; CI: confidence interval; DAPSA: Disease Activity index for Psoriatic Arthritis; DAPSA28: Disease Activity index for Psoriatic Arthritis in 28 joints; EPV: events-per-variable per available independent variable; ID: inactive disease; LDA: low disease activity; OR: odds ratio; PGA: Patient Global Assessment; HAQ: Health Assessment Questionnaire; PsA: psoriatic arthritis. Values in bold indicate statistically significant results. < 20 patients: rates are presented if more than 20 patients had available data. NC: not calculated, comparisons are presented if more than 50 patients per group had more than 50% available data. < 5 EPV: comparisons are presented if EPV ≥ 5.

^a *P* < 0.05.

^b *P* < 0.001

^c Values adjusted for age, gender, GDP per capita, time since diagnosis and baseline ASDAS-CRP.

^d Values adjusted for age, gender, GDP per capita, time since diagnosis and baseline DAPSA28.

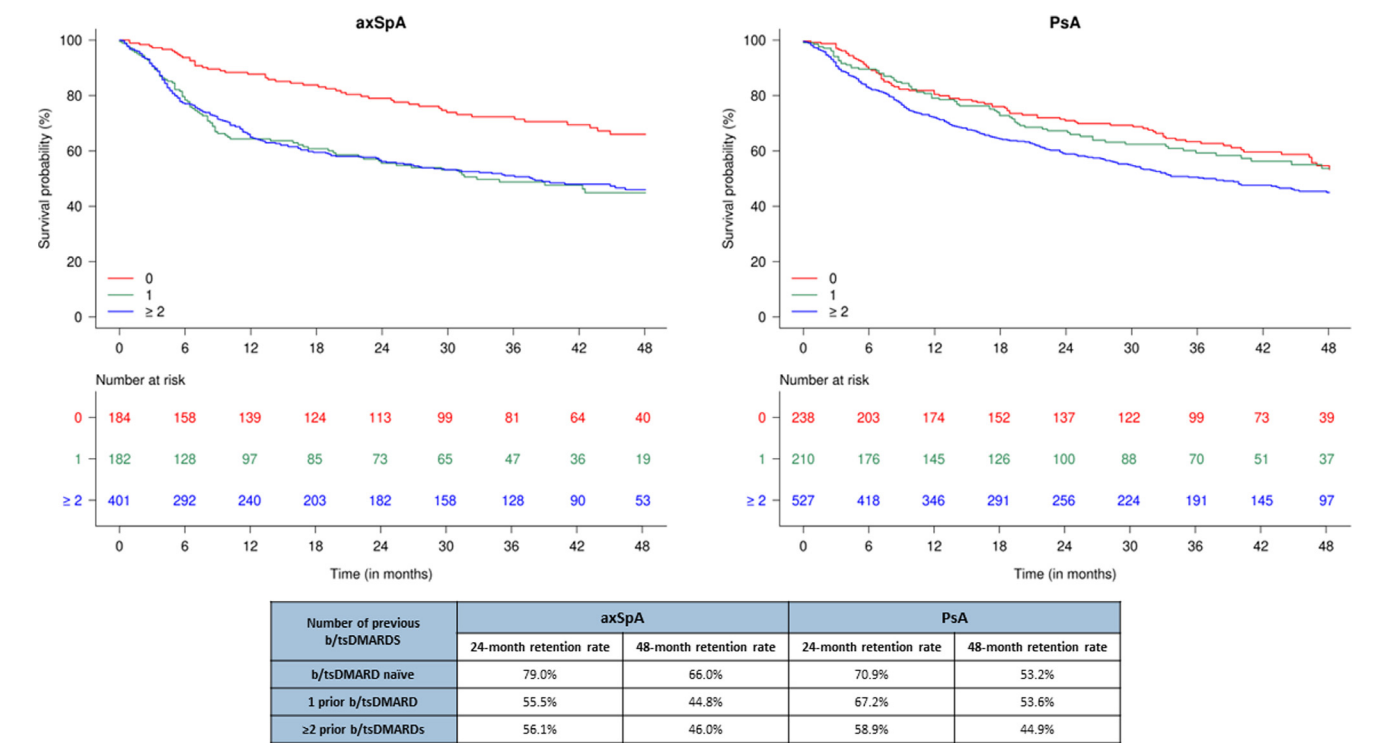


Fig. 1. Kaplan-Meier curve showing the survival probability for secukinumab in patients with axSpA and PsA, stratified by the number of previous b/tsDMARDs. axSpA: axial spondyloarthritis; b/tsDMARD: biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; PsA: psoriatic arthritis.

diagnosis of axSpA in patients having experienced a lack of efficacy of a first b/tsDMARD at 12 weeks is important before initiating a further b/tsDMARD [10].

Our real-world study is the first to report both remission and LDA rates after 4 years of secukinumab therapy. The effect of secukinumab on remission and LDA rates has been investigated in several RCTs in both axSpA and PsA [39–42], and also in real-world cohorts [24,43], all reporting beneficial effects up to 24 months. Similarly, we observed an improvement in all PROs and disease activity measures until 48 months of follow-up in patients remaining on therapy. Although baseline PROs across treatment lines were similar, we observed numerically higher remission and LDA rates in b/tsDMARD naïve patients than in patients with 1 or ≥ 2 prior b/tsDMARDs, at 24 and 48 months, both in axSpA and PsA. Statistically significant differences were found between the b/tsDMARD naïve and ≥ 2 prior b/tsDMARDs groups at 24 months in both axSpA and PsA, while comparison between LDA rates at 48 months was rarely possible due to a limited number of patients. These results are again in line with those previously found in TNFi studies. In EuroSpA, similar baseline PROs across treatment lines in patients treated with TNFi in both axSpA and PsA have also been reported [44,45]. Moreover, prior studies have shown that b/tsDMARD naïve patients have higher remission rates than TNFi-experienced patients after 24 months of TNFi-exposure, in both axSpA and PsA [18,45].

In addition, the 24-month PRO remission rates for pain, fatigue, PGA and HAQ in b/tsDMARD naïve axSpA patients receiving secukinumab in the current study (43%, 37%, 55% and 47%, respectively) were fairly comparable to those reported in EuroSpA data by Ørnberg et al. in b/tsDMARD naïve axSpA patients receiving a first TNFi (54%, 47%, 53% and 65%, respectively) [18]. At baseline, the b/tsDMARD naïve patients initiating secukinumab had higher percentages of males (71% vs. 58%), HLA-B27 positivity (80% vs. 75%), radiographic sacroiliitis (83% vs. 76%) and higher CRP values (11 vs. 8 mg/L), than those initiating TNFi as their first b/tsDMARD. However, there were no differences in age, BMI or PROs levels between

these two populations. It is important to underline that data from different studies cannot be directly compared, and it seems likely that patients who used secukinumab as their first b/tsDMARD from 2015–2018 constitute a particular patient subset, since EULAR recommendations in this period recommended TNFi as the first b/tsDMARD [46].

There are no recommendations in the literature regarding the cut-off values for PRO remission in either axSpA or PsA. Therefore, similar to previous studies within the EuroSpA collaboration [9,24], we chose to base our cut-offs on the ASAS working group's definition of partial remission in axSpA, including a value of < 20 in each of the four domains: PGA, pain, function and inflammation [21], and we also applied these cut-off values to PsA patients to make comparisons feasible, although this meant that we were less stringent on pain remission for PsA patients than the MDA criteria [22]. Similarly, there is no consensus on the best cut-off for BASDAI LDA and ID in axSpA, and the use of the BASDAI cut-offs < 20 and < 40 were chosen since a value < 40 is often considered to define LDA [47].

Our study has several limitations. Firstly, missingness, inherent to all registry studies, was an issue for outcome data, both at secukinumab treatment start and during follow-up. Results presented in this study are for the patients remaining on treatment at the respective time-points, and we have particularly low numbers available for the 48-month follow-up. We used MICE to overcome missing baseline covariates. Secondly, heterogeneity in registry design and data collection across EuroSpA registries have been reported by Linde et al. [48], and our data also show variations in baseline characteristics across registries. Similar to other observational studies, heterogeneity of patients and selection bias potentially present may have influenced effectiveness measures. Thirdly, we did not have data on dose changes or modifications of dosing frequency during therapy. Finally, patients included in our study started secukinumab between January 1st 2015 and March 31st 2018. In Europe, secukinumab was approved for PsA and r-axSpA in 2015 [49], but for nr-axSpA only in 2020 [50]. In our cohort, 25% of the axSpA patients with available data on radiographic status had nr-

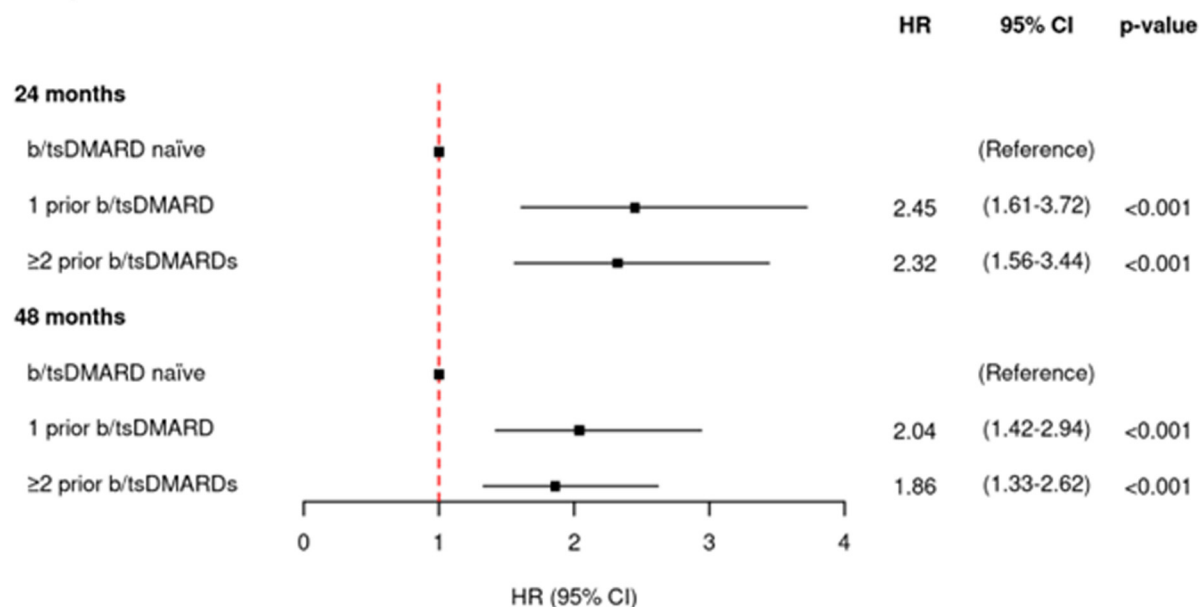
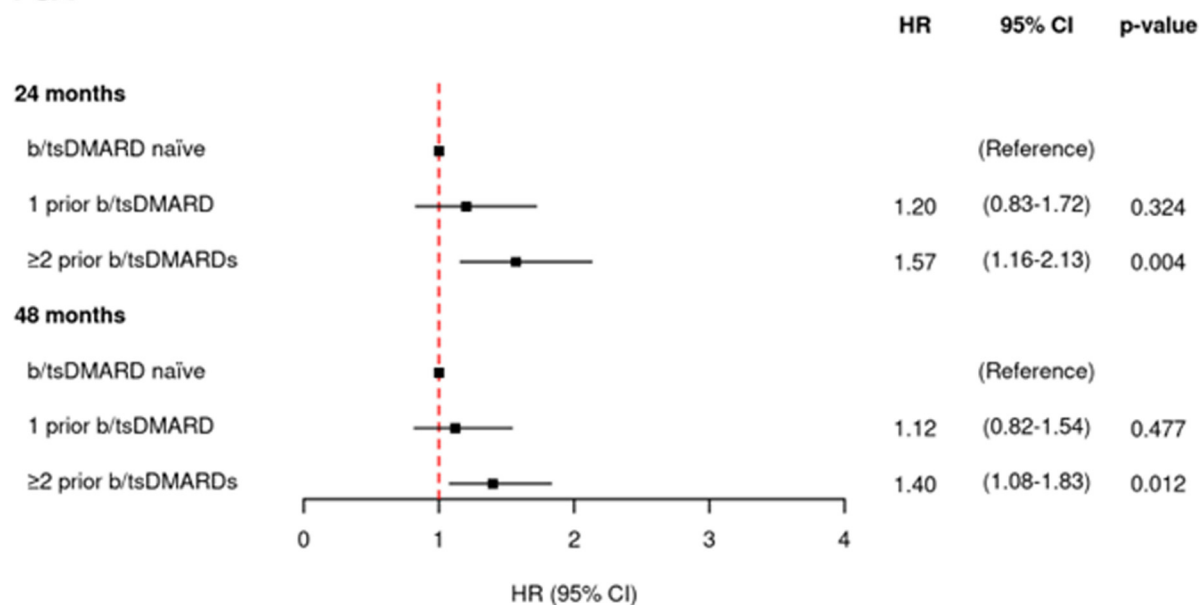
axSpA**PsA**

Fig. 2. Hazard Ratios for having withdrawn secukinumab at 24 and 48 months in patients with axSpA and PsA, stratified by the number of previous b/tsDMARDs. Results of adjusted Cox regression analyses. axSpA: axial spondyloarthritis; b/tsDMARD: biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; CI: confidence interval; HR: hazard ratio for withdrawing; PsA: psoriatic arthritis. Values adjusted for age, gender, GDP per capita, time since diagnosis and baseline DAPSA28.

axSpA, and thus a minority of our included patients was receiving secukinumab off label.

An important strength of our study is that we were able to investigate outcomes in both axSpA and PsA patients in a large prospective observational cohort of patients initiating secukinumab in real-life settings. The generalizability of our results is high, due to the inclusion of data from 13 registries across Europe and the high number of patients.

In conclusion, this large real-world study demonstrated secukinumab retention rates of approximately 50% after four years in both axSpA and PsA, which is comparable to previously reported TNFi retention rates. b/tsDMARD naïve patients had higher retention and remission rates over 48 months compared to patients with prior b/tsDMARD exposure, particularly in axSpA.

Funding

The EuroSpA collaboration is financially supported by Novartis. Novartis had no influence on the data collection, statistical analyses, manuscript preparation, or decision to submit.

Disclosure of interest

Marion Pons, Stylianos Georgiadis, Zohra Faizy Ahmadzay, Jette Heberg, Lykke Midtbøll Ørnbjerg: research grant from Novartis and UCB (paid to employer); Sara Nysom Christiansen, Simon Horskjær Rasmussen: research grant from Novartis (paid to employer); Mikkel Østergaard: Research grant from Abbvie, Amgen, BMS, Merck, Novartis and UCB and consulting and/or speaker fees from

Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Galapagos, Gilead, Hospira, Janssen, MEDAC, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, UCB; Bente Glintborg: research grants from Pfizer, Abbvie, BMS, Sandoz; Anne Gitte Loft: consulting fees from Janssen, Lilly, Novartis, UCB and speakers fees from AbbVie, Novartis, Pfizer, paid instructor from Pfizer; Isabel Castrejon: consulting and/or speaker fees from BMS, Eli-Lilly, Galapagos, Gilead, Janssen, Novartis, MSD, Pfizer, GSK; Fernando Sánchez-Alonso: None; Florenzo Iannone: research grant from BMS, Galapagos, Pfizer and consulting and/or speakers fees from Abbvie, Amgen, AstraZeneca, BMS, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, UCB; Dan Nordström: research grant from MSD, consulting fees from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB, and speaker fees from Novartis, Pfizer, UCB; Anna-Mari Hokkanen: Research grant from MSD; Adrian Ciurea: None; Michael J. Nissen: research grant from Novartis and Pfizer and consulting and/or speaker fees from Abbvie, Eli Lilly, Janssens, Novartis, Pfizer; Jakub Závada: consulting fees from Abbvie, AstraZeneca and speakers fees from Abbvie, Eli-Lilly, Sandoz, Novartis, Egis, UCB, Sanofi, AstraZeneca, Sobi; Karel Pavelka: Consulting fees from Abbvie, UCB, Pfizer, Eli Lilly, Celltrion, MSD, Novartis and speaker fees from Abbvie, Amgen, Pfizer, Eli Lilly, Viartis, Fresenius, Novartis; Ziga Rotar: consulting fees from Abbvie, Novartis, Eli Lilly, Pfizer, Janssen, SOBI, swixx BioPharma, AstraZeneca, and speaker fees from Abbvie, Amgen, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen; Katja Perdan Pirkmajer: consulting fees from Abbvie, Novartis, Medis, Eli Lilly, Pfizer, Boehringer Ingelheim and speaker fees from Abbvie, Novartis, MSD, Medis, Eli Lilly, Pfizer, Lek, Janssen; Brigitte Michelsen: research grant from Novartis and the centre for treatment of Rheumatic and Musculoskeletal Diseases (REMEDY) is funded as a Centre for Clinical Treatment Research by The Research Council of Norway (project 328657) and speaker fees from Novartis; Pawel Mielnik: consulting fees from Galapagos; Miguel Bernades: none; Nikita Khmelinskii: consulting fees from Abbvie, AstraZeneca, GSK and speakers fees from AstraZeneca, GSK, Novartis; Karin Laas: speaker fees from Abbvie, Johnson and Johnson, Novartis, Pfizer; Sigrid Vorobjov: none; Catalin Codreanu: consulting and/or speaking fees from AbbVie, Amgen, Boehringer Ingelheim, Ewopharma, Lilly, Novartis, Pfizer; Gary J. Macfarlane: research grant from GSK; Gareth T. Jones: research grants (paid to employer) from Abbvie, Pfizer, UCB, Amgen, GSK and speaker fees from Janssen; Bjorn Gudbjornsson: None; Olafur Pálsson: None; Johan K Wallman: research grant from AbbVie, Amgen, Eli Lilly, Novartis, Pfizer and speaker fees from AbbVie, Amgen; Irene van der Horst-Bruinsma: Unrestricted Grants received for investigator initiated studies from MSD, Pfizer, AbbVie, UCB. Fees received for lectures from BMS, AbbVie, Pfizer, MSD, UCB, consulting fees from AbbVie, UCB, MSD, Novartis, Lilly and speaker fees from UCB; Fatos Onen: Research grant from Pfizer and speaker fees from AbbVie, Amgen, Celltrion, Lilly, Pfizer, Roche, Novartis, Abdi Ibrahim, UCB; Merete Lund Hetland: Research grants (paid to employer) from Abbvie, Biogen, BMS, Celltrion, Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Medac, Pfizer, Roche, Samsung Biopics, Sandoz, Novartis, Nordforsk, consulting fees from Abbvie (paid to employer), chaired the steering committee of the Danish Rheumatology Quality Registry (DANBIO, DRQ), which receives public funding from the hospital owners and funding from pharmaceutical companies and speaker fees from Pfizer, Medac, Sandoz (paid to employer) and Novartis.

Acknowledgements

On behalf of the EuroSpA Scientific Committee, the authors acknowledge Novartis Pharma AG for supporting the EuroSpA collaboration. Novartis had no influence on the data collection, sta-

tistical analyses, manuscript preparation or decision to submit for publication.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jbspin.2024.105824>.

Références

- [1] Sieper J, Poddubny D. Axial spondyloarthritis. *Lancet* 2017;390:73–84, [http://dx.doi.org/10.1016/S0140-6736\(16\)31591-4](http://dx.doi.org/10.1016/S0140-6736(16)31591-4).
- [2] Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med* 2017;376:957–70, <http://dx.doi.org/10.1056/NEJMRA1505557>.
- [3] Baeten D, Baraliakos X, Braun J, et al. Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. *Lancet* 2013;382:1705–13, [http://dx.doi.org/10.1016/S0140-6736\(13\)61134-4](http://dx.doi.org/10.1016/S0140-6736(13)61134-4).
- [4] McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* 2015;386:1137–46, [http://dx.doi.org/10.1016/S0140-6736\(15\)61134-5](http://dx.doi.org/10.1016/S0140-6736(15)61134-5).
- [5] Braun J, Baraliakos X, Heldmann F, et al. Tumor necrosis factor alpha antagonists in the treatment of axial spondyloarthritis. *Expert Opin Investig Drugs* 2014;23:647–59.
- [6] Braun J, Baraliakos X, Deodhar A, et al. Effect of secukinumab on clinical and radiographic outcomes in ankylosing spondylitis: 2-year results from the randomised phase III MEASURE 1 study. *Ann Rheum Dis* 2017;76:1070–7, <http://dx.doi.org/10.1136/annrheumdis-2016-209730>.
- [7] McInnes IB, Mease PJ, Ritchlin CT, et al. Secukinumab sustains improvement in signs and symptoms of psoriatic arthritis: 2 year results from the phase 3 FUTURE 2 study. *Rheumatology (Oxford)* 2017;56:1993–2003, <http://dx.doi.org/10.1093/rheumatology/kex301>.
- [8] Michelsen B, Georgiadis S, Di Giuseppe D, et al. Real-world six- and twelve-month drug retention, remission, and response rates of secukinumab in 2017 patients with psoriatic arthritis in thirteen European countries. *Arthritis Care Res* 2022;74:1205–18, <http://dx.doi.org/10.1002/acr.24560>.
- [9] Michelsen B, Lindström U, Codreanu C, et al. Drug retention, inactive disease and response rates in 860 patients with axial spondyloarthritis initiating secukinumab treatment: routine care data from 13 registries in the EuroSpA collaboration. *RMD Open* 2020;6:e001280, <http://dx.doi.org/10.1136/rmdopen-2020-001280>.
- [10] Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. *Ann Rheum Dis* 2023;82:19–34, <http://dx.doi.org/10.1136/ard-2022-223296>.
- [11] Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis* 2020;79:700–12, <http://dx.doi.org/10.1136/annrheumdis-2020-217159>.
- [12] <https://europa.eu/>.
- [13] van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984;27:361–8, <http://dx.doi.org/10.1002/art.1780270401>.
- [14] Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol* 1994;21:2281–5.
- [15] 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.
- [16] Schoels M, Aletaha D, Funovits J, et al. Application of the DAREA/DAPSA score for assessment of disease activity in psoriatic arthritis. *Ann Rheum Dis* 2010;69:1441–7, <http://dx.doi.org/10.1136/ard.2009.122259>.
- [17] Michelsen B, Sexton J, Smolen JS, 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, <http://dx.doi.org/10.1136/annrheumdis-2018-213463>.
- [18] Ørnberg LM, Rugbjerg K, Georgiadis S, et al. One-third of European patients with axial spondyloarthritis reach pain remission with routine care tumor necrosis factor inhibitor treatment. *J Rheumatol* 2023;50:1009–119, <http://dx.doi.org/10.3899/jrheum.220459> [*jrheum.220459*].
- [19] Machado PM, Landewé R, Heijde D, et al. Ankylosing Spondylitis Disease Activity Score (ASDAS): 2018 update of the nomenclature for disease activity states. *Ann Rheum Dis* 2018;77:1539–40, <http://dx.doi.org/10.1136/annrheumdis-2018-213184>.
- [20] Schoels MM, Aletaha D, Alasti F, et al. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. *Ann Rheum Dis* 2016;75:811–8, <http://dx.doi.org/10.1136/annrheumdis-2015-207507>.
- [21] Anderson JJ, Baron G, Van Der Heijde D, et al. Ankylosing spondylitis assessment group preliminary definition of short-term improvement in ankylosing spondylitis. *Arthritis Rheum* 2001;44:1876–86, [http://dx.doi.org/10.1002/1529-0131\(200108\)44:8<1876::AID-ART326>3.0.CO;2-F](http://dx.doi.org/10.1002/1529-0131(200108)44:8<1876::AID-ART326>3.0.CO;2-F).

- [22] Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. *Ann Rheum Dis* 2010;69:48–53, <http://dx.doi.org/10.1136/ard.2008.102053>.
- [23] Felson DT, Smolen JS, Wells G, et al. American College of Rheumatology/European League Against Rheumatism provisional definition of remission in rheumatoid arthritis for clinical trials. *Ann Rheum Dis* 2011;70:404–13.
- [24] Christiansen SN, Horskjær Rasmussen S, Pons M, et al. Patient-reported outcomes in axial spondyloarthritis and psoriatic arthritis patients treated with secukinumab for 24 months in daily clinical practice. *Semin Arthritis Rheum* 2024;65:152388, <http://dx.doi.org/10.1016/j.semarthrit.2024.152388>.
- [25] Dixon WG, Carmona L, Finckh A, et al. EULAR points to consider when establishing, analysing and reporting safety data of biologics registers in rheumatology. *Ann Rheum Dis* 2010;69:1596–602, <http://dx.doi.org/10.1136/ard.2009.125526>.
- [26] Kristensen LE, Saxne T, Geborek P. The LUNDEX, a new index of drug efficacy in clinical practice: results of a five-year observational study of treatment with infliximab and etanercept among rheumatoid arthritis patients in Southern Sweden. *Arthritis Rheum* 2006;54:600–6, <http://dx.doi.org/10.1002/art.21570>.
- [27] Azur MJ, Stuart EA, Frangakis C, et al. Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res* 2011;20:40–9, <http://dx.doi.org/10.1002/mpr.329>.
- [28] Chimenti MS, Fonti GL, Conigliaro P, et al. One-year effectiveness, retention rate, and safety of secukinumab in ankylosing spondylitis and psoriatic arthritis: a real-life multicenter study. *Expert Opin Biol Ther* 2020;20:813–21, <http://dx.doi.org/10.1080/14712598.2020.1761957>.
- [29] Favalli EG, Selmi C, Becciolini A, et al. Eight-year retention rate of first-line tumor necrosis factor inhibitors in spondyloarthritis: a multicenter retrospective analysis. *Arthritis Care Res* 2017;69:867–74, <http://dx.doi.org/10.1002/acr.20390>.
- [30] Lie E, Kristensen LE, Forsblad-d'Elia H, et al. The effect of comedication with conventional synthetic disease modifying antirheumatic drugs on TNF inhibitor drug survival in patients with ankylosing spondylitis and undifferentiated spondyloarthritis: results from a nationwide prospective study. *Ann Rheum Dis* 2015;74:970–8, <http://dx.doi.org/10.1136/annrheumdis-2014-206616>.
- [31] Nissen MJ, Ciurea A, Bernhard J, et al. The Effect of comedication with a conventional synthetic disease-modifying antirheumatic drug on drug retention and clinical effectiveness of anti-tumor necrosis factor therapy in patients with axial spondyloarthritis. *Arthritis Rheumatol* 2016;68:2141–50, <http://dx.doi.org/10.1002/art.39691>.
- [32] Deodhar A, Yu D. Switching tumor necrosis factor inhibitors in the treatment of axial spondyloarthritis. *Semin Arthritis Rheum* 2017;47:343–50, <http://dx.doi.org/10.1016/j.semarthrit.2017.04.005>.
- [33] Fagerli KM, Lie E, van der Heijde D, et al. Switching between TNF inhibitors in psoriatic arthritis: data from the NOR-DMARD study. *Ann Rheum Dis* 2013;72:1840–4, <http://dx.doi.org/10.1136/annrheumdis-2012-203018>.
- [34] Dougados M, Lardy-Cléaud A, Desfleurs E, et al. Impact of the time of initiation and line of biologic therapy on the retention rate of secukinumab in axial spondyloarthritis (axSpA): data from the French multicentre retrospective FORSYA study. *RMD Open* 2024;10:e003942, <http://dx.doi.org/10.1136/rmdopen-2023-003942>.
- [35] Dougados M, Lucas J, Desfleurs E, et al. Factors associated with the retention of secukinumab in patients with axial spondyloarthritis in real-world practice: results from a retrospective study (FORSYA). *RMD Open* 2023;9:e002802, <http://dx.doi.org/10.1136/rmdopen-2022-002802>.
- [36] Salaffi F, De Angelis R, Carotti M, et al. Fibromyalgia in patients with axial spondyloarthritis: epidemiological profile and effect on measures of disease activity. *Rheumatol Int* 2014;34:1103–10, <http://dx.doi.org/10.1007/s00296-014-2955-9>.
- [37] López-Medina C, Moltó A. Comorbid pain in axial spondyloarthritis, including fibromyalgia. *Ther Adv Musculoskelet Dis* 2020;12, <http://dx.doi.org/10.1177/1759720X20966123> [1759720X20966123].
- [38] Iannone F, Nivuvori M, Fornaro M, et al. Comorbid fibromyalgia impairs the effectiveness of biologic drugs in patients with psoriatic arthritis. *Rheumatology (Oxford)* 2020;59:1599–606, <http://dx.doi.org/10.1093/rheumatology/kez505>.
- [39] Deodhar A, Conaghan PG, Kvien TK, et al. Secukinumab provides rapid and persistent relief in pain and fatigue symptoms in patients with ankylosing spondylitis irrespective of baseline C-reactive protein levels or prior tumour necrosis factor inhibitor therapy: 2-year data from the MEASURE 2 study. *Clin Exp Rheumatol* 2019;37:260–9.
- [40] Strand V, Mease P, Gossec L, et al. Secukinumab improves patient-reported outcomes in subjects with active psoriatic arthritis: results from a randomised phase III trial (FUTURE 1). *Ann Rheum Dis* 2017;76:203–7, <http://dx.doi.org/10.1136/annrheumdis-2015-209055>.
- [41] McInnes IB, Mease PJ, Schett G, et al. Secukinumab provides rapid and sustained pain relief in psoriatic arthritis over 2 years: results from the FUTURE 2 study. *Arthritis Res Ther* 2018;20:113, <http://dx.doi.org/10.1186/s13075-018-1610-3>.
- [42] Kvien TK, Conaghan PG, Gossec L, et al. Secukinumab and sustained reduction in fatigue in patients with ankylosing spondylitis: long-term results of two phase III randomized controlled trials. *Arthritis Care Res* 2022;74:759–67, <http://dx.doi.org/10.1002/acr.24517>.
- [43] Williams T, Wadeley A, Bond D, et al. Real-world experience of secukinumab treatment for ankylosing spondylitis at the Royal National Hospital for Rheumatic Diseases Bath. *Clin Rheumatol* 2020;39:1501–4, <http://dx.doi.org/10.1007/s10067-020-04944-5>.
- [44] Linde L, Ørnberg LM, Brahe CH, et al. Second and third TNF inhibitors in European patients with axial spondyloarthritis: effectiveness and impact of the reason for switching. *Rheumatol Oxf Engl* 2023;1–11, <http://dx.doi.org/10.1093/rheumatology/kead494> [kead494].
- [45] Ørnberg LM, Rugbjerg K, Georgiadis S, et al. Patient-reported outcomes and PRO remission rates in 12,262 biologic-naïve patients with psoriatic arthritis treated with TNF-inhibitors in routine care. *J Rheumatol* 2024;51:378–89, <http://dx.doi.org/10.3899/jrheum.2023-0764> [jrheum.2023-0764].
- [46] van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis* 2017;76:978–91, <http://dx.doi.org/10.1136/annrheumdis-2016-210770>.
- [47] Arida A, Protogerou AD, Konstantonis G, et al. Subclinical atherosclerosis is not accelerated in patients with ankylosing spondylitis with low disease activity: new data and meta-analysis of published studies. *J Rheumatol* 2015;42:2098–105, <http://dx.doi.org/10.3899/jrheum.150316>.
- [48] Linde L, Ørnberg LM, Rasmussen SH, et al. Commonalities and differences in set-up and data collection across European spondyloarthritis registries – results from the EuroSpA collaboration. *Arthritis Res Ther* 2023;25:205, <http://dx.doi.org/10.1186/s13075-023-03184-7>.
- [49] [https://www.novartis.com/news/media-releases/novartis-receives-two-landmark-european-approvals-cosentyx-treat-patients-ankylosing-spondylitis-and-psoriatic-arthritis#:~:text=Basel%2C%20November%2023%2C%202015%20%2D,and%20psoriatic%20arthritis%20\(PsA\).](https://www.novartis.com/news/media-releases/novartis-receives-two-landmark-european-approvals-cosentyx-treat-patients-ankylosing-spondylitis-and-psoriatic-arthritis#:~:text=Basel%2C%20November%2023%2C%202015%20%2D,and%20psoriatic%20arthritis%20(PsA).)
- [50] [https://www.novartis.com/news/media-releases/novartis-cosentyx-gains-fourth-indication-eu-first-class-approval-axial-spondyloarthritis-spectrum#:~:text=Basel%2C%20April%2029%2C%202020%20E2%80%944,spondyloarthritis%20\(nr%2DaxSpA\).](https://www.novartis.com/news/media-releases/novartis-cosentyx-gains-fourth-indication-eu-first-class-approval-axial-spondyloarthritis-spectrum#:~:text=Basel%2C%20April%2029%2C%202020%20E2%80%944,spondyloarthritis%20(nr%2DaxSpA).)