Persistence of advanced systemic pharmacological treatment of moderate-to-severe psoriasis among bio-naive patients-A retrospective register-based cohort study in Finland and Sweden

Tskhvarashvili, G.

John Wiley and Sons Inc
2025-03

Tskhvarashvili, G, Aher, K, Sveide, I, Katus, U, Westerlund, A, Hoti, F, Wennerström, C, Hassan, F, Lee, J, Hermanrud, C, Johnsson, I, Passey, A, Nissinen, R, Polesie, S, Mälkönen, T & Saarelainen, L 2025, 'Persistence of advanced systemic pharmacological treatment of moderate-to-severe psoriasis among bio-naive patients-A retrospective register-based cohort study in Finland and Sweden', Journal of the European Academy of Dermatology and Venereology, vol. 39, no. S1, pp. 50-64. https://doi.org/10.1111/jdv.20198

http://hdl.handle.net/10138/593280
10.1111/jdv.20198

Received: 21 July 2023 | Accepted: 13 June 2024

DOI: 10.1111/jdv.20198

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

ORIGINAL ARTICLE

Persistence of advanced systemic pharmacological treatment of moderate-to-severe psoriasis among bio-naïve patients—A retrospective register-based cohort study in Finland and Sweden

G. Tskhvarashvili[1] | K. Aher[2] | I. Sveide[3] | U. Katus[4] | A. Westerlund[5] | F. Hoti[6] | C. Wennerström[7] | F. Hassan[8] | J. Lee[9] | C. Hermanrud[7] | I. Johnsson[7] | A. Passey[7] | R. Nissinen[10] | S. Polesie[11,12] | T. Mälkönen[13] | L. Saarelainen[14]

[1]Epidemiology and Database Studies, IQVIA, Tallinn, Estonia

[2]Biostatistics, IQVIA, Tallinn, Estonia

[3]Biostatistics, IQVIA, Mölndal, Sweden

[4]Epidemiology and Database Studies, IQVIA, Tartu, Estonia

[5]Epidemiology and Database Studies, IQVIA, Solna, Sweden

[6]Biostatistics, IQVIA, Espoo, Finland

[7]Janssen-Cilag AB, Solna, Sweden

[8]Janssen-Cilag, High Wycombe, UK

[9]Janssen-Cilag A/S, Birkerød, Denmark

[10]Janssen-Cilag Oy, Espoo, Finland

[11]Department of Dermatology and Venereology, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[12]Sahlgrenska University Hospital, Department of Dermatology and Venereology, Region Västra Götaland, Gothenburg, Sweden

[13]Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland

[14]Epidemiology and Database Studies, IQVIA, Espoo, Finland

Correspondence
L. Saarelainen, Epidemiology and Database Studies, IQVIA, Espoo, Finland.
Email: laura.saarelainen@iqvia.com

Abstract

Background: Plaque psoriasis (PsO) requires long-term treatment for symptom control and remission; thus, a long-term pharmacological intervention is necessary. Treatment persistence reflects long-term therapeutic effectiveness and tolerance.

Objectives: This study investigates drug persistence and compares treatment discontinuation rates across biologic agents and apremilast used by PsO patients in Finland and Sweden.

Methods: This retrospective register-based cohort study included bio-naïve patients (≥18 years) with moderate-to-severe PsO, who initiated treatment with abatacept, adalimumab, brodalumab, certolizumab pegol, etanercept, golimumab, guselkumab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab or apremilast during 2008–2020 in Finland or Sweden. The main analysis evaluated persistence (based on duration of continuous treatment) and compared rates of treatment discontinuation using guselkumab as reference drug, during 2018–2020 in Finland. Treatment discontinuation was assessed by survival analysis of the time to first drug discontinuation, including switching to other study drugs. Due to limited sample size ($n < 20$), certain biologics (abatacept, brodalumab, certolizumab pegol, etanercept, golimumab, risankizumab and tildrakizumab) were excluded from the persistence analysis.

Results: In Finland, 709 patients fulfilled the inclusion criteria during 2018–2020 for the main analysis. The highest persistence was observed for guselkumab and ustekinumab with 90 and 85% of treated patients, respectively, continuing treatment for ≥1 year. Comparable results were observed in the expanded cohort analysis (index starting in 2008; 2745 bio-naïve patients in Finland and 10,970 in Sweden). Furthermore, patients treated with guselkumab in Finland showed lower treatment discontinuation rates compared to other study drugs.

Conclusion: Guselkumab and ustekinumab demonstrated high persistence as measured by continued treatment for at least 1 year. Furthermore, these treatments demonstrated lower rates of discontinuation compared to other study drugs included in the analysis. Understanding the balance between efficacy and feasibility in treatment decisions is crucial, as feasibility may impact persistency outcomes and potentially increase persistency rates.

INTRODUCTION

Plaque psoriasis (PsO), also known as psoriasis vulgaris, is a chronic, immune-mediated inflammatory skin condition, with associated comorbidities, such as depression and metabolic syndrome, reducing the quality of life of affected individuals.[1,2] Psoriasis has a global prevalence rate of 2%–3% and an age-standardized incidence rate of 57.8 per 100,000 people.[3,4] The prevalence of PsO across geographical regions varies from 0.14% in East Asia to 1.92% in Western Europe, including Finland and Sweden.[5] Moderate-to-severe PsO, which is generally defined as having extensive or widespread disease signs and symptoms, may have a major impact on quality of life, with around 90% of the patients requiring long-term treatment.[6]

Biological treatments targeting specific components of the immune system have achieved favourable treatment outcomes for moderate-to-severe PsO, thereby changing the treatment landscape.[6,7] However, biological therapies for PsO are commonly discontinued due to lack or loss of efficacy or adverse events.[8] Additionally, apremilast is an orally administered systemic phosphodiesterase-4 inhibitor, indicated for patients not responding to or with a contraindication to other systemic therapies and who are eligible for systemic treatment.[9,10]

Treatment persistence, also referred to as drug survival, is considered an indirect indicator of treatment effectiveness and tolerability.[11] PsO is a chronic disease, and continuous treatment is necessary for optimal symptom control. Therefore, discontinuation of treatment is not recommended.[8,12] A long-term observational study based on quality registers reported that nearly 77% of patients with PsO continued treatment for ≥1 year; however, treatment persistence decreased over longer periods (63% continued for ≥2 years and 53% for ≥3 years).[12]

Real-world studies describing utilization of biologic treatments or apremilast for moderate-to-severe PsO, particularly in the Nordic countries, are limited. To address this research gap, we conducted a retrospective cohort study using nationwide registers in two Nordic countries (Finland and Sweden). The primary objective of this study was to describe treatment persistence and compare treatment discontinuation rates across biologic agents and apremilast. The main analyses were performed during a study period of 2018–2020 in Finland, to account for large discrepancies in follow-up time for newer therapies compared to those in clinical use for many years. Additionally, analyses spanning the full study period (2008–2020) were performed separately in Finland and Sweden.

MATERIALS AND METHODS

This retrospective register-based cohort study assessed and compared the persistence of each study agent (abatacept, adalimumab, brodalumab, certolizumab pegol, etanercept, golimumab, guselkumab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab and apremilast) among bio-naïve adult patients with moderate-to-severe PsO in Finland and Sweden.

Patient-level data for the entire population were obtained from nationwide registers in Finland and Sweden (Table S1), using unique personal identification numbers assigned to all residents in the two countries, thereby enabling linkage of data to different registers. Individual-level pseudonymized data were used. The main variables were the study drugs and variables used to define persistence. A complete list of variables is provided in Table S2. Dosage assumptions to define drug supplies and the induction dose for all dispensations were based on the administrative instructions in the summary of product characteristics (SPC) of each drug (Table S3). The Ethics Committee of the Hospital District of Helsinki and Uusimaa in Finland, and a regional ethical review board in Sweden, approved this study, and informed consent was not required for this registry-based study (Table S1).

Patients ≥18 years of age at treatment initiation (TI), with a diagnosis of PsO (International statistical classification of diseases and related health problems, 10th revision [ICD-10] L40.0) or L40.9 code (Sweden only), and drug dispensations with PsO-specific special reimbursement codes for study drugs (Finland only; reimbursement numbers 319 and 377 [apremilast]) were included in the study. The main analyses included patients who initiated treatment with a study drug during the period of 2018–2019 in Finland, while expanded analyses included patients who initiated treatment between 2008 and 2020 in Finland or Sweden (Figure S1). Index date was defined (TI) as the date of the first dispensation of any study drug during the study period.

Patients who were treated with study drugs or efalizumab within 24 months before the start of the study period; had dispensations of ≥2 study drugs at TI; had a primary diagnosis of PsO (ICD-10 code L40.0; reimbursement numbers 319 and 377 in Finland) exclusively after TI; or had non-primary diagnoses of PsO before TI; and had ≤12 months of data available before TI were excluded from the study. Furthermore, patients on study drugs with reimbursement codes for other indications, such as gastrointestinal disease or hidradenitis suppurativa, were also excluded.

Patients were followed from TI until death, emigration, the 31st day of a continuous inpatient stay, beginning of pregnancy (40 weeks prior to delivery), initiation of efalizumab or the end of the study period, whichever occurred first.

The definition of persistence was based on the time from the first dispensation of a study drug until discontinuation, including switching to another study drug (definitions available at Table S4). Uncertainty related to actual drug use was addressed using grace periods, defined as 100% duration of the preceding drug supply, and this indicated the maximum time the patient was allowed not to have drug supply to be considered under continuous exposure period.

Descriptive statistics were used to summarize persistence and describe the percentage of patients who continued

TABLE 1 Patient characteristics for the main analysis: bio-naïve patients with PsO per study drug in Finland during 2018–2020.[a]

Patient characteristics		Study drugs					
		Guselkumab ($n=119$)	Adalimumab ($n=44$)	Apremilast ($n=229$)	Ixekizumab ($n=67$)	Secukinumab ($n=133$)	Ustekinumab ($n=104$)
Age at treatment initiation	18–34	19 (15.97%)	7 (15.91%)	18 (7.86%)	10 (14.93%)	17 (12.78%)	13 (12.50%)
	35–44	28 (23.53%)	16 (36.36%)	36 (15.72%)	13 (19.40%)	34 (25.56%)	25 (24.04%)
	45–54	25 (21.01%)	11 (25.00%)	59 (25.76%)	16 (23.88%)	28 (21.05%)	22 (21.15%)
	55–64	26 (21.85%)	5 (11.36%)	44 (19.21%)	17 (25.37%)	32 (24.06%)	22 (21.15%)
	≥65	21 (17.65%)	5 (11.36%)	72 (31.44%)	11 (16.42%)	22 (16.54%)	22 (21.15%)
	Mean (SD)	50.05 (14.12)	46.13 (12.99)	55.75 (14.71)	50.51 (14.21)	50.76 (13.76)	51.53 (14.57)
	Median (Q1, Q3)	52.10 (39.45–60.85)	43.45 (37.35–54.20)	55.30 (46.10–67.70)	50.10 (39.55–61.05)	50.60 (41.00–62.80)	51.85 (41.07–63.05)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring
Sex	Male	80 (67.23%)	23 (52.27%)	114 (49.78%)	45 (67.16%)	84 (63.16%)	71 (68.27%)
	Female	39 (32.77%)	21 (47.73%)	115 (50.22%)	22 (32.84%)	49 (36.84%)	33 (31.73%)
Education	Secondary education	57 (47.90%)	23 (52.27%)	109 (47.60%)	36 (53.73%)	56 (42.11%)	54 (51.92%)
	Higher education	40 (33.61%)	14 (31.82%)	79 (34.50%)	18 (26.87%)	47 (35.34%)	34 (32.69%)
	Missing	22 (18.49%)	7 (15.91%)	41 (17.90%)	13 (19.40%)	30 (22.56%)	16 (15.38%)
Index year at treatment initiation	2018	11 (9.24%)	18 (40.91%)	98 (42.79%)	32 (47.76%)	83 (62.41%)	70 (67.31%)
	2019	108 (90.76%)	26 (59.09%)	131 (57.21%)	35 (52.24%)	50 (37.59%)	34 (32.69%)
Dispensations of conventional systemic drugs for psoriasis vulgaris 24 months before index date							
Acitretin	No	87 (73.11%)	35 (79.55%)	165 (72.05%)	42 (62.69%)	102 (76.69%)	69 (66.35%)
	Yes	32 (26.89%)	9 (20.45%)	64 (27.95%)	25 (37.31%)	31 (23.31%)	35 (33.65%)
Ciclosporin	No	112 (94.12%)	40–43 (90.91%–97.73%)	216 (94.32%)	62 (92.54%)	121 (90.98%)	100–103 (96.15%–99.04%)
	Yes	7 (5.88%)	<5	13 (5.68%)	5 (7.46%)	12 (9.02%)	<5
Methotrexate	No	24 (20.17%)	14 (31.82%)	98 (42.79%)	15 (22.39%)	27 (20.30%)	31 (29.81%)
	Yes	95 (79.83%)	30 (68.18%)	131 (57.21%)	52 (77.61%)	106 (79.70%)	73 (70.19%)
Any conventional systemic drugs (acitretin, ciclosporin, methotrexate)	No	12 (10.08%)	7 (15.91%)	59 (25.76%)	8 (11.94%)	18 (13.53%)	18 (17.31%)
	Yes	107 (89.92%)	37 (84.09%)	170 (74.24%)	59 (88.06%)	115 (86.47%)	86 (82.69%)
Number of conventional systemic drugs (acitretin, ciclosporin, methotrexate)	None	12 (10.08%)	7 (15.91%)	59 (25.76%)	8 (11.94%)	18 (13.53%)	18 (17.31%)
	1	82 (68.91%)	31 (70.45%)	132 (57.64%)	37 (55.22%)	83 (62.41%)	60 (57.69%)
	2–3	25 (21.01%)	6 (13.64%)	38 (16.59%)	22 (32.84%)	32 (24.06%)	26 (25.00%)
	Mean (SD)	1.13 (0.59)	0.98 (0.55)	0.91 (0.65)	1.22 (0.67)	1.12 (0.64)	1.08 (0.65)
	Median (Q1, Q3)	1.00 (1.00–1.00)	1.00 (1.00–1.00)	1.00 (0.00–1.00)	1.00 (1.00–2.00)	1.00 (1.00–1.00)	1.00 (1.00–1.25)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring

TABLE 1 (Continued)

Patient characteristics		Study drugs					
		Guselkumab (*n* = 119)	**Adalimumab (*n* = 44)**	**Apremilast (*n* = 229)**	**Ixekizumab (*n* = 67)**	**Secukinumab (*n* = 133)**	**Ustekinumab (*n* = 104)**
Dispensation of conventional systemic drugs during exposure to any study drugs							
Concomitant acitretin use	No	115–118 (96.64%–99.16%)	44 (100.00%)	225–228 (98.25%–99.56%)	67 (100.00%)	129–132 (96.99%–99.25%)	100–103 (96.15%–99.04%)
	Yes	<5	0 (0.00%)	<5	0 (0.00%)	<5	<5
Concomitant methotrexate use	No	110 (92.44%)	30 (68.18%)	194 (84.72%)	61 (91.04%)	117 (87.97%)	97 (93.27%)
	Yes	9 (7.56%)	14 (31.82%)	35 (15.28%)	6 (8.96%)	16 (12.03%)	7 (6.73%)
Concomitant ciclosporin use	No	105 (88.24%)	30 (68.18%)	188 (82.10%)	61 (91.04%)	112 (84.21%)	95 (91.35%)
	Yes	14 (11.76%)	14 (31.82%)	41 (17.90%)	6 (8.96%)	21 (15.79%)	9 (8.65%)
Other systemic drugs for moderate-to-severe psoriasis vulgaris 24 months before index date							
Dimethyl fumarate	No	119 (100.00%)	44 (100.00%)	229 (100.00%)	67 (100.00%)	133 (100.00%)	104 (100.00%)
	Yes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infliximab	No	119 (100.00%)	44 (100.00%)	229 (100.00%)	67 (100.00%)	133 (100.00%)	104 (100.00%)
	Yes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leflunomide	No	119 (100.00%)	40–43 (90.91%–97.73%)	213 (93.01%)	63–66 (94.03%–98.51%)	128 (96.24%)	104 (100.00%)
	Yes	0 (0.00%)	<5	16 (6.99%)	<5	5 (3.76%)	0 (0.00%)
Tofacitinib	No	119 (100.00%)	44 (100.00%)	229 (100.00%)	67 (100.00%)	133 (100.00%)	104 (100.00%)
	Yes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Characteristics related to psoriasis vulgaris							
Drug dispensation with a drug reimbursement number 319 and 377	No dispenses	0 (0.00%)	<5	<5	<5	5 (3.76%)	<5
	1 dispense	119 (100.00%)	40–43 (90.91%–97.73%)	225–228 (98.25%–99.56%)	63–66 (94.03%–98.51%)	128 (96.24%)	100–103 (96.15%–99.04%)
	2 dispenses	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	>2 dispenses	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Drug dispensation with a drug reimbursement number 313, 281, 319 or 377	No dispenses	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)	0 (0.00%)
	1 dispense	119 (100.00%)	44 (100.00%)	225–228 (98.25%–99.56%)	67 (100.00%)	133 (100.00%)	104 (100.00%)
	2 dispenses	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	>2 dispenses	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

(Continues)

TABLE 1 (Continued)

Patient characteristics		Study drugs					
		Guselkumab (*n* = 119)	**Adalimumab (*n* = 44)**	**Apremilast (*n* = 229)**	**Ixekizumab (*n* = 67)**	**Secukinumab (*n* = 133)**	**Ustekinumab (*n* = 104)**
Time since first PsO diagnosis	<2 years	38 (31.93%)	9 (20.45%)	57 (24.89%)	30 (44.78%)	48 (36.09%)	29 (27.88%)
	2–6 years	29 (24.37%)	12 (27.27%)	47 (20.52%)	12 (17.91%)	30 (22.56%)	22 (21.15%)
	≥7 years	52 (43.70%)	23 (52.27%)	121–124 (52.84%–54.15%)	25 (37.31%)	55 (41.35%)	53 (50.96%)
	Missing	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)	0 (0.00%)
	Mean (SD)	6.89 (6.71)	8.78 (6.47)	8.68 (6.64)	6.11 (7.15)	6.88 (6.73)	8.23 (7.01)
	Median (Q1, Q3)	4.51 (1.22–11.65)	7.30 (2.69–13.70)	7.75 (2.06–14.47)	2.42 (0.02–9.84)	4.83 (0.68–12.12)	7.03 (1.77–13.90)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring
Dermatologist/rheumatologist as prescriber of first dispensation of treatment line	No	<5	<5	11 (4.80%)	<5	0 (0.00%)	<5
	Dermatologist	92–95 (77.31%–79.83%)	34 (77.27%)	111 (48.47%)	51–57 (76.12%–85.07%)	98–101 (73.68%–75.94%)	79–82 (75.96%–78.85%)
	Rheumatologist	0 (0.00%)	<5	56 (24.45%)	<5	<5	0 (0.00%)
	Missing	23 (19.33%)	6 (13.64%)	51 (22.27%)	8 (11.94%)	31 (23.31%)	21 (20.19%)
Number of dermatologist visits 12 months before index date	No visits	19 (15.97%)	<5	62 (27.07%)	15 (22.39%)	32 (24.06%)	13 (12.50%)
	1–5 visits	54 (45.38%)	25–28 (56.82%–63.64%)	88 (38.43%)	32 (47.76%)	50 (37.59%)	51 (49.04%)
	6–9 visits	27 (22.69%)	10 (22.73%)	32 (13.97%)	9 (13.43%)	17 (12.78%)	23 (22.12%)
	≥10 visits	19 (15.97%)	5 (11.36%)	47 (20.52%)	11 (16.42%)	34 (25.56%)	17 (16.35%)
	Mean (SD)	6.21 (7.13)	5.43 (5.55)	6.43 (8.93)	5.94 (8.30)	7.44 (9.71)	6.38 (7.58)
	Median (Q1, Q3)	4.00 (2.00–7.00)	4.50 (2.00–6.50)	3.00 (0.00–8.00)	3.00 (1.00–6.00)	4.00 (1.00–11.00)	4.00 (2.00–7.00)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring
Number of rheumatologist visits 12 months before index date	No visits	114 (95.80%)	28–31 (63.64%–70.45%)	147 (64.19%)	54 (80.60%)	108 (81.20%)	92–95 (88.46%–91.35%)
	1–2 visits	5 (4.20%)	12 (27.27%)	38 (16.59%)	8 (11.94%)	17 (12.78%)	8 (7.69%)
	≥3 visits	0 (0.00%)	<5	44 (19.21%)	5 (7.46%)	8 (6.02%)	<5
	Mean (SD)	0.05 (0.26)	0.93 (2.13)	1.29 (2.54)	0.88 (3.48)	0.60 (2.30)	0.21 (0.72)
	Median (Q1, Q3)	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.00 (0.00–2.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring

TABLE 1 (Continued)

Patient characteristics		Study drugs					
		Guselkumab (*n* = 119)	Adalimumab (*n* = 44)	Apremilast (*n* = 229)	Ixekizumab (*n* = 67)	Secukinumab (*n* = 133)	Ustekinumab (*n* = 104)
Number of any specialist outpatient encounters 12 months before index date	No visits	10 (8.40%)	0 (0.00%)	14 (6.11%)	10 (14.93%)	17 (12.78%)	6 (5.77%)
	1–3 visits	28 (23.53%)	7 (15.91%)	34 (14.85%)	15 (22.39%)	25 (18.80%)	22 (21.15%)
	4–5 visits	15 (12.61%)	<5	29 (12.66%)	8 (11.94%)	22 (16.54%)	14 (13.46%)
	6–9 visits	38 (31.93%)	14–17 (31.82%–38.64%)	55 (24.02%)	14 (20.90%)	15 (11.28%)	26 (25.00%)
	10–17 visits	13 (10.92%)	8 (18.18%)	46 (20.09%)	6 (8.96%)	23 (17.29%)	18 (17.31%)
	≥18 visits	15 (12.61%)	11 (25.00%)	51 (22.27%)	14 (20.90%)	31 (23.31%)	18 (17.31%)
	Mean (SD)	8.36 (8.86)	12.70 (13.20)	11.72 (10.95)	10.72 (14.11)	10.90 (12.09)	10.89 (14.24)
	Median (Q1, Q3)	6.00 (3.00–9.00)	8.00 (5.75–17.25)	8.00 (4.00–15.00)	6.00 (2.00–14.00)	6.00 (3.00–16.00)	7.00 (3.00–13.00)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring
Any phototherapy received 12 months before index date	No	114 (95.80%)	40–43 (90.91%–97.73%)	191 (83.41%)	63–66 (94.03%–98.51%)	118 (88.72%)	97 (93.27%)
	Yes	5 (4.20%)	<5	38 (16.59%)	<5	15 (11.28%)	7 (6.73%)
Number of phototherapy occasions 12 months before index date	None	114 (95.80%)	40–43 (90.91%–97.73%)	191 (83.41%)	63–66 (94.03%–98.51%)	118 (88.72%)	97 (93.27%)
	1	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	2	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	≥3	5 (4.20%)	<5	38 (16.59%)	<5	15 (11.28%)	7 (6.73%)
Being hospitalized with PsO as the main discharge diagnosis 12 months before index date	No	28 (23.53%)	10 (22.73%)	74 (32.31%)	21 (31.34%)	53 (39.85%)	22 (21.15%)
	Yes	91 (76.47%)	34 (77.27%)	155 (67.69%)	46 (68.66%)	80 (60.15%)	82 (78.85%)
Comorbidities and co-medications from 24 months before index date							
Psoriatic arthritis	No	111 (93.28%)	21 (47.73%)	146 (63.76%)	53 (79.10%)	91 (68.42%)	86 (82.69%)
	Yes	8 (6.72%)	23 (52.27%)	83 (36.24%)	14 (20.90%)	42 (31.58%)	18 (17.31%)
Crohn's disease	No	115–118 (96.64%–99.16%)	40–43 (90.91%–97.73%)	225–228 (98.25%–99.56%)	67 (100.00%)	133 (100.00%)	100–103 (96.15%–99.04%)
	Yes	<5	<5	<5	0 (0.00%)	0 (0.00%)	<5
Ulcerative colitis	No	115–118 (96.64%–99.16%)	40–43 (90.91%–97.73%)	225–228 (98.25%–99.56%)	67 (100.00%)	133 (100.00%)	100–103 (96.15%–99.04%)
	Yes	<5	<5	<5	0 (0.00%)	0 (0.00%)	<5
Ankylosing spondylitis	No	119 (100.00%)	44 (100.00%)	229 (100.00%)	63–66 (94.03%–98.51%)	129–132 (96.99%–99.25%)	104 (100.00%)
	Yes	0 (0.00%)	0 (0.00%)	0 (0.00%)	<5	<5	0 (0.00%)

(Continues)

TABLE 1 (Continued)

Patient characteristics		Study drugs					
		Guselkumab ($n=119$)	Adalimumab ($n=44$)	Apremilast ($n=229$)	Ixekizumab ($n=67$)	Secukinumab ($n=133$)	Ustekinumab ($n=104$)
Rheumatoid arthritis	No	119 (100.00%)	44 (100.00%)	225–228 (98.25%–99.56%)	63–66 (94.03%–98.51%)	129–132 (96.99%–99.25%)	104 (100.00%)
	Yes	0 (0.00%)	0 (0.00%)	<5	<5	<5	0 (0.00%)
Juvenile rheumatoid arthritis	No	119 (100.00%)	44 (100.00%)	225–228 (98.25%–99.56%)	67 (100.00%)	133 (100.00%)	104 (100.00%)
	Yes	0 (0.00%)	0 (0.00%)	<5	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiovascular disease[b]	No	111 (93.28%)	40–43 (90.91%–97.73%)	188 (82.10%)	57 (85.07%)	117 (87.97%)	92 (88.46%)
	Yes	8 (6.72%)	<5	41 (17.90%)	10 (14.93%)	16 (12.03%)	12 (11.54%)
Diabetes mellitus (type I or II)	No	96 (80.67%)	35 (79.55%)	186 (81.22%)	56 (83.58%)	118 (88.72%)	83 (79.81%)
	Yes	23 (19.33%)	9 (20.45%)	43 (18.78%)	11 (16.42%)	15 (11.28%)	21 (20.19%)
Recorded obesity	No	113 (94.96%)	40–43 (90.91%–97.73%)	217 (94.76%)	63–66 (94.03%–98.51%)	126 (94.74%)	97 (93.27%)
	Yes	6 (5.04%)	<5	12 (5.24%)	<5	7 (5.26%)	7 (6.73%)
Psychiatric diagnoses (main definition)	No	115–118 (96.64%–99.16%)	40–43 (90.91%–97.73%)	221 (96.51%)	63–66 (94.03%–98.51%)	128 (96.24%)	100–103 (96.15%–99.04%)
	Yes	<5	<5	8 (3.49%)	<5	5 (3.76%)	<5
Charlson comorbidity index score	0	102 (85.71%)	38 (86.36%)	160 (69.87%)	55 (82.09%)	114 (85.71%)	82 (78.85%)
	1	8 (6.72%)	<5	29 (12.66%)	6 (8.96%)	10 (7.52%)	9 (8.65%)
	2	5 (4.20%)	<5	23 (10.04%)	<5	<5	10 (9.62%)
	3	<5	<5	10 (4.37%)	<5	<5	<5
	≥4	<5	<5	7 (3.06%)	<5	<5	<5
	Mean (SD)	0.27 (0.77)	0.30 (0.85)	0.62 (1.19)	0.39 (1.06)	0.33 (1.10)	0.38 (0.85)
	Median (Q1, Q3)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–1.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	Min–Max	Censoring	Censoring	Censoring	Censoring	Censoring	Censoring
Number of co-medications 24 months before index date	0	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
	1–9	60 (50.42%)	20 (45.45%)	71 (31.00%)	28 (41.79%)	63 (47.37%)	41 (39.42%)
	≥10	59 (49.58%)	24 (54.55%)	158 (69.00%)	39 (58.21%)	70 (52.63%)	63 (60.58%)
Cardiovascular disease (primary care diagnoses)	No	106 (89.08%)	39 (88.64%)	172 (75.11%)	55 (82.09%)	105 (78.95%)	87 (83.65%)
	Yes	13 (10.92%)	5 (11.36%)	57 (24.89%)	12 (17.91%)	28 (21.05%)	17 (16.35%)
Diabetes mellitus (type I or II) (primary care diagnoses)	No	100 (84.03%)	38 (86.36%)	194 (84.72%)	60 (89.55%)	123 (92.48%)	88 (84.62%)
	Yes	19 (15.97%)	6 (13.64%)	35 (15.28%)	7 (10.45%)	10 (7.52%)	16 (15.38%)

TABLE 1 (Continued)

Patient characteristics		Study drugs					
		Guselkumab (*n* = 119)	Adalimumab (*n* = 44)	Apremilast (*n* = 229)	Ixekizumab (*n* = 67)	Secukinumab (*n* = 133)	Ustekinumab (*n* = 104)
Psychiatric diagnoses (primary care diagnoses)	No	113 (94.96%)	40–43 (90.91%–97.73%)	214 (93.45%)	62 (92.54%)	126 (94.74%)	100–103 (96.15%–99.04%)
	Yes	6 (5.04%)	<5	15 (6.55%)	5 (7.46%)	7 (5.26%)	<5

[a]Patients with >20 observations at treatment initiation are shown in the table.
[b]Cardiovascular diseases include hypertension, a history of cardiovascular events, and hypercholesterolemia and mixed hyperlipidaemia.

treatment at 12 months, for each study drug. A competing risk analysis was performed using the cumulative incidence estimator (Aalen-Johansen)[13] of the time to the first treatment discontinuation, considering death as a competing risk event. Unadjusted cumulative incidence curves for each study drug were used to evaluate persistence. Rate of treatment discontinuation was analysed using Cox proportional hazards regression (Cox PH), with guselkumab as a reference drug. Unadjusted (crude) hazard ratios (HRs) with 95% confidence intervals (CIs) were derived without any other variables in the model. Adjusted estimates were generated to include covariates (Table S2) in the model and account for confounding bias. Potential confounders were carefully selected for the covariate-adjusted Cox PH regression model (Table S2).

Shorter follow-up periods for newer biologics, such as brodalumab, guselkumab, ixekizumab and risankizumab, necessitated restricting the study period to 2018–2020. The unadjusted cumulative incidence and discontinuation rate analyses were repeated to estimate bias due to higher likelihood of treatment censoring when drugs had less time on the market. Furthermore, the expanded cohort analyses for treatment persistence included separate study populations from Finland and Sweden and were conducted from 2008 to 2020. This study focused on the 2018–2020 cohort in Finland, for which persistence and rates of treatment discontinuation were assessed for a maximum of 3 years (TI during 2018–2019, when all drugs were available; follow-up through the end of 2020). Sweden was not included in the analysis due to small sample size. Furthermore, due to limited sample size ($n < 20$), certain biologics (abatacept, brodalumab, certolizumab pegol, etanercept, golimumab, risankizumab and tildrakizumab) were excluded from the persistence analysis.

Sensitivity analyses were performed for the 2018–2020 cohort from Finland. Potential misclassification of exposure was addressed by sensitivity analyses that considered various grace periods (0 days, 90 days and 50% duration of the preceding drug supply) and administration frequencies (assuming maintenance without induction [Table S4]).

Furthermore, for the main analyses, potential impact of residual confounding was assessed by the E-values for the point estimate and for the 95% CI limit that was closest to null.[14] The estimated impact of observed variables was used as a reference for the *E*-values, by assuming that residual confounding is related to and not more influential than individual measured variables.

RESULTS

Baseline characteristics and patient demographics

The main analysis performed during the period of 2018–2020 included 709 patients in Finland, with a mean (SD) age ranging between 37.48 (14.52) years and 55.75 (14.71) years across different treatment groups. Psoriatic arthritis was the

most common comorbidity, and methotrexate was the most commonly prescribed conventional systemic drug (Table 1).

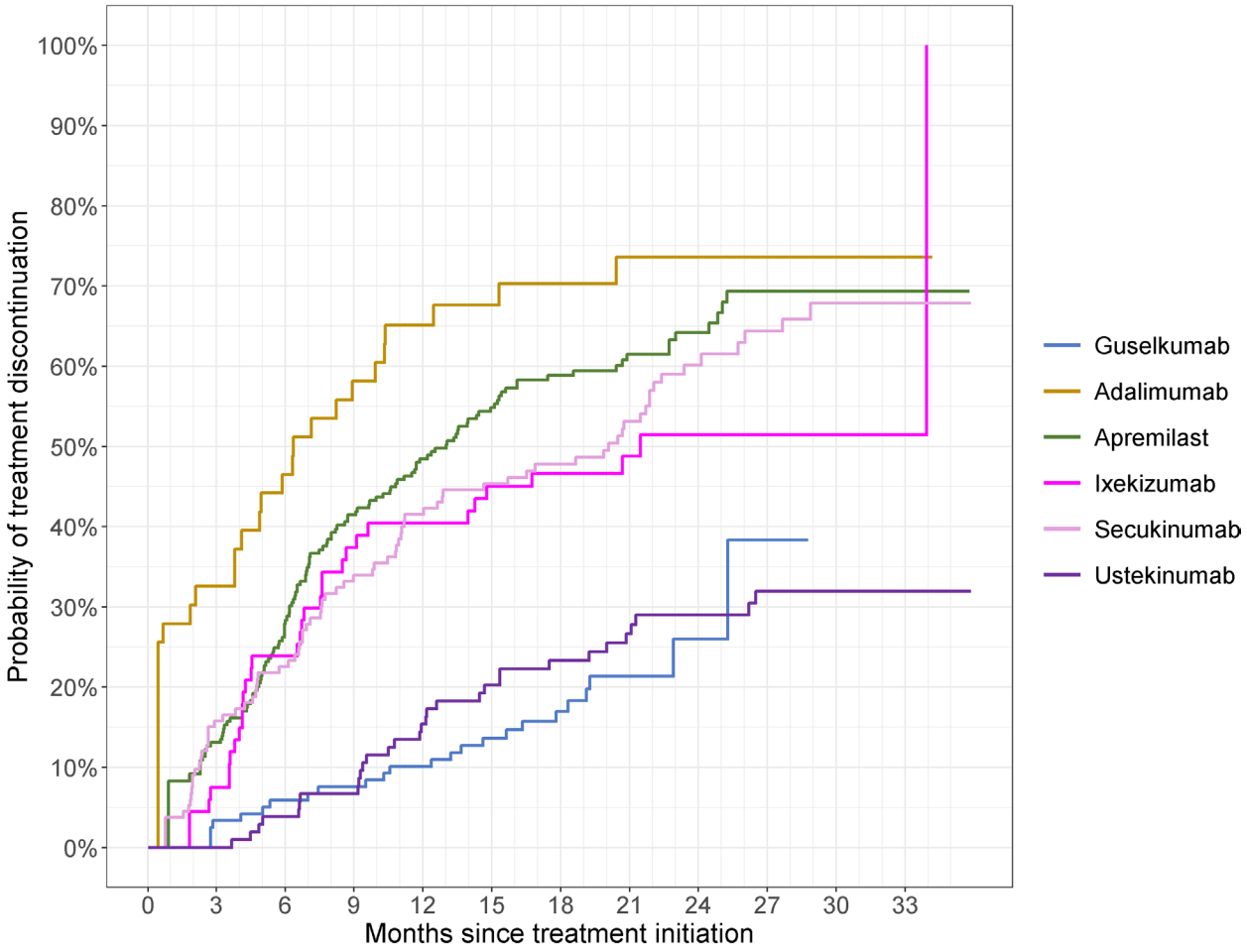
In the main analysis, patients treated with ustekinumab had the longest mean duration of follow-up (697 days), followed by guselkumab (540 days), while those treated with certolizumab pegol had the shortest mean duration of follow-up (229 days).

The expanded 2008–2020 cohorts included 2745 and 10,970 bio-naïve patients with moderate-to-severe PsO from Finland and Sweden registers, respectively. The total number of patients per study drug and baseline characteristics are presented in Tables S5 and S6A for Finland and Tables S5 and S6B for Sweden.

Similar to the main analysis, patients treated with ustekinumab had the longest mean duration of follow-up (1284 days in Finland and 906 days in Sweden), while those treated with risankizumab had the shortest mean duration of follow-up (197 days in Finland and 224 days in Sweden). However, due to its delayed entry into the market (reimbursement in Sweden in June 2019 and in Finland in January 2020), the risankizumab cohort had a maximum follow-up time of 1 year and the results may not be comparable with other drugs in the expanded analyses.

Descriptive persistence

In the 2018–2020 cohort from Finland (i.e. main analysis), the highest persistence was observed for guselkumab and ustekinumab, with 90% and 82%, respectively, of patients continuing treatment for ≥1 year (Figure 1). Furthermore, the expanded 2008–2020 cohort from Finland had the highest



Number of patients at risk per each drug

Guselkumab	119	112	106	68	7	0
Adalimumab	44	23	15	9	<5	<5
Apremilast	229	167	115	72	29	15
Ixekizumab	67	51	39	33	13	7
Secukinumab	133	103	77	61	29	15
Ustekinumab	104	99	85	72	48	35

FIGURE 1 Unadjusted cumulative incidence estimates for treatment discontinuation by drug among bio-naïve patients with PsO in Finland during 2018–2020[1]. [1]Patients with >20 observations at treatment initiation are shown in the graph.

persistence for guselkumab, with 90% of patients continuing treatment for ≥1 year, followed by ustekinumab (85%) (Figure 2a). In Sweden, where persistence for guselkumab was not measured due to small sample size, ustekinumab (73%) and risankizumab (60%) showed the highest persistence (Figure 2b).

Comparative rates of discontinuation

In the 2018–2020 cohort from Finland (i.e. main analysis), patients treated with guselkumab showed a lower rate of treatment discontinuation compared to adalimumab (adjusted hazard ratio [aHR] = 8.00, 95% CI: 4.33–14.77), apremilast (aHR = 4.81, 95% CI: 3.05–7.58), ixekizumab (aHR = 3.15, 95% CI: 1.84–5.37) and secukinumab (aHR = 3.81, 95% CI: 2.42–6.01); crude HRs and aHRs are available in Table 2. Ustekinumab and guselkumab had comparable rates of treatment discontinuation (Figure 3). Due to small sample size, Sweden was omitted from this analysis.

Estimated HRs indicated that the most relevant predictor of treatment discontinuation, apart from the study drug, was the number of dermatologist encounters within the 12 months prior to the index date. Greatest probability (HR = 1.41, 95% CI: 1.00–1.98) was observed for patients with >10 visits. All adjusted E-values of the point estimates (Table 2) were greater than the HR of that predictor. Given that none of the observed effects of study drugs (Table 2) could be explained by any individual observed confounder alone, we assess that it is unlikely that the effect sizes would be explained by unmeasured confounding.

The expanded cohort with treatment index during the period of 2008–2020 showed similar results; patients treated with guselkumab or ustekinumab showed a significantly lower rate of treatment discontinuation than those treated with adalimumab (Table S7A for Finland and Table S7B for Sweden and Figure S2).

Sensitivity analyses for treatment discontinuation rates using various grace periods (50% duration of the preceding drug supply, 90 days), or assuming maintenance therapy without induction, showed that the main and sensitivity analyses had comparable results for most of the therapies (Figure 4). Despite differences in the estimates, the overall statistical significance and the direction of the associations were consistent across analyses. However, when applying a grace period of 0 days, the association became statistically non-significant for patients treated with apremilast and ixekizumab.

DISCUSSION

This retrospective register-based cohort study described persistence for biologic drugs or apremilast in bio-naïve patients with moderate-to-severe PsO in Finland and Sweden. Results of the main analysis demonstrated that patients treated with guselkumab or ustekinumab had the highest persistence, defined as continued treatment for ≥1 year in Finland. In previous studies, guselkumab has also demonstrated high efficacy, safety and tolerance among patients with moderate-to-severe PsO.[15–17] The FINGUS study involving Finnish patients with moderate-to-severe PsO reported a persistence probability of 86% at 1 year with guselkumab treatment.[18] Similarly, high persistence probabilities ranging between 65% and 94% have been reported for guselkumab in several real-world studies with varying follow-up periods.[19–21] Recent studies in Europe have also reported positive results among patients treated

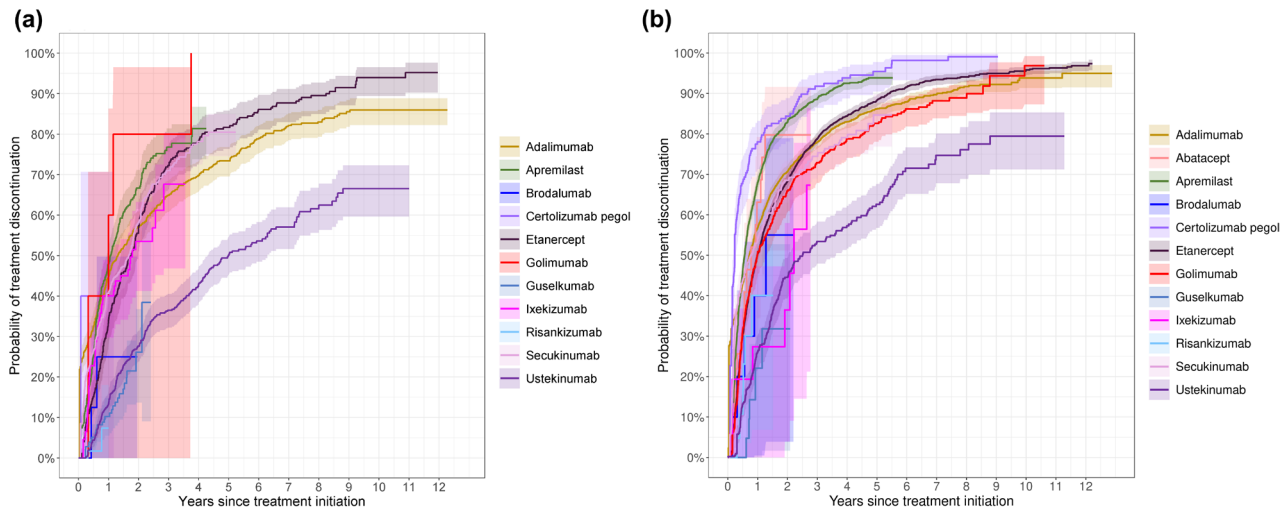


FIGURE 2 Unadjusted cumulative incidence estimates for treatment discontinuation by drug among bio-naïve patients with PsO in Finland and Sweden during 2008–2020[1]. (a) Treatment discontinuation in Finland. (b) Treatment discontinuation in Sweden. [1]Non-parametric crude cumulative incidence of treatment discontinuation with patient death as a competing risk.

TABLE 2 Results in Finland for discontinuation analysis, bio-naïve PsO, while guselkumab as a referent drug was used during 2018–2020.

Study drugs	Number of treatment discontinuations	Person-years	Incidence rate per 1 person-year (95% CI)	Crude HR (95% CI)	aHR[a] (95% CI)	Crude E-value (95% CI limit)	Adjusted E-value (95% CI limit)
Main analysis ($n = 709$ patients)							
Guselkumab	24	176.04	0.14 (0.09–0.20)	Reference level	Reference level	Reference level	Reference level
Adalimumab	31	35.40	0.88 (0.62–1.25)	6.53 (3.67–11.63)	8.00 (4.33–14.77)	6.45 (4.28)	7.37 (4.84)
Apremilast	144	251.75	0.57 (0.49–0.67)	4.22 (2.77–6.42)	4.81 (3.05–7.58)	4.74 (3.43)	5.22 (3.71)
Ixekizumab	34	86.35	0.39 (0.28–0.55)	2.99 (1.77–5.04)	3.15 (1.84–5.37)	3.65 (2.33)	3.80 (2.42)
Secukinumab	81	177.17	0.46 (0.37–0.57)	3.51 (2.25–5.46)	3.81 (2.42–6.01)	4.13 (2.89)	4.40 (3.07)
Ustekinumab	31	198.50	0.16 (0.11–0.22)	1.28 (0.76–2.15)	1.35 (0.80–2.29)	1.65 (1.00)	1.77 (1.00)
Sensitivity analysis with a grace period of 0 days ($n = 709$ patients)							
Guselkumab	113	41.86	2.70 (2.24–3.25)	Reference level	Reference level	Reference level	Reference level
Adalimumab	43	4.71	9.13 (6.77–12.31)	3.37 (1.88–6.02)	4.09 (2.33–7.18)	4.00 (2.47)	4.63 (2.97)
Apremilast	221	73.62	3.00 (2.63–3.43)	1.05 (0.82–1.35)	1.15 (0.87–1.53)	1.23 (1.00)	1.44 (1.00)
Ixekizumab	66	20.56	3.21 (2.52–4.09)	0.89 (0.70–1.13)	0.93 (0.72–1.19)	1.40 (1.00)	1.29 (1.00)
Secukinumab	131	27.83	4.71 (3.97–5.59)	1.73 (1.30–2.30)	1.90 (1.44–2.52)	2.28 (1.69)	2.49 (1.89)
Ustekinumab	102	28.97	3.52 (2.90–4.28)	1.08 (0.86–1.35)	1.10 (0.87–1.39)	1.28 (1.00)	1.34 (1.00)
Sensitivity analysis with a grace period of 90 days ($n = 709$ patients)							
Guselkumab	18	180.59	0.10 (0.06–0.16)	Reference level	Reference level	Reference level	Reference level
Adalimumab	25	54.28	0.46 (0.31–0.68)	4.85 (2.62–8.99)	6.17 (3.19–11.94)	5.24 (3.28)	6.20 (3.84)
Apremilast	139	275.82	0.50 (0.43–0.60)	5.20 (3.19–8.48)	5.72 (3.36–9.74)	5.51 (3.84)	5.89 (4.00)
Ixekizumab	24	108.79	0.22 (0.15–0.33)	2.26 (1.24–4.13)	2.43 (1.32–4.49)	2.90 (1.59)	3.09 (1.72)
Secukinumab	60	224.67	0.27 (0.21–0.34)	2.79 (1.66–4.68)	3.09 (1.82–5.25)	3.45 (2.19)	3.75 (2.39)
Ustekinumab	29	198.74	0.15 (0.10–0.21)	1.54 (0.85–2.78)	1.63 (0.89–2.99)	2.03 (1.00)	2.15 (1.00)
Sensitivity analysis with a grace period of 50% ($n = 709$ patients)							
Guselkumab	35	164.21	0.21 (0.15–0.30)	Reference level	Reference level	Reference level	Reference level
Adalimumab	34	30.40	1.12 (0.80–1.57)	5.12 (3.05–8.61)	6.07 (3.48–10.58)	5.45 (3.70)	6.13 (4.10)
Apremilast	160	220.31	0.73 (0.62–0.85)	3.31 (2.32–4.73)	3.74 (2.56–5.45)	3.95 (2.97)	4.33 (3.22)
Ixekizumab	45	70.42	0.64 (0.48–0.86)	3.01 (1.93–4.68)	3.29 (2.10–5.16)	3.67 (2.53)	3.94 (2.72)
Secukinumab	94	145.25	0.65 (0.53–0.79)	3.10 (2.11–4.53)	3.43 (2.32–5.07)	3.75 (2.74)	4.06 (2.97)
Ustekinumab	43	180.04	0.24 (0.18–0.32)	1.24 (0.81–1.91)	1.28 (0.83–1.98)	1.59 (1.00)	1.66 (1.00)
Sensitivity analysis assuming maintenance treatment without an initial induction treatment ($n = 709$ patients)							
Guselkumab	22	179.36	0.12 (0.08–0.19)	Reference level	Reference level	Reference level	Reference level
Adalimumab	27	48.28	0.56 (0.38–0.82)	4.72 (2.70–8.25)	5.80 (3.17–10.62)	5.14 (3.36)	5.94 (3.82)
Apremilast	144	251.75	0.57 (0.49–0.67)	4.86 (3.13–7.55)	5.57 (3.43–9.03)	5.25 (3.78)	5.78 (4.06)
Ixekizumab	30	99.17	0.30 (0.21–0.43)	2.54 (1.48–4.37)	2.66 (1.52–4.63)	3.20 (1.95)	3.32 (2.01)
Secukinumab	71	203.70	0.35 (0.28–0.44)	2.99 (1.88–4.74)	3.23 (2.01–5.21)	3.65 (2.47)	3.88 (2.62)
Ustekinumab	31	199.21	0.16 (0.11–0.22)	1.37 (0.80–2.35)	1.46 (0.84–2.53)	1.80 (1.00)	1.93 (1.00)

aHR, adjusted HR; CI, Confidence interval; HR, Hazard ratio; PsO, Psoriasis vulgaris.

[a]Covariates used for adjustment are listed in Table S3.

with ustekinumab and guselkumab. The French National Health Insurance Database study conducted using data from 16,545 bio-naïve patients with PsO treated with adalimumab, etanercept, infliximab or ustekinumab showed that ustekinumab had the highest 1 year persistence probability (85%).[22] These findings highlight the consistency and comparability of our results with those from other large-scale European registry-based studies. Furthermore, two prospective cohort studies of patients with PsO, which used data from the British Association of Dermatologists Biologics and Immunomodulators Register and Danish nationwide registries, reported that guselkumab had the highest drug survival rates among all biologics included in the study.[23] The US-based retrospective study by Fitzgerald et al. reported a higher persistence rate at 24 months for guselkumab compared with other biologics.[24]

Furthermore, our results showed that guselkumab had a lower treatment discontinuation rate compared to other

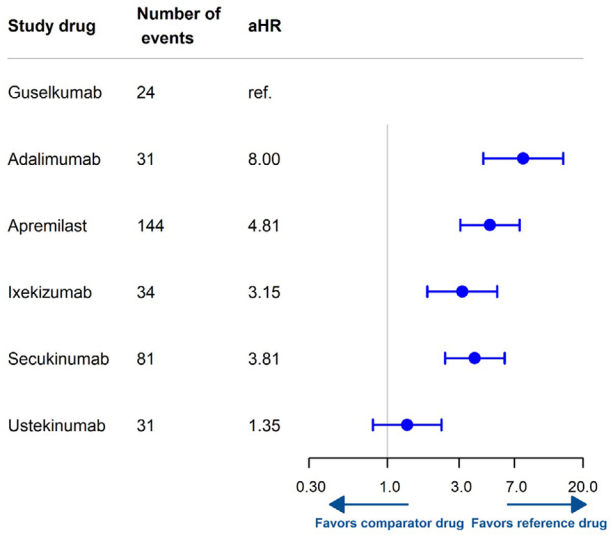


FIGURE 3 Adjusted hazard ratios for treatment discontinuation by drug among bio-naïve patients with PsO in Finland during 2018–2020.[1] aHR, adjusted Hazard ratio; PsO, Psoriasis vulgaris. [1]Patients with >20 observations at treatment initiation are shown in the graph. Adjustments used in the model are available in Methods section. Full HRs, CIs, unadjusted and adjusted, are provided in Table 2. CIs included 1, meaning that no clinically relevant differences were noted in comparative treatment discontinuation analysis, while study drug was compared to guselkumab.

biologic drugs in the main analysis, after accounting for the differences in baseline characteristics. These findings are consistent with results from other European registry-based studies demonstrating guselkumab's high persistency compared to other biologics, except ustekinumab.[11,25]

A major strength of our study is its robust design. Biases related to differences in drug availability and treatment practices over time and uncertainties regarding actual treatment discontinuation dates were accounted for by various sensitivity analyses, and the results remained aligned. Despite differences in the observed HRs, the overall statistical significance and direction of the associations were consistent across analyses, supporting our conclusions regarding the higher persistence of guselkumab compared to other biologic drugs or apremilast, and emphasizing the appropriateness of the main definitions, dosage assumptions and methods used in this study. The data included in this study were taken from comprehensive nationwide registers, encompassing the entire populations of Finland and Sweden.

Potential limitations of our study include potential bias due to unmeasured confounding, such as disease severity and drug use during hospitalizations. Attempts were made to reduce confounding through model adjustment for analyses for each country and inclusion of baseline measures of potential confounders in the statistical analyses. We also performed bias analyses using *E*-values and inferred that the likelihood of effect sizes explainable by unmeasured confounding was low but cannot be completely ruled out. Immortal time bias was minimal as the follow-up period began on the date of initiating drug use and not on the date of diagnosis. Also, all dispensations of study drugs for patients within the 24 months before the start of the study period were excluded. Furthermore, due to limited sample size, propensity score methods could not be applied. This increases the likelihood of errors in the estimation of effects due to model misspecification.

Lastly, the change in treatment targets from PASI 75 to PASI 90–100 with introduction of more efficacious therapies may have led to quicker discontinuation of less-effective therapies.[26–28]However, analyses for the 2018–2020 timeframe are less likely to be subject to this potential bias compared with the expanded 2008–2020 analyses.

Other potential limitations of the study pertain to information bias. The diagnosis of PsO was captured based on diagnostic codes, which are subject to differences in coding practices among physicians, regions and countries. In Finland, the Hospital Discharge Register data did not cover diagnoses obtained in the private healthcare sector, thereby indicating gaps in the diagnostic data. However, individuals having any encounters in a secondary care setting (e.g. outpatient and inpatient hospital care) during the period from 2008 to 2020 could be considered for this study. Furthermore, the registers did not contain information on inpatient drug use and therefore were unknown.[29] To reduce exposure uncertainty, follow-up was censored for long inpatient stays (>30 days). Also, the prescription registers did not specify indications for the study drugs, thereby raising the possibility of their use for conditions other than PsO, such as Crohn's disease or rheumatoid arthritis. However, in Finland, special reimbursement codes were utilized to identify use of study drugs specifically for the treatment of PsO. Furthermore, patients initiating study drugs that received marketing authorization relatively later compared to others (e.g. brodalumab, certolizumab pegol and risankizumab) were subject to more limited time for follow-up, resulting in insufficient numbers of patients for deriving meaningful conclusions from the analyses. Please note that tildrakizumab was not used in Finland and Sweden during the study period (2008–2020) because it was not available (in Sweden, tildrakizumab achieved reimbursement in November 2022 while in Finland, reimbursement was achieved in March 2023).

When considering the balance between efficacy and feasibility in treatment decisions, it is important to acknowledge that this compromise can impact the results when assessing treatment persistence. If doctors prioritize feasibility over efficacy in certain cases, such as opting for a treatment regimen that is more convenient for the patient but may have a slightly reduced immediate effect, it can influence the overall treatment persistence outcomes. Understanding this dynamic is crucial when analysing the long-term effectiveness and patient adherence to treatment plans, especially considering that some biologics, such as ustekinumab, are administered every 12th week, which could contribute to increased persistence rates for certain patient populations.

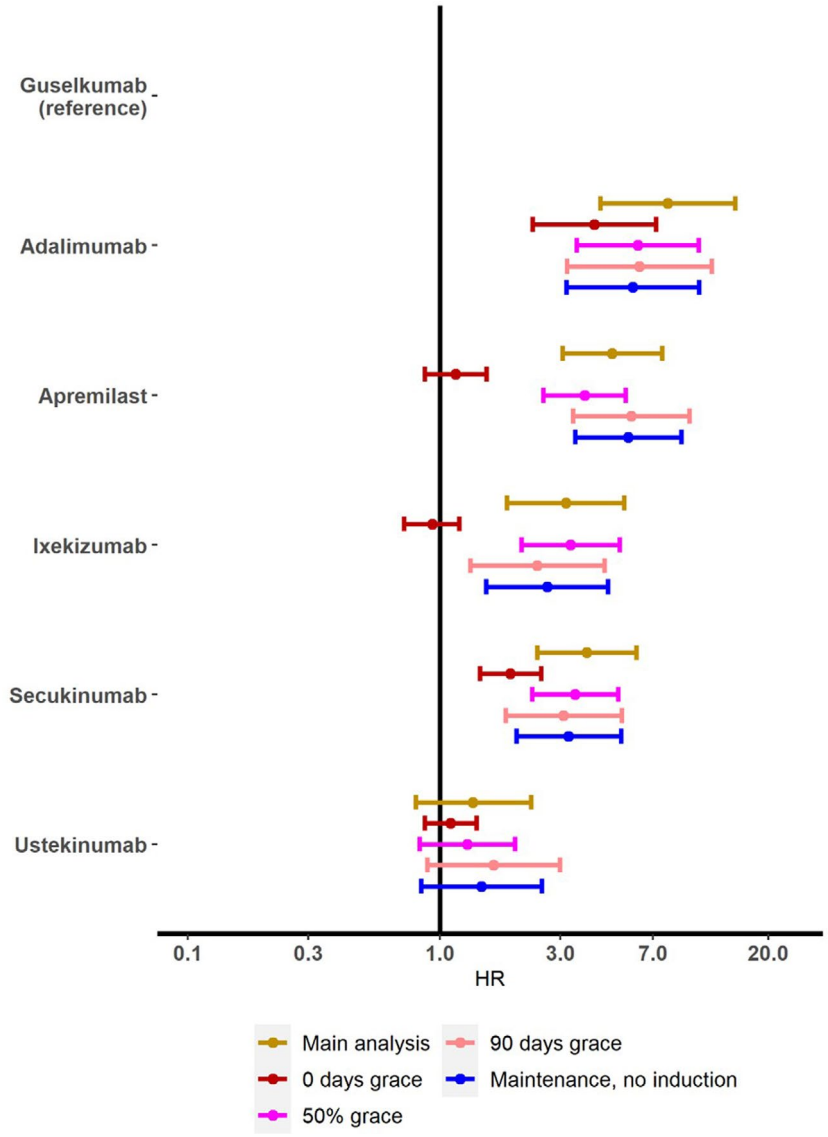


FIGURE 4 Sensitivity analysis for treatment discontinuation by drug among bio-naïve patients with PsO in Finland during 2018–2020.[1] aHR, adjusted Hazard ratio; PsO, Psoriasis vulgaris. [1]Patients with >20 observations at treatment initiation are shown in the graph. Adjustments used in the model are available in Methods section. Full HRs, CIs, unadjusted and adjusted, are provided in Table 2. The following grace periods were used: 0 days and 90 days and 50% duration of the preceding drug supply. CIs included 1, meaning that no clinically relevant differences were noted in comparative treatment discontinuation analysis, while study drug was compared to guselkumab.

CONCLUSIONS

The vast majority of patients treated with guselkumab and ustekinumab demonstrated high persistence as measured by continued treatment for at least 1 year. Furthermore, these therapies showed lower rates of discontinuation compared to other biologics or apremilast, in treating moderate-to-severe PsO during the study period, after adjusting for baseline characteristics. Although persistence may reflect a variety of parameters, these results support the notion that guselkumab and ustekinumab possess better effectiveness and tolerability compared to other biologic drugs in a real-world setting in Finland and Sweden. Nonetheless, further research on long-term persistence of biologic therapies in moderate-to-severe PsO is warranted to verify these results, especially if sample size limitations (which led to the exclusion of certain treatments) can be overcome with updated data.

ACKNOWLEDGEMENTS

We acknowledge and thank Elisabeth Björkqvist, Katja Hakkarainen, Juha Mehtälä and Leyla Nunez for their contribution in writing the study protocols and for their scientific contributions; Dhanya Mukundan and Suchitra Jagannathan for providing support with the medical writing and interpretation of the results; Matti Rantanen and Eric Beohou for their support in code development and code revisions; Saara Hetemäki for the data access coordination in Finland; Li Hantler and Susanna Jokinen for the data access coordination in Sweden; and Samron Brhane Gebregergish,

Nallely Ramirez-Solano and Fabian Mancera for project coordination and support during the study.

FUNDING INFORMATION

This study was funded by Janssen-Cilag Oy. The sponsor of the study could comment on the study design, interpretation of data, and the writing of the manuscript. However, the sponsor had no role in the data collection or analysis.

CONFLICT OF INTEREST STATEMENT

GT, KA, IS, UK, AW, FH and LS are/were employees of IQVIA, a company that performs commissioned pharmacoepidemiological studies for several pharmaceutical companies. CW, FH, JL, CH, IJ, AP and RN are/were employees of Janssen-Cilag. SP and TM are consultants of IQVIA to provide medical expertise.

DATA AVAILABILITY STATEMENT

The patient-level data that support the findings of this study are not available for third-party data vendors, due to public Nordic data legislation.

REFERENCES

1. Augustin M, Dauden E, Mrowietz U, Konstantinou MP, Gerdes S, Rissler M, et al. Baseline characteristics of patients with moderate-to-severe psoriasis according to previous systemic treatment exposure: the PROSE study population. J Eur Acad Dermatol Venereol. 2020;34(11):2548–56.
2. Banaszczyk K. Tildrakizumab in the treatment of psoriasis—literature review. Reumatologia. 2019;57(4):234–8.
3. Foundation NP. Psoriasis Statistics. 2023. Accessed on March 2023. Available at: https://www.psoriasis.org/psoriasis-statistics/ (last accessed 23 March 2023).
4. Damiani G, Bragazzi NL, Karimkhani Aksut C, Wu D, Alicandro G, McGonagle D, et al. The global, regional, and National Burden of psoriasis: results and insights from the global Burden of disease 2019 study. Front Med (Lausanne). 2021;8:743180.
5. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020;369:m1590.
6. Sawyer LM, Cornic L, Levin L, Gibbons C, Møller AH, Jemec GB. Long-term efficacy of novel therapies in moderate-to-severe plaque psoriasis: a systematic review and network meta-analysis of PASI response. J Eur Acad Dermatol Venereol. 2019;33(2):355–66.
7. Sbidian E, Chaimani A, Garcia-Doval I, Do G, Hua C, Mazaud C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2017;12(12):Cd011535.
8. Menter A, Papp KA, Gooderham M, Pariser DM, Augustin M, Kerdel FA, et al. Drug survival of biologic therapy in a large, disease-based registry of patients with psoriasis: results from the psoriasis longitudinal assessment and registry (PSOLAR). J Eur Acad Dermatol Venereol. 2016;30(7):1148–58.
9. Afra TP, Razmi TM, Dogra S. Apremilast in psoriasis and beyond: big hopes on a small molecule. Indian Dermatol Online J. 2019;10(1):1–12.
10. Gisondi P, Girolomoni G. Apremilast in the therapy of moderate-to-severe chronic plaque psoriasis. Drug Des Devel Ther. 2016;10:1763–70.
11. Yiu ZZN, Becher G, Kirby B, Laws P, Reynolds NJ, Smith CH, et al. Drug survival associated with effectiveness and safety of treatment with Guselkumab, Ixekizumab, Secukinumab, Ustekinumab, and adalimumab in patients with psoriasis. JAMA Dermatol. 2022;158(10):1131–41.
12. Warren RB, Smith CH, Yiu ZZN, Ashcroft DM, Barker JNWN, Burden AD, et al. Differential drug survival of biologic therapies for the treatment of psoriasis: a prospective observational cohort study from the British Association of Dermatologists biologic interventions register (BADBIR). J Invest Dermatol. 2015;135(11):2632–40.
13. Aalen OO, Johansen S. An empirical transition matrix for non-homogeneous Markov chains based on censored observations. Scand J Stat. 1978;5(3):141–50. http://www.jstor.org/stable/4615704
14. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. Ann Intern Med. 2017;167(4):268–74.
15. Bonifati C, Morrone A, Cristaudo A, Graceffa D. Effectiveness of anti-interleukin 23 biologic drugs in psoriasis patients who failed anti-interleukin 17 regimens. A real-life experience. Dermatol Ther. 2021;34(1):e14584.
16. Ruggiero A, Fabbrocini G, Cinelli E, Megna M. Efficacy and safety of guselkumab in psoriasis patients who failed ustekinumab and/or anti-interleukin-17 treatment: a real-life 52-week retrospective study. Dermatol Ther. 2021;34(1):e14673.
17. Megna M, Potestio L, Ruggiero A, Camela E, Fabbrocini G. Guselkumab is efficacious and safe in psoriasis patients who failed anti-IL17: a 52-week real-life study. J Dermatolog Treat. 2022;33(5):2560–4.
18. Mälkönen T, Nuutinen P, Hallinen T, Soini E, Nissinen R, Wennerstöm C, et al. Guselkumab treatment outcomes and persistence in a nationwide real-world cohort of patients with plaque psoriasis. Acta Derm Venereol. 2022;102:adv00631.
19. Xu C, Teeple A, Wu B, Fitzgerald T, Feldman SR. Treatment adherence and persistence of seven commonly prescribed biologics for moderate to severe psoriasis and psoriatic arthritis in a U.S. commercially insured population. J Dermatolog Treat. 2022;33(4):2270–7.
20. Torres T, Puig L, Vender R, Lynde C, Piaserico S, Carrascosa JM, et al. Drug survival of IL-12/23, IL-17 and IL-23 inhibitors for psoriasis treatment: a retrospective multi-country, multicentric cohort study. Am J Clin Dermatol. 2021;22(4):567–79. (In eng).
21. Ruiz-Villaverde R, Rodriguez-Fernandez-Freire L, Armario-Hita JC, Pérez-Gil A, Galán-Gutiérrez M. Guselkumab: mid-term effectiveness, drug survival, and safety in real clinical practice. Dermatol Ther. 2021;34(2):e14798.
22. Sbidian E, Mezzarobba M, Weill A, Coste J, Rudant J. Persistence of treatment with biologics for patients with psoriasis: a real-world analysis of 16 545 biologic-naïve patients from the French National Health Insurance database (SNIIRAM). Br J Dermatol. 2019;180(1):86–93.
23. Egeberg A, Rosenø NAL, Aagaard D, Lørup EH, Nielsen ML, Nymand L, et al. Drug survival of biologics and novel immunomodulators for rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis, and psoriasis - a nationwide cohort study from the DANBIO and DERMBIO registries. Semin Arthritis Rheum. 2022;53:151979. (In eng). https://doi.org/10.1016/j.semarthrit.2022.151979
24. Fitzgerald T, Zhdanava M, Pilon D, Shah A, Hilts A, Lefebvre P, et al. Long-term psoriasis control with Guselkumab, adalimumab, Secukinumab, or Ixekizumab in the USA. Dermatol Ther (Heidelb). 2023;13(4):1053–68.
25. Schmitt-Egenolf M, Freilich J, Stelmaszuk-Zadykowicz NM, Apol E, Hansen JB, Levin L. Drug persistence of biologic treatments in psoriasis: a Swedish National Population Study. Dermatol Ther (Heidelb). 2021;11(6):2107–21.
26. Nast A, Smith C, Spuls PI, Avila Valle G, Bata-Csörgö Z, Boonen H, et al. EuroGuiDerm guideline on the systemic treatment of psoriasis vulgaris—part 1: treatment and monitoring recommendations. J Eur Acad Dermatol Venereol. 2020;34(11):2461–98. (In eng). https://doi.org/10.1111/jdv.16915
27. Torres T, Puig L. Treatment goals for psoriasis: should PASI 90 become the standard of care? Actas Dermosifiliogr. 2015;106(3):155–7.

28. Choi S, Oh S, Yoon HS. Association between short-term PASI90 achievement and drug survival of biologics in patients with psoriasis. Ann Dermatol. 2022;34(3):173–81. (In eng). https://doi.org/10.5021/ad.2022.34.3.173
29. Furu K, Wettermark B, Andersen M, Martikainen JE, Almarsdottir AB, Sørensen HT. The Nordic countries as a cohort for pharmacoepidemiological research. Basic Clin Pharmacol Toxicol. 2010;106(2):86–94. (In eng). https://doi.org/10.1111/j.1742-7843.2009.00494.x

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Tskhvarashvili G, Aher K, Sveide I, Katus U, Westerlund A, Hoti F, et al. Persistence of advanced systemic pharmacological treatment of moderate-to-severe psoriasis among bio-naïve patients—A retrospective register-based cohort study in Finland and Sweden. J Eur Acad Dermatol Venereol. 2025;39(Suppl. 1):50–64. https://doi.org/10.1111/jdv.20198