Supplementary Material

The PROPER Study: A 48-Week, Pan-European, Real-World Study of Biosimilar SB5 Following Transition from Reference Adalimumab in Patients with Immune-Mediated Inflammatory Disease

Ulf Müller-Ladner[1] • Axel Dignass[2] • Karl Gaffney[3] • Deepak Jadon[4] • Marco Matucci-Cerinic[5,6] • Triana Lobaton[7] • Philippe Carron[8] • Javier P. Gisbert[9] • Ira Pande[10] • Maximilian Utzinger[11] • Janet Addison[12]

Correspondence:

Professor Ulf Müller-Ladner

Department of Rheumatology and Clinical Immunology

Justus-Liebig University Giessen

Campus Kerckhoff

Benekestr. 2–8

D-61231 Bad Nauheim

Germany

E-mail: u.mueller-ladner@kerckhoff-klinik.de

Telephone: + 49-6032-9962101

1. Supplementary Methods

1.1 Interim Analyses

Interim analyses have been presented in the form of abstracts and posters at international and national congresses as follows:

1) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. AB0311 The PROPER study: results of the first interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis. Ann Rheum Dis. 2020;79(suppl 1):1454-5.
2) Müller-Ladner U, Zinke S, Liebhaber A, Utzinger M, Addison J. The PROPER study: a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab; an interim analysis of patients from the German rheumatoid arthritis cohort [abstract]. German Society for Rheumatology. German Society for Orthopedic Rheumatology. German Rheumatology Congress 2020, 48th Congress of the German Society for Rheumatology (DGRh), 34th Annual Meeting of the German Society for Orthopedic Rheumatology (DGORh). Sept 9, 2020; sine loco [digital], Sept 9–12, 2020. Düsseldorf: German Medical Science GMS Publishing House; 2020. DocRA.46.
3) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. The PROPER study: results of the first interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis [abstract]. Arthritis Rheumatol. 2020;72(suppl 10).
4) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. The PROPER study: a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab; an interim analysis of patients from the German rheumatoid arthritis cohort. Poster presented at German Rheumatology Congress 2020, 48th Congress of the German Society for Rheumatology (DGRh), 34th Annual Meeting of the German Society for Orthopedic Rheumatology (DGORh); Sept 9–12, 2020; all-virtual.
5) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. The PROPER study: results of an interim analysis of a pan-EU real-world study of SB5 biosimilar

following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis, or psoriatic arthritis. Poster presented at the American College of Rheumatology Convergence 2020 Annual Meeting; 07 Nov 2020; all-virtual.

6) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. AB0204 The PROPER study: interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis, or psoriatic arthritis. Ann Rheum Dis. 2021;80(suppl 1):1126-7.

7) Dignass A, Gisbert JP, Schubert S, Ehelhalt R, Mohr CF, Freudensprung U, et al. The PROPER study: interim analysis of a pan-European real-world study of SB5 adalimumab biosimilar after transition from reference adalimumab in patients with Crohn's disease. Z Gastroenterol. 2021;59(08):e170-1.

8) Dignass A, Gisbert J, Freudensprung U, Addison J. P469 The PROPER study: interim analysis of a pan-European real-world study of SB5 adalimumab biosimilar after transition from reference adalimumab in patients with Crohn's disease. J Crohns Colitis. 2021;15(suppl 1):S459-60.

9) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. The PROPER study: results of the first 48-week interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis [abstract]. Arthritis Rheumatol. 2021;73(suppl 10).

10) Müller-Ladner U, Gaffney K, Jadon D, Freudensprung U, Addison J. The PROPER study: results of the first 48-week interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis. Poster presented at ACR Convergence 2021 Annual Meeting; 07 Nov 2021; all-virtual.

11) Dignass A, Gisbert J, Freudensprung U, Addison J. The PROPER study: interim analysis of a pan-European real-world study of SB5 adalimumab biosimilar after transition from reference adalimumab in patients with Crohn's disease. Poster presented at 16th Congress of ECCO; European Crohn's and Colitis Organisation; July 2–3 and 8–10, 2021; all-virtual.

12) Müller-Ladner U, Zinke S, Liebhaber A, Mohr C, Addison J. The PROPER study: interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients from the Germany rheumatoid arthritis or

psoriatic arthritis cohort. Poster presented at German Rheumatology Congress 2021, 49th Congress of the German Society for Rheumatology (DGRh), 35th Annual Meeting of the German Society for Orthopedic Rheumatology (DGORh); 15–18 Sep 2021; all-virtual.

13) Dignass AU, Gisbert JP, Bossa F, Freudensprung U, Addison J. P434 The PROPER study: interim analysis of a Pan-European real-world study of SB5 adalimumab biosimilar after transition from reference adalimumab in patients with Crohn's disease. J Crohns Colitis. 2022;16(suppl 1):i418.

14) Dignass AU, Gisbert JP, Bossa F, Freudensprung U, Addison J. The PROPER study: interim analysis of a pan-European real-world study of SB5 adalimumab biosimilar after transition from reference adalimumab in patients with Crohn's disease. Poster presented at 17th Congress of ECCO; European Crohn's and Colitis Organisation; 16–19, February 2022; all-virtual.

15) Müller-Ladner U, Gaffney K, Jadon D, Matucci-Cerinic M, Chamizo Carmona E, Freudensprung U, et al. AB0348 The PROPER study: a 48-week analysis of a PAN-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients with rheumatoid arthritis, axial spondyloarthritis or psoriatic arthritis. Ann Rheum Dis. 2022;81(suppl 1):1299-1300.

16) Müller-Ladner U, Gaffney K, Jadon D, Matucci-Cerinic M, Chamizo E, Addison J. The PROPER study: interim analysis of a pan-EU real-world study of SB5 biosimilar following transition from reference adalimumab in patients from the Germany rheumatoid arthritis or psoriatic arthritis cohort. Poster presented at German Rheumatology Congress 2022, 50th Congress of the German Society for Rheumatology (DGRh), 36th Annual Meeting of the German Society for Orthopedic Rheumatology (DGORh), 32nd Annual Meeting of the Society for Child and Adolescent Rheumatology (GKJR); Aug 31 to Sept 3, 2022; Berlin.

1.2 Disease Activity and Patient-Reported Outcome Measures

Table S1 Disease activity measures, scores, and indications

Disease activity measure	Summary of questionnaire design	Clinical status: score thresholds	Possible scores	Indication
DAS28-CRP$_{conv}$	The DAS28-CRP and DAS28-ESR comprise four components: number of swollen joints, number of tender joints, CPR or ESR level, and patient assessment of activity of disease. The total score is calculated. A converted DAS28-CRP was derived using the following conversion factor from DAS28-ESR: DAS28-CRP$_{conv}$=1.1953e$^{0.2487(DAS28-ESR)}$[1]	Remission: ≤ 2.4 Low activity: > 2.4–2.9 Moderate activity: > 2.9–4.6 High activity: > 4.6	0–9.8[a]	RA PsA (German patients)
BASDAI	The BASDAI comprises six questions (fatigue, pain, swelling, discomfort, stiffness severity, and duration). Responses are on a 10-cm VAS, where 0 cm is the least and 10 cm denotes the most possible symptoms. The total score was determined by: BASDAI = {(Q1+Q2+Q3+Q4) + ([Q5+ Q6]/2)}/5	Low disease activity < 4	0–10[a]	axSpA
FFbH	A Germany-specific questionnaire comprising 18 items focusing on the ability to perform activities of daily living (e.g., writing by hand or sitting on an unpadded chair for 1 hour). There are three possible responses: “Yes” (2 points), “with difficulty” (1 point), and “no or only with outside help” (0 points). The points of all questions are summed, multiplied by 100, and then divided by the maximum score. The resulting percentage describes the functional capacity of the patient[c]	–	0–100[b]	RA
HBI	A questionnaire comprising five components focusing on: (1) patient well-being (0–4 points); (2) abdominal pain (0–3 points); (3) number of liquid or soft stools (1–25 points); (4) abdominal mass (0–3 points); (5) complications (0–8 points); for all questions the lowest number represents the best possible condition. The total score is calculated by summing the scores of all five parameters	Remission: < 5 Mild activity: 5–7 Moderate activity: 8–16 Severe activity: > 16	0–43[a]	CD
PsARC	Four items: swollen joints, tender joints, and Patient Global Assessment and Physician Global Assessment of disease activity. Responses involved counting (separately) the number of swollen joints (from 66 joints) and tender joints (from 68 joints), and assessing patient perception of their disease state on a 5-point Likert scale from 0 (best possible condition) to 5 (worst possible condition). Only the SJC and TJC were used in this analysis[d]	Inactive disease: SJC < 3 or TJC < 3 (both scores must be available) Active disease: SJC of ≥3 TJC of ≥3	SJC: 0–66[a] TJC: 0–68[a]	PsA
PMS	Three items: stool frequency (0–3), rectal bleeding (0–3), and Physician Global Assessment (0–3). The total score was calculated by summing the scores of all three parameters	Remission: < 2 Mild activity: 2–4 Moderate activity: 5–7 Severe activity: > 7	0–9[a]	UC

axSpA axial spondyloarthritis, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *CD* Crohn’s disease, DAS28-*CRP* Disease Activity Score in 28 joints using C-reactive protein, *DAS28-CRP$_{conv}$* Disease Activity Score in 28 joints using C-reactive protein converted from the Disease Activity Score in 28 joints using erythrocyte sedimentation rate, *DAS28-ESR* Disease Activity Score in 28 joints using erythrocyte sedimentation rate, *FFbH* Funktionsfragebogen Hannover, *HBI* Harvey-Bradshaw Index, *PMS* partial Mayo score, *PsA* psoriatic arthritis, *PsARC* Psoriatic Arthritis Response Criteria, *Q* question, RA rheumatoid arthritis, *SJC* swollen joint count, *TJC* tender joint count, *UC* ulcerative colitis, *VAS* visual analog scale

[a] Lower scores indicate less active disease. [b] Higher scores indicate less active disease. [c] Only functional capacity was captured. [d] Joint counts were used to evaluate candidate predictors at baseline, and while PsARC Physician and Patient Global Assessment scores of disease activity were collected, it is not customary to produce a single composite score for PsARC

Table S2 Patient satisfaction and patient-reported outcome measures, scores, and indications

PROM	Summary of questionnaire design	Possible scores	Indication
PSQ	Comprised three general (SB5 administration-device-independent) questions and four device-specific questions (three for the pen and one for the syringe), with responses recorded on a 5-point Likert scale, from 0 "very dissatisfied, very difficult, or very unclear" to 4 "very satisfied, very simple, or very clear":[a] (1) Ease of administration of the injection (2) Ease of holding the device (3) Duration of the injection (4) Device Pre-filled pen a. Injection without additional pressing of a button b. Clarity of acoustic signals (click) c. Indication of completed injection Pre-filled syringe a. Ease of using the plunger	–	RA, axSpA, PsA, CD, and UC
HAQ-DI	Eight sections, with two or three questions per section: dressing and grooming, arising, eating, walking, hygiene, reach, grip, activities. Scoring is on a scale of 0 (without any difficulty) to 3 (unable to do). The assigned scores for each of the eight sections (i.e., the worst score) are summed and divided by 8	0–3[b]	RA, axSpA, and PsA
BASFI	Ten questions: putting on socks, bending forward, reaching up, getting up from an armless chair, getting up off the floor, standing unsupported, climbing 12–15 steps, looking over the shoulder, doing physically demanding activities, doing a full day of activities. Responses are on a scale ranging from 0 (no limitation) to 10 (maximal limitation in function). The final score is the average of all questions	0–10[b]	axSpA
IBD-Control-8 **IBD-Control VAS score**	The IBD-Control comprises five categories with 14 questions: IBD well controlled (Q1a), treatment is useful in controlling (Q1b), change in bowel symptoms (Q2a), missing planned activities (Q3a), night symptoms (Q3b), pain or discomfort (Q3c), energy and fatigue (Q3d), anxiety or depressed (Q3e), change of treatment (Q3f), discuss alternate types of drugs (Q4a), discuss ways to adjust own treatment (Q4b), discuss side effects (Q4c), discuss newly occurred symptoms (Q4d), overall control of IBD (Q5). Each question within categories 1, 3, and 4 is answered by yes/not sure/no. For analysis, the best possible answer corresponded to 2 points, not sure corresponded to 1 point, and the worst possible answer corresponded to 0 points. For category 3, the possible answers ware better/no change/worse. Q5 is scored on a VAS, from 0 (worst possible control) to 100 (best possible control). The IBD-Control-8 sub-score was calculated by summing up the scores of questions Q1a, Q1b, Q3a, Q3b, Q3c, Q3d, Q3e, and Q3f. The resulting sub-score ranged from 0 to 16 (0 = worst control). Only the IBD-Control-8 sub-score and the IBD-Control VAS score were analyzed	IBD-Control-8: 0–16[c] IBD-Control VAS score: 0–100[c]	CD and UC

axSpA axial spondyloarthritis, *BASFI* Bath Ankylosing Spondylarthritis Functional Index, *CD* Crohn's disease, *HAQ-DI* Health Disability Questionnaire–Disability Index, *IBD* inflammatory bowel disease, *IBD-Control(-8)* Inflammatory Bowel Disease – Control Questionnaire (eight-question sub-score), *PROM* patient-reported outcome measure, *PsA* psoriatic arthritis, *PSQ* Patient Satisfaction Questionnaire, *RA* rheumatoid arthritis, *VAS* visual analog scale, *UC* ulcerative colitis

[a] Some data may be presented using a condensed, 3-point Likert scale, where 0 = "very dissatisfied or dissatisfied", "very difficult or difficult", or "very unclear or unclear"; 1 = "neutral"; 2 = "very satisfied or satisfied", "very simple or simple", or "very clear or clear". [b] Lower scores indicate better outcomes (ie, lower level of functional impairment). [c] Higher scores indicate better outcomes (ie, lower level of functional impairment)

Table S3 Criteria used to define SAEs, a causal relationship of AEs to SB5, and the severity of AEs

	Defining Criteria
SAEs	An SAE was defined as any untoward medical occurrence that at any dose: • Resulted in death • In the view of the investigator, placed the subject at immediate risk of death (a life-threatening event), not including an event that, had it occurred in a more severe form, might have caused death • Required inpatient hospitalization or prolongation of existing hospitalization • Resulted in persistent or significant disability/incapacity • Resulted in a congenital anomaly/birth defect • Was a medically important event, defined as an AE that, in the opinion of the investigator may have jeopardized the subject or required intervention to prevent one of the other listed outcomes (e.g., allergic bronchospasm requiring intensive treatment in an emergency room or convulsions occurring at home that did not require inpatient hospitalization)
Relatedness of AEs to SB5	• Relatedness was decided by the study physician
Severity of AEs	*Mild:* Symptom(s) barely noticeable to patient or does not make patient uncomfortable; does not influence performance or functioning; prescription drug not ordinarily needed for relief of symptom(s) but may be given because of personality of patient *Moderate:* Symptom(s) of a sufficient severity to make subject uncomfortable; performance of daily activity is influenced; subject is able to continue in study; treatment for symptom(s) may be needed *Severe:* Symptom(s) cause severe discomfort; symptoms cause incapacitation or significant impact on patient's daily life; severity may cause cessation of study treatment; treatment for symptom(s) may be given and/or patient hospitalized

AE adverse event, *SAE* serious adverse event

1.3 Determination of the Sample Size

Sample size scenarios were calculated for each indication cohort (rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis, Crohn's disease, and ulcerative colitis). A basic clinical prediction model was established for the primary outcome "evaluation of candidate predictors of persistence on SB5", for each cohort. Reliable estimates required a sufficient number of events per candidate predictor. A Cox regression model was built assuming the need for a minimum of 10 events per candidate predictor variable. For the sample size scenarios shown in **Table S4**, the event is defined as "SB5 discontinuation within the 48 weeks follow-up time of this study". Patients not having experienced the event were assumed to have remained on SB5 throughout the study.

Table S4 Sample size scenarios

Scenario	Sample size (*N*)	Event rate of an endpoint	Events of an endpoint (*n*)	Events per candidate predictor variable (*n*)	Candidate predictor variable (*n*)
#1	100	10%	10	10	1
#2[a]		20%	20		2
#3	200	10%	20	10	2
#4		20%	40		4
#5	300	10%	30	10	3
#6		20%	60		6
#7	400	10%	40	10	4
#8		20%	80		8

[a] Scenario #2 indicates that in establishing two predictors, at least 20 events (in total) were needed

2. Supplementary Results

2.1 Supplementary Tables

Table S5 Absolute disease activity and PROM scores over time

Indication	Disease activity measure/PROM	*n*	Mean ± SD	Median	95% CI
RA	DAS28-CRP_{conv}				
	Baseline	191	2.4 ± 0.8	2.3	2.3–2.5
	Week 12	128	2.5 ± 0.7	2.4	2.4–2.6
	Week 24	133	2.5 ± 0.8	2.4	2.3–2.6
	Week 48	154	2.4 ± 0.8	2.3	2.3–2.6
	FFbH				
	Baseline	41	78.0 ± 20.9	81.0	71.4–84.7
	Week 12	44	78.9 ± 19.4	83.5	73.0–84.8
	Week 24	42	75.4 ± 22.7	79.5	68.3–82.4
	Week 48	63	73.5 ± 21.9	81.0	68.0–79.0
	HAQ-DI				
	Baseline	49	0.8 ± 0.7	1.0	0.6–1.0
	Week 12	45	0.8 ± 0.7	1.0	0.6–1.0
	Week 24	47	0.8 ± 0.7	0.6	0.6–1.0
	Week 48	58	0.8 ± 0.7	0.8	0.6–1.0
axSpA	BASDAI				
	Baseline	116	2.7 ± 1.8	2.4	2.3–3.0
	Week 12	38	3.8 ± 1.7	3.9	3.2–4.3
	Week 24	49	3.3 ± 2.3	2.8	2.7–4.0
	Week 48	59	2.6 ± 1.8	2.3	2.1–3.1
	BASFI				
	Baseline	47	3.4 ± 2.5	3.2	2.6–4.1
	Week 12	20	3.7 ± 2.5	3.0	2.5–4.8
	Week 24	22	3.7 ± 2.2	3.6	2.7–4.6
	Week 48	20	3.5 ± 2.4	4.0	2.3–4.6
PsA	PsARC (swollen joint score)				
	Baseline	131	0.6 ± 1.4	0	0.3–0.8
	Week 12	46	0.7 ± 1.5	0	0.2–1.2
	Week 24	58	1.0 ± 3.2	0	0.2–1.8
	Week 48	63	0.7 ± 1.8	0	0.3–1.2
	PsARC (tender joint score)				
	Baseline	131	1.6 ± 3.9	0	1.0–2.3
	Week 12	46	1.7 ± 3.4	0	0.7–2.7
	Week 24	58	3.2 ± 7.8	0	1.1–5.2
	Week 48	63	1.1 ± 2.0	0	0.6–1.6
	HAQ-DI				
	Baseline	60	0.6 ± 0.7	0.4	0.4–0.8
	Week 12	28	0.6 ± 0.7	0.3	0.3–0.9
	Week 24	30	0.5 ± 0.6	0.3	0.3–0.7
	Week 48	39	0.6 ± 0.6	0.4	0.4–0.7
CD	HBI				
	Baseline	430	2.4 ± 2.7	2.0	2.1–2.6
	Week 12	240	2.5 ± 3.6	2.0	2.1–3.0
	Week 24	268	2.6 ± 3.3	2.0	2.2–3.0
	Week 48	289	2.4 ± 2.8	2.0	2.0–2.7
	IBD-Control (VAS)				
	Baseline	117	85.0 ± 16.7	90.0	81.9–88.1
	Week 12	79	80.9 ± 18.8	85.0	76.7–85.1
	Week 24	92	83.8 ± 15.7	85.0	80.5–87.0
	Week 48	90	78.2 ± 22.1	80.5	73.6–82.9
	IBD-Control-8				
	Baseline	120	13.3 ± 3.5	14.0	12.6–13.9
	Week 12	78	12.2 ± 4.5	14.0	11.2–13.2
	Week 24	93	12.8 ± 3.3	14.0	12.1–13.5
	Week 48	89	12.2 ± 3.6	14.0	11.5–13.0
UC	PMS				
	Baseline	12	1.3 ± 1.6	0.5	0.2–2.3
	Week 12	3	0.7 ± 1.2	0.0	–2.2 to 3.5
	Week 24	2	1.0 ± 0.0	1.0	–
	Week 48	6	0.7 ± 0.8	0.5	–0.2 to 1.5

axSpA axial spondyloarthritis, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BASFI* Bath Ankylosing Spondylarthritis Functional Index, *CD* Crohn's disease, *CI* confidence interval, *DAS28-CRP_{conv}* Disease Activity Score in 28 joints using C-reactive protein converted from Disease Activity Score in 28 joints using erythrocyte sedimentation rate, *FFbH* Funktionsfragebogen Hannover, *HAQ-DI* Health Disability Questionnaire–Disability Index, *HBI* Harvey-Bradshaw Index, *IBD-Control(-8)* Inflammatory Bowel Disease – Control Questionnaire (eight-question subscore), *PMS* partial Mayo score, *PROM* patient-reported outcome measure, *PsA* psoriatic arthritis, *PsARC* Psoriatic Arthritis Response Criteria, *RA* rheumatoid arthritis, *SD* standard deviation, *UC* ulcerative colitis, *VAS*, visual analog scale

Table S6 SB5 dosing regimen at baseline and Week 48

	RA *N* = 207	axSpA *N* = 127	PsA *N* = 162	CD *N* = 447	UC *N* = 12
Dose frequency, *n* (%)					
Baseline					
40 mg Q2W	138 (67.0)	110 (86.6)	148 (91.4)	315 (70.8)	6 (50.0)
40 mg QW	0	0	0	45 (10.1)	3 (25.0)
40 mg other	45 (21.8)	7 (5.5)	8 (4.9)	36 (8.1)	1 (8.3)
Week 48					
40 mg Q2W	132 (72.5)	93 (87.7)	125 (91.9)	247 (72.6)	4 (57.1)
40 mg QW	1 (0.5)	1 (0.9)	2 (1.5)	58 (17.1)	2 (28.6)
40 mg other	47 (25.8)	11 (10.4)	8 (5.9)	30 (8.8)	1 (14.3)

axSpA axial spondyloarthritis, *CD* Crohn's disease, *PsA* psoriatic arthritis, *Q2W*, once every 2 weeks, *QW,* once weekly, *RA* rheumatoid arthritis, *UC* ulcerative colitis

Table S7 Patient status at the end of the study (Week 48)

	Indication					
	RA	**axSpA**	**PsA**	**CD**	**UC**	**Total**
	***n* = 207**	***n* = 127**	***n* = 162**	***n* = 447**	***n* = 12**	***N* = 955**
Reason for study withdrawal, n (%)	3 (1.4)	0	6 (3.7)	14 (3.1)	0	23 (2.4)
Lost to follow-up	2 (1.0)	0	3 (1.9)	3 (0.7)	0	8 (0.8)
Physician decision	0	0	1 (0.6)	4 (0.9)	0	5 (0.5)
Patient withdrew consent	0	0	1 (0.6)	2 (0.4)	0	3 (0.3)
Patient death	0	0	0	0	0	0
Other	1 (0.5)	0	1 (0.6)	5 (1.1)	0	7 (0.7)
Patients completed Week 48, n (%)	204 (98.6)	127 (100)	156 (96.3)	433 (96.9)	12 (100)	932 (97.6)
Reason for SB5 discontinuation, n (%)	38 (18.4)	27 (21.3)	34 (21.0)	128 (28.6)	6 (50.0)	233 (24.4)
Adverse event[a]	12 (5.8)	6 (4.7)	10 (6.2)	51 (11.4)	0	79 (8.3)
Patient decision	4 (1.9)	3 (2.4)	5 (3.1)	34 (7.6)	1 (8.3)	47 (4.9)
Physician decision	4 (1.9)	6 (4.7)	1 (0.6)	27 (6.0)	2 (16.7)	40 (4.2)
Secondary loss of response	5 (2.4)	3 (2.4)	10 (6.2)	6 (1.3)	1 (8.3)	25 (2.6)
Cost	6 (2.9)	0	0	0	0	6 (0.6)
Mandated by health authority/payer	0	3 (2.4)	1 (0.6)	0	0	4 (0.4)
Other	7 (3.4)	6 (4.7)	7 (4.3)	10 (2.2)	2 (16.7)	32 (3.4)
SB5 ongoing at Week 48, n %)	169 (81.6)	100 (78.7)	128 (79.0)	319 (71.4)	6 (50.0)	722 (75.6)

axSpA axial spondyloarthritis, *CD* Crohn's disease, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis, *UC* ulcerative colitis

[a] The most common adverse event causing SB5 discontinuation was injection-site reaction (n=66, 6.9%)

Table S8 Change from baseline in PROMs (total scores) over time in patients with RA, axSpA, PsA, and CD

Indication (PROM)	Timepoint	*n*	Mean ± SD[a]	Median	95% CI[a]
RA (HAQ-DI)	Week 12	37	–0.02 ± 0.29	0	–0.12 to 0.08
	Week 24	35	0.09 ± 0.39	0.13	–0.05 to 0.22
	Week 48	34	0.10 ± 0.46	0.06	–0.06 to 0.27
axSpA (BASFI)	Week 12	11	0.43 ± 1.19	0.30	–0.37 to 1.23
	Week 24	13	0.34 ± 1.50	0.30	–0.57 to 1.25
	Week 48	13	–0.04 ± 1.49	0.40	–0.94 to 0.86
PsA (HAQ-DI)	Week 12	19	0.07 ± 0.21	0	–0.04 to 0.17
	Week 24	23	0.08 ± 0.28	0	–0.04 to 0.20
	Week 48	34	–0.02 ± 0.38	0	–0.15 to 0.12
CD (IBD-Control [VAS])	Week 12	68	–0.8 ± 14.2	0	–4.2 to 2.6
	Week 24	73	0.3 ± 17.2	0	–3.7 to 4.3
	Week 48	60	–2.6 ± 18.7	0	–7.5 to 2.2

axSpA axial spondyloarthritis, *BASFI* Bath Ankylosing Spondylarthritis Functional Index, *CD* Crohn's disease, *CI* confidence interval, *HAQ-DI* Health Disability Questionnaire–Disability Index, *IBD-Control* Inflammatory Bowel Disease – Control Questionnaire, *PROM* patient-reported outcome measure, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis, *SD* standard deviation, *VAS* visual analog scale

[a] Where available, data are cited to two decimal places to avoid rounding of some numbers to "0.0"

Table S9 SAEs by high-level term and causality

Indication[a]	High-level term	Related to SB5	Events (*n*)
RA (*n* = 207)	Abdominal and GI infections	No	1
	Coronary artery disorders NEC	No	1
	Coronavirus infections	No	1
	Depressive disorders	No	1
	Lower respiratory tract and lung infections	No	1
	Paresthesias and dysesthesias	No	1
	Parvoviral infections	No	1
	Herpes viral infections	Yes	1
	Lower respiratory tract and lung infections	Yes	1
		Total	9
axSpA (*n* = 127)	CNS hemorrhages and cerebrovascular accidents	No	1
	Supraventricular arrhythmias	No	1
		Total	2
PsA (*n* = 162)	Breast and nipple neoplasms malignant	No	1
	Cholecystitis and cholelithiasis	No	1
	Coronavirus infections	No	1
	Ischemic coronary artery disorders	No	2
	Motor neuron diseases	No	2
	Non-site-specific injuries NEC	No	1
	Breathing abnormalities	Yes	1
		Total	9
CD (*n* = 447)	Anemias NEC	No	1
	Anal and rectal stenosis and obstruction	No	1
	Aortic valvular disorders	No	1
	Colitis (excluding infective)	No	2
	Depressive disorders	No	1
	Duodenal and small intestinal stenosis and obstruction	No	2
	GI and abdominal pains (excluding oral and throat)	No	1
	GI fistulae	No	1
	GI stenosis and obstruction NEC	No	1
	General nutritional disorders NEC	No	1
	Infections NEC	No	1
	Intervertebral disc disorders NEC	No	1
	Ischemic coronary artery disorders	No	1
	Large intestinal stenosis and obstruction	No	1
	Menstruation and uterine bleeding NEC	No	1
	Non-site-specific procedural complications	No	1
	Esophageal ulcers and perforation	No	1
	Psychiatric symptoms NEC	No	1
	Skin and subcutaneous tissue ulcerations	No	1
	Suicidal and self-injurious behavior	No	1
	Thyroid disorders NEC	No	1
	Abdominal and GI infections	Yes	1
	GI fistulae	Yes	1
	GI stenosis and obstruction NEC	Yes	1
	Supraventricular arrhythmias	Yes	1
		Total	27

axSpA axial spondyloarthritis, *CD* Crohn's disease, *CNS*, central nervous system, *GI* gastrointestinal, *NEC* not elsewhere classified, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis, *SAE* serious adverse event

[a] There were no SAEs in the ulcerative colitis cohort

Table S10 Patient satisfaction with data from a condensed, 3-point Likert scale

Patient satisfaction factor	PSQ responses at baseline and Week 48[a]	Indication				
		RA, *n* (%)	axSpA, *n* (%)	PsA, *n* (%)	CD, *n* (%)	UC, *n* (%)
Ease of administration of the injection	Baseline					
	Very difficult or difficult	3 (16.7)	0	4 (20.0)	26 (16.3)	0
	Neutral	5 (27.8)	1 (16.7)	0	25 (15.6)	0
	Simple or very simple	10 (55.6)	5 (83.3)	16 (80.0)	109 (68.1)	0
	Week 48					
	Very difficult or difficult	19 (13.1)	15 (18.3)	13 (16.3)	32 (11.8)	3 (60.0)
	Neutral	29 (20.0)	13 (15.9)	4 (5.0)	49 (18.1)	0
	Simple or very simple	97 (66.9)	54 (65.9)	63 (78.8)	190 (70.1)	2 (40.0)
Ease of holding the device	Baseline					
	Very difficult or difficult	3 (16.7)	0	2 (10.0)	28 (17.5)	0
	Neutral	4 (22.2)	2 (28.6)	1 (5.0)	27 (16.9)	0
	Simple or very simple	11 (61.1)	5 (71.4)	17 (85.0)	105 (65.6)	0
	Week 48					
	Very difficult or difficult	17 (11.8)	5 (6.2)	10 (12.5)	27 (10.0)	2 (40.0)
	Neutral	34 (23.6)	16 (19.8)	5 (6.3)	43 (15.9)	0
	Simple or very simple	93 (64.6)	60 (74.1)	65 (81.3)	200 (74.1)	3 (60.0)
Duration of the injection	Baseline					
	Very dissatisfied or dissatisfied	2 (11.1)	1 (16.7)	3 (15.0)	21 (13.1)	0
	Neutral	6 (33.3)	2 (33.3)	2 (10.0)	35 (21.9)	0
	Satisfied or very satisfied	10 (55.6)	3 (50.0)	15 (75.0)	104 (65.0)	0
	Week 48					
	Very dissatisfied or dissatisfied	18 (12.5)	7 (8.5)	11 (13.8)	37 (13.7)	2 (40.0)
	Neutral	31 (21.5)	18 (22.0)	15 (18.8)	63 (23.3)	2 (40.0)
	Satisfied or very satisfied	95 (66.0)	57 (69.5)	54 (67.5)	170 (63.0)	1 (20.0)
Device	Baseline					
	Pen	13 (72.2)	5 (71.4)	19 (95.0)	128 (80.0)	0
	Syringe	5 (27.8)	2 (28.6)	1 (5.0)	32 (20.0)	0
	Week 48					
	Pen	115 (79.3)	73 (89.0)	71 (88.8)	232 (86.6)	5 (100)
	Syringe	30 (20.7)	9 (11.0)	9 (11.3)	36 (13.4)	0
Injection without additional pressing of a button (pen only)	Baseline					
	Very dissatisfied or dissatisfied	1 (7.7)	1 (25.0)	4 (21.1)	38 (29.7)	0
	Neutral	5 (38.5)	1 (25.0)	0	26 (20.3)	0
	Satisfied or very satisfied	7 (53.8)	2 (50.0)	15 (78.9)	64 (50.0)	0
	Week 48					
	Very dissatisfied or dissatisfied	22 (19.1)	22 (30.6)	15 (21.4)	54 (23.4)	2 (40.0)
	Neutral	24 (20.9)	7 (9.7)	11 (15.7)	43 (18.6)	1 (20.0)
	Satisfied or very satisfied	69 (60.0)	43 (59.7)	44 (62.9)	134 (58.0)	2 (40.0)

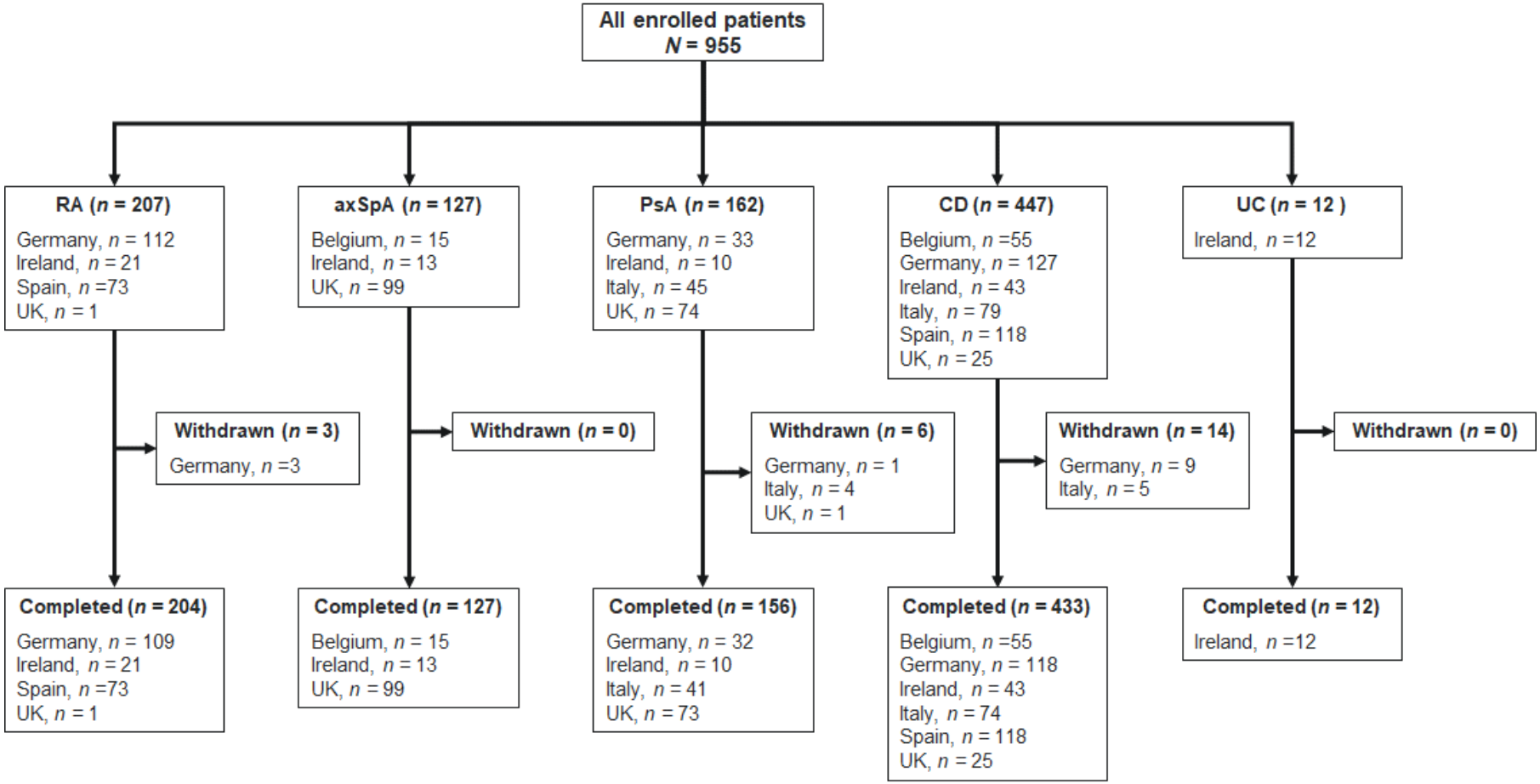
Clarity of acoustic (click) signals (pen only)	Baseline					
	Very unclear or unclear	1 (7.7)	0	0	6 (4.7)	0
	Neutral	5 (38.5)	0	1 (5.3)	16 (12.5)	0
	Clear or very clear	7 (53.8)	5 (100.0)	18 (94.7)	106 (82.8)	0
	Week 48					
	Very unclear or unclear	7 (6.1)	6 (8.2)	3 (4.2)	16 (6.9)	3 (60.0)
	Neutral	27 (23.5)	6 (8.2)	3 (4.2)	29 (12.6)	0
	Clear or very clear	81 (70.4)	61 (83.6)	65 (91.5)	186 (80.5)	2 (40.0)
Indication of completed injection (pen only)	Baseline					
	Very unclear or unclear	1 (7.7)	0	0	6 (4.7)	0
	Neutral	3 (23.1)	0	1 (5.6)	11 (8.6)	0
	Clear or very clear	9 (69.2)	5 (100.0)	17 (94.4)	111 (86.7)	0
	Week 48					
	Very unclear or unclear	6 (5.2)	5 (6.9)	3 (4.2)	18 (7.8)	3 (60.0)
	Neutral	25 (21.7)	4 (5.6)	7 (9.9)	29 (12.6)	0
	Clear or very clear	84 (73.0)	63 (87.5)	61 (85.9)	183 (79.6)	2 (40.0)
Ease of using the plunger (syringe only)	Baseline					
	Very difficult or difficult	0	0	1 (100.0)	7 (21.9)	0
	Neutral	1 (20.0)	0	0	6 (18.8)	0
	Simple or very simple	4 (80.0)	2 (100.0)	0	19 (59.4)	0
	Week 48					
	Very difficult or difficult	6 (20.0)	0	4 (44.4)	5 (13.9)	0
	Neutral	5 (16.7)	3 (33.3)	0	4 (11.1)	0
	Simple or very simple	19 (63.3)	6 (66.7)	5 (55.6)	27 (75.0)	0

axSpA axial spondyloarthritis, *CD* Crohn's disease, *PsA* psoriatic arthritis, *PSQ* Patient Satisfaction Questionnaire, *RA* rheumatoid arthritis, *UC* ulcerative colitis

[a] Although data were collected using a 5-point Likert scale, these data have been condensed to 3-point Likert responses, where 0 = "very dissatisfied or dissatisfied", "very difficult or difficult", or "very unclear or unclear"; 1 = "neutral"; 2 = "very satisfied or satisfied", "very simple or simple", or "very clear or clear"

2.2 Supplementary Figure

Fig. S1 Disposition of enrolled patients by disease and country



axSpA axial spondyloarthritis, *CD* Crohn's disease, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis, *UC* ulcerative colitis, UK, United Kingdom

Supplementary Reference

1. Leong KP, Tan JWL, Gao X, Koh ET, Group TRAS. Conversion among the 28-joint count activity indices for rheumatoid arthritis. Eur J Rheumatol. 2020;7(3):105-11. https://doi:10.5152/eurjrheum.2020.19199.