

**Title:**

Real-world evidence of clinical outcomes of the use of the adalimumab biosimilar SB5 in rheumatic and digestive IMiDs: 12-month data from the PERFUSE study

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**Supplementary Table S1** Disease activity scores and cut-offs used for this study.

**Supplementary Table S3A** Complete listing of physician-reported comorbidities and co-treatments at baseline for the rheumatology cohort.

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**Supplementary Table S4** Evolution of disease activity scores between baseline and M12 (significant differences are bolded,  $p < 0.05$ ).

**Supplementary Table S5** CRP concentration at baseline and M12. Results are presented in mg/mL and significant population-level differences between M0 and M12 are bolded ( $p < 0.05$ ).

**Supplementary Figure S6** Evolution of CRP levels (in mg/L) between baseline (M0, dark grey) and 12 months (M12, light grey). Error bars are 95% confidence intervals. Statistically significant ( $p < 0.05$ ) population-level differences are presented with a star. Results are presented for all patients with data at each time point. **A.** Naïve populations. **B.** Switched populations. A blue line denotes the upper limit of what are considered acceptable CRP levels (10 mg/L).

**Supplementary Table S7** Kaplan-Meier estimates for persistence. For all values presented, the numerator was the number of patients remaining at that time point and the denominator was the number of enrolled patients who had received at least one dose of SB5.

**Supplementary Table S1.** Disease activity scores and cut-offs used for this study.

Score	DAS28-ESR	DAS28-CRP	BASDAI	HBI	SCCAI
<b>Indications</b>	RA; PsA	RA; PsA	PsA; AS	CD	UC
<b>Remission</b>	<2.6	<2.4	N/A	<5	N/A
<b>LDA</b>	[2.6; 3.2]	[2.4; 3.9]	<4	[5; 7]	<5
<b>MDA</b>	]3.2; 5.1]	]2.9; 4.64]	N/A	]8; 16]	N/A
<b>HDA</b>	>5.1	>4.64	≥4	>16	≥5
<b>Reference</b>	Fleischmann et al. [20]		Garrett et al. [17]	Bradshaw [18]	Jowett et al. [21]

AS = ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CD = Crohn's disease; CRP = C-reactive protein; DAS28 = Disease Activity Score (28 joint); ESR = erythrocyte sedimentation rate; HBI = Harvey-Bradshaw Index; HDA = high disease activity; LDA = low disease activity; MDA = moderate disease activity; N/A = Not Applicable; PsA = psoriatic arthritis; RA = rheumatoid arthritis; SCCAI = Simple Clinical Colitis Activity Index; UC = ulcerative colitis.

**Supplementary Table S3A.** Complete listing of physician-reported comorbidities and co-treatments at baseline for the rheumatology cohort.

Rheumatology Cohort	Naïve patients			Switched patients <sup>a</sup>		
	RA N=77	PsA N=48	AS N=194	RA N=39	PsA N=30	AS N=119
<b>Comorbidities at baseline, n (%)</b>						
<b>Patients with at least 1 comorbidity</b>	<b>26 (33.8%)</b>	<b>26 (54.2%)</b>	<b>83 (42.8%)</b>	<b>20 (51.3%)</b>	<b>17 (56.7%)</b>	<b>58 (48.7%)</b>
Anxiety or Panic Attacks	-	4 (8.3%)	12 (6.2%)	3 (7.7%)	2 (6.7%)	6 (5.0%)
Arterial Disease (Other than Cerebral Arteries and Heart) / Arteritis of the Lower Limbs / Arteriosclerosis	2 (2.6%)	2 (4.2%)	8 (4.1%)	3 (7.7%)	5 (16.7%)	7 (5.9%)
Asthma	4 (5.2%)	2 (4.2%)	11 (5.7%)	1 (2.6%)	2 (6.7%)	4 (3.4%)
Back Pain (Disc Disease, Compressed Lumbar Spine, Chronic Low Back Pain)	2 (2.6%)	9 (18.8%)	26 (13.4%)	2 (5.1%)	2 (6.7%)	14 (11.8%)
Chronic Obstructive Bronchitis/Adult Respiratory Distress Syndrome/Lung Disease/Emphysema	5 (6.5%)	3 (6.3%)	9 (4.6%)	1 (2.6%)	-	1 (0.8%)
Congestive Heart Failure (or Heart Disease)	3 (3.9%)	-	3 (1.5%)	1 (2.6%)	-	4 (3.4%)
Depression	3 (3.9%)	7 (14.6%)	13 (6.7%)	5 (12.8%)	2 (6.7%)	8 (6.7%)
Digestive Disease (Ulcers, Hiatus Hernia, Reflux)	3 (3.9%)	5 (10.4%)	13 (6.7%)	2 (5.1%)	-	10 (8.4%)
Hearing Impairment (Such as Deafness Despite Hearing Aid)	-	-	4 (2.1%)	-	-	2 (1.7%)
History of Myocardial Infarction	2 (2.6%)	1 (2.1%)	2 (1.0%)	2 (5.1%)	2 (6.7%)	2 (1.7%)
History of Stroke or Transitory Ischaemic Attack	-	-	2 (1.0%)	-	-	3 (2.5%)
Neurological Disease (Such as Multiple Sclerosis or Parkinson's Disease)	-	-	1 (0.5%)	-	-	1 (0.8%)
Obesity	5 (6.5%)	8 (16.7%)	20 (10.3%)	2 (5.1%)	7 (23.3%)	16 (13.4%)
Osteoporosis	6 (7.8%)	2 (4.2%)	2 (1.0%)	9 (23.1%)	1 (3.3%)	5 (4.2%)

Type 1 or 2 (Insulin or Non-Insulin Dependent) Diabetes	3 (3.9%)	6 (12.5%)	7 (3.6%)	3 (7.7%)	3 (10.0%)	9 (7.6%)
Visual Disturbances (Such as Cataracts, Glaucoma, Macular Degeneration)	1 (1.3%)	2 (4.2%)	8 (4.1%)	2 (5.1%)	-	4 (3.4%)
Other	-	1 (2.1%)	3 (1.5%)	2 (5.1%)	1 (3.3%)	2 (1.7%)
<b>Patients taking co-treatments at baseline, n (%)</b>						
<b>Patients with at least one co-treatment</b>	<b>65 (84.4%)</b>	<b>28 (58.3%)</b>	<b>35 (18.0%)</b>	<b>23 (59.0%)</b>	<b>8 (26.7%)</b>	<b>10 (8.4%)</b>
Methotrexate	49 (63.6%)	22 (45.8%)	26 (13.4%)	18 (46.2%)	6 (20.0%)	6 (5.0%)
Prednisone	31 (40.3%)	-	-	3 (7.7%)	-	1 (0.8%)
Leflunomide	14 (18.2%)	5 (10.4%)	1 (0.5%)	3 (7.7%)	-	-
Prednisone	-	3 (6.3%)	13 (6.7%)	-	1 (3.3%)	-
Prednisolone	-	-	-	2 (5.1%)	-	-
Sulfasalazine	1 (1.3%)	1 (2.1%)	1 (0.5%)	-	1 (3.3%)	3 (2.5%)
Hydroxychloroquine	1 (1.3%)	-	-	-	-	-

<sup>a</sup> Both from reference and from biosimilar adalimumab.

AS = ankylosing spondylitis; PsA = psoriatic arthritis; RA = rheumatoid arthritis.

**Supplementary Table S3B.** Complete listing of physician-reported comorbidities and co-treatments at baseline for the gastroenterology cohort.

Gastroenterology Cohort	Naïve Patients		Switched Patients <sup>a</sup>	
	CD N=208	UC N=74	CD N=108	UC N=14
<b>Patients with comorbidities, n (%)</b>				
<b>Patients with least one comorbidity</b>	<b>74 (35.6%)</b>	<b>24 (32.4%)</b>	<b>42 (38.9%)</b>	<b>3 (21.4%)</b>
Ankylosing Spondylitis	12 (5.8%)	2 (2.7%)	10 (9.3%)	1 (7.1%)
Asthma	6 (2.9%)	3 (4.1%)	5 (4.6%)	-
Chronic Bronchitis	-	-	2 (1.9%)	-
Erythema Nodosum	4 (1.9%)	-	1 (0.9%)	-
Peripheral Rheumatism	14 (6.7%)	2 (2.7%)	7 (6.5%)	1 (7.1%)
Primary Sclerosing Cholangitis	2 (1.0%)	1 (1.4%)	2 (1.9%)	-
Pyoderma Gangrenosum	1 (0.5%)	-	1 (0.9%)	-
Sacroiliitis	2 (1.0%)	1 (1.4%)	2 (1.9%)	-
Thrombophlebitis	2 (1.0%)	1 (1.4%)	3 (2.8%)	1 (7.1%)
Uveitis	2 (1.0%)	2 (2.7%)	3 (2.8%)	-
Other	51 (24.5%)	16 (21.6%)	26 (24.1%)	1 (7.1%)
<b>Patients taking co-treatments at baseline, n (%)</b>				
<b>Patients with least one co-treatment</b>	<b>108 (51.9%)</b>	<b>54 (73.0%)</b>	<b>20 (18.5%)</b>	<b>2 (14.3%)</b>
Azathioprine	56 (26.9%)	18 (24.3%)	8 (7.4%)	-
5-ASA Oral	13 (6.3%)	25 (33.8%)	-	2 (14.3%)
Methotrexate	7 (3.4%)	5 (6.8%)	5 (4.6%)	-
5-ASA Topical	1 (0.5%)	14 (18.9%)	-	-
Budesonide	10 (4.8%)	4 (5.4%)	-	-
6-Mercaptopurine	4 (1.9%)	-	2 (1.9%)	-
Other	48 (23.1%)	28 (37.8%)	7 (6.5%)	-

<sup>a</sup> Both from reference and from biosimilar adalimumab.

5-ASA = 5-aminosalicylic acid; CD = Crohn's disease; UC = ulcerative colitis.

**Supplementary Table S4.** Disease activity scores at baseline and M12 and change from baseline.

Group & Disease		Score	Baseline (M0)		Month 12 (M12)		Evolution <sup>b</sup>	
			n	Mean [95% CI]	n	Mean [95% CI]	n (pairs)	Mean [95% CI]
Naïve	RA	DAS28-ESR	23	4.5 [4.2; 4.9]	13	2.8 [2.3; 3.3]	<b>6</b>	<b>-1.3 [-2.2; -0.5]</b>
		DAS28-CRP	29	4.3 [3.8; 4.8]	13	2.8 [2.3; 3.4]	<b>9</b>	<b>-1.6 [-2.3; -0.3]</b>
	PsA	BASDAI	19	5.6 [4.7; 6.4]	11	4.1 [2.6; 5.5]	6	-1.7 [-3.6; 0.2]
		DAS28-ESR	14	3.4 [2.7; 4.1]	6	2.1 [0.5; 3.7]	4	-0.9 [-3.5; 1.7]
		DAS28-CRP	8	4.1 [3.4; 4.8]	12	2.4 [1.8; 2.9]	3	-2.4 [-3.6; -1.1]
	AS	BASDAI	117	5.5 [5.2; 5.8]	46	3.6 [2.9; 4.2]	<b>38</b>	<b>-1.9 [-2.4; -1.3]</b>
	CD	HBI	137	4.1 [3.5; 4.8]	62	1.5 [0.9; 2.2]	<b>50</b>	<b>-2.8 [-3.9; -1.7]</b>
	UC	SCCAI	43	5.8 [4.6; 6.9]	13	2 [0.7; 3.3]	10	-3.4 [-6.9; 0.1]
Switched <sup>a</sup>	RA	DAS28-ESR	13	2.4 [1.7; 3.1]	8	2.5 [1.3; 3.7]	6	-0.4 [-1.4; 0.6]
		DAS28-CRP	5	1.8 [1.4; 2.1]	4	2.2 [1.7; 2.8]	1	-0.1 [N/A; N/A]
	PsA	BASDAI	8	3.4 [1.7; 5]	3	4.3 [1.9; 6.6]	2	1.5 [-0.5; 3.4]
		DAS28-ESR	3	2.6 [1.6; 3.5]	3	3 [1.6; 5.8]	1	-1.4 [N/A; N/A]
		DAS28-CRP	4	3.3 [1.8; 4.8]	2	3.5 [2; 5.1]	1	1.2 [N/A; N/A]
	AS	BASDAI	57	3.2 [2.7; 3.7]	26	2.7 [1.9; 3.5]	20	-0.4 [-1.0; 0.1]
	CD	HBI	81	2.3 [1.6; 2.9]	49	2.1 [1.3; 2.9]	33	-0.9 [-2.0; 0.1]
	UC	SCCAI	8	0.5 [0; 1.1]	5	1.4 [0; 3.3]	3	-0.3 [-3.2; 2.5]

<sup>a</sup> Both from reference and from biosimilar adalimumab.

<sup>b</sup> Data only for patients with data available at both time points.

Significant differences are bolded, p<0.05.

AS = ankylosing spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CD = Crohn's disease; CI = confidence interval; CRP = C-reactive protein; DAS28 = Disease Activity Score (28 joint); ESR = erythrocyte sedimentation rate; HBI = Harvey-Bradshaw Index; N/A = Not Applicable; PsA = psoriatic arthritis; RA = rheumatoid arthritis; SCCAI = Simple Clinical Colitis Activity Index; UC = ulcerative colitis.

**Supplementary Table S5.** CRP concentration at baseline and M12.

Group & Disease		Baseline (M0)		Month 12 (M12)	
		n	Mean [95% CI]	n	Mean [95% CI]
Naïve	<b>RA</b>	<b>32</b>	<b>18.8 [9.4; 28.1]</b>	<b>20</b>	<b>3.5 [1.3; 5.6]</b>
	<b>PsA</b>	<b>20</b>	<b>16.3 [5; 27.6]</b>	<b>15</b>	<b>1.9 [1.1; 2.7]</b>
	<b>AS</b>	<b>93</b>	<b>10.7 [8; 13.4]</b>	<b>48</b>	<b>4.6 [2.3; 7]</b>
	<b>CD</b>	101	12.6 [9.1; 16]	63	7.4 [3.4; 11.5]
	<b>UC</b>	42	12 [4.3; 19.6]	15	3.1 [0.1; 6.2]
Switched <sup>a</sup>	<b>RA</b>	13	4.3 [1.1; 7.5]	15	4.9 [0.1; 9.8]
	<b>PsA</b>	9	2.5 [0.5; 4.5]	10	2.6 [0.5; 4.7]
	<b>AS</b>	37	3.2 [1.9; 4.5]	32	2.3 [1.6; 3.0]
	<b>CD</b>	33	7.5 [1; 14]	29	5.6 [0; 12.5]
	<b>UC</b>	2	0.1 [0; 0.2]	2	1.5 [0; 2.9]

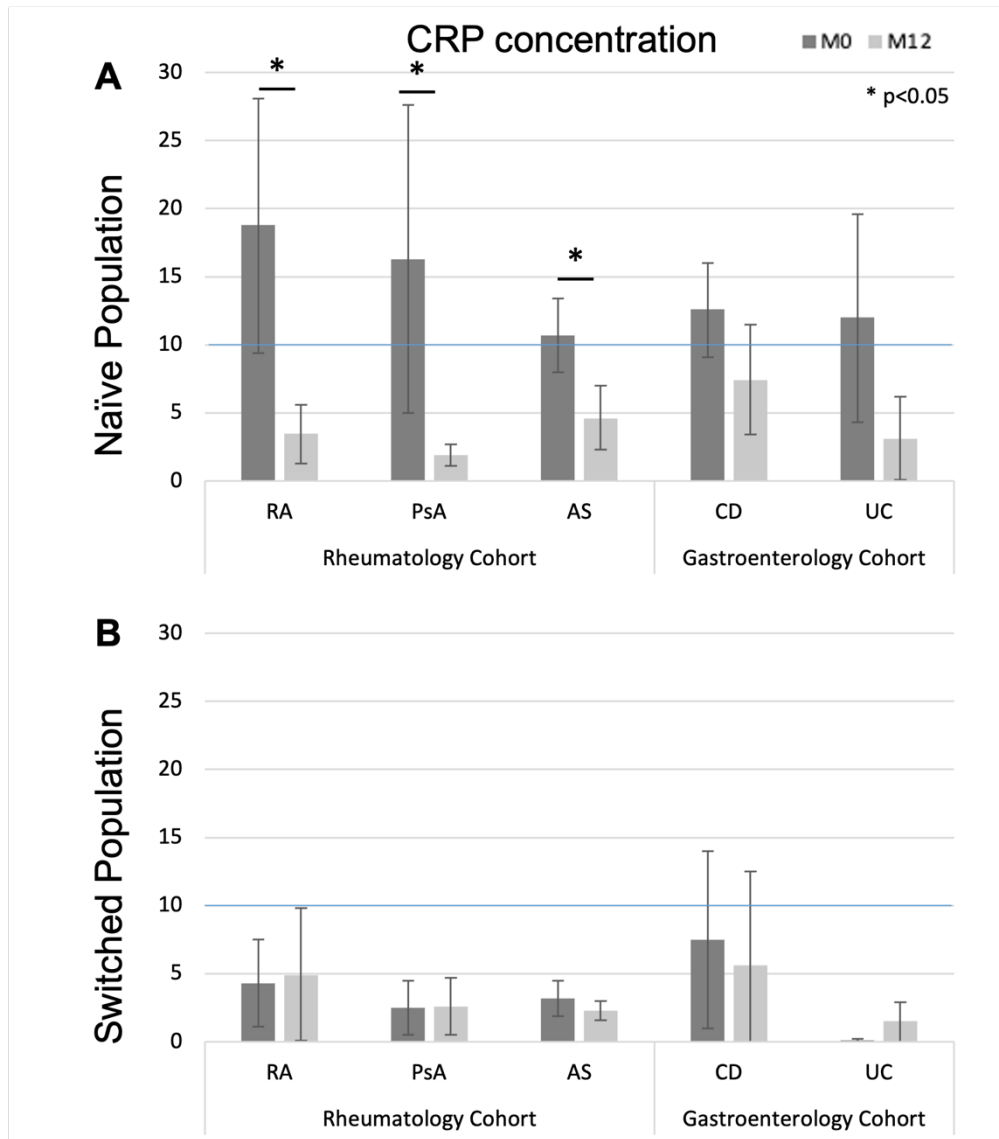
<sup>a</sup> From reference and/or from other biosimilar adalimumab.

Results are presented in mg/mL and significant population-level differences between M0 and M12 are bolded ( $p < 0.05$ ).

AS = ankylosing spondylitis; CD = Crohn's disease; CI = confidence interval; CRP = C-reactive protein; PsA = psoriatic arthritis; RA = rheumatoid arthritis; UC = ulcerative colitis.



**Supplementary Figure S6** Evolution of CRP levels (in mg/L) between baseline (M0, dark grey) and 12 months (M12, light grey). Error bars are 95% confidence intervals. Statistically significant ( $p < 0.05$ ) population-level differences are presented with a star. Results are presented for all patients with data at each time point. **A.** Naïve populations. **B.** Switched populations. A blue line denotes the upper limit of what are considered acceptable CRP levels (10 mg/L).



**Supplementary Table S7.** Kaplan-Meier estimates for persistence.

Group & Disease		Month 3 (M3)	Month 6 (M6)	Month 12 (M12)
<b>Naïve Median [95% CI]</b>	<b>RA (N=77)</b>	89.5 [80.1; 94.6]	75.0 [63.7; 83.3]	58.6 [46.5; 68.8]
	<b>PsA (N=48)</b>	91.5 [79.0; 96.7]	80.9 [66.5; 89.6]	65.3 [49.7; 77.1]
	<b>AS (N=194)</b>	91.13 [86.1; 94.4]	75.7 [69.0; 81.2]	55.8 [48.3; 62.6]
	<b>CD (N=208)</b>	90.8 [85.9; 94.0]	82.9 [77.0; 87.4]	69.9 [63.0; 75.7]
	<b>UC (N=74)</b>	76.7 [65.2; 84.8]	63.0 [50.9; 72.9]	42.1 [30.7; 53.1]
<b>Switched from reference Median [95% CI]</b>	<b>RA (N=37)</b>	86.2 [69.9; 94.0]	75.1 [57.5; 86.2]	58.0 [40.2; 72.2]
	<b>PsA (N=29)</b>	75.9 [55.9; 87.7]	69.0 [48.8; 82.5]	55.2 [35.6; 71.0]
	<b>AS (N=113)</b>	86.6 [78.8; 91.7]	73.0 [63.7; 80.3]	57.0 [47.2; 65.7]
	<b>CD (N=103)</b>	89.3 [81.6; 93.9]	75.6 [66.1; 82.8]	63.4 [53.2; 72.0]
	<b>UC (N=13)</b>	84.6 [51.2; 95.9]	53.9 [24.8; 76.0]	53.9 [24.8; 76.0]
<b>Switched from another biosimilar Median [95% CI]</b>	<b>RA (N=2)</b>	100 [100; 100]	100 [100; 100]	100 [100; 100]
	<b>PsA (N=1)</b>	100 [100; 100]	100 [100; 100]	100 [100; 100]
	<b>AS (N=6)</b>	60.0 [12.6; 88.2]	40.0 [5.2; 75.3]	20.0 [0.8; 58.2]
	<b>CD (N=5)</b>	60.0 [12.6; 88.2]	60.0 [12.6; 88.2]	60.0 [12.6; 88.2]
	<b>UC (N=1)</b>	100 [100; 100]	N/A [N/A; N/A]	N/A [N/A; N/A]
<b>Switched from reference or another biosimilar Median [95% CI]</b>	<b>RA (N=39)</b>	86.9 [71.4; 94.3]	76.4 [59.5; 86.9]	60.1 [42.7; 73.7]
	<b>PsA (N=30)</b>	76.7 [57.2; 88.1]	70.0 [50.3; 83.1]	56.7 [37.3; 72.1]
	<b>AS (N=119)</b>	85.5 [77.7; 90.7]	71.6 [62.4; 78.9]	55.4 [45.8; 64.0]
	<b>CD (N=108)</b>	88.0 [80.2; 92.8]	74.9 [65.5; 82.0]	63.3 [53.4; 71.7]
	<b>UC (N=14)</b>	85.7 [53.9; 96.2]	56.3 [27.2; 77.6]	56.3 [27.2; 77.6]

For all values presented, the numerator was the number of patients remaining at that time point and the denominator was the number of enrolled patients who were treated with SB5.

AS = ankylosing spondylitis; CD = Crohn's disease; CI = confidence interval; PsA = psoriatic arthritis; RA = rheumatoid arthritis; UC = ulcerative colitis.