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Real-World Effectiveness and Safety of SDZ-ADL (Adalimumab Biosimilar) in Patients with Psoriasis from the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR)

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Abstract: SDZ-ADL is a biosimilar of reference adalimumab. Here, the safety and effectiveness data of SDZ-ADL from the British Association of Dermatologists Biologic and Immuno-modulators Register (BADBIR) are reported. In the safety set, data of SDZ-ADL were compared with conventional systemics data. In the effectiveness set, the effectiveness and quality-of-life of patients treated with SDZ-ADL as a first-time biologic, or who switched from a previous biologic to SDZ-ADL, were assessed using the Psoriasis Activity Severity Index (PASI) and Dermatology Life Quality Index (DLQI), respectively. A total of 565 (incidence rate (IR) per 1000 person-years 29.1, 95% CI 26.8–31.6) serious infections and 48 (IR 2.5, 95% CI 1.8–3.3) myocardial infarction events were reported in the conventional systemics cohort compared with four (IR 31.5, 95% CI 8.6–80.7) and one (IR 7.9, 95% CI 0.2–43.9) in the biologic cohort, respectively. One patient (0.7% (1/136)) reported injection-site pain in the biologic cohort. At 12 months, PASI $\leq$ 2 was achieved in 84.6% (11/13) and 76.9% (10/13) and DLQI 0/1 was achieved in 70% (7/10) and 75% (3/4) of patients in the biologic-naïve and biologic-switch cohorts, respectively. After one year of therapy, 82.7% (110/133) patients remained on SDZ-ADL. SDZ-ADL was well-tolerated and effective in patients with psoriasis.

Keywords: safety; effectiveness; psoriasis

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1. Introduction

Psoriasis is a chronic inflammatory immune-mediated disease that affects the skin; it has a prevalence of approximately 2% in Europe and North America [1,2]. Although there are several clinical manifestations of psoriasis, plaque psoriasis accounts for 90% of cases [2]. Comorbid diseases of psoriasis include psoriatic arthritis (PsA), depression, Crohn's disease, and cardiovascular disorders, all of which compound the detrimental impact of this disease on a patient's quality of life (QoL) [3–5].

Research on the disease mechanism of psoriasis has highlighted the central role of the pro-inflammatory cytokine, tumour necrosis factor (TNF)-α [2]. GP2017 (SDZ-ADL, Hyrimoz® Sandoz GmbH, Langkampfen, Austria)—a biosimilar of the reference anti-TNF-α monoclonal antibody adalimumab (ref-ADL)—is approved for the treatment of various immune-mediated inflammatory diseases, including psoriasis, PsA, and hidradenitis suppurativa (HS) [6].

SDZ-ADL binds specifically to TNF and blocks its interaction with the p55 and p75 cell surface TNF receptors, thereby neutralising its biological function. SDZ-ADL also modulates TNF-induced or regulated biological responses (e.g., changes in endothelial leukocyte adhesion molecule-1 (ELAM-1), vascular cell adhesion molecule-I (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) levels) [7].

Functional and pharmacological studies have demonstrated equivalency between SDZ-ADL and ref-ADL [8], and the ADACCESS and ADMYRA Phase III clinical trials have both confirmed the equivalent safety and efficacy of SDZ-ADL to ref-ADL in patients with moderate-to-severe chronic plaque psoriasis and rheumatoid arthritis (RA), respectively [7,9].

The ADACCESS Phase III confirmatory study also assessed the impact of multiple switches between SDZ-ADL and ref-ADL [10]. The 51-week study revealed no differences in efficacy, safety, or immunogenicity after four switches (at Weeks 17, 23, 29, and 35) between the switch group (n = 126) and the continuous treatment group (n = 253) where patients remained on the same treatment (SDZ-ADL or ref-ADL) throughout the study. Furthermore, treatment with SDZ-ADL and ref-ADL resulted in comparable improvements in patient-reported outcomes (PROs) as well as in QoL scores. Switching between SDZ-ADL and ref-ADL had no negative impact on PROs [9].

The British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR) is a large, representative, prospective, ongoing pharmacovigilance registry of patients with psoriasis in the United Kingdom (UK) and Republic of Ireland (RoI) [11]. Data are collected from patients and clinicians/nurses on a regular basis to assess changes in therapy and to obtain information regarding adverse events (AEs). Patient records are also linked to national cancer and death registers to provide lifelong follow-up. Although specifically designed to collect safety data, drug survival, effectiveness, and QoL data may also be derived from this extensive national registry, making it an ideal resource to assess real-world evidence (RWE) on the use of SDZ-ADL in patients with psoriasis.

The aim of this report was to assess the safety of SDZ-ADL compared with conventional systemic therapies from the BADBIR. As secondary outcomes, this study assessed the real-world effectiveness and the impact on QoL using the Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI), respectively [12,13] in biologic-naïve patients and in biologic-experienced patients who switched treatment from another biologic to SDZ-ADL.

2. Results

2.1. Safety Set: The Conventional Systemics Cohort Compared with the SDZ-ADL Cohort

The safety set (SS) comprised 136 patients in the SDZ-ADL cohort (biologic-naïve: n = 46; biologic-switch: n = 90) and 5919 patients in the conventional systemics cohort (Table 1).

The mean ± standard deviation (SD) age of patients at study entry was 44.9 ± 13.3 in the SDZ-ADL cohort and 43.6 ± 14.5 years in the conventional systemics cohort; the corresponding mean ± SD disease durations were 20.9 ± 14.2 and 18.2 ± 13.3 years (Table 2).

Table 1. Baseline demographic characteristics of patients registered in the conventional and SDZ-ADL cohort from the safety set.

	Conventional Systemics Cohort (n = 5919)	SDZ-ADL Cohort (n = 136) *	
	Conventional Systemics	Biologics-Naïve	Biologic-Switch #
Cumulative number of registrations from 27 September 2007	5919	46	90
Cumulative number by gender			
Male	3333	29	52
Female	2586	17	38
Cumulative number by age at registration			
<16	39	0	0
16–18	101	0	1
19–34	1697	7	21
35–44	1405	14	29
45–54	1355	11	22
55–64	820	7	9
65–74	402	7	7
75+	100	0	1

* At the study end on 31 July 2021, a total of 136 patients were registered on the SDZ-ADL cohort of the safety set. # Biologic-experienced patients who switched from a previous biologic treatment to SDZ-ADL within the previous 6 months of baseline.

Table 2. Baseline disease characteristics of patients registered in the SDZ-ADL and conventional systemic cohorts from the safety set.

		SDZ-ADL Cohort			Conventional Systemics Cohort		
	Sex	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age (years)	Male	81	45.6	13.9	3333	44.1	14
	Female	55	43.8	12.5	2586	43	15.1
	Total	136	44.9	13.3	5919	43.6	14.5
Disease duration (years)	Male	81	20.5	14.8	3321	17.2	12.4
	Female	55	21.5	13.3	2580	19.5	14.3
	Total	136	20.9	14.2	5901	18.2	13.3
No. of comorbidities N (%)	0	46 (33.8)			2142 (36.2)		
	0–2	84 (61.8)			3280 (55.4)		
	3–4	4 (2.9)			381 (6.4)		
	5+	2 (1.5)			116 (2.0)		
	Total	136			5919		

N, number of participants in the population; SD, standard deviation.

In total, 55.4% (3280/5919) of patients in the conventional systemics cohort and 61.8% (84/136) in the SDZ-ADL cohort had one to two comorbidities (Table 2).

A total of 565 serious infections were reported (incidence rate (IR) per 1000 person-years 29.1; 95% confidence interval (CI) 26.8–31.6) in the conventional systemics cohort while four were reported (IR 31.5; 95% CI 8.6–80.7) in the SDZ-ADL cohort. In the conventional systemics cohort, 60 respiratory (non-infectious) events (IR 3.1; 95% CI 2.4–4.0) were reported, but there were none in the SDZ-ADL cohort; 48 (IR 2.5; 95% CI 1.8–3.3) myocardial infarction events were reported in the conventional systemics cohort and one (IR 7.9; 95% CI 0.2–43.9) was reported in the SDZ-ADL cohort (Table 3). Only one patient (1/136 [0.7%]) reported injection site pain in the SDZ-ADL cohort.

Table 3. Safety data from the safety set.

	Conventional Systemics (*n* = 5919)		SDZ-ADL (*n* = 136) *	
Event	**No. of Events**	**IR/1000 (95% CI)**	**No. of Events**	**IR/1000 (95% CI)**
Total serious event	565	29.1 (26.8, 31.6)	4	31.5 (8.6, 80.7)
Pneumonia	151	7.8 (6.6, 9.1)	1	7.9 (0.2, 43.9)
Septicaemia	43	2.2 (1.6, 3.0)	0	0.0 (0.0, 29.0)
Opportunistic infection	7	0.4 (0.1, 0.7)	0	0.0 (0.0, 29.0)
Soft tissue and skin infection	100	5.2 (4.2, 6.3)	1	7.9 (0.2, 43.9)
Cellulitis	58	3.0 (2.3, 3.9)	1	7.9 (0.2, 43.9)
Other	42	2.2 (1.6, 2.9)	0	0.0 (0.0, 29.0)
Other serious infection	252	13.0 (11.4, 14.7)	2	15.7 (1.9, 56.9)
Tuberculosis	0	0.0 (0.0, 0.2)	0	0.0 (0.0, 29.0)
Cardiac SAE	164	8.5 (7.2, 9.9)	1	7.9 (0.2, 43.9)
Congestive heart failure (new or worsening)	17	0.9 (0.5, 1.4)	0	0.0 (0.0, 29.0)
Myocardial infarction	48	2.5 (1.8, 3.3)	1	7.9 (0.2, 43.9)
Central demyelination	0	0.0 (0.0, 0.2)	0	0.0 (0.0, 29.0)
Peripheral neuropathy	3	0.2 (0.0, 0.5)	0	0.0 (0.0, 29.0)
Cerebrovascular accident	52	2.7 (2.0, 3.5)	0	0.0 (0.0, 29.0)
Skin (non-cancer)	207	10.7 (9.3, 12.2)	0	0.0 (0.0, 29.0)
Total haematologic events	15	0.8 (0.4, 1.3)	0	0.0 (0.0, 29.0)
Aplastic anaemia	3	0.2 (0.0, 0.5)	0	0.0 (0.0, 29.0)
Total malignant events	308	7.3 (6.5, 8.2)	0	0.0 (0.0, 13.4)
Lymphoproliferative	17	0.4 (0.2, 0.6)	0	0.0 (0.0, 13.4)
Lymphoma	11	0.3 (0.1, 0.5)	0	0.0 (0.0, 13.4)
Myeloma	2	0.0 (0.0, 0.2)	0	0.0 (0.0, 13.4)
Leukaemia	4	0.1 (0.0, 0.2)	0	0.0 (0.0, 13.4)
Skin cancer	127	3.0 (2.5, 3.6)	0	0.0 (0.0, 13.4)
Non-melanoma skin-cancer	118	2.8 (2.3, 3.4)	0	0.0 (0.0, 13.4)
Melanoma	9	0.2 (0.1, 0.4)	0	0.0 (0.0, 13.4)
Other skin cancer	0	0.0 (0.0, 0.1)	0	0.0 (0.0, 13.4)
Solid tumours	162	3.8 (3.3, 4.5)	0	0.0 (0.0, 13.4)
Brain neoplasms	2	0.0 (0.0, 0.2)	0	0.0 (0.0, 13.4)
Glioblastoma	1	0.0 (0.0, 0.1)	0	0.0 (0.0, 13.4)
Other brain neoplasm	1	0.0 (0.0, 0.1)	0	0.0 (0.0, 13.4)
Pregnancy	126	14.6 (12.1, 17.3)	0	0.0 (0.0, 77.4)
Death	183	4.3 (3.7, 5.0)	0	0.0 (0.0, 24.2)

95% CI, 95% confidence interval; IR/1000, incidence rate per 1000 person years; SAE, serious adverse events. * At study end on 31 July 2021, a total of 136 patients were registered on the SDZ-ADL cohort of the safety set.

For the IR of first events, the IR of total serious infections was 9.5 (95% CI 8.6–10.5; *n* = 380) in the conventional systemics cohort and 6.3 (95% CI 2.03–19.5; *n* = 3) in the SDZ-ADL cohort, and the unadjusted and adjusted hazard ratio (HR) values for the total serious infections were 0.53 (95% CI 0.17–1.64) and 0.60 (95% CI 0.19–1.86), respectively (Table 4). The IR for soft tissue and skin infection was 2.2 (95% CI 1.8–2.7; *n* = 91) in the conventional systemics cohort and 2.1 (95% CI 0.3–14.8; *n* = 1) in the SDZ-ADL cohort, and

the unadjusted and adjusted HR values for the soft tissue and skin infections were 0.74 (95% CI 0.10–5.34) and 0.86 (95% CI 0.12–6.26), respectively (Table 4). The IR for myocardial infarction was 1.1 (95% CI 0.8–1.5; n = 47) in the conventional systemics cohort and 2.1 (95% CI 0.3–14.8; n = 1) in the SDZ-ADL cohort, and the unadjusted and adjusted HR values for myocardial infarction were 1.53 (95% CI 0.21–11.13) and 1.71 (95% CI 0.23–12.53), respectively (Table 4). No new safety signals were observed.

Table 4. Number and rates of first events, including unadjusted and adjusted hazard ratios per 1000 person years in the safety set.

	Conventional Systemics (n = 5919)		**SDZ-ADL (n = 136)**		**HR**	
SAEs	**N**	**IR/1000 (95% CI)**	**N**	**IR/1000 (95% CI)**	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)**
Total serious infection	380	9.5 (8.6, 10.5)	3	6.3 (2.03, 19.5)	0.53 (0.17, 1.64)	0.60 (0.19, 1.86)
Pneumonia	114	2.7 (2.3, 3.3)	1	2.1 (0.3, 14.8)	0.58 (0.08, 4.18)	0.64 (0.09, 4.58)
Septicaemia	38	0.9 (0.7, 1.2)	0	-	-	-
Opportunistic infection	7	0.2 (0.1, 0.3)	0	-	-	-
Soft tissue and skin infection	91	2.2 (1.8, 2.7)	1	2.1 (0.3, 14.8)	0.74 (0.10, 5.34)	0.86 (0.12, 6.26)
Cellulitis	60	1.4 (1.1, 1.9)	1	2.1 (0.3, 14.8)	1.15 (0.16, 8.29)	1.28 (0.18, 9.39)
Other soft tissue and skin infection	39	0.9 (0.7, 1.3)	0	-	-	-
Other serious infection	210	5.1 (4.5, 5.9)	2	4.2 (1.05, 16.7)	0.66 (0.16, 2.67)	0.74 (0.18, 2.97)
Tuberculosis	0	-	0	-	-	-
Respiratory (non-infection)	50	1.2 (0.9, 1.6)	0	-	-	-
Cardiac SAE	132	3.2 (2.7, 3.8)	1	2.1 (0.3, 14.8)	0.55 (0.08, 3.92)	0.56 (0.08, 3.99)
congestive heart failure (new or worsening)	12	0.3 (0.2, 0.5)	0	-	-	-
Myocardial infarction	47	1.1 (0.8, 1.5)	1	2.1 (0.3, 14.8)	1.53 (0.21, 11.13)	1.71 (0.23, 12.53)
Other cardiac events	86	2.1 (1.7, 2.6)	0	-	-	-
Nervous system SAE	88	2.1 (1.7, 2.6)	0	-	-	-
Central demyelination	0	-	0	-	-	-
Peripheral neuropathy	3	0.1 (0.02, 0.2)	0	-	-	-
Cerebrovascular accident	47	1.1 (0.8, 1.5)	0	-	-	-
Total haematologic events	13	0.3 (0.2, 0.5)	0	-	-	-
Total malignant events	207	5.1 (4.4, 5.8)	0	-	-	-
Death	183	4.4 (3.8, 5.1)	0	-	-	-

95% CI, 95% confidence interval; HR, hazard ratio; IR/1000, incidence rate per 1000 person years; SAE, serious adverse event.

2.2. Effectiveness Set: The Biologic-Naïve and Biologic-Switch Cohorts

The effectiveness set (ES) comprised 133 patients (biologic-naïve: n = 46; biologic-switch: n = 87). Data from three patients were missing. The mean ± SD age of patients at study entry was 45.9 ± 12.6 years in the biologic-naïve cohort and 44.1 ± 13.6 years in the biologic-switch cohort; the mean disease durations were 19.2 ± 13.4 and 21.9 ± 14.8 years, respectively (Table 5).

Table 5. Baseline demographics and clinical characteristics of the effectiveness set.

	Effectiveness Set (n = 133) **								
	Biologic-Naïve (n = 46; 34.6%)				Biologic-Switch (n = 87; 65.4%)				p Value *
Characteristics	**N**	**Mean (SD)**	**Median (IRQ)**	**Range**	**N**	**Mean (SD)**	**Median (IRQ)**	**Range**	
Follow-up (years)	46	1.9 (0.6)	2.0	(1.8–2.4)	87	1.8 (0.7)	2.0	(1.6–2.3)	0.535
Age (years)	46	45.9 (12.6)	45.0	(36.0–56.0)	87	44.1 (13.6)	43.0	(36.0–52.0)	0.571
Age of onset (years)	46	26.7 (12.3)	27.5	(17.0–37.0)	87	22.3 (13.6)	20.0	(14.0–28.0)	**0.009**
Disease duration (years)	46	19.2 (13.4)	16.0	(9.0–26.0)	87	21.9 (14.8)	19.0	(10.0–30.0)	0.578
Weight (kg)	36	85.5 (18.7)	83.4	(68.6–99.5)	81	88.4 (20.8)	86.3	(72.9–99.2)	0.639
Height (kg)	44	169.5 (9.7)	170.0	(161.0–176.0)	87	169.4 (11.1)	170.0	(160.0–177.0)	1.000
BMI (kg/m^2)	36	29.4 (5.3)	28.4	(25.9–33.0)	81	30.8 (6.9)	29.7	(26.2–33.3)	0.475
Waist circumference (cm)	30	84.9 (23.2)	90.0	(78.0–100.0)	78	102.6 (17.5)	102.0	(89.8–111.0)	**0.010**
Baseline PASI #	39	12.9 (5.3)	11.5	(10.5–12.6)	26	2.1 (4.0)	0.3	(0.0–1.9)	**0.001**
Baseline DLQI ##	38	17.2 (5.9)	16.0	(13.0–22.0)	17	2.9 (3.4)	2.0	(0.0–4.0)	**0.001**
Psoriatic arthritis, N (%)	46	11 (23.9)			87	22 (25.3)			0.861
No. of comorbidities	46	1.5 (1.9)	0.0	(0.0–3.0)	87	1.3 (1.2)	1.0	(0.0–2.0)	**0.002**
No. of skin cancers/pre-skin cancers	46	0.0 (0.1)	0.0	0.0–0.0	87	0	0	0	-
No. of biologics prior to Hyrimoz	46	0	0	0	87	1.3 (0.6)	1.0	1.0–1.0	-
Previous systemics, N (%):	46				87				
Methotrexate		36 (78.3)				64 (73.6)			0.551
Acitretin		13 (28.3)				39 (44.8)			0.063
Mycophenolate mofetil		0				2 (2.3)			0.300
Ciclosporin		31 (67.4)				55 (63.2)			0.632
Hydroxycarbamide		1 (2.2)				1 (1.2)			0.644
Fumaric acidEsters		10 (21.7)				12 (13.8)			0.241
PUVA		2 (4.4)				2 (2.3)			0.510

BMI, body mass index; DLQI, dermatology life quality index; IRQ, interquartile range; PASI, psoriasis area severity index; PUVA, psoralen + ultraviolet light A. * p-value is calculated for biologic-naive vs. biologic-switch cohorts only and is not calculated if the number of observations is equal to 0. ** At study end on 1 August 2021, 133 patients in total were registered in the effectiveness set due to missing data from three patients. # Baseline PASI score reported within 6 months of the drug start date (−183 to 0 days) was defined as baseline PASI. ## Baseline DLQI score reported within 6 months of the drug start date (−183 to 0 days) was defined as baseline DLQI.

The mean ± SD number of comorbidities was 1.5 ± 1.9 in the biologic-naïve cohort and 1.3 ± 1.2 in the biologic-switch cohort. The mean ± SD baseline PASI (12.9 ± 5.3 (n = 39)) and DLQI (17.2 ± 5.9 (n = 38)) scores were higher in the biologic-naïve cohort than in the biologic-switch cohort (PASI score: 2.1 ± 4.0 (n = 26); DLQI score: 2.9 ± 3.4 (n = 17)) (Table 5).

At 6 months of treatment, most patients achieved PASI score ≤ 2 in the biologic-naïve (17/22 (77.3%)) and biologic-switch (20/26 (76.9%)) cohorts. At 12 months, a PASI score ≤ 2

was achieved in 84.6% (11/13) of patients in the biologic-naïve cohort and by 76.9% (10/13) in the biologic-switch cohort (Table 6).

Table 6. Percentage of patients achieving PASI $\leq$ 2 score and DLQI 0 or 1 score at 6 and 12 months in biologic-naive and biologic-switch cohorts of the effectiveness set.

Time Point	PRO Achieved	Biologic-Naïve n (%)	Biologic-Switch n (%)
6 months	PASI $\leq$ 2	17 (77.3)	20 (76.9)
	DLQI 0 or 1	9 (42.9)	8 (80.0)
12 months	PASI $\leq$ 2	11 (84.6)	10 (76.9)
	DLQI 0 or 1	7 (70.0)	3 (75.0)

DLQI, Dermatology Life Quality Index; n, number of participants; PASI, Psoriasis Activity Severity Index; PRO, patient-reported outcome.

At 6 months of treatment, 42.9% (9/21) of patients in the biologic-naïve cohort and 80.0% (8/10) in the biologic-switch cohort had a DLQI score of 0 to 1, indicating no impairment in health-related QoL. At 12 months, DLQI 0 to 1 scores were achieved in 70.0% (7/10) and 75.0% (3/4) of the biologic-naïve and biologic-switch cohorts, respectively (Table 6).

At the end of the one-year observation, a total of 82.7% (110/133) of patients (biologic-naïve: 84.8% (39/46); biologic-switch: 71/87 (81.6%)) remained on SDZ-ADL treatment (Table 7). At the median follow-up of two years, the primary reasons for patients discontinuing treatment (biologic-naïve: 7/46; biologic-switch: 16/87) were ineffectiveness and AEs (Table 7).

Table 7. Proportion of patients that stopped treatment in the biologic-naïve and biologic-switch cohorts of the effectiveness set.

Reason for Stopping Treatment	Biologic-Naïve *n* = 46 (34.6%)		Biologic-Switch *n* = 87 (65.4%)		Full Cohort *n* = 133 (100%)	
	n (%)	Time to Interruption * (IQR)	n (%)	Time to Interruption * (IQR)	N (%)	Time to Interruption * (IQR)
Did not stop	39 (84.8)	-	71 (81.6)	-	110 (82.7)	-
Adverse events	3 (6.5)	0.3 (0.2–0.8)	11 (12.6)	0.5 (0.2–0.6)	14 (10.5)	0.4 (0.2–0.6)
Ineffectiveness	1 (2.2)	0.5 (0.5–0.5)	3 (3.5)	0.5 (0.2–2.4)	4 (3.0)	0.5 (0.3–1.5)
Other **	3 (6.5)	0.9 (0.3–1.4)	2 (2.3)	0.4 (0.4–0.5)	5 (3.8)	0.5 (0.4–0.9)

IQR, interquartile range; n, number of participants; N, number of participants in the full cohort. * Median with 25–75% interquartile range (IQR) of follow-up time in years for the full cohort is 2.0 (1.7–2.3). ** Other reasons include contraindication, financial consideration, patient choice, patient non-compliance, remission, and clinical trial enrolment.

3. Discussion

The current study supports previous studies that indicate SDZ-ADL matches the safety and effectiveness of ref-ADL in the treatment of patients with psoriasis [7,9,10]. Moreover, the results indicate no increase in terms of reported serious AEs compared to conventional systemic therapies, reinforcing the established safety profile of adalimumab, and showing no difference in the risk of safety events for patients treated with SDZ-ADL.

The long-term safety of ref-ADL treatment for 10 indications (psoriasis, HS, RA, ankylosing spondylitis, non-radiographic axial spondyloarthritis, peripheral spondyloarthritis, PsA, Crohn's disease, ulcerative colitis, and uveitis) was examined in 29,967 patients from 77 randomised, controlled, open-label, and long-term extension clinical trials representing 56,916 patient-years of exposure [14]. The analysis demonstrated that rates of serious AEs

remained low, which is consistent with previously reported TNF inhibitors [15], and that no new safety findings were noted with increased ref-ADL exposure [14].

The SS analysis reported long-term disease durations in the SDZ-ADL and conventional systemics cohorts at baseline, and most patients in both cohorts had one to two comorbidities. This suggests a need for cost-effective therapies that help to minimise and control the long-term disease burden on patients without increasing the risk of complications associated with AEs or comorbidities.

The ES analysis demonstrated the effectiveness of SDZ-ADL with continued improvements observed in PASI and DLQI scores from baseline at 6 months and up to 12 months of treatment. Over 70% of patients in both the biologic-naïve and biologic-switch cohorts achieved a PASI score ≤ 2 and a score of DLQI 0 to 1. Most patients in both cohorts continued treatment for a median of two years. Although drug survival data were not available, these results might indicate that there is no difference from previously reported data in treatment retention with ref-ADL or other ADL biosimilars [16,17].

The results of this study also support the findings of the ADACCESS Phase III confirmatory study, which demonstrated the efficacy and safety of SDZ-ADL in patients with moderate-to-severe psoriasis and demonstrated that SDZ-ADL matched ref-ADL in efficacy and safety [9]. The ADACCESS study also demonstrated that switching four times between SDZ-ADL and ref-ADL between Week 17 and Week 51 had no effect on improvements in DLQI score compared to non-switch cohorts who remained on the same therapy assigned at baseline (SDZ-ADL or ref-ADL) throughout the study. In the ADACCESS study, the proportion of patients that achieved a score of DLQI 0 to 1 at Week 17 was 51.7% (104/201) in the SDZ-ADL cohort and 49.5% (99/200) in the ref-ADL cohort. After the switch period, the same score was achieved at Week 51 by 61.0% (61/100) of non-switch patients who continued SDZ-ADL, 56.7% (59/104) of non-switch patients who continued ref-ADL, 51.1% (24/47) of patients who switched to SDZ-ADL, and 56.0% (28/50) of patients who switched to ref-ADL [9]. These results highlight the similarities between SDZ-ADL and ref-ADL, and therefore, QoL is not impacted when switches are made [9]. In our study, although information about previous biologic therapy of the biologic-switch cohort was not available, the low mean PASI (2.1) and DLQI (2.9) scores at baseline suggest that most patients likely switched from ref-ADL or other ADL biosimilars. The high proportions of patients achieving scores of PASI ≤ 2 or DLQI 0 to 1 at both 6 and 12 months highlight that switching treatments had no impact on effectiveness and QoL, thus confirming the results of the ADACCESS study.

The effectiveness and safety of SDZ-ADL in real-world conditions have also been demonstrated in other psoriasis registry studies that have explored data from the Biologic Treatment in Danish Dermatology (DERMBIO) registry [18] and from registries that collect data on other indications such as the Danish rheumatologic database (DANBIO) and the Swedish Rheumatology Quality (SRQ) database which contain data on RA, PsA, and axial spondyloarthritis [19,20]. In 2018, patients in Denmark switched treatment from ref-ADL to either SDZ-ADL or Imraldi (SB5) [19]. Overall, the combined one-year treatment retention rate for the biosimilars was high in the DANBIO registry study (89.5% (Kaplan–Meier estimation)) and was comparable to ref-ADL in the DERMBIO registry study (92.0% vs. 92.1%, respectively (95% CI 89.0–94.9)) [18]. Results from these studies also demonstrated that the overall estimated risk of withdrawal was low, and that disease activity did not change after a switch. Similar treatment retention between SDZ-ADL and ref-ADL was observed in biologic-naïve patients and in patients who switched from ref-ADL in a study using data from the SRQ database [20].

RWE studies are important to understand the effectiveness of a treatment outside of the stringent settings of a clinical trial and to account for patients who would be categorised as ineligible for such trials [21]. Classical clinical trials are designed to minimise extraneous variables that are commonly exhibited in the real world such as variations in clinical care and in clinical characteristics. Reducing these natural variations limits the range of observable treatment outcomes that would otherwise be observed in the real-world setting.

To obtain a holistic understanding of intervention effectiveness and realistic treatment outcomes, data from clinical trials should be used together with data from RWE studies that use high-quality data from healthcare databases [22,23]. The insights gained from this approach can support physicians and other healthcare professionals to broadly adopt and integrate biosimilars into their practice.

As with all RWE studies, missing data points can lead to limitations in a study. Changes from baseline in PASI and DLQI scores in the ES study were not reported because of high proportions of unavailable data at the time of collection. Reasons for this included a delay between data collection and data being entered by the reporting healthcare provider; no collection of data in the windows of 4–8 months and 10–14 months; and limited data availability in 2020 because of the COVID-19 pandemic.

4. Materials and Methods

This study was conducted at the University of Manchester under the auspices of the British Association of Dermatologists.

4.1. Recruitment and Baseline Data Collection

SDZ-ADL was approved by the European Medicines Agency (EMA) in July 2018 for the treatment of psoriasis. The BADBIR (latest protocol version 19: BAD Biological Interventions for Psoriasis Register) began the recruitment of patients with a dermatologist-confirmed diagnosis of psoriasis who had started treatment with SDZ-ADL when Sandoz joined the register in December 2018. Study participants were enrolled by a dermatologist or nurse who completed a baseline registration form in the BADBIR database [24]. Patients were enrolled from 20 December 2018, safety data were analysed up until a cut-off date of 31 July 2021 in the SS, and effectiveness data were analysed up until 1 August 2021 in the ES.

4.2. Safety Set and Effectiveness Set Analyses

In the SS, patients who either started on or switched to SDZ-ADL in the 6 months prior to study commencement were assigned to the biologic cohort (SDZ-ADL cohort) and compared with patients assigned to a conventional systemics cohort (patients who were treated with conventional systemics within the 6 months prior to study commencement and who remained on conventional systemic therapy throughout the study). The conventional systemics cohort included biologic-naïve patients with psoriasis treated with either acitretin, ciclosporin, fumaric acid esters, hydroxycarbamide, methotrexate, or psoralen + ultraviolet light A. Patients in the conventional systemics cohort had scores of PASI $\geq$ 10 and DLQI $\geq$ 10 at baseline (unless they were switching between conventional systemics).

In the ES, patients with psoriasis who received SDZ-ADL as their first biologic drug within 6 months of study commencement were assigned to the biologic-naïve cohort and those who were treated with another biologic prior to switching to SDZ-ADL within 6 months of study commencement were assigned to the biologic-switch cohort. Both cohorts were assessed at 6 and 12 months after treatment commencement for effectiveness using the PASI and for QoL using the DLQI.

For both the SS and ES, baseline data regarding diagnosis, disease activity, previous and current anti-psoriatic therapies, types and number of comorbidities, and medication lists were captured at baseline by the reporting healthcare professional.

4.3. Analysis of Serious Adverse Events in the Safety Set

The Cox proportional hazards model was used to compare event rates between the SDZ-ADL cohort and the conventional systemics cohort when $\geq$10 AEs across the two cohorts were observed with at least one event in each cohort. Unadjusted and adjusted HRs were used to compare IRs (per 1000 person-years CI = 95%) between the SDZ-ADL and conventional systemics cohorts. The models were adjusted using deciles of a propensity score that was calculated using variables recorded at the start of therapy, including age, sex,

disease duration, body mass index (BMI), number of comorbidities, previous ultraviolet therapy, and smoking status. Interactions between variables (age × sex, age × disease duration, age × number of comorbidities) were also analysed.

Missing baseline data were replaced using multiple imputation (20 datasets generated). The regression models included a single first event per patient.

The risk window for all AEs except for death or malignancy was from the initiation of therapy up to 90 days after the end of therapy, death, or the end of data collection, whichever occurred first. SAEs that occurred after the risk window were not counted towards IR estimations. However, where a patient switched therapy within 90 days of discontinuing the first therapy, the risk window overlapped, and therefore, both therapies contributed to the IR estimation.

For analysis of the risk of death, the risk window was from the initiation of therapy until 90 days after the end of therapy, death, or the cut-off date of 31 July 2021, whichever occurred first. Deaths that occurred after this window did not count towards IR estimations. For the conventional systemics cohort, the follow-up time started at study entry and continued until death, the cut-off date, or until the patient started a biologic drug.

For analyses of the risk of malignancy, the risk window for any biologic therapy included all person-time in the register (since starting that biologic therapy) and extended until the cut-off date of 31 July 2021 or the date of death, whichever occurred first. Where a malignancy was diagnosed after a second agent had commenced, both agents contributed to the IR estimations. For the conventional systemics cohort, the follow-up time started at study entry and continued until death, the cut-off date, or commencement of a biologic drug.

At the end of the study, IRs were recalculated with complete data and reflected appropriate risk windows for the AEs of interest. Cancer IRs were also calculated to reflect the experience of patients who had or had not switched therapies.

4.4. Effectiveness Analysis: The Biologic-Naïve Versus Biologic-Switch Cohort

Patients with PASI and DLQI scores recorded at 6 and 12 months after commencing SDZ-ADL were analysed. PASI and DLQI scores recorded between 4 and 8 months (121 and 244 days) and between 10 and 14 months (304 and 426 days) after commencing SDZ-ADL were used for 6- and 12-month PASI and DLQI scores. If multiple PASI or DLQI scores were recorded in these windows, the lowest values that were recorded at Day 183 (Month 6) and at Day 365 (Month 12) were selected. Additional time points up to 1 year at Months 6 and 12 are presented in the results based on the proportions of patients in the biologic-naïve and biologic-switch cohorts with reported PASI and DLQI scores.

An analysis of drug persistence (survival analysis) could not be performed because it required 1000 person-years of follow-up to produce 6-month estimates, and these data were not available. Therefore, we analysed the number of patients on SDZ-ADL treatment only at the end of the observation. Additionally, data on the previous biologic therapy of patients in the biologic-switch cohort were not available.

4.5. Data Collection at the 3-Year Follow-Up

Data on changes to therapies (biologic and conventional), disease activity, and the development of any serious AEs or non-serious AEs (regardless of whether they resulted in drug discontinuation) were collected every 6 months from the start of the study up to 3 years. National healthcare data provided additional information on all patients who died, developed a malignancy, or were hospitalised overnight (England, Scotland, and Wales only).

5. Conclusions

Overall, the safety, effectiveness, and discontinuation rates observed in this study are consistent with those in clinical trials and RWE studies of SDZ-ADL as well as with data reported for ref-ADL and other adalimumab biosimilars. Moreover, there was no

increased risk of SAEs in patients treated with SDZ-ADL compared to a conventional systemic therapy cohort, reinforcing the safety of SDZ-ADL in patients with psoriasis.

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Institutional Review Board Statement: BADBIR was approved in March 2007 by the NHS (National Health Service) Research Ethics Committee North-West England, reference 07/MRE08/9.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. All patients gave written consent for their participation in the registry. Patients are made aware of pharmaceutical company involvement as part of their consent.

Data Availability Statement: The BAD receives funding and has a generic contract with the pharmaceutical companies whose products are being monitored, including Sandoz Hexal UK Limited. The University of Manchester is the sponsor of the study. The project will be steered by a steering group, a Data Monitoring Committee * and ethics committee under the auspices of the BAD and will operate independently from direct industry involvement. * A Data Monitoring Committee (DMC) has been established, analogous to a Data Safety & Monitoring Board established for major clinical trials. The DMC is independent of the principal investigators and also of any of the pharmaceutical industries involved and has the power to request interim analyses and advise on the timing and nature of any publications. The DMC includes at least one epidemiologist, a dermatologist, and a statistician. Sandoz Hexal is committed to sharing patient-level data and supporting clinical documents from eligible studies with qualified external researchers. These requests are reviewed and approved by an independent review panel based on scientific merit. All data provided are anonymised to respect the privacy of patients who have participated in the study in line with applicable laws and regulations. Some of the results in this manuscript were published at the European Academy of Dermatology and Venereology (EADV) 2021 Effectiveness and Safety of GP2017 (Adalimumab Biosimilar) in Patients with Psoriasis: Real-world Evidence from the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR), poster number 1306.

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