Supplementary Material

Treatment with SDZ-ADL, an Adalimumab Biosimilar, in Patients with Rheumatoid Arthritis, Psoriasis, or Psoriatic Arthritis: Results of Patient-reported Outcome Measures from Two Phase III Studies (ADMYRA and ADACCESS)

Andrew Blauvelt[1], Craig L. Leonardi[2], Norman Gaylis[3], Julia Jauch Lembach[4], Alison Balfour[4], Lena Lemke[4], Sohaib Hachaichi[5], Ines Brueckmann[5], Teodora Festini[4], Piotr Wiland[6]

[1]Oregon Medical Research Center, Portland, OR, USA

[2]Central Dermatology, St Louis, MO, USA

[3]Arthritis & Rheumatic Disease Specialties, Aventura, FL, USA

[4]Global Clinical Development, Biopharmaceuticals, Hexal AG, Holzkirchen, Germany

[5]Global Medical Affairs, Biopharmaceuticals, Hexal AG, Holzkirchen, Germany

[6]Department of Rheumatology and Internal Medicine, Wrocław Medical University, Wrocław, Poland

Corresponding author:

Andrew Blauvelt, M.D., M.B.A.

Oregon Medical Research Center

9495 Locust St., Suite G

Portland, OR 97223, USA

Email: ablauvelt@oregonmedicalresearch.com

Telephone: 503-245-1525

Fax: 503-245-031

BioDrugs, 2021

Patient-reported outcome assessments

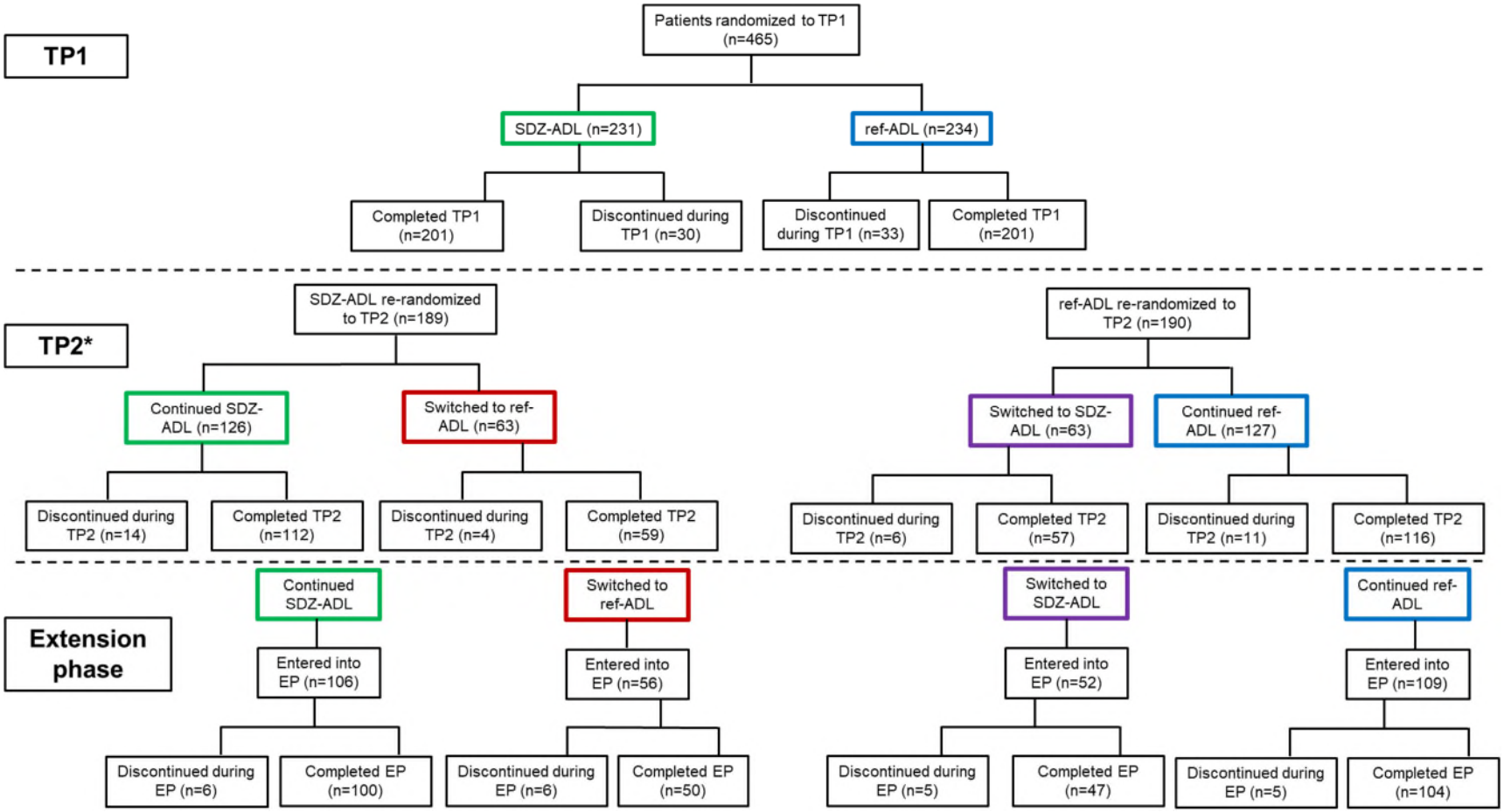
Dermatology Life Quality Index (DLQI) is a 10-item, general dermatology-specific instrument that has been extensively used in psoriasis (PsO) clinical trials [1]. Each item on the scale has four response categories ranging from 0 (“not at all”) to 3 (“very much”). The DLQI total is a sum of the ten questions, and the scores range from 0 to 30. Higher scores indicate greater impairment in health-related quality of life (HRQoL). The EuroQol five-dimension (EQ-5D™) is a trademark of the EuroQol Group and is a generic instrument to assess patient health status. It provides a simple descriptive profile and a single index value for health status. The EuroQol five-dimension health status questionnaire version 2 (EQ-5D-5L v2) consists of two pages: the EQ-5D-5L descriptive system (providing categorical data) and the EQ-5D visual analog scale (VAS; providing continuous data). The EQ-5D-5L descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five response levels: no problems, slight problems, moderate problems, severe problems, and extreme problems [2]. The EQ-5D-5L VAS ranges from 0 to 100, where 0 represents the worst and 100 the best imaginable health status. Lower scores indicate worse HRQoL. HAQ-DI scores were used to assess physical function in patients with psoriatic arthritis (PsA) [3, 4]. There are 20 items in eight categories of functioning, and each item is scored on a four-point scale from 0 to 3, representing “without any difficulty” (0), “with some difficulty” (1), “with much difficulty” (2), and “unable to do” (3). The eight scores of the eight sections are summed and divided by 8 to provide the total Health Assessment Questionnaire Disability Index (HAQ-DI) score. The range for this score is 0–3. Higher scores indicate greater HRQoL impairment.

Functional Assessment of Chronic Illness Therapy–Fatigue Scale (FACIT-Fatigue©) is a 13-item questionnaire [5, 6] that assesses self-reported fatigue and its impact on daily activities and function. Scores range from 0 to 52, with lower scores indicating more fatigue. The Patient Global Assessment (PtGA) was performed using a 100-mm VAS ranging from “very good” to “very poor,” after the question, "Considering all the ways rheumatoid arthritis affects you, please indicate with a vertical mark (|) through the horizontal line how well you are doing.” To enhance objectivity, the physician was unaware of the

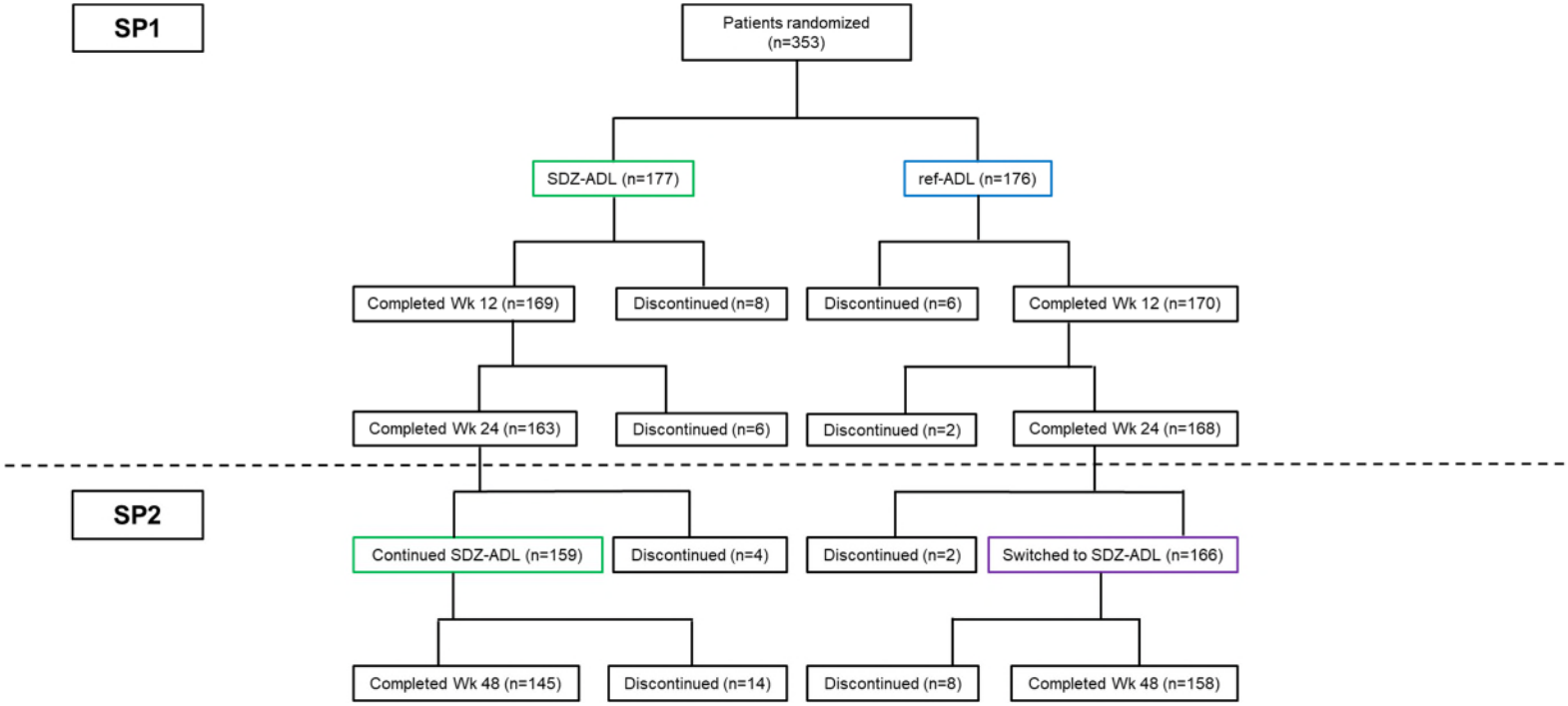
specific PtGA of disease activity when performing his/her own assessment on that patient. The patient assessment of rheumatoid arthritis pain was performed using a 100-mm VAS ranging from “no pain” to “unbearable pain” after the question, “Please indicate with a vertical mark (|) through the horizontal line the most pain you had from your rheumatoid arthritis over the last 24 hours.”

Fig S1. Patient disposition

a) ADACCESS study



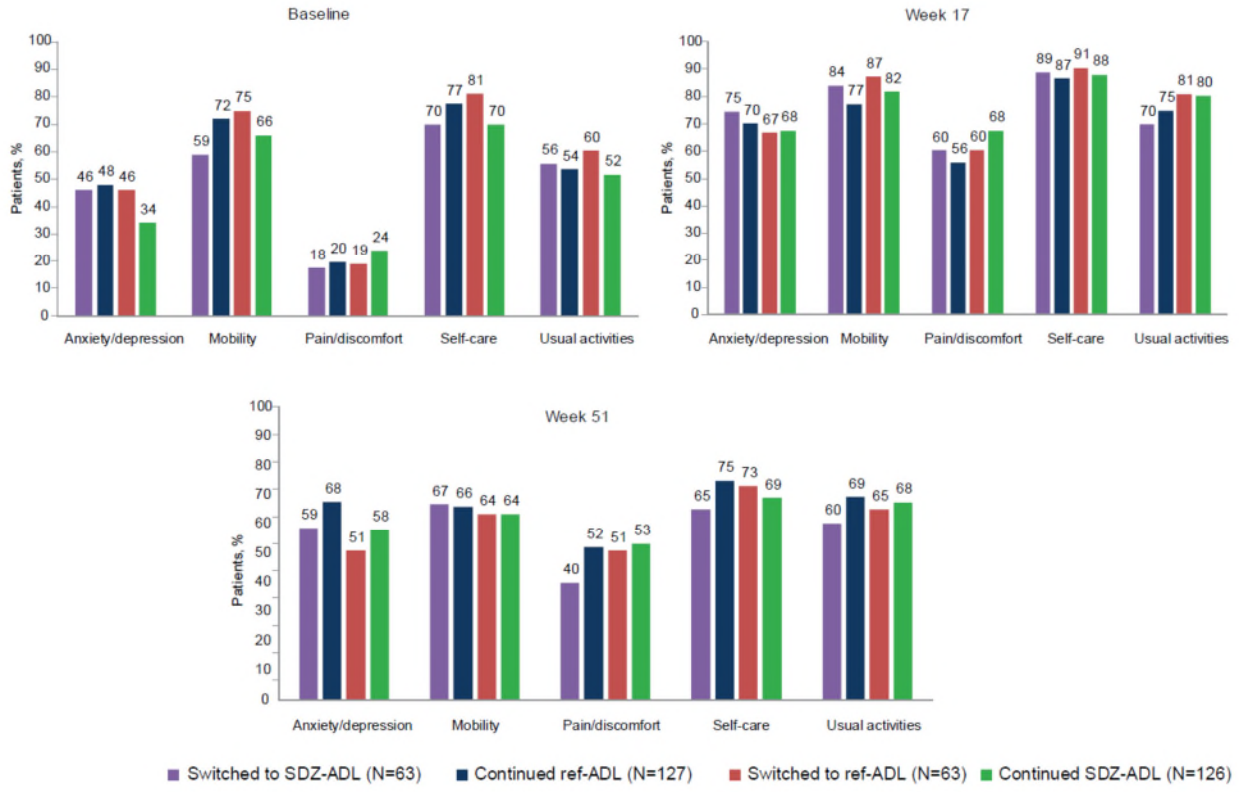
b) ADMYRA study



*Patients who had achieved at least 50% improvement in PASI at Wk 16 were re-randomized (2:1) at Wk 17 to enter TP2.

EP extension phase (Wk 35 to Wk 51), *n* number of patients, *PASI* Psoriasis Area and Severity Index, *ref-ADL* reference adalimumab, *SDZ-ADL* Sandoz biosimilar adalimumab, *SP1* study period 1 (randomization to Wk 24), *SP2* study period 2 (Wk 24 to Wk 48), *TP1* treatment period 1 (randomization to Wk 17), *TP2* treatment period 2 (Wk 17 to Wk 35), *Wk* week

Fig. S2 Patients with moderate-to-severe plaque PsO with a score of 1 (no problems) for each of the EQ-5D-5L dimensions (ADACCESS study; TP2 + EP FAS)

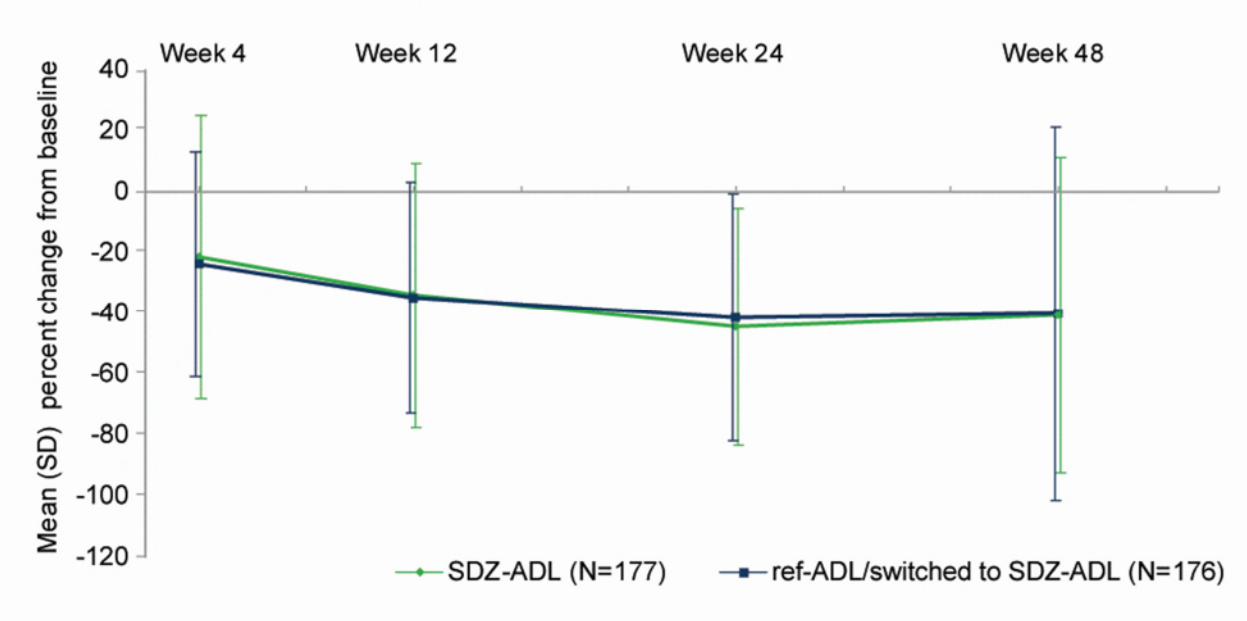


TP2 + EP FAS consists of all patients who were re-randomized into TP2. Patients were analyzed according to the treatment assigned at re-randomization

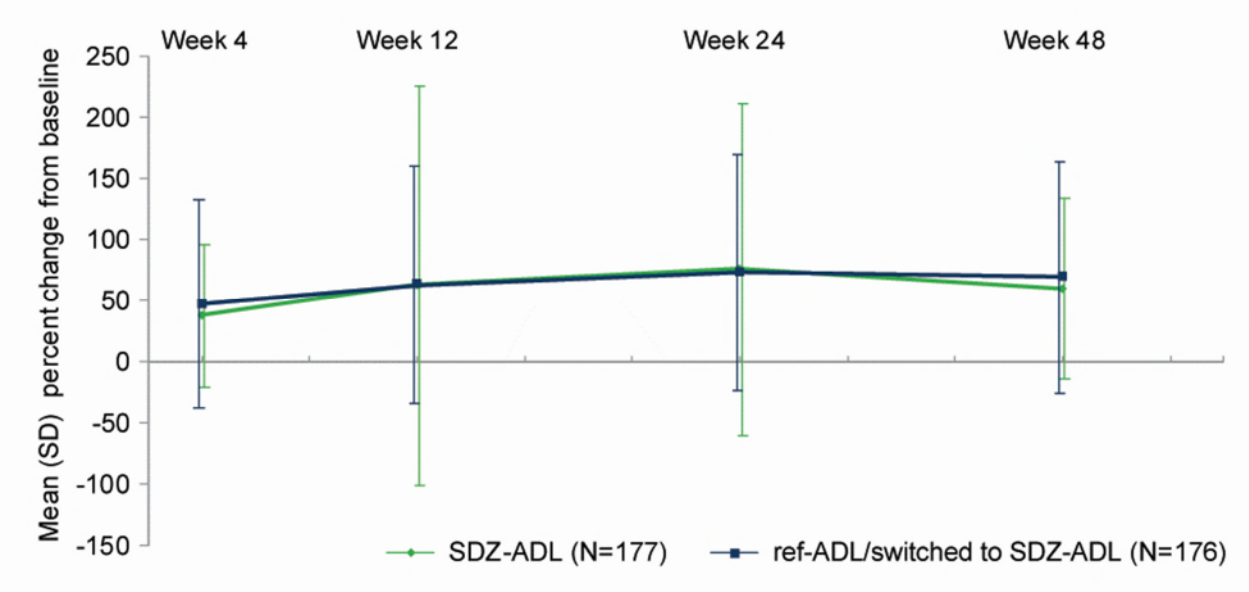
EP extension phase, *EQ-5D-5L* EuroQol five-dimension health status questionnaire, *FAS* full analysis set, *PsO* psoriasis, *ref-ADL* reference adalimumab, *SDZ-ADL* Sandoz biosimilar adalimumab, *TP2* treatment period 2

Fig. S3 Percent change from baseline in HAQ-DI and FACIT-Fatigue scores up to Week 48 in patients with moderate-to-severe RA (ADMYRA study; SP1 FAS)

(a) HAQ-DI



(b) FACIT-Fatigue



SP1 FAS includes all randomized patients in whom the study drug was administered. Panel (**a)** depicts percent change from baseline in HAQ-DI scores. For HAQ-DI, the range of possible scores is 0–3 (0

being the best possible score and 3 the worst), and panel (**b)** depicts the percent change from baseline in the FACIT-Fatigue score (ranges from 0 to 52), with lower scores indicating more fatigue

FACIT Functional Assessment of Chronic Illness Therapy, *FAS* full analysis set, *HAQ-DI* Health Assessment Questionnaire Disability Index, *RA* rheumatoid arthritis, *ref-ADL* reference adalimumab, *SD* standard deviation, *SDZ-ADL* Sandoz biosimilar adalimumab, *SP1* study period 1

Table S1 Demographics and baseline disease characteristics of patients with moderate-to-severe plaque PsO (ADACCESS study; TP1 FAS, TP2 + EP FAS)

	TP1		TP2			
	SDZ-ADL N=231	**ref-ADL N=234**	**Switched to SDZ-ADL N=63**	**Continued ref-ADL N=127**	**Switched to ref-ADL N=63**	**Continued SDZ-ADL N=126**
Age, years	45.6 (14.2)	46.9 (14.1)	47.6 (14.3)	48.0 (13.8)	47.0 (14.2)	46.2 (14.3)
Female, n (%)	89 (38.5)	92 (39.3)	29 (46.0)	46 (36.2)	27 (42.9)	46 (36.5)
Duration since initial diagnosis of PsO, years	15.3 (12.6)	16.9 (14.6)	16.3 (14.2)	16.6 (14.0)	17.0 (14.3)	14.5 (12.0)
PASI[a]	19.9 (8.6)	20.2 (7.7)	19.7 (6.9)	20.8 (8.1)	19.1 (7.1)	20.6 (8.8)
DLQI	14.1 (7.8)	13.5 (7.6)	13.1 (7.4)	13.7 (7.7)	12.3 (7.7)	14.5 (7.7)
EQ-5D-5L score	69.7 (22.5)	69.2 (23.0)	70.7 (24.1)	68.3 (23.1)	72.7 (20.6)	68.2 (23.3)
Psoriatic arthritis present, n (%)	52 (22.5)	46 (19.7)	13 (20.6)	25 (19.7)	15 (23.8)	24 (19.0)
HAQ-DI score[b]	0.6 (0.6)	0.7 (0.6)	0.9 (0.6)	0.6 (0.5)	0.6 (0.7)	0.7 (0.6)

The table is adapted from Blauvelt et al publication [7]. [a]Assessed at randomization; [b]Performed only in patients with psoriatic arthritis. All values are mean (SD) unless otherwise stated. TP1 FAS consisted of all randomized patients in whom the study treatment had been administered during TP1. TP2 + EP FAS consisted of all patients who were re-randomized into TP2

DLQI Dermatology Life Quality Index, *EP* extension phase, *EQ-5D-5L* EuroQol five-dimension health status questionnaire, *FAS* full analysis set, *HAQ-DI* Health Assessment Questionnaire Disability Index, *PASI* Psoriasis Area and Severity Index, *PsO* psoriasis, *ref-ADL* reference adalimumab, *SD* standard deviation, *SDZ-ADL* Sandoz biosimilar adalimumab, *TP1* treatment period 1, *TP2* treatment period 2

Table S2 Demographics and baseline disease characteristics of patients with moderate-to-severe RA (ADMYRA study; SP1, SP2 FAS)

	SP1		SP2	
	SDZ-ADL N=177	**ref-ADL N=176**	**Continued SDZ-ADL N=159**	**ref-ADL/switched to SDZ-ADL N=166**
Age, years	52.8 (12.8)	53.8 (12.2)	52.9 (12.5)	53.5 (12.3)
Female, n (%)	153 (86.4)	142 (80.7)	135 (84.9)	132 (79.5)
Duration of RA, years	8.1 (8.2)	7.4 (7.7)	8.0 (8.1)	7.1 (7.5)
HAQ-DI© score	1.49 (0.6)	1.46 (0.6)	1.48 (0.7)	1.44 (0.6)
FACIT-Fatigue score	24.71 (8.8)	25.33 (10.1)	24.86 (8.9)	25.47 (10.1)
PhGA of disease activity (VAS, mm)	65.4 (16.4)	64.3 (16.2)	65.0 (16.9)	64.2 (16.0)
PtGA of disease activity (VAS, mm)	64.4 (17.4)	65.2 (18.5)	64.1 (17.7)	65.3 (18.5)
PtGA of pain (VAS, mm)	64.1 (18.7)	64.3 (18.4)	63.9 (19.0)	64.2 (18.5)

The table is adapted from Wiland et al publication [8]. All values are mean (SD) unless otherwise stated. SP1 FAS consisted of all randomized patients in whom the study drug was administered. SP2 FAS consisted of all SP1 FAS patients who entered SP2

FACIT Functional Assessment of Chronic Illness Therapy, *FAS* full analysis set, *HAQ-DI* Health Assessment Questionnaire Disability Index, *PhGA* Physician Global Assessment, *PtGA* Patient Global Assessment, *RA* rheumatoid arthritis, *ref-ADL* reference adalimumab, *SD* standard deviation, *SDZ-ADL* Sandoz biosimilar adalimumab, *SP1* study period 1, *SP2* study period 2, *VAS* visual analog scale

Table S3 Percent change in DLQI subscale scores in patients with moderate-to-severe plaque PsO (ADACCESS study; TP2 + EP FAS)

DLQI	**Baseline**				**Week 17**				**Week 51**			
subscale scores	Switched to SDZ-ADL N=63	Continued ref-ADL N=127	Switched to ref-ADL N=63	Continued SDZ-ADL N=126	Switched to SDZ-ADL N=63	Continued ref-ADL N=127	Switched to ref-ADL N=63	Continued SDZ-ADL N=126	Switched to SDZ-ADL N=63	Continued ref-ADL N=127	Switched to ref-ADL N=63	Continued SDZ-ADL N=126
Symptoms and feelings	4.2 (1.6)	3.9 (1.7)	3.9 (1.6)	4.1 (1.4)	−69.8 (32.0)	−69.6 (32.6)	−65.4 (41.8)	−72.0 (32.0)	−62.1 (37.0)	−78.0 (46.6)	−74.2 (33.7)	−79.8 (33.9)
Daily activities	2.9 (1.9)	2.9 (1.8)	2.7 (1.9)	3.2 (1.9)	−70.4 (46.7)	−75.6 (38.2)	−73.5 (47.3)	−79.9 (31.0)	−73.7 (39.7)	−84.3 (27.0)	−75.2 (43.1)	−88.0 (25.8)
Leisure	2.1 (1.9)	2.4 (1.9)	2.0 (1.8)	2.7 (2.0)	−82.0 (31.9)	−77.4 (38.1)	−80.2 (30.1)	−80.6 (31.9)	−82.8 (32.2)	−90.7 (20.5)	−88.0 (28.9)	−88.0 (28.7)
Work/school	0.9 (1.0)	1.1 (1.1)	1.0 (1.2)	1.2 (1.2)	−73.5 (49.8)	−78.5 (39.1)	−78.6 (35.5)	−74.7 (42.4)	−76.2 (41.4)	−81.8 (35.4)	−67.3 (64.9)	−72.5 (62.5)
Personal relationships	1.8 (1.9)	2.1 (2.0)	1.7 (1.9)	2.1 (2.1)	−77.2 (47.1)	−80.8 (33.6)	−73.3 (32.9)	−80.7 (30.9)	−81.6 (55.4)	−82.3 (50.7)	−84.5 (30.2)	−88.8 (28.1)
Treatment	1.3 (1.2)	1.3 (1.1)	1.0 (1.0)	1.2 (1.1)	−81.2 (30.9)	−74.9 (45.7)	−80.3 (34.4)	−80.8 (33.0)	−81.5 (32.2)	−84.2 (36.0)	−78.6 (47.2)	−79.0 (45.4)

Values at baseline are mean (SD). Values at Weeks 17 and 51 are mean percent change (SD). At each time point, only patients with a value at both baseline and post-baseline were included. Scores range from 0 to 30; higher scores indicate greater impairment in health-related quality of life. Subscale scores (range): symptoms and feelings (0–6); daily activities (0–6); leisure (0–6); work/school (0–3); personal relationships (0–6); and

treatment (0–3). At each time point, only patients with a value at both baseline and post-baseline were included. TP2 + EP FAS consists of all patients who were re-randomized into TP2. Patients were analyzed according to the treatment assigned at re-randomization

DLQI Dermatology Life Quality Index, *EP* extension phase, *FAS* full analysis set, *PsO* psoriasis, *ref-ADL* reference adalimumab, *SD* standard deviation, *SDZ-ADL* Sandoz biosimilar adalimumab, *TP2* treatment period 2

References

1. Finlay AY, Khan GK. Dermatology life quality index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol. 1994;19:210–6.
2. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20:1727–36.
3. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum. 1980;23:137–45.
4. Bruce B, Fries JF. The health assessment questionnaire (HAQ). Clin Exp Rheumatol. 2005;23:S14–8.
5. Cella D, Yount S, Sorensen M, Chartash E, Sengupta N, Grober J. Validation of the functional assessment of chronic illness therapy fatigue scale relative to other instrumentation in patients with rheumatoid arthritis. J Rheumatol. 2005;32(5):811–19.
6. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the functional assessment of cancer therapy (FACT) measurement system. J Pain Symptom Manage. 1997;13:63–74.
7. Blauvelt A, Lacour JP, Fowler JF Jr, Weinberg JM, Gospodinov D, Schuck E, et al. Phase III randomized study of the proposed adalimumab biosimilar GP2017 in psoriasis: impact of multiple switches. Br J Dermatol. 2018;179(3):623–31.
8. Wiland P, Slawomir J, Dokoupilová E, Brandt-Jürgens J, Miranda-Limón JM, Cantalejo Moreira M, et al. Switching to Biosimilar SDZ-ADL in Patients with Moderate-to-Severe Active Rheumatoid Arthritis: 48-Week Efficacy, Safety and Immunogenicity Results From the Phase III, Randomized, Double-Blind ADMYRA Study. Biodrugs 2020 34 (6):809–23.