SUPPLEMENTARY MATERIAL

Randomised study of PF-06410293, an adalimumab (ADL) biosimilar, compared with reference ADL for the treatment of active rheumatoid arthritis: results from week 26–52, including a treatment switch from reference ADL to PF-06410293

Roy M. Fleischmann, Daniel F. Alvarez, Amy E. Bock, Carol Cronenberger, Ivana Vranic, Wuyan Zhang, Rieke Alten

Supplemental table 1. All-causality TEAEs occurring in ≥2% of patients in any treatment group (safety population)*

SOC and PT	ADL-PF/ADL-PF (n=283)	ADL-EU/ADL-EU (n=135)	ADL-EU/ADL-PF (n=133)
Number of AEs	243	112	100
Patients with any AE, n (%)	123 (43.5)	60 (44.4)	51 (38.3)
Blood and lymphatic system disorders	9 (3.2)	7 (5.2)	2 (1.5)
Neutropenia	2 (0.7)	4 (3.0)	2 (1.5)
Infections and infestations	49 (17.3)	23 (17.0)	28 (21.1)
Bronchitis	1 (0.4)	0	4 (3.0)
Upper respiratory tract infection	4 (1.4)	5 (3.7)	6 (4.5)
Urinary tract infection	3 (1.1)	1 (0.7)	5 (3.8)
Viral upper respiratory tract infection	15 (5.3)	5 (3.7)	6 (4.5)
Injury, poisoning and procedural complications	12 (4.2)	3 (2.2)	5 (3.8)
Fall	4 (1.4)	1 (0.7)	4 (3.0)
Investigations	22 (7.8)	13 (9.6)	10 (7.5)
Blood creatinine increased	1 (0.4)	3 (2.2)	0

Alanine aminotransferase increased	5 (1.8)	4 (3.0)	4 (3.0)
Aspartate aminotransferase increased	3 (1.1)	4 (3.0)	1 (0.8)
Musculoskeletal and connective tissue disorders	21 (7.4)	13 (9.6)	10 (7.5)
Rheumatoid arthritis	4 (1.4)	2 (1.5)	3 (2.3)
Nervous system disorders	14 (4.9)	1 (0.7)	5 (3.8)
Headache	9 (3.2)	1 (0.7)	2 (1.5)
Vascular disorders	12 (4.2)	5 (3.7)	3 (2.3)
Hypertension	8 (2.8)	3 (2.2)	3 (2.3)

*Includes all AEs starting on or after the first injection of study drug in TP2, and ongoing AEs at the start of TP2 that worsened on or after the first injection of study drug in TP2.

ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; AE, adverse event; PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event; TP2, treatment period 2.

Supplemental table 2. Summary of all-causality SAE SOCs reported by ≥2% of patients in any treatment group (safety population)*

SOC and PT	ADL-PF/ADL-PF (n=283)	ADL-EU/ADL-EU (n=135)	ADL-EU/ADL-PF (n=133)
Patients with any TEAE, n (%)	4 (1.4)	6 (4.4)	3 (2.3)
Infections and infestations	1 (0.4)	3 (2.2)	0
Bronchopulmonary aspergillosis	0	1 (0.7)	0
Ear infection	1 (0.4)	0	0
Gastroenteritis salmonella	0	1 (0.7)	0
Pneumonia	0	1 (0.7)	0

*Includes all AEs starting on or after the first injection of study drug in TP2, and ongoing AEs at the start of TP2 that worsened on or after the first injection of study drug in TP2.

ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; AE, adverse event; PT, preferred term; SAE, serious adverse event; SOC, system organ class; TP2, treatment period 2.

Supplemental table 3. Grade 3 or higher all-causality SOCs reported by ≥1% of patients in any treatment group (safety population)

SOC and PT	ADL-PF/ADL-PF (n=283)	ADL-EU/ADL-EU (n=135)	ADL-EU/ADL-PF (n=133)
Number of AEs	10	8	4
Patients with any TEAE, n (%)	7 (2.5)	7 (5.2)	4 (3.0)
Infections and infestations	1 (0.4)	2 (1.5)	1 (0.8)
Ear infection	1 (0.4)	0	0
Gastroenteritis salmonella	0	1 (0.7)	0
Pneumonia	0	1 (0.7)	0
Urinary tract infection	0	0	1 (0.8)
Vascular disorders	1 (0.4)	2 (1.5)	0
Hypertension	1 (0.4)	1 (0.7)	0
Venous thrombosis limb	0	1 (0.7)	0

ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; AE, adverse event; PT, preferred term; SOC, system organ class; TEAE, treatment-emergent adverse event.

Supplemental table 4. Mean (SD) serum drug trough concentrations (ng/mL) versus time by NAb status during TP2

	ADL-PF/ADL-PF		ADL-EU/ADL-EU		ADL-EU/ADL-PF	
Visit (0 hours post-dose)	**ADA+/NAb+**	**ADA+/NAb−**	**ADA+/NAb+**	**ADA+/NAb−**	**ADA+/NAb+**	**ADA+/NAb−**
Day 183						
Mean	912	8034	1239	6036	535	6166
SD	1420.7	4355.5	2180.9	3981.6	1013.0	4291.8
N	51	95	22	57	20	46
NALQ*	23	95	9	56	6	46
Day 211						
Mean	917	7589	1329	5705	807.3	6325
SD	1545.5	4327.8	2054.0	4026.9	1066.4	3987.1
N	48	96	22	56	20	46
NALQ*	24	96	11	55	9	46
Day 253						
Mean	942	7369	1258	6257	1143	6462

	ADL-PF/ADL-PF		ADL-EU/ADL-EU		ADL-EU/ADL-PF	
Visit (0 hours post-dose)	**ADA+/NAb+**	**ADA+/NAb−**	**ADA+/NAb+**	**ADA+/NAb−**	**ADA+/NAb+**	**ADA+/NAb−**
SD	1936.3	3902.2	1823.8	4706.9	1645.5	4397.4
N	45	94	18	55	20	44
NALQ*	17	94	10	54	8	44
Day 365						
Mean	1076	6603	1054	5268	1598	6423
SD	2150.9	3521.3	1825.6	4049.2	2539.9	4599.8
N	43	93	17	55	19	45
NALQ*	15	91	7	53	9	44
EOT/ET/Day 547						
Mean	1234	2093	683	2342		
SD	1491.0	3386.2	1183.6	2147.5		
N	7	3	3	2	1	0
NALQ*	4	2	1	2	0	
Follow-up/Day 575						

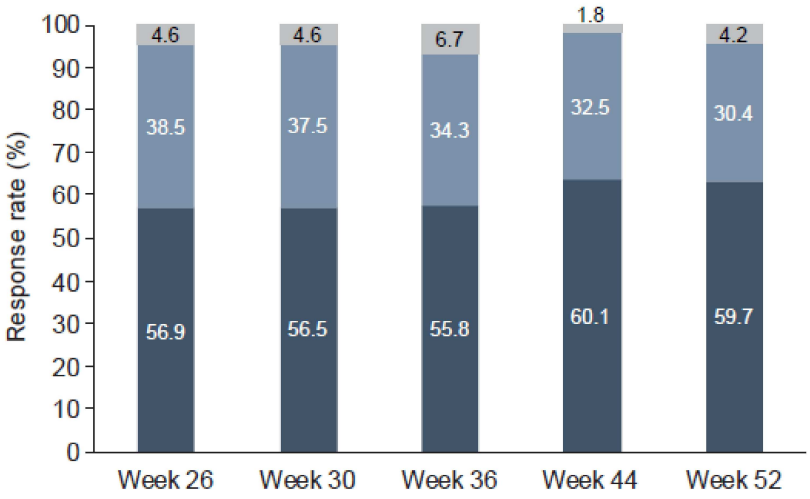
	ADL-PF/ADL-PF		ADL-EU/ADL-EU		ADL-EU/ADL-PF	
Visit (0 hours post-dose)	**ADA+/NAb+**	**ADA+/NAb−**	**ADA+/NAb+**	**ADA+/NAb−**	**ADA+/NAb+**	**ADA+/NAb−**
Mean		279			1240	
SD						
N	4	1	2	0	1	0
NALQ*	0	1	0		1	

*Summary statistics were calculated by setting concentration values below the lower limit of quantification (250 ng/mL) to zero. Summary statistics were not presented if NALQ was zero.

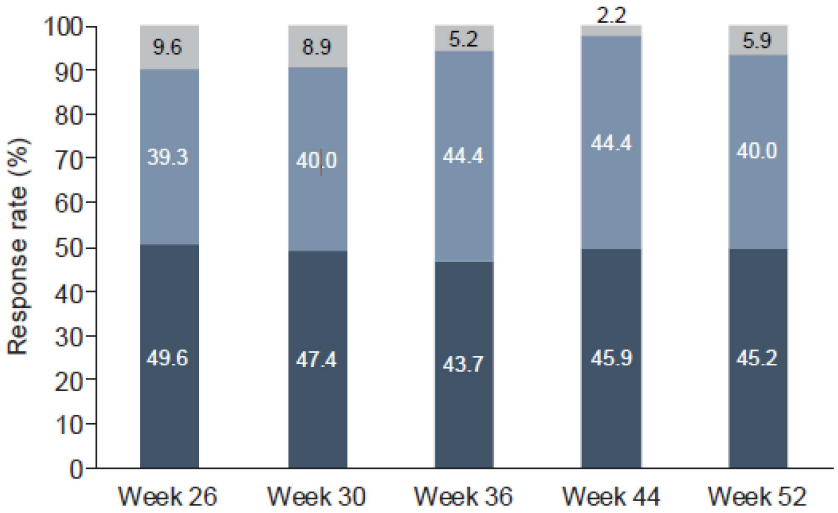
ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; EOT, end of treatment; ET, early termination; N, number of observations with non-missing concentrations; NAb, neutralising antibody; NALQ, number of observations above the lower limit of quantification; SD, standard deviation.

Supplemental figure 1. EULAR response rates by visit (ITT population) in patients treated with a) ADL-PF/ADL-PF; b) ADL-EU/ADL-EU; and c) ADL-EU/ADL-PF

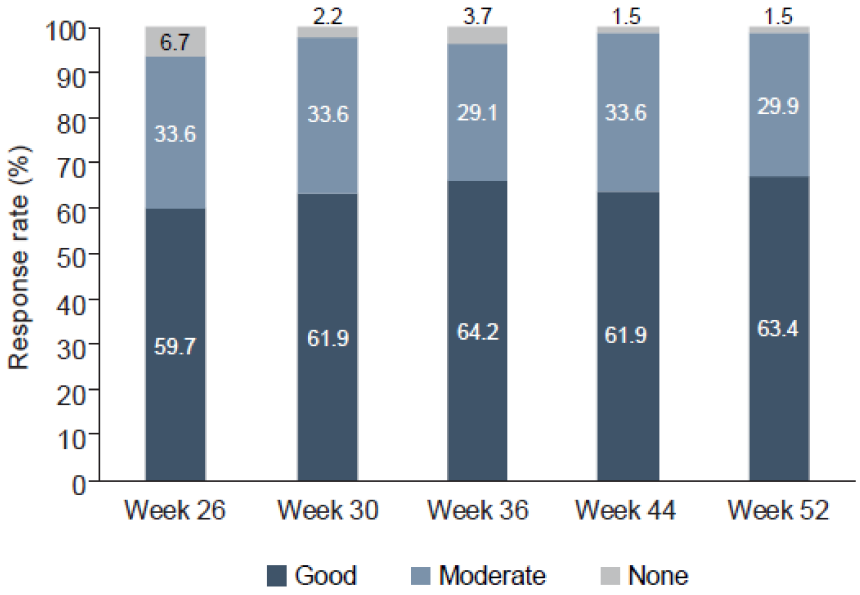
A) EULAR response rates by visit (ITT population) in patients treated with ADL-PF/ADL-PF



B) EULAR response rates by visit (ITT population) in patients treated with ADL-EU/ADL-EU

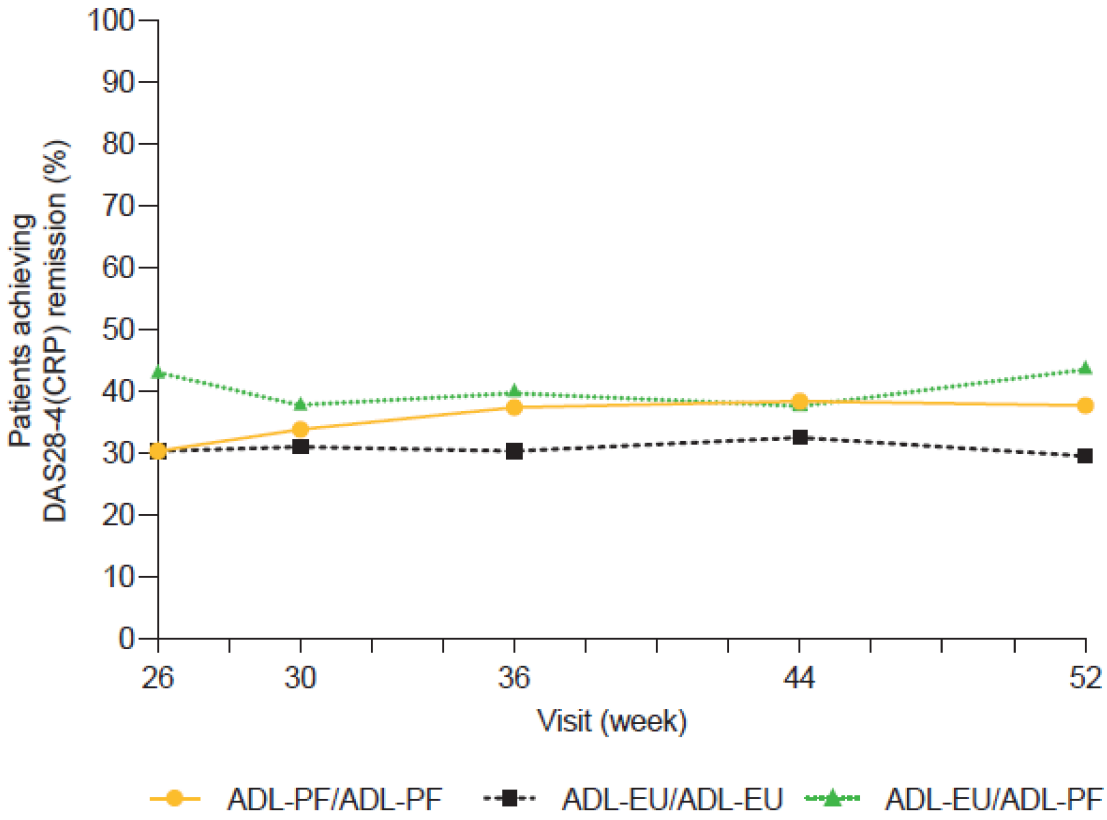


C) EULAR response rates by visit (ITT population) in patients treated with ADL-EU/ADL-PF



ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; EULAR, European League Against Rheumatism; ITT, intent-to-treat.

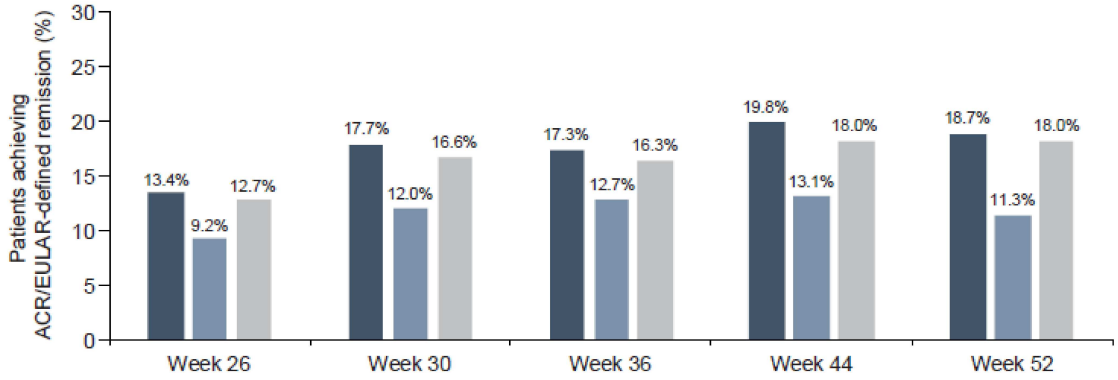
Supplemental figure 2. DAS28-4(CRP) <2.6 by visit (ITT population)



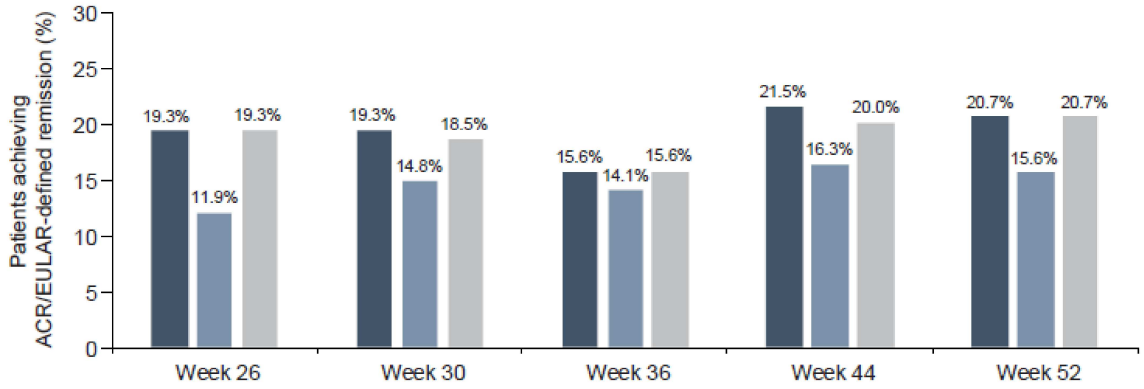
ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; CRP, C-reactive protein; DAS, Disease Activity Score; ITT, intent-to-treat.

Supplemental figure 3. ACR/EULAR-defined remission by visit (ITT population) in patients treated with a) ADL-PF/ADL-PF; b) ADL-EU/ADL-EU; and c) ADL-EU/ADL-PF

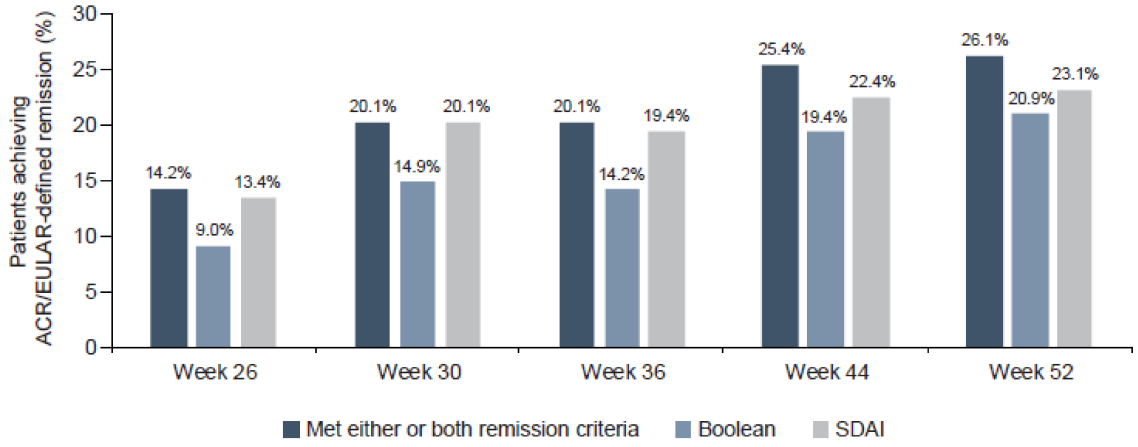
A) ACR/EULAR-defined remission by visit (ITT population) in patients treated with ADL-PF/ADL-PF



B) ACR/EULAR-defined remission by visit (ITT population) in patients treated with ADL-EU/ADL-EU

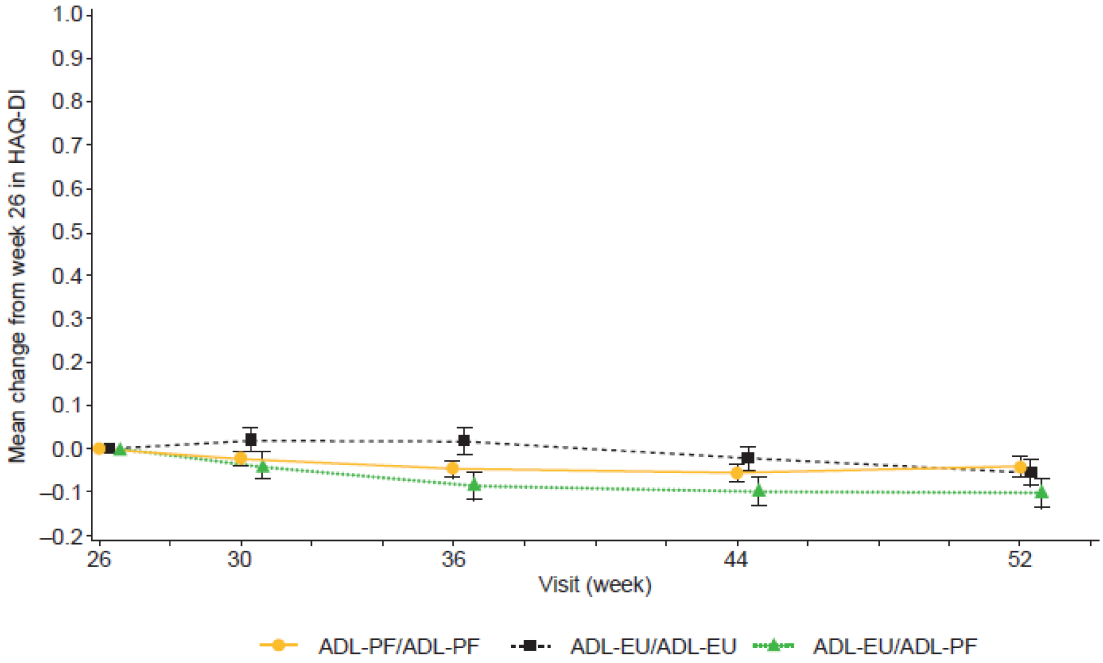


C) ACR/EULAR-defined remission by visit (ITT population) in patients treated with ADL-EU/ADL-PF



ACR, American College of Rheumatology; ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; EULAR, European League Against Rheumatism; ITT, intent-to-treat; SDAI, Simplified Disease Activity Index.

Supplemental figure 4. Mean change (±SE) from week 26 (pre-dose) in HAQ-DI by visit (ITT population)



ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; HAQ-DI, Health Assessment Questionnaire–Disability Index; ITT, intent-to-treat; SE, standard error.