Effectiveness of Etanercept in Rheumatoid Arthritis: Real-World Data From the German Non-Interventional Study ADEQUATE With Focus on Treat-to-Target and Patient-Reported Outcomes

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Supplementary Table S1 Overview of data from routine clinical practice

	Visit 1 week 0	Visit 2 week 12	Visit 3 week 24	Visit 4 week 36	Visit 5 week 52
Medical history	x				
Participation in the 'TOGETHER' program[a]	x				
Inclusion/exclusion criteria	x				
Treatment/medications					
Prior treatment	x				
Treatment with etanercept	x	x	x	x	x
Concomitant treatment		x	x	x	x
Safety parameters					
Physical examination	x				
Laboratory	x	x	x	x	x
AE documentation		x	x	x	x
Effectiveness					
Examination of joints	x	x	x	x	x
Morning stiffness	x	x	x	x	x
Patient and physician global assessment	x	x	x	x	x
Pain	x	x	x	x	x
Fatigue	x	x	x	x	x
Health outcomes					
FFbH	x	x	x	x	x
PHQ-2	x	x	x	x	x

[a] The 'TOGETHER' program, sponsored by Pfizer, aims to improve patient treatment compliance by special trainings and engagements

AE adverse event, *FFbH* Hannover Functional Questionnaire, *PHQ-2* Patient Health Questionnaire-2

Supplementary Table S2 Number of patients recorded at each visit

Time point	Number of patients documented, *n* (%)[a]
Visit 1 (week 0)	824 (100.0)
Visit 2 (week 12)	799 (97.0)
Visit 3 (week 24)	672 (81.6)
Visit 4 (week 36)	568 (68.9)
Visit 5 (week 52)	508 (61.7)

[a] Includes patients who discontinued (for any reason), therefore number of patients documented includes patients listed at non-completers for this visit

Supplementary Table S3 Common (> 3% of patients) concomitant medications[a] given at least once during the study treatment period

	Patients with RA (*N* = 824)
Any concomitant medication	743 (90.2)
Methotrexate	379 (46.0)
Prednisolone	260 (31.6)
Folic acid	135 (16.4)
Colecalciferol	122 (14.8)
Ibuprofen	70 (8.5)
Pantoprazole	67 (8.1)
Metamizole	57 (6.9)
Diclofenac	48 (5.8)
Etoricoxib	45 (5.5)
Prednisone	39 (4.7)
Leflunomide	36 (4.4)
Levothyroxine	35 (4.2)
Ramipril	34 (4.1)
Celecoxib	30 (3.6)
Bisoprolol	30 (3.6)
Valoron n /00628301	29 (3.5)
Acetylsalicylic acid	27 (3.3)

[a] Concomitant medications were documented as free text, coded according to the World Health Organization – Drug Dictionary and analyzed by International Nonproprietary Name

RA, rheumatoid arthritis

Supplementary Table S4 Concomitant diseases recorded at baseline[a]

Concomitant diseases, *n* (%)	
Vascular disorders	343 (41.6)
Hypertension	296 (35.9)
Essential hypertension	37 (4.5)
Musculoskeletal and connective tissue disorders	297 (36.0)
Osteoarthritis	108 (13.1)
Osteoporosis	98 (11.9)
Metabolism and nutrition disorders	231 (28.0)
Type 2 diabetes mellitus	71 (8.6)
Obesity	37 (4.5)
Endocrine disorders	96 (11.7)
Hypothyroidism	38 (4.6)
Respiratory, thoracic, and mediastinal disorders	93 (11.3)
Chronic obstructive pulmonary disease	34 (4.1)
Asthma	31 (3.8)
Cardiac disorders	91 (11.0)
Coronary artery disease	41 (5.0)
Psychiatric disorders	66 (8.0)
Depression	48 (5.8)
Nervous system disorders	74 (9.0)
Renal and urinary disorders	64 (7.8)
Chronic kidney disease	37 (4.5)
Surgical and medical procedures	62 (7.5)
Gastrointestinal disorders	49 (5.9)
Infections and infestations	34 (4.1)
Neoplasms (benign, malignant, and unspecified)	33 (4.0)
Hepatobiliary disorders	28 (3.4)
Skin and subcutaneous tissue disorders	26 (3.2)

[a] Concomitant diseases were documented as free text entries, coded according to MedDRA and tabulated by primary system organ class and preferred term (up to two most common preferred terms). Only conditions occurring in ≥ 3% of patients are included in the table.

MedDRA Medical Dictionary for regulatory Activities

Supplementary Table S5 Disease activity in patients with RA according to alternative disease activity scores

Disease activity score, *n* (%)						
SDAI	**Week**	***n***	**SDAI remission (≤ 3.3)**	**Low SDAI (> 3.3–11.0)**	**Moderate SDAI (11.1–26.0)**	**High SDAI (> 26.0)**
	0	809	0 (0.0)	46 (5.7)	336 (41.5)	319 (39.4)
	12	794	64 (8.1)	270 (34.0)	261 (32.9)	61 (7.7)
	24	664	75 (11.3)	293 (44.1)	158 (23.8)	42 (6.3)
	36	561	72 (12.8)	264 (47.1)	134 (23.9)	30 (5.3)
	52	502	83 (16.5)	258 (51.4)	90 (17.9)	27 (5.4)
CDAI	**Week**	***n***	**CDAI remission (≤ 2.8)**	**Low CDAI (> 2.8–10.0)**	**Moderate CDAI (10.1–22.0)**	**High CDAI (> 22.0)**
	0	809	0 (0.0)	46 (5.7)	293 (36.2)	392 (48.5)
	12	794	73 (9.2)	311 (39.2)	263 (33.1)	94 (11.8)
	24	664	97 (14.6)	328 (49.4)	180 (27.1)	64 (9.6)
	36	561	91 (16.2)	304 (54.2)	146 (26.0)	46 (8.2)
	52	502	100 (19.9)	293 (58.4)	106 (21.1)	34 (6.8)
ACR/ EULAR	**Week**	***n***	**Remission criteria[a] met**		**Remission criteria not met**	
	0	806	1 (0.1)		805 (99.9)	
	12	780	9 (1.2)		771 (98.8)	
	24	651	19 (2.9)		632 (97.1)	
	36	543	19 (3.5)		524 (96.5)	
	52	485	17 (3.5)		468 (96.5)	

[a] TJC ≤ 1, SJC ≤ 1, CRP ≤ 1 mg/dL, patient global assessment of disease activity ≤ 10.

ACR American College of Rheumatology, *CDAI* Clinical Disease Activity Index, *CRP* C-reactive protein, *EULAR* European League Against Rheumatism, *RA* rheumatoid arthritis, *SDAI* Simple Disease Activity Index, *SJC* swollen joint count, *TJC* tender joint count

Supplementary Table S6A Logistic regression analysis on patients with RA with DAS28 > 3.2 at week 36

			Wald CI for parameters		Wald CI for odds ratios		
Parameter	**Category**	**Pr > chi-square**	**Estimate**	**95% confidence limits**	**Compared categories**	**Estimate**	**95% confidence limits**
Duration of disease (years)		0.835	0.004	–0.032, 0.039		1.004	0.969, 1.040
Disease activity at baseline	Mild[a]	0.083	–2.350	–5.007, 0.307	Mild[a] vs. Severe[c]	0.095	0.007, 1.360
	Moderate[b]	0.018	–1.101	–2.012, –0.190	Moderate[b] vs. Severe[c]	0.332	0.134, 0.827
Patient assessment fatigue		0.618	–0.005	–0.023, 0.014		0.995	0.977, 1.014
Patient assessment pain activity		0.383	0.016	–0.020, 0.053		1.017	0.980, 1.055
Patient assessment disease activity		0.969	0.001	–0.042, 0.043		1.001	0.959, 1.044
Physician's assessment disease activity		0.095	–0.027	–0.059, 0.005		0.973	0.942, 1.005
PHQ-2 score		0.520	0.109	–0.222, 0.439		1.115	0.801, 1.552

[a] DAS28 ≤ 3.2

[b] DAS28 > 3.2–5.1

[c] DAS28 > 5.1

CI confidence interval, *DAS28* Disease Activity Score in 28 joints, *PHQ-2* Patient Health Questionnaire-2*, RA* rheumatoid arthritis

Supplementary Table S6B Logistic regression analysis on patients with RA with DAS28 > 3.2 at week 52

			Wald CI for parameters			Wald CI for odds ratios			
Parameter	**Category**	**Pr > chi-square**	**Estimate**	**95% confidence limits**		**Compared categories**	**Estimate**	**95% confidence limits**	
Duration of disease (years)		0.097	0.049	–0.009,	0.107		1.050	0.991,	1.112
Disease activity at baseline	Mild[a]/Moderate[b]	0.365	–0.586	–1.854,	0.681	Mild[a]/Moderate[b] vs. Severe[c]	0.556	0.157,	1.977
Patient assessment fatigue		0.272	0.012	–0.009,	0.033		1.012	0.991,	1.034
Patient assessment pain activity		0.352	–0.020	–0.061,	0.022		0.981	0.941,	1.022
Patient assessment disease activity		0.132	0.032	–0.010,	0.074		1.033	0.990,	1.077
Physician's assessment disease activity		0.568	–0.012	–0.055,	0.030		0.988	0.946,	1.031
PHQ-2 score		0.440	–0.145	–0.514,	0.224		0.865	0.598,	1.250

[a] DAS28 ≤ 3.2

[b] DAS28 > 3.2–5.1

[c] DAS28 > 5.1

CI confidence interval, *DAS28* Disease Activity Score in 28 joints, *PHQ-2* Patient Health Questionnaire-2, *RA* rheumatoid arthritis

Supplementary Table S7 List of all investigators of the ADEQUATE study[a]

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Klaus Krueger	München
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Uwe Schwichtenberg	Bremen
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Sylvia Berger	Naunhof
Frank Zeiger	Leipzig
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Brigitte Otte	Wesel
Frank Schumann	Reken
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Uwe Mall	Bremen
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Jochen Walter	Rendburg
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Thilo Klopsch	Neubrandenburg
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Charlotte Moebius	Schwerin
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Elisabeth Staender	Schwerin
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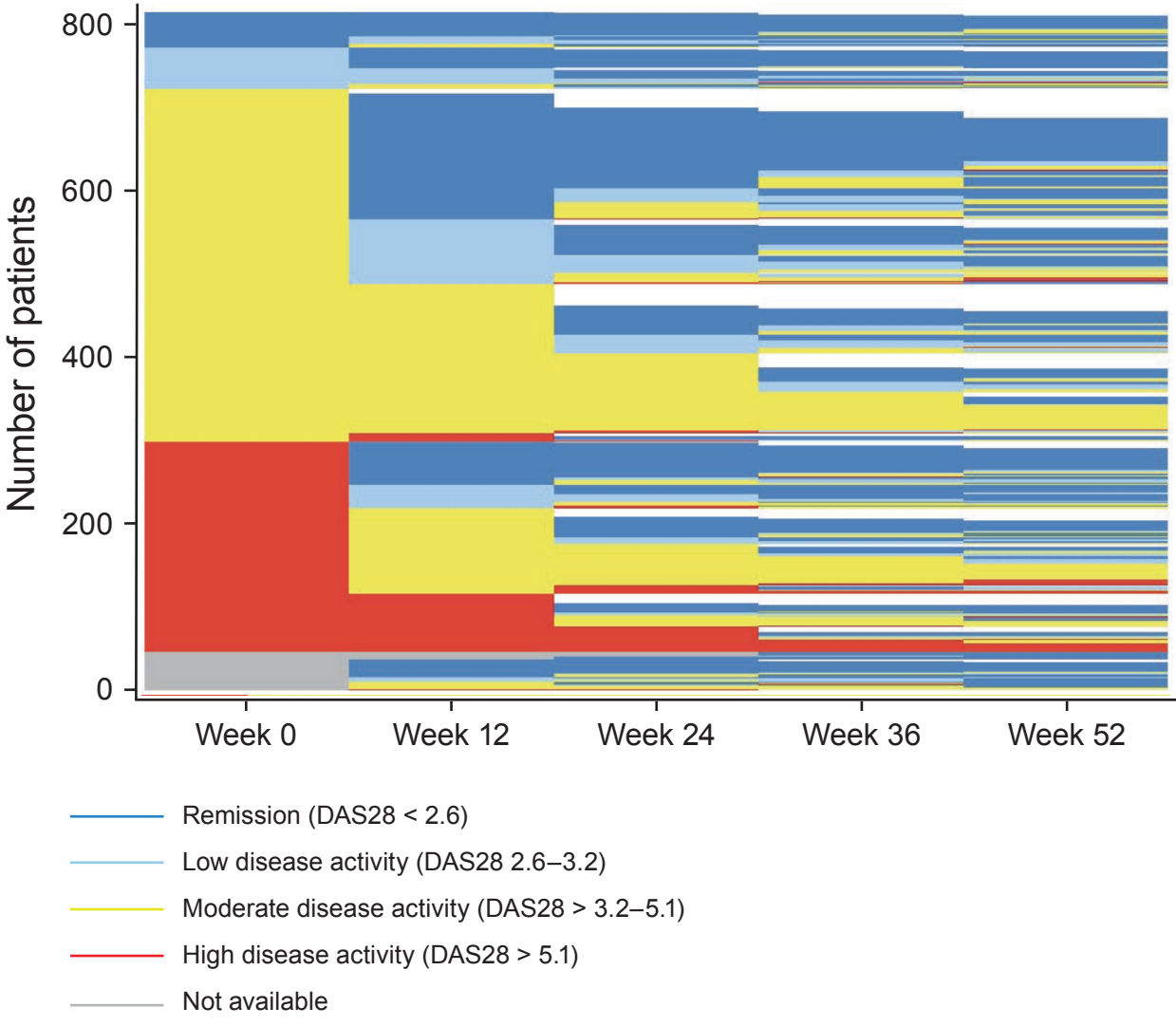
Parysa Alborz	Köln

[a] Includes investigators who recruited patients with axial spondyloarthritis, psoriatic arthritis, and plaque psoriasis.

[b] Unless specified otherwise, investigators were based at private practices.

Supplementary Fig. 1 Course of disease in patients with RA (LOCF)



DAS28, Disease Activity Score in 28 joints; *LOCF*, last observation carried forward; *RA*, rheumatoid arthritis