ELECTRONIC SUPPLEMENTARY MATERIAL FOR:

Retention Rate, Efficacy, and Safety of the Biosimilar CT-P13 versus Reference Infliximab in Patients with Ankylosing Spondylitis: A Propensity Score Matched Analysis from the Korean College of Rheumatology Biologics Registry

Journal: *BioDrugs 2020*

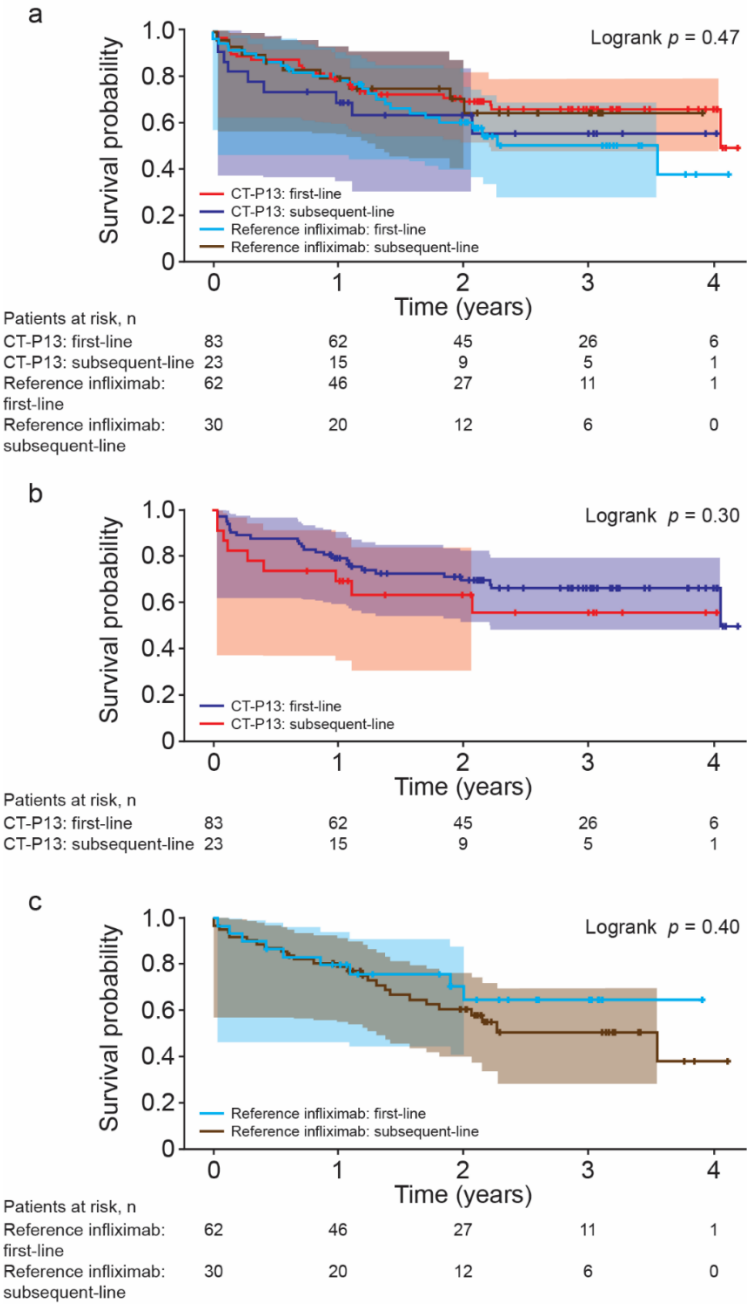
Hyoun-Ah Kim, Eunyoung Lee, Sun-Kyung Lee, Yong-Beom Park, Kichul Shin*

***Corresponding author:** Kichul Shin

Division of Rheumatology, Seoul Metropolitan Government-Seoul National University Hospital Boramae Medical Center, Seoul, Republic of Korea

Email: kideb1@gmail.com

Fig S1 Drug retention[a] up to 4 years by treatment line, overall (**a**), for CT-P13 (**b**), and reference infliximab (**c**) analyzed by Kaplan–Meier and Hall and Wellner methods to account for the varied follow-up periods of different patients due to the prospective, observational design of the KOBIO registry



[a]Defined as time to discontinuation or change of biologic therapy

Shading indicates 95% Hall-Wellner bands. + indicates censored patients

KOBIO Korean College of Rheumatology Biologics

Table S1 Baseline patient characteristics between patients who were included in the study (matched) and patients who were not included in the study (unmatched) after propensity score matching

Characteristics	**Overall (*N* = 256)**	**Unmatched (*n* = 132)**	**Matched (*n* = 124)**	***p*-value**
Age at start, years	39.0 ± 12.9	39.4 ± 12.5	38.6 ± 13.3	0.65
Disease duration, years	4.1 ± 5.3	4.0 ± 5.4	4.2 ± 5.2	0.76
Male, *n* (%)	186 (73)	92 (70)	94 (76)	0.27
Smoking history, *n* (%)				
Ex-smoker	52 (20)	26 (20)	26 (21)	
Current smoker	70 (27)	37 (28)	33 (27)	0.95
Never	134 (52)	69 (52)	65 (52)	
BMI, kg/m^2	23.8 ± 3.2	23.8 ± 3.2	23.8 ± 3.2	0.97
Swollen joint counts	0.8 ± 3.2	0.9 ± 3.8	0.8 ± 2.4	0.78
Tender joint counts	1.4 ± 4.6	1.7 ± 5.6	1.1 ± 3.1	0.29
BASDAI	6.3 ± 1.9	7.0 ± 1.5	5.5 ± 1.9	<0.001*
Patient's GA	6.4 ± 2.1	6.9 ± 1.9	5.8 ± 2.1	<0.001*
ASDAS-ESR	3.7 ± 1.0	4.0 ± 0.9	3.4 ± 1.0	<0.001*
ASDAS-CRP	3.7 ± 1.2	4.0 ± 1.3	3.4 ± 1.0	<0.001*
ESR test result, *n* (%)				
Normal	86 (34)	42 (32)	44 (36)	0.50
ESR	35.4 ± 31.1	35.8 ± 30.4	34.9 ± 31.9	0.82
CRP test result, *n* (%)				
Normal	75 (30%)	36 (27%)	39 (32%)	0.43
CRP	2.1 ± 2.9	2.0 ± 2.6	2.3 ± 3.2	0.38
HLA-B27, *n* (%)				
No	19 (7)	8 (6)	11 (9)	
Positive	201 (79)	103 (78)	98 (79)	0.11
Negative	36 (14)	21 (16)	15 (12)	

Data presented are mean (standard deviation), unless otherwise indicated *Significant *p*-value ($p < 0.05$)

ASDAS Ankylosing Spondylitis Disease Activity Score, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BMI* body mass index, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *GA* global assessment, *HLA-B27* human leukocyte antigen-B27

Table S2 Baseline patient characteristics after propensity score matching (patients who received first-line biologic therapy)

Characteristics	**Overall (*N* = 179)**	**CT-P13 (*n* = 98)**	**Reference infliximab (*n* = 81)**	***p*-value**
Age at start, years	39.6 ± 13.6	38.7 ± 13.4	40.6 ± 13.8	0.20
Disease duration, years	3.3 ± 4.7	3.9 ± 5.2	2.5 ± 3.8	0.01*
Male, *n* (%)	135 (75)	78 (80)	57 (70)	0.43
Smoking history, *n* (%)				
Ex-smoker	37 (21)	20 (20)	17 (21)	
Current smoker	49 (27)	25 (26)	24 (30)	0.54
Never	93 (52)	53 (54)	40 (49)	
BMI, kg/m^2	23.6 ± 3.3	24.3 ± 3.2	23.4 ± 3.4	0.41
Swollen joint counts	0.6 ± 1.9	0.7 ± 2.4	0.5 ± 1.2	0.27
Tender joint counts	0.7 ± 1.8	0.9 ± 2.1	0.6 ± 1.2	0.19
BASDAI	5.5 ± 2.0	5.4 ± 1.9	5.6 ± 2.0	0.45
Patient's GA	5.9 ± 2.2	5.7 ± 2.1	6.1 ± 2.2	0.85
ASDAS-ESR	3.5 ± 1.1	3.4 ± 1.0	3.7 ± 1.1	0.07
ASDAS-CRP	3.4 ± 1.1	3.4 ± 1.0	3.5 ± 1.2	0.42
ESR test result, *n* (%)				
Normal	57 (32)	34 (35)	23 (29)	0.25
ESR	37.3 ± 32.1	33.9 ± 31.3	41.5 ± 32.8	0.11
CRP test result, *n* (%)				
Normal	55 (31)	27 (28)	28 (35)	0.87
CRP	2.4 ± 3.2	2.2 ± 2.8	2.5 ± 3.5	0.63
HLA-B27, *n* (%)				
No	15 (8)	11 (11)	4 (5)	
Positive	148 (83)	77 (79)	71 (88)	0.11
Negative	16 (9)	10 (10)	6 (7)	

Data presented are mean (standard deviation), unless otherwise indicated

*Significant *p*-value ($p < 0.05$)

ASDAS Ankylosing Spondylitis Disease Activity Score, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BMI* body mass index, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *GA* global assessment, *HLA-B27* human leukocyte antigen-B27

Table S3 Baseline characteristics after propensity score matching for patients who received subsequent-line treatment

Characteristics	**Overall (*N* = 69)**	**CT-P13 (*n* = 26)**	**Reference infliximab (*n* = 43)**	***p*-value**
Age at start, years	38.1 ± 12.9	38.3 ± 13.2	38.0 ± 12.8	0.58
Disease duration, years	6.8 ± 6.0	5.4 ± 5.2	7.6 ± 6.3	0.005*
Male, *n* (%)	49 (71)	16 (62)	33 (77)	0.81
Smoking history, *n* (%)				
Ex-smoker	14 (20)	6 (23)	8 (19)	
Current smoker	22 (32)	8 (31)	14 (33)	0.48
Never	33 (48)	12 (46)	21 (49)	
BMI, kg/m^2	22.7 ± 2.8	23.1 ± 2.9	22.2 ± 2.7	0.22
Swollen joint counts	0.5 ± 1.7	1.0 ± 2.6	0.2 ± 0.7	0.10
Tender joint counts	0.9 ± 3.5	1.8 ± 5.4	0.4 ± 1.2	0.17
BASDAI	5.5 ± 1.9	6.0 ± 1.8	5.3 ± 1.9	0.91
Patient's GA	5.6 ± 2.1	6.4 ± 1.9	5.2 ± 2.1	0.46
ASDAS-ESR	3.3 ± 1.0	3.7 ± 1.1	3.1 ± 0.9	0.07
ASDAS-CRP	3.1 ± 1.1	3.5 ± 1.1	2.9 ± 1.1	< 0.001*
ESR test result, *n* (%)				
Normal	27 (39)	10 (38)	17 (40)	0.49
ESR	31.3 ± 27.0	38.8 ± 34.3	26.8 ± 20.5	0.05
CRP test result, *n* (%)				
Normal	35 (51)	12 (46)	23 (55)	0.011*
CRP	1.8 ± 3.3	2.5 ± 4.3	1.3 ± 2.5	0.014*
HLA-B27, *n* (%)				
No	2 (3)	.	2 (5)	
Positive	58 (84)	21 (81)	37 (86)	0.57
Negative	9 (13)	5 (19)	4 (9)	

Data presented are mean (standard deviation), unless otherwise indicated

*Significant *p*-value ($p < 0.05$)

ASDAS Ankylosing Spondylitis Disease Activity Score, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *BMI* body mass index, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *GA* global assessment, *HLA-B27* human leukocyte antigen-B27

Table S4 Prior TNF inhibitors and reasons for changing treatment to CT-P13 or reference infliximab in patients who received subsequent-line treatment

Prior TNF inhibitor **Reason for changing treatment**	**CT-P13** **(*n* = 26)**	**Reference infliximab** **(*n* = 43)**
Adalimumab		
Adverse event	1	5
Inefficacy	7	7
Other		1[a]
CT-P13		
Unknown	2[b]	3
Etanercept		
Adverse event	1	5
Inefficacy	6	5
Other	1[c]	1[d]
Unknown	1	
Reference infliximab		
Inefficacy	1	
Other	2[e]	
Unknown	3	16[b]
Unknown		
Inefficacy	1	

[a]Insurance (*n* = 1)

[b]Reflects treatment that was stopped and restarted with the same biologic

[c]Tremor (*n* = 1)

[d]Patient's will (*n* = 1)

[e]Insurance (*n* = 1) and investigator decision (*n* = 1)

TNF tumor necrosis factor

Table S5 Treatment duration by treatment line

	CT-P13 (*n* = 124)	**Reference infliximab (*n* = 124)**	***p*-value***
All patients			
N	124	124	-
Median, years [IQR]	2.06 [0.99–3.05]	1.75 [0.97–2.24]	0.11
First line			
N	82	62	-
*N*miss[a]	16	19	-
Median, years [IQR]	2.13 [1.02–3.07]	1.64 [0.99–2.18]	0.06
Subsequent line			
N	23	30	-
*N*miss[a]	3	13	-
Median, years [IQR]	1.11 [0.41–2.99]	1.85 [0.95–2.58]	0.75

*The *p*-value was calculated from the two-sided Wilcoxon rank-sum test

[a]*N*miss indicates the number of patients with missing data after initial enrollment

IQR interquartile range

Table S6 Subsequent biologic drugs administered after change from CT-P13 or reference infliximab

Changed to	From CT-P13 (*N* = 21)			From reference infliximab (*N* = 14)		
	Overall (*N* = 21)	First line (*n* = 15)	Subsequent line (*n* = 6)	Overall (*N* = 14)	First line (*n* = 10)	Subsequent line (*n* = 4)
Etanercept	1		1	2	1	1
Reference infliximab	2	2				
CT-P13				3	2	1
Adalimumab	7	5	2	7	5	2
Golimumab	11	8	3	2	2	

Table S7 Efficacy measurements at baseline and at each follow-up in CT-P13-treated and reference infliximab-treated patients

		CT-P13 (*n* = 124)		Reference infliximab (*n* = 124)		*p*-value†
		n	**Median**	***n***	**Median**	
BASDAI	Baseline	124	5.75	124	5.9	0.74
	Year 1	100	2.4	85	3	0.09
	Year 2	62	1.8	51	2.1	0.34
	Year 3	38	1.55	19	2.1	0.68
	Year 4	12	1.75	5	2.6	0.64
ESR	Baseline	124	26	124	28	0.44
	Year 1	102	9	87	11	0.19
	Year 2	63	9.5	51	10	0.77
	Year 3	39	10	19	6	0.06
	Year 4	12	15	5	13	0.54
CRP	Baseline	124	0.97	124	0.53	0.09
	Year 1	88	0.17	85	0.13	0.72
	Year 2	48	0.23	50	0.09	0.02*
	Year 3	25	0.19	18	0.08	0.04*
	Year 4	6	0.5	4	0.12	0.04*
ASDAS-ESR	Baseline	124	3.4	124	3.4	0.92
	Year 1	109	1.9	93	2.2	0.04*
	Year 2	70	1.8	57	1.9	0.66
	Year 3	43	1.4	22	1.4	0.83
	Year 4	14	1.85	5	1.3	-
ASDAS-CRP	Baseline	124	3.4	124	3.2	0.14
	Year 1	109	1.6	93	1.7	0.40
	Year 2	70	1.6	57	1.3	0.20
	Year 3	43	1.5	22	1.05	0.12
	Year 4	14	1.7	5	1.3	0.21
Patient's GA	Baseline	124	6	124	6	0.42
	Year 1	107	3	91	4	0.03*
	Year 2	68	2	57	3	0.32
	Year 3	42	2	22	2.5	0.29
	Year 4	14	2	5	2	0.85

*Significant *p*-value ($p < 0.05$)

†*p*-values were calculated using the two-sided Wilcoxon rank-sum test

ASDAS Ankylosing Spondylitis Disease Activity Score, *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *GA* global assessment

Table S8 Summary of AEs in the CT-P13 and reference infliximab groups

	CT-P13 (*n* = 124)	**Reference infliximab (*n* = 124)**
Patients reporting AEs, *n* (%)	65 (52.4)	52 (41.9)
Patients with study drug-related AEs, *n* (%)	23 (18.5)	19 (15.3)
Total AE cases, *n*	214	151
Total AE cases according to severity, *n*		
Mild/grade 1	124	78
Moderate/grade 2	76	62
Severe/grade 3	10	11
Undefined	4	
Total AE cases according to relationship with treatment, *n*		
Related	60	42
Unrelated	123	81
Indeterminate	30	28
Undefined	1	

AE adverse event

Table S9 Treatment-related adverse events occurring in ≥ 1 patient if grade ≥ 3, or ≥ 2 patients overall if grade 1–2 in intensity

	CT-P13		Reference infliximab	
	Grade 1–2	**Grade 3**	**Grade 1–2**	**Grade 3**
Acute kidney injury			2	
Chronic urticaria	3			
Common cold	4[a]			
Gastric ulcer			2	
Gastritis	2			
Headache	2			
Herpes zoster			1	
Infusion or injection site reaction	8	1	8	
Leukopenia	1			
Mycobacterium tuberculosis infection		1	3	3
Psoriasis			2	
Sinusitis	1			
Skin rash	6		1	
Tinea pedis	1			
Transaminitis	3		2	
Upper respiratory infection	2			
Uveitis	4	1	3	
Other infection			1	
Not specified	9			

Data are number of adverse events

[a]Recurrent in one patient