

Pragmatic trial baricitinib versus First biological in “Tight Control” Patients suffering from Rheumatoid Arthritis (PERFECTRA) – Supplemental Material

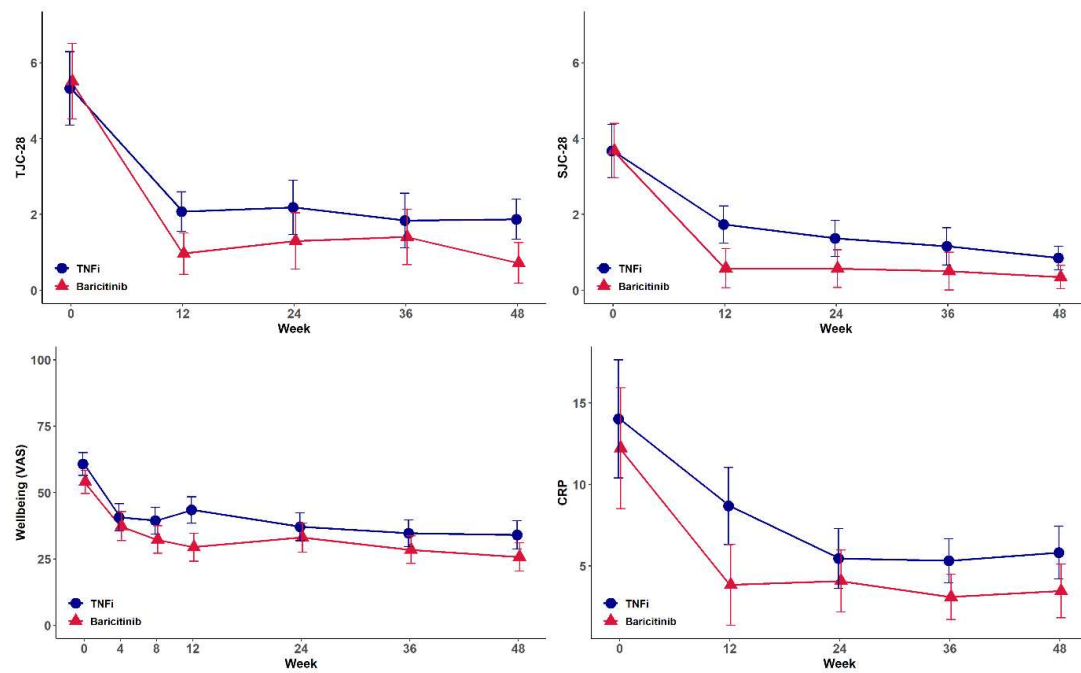


Figure 1 Estimated Marginal Means in individual DAS28-CRP components at weeks 0, 12, 24, 36, and 48

Error bars represent 95% Wald CI. DAS28-CRP: Disease Activity Score with 28-joint count C-reactive protein, TNFi: Tumor necrosis factor inhibitors, VAS: visual analog scale, TJC: tender joint count, SJC: swollen joint count

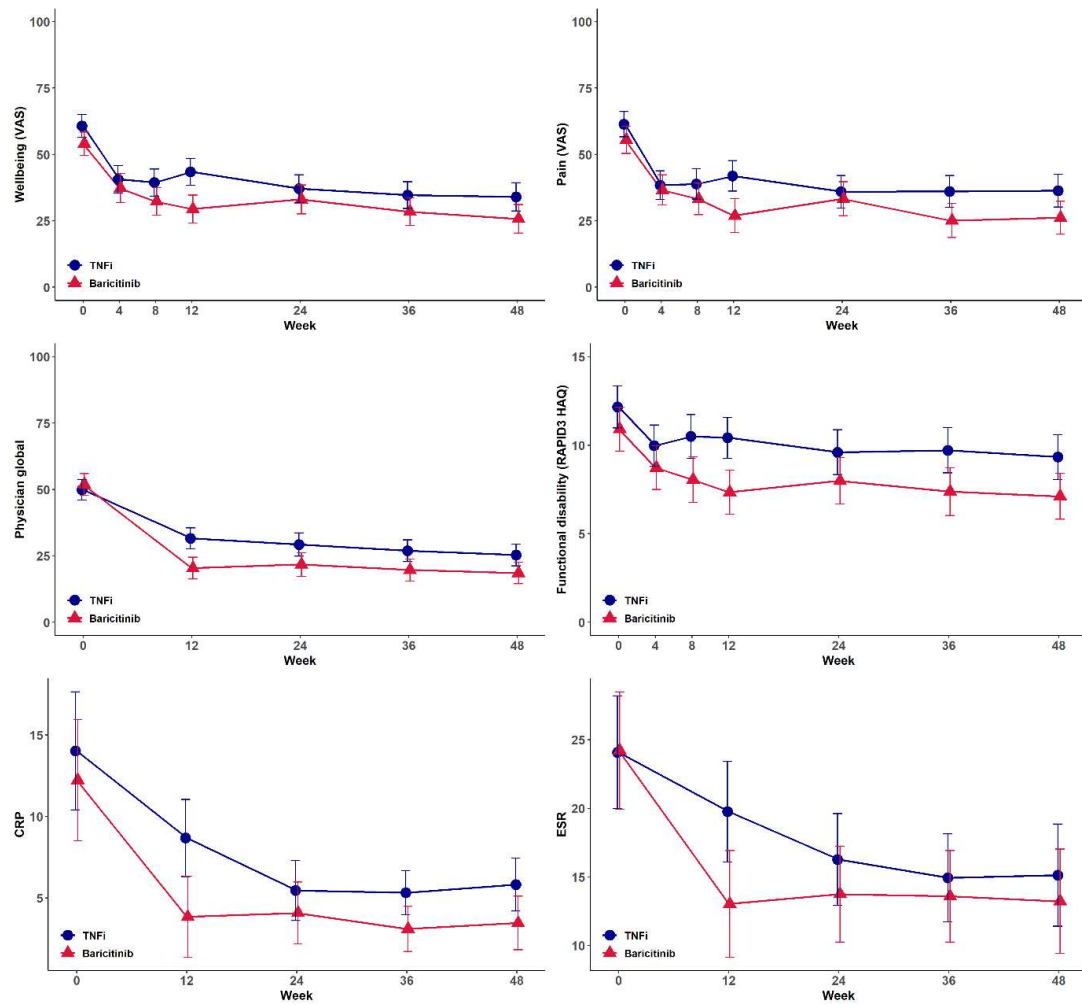


Figure 2 Estimated Marginal Means in VAS Wellbeing, VAS Disease Activity, VAS Pain, functional disability with HAQ, physician global and VAS Fatigue at weeks 0, 12, 24, 36, and 48

Error bars represent 95% Wald CI. DAS28-CRP: Disease Activity Score with 28-joint count C-reactive protein, TNFi: Tumor necrosis factor inhibitors, VAS: visual analog scale, RAPID3 HAQ: Rapid Health Assessment Questionnaire-II

Measure	Intercept	Group		Time		Group x Time	
	value (std. error)	value (std. error)	p-value	value (std. error)	p-value	value (std. error)	p-value
DAS28-CRP	3.7	-0.3 (0.14)	0.00	0.0 (0.00)	0.000	0.0 (0.00)	0.47
CDAI	16.9	-2.0 (1.05)	0.05	-0.2 (0.03)	0.318	0.0 (0.00)	0.32
CRP	11.8	-2.7 (2.02)	0.00	-0.2 (0.040)	0.00	0.0 (0.05)	0.92
ESR	22.6	-2.6 (2.78)	0.35	-0.2 (0.04)	0.00	0.0 (0.06)	0.93
SJC	3.05	-0.47 (0.32)	0.13	-0.05 (0.00)	0.00	-0.01 (0.01)	0.57
TJC	4.2	-0.2 (0.53)	0.65	-0.1 (0.01)	0.00	0.0 (0.01)	0.24
Physician Global	44.0	-4 (2.55)	0.15	0.0 (0.05)	0.00	0.0 (0.08)	0.20
Wellbeing	49.0	-7.0 (1.93)	0.00	0.0 (0.06)	0.00	0.0 (0.08)	0.89
RAPID3 HAQ	11.1	-1.7 (0.78)	0.03	0.0 (0.01)	0.0001	0.0 (0.02)	0.42
Pain	48.0	-5.0 (3.07)	0.10	0.0 (0.06)	0.00	0.0 (0.09)	0.32
Fatigue	53.0	-6.0 (3.50)	0.10	0.0 (0.10)	0.000	0.0 (0.10)	0.60

Table 1 Fixed effects estimates of mixed model analysis for secondary endpoints outcome measures

DAS28-CRP: Disease Activity Score with 28-joint count C-reactive protein, CDAI: clinical disease activity index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, SJC: swollen joint count, TJC: tender joint count, RAPID3 HAQ: Rapid Health Assessment Questionnaire-II

	TNFi strategy	Baricitinib strategy	P-value overall
Week 0	0.00 (0.00; 2.00)	0.00 (0.00; 1.12)	0.407
Week 48	1.00 (0.00; 3.12)	0.00 (0.00; 1.62)	0.099
Progression	0.00 (0.00; 1.00)	0.00 (0.00; 0.50)	0.121

Table 2 Median SHS scores at baseline and week 48 with 95% Wald CI

SHS: Sharp/van der Heijde Scores, TNFi: Tumor necrosis factor inhibitors

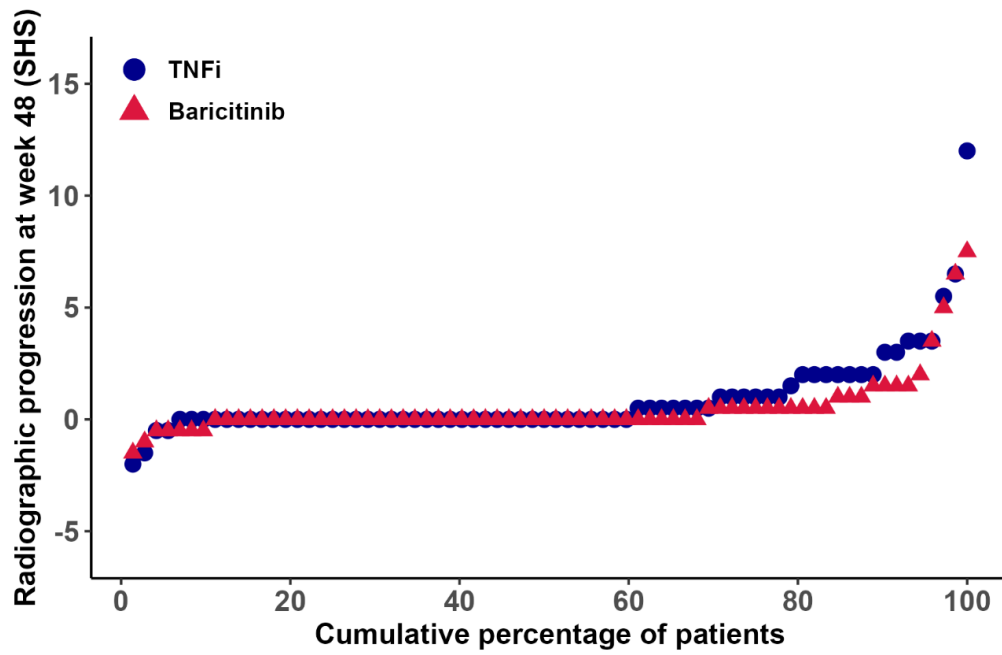


Figure 3 SHS cumulative probability plot

SHS: Sharp/van der Heijde Scores, TNFi: Tumor necrosis factor inhibitors

	Original formulation by attending physician	Translation In English when applicable	Baricitinib strategy	TNFi	While on Baricitinib	While on TNFi
SAE	Tibial plateau fracture left after trauma		0	1	0	1
	myocard infarct		1	0	1	0
	Diaphragmatic herniation after gastric bypass <sup>β</sup>		0	1	0	0
	beklemde navelbreuk	strangulated umbilical hernia	0	1	0	1
	bilateral pneumonia <sup>θ</sup>		1	0	1	0
	infection of urinary tract <sup>θ</sup>		1	0	1	0
	conjunctivitis <sup>θ</sup>		1	0	1	0
	total knee arthroplasty		1	0	1	0
	gemetastaseerd cholangiocarcinoom	metastatic cholangiocarcinoma	0	1	0	1
	esophageal carcinoma		0	1	0	1
cerebral concussion		1	0	1	0	
AE						
airways	dyspnoea		0	1	0	1
Blood	glucose <sup>δ (2) θ α</sup>	dysregulated glucose metabolism	3	1	1	3
	increase of cholesterol <sup>θ (2) φ</sup>		3	0	3	0
	increase of lipids <sup>θ</sup>		1	0	1	0
	leucopenia <sup>α</sup>		0	1	0	1
carcinoma	carcinoma		0	1	0	1
Cold	cold <sup>δ λ α</sup>		2	1	0	3
Cough	cough <sup>θ α</sup>		1	1	1	1
Cramp	cramp		0	1	0	1
disordered appetite	disordered appetite <sup>α (2) ς</sup>		4	0	4	0
dizziness	dizziness <sup>δ μ</sup>		1	3	0	4
Edema	edema <sup>ξ</sup>		1	0	1	0
Fatigue	fatigue <sup>δ θ (3) α (3)</sup>		6	2	6	2
Fever	fever <sup>μ</sup>		2	0	1	1
fractures	fractures		2	1	1	2
Gaining	gaining weight <sup>δ θ (4)</sup>		4	1	4	1
GI tract	diarrhea <sup>θ α</sup>		3	0	3	0
	GI complaints <sup>θ (2) ε (2) ν α (2)</sup>		4	4	6	1
	nausea <sup>δ (10) θ (4) ρ α (11)</sup>		5	24	10	19
Head	dry eyes <sup>δ</sup>		0	1	0	1
	dry nose <sup>δ</sup>		0	1	0	1
	runny nose <sup>δ</sup>		0	1	0	1
	tinnitus <sup>δ</sup>		1	2	1	2
hypertension	hypertension <sup>δ (2) θ (2) χ α</sup>		3	3	3	2
Infection	airways <sup>π (2) θ ν (3) α</sup>		1	7	1	7
	bursitis <sup>ν α</sup>		0	2	0	0
	cold sore <sup>θ ν σ α</sup>		1	3	1	2
	COVID-19 <sup>ν</sup>		4	2	2	3

	eye <sup>θ</sup> γ α	1	2	2	1	
	flu <sup>μ</sup>	1	2	0	3	
	fungal <sup>δ</sup>	1	1	1	1	
	prostate	1	0	1	0	
	shingles <sup>θ</sup>	1	0	1	0	
	sinusitis <sup>θ</sup>	0	1	1	0	
	skin <sup>θ</sup> β α	0	3	2	1	
	throat <sup>δ</sup>	0	1	0	1	
	tooth	0	1	0	1	
	urinary tract <sup>δ</sup> (2) θ (6) γ (2)	5	7	6	6	
	viral <sup>θ</sup>	1	0	1	0	
inflammation	tendon	0	2	0	2	
	throat <sup>θ</sup> (2)	0	2	0	2	
insomnia	insomnia <sup>δ</sup>	1	1	1	1	
Kidney	renal dysfunction <sup>ε</sup> θ	1	1	2	0	
less blood loss during period	less blood loss during period	1	0	1	0	
Liver	increased liver values <sup>θ</sup> ε τ α (8)	2	10	4	6	
Malaise	malaise <sup>δ</sup>	0	1	0	1	
Mouth	burning sensation <sup>θ</sup>	1	0	1	0	
	change of taste <sup>δ</sup> θ (2)	2	1	2	1	
	mouth sore <sup>θ</sup>	1	0	1	0	
	mucus <sup>α</sup>	0	1	0	1	
	sensitive skin <sup>θ</sup>	1	0	1	0	
Other	Body feels warm after Enbrel injection <sup>γ</sup>	0	1	0	1	
	dental problems <sup>α</sup>	0	1	0	1	
	Dupuytren	1	0	0	1	
	fall	1	0	1	0	
	feeling of pressure on the chest <sup>α</sup>	0	1	1	0	
	Hernia cicatricialis	1	0	1	0	
	hernia with ulcer	1	0	0	1	
	HNP	1	0	1	0	
	hot flashes <sup>θ</sup> (2) γ	2	1	2	1	
	increase activity glandula parotis right	0	1	0	1	
	increase PSA value	0	1	0	1	
	Macrocytaire anemia <sup>θ</sup>	macrocytic anemia	1	0	1	0
	mortonse neurose right foot	Morton's neuropathy	0	1	0	1
	Not feeling well for a few hours <sup>δ</sup>		0	1	0	1
	numbness and tingling sensation of hands and feet <sup>η</sup>		0	1	0	1
	shaky <sup>α</sup> δ		2	0	0	2
	swollen hands and feet during hot summer		1	0	1	0
trombosflebitis		0	1	0	1	
Pain	chest <sup>λ</sup>	0	2	0	2	
	head <sup>δ</sup> θ (5) γ α	9	6	11	4	
	leg <sup>θ</sup> γ	1	1	1	1	

	stomach <sup>α</sup>		0	1	0	1
	throat <sup>θ</sup>		0	2	1	1
perspiration	perspiration <sup>μ</sup>		1	0	0	1
restless	restless <sup>λ</sup>		1	0	1	0
Skin	bruise <sup>δ θ γ α ι</sup>		3	3	4	2
	cellulitis <sup>θ</sup>		1	0	1	0
	rash/itch/eczema <sup>δ (5) θ (7) γ (4) ε α τ (2) κ</sup>		8	17	7	15
	wound		0	1	0	1
aggravation of complaints	omarthrose right <sup>λ</sup>		1	0	1	0
	reumatoide arthritis <sup>θ</sup>	Rheumatoid arthritis	2	0	2	0

Table 3 SAE and AE full overview

(S)AE's that are attributed to medication according to prescribing physicians is indicated by footnotes: α Methotrexat, β Benepali, γ Etanercept, δ Adalimumab, ε Hydroxychloroquine, ζ Arthrotec, η Pravastatine, θ baricitinib, ι Prednisolon, κ Tocilizumab, λ Leflunomide, μ Infliximab, ν Meloxicam, ξ Amlodipine, π amgevita, ρ Celecoxib, ς Sulfasalazine, σ Filgotinib, τ Sarilumab, φ rosuvastatine, χ hydrochloorthiazide.

(S)AE without a footnote are not attributed to medication according to prescribing physician.

The number in brackets following the footnote indicates the amount of AE (>1) that were thought to be related to the medication used according to physicians, TNFi: tumor necrosis factor inhibitors



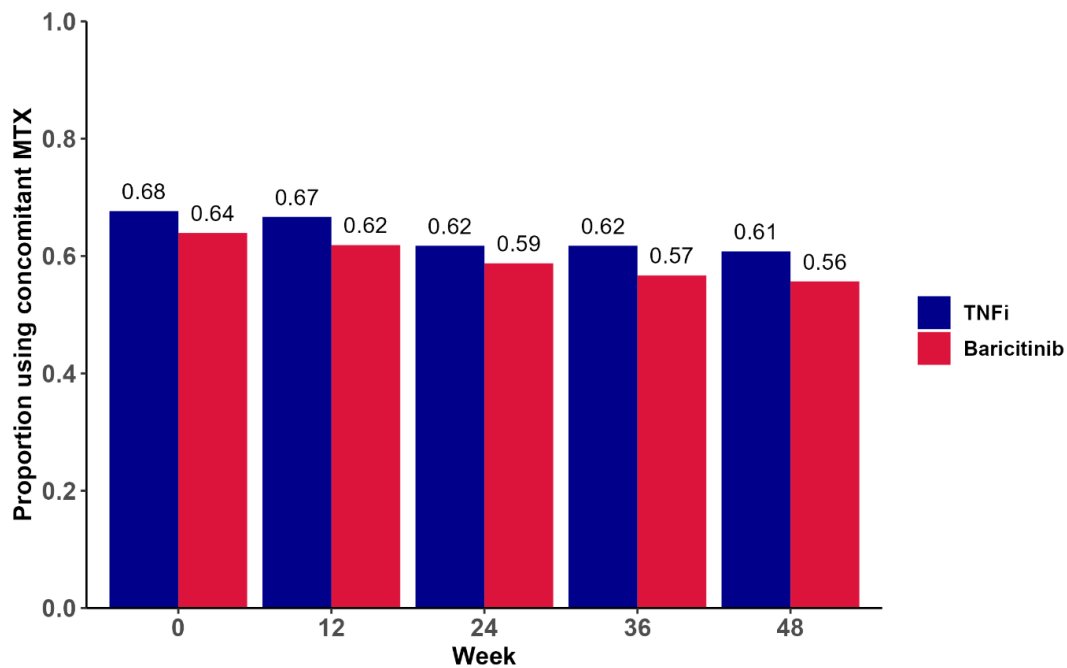


Figure 4 Concomitant MTX use for Baricitinib strategy group and TNFi strategy group  
 MTX: Methotrexate, TNFi: Tumor necrosis factor inhibitors

Switch frequency in first 12 weeks	TNFi strategy (N)	Baricitinib strategy
0	82	68
1	11	17
2	6	4
3	0	3
4	3	4
5	0	1

Table 4 Frequency table showing N of patients changing MTX dose in the first 12 weeks.

MTX: methotrexate. No statistically significant difference between groups ( $P=0.21$ ).