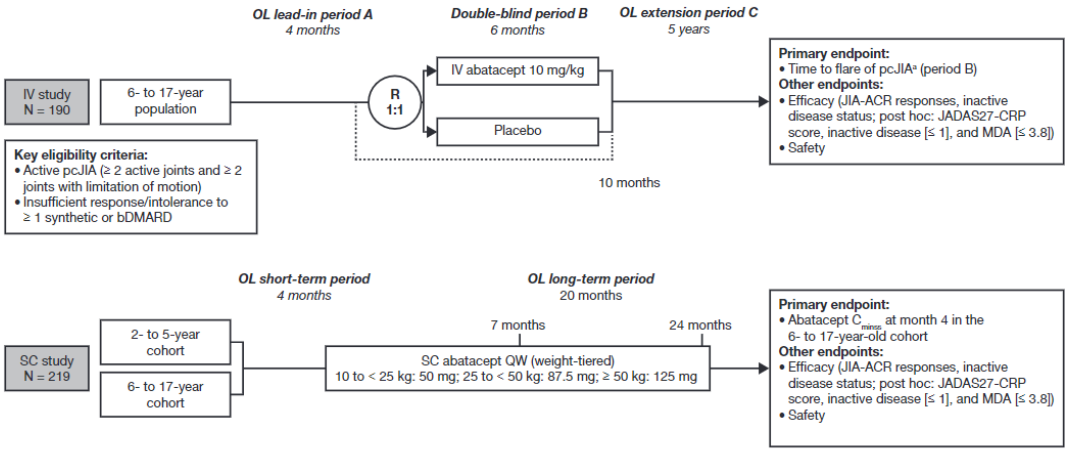
Supplementary Figure S1. Study design: IV and SC abatacept in pcJIA.

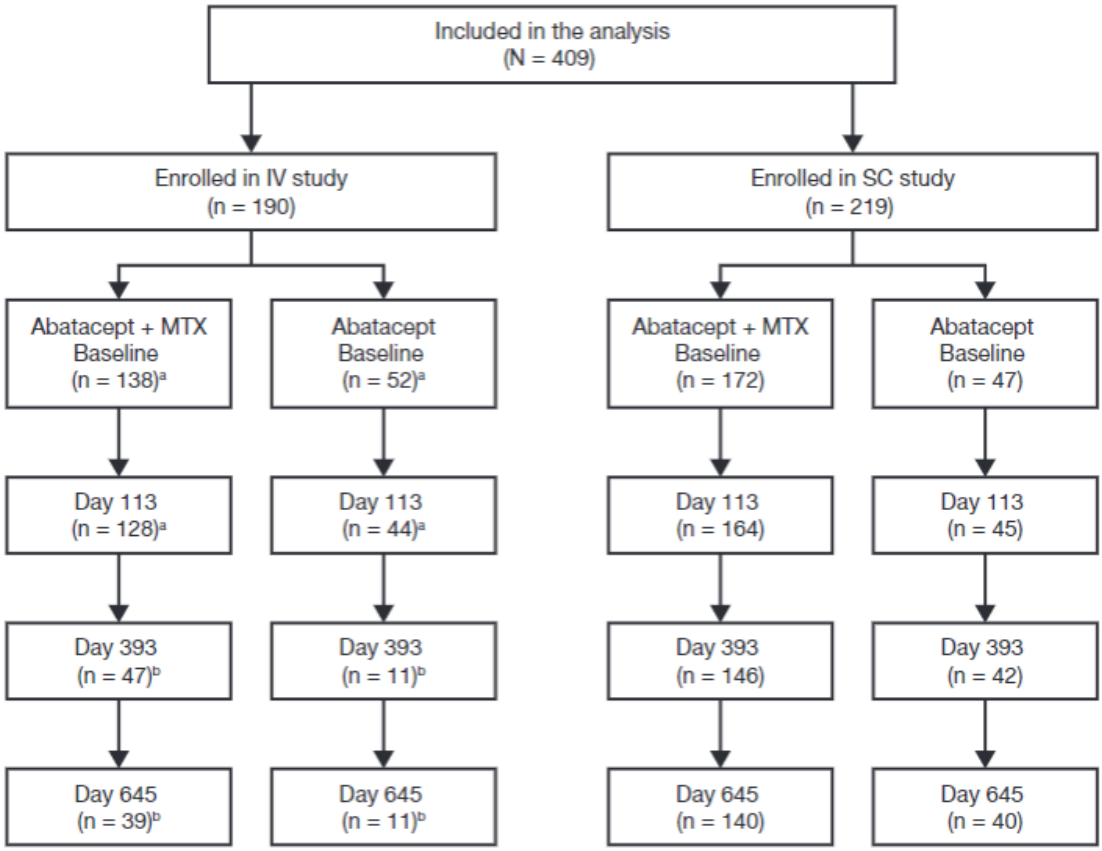


[a]Flare was defined as worsening of ≥ 30% in ≥ 3 of the 6 ACR core-response variables for JIA, and ≥ 30% improvement in 1 variable during the double-blind period; inactive disease was defined as absence of active joints, Physician Global Assessment of disease severity ≤ 10 mm, and ESR ≤ 20 mm/h (IV study) or CRP ≤ 0.6 mg/dL (SC study). The dashed line for the IV study shows the option for non-responders in period A to receive OL treatment with abatacept in period C.

ACR: American College of Rheumatology; bDMARD: biologic disease-modifying antirheumatic drug; C_{minss}: steady-state serum trough concentration; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IV: intravenous; JADAS27: Juvenile Arthritis Disease Activity Score in 27 joints; MDA: minimal disease activity; OL: open-label; pcJIA: polyarticular-course juvenile idiopathic arthritis; R: randomization; SC: subcutaneous.

Ruperto et al. J Rheumatol 2023. doi:10.3899/jrheum.2022-1320

Supplementary Figure S2. Evaluable patient population for efficacy assessment by trial, time point, and MTX use.



[a]Includes all treated patients in period A.

[b]Includes all patients randomized to abatacept in period B; day 393 corresponds with day 85 of period C and day 645 corresponds with day 673 of period C.

IV: intravenous; MTX: methotrexate; SC: subcutaneous.

Ruperto et al. J Rheumatol 2023. doi:10.3899/jrheum.2022-1320

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Baseline demographics and disease characteristics by study treatment and reason for MTX discontinuation for all treated patients.

	SC Abatacept[a]			IV Abatacept		
	Abatacept + MTX, n = 172	Abatacept Monotherapy (MTX LOE), n = 14	Abatacept Monotherapy (MTX Intolerance), n = 22	Abatacept + MTX n = 138	Abatacept Monotherapy (MTX LOE), n = 23	Abatacept Monotherapy (MTX Intolerance), n = 21
Duration of JIA, months	12.0 (0.0–36.0)	24.0 (12.0–60.0)	12.0 (0.0–36.0)	36.0 (12.0–72.0)	84.0 (36.0–108.0)	84.0 (36.0–108.0)
JIA categories, n (%)						
Polyarticular RF−	97 (56.4)	6 (42.9)	14 (63.6)	55 (39.9)	14 (60.9)	7 (33.3)
Oligoarticular	24 (14.0)	3 (21.4)	3 (13.6)	17 (12.3)	4 (17.4)	10 (47.6)
Polyarticular RF+	38 (22.1)	4 (28.6)	4 (18.2)	34 (24.6)	1 (4.3)	0 (0.0)
Systemic	5 (2.9)	0 (0.0)	0 (0.0)	31 (22.5)	4 (17.4)	4 (19.0)
Other	8 (4.7)	1 (7.1)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)
Physician Global Assessment, 0–100 mm VAS[b]	49.3 (35.0–64.2)	34.4 (22.0–72.0)	58.0 (28.0–71.0)	50.5 (38.0–65.0)	60.0 (45.0–77.0)	59.0 (45.0–68.0)

Ruperto et al. J Rheumatol 2023. doi:10.3899/jrheum.2022-1320

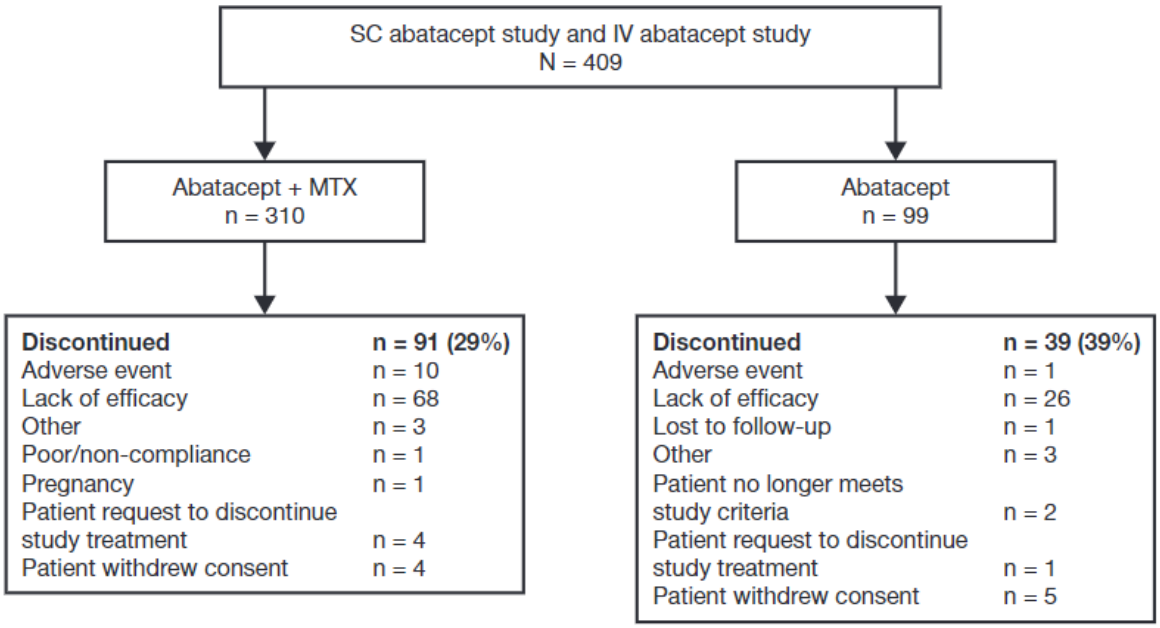
Parent Global Assessment of patient overall well-being, 0–100 mm VAS [b]	47.8 (21.8–66.3) (n = 171)	33.3 (13.0–59.6)	52.4 (39.0–66.3)	47.0 (28.0–59.0)	37.0 (13.0–63.0)	38.0 (8.0–61.0)
CHAQ-DI	1.0 (0.5–1.6) (n = 171)	0.8 (0.1–1.6)	0.9 (0.4–1.9)	1.3 (0.8–1.9)	1.3 (0.4–1.8)	1.0 (0.6–1.3)
Active joints	10.0 (6.0–18.0)	5.0 (4.0–9.0)	8.5 (6.0–16.0)	12.5 (6.0–25.0)	12.0 (6.0–34.0)	11.0 (6.0–15.0)
Joints with LOM	8.5 (5.0–15.0)	4.0 (2.0–10.0)	9.0 (7.0–13.0)	12.5 (6.0–26.0)	11.0 (4.0–30.0)	12.0 (8.0–15.0)
CRP, mg/dL	0.3 (0.1–1.0)	0.3 (0.1–0.8)	0.1 (0.1–0.5)	1.4 (0.2–5.8)	1.3 (0.3–2.8)	0.9 (0.3–3.1)
JADAS27-CRP	18.8 (13.2–25.0)	12.0 (6.3–25.4)	21.1 (13.5–25.2)	21.7 (15.5–31.1)	19.3 (14.5–36.3)	19.6 (13.5–24.4)
Pain VAS < 35 mm, n (%)	63 (36.6)	5 (35.7)	4 (18.2)	50 (36.2)	6 (26.1)	9 (42.9)
Prior biologic use, n (%)	32 (18.6)	9 (64.3)	9 (40.9)	30 (21.7)	14 (60.9)	9 (42.9)
MTX dose, mg/kg/week	0.4 (0.3–0.5)	NA	NA	0.4 (0.3–0.6)	NA	NA
Prednisone equivalent dose, mg/kg/day	0.15 (0.09–0.18) (n = 54)	0.13 (0.07–0.18) (n = 2)	0.17 (0.12–0.22) (n = 2)	0.14 (0.11–0.18) (n = 71)	0.15 (0.10–0.19) (n = 11)	0.14 (0.09–0.19) (n = 5)

Data are presented as median (Q1–Q3) unless otherwise noted.

[a]Data presented reflect the cohort aged 2–17 years. [b]A score of 0 corresponds with “very well” and “inactive disease” for Parent Global Assessment of patient overall well-being and Physician Global Assessment, respectively.

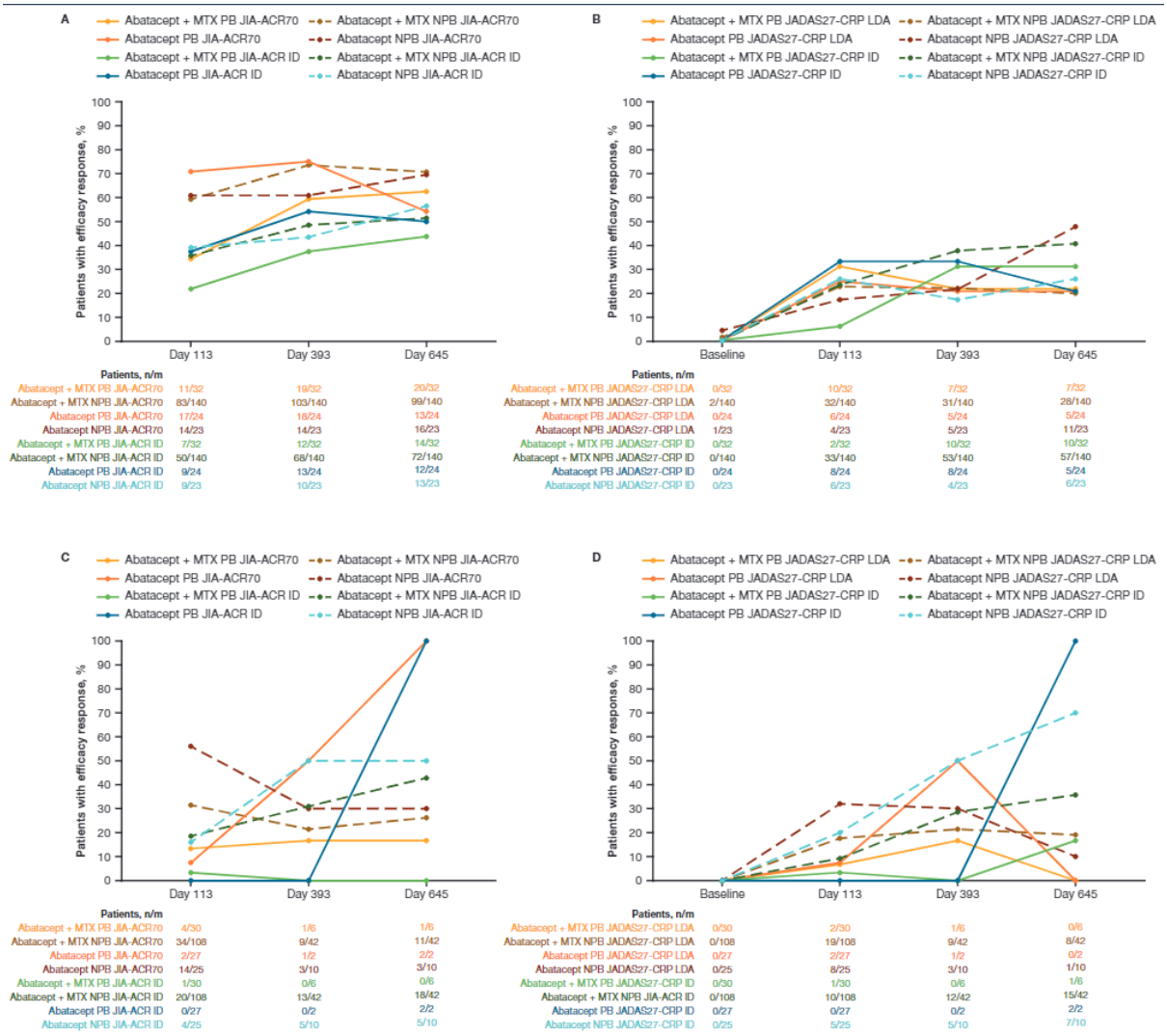
CHAQ-DI: Childhood Health Assessment Questionnaire–Disability Index; CRP: C-reactive protein; IV: intravenous; JADAS27-CRP: Juvenile Arthritis Disease Activity Score in 27 joints using CRP; JIA: juvenile idiopathic arthritis; LOE: loss of efficacy; LOM: limitation of motion; MTX: methotrexate; NA: not applicable; RF: rheumatoid factor; SC: subcutaneous; VAS: visual analog scale.

Supplementary Figure S3. Patient disposition by abatacept monotherapy and combination therapy (abatacept + MTX) use.



IV: intravenous; MTX: methotrexate; SC: subcutaneous.

Supplementary Figure S4. Efficacy responses over time by MTX and prior biologic use in patients with pcJIA receiving abatacept + MTX or abatacept monotherapy within the SC study[a] (A and B) and the IV study[b] (C and D).



[a]Includes all treated patients. [b]Includes all patients randomized to abatacept during period B. ID: inactive disease; IV: intravenous; JADAS27-CRP: Juvenile Arthritis Disease Activity Score in 27 joints using C-reactive protein; JIA-ACR70: 70% improvement in juvenile idiopathic arthritis-American College of Rheumatology criteria; LDA: low disease activity; MTX: methotrexate; PB: prior biologic use; pcJIA: polyarticular-course juvenile idiopathic arthritis; n/m: number of patients with efficacy response/number of patients in the analysis; NPB: no prior biologic use; SC: subcutaneous.

Supplementary Table S2. Summary of exposure adjusted adverse events by age and MTX use in the SC study for all treated patients.

	SC Abatacept 2- to 5-year-old Cohort		SC Abatacept 6- to 17-year-old Cohort	
	Abatacept + MTX, n = 36	Abatacept, n = 10	Abatacept + MTX, n = 136	Abatacept, n = 37
SAEs	4 (6.3)	1 (5.6)	11 (4.8)	5 (7.8)
Overall AEs	264 (417.7)	78 (433.3)	761 (332.0)	128 (200.3)
AEs related to study drug	88 (139.2)	19 (105.6)	144 (62.8)	31 (48.5)
AEs of special interest				
Malignancy	0 (0)	0 (0)	1 (0.4)	0 (0)
Autoimmune disease	0 (0)	0 (0)	3 (1.3)	0 (0)
Infections and infestations	124 (196.2)	29 (161.1)	297 (129.6)	60 (93.9)
Acute tonsilitis	0 (0)	0 (0)	0 (0)	0 (0)
Bronchitis	5 (7.9)	0 (0)	4 (1.7)	3 (4.7)
Cellulitis	0 (0)	1 (5.6)	0 (0)	0 (0)
Ear infection	2 (3.2)	0 (0)	2 (0.9)	0 (0)
Enterobiasis	0 (0)	1 (5.6)	1 (0.4)	0 (0)
Gastroenteritis	4 (6.3)	2 (11.1)	13 (5.7)	4 (6.3)
Impetigo	2 (3.2)	0 (0)	1 (0.4)	0 (0)
Influenza	2 (3.2)	2 (11.1)	15 (6.5)	3 (4.7)
Laryngitis	0 (0)	1 (5.6)	0 (0)	1 (1.6)
Nasopharyngitis	30 (47.5)	9 (50.0)	74 (32.3)	14 (21.9)
Otitis media	2 (3.2)	0 (0)	0 (0)	2 (3.1)
Pharyngitis	7 (11.1)	0 (0)	12 (5.2)	1 (1.6)
Rhinitis	15 (23.7)	1 (5.6)	13 (5.7)	4 (6.3)
Scarlet fever	2 (3.2)	1 (5.6)	0 (0)	0 (0)
Sinusitis	1 (1.6)	1 (5.6)	10 (4.4)	2 (3.1)
Tonsilitis	7 (11.1)	0 (0)	6 (2.6)	2 (3.1)

Ruperto et al. J Rheumatol 2023. doi:10.3899/jrheum.2022-1320

Tracheitis	0 (0)	1 (5.6)	0 (0)	0 (0)
Upper respiratory tract infection	10 (15.8)	5 (27.8)	56 (24.4)	6 (9.4)
Urinary tract infection	1 (1.6)	0 (0)	10 (4.4)	3 (4.7)
Varicella	3 (4.7)	0 (0)	0 (0)	0 (0)
Viral infection	0 (0)	0 (0)	0 (0)	1 (1.6)
GI disorders	39 (61.7)	14 (77.8)	101 (44.1)	16 (25.0)
Abdominal pain	3 (4.7)	1 (5.6)	12 (5.2)	5 (7.8)
Aphthous ulcer	2 (3.2)	1 (5.6)	7 (3.1)	0 (0)
Mouth ulceration	0 (0)	0 (0)	0 (0)	3 (4.7)
Nausea	4 (6.3)	3 (16.7)	28 (12.2)	0 (0)
Vomiting	8 (12.7)	1 (5.6)	15 (6.5)	3 (4.7)
Hepatobiliary disorders	0 (0)	0 (0)	2 (0.9)	0 (0)
Hepatic enzyme increases	2 (3.2)	0 (0)	0 (0)	0 (0)

All values shown as n (IR/100 patient-years).

AE: adverse event; GI: gastrointestinal; IR: incidence rate; MTX: methotrexate; SAE: serious adverse event; SC: subcutaneous.

Ruperto et al. J Rheumatol 2023. doi:10.3899/jrheum.2022-1320

Supplementary Table S3. Abatacept C_{minss} values at day 113 by MTX use.

	SC Abatacept[a,b]		IV Abatacept[b,c]	
	Abatacept + MTX, n = 128	Abatacept, n = 37	Abatacept + MTX, n = 115	Abatacept, n = 35
C_{minss} at day 113	43.6 (9.3–122.1)	46.0 (15.8–97.0)	10.9 (0.2–61.6)	11.9 (0.5–39.7)

Values presented as mean (min–max).

[a]2- to 17-year-old cohort.

[b]Data for C_{minss} at day 113 reflect the time of the primary pharmacokinetic endpoint for the SC study and the duration of period A for the IV study.

[c]6- to 17-year-old cohort.

C_{minss}: abatacept minimum steady-state trough concentration; IV: intravenous; MTX: methotrexate; SC: subcutaneous.

Ruperto et al. J Rheumatol 2023. doi:10.3899/jrheum.2022-1320