Table SI. Patient and treatment characteristics in all paediatric patients with psoriasis at start of methotrexate treatment and split for patients with folic acid once weekly vs 6 times weekly

	All patients[a] (*n* = 105)	Patients with FA once weekly (*n* = 48)	Patients with FA 6 times weekly (*n* = 53)	*p*-value[d]
Patient characteristics				
Sex (male), *n* (%)	43 (41.0)	24 (50.0)	19 (35.8)	0.217
Age, years, mean (SD) [range]	14.1 (3.1) [5.7–17.9]	14.3 (2.9) [6.5–17.9]	13.9 (3.3) [5.7–17.8]	0.724
BMI[b], *n* (%)				0.063
Thinness	9 (8.6)	4 (8.3)	3 (5.7)	
Normal weight	74 (70.5)	29 (60.4)	43 (81.1)	
Overweight/obesity	22 (21.0)	15 (31.3)	7 (13.2)	
Psoriasis location[c], n (%)				
Scalp	104 (99.0)	47 (97.9)	53 (100.0)	0.960
Inverse	47 (44.8)	19 (39.6)	25 (47.2)	0.571
Unguium	17 (16.2)	11 (22.9)	6 (11.3)	0.197
Psoriasis duration, median (IQR) [range]	4.1 (4.8) [0.3–14.7]	4.1 (5.9) [0.3–10.8]	4.3 (4.2) [0.5–14.7]	0.778
PASI (0–72), mean (SD) [range]	10.2 (6.2) [3.0–42.4]	11.1 (6.7) [3.2–42.4]	9.5 (5.5) [3.0–32.4]	0.192
BSA (0–100), mean (SD) [range]	14.7 (13.2) [2.5–76.0]	15.8 (15.7) [2.6–76.0]	13.9 (10.8) [2.5–59.0]	0.490
PGA (0–5), mean (SD) [range]	3.3 (1.0) [1.0–5.0]	3.3 (0.8) [1.0–5.0]	3.2 (0.8) [2.0–5.0]	0.373
CDLQI (0–30), mean (SD) [range]	10.2 (5.0) [1.0–24.0]	9.9 (5.2) [1.0–19.0]	10.6 (4.8) [2.0–24.0]	0.477
Treatment characteristics				
Treatment duration, years, mean (SD) [range]	1.8 (1.6) [0.1–8.0]	2.4 (2.0) [0.2–8.0]	1.1 (0.8) [0.06–3.1]	**< 0.001**
Dose in mg/kg/week, mean (SD) [range]	0.27 (0.09) [0.02–0.51]	0.26 (0.10) [0.02–0.50]	0.28 (0.09) [0.16–0.51]	0.188
Administration route, *n* (%)				0.944
Oral	103 (98.1)	47 (97.9)	52 (98.1)	
Subcutaneous	2 (1.9)	1 (2.1)	1 (1.9)	

[a]All patients including 4 patients who switched from FA once weekly to 6 times weekly or vice versa during follow-up (these 4 patients were not included in the FA regimen groups). [b]Cut-offs for overweight/obesity were based on The extended International Obesity Taskforce (IOTF) body mass index (BMI) cut-offs for thinness, overweight and obesity by Cole et al. [c]Total number of patients does not equal sum of patients reporting different locations of psoriasis because more than 1 location of psoriasis can be reported in the same patient. [d]Comparison by Mann–Whitney *U* test in case of non-normal distributed continuous variables, by independent sample *t*-tests in case of normal continuous data and by χ^2 tests or Fisher's exact tests for categorical data.
BSA: body surface area; CDLQI: Children's Dermatology Life Quality Index; IQR: interquartile range; FA: folic acid; PASI: Psoriasis Area and Severity Index; PGA: Physician Global Assessment; SD: standard deviation. *p*-values in bold are considered to be statistically significant.

Table SII. Cox regression model used to compare the occurrence of persistent gastrointestinal adverse events between folic acid regimens

	Estimate	95% CI	*p*-value
First model including all confounders			
FA regimen			0.160
FA once per week	0[a]		
FA 6 times per week	0.620	0.318–1.207	
Sex			0.346
Male	0.728	0.376–1.410	
Female	0[a]		
BMI at baseline			0.999
Underweight/normal weight	0[a]		
Overweight/obesity	1.001	0.389–2.577	
Age, years	0.998	0.843–1.181	0.980
MTX dose in mg/kg at baseline	0.592	0.002–209.9	0.861
Final model (after exclusion of confounders that did not alter the unadjusted exposure-outcome effect by 10% or more)			
FA regimen			0.196
FA once per week	0[a]		
FA 6 times per week	0.656	0.346–1.243	

[a]This parameter was set to zero because it is redundant.
BMI: body mass index; CI: confidence interval; FA: folic acid; MTX: methotrexate.

Table SIII. Final logistic regression models used for comparison of effectiveness between folic acid regimens

Variable	Estimate	95% CI	*p*-value
Last observation carried forward (LOCF) analysis			
Absolute PASI ≤3.0			
Week 12			
FA regimen			0.358
FA once per week	0[a]		
FA 6 times per week	1.542	0.613–3.878	
Week 24			
FA regimen			0.333
FA once per week	0[a]		
FA 6 times per week	0.673	0.302–1.501	
Week 36			
FA regimen			0.190
FA once per week	0[a]		
FA 6 times per week	0.566	0.242–1.326	
BMI at baseline			**0.013**
Underweight/normal weight	0[a]		
Overweight/obesity	0.234	0.075–0.732	
Week 48			
FA regimen			0.562
FA once per week	0[a]		
FA 6 times per week	0.783	0.341–1.794	
Age, years	1.175	0.951–1.452	0.134
Absolute PASI ≤2.0			
Week 12			
FA regimen			0.065
FA once per week	0[a]		
FA 6 times per week	2.874	0.937–8.815	
Week 24			
FA regimen			0.788
FA once per week	0[a]		
FA 6 times per week	0.889	0.376–2.100	
Week 36			
FA regimen			0.621
FA once per week	0[a]		
FA 6 times per week	0.793	0.315–1.992	
BMI at baseline			**0.027**
Underweight/normal weight	0[a]		
Overweight/obesity	0.173	0.036–0.820	
Age in years	1.654	0.645–4.242	0.295
Week 48			
FA regimen			0.713
FA once per week	0[a]		
FA 6 times per week	0.848	0.351–2.046	
Sex			0.176
Male	0.532	0.213–1.328	
Female	0[a]		
As treated analysis			
Absolute PASI ≤3.0			
Week 12			
FA regimen			0.358
FA once per week	0[a]		
FA 6 times per week	1.542	0.613–3.878	
Week 24			
FA regimen			0.972
FA once per week	0[a]		
FA 6 times per week	0.972	0.404–2.400	
Week 36			
FA regimen			0.818
FA once per week	0[a]		
FA 6 times per week	0.888	0.323–2.422	
BMI at baseline			**0.026**
Underweight/normal weight	0[a]		
Overweight/obesity	0.157	0.031–0.798	
Week 48			
FA regimen			0.130
FA once per week	0[a]		
FA 6 times per week	2.400	0.772–7.459	
Absolute PASI ≤2.0			
Week 12			
FA regimen			0.065
FA once per week	0[a]		
FA 6 times per week	2.874	0.937–8.815	
Week 24			
FA regimen			0.822
FA once per week	0[a]		
FA 6 times per week	1.115	0.430–2.893	
Week 36			
FA regimen			0.361
FA once per week	0[a]		
FA 6 times per week	1.621	0.575–4.567	
Week 48			
FA regimen			0.199
FA once per week	0[a]		
FA 6 times per week	2.000	0.694–5.764	

[a]This parameter was set to zero because it is redundant.
BMI: body mass index; CI: confidence interval; FA: folic acid; MTX: methotrexate. *p*-values in bold are considered to be statistically significant.

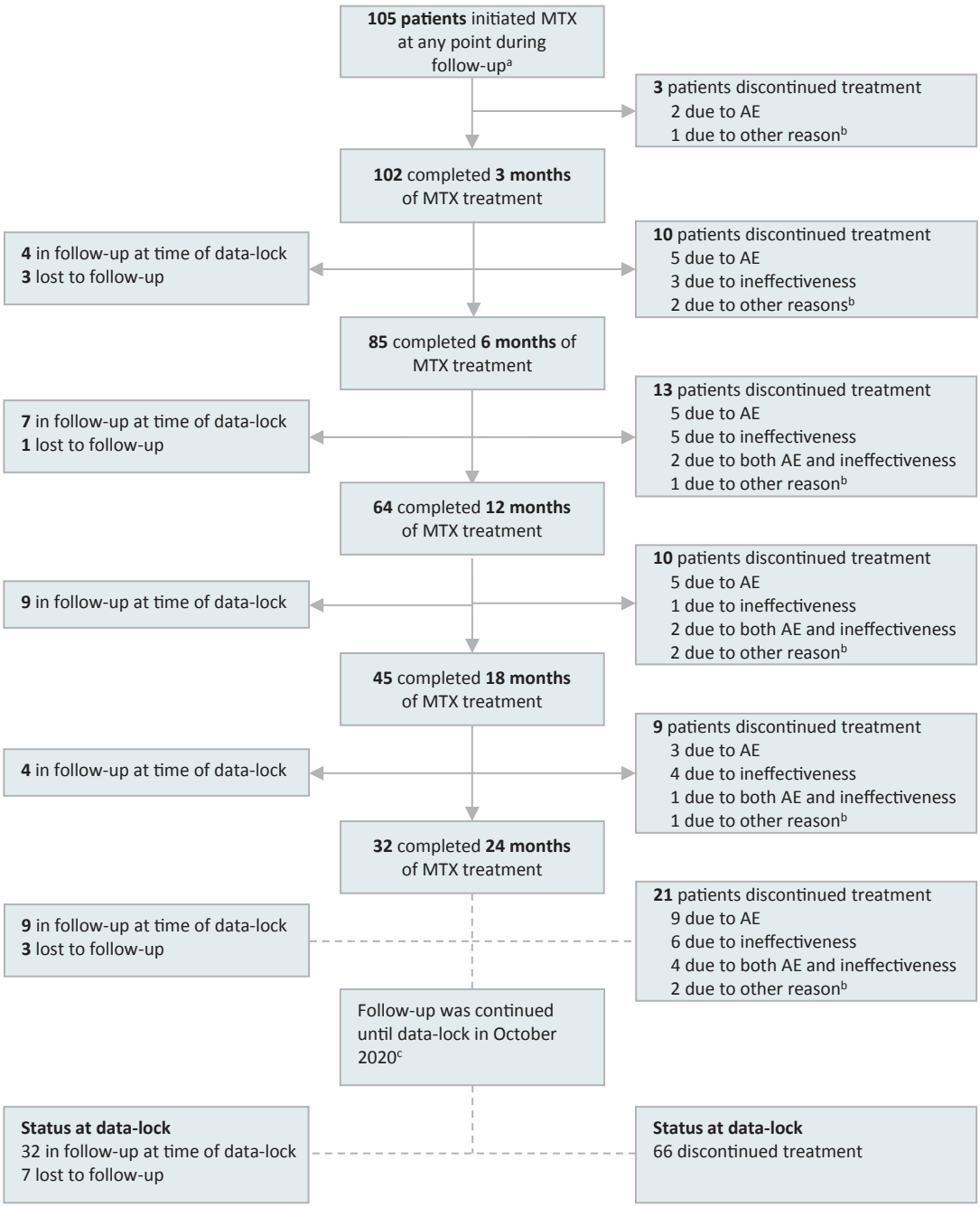
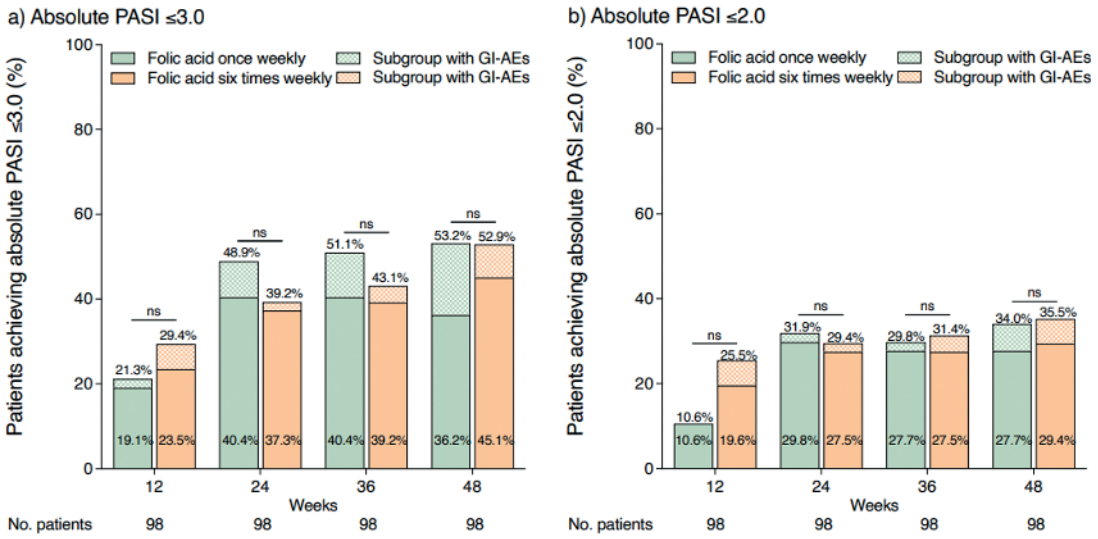


Fig. S1. Flowchart of treatment status of patients during follow-up in the Child-CAPTURE. Since the inclusion of patients in the Child-CAPTURE and MTX initiation is continuously ongoing, some patients might only have a short follow-up time at time of data-lock, although still being actively treated with methotrexate (MTX). Hence, patients had different follow-up times at the moment of data-lock, with patients who discontinued MTX or were lost to follow-up, but also patients who were on active treatment at data-lock. This flowchart shows the number of patients who completed a certain time-point of follow-up. [a]Patients were included in this study if they initiated MTX at any point during the Child-CAPTURE from September 2008 to data-lock in October 2020. [b]Other reasons: remission of psoriasis ($n = 5$), patients' own decision ($n = 2$) a desire to consume alcohol ($n = 2$). [c]Follow-up time until either MTX discontinuation or data-lock ranges from 1 to 96 months. AE: adverse event.

Last observation carried forward (LOCF) analyes



As treated analyses

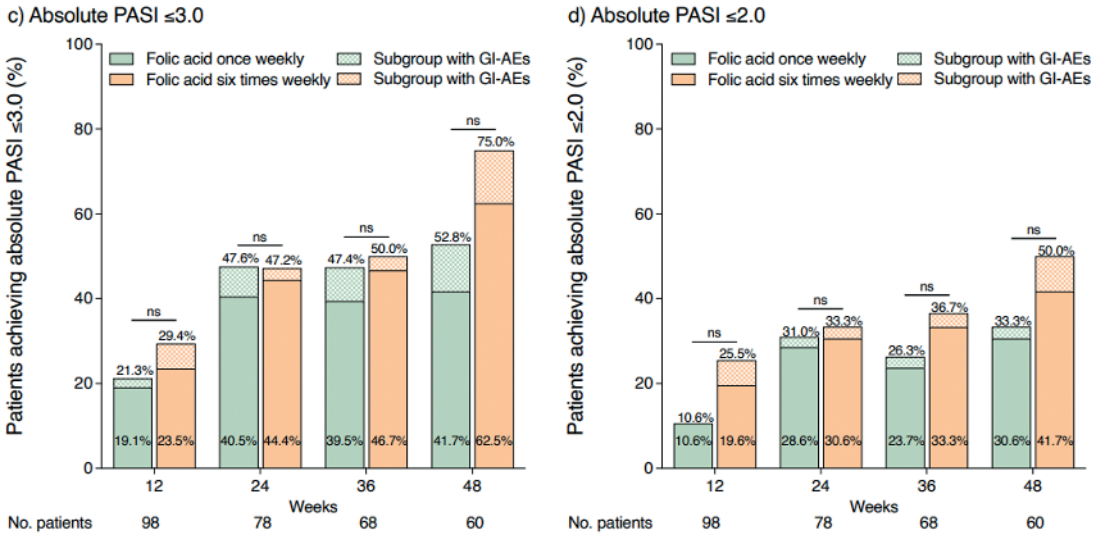


Fig. S2. Percentage of paediatric patients treated with methotrexate (MTX) with folic acid once weekly vs 6 times weekly achieving an absolute PASI ≤3.0 and ≤2.0 without and with persistent gastrointestinal adverse events. An additional distinction was made between patients with and without persistent gastrointestinal adverse events at all time-points. Logistic regression models were used to compare folic acid once weekly vs 6 times weekly. The following possible confounders were incorporated in the models: sex, age at start of MTX, body mass index at start of MTX and dose in mg/kg at start of MTX. Only confounders that altered the unadjusted exposure-outcome effect by 10% or more were retained in the models. LOCF: last observation carried forward; NS: not significant; GI-AEs: gastrointestinal adverse events; PASI: Psoriasis Area and Severity Index.