

SUPPLEMENTARY MATERIAL

Prevention of disease flares by risk-adapted stratification of therapy withdrawal in juvenile idiopathic arthritis: Results from the PREVENT-JIA trial

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Suppl. Table S1. Inclusion and exclusion criteria of the PREVENT-JIA study

Inclusion criteria	Exclusion criteria
Any JIA subcategory	Persistent Oligoarthritis Systemic JIA with systemic features within 1 year prior to inclusion
Clinically inactive disease No joint with active arthritis No fever No rash No serositis No splenomegaly No lymphadenopathy No active uveitis No elevation in ESR/CRP	History of MAS
Physicians global assessment of disease activity indicates no activity for at least 6 months	History of active Uveitis
Approved medication: DMARDs and/ or biologics on a stable dose; (+/- NSAIDs)	Withdrawal of any biological drug in past has been unsuccessful
Steroids withdrawn at least 1 month before remission	Steroids in the month before remission
No Intraarticular joint injections within the last 6 months before remission	Intraarticular joint injections within the last 6 months before remission

Suppl. Table S2. Criteria of inactive disease and remission

Clinically inactive disease
<ul style="list-style-type: none">• No joints with active arthritis• No fever, rash, serositis, splenomegaly, or generalized lymphadenopathy attributable to JIA• No active uveitis• Normal ESR or CRP (if both are tested, both must be normal)• Physician's global assessment of disease activity indicates no disease activity (i.e., best score attainable on the scale used)
Clinical remission on medication
The criteria for inactive disease must be met for a minimum of 6 continuous months while the patient is on medication
Clinical remission off medication
The criteria for inactive disease must be met for a minimum of 12 continuous months while off all anti-arthritis and anti-uveitis medications

Suppl. Table S3. Final medication in the PREVENT-JIA group and the respective BiKeR control group

	Patients who reached I1 under medication		Patients who stopped therapy following I1	
	PREVENT-JIA	BiKeR (matched)	PREVENT-JIA	BiKeR
All Patients	100 ¹	100 ²	91 ³	118 ⁴
cDMARDs				
MTX	77 (77%)	79 (79%)	70 (77%)	33 (28%)
Leflunomid	2 (2%)	0	2 (2%)	0
bDMARDs				
Abatacept	2 (2%)	0	2 (2%)	0
Adalimumab	4 (4%)	1 (1%)	4 (4%)	6 (5%)
Canakinumab	0	0	0	0
Etanercept	12 (12%)	10 (10%)	10 (11%)	46 (39%)
Golimumab	0	0	0	0
Infliximab	0	0	0	0
Tocilizumab	0	1 (1%)	0	1 (1%)
Combination				
MTX + Abatacept	1 (1%)	1 (1%)	1 (1%)	0
MTX + Adalimumab	0	1 (1%)	0	5 (4%)
Leflunomid + Adalimumab	0	0	0	1 (1%)
MTX + Canakinumab	0	1 (1%)	0	0
MTX + Etanercept	1 (1%)	5 (5%)	1 (1%)	17 (14%)
MTX + Golimumab	0	0	0	3 (3%)
MTX + Infliximab	0	1 (1%)	0	2 (2%)
MTX + Tocilizumab	1 (1%)	0	1 (1%)	4 (3%)

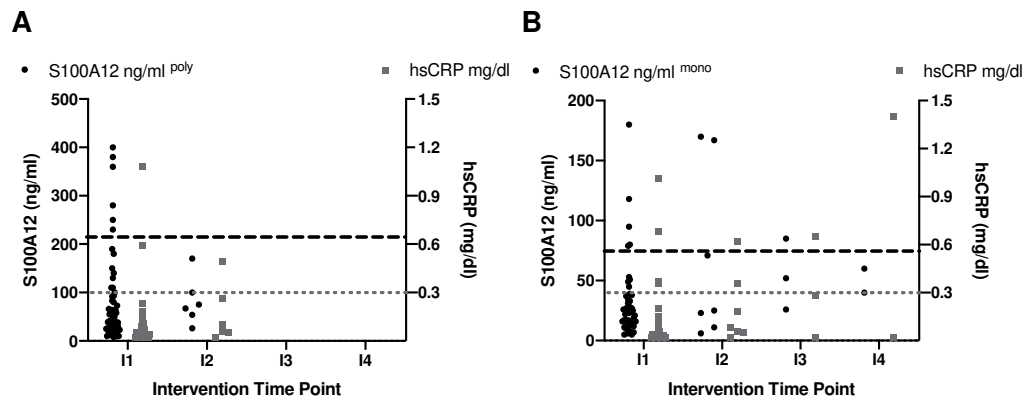
¹ PREVENT-JIA patients who reached the first intervention time point I1.

² Of the 430 eligible patients from the BiKeR registry who reached clinical remission on medication, remained inactive for at least further 6 months on medication and reached the corresponding first intervention time point I1, 100 patients were selected so that the JIA subtype and the type of final therapy of a pair of individual PREVENT-JIA and BiKeR patients matched exactly (final therapy type 1: csDMARD without additional bDMARDs, type 2: bDMARDs with or without additional csDMARD), and the duration of therapy matched as well as possible (duration from treatment start until inactive disease on stable medication).

³ PREVENT-JIA patients who stopped treatment within the one-year intervention phase.

⁴ A number of 118 eligible patients from the BiKeR registry reached the corresponding first intervention time point I1 and stopped treatment within a one-year period corresponding to the intervention phase of the PREVENT-JIA study.

Suppl. Figure S1. Biomarker values



A) Results for S100A12 (black circles) and hsCRP (grey squares) obtained in patient samples (I1: n=53; I2: n=6) in which the polyclonal S100A12 assay was used. The black dashed line indicates the assay-specific S100A12 cut-off at 175 ng/ml, while the grey dotted line shows the cut-off for hsCRP at 0.3 mg/dl. The polyclonal S100A12 assay was applied until June 2015 and therefore not used for any samples at later intervention time points I3 or I4. **B)** Results of the monoclonal S100A12 ELISA (black circles) and hsCRP (grey squares) for samples (n=59; I1: n=47; I2: n=7; I3: n=2; I4: n=2) collected beyond June 2015. The black dashed line indicates the assay-specific S100A12 cut-off at 75 ng/ml, while the grey dotted line shows the cut-off for hsCRP at 0.3 mg/dl.