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Steroids withdrawn at least 1 month before remission	Steroids in the month before remission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
• 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%)

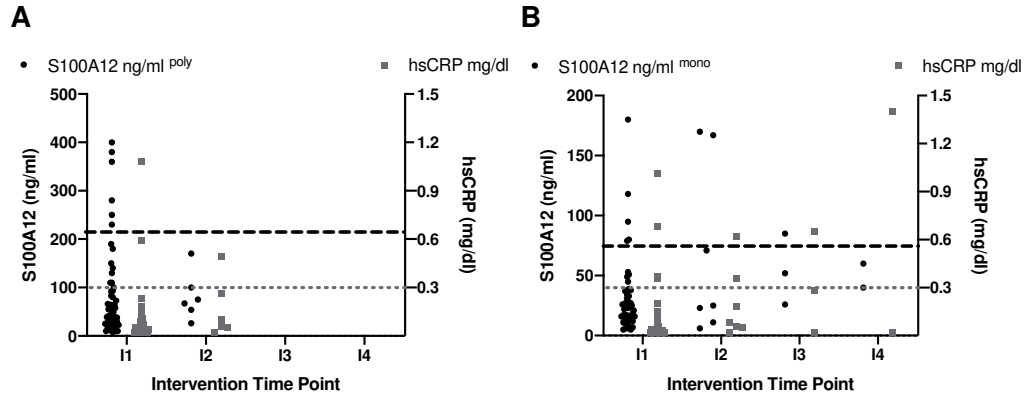
[1] PREVENT-JIA patients who reached the first intervention time point I1.

[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.