Results: There were no significant differences in gender, age, clinical manifestations, and laboratory findings between IgAV and IgAVN patients (Table 1). sCD40L levels were higher (median 1938.1 vs 754.9 pg/mL, $p=0.04$) whereas sST2 levels were lower (median 862.8 vs 2302.8 pg/mL, $p=0.02$) in the patients who developed IgAV nephritis (Figure 1). sRAGE levels were higher and IL18 levels were lower in IgAVN patients but did not reach statistical significance, probably due to the low number of patients. The other parameters did not show any specific pattern.

Table 1.

	IgAV (n=4)	IgAVN (n=4)	p value
Gender	2F, 2M	1F, 3M	0.49
Age at disease onset	9.0±5.4	10.3±3.4	0.68
Arthralgia/arthritis	50%	75%	0.49
GIS involvement	75%	50%	0.49
Haemoglobine (gr/dL)	12.4±2.3	12.3±0.6	0.95
White blood cells, $\times 10^9/L$	11150±1933	8525±1497	0.08
Platelets $\times 10^9/L$	290250±87328	269250±38741	0.68
Erythrocyte sedimentation rate (mm/hr)	10.5±9.1	21.0±14	0.26
C-reactive protein (mg/dL)	0.63±0.03	1.16±0.96	0.39

Data are given as mean±SD

Figure 1.

Soluble CD40 ligand (sCD40L) is expressed on platelets and released on activation. It is proinflammatory for endothelial cells and promotes coagulation by inducing expression of tissue factor on monocytes and endothelial cells². It was investigated in acute coronary syndrome and was suggested as a risk factor for vascular damage.² Furthermore, the levels of sCD40L were shown to be correlated with disease activity in ANCA-associated vasculitis³. Thus in IgAV, sCD40L may be associated with the involvement of the kidney vasculature, which represents the more severe form of the disease. Receptor for advanced glycation end-products (RAGE) is another marker for endothelial damage and vasculitis which was higher in IgAVN, as well.

IL33 is expressed by epithelial and endothelial cells and overexpression of IL33 have been shown in large vessel vasculitis⁴. sST2 acts as a decoy receptor and inhibits IL33 signalling⁴. It was interesting to see that the levels of the IL-18 and sST2, which are members of IL-1 family, were lower in IgAVN patients.

Conclusion: Although the number of the patients were limited in this pilot study, we suggest that sCD40L and sRAGE might be used to predict the development of renal disease in IgAV patients. Further studies with larger number of patients are needed to confirm our findings.

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Pediatric Rheumatology - Clinical

POS0075

SAFETY AND EFFICACY OF GOLIMUMAB FOR THE TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS - AN UPDATE FROM THE BIKER REGISTRY

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Background: Golimumab (GOL) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years and older. Data on long-term safety of GOL in this indication are limited.

Objectives: To assess long-term safety and efficacy of GOL in pJIA patients.

Methods: In this ongoing non-interventional observational study, clinical characteristics, disease activity and safety parameters were analysed using the German Biologics in Paediatric Rheumatology (BiKeR) registry. 81 pJIA-patients treated with GOL were body weight-matched with 162 patients receiving alt. tumor necrosis factor inhibitors (TNFi) and 81 biologic-naïve patients under methotrexate (MTX)-therapy.

Results: Baseline parameters of GOL patients differed from the alternative TNFi and MTX cohorts. In patients starting with GOL treatment, disease duration was longer, corticosteroid use was less and disease activity, measured by the mean number of active joints and the JADAS10, was lower (Table 1).

The long-term clinical efficacy of GOL in pJIA is highlighted by a decrease of the mean JADAS 10 from 11.6 (baseline) to 5.2 after 24 months. After 2 years, a JADAS 10 minimal disease activity was reached by 44.4 % of patients, whereas 22.2 % of patients were in remission and the JIA ACR 30/50/70/90 response rates were 77.8/72.2/66.7/55.6% respectively.

AE, SAE and infectious AE rates between the three cohorts were comparable (Table 1). In the GOL cohort, 4 SAE (1 uveitis, 1 arthritis flare, 1 fibromyalgia syndrome and 1 abscess) were reported, while in the alt. TNFi group 7 SAEs and in the MTX cohort 1 SAE were noted (Table 1). One serious infectious event (1 abscess) was documented in the GOL cohort, 2 alt. TNFi patients had influenza and no serious infectious events were seen in the MTX control group.

Few autoimmune processes occurred: 2 incident events in the GOL cohort (1 uveitis, 1 psoriasis), 3 cases in the alt. TNFi group (2 uveitis, 1 psoriasis,) and 1 event in MTX-patients (celiac disease) (Table 1). Out of the 20 GOL patients with preexisting uveitis at baseline, 6 had flare events; there were no reported uveitis flares of the 17 patients in the alt. TNFi group and no patients with preexisting uveitis in the MTX-group. No malignancies or deaths were reported.

Conclusion: Our interim results show an acceptable safety profile of GOL therapy, comparable to treatment with alt. TNFi or MTX. No new safety signals occurred. The efficacy outcome data confirm long-term benefits of GOL treatment in pJIA patients.

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Table 1. Baseline parameters and adverse events

	GOL n=81	alt. TNFi n=162	MTX n=81	p-value ∞ GOL vs alt. TNFi	p-value ∞ GOL vs MTX
Gender female °	67 (83)	127 (78)	64 (79)	0.5	0.7
Disease duration (yrs)	7.1±4.3	4.3±3.7	1.2±2.1	<0.0001	<0.0001
RF neg. Polyarthriti ^s °	40 (49)	79 (49)	50 (62)	1.0	0.15
RF pos. Polyarthriti ^s °	8 (10)	22 (14)	16 (20)	0.5	0.1
Extended Oligoarthritis °	30 (37)	54 (33)	13 (16)	0.6	0.004
Psoriatic arthriti ^s °	3 (4)	7 (4)	2 (3)	1.0/1.0	1.0
Pretreatment bDMARD °	68 (84.0)	35 (21.6)	0	<0.0001	<0.0001
Concomitant systemic steroids, n (%)	13 (16)	38 (24)	39 (48)	0.2	<0.0001
Active joint count #	4.6±4.8	4.9±5.7	9.6±6.5	0.4	<0.0001
CHAQ DI #	0.4±0.5	0.5±0.5	0.6±0.6	0.1	0.02
JADAS10 #	11.6±6.2	12.1±6.1	16.8±5.3	0.6	<0.0001
AE *	91 (107.4; 88-132)	213 (88.7; 78-101)	113 (119.8; 100-144)	0.1	0.4
SAE *	4 (4.7; 2-13)	7 (2.9; 1-6)	1 (1.1; 0.1-8)	0.4	0.2
Serious infections *	1 (1.2; 0.2-8.4)	2 (0.8; 0.2-3.3)	0	0.7	n.a.
Autoimmune process (%)	2 (2.4)	3 (1.9)	1 (1.2)	1.0	1.0
Patients with uveitis new manifestation after study entry *	1 (1.2; 0.2-8)	2 (0.8; 0.5-3)	0	0.7	n.a.
Patients with uveitis flare events with preexisting uveitis at baseline *	6 (7.1; 3-16)	0	0	n.a.	n.a.

Rheumatoid factor (RF), biologic disease modifying antirheumatic drug (bDMARD), childhood health assessment questionnaire disability index (CHAQ DI), juvenile arthritis disease activity index (JADAS), adverse event (AE), patient year (PY), ° n (%), # mean (SD), * n (rate/100PY; 95%CI), Golimumab (GOL), alternative tumor necrosis factor inhibitor (alt. TNFi), methotrexate (MTX), ∞ by t-test or χ^2 -test as appropriate.

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POS0076

S100A8/A9 AND S100A12 AS POTENTIAL PREDICTIVE BIOMARKERS OF ABATACEPT RESPONSE IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Background: The calcium-binding proteins S100A8/A9 (calprotectin) and S100A12 (extracellular newly identified receptor for advanced glycation end-products binding protein [EN-RAGE]) are involved in multiple signalling pathways to mediate inflammation, can be secreted by activated monocytes/macrophages and exhibit cytokine-like extracellular functions. Circulating levels of these proteins have been associated with disease and clinical responses in systemic juvenile idiopathic arthritis (sJIA), including treatment response.¹ Studies suggest that serum S100A8/A9 and S100A12, which are released at inflammation sites, are more specific biomarkers of local inflammation (e.g. in the synovium) than systemic biomarkers such as CRP and ESR.^{2,3}

Objectives: To investigate if baseline S100A8/A9 and S100A12 predict clinical response to abatacept treatment in polyarticular JIA (pJIA), and to assess

whether changes from baseline in S100A8/A9 or S100A12 can be better prognostic markers for response to abatacept treatment than CRP in pJIA.

Methods: Data are from a phase III trial of SC abatacept for the treatment of pJIA (NCT01844518).⁴ This 24-month, single-arm, open-label, international, multi-centre, two-part study included male and female patients with pJIA aged 2–17 years. This analysis examined the correlation between biomarkers (S100A8/A9, S100A12 and high-sensitivity CRP [hsCRP]) and disease activity (measured using Juvenile Arthritis Disease Activity Score [JADAS]) at baseline, baseline biomarker values as predictors of future treatment response (ACR and JADAS endpoints), and the correlation between change from baseline in biomarker values and treatment response at Day 113.

Results: Of 219 total patients, 158 (72%) had S100A8/A9 values and 155 (71%) had S100A12 values at baseline. Median S100A8/A9 and S100A12 values were 3295 ng/mL (normal range, 716–3004 ng/mL) and 176 ng/mL (normal range, 32–385 ng/mL), respectively. S100A8/A9, S100A12 and hsCRP (median 0.20 mg/dL; normal ≤0.6 mg/dL) had a low-to-moderate but significant association with disease activity at baseline; coefficients for associations between JADAS71-CRP low disease activity (LDA) and the biomarkers S100A8/A9, S100A12 and hsCRP were 0.23 (p=0.0038), 0.16 (p=0.0448) and 0.26 (p=0.0001), respectively. Baseline S100A8/A9 level above the median was associated with lower odds of ACR100 at Day 113 (p=0.0052). Figure 1 shows the associations of baseline biomarker values with Day 113 ACR and JADAS scores in the overall population. Baseline S100A8/A9 or S100A12 did not significantly influence ACR50 or ACR70 responses at Day 113, but high baseline values were associated with reduced odds of ACR90 (p=0.01), ACR100 (p=0.005), ACR-inactive disease (ID) (p=0.0001), and JADAS71-CRP (LDA) (p=0.02). By Day 477, elevated baseline S100A12 was still significantly associated with lower odds of ACR100 overall (0.467; p=0.0248) but baseline S100A8/A9 was not; at Day 645, neither was significantly associated with ACR100 response. At Day 113, changes from baseline in S100A8/A9 and S100A12 were correlated with ACR100 (coefficients of 0.22 [p=0.0082] and 0.26 [p=0.0015], respectively) and with ACR-ID (0.22 [p=0.0067] and 0.26 [p=0.0014], respectively); change in hsCRP was not significantly correlated with disease response.

Conclusion: S100A8/A9 and S100A12 may serve as prognostic biomarkers to predict response to abatacept treatment at Day 113. Changes from baseline S100A8/A9 and S100A12 levels were more highly correlated with efficacy outcomes including ACR100 and ACR-ID at Day 113 compared with hsCRP.

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Figure 1. Effect of baseline S100A8/A9 or S100A12 level on efficacy response at Day 113 in the overall population

ACR50/70/90/100=50/70/90/100% improvement in ACR criteria; ID=inactive disease; JADAS71-CRP=Juvenile Arthritis Disease Activity Score in 71 joints using CRP; LDA=low disease activity; OR=odds ratio.

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