TRAF7, MAFB), and Toll-like receptor signaling (*TLR1, IRAK2 MYD88, TOLLIP, TICAM1, TRAM1*).

Conclusion: Changes in individual CpGs, DMRs, and inflammatory pathways were detected in baseline samples of psoriasis converters compared to non-converters. These preliminary data support our hypothesis that DNA methylation changes occur early in PsA pathogenesis and can potentially serve as prognostic biomarkers of future onset of arthritis in psoriasis patients.

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THURSDAY, 13 JUNE 2019

Adults are just grown up children! Discuss

OP0204 EMAPALUMAB, AN INTERFERON GAMMA (IFN-Y)-BLOCKING MONOCLONAL ANTIBODY, IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME (MAS) COMPLICATING SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

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Background: MAS is a severe complication of rheumatic diseases, most frequently sJIA, caused by excessive activation and expansion of T cells and macrophages. It is characterized by fever, hepatosplenomegaly, liver dysfunction, cytopenias, coagulation abnormalities and hyperferritinemia, possibly progressing to multiple organ failure and death. MAS is categorized as a secondary form of HLH. A vast body of evidence points to uncontrolled overproduction of IFNγ as a major driver of hyperinflammation and hypercytokinemia in MAS and HLH. Emapalumab has been shown to effectively control disease activity in patients with primary HLH.

Objectives: To assess the pharmacokinetics (PK), efficacy and safety of intravenous (IV) emapalumab in patients with MAS and confirm the proposed dose regimen.

Methods: This is a pilot open-label single arm international study (NCT03311854). Patients had to have MAS (defined according to the 2016 ACR/EULAR classification criteria), on a background of confirmed, or high presumption of, sJIA, and inadequate response to high-dose IV glucocorticoids. Emapalumab initial dose was 6 mg/kg and treatment was continued at 3 mg/kg, twice weekly for a total of 4 weeks or less upon achievement of complete response. Serum concentrations of emapalumab, IFNγ-induced chemokine CXCL9 and sIL2R were measured. Safety assessments included adverse events (AEs) and laboratory abnormalities. Efficacy was defined as complete response by week 8, i.e. absence of MAS clinical signs plus white blood cell and platelet counts above lower limit of normal, LDH, AST/ALT<1.5 x upper limit of normal, fibrinogen >100 mg/dL, and ferritin decreased by ≥80% or to <2000 ng/mL, whichever was lower. Twin protocols are in place to recruit 5 patients each in Europe and North America (trial not started yet). We report data on the 6 patients recruited in the European protocol.

PK/PD parameters	Baseline	Week 1	Week 2	EOT	Week 8
Emapalumab (ug/mL) Median (range) trough levels	n.a.	48 (35-84)	88 (49-156)	112 (88-247)	58 (2-120)
CXCL9 (r.r. ≤ 300 pg/mL) Median (range) serum levels	8,506 (1,518-98,121)	465 (192-768)	134 (80-499)	109 (80-156)	120 (80-249)
sIL2R (r.r. ≤ 2000 pg/mL) Median (range) serum levels	4,350 (1,664-20,954)	4,161 (1,883-17,059)	2,184 (909-8,090)	1,095 (571-2,045)	1,083 (442-1,271)

Laboratory parameters	Baseline	EOT	Week 8
Platelet count < LLN, n. pts Median (range)	5 132.5 (70-229)	1 269.5 (133-455)	None 387.5 (214-455)
Ferritin > 2,000 ng/mL, n. pts Median (range)	5 21,668 (716-192,548)	None 322 (49-1222)	None 116 (38-258)
AST (IU/L) > 1.5 x ULN, n. pts Median (range)	4 136.5 (43-1507)	None 25.5 (19-39)	None 30.5 (18-43)
ALT (IU/L) > 1.5 x ULN, n. pts Median (range)	6 176.0 (95-852)	2 44.0 (23-76)	None 37.5 (27-48)
LDH (IU/L) > 1.5 x ULN, n. pts Median (range)	6 2,063 (727-12,734)	1 662 (423-810)	None 542 (423-579)
Fibrinogen (mg/dL) < LLN, n. pts Median (range)	3 203.5 (110-465)	None 240 (200-302)	None 271 (210-361)

EOT: end of treatment; LLN: lower limit of normal; ULN: upper limit of normal; r.r.: reference range

Results: Six patients (5 females, median age 11 years, range: 2-25 years) received emapalumab according to the prescribed dose regimen. Treatment duration ranged from 3 (2 patients) to 4 weeks. Prior to emapalumab, all patients failed methylprednisolone pulses, in 2 patients plus cyclosporine A (CsA) and in 2 patients plus CsA and anakinra. The achieved emapalumab concentrations led to rapid neutralization of IFNγ as indicated by CXCL9 levels and subsequent deactivation of T cells as indicated by sIL2R levels. In all patients, complete response was achieved by week 8, in 4 patients by end of treatment (Table). Systemic glucocorticoids were weaned in all patients. Emapalumab infusions were well tolerated and none of the patients discontinued emapalumab. A CMV reactivation was reported by investigator as a serious event possibly related to emapalumab, but resolved completely with treatment.

Conclusion: Emapalumab administration with the tested dosing regimen led to rapid neutralization of IFNγ as shown by normalization of CXCL9, associated with evidence of decreased T cell activation. In all patients, emapalumab treatment was effective in controlling MAS with a favourable safety profile.

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OP0205 LIVE ATTENUATED VACCINES IN PEDIATRIC RHEUMATIC DISEASES ARE SAFE: MULTICENTER, RETROSPECTIVE DATA COLLECTION

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Background: Common practice is to withhold vaccination with live-attenuated vaccines in patients with rheumatic diseases on high-dose DMARDs, glucocorticosteroids or biological agents, due to limited safety data, and the (theoretical) risk of introducing an infectious disease to the patient. Evidence for this approach is low. We collected data from pediatric rheumatologists who vaccinate these patients, to obtain additional safety data, which might update and revise this approach.

Objectives: To collect retrospective data in patients with JIA and other diseases who received live booster MMR or MMRV while on DMARDs, glucocorticosteroids or biological agents.

Methods: Data from 13 pediatric rheumatology centers in 10 countries were collected.

Results: 234 patients were reported; mean age 5± 2.7, 70% girls. 206 had JIA;. 46% oligoarticular, 36% polyarticular, 8% systemic, 5% SPA types, 5% JIA and uveitis. 48% of JIA patients were in remission on medication. Disease activity was low in 38%, high in 2%, moderate in 7%; 11 patients had juvenile dermatomyositis, 3 systemic and 2 localized scleroderma, 4 isolated idiopathic uveitis, 1 CINCA syndrome, 1 MKD, and 1 FMF.

110 patients had MMR/V booster while on MTX; 3 reported mild side-effects of local skin reaction and pain, none had disease flare. 76 had booster while on MTX + anti-TNF; 7 reported mild and transient adverse events of local skin reaction, fever and URTI. 39 had booster while on anti-TNF alone; 1 reported fever. 3 had

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booster while on tocilizumab, 7 on anakinra, and 5 on canakinumab. There was no relation between disease activity, type or duration, sex, age and outcome of vaccinations. No vaccine infection related to measles, rubella, mumps and varicella were reported.

Conclusion: This large, retrospective data collection demonstrates that live-attenuated booster vaccine is probably safe in children with rheumatic diseases, on immunosuppressive therapies. This strengthens the new PRES recommendation: "Vaccination of live-attenuated vaccines in patients on high-dose DMARD, high-dose glucocorticosteroids or biological agents can be considered on a case-by-case basis, weighing the risk of infections against the hypothetical risk of inducing infection through vaccination." These data provide the basis for a large, prospective data collection study that is planned by the PReS vaccination study group. It will increase the current level of evidence for the safety of vaccinations in our pediatric rheumatology population.

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Exercise – more than a wonderdrug

OP0206-HPR BENEFICIAL LONG-TERM EFFECT OF A SUPERVISED EXERCISE PROGRAM ON PHYSICAL ACTIVITY LEVEL IN PATIENTS WITH AXIAL SPONDYLOARTHRTIS: 12 MONTHS FOLLOW-UP OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Background: Exercise is recommended in the management of axial spondyloarthritis (axSpA)[1] as it may reduce the burden of the disease.[2] Despite this, patients with axSpA tend to have a low physical activity (PA) level[3] and few patients engage in high intensities of exercise[4].

Objectives: To investigate the long-term effect of a three months supervised exercise program on PA-level in patients with axSpA.

Methods: 100 patients with axSpA were randomized to either an exercise group (EG) or a no-intervention control group (CG). The exercise group participated in a three months high intensity cardiorespiratory and strength exercise program supervised by a physiotherapist. PA-level was a secondary outcome measured at 12 months follow-up with a standardised questionnaire (frequency, duration, intensity and mode)[5]. Being physically active was defined as $\geq$1 hour/week with high intensity PA. Statistical analyses were performed on an intention-to-treat basis using chi-square tests and logistic regression.

Results: A total of 87 of 100 (87%) patients were included in the analyses (table 1). At 12 months follow-up, significantly more patients in the EG than in the CG were physically active, p<0.001 (figure 1). Further, significantly more patients in the EG than in the CG exercised 2-3 times per week (25 [58%] vs. 15 [34%], p=0.02). Fewer patients in the EG reported to exercise at a low intensity level (low intensity reported by 3 [8%] in the EG vs. 14 [44%] in the CG, p=0.002). The regression analysis showed that participating in the exercise program (p<0.001) and earlier exercise experience (p=0.01) were the factors most associated with being physically active at 12 months follow-up (table 2).

Table 1. Baseline descriptive of the exercise group and the control group

	Exercise group (n=43)	Control group (n=44)
Age, years, mean (min-max)	45.5 (23-68)	47.4 (24-69)
Sex, male, n (%)	22 (51%)	20 (46%)
Radiographic axSpA	32 (74%)	28 (64%)
TNF-inhibitor, n (%)	38 (44%)	20 (46%)
ASDAS, mean (SD)	2.6 (0.7)	2.5 (0.7)

ASDAS, Ankylosing Spondylitis Disease Activity Score

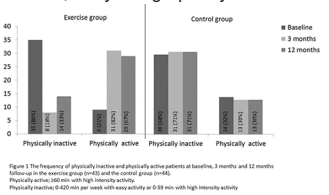

Figure 1 The frequency of physically inactive and physically active patients at baseline, 3 months and 12 months follow-up in the exercise group (n=43) and the control group (n=44).
Physically active; ≥60 min with high intensity activity.
Physically inactive; 0-420 min per week with easy activity or 0-59 min with high intensity activity

Conclusion: A three month supervised exercise program delivered by physiotherapists had a significant long-term beneficial effect on PA-level in patients with axSpA. As regular exercise is an important part of the treatment recommendations for patients with axSpA[1], the results indicate that a time-limited supervised exercise program may be used as an effective intervention to succeed in reaching this recommendation.

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Getting a grip on the co-morbidities in gout

OP0207 URATE-LOWERING THERAPY WITH VERINURAD AND FEBUXOSTAT REDUCES SERUM URIC ACID AND ALBUMINURIA IN HYPERURICEMIC PATIENTS WITH DIABETES

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Background: Hyperuricemia is implicated as a major risk factor for chronic kidney disease (CKD), and emerging clinical data suggest that lowering serum uric acid (sUA) may protect kidney function by reducing albuminuria and slowing the rate of CKD progression. We evaluated the efficacy and safety of an intensive sUA-lowering strategy of verinurad (RDEA3170), a novel urate transport inhibitor of URAT1, and febuxostat in patients with Type 2 diabetes mellitus (T2DM) and albuminuria (clinicaltrials.gov: NCT03118739).

Objectives: To compare the efficacy of verinurad + febuxostat to placebo in reducing albuminuria in patients with T2DM.

Methods: A Phase 2 parallel group, randomised, double-blind, placebo-controlled clinical trial. Patients were assigned 1:1 to either verinurad 9 mg + febuxostat 80 mg (n=32) or placebo (n=28). Inclusion criteria: aged $\geq$18 years, sUA concentration $\geq$6.0 mg/dL, estimated glomerular filtration rate (eGFR) $\geq$30 mL/min/1.73 m^2, urinary albumin-to-creatinine ratio (UACR) 30–3500 mg/g and T2DM diagnosis. Exclusion criteria: history of gout or recent treatment with urate-lowering therapy. The primary endpoint was change in UACR. Secondary endpoints included sUA, renal function biomarkers, and eGFR.

Results: Baseline characteristics were similar between groups. For treatment vs placebo, respectively, mean (SD) sUA was 7.5 (1.6) vs 7.0 (0.8) mg/dL, eGFR was 59.2 (25.3) vs 68.1 (23.2) mL/min/1.73 m^2, and UACR was 459 (825) vs 412 (548) mg/g at baseline. The study met the primary endpoint as verinurad/febuxostat reduced UACR by 39% vs placebo after 12 weeks of treatment (p=0.07,

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