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- γ)-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 IFN γ 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, IFN γ -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 $\geq 80\%$ 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 (ng/mL)	n.s.	48 (35-84)	88 (49-156)	112 (88-247)	58 (2-120)
CXCL9 (x < 300 pg/mL)	8,506 Median (range)	465 (1518-96,121)	134 (80-409)	109 (80-156)	120 (80-249)
sIL2R (x < 2000 ng/mL)	4,350 Median (range)	4,161 (1,664-20,954)	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	5	1	None		
Median (range)	132.5 (70-229)	269.5 (133-455)	387.5 (214-455)		
Ferritin > 2,000 ng/mL, n, pts	5	None	None		
Median (range)	21,668 (716-192,548)	323 (69-1222)	116 (38-258)		
AST (IU/L) > 1.5 x ULN, n, pts	4	None	None		
Median (range)	136.5 (43-1507)	25.5 (19-39)	30.5 (18-43)		
ALT (IU/L) > 1.5 x ULN, n, pts	6	2	None		
Median (range)	176.0 (95-852)	44.0 (23-76)	37.5 (27-48)		
LDH (IU/L) > 1.5 x ULN, n, pts	6	None	None		
Median (range)	2,063 (727-12,734)	662 (423-810)	542 (423-579)		
Fibrinogen (mg/dL) < LLN, n, pts	3	None	None		
Median (range)	203.5 (110-465)	240 (200-302)	271 (210-361)		

EOT: end of treatment; LLN: lower limit of normal; ULN: upper limit of normal; x: 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 IFN γ 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 IFN γ 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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[1] Ravelli A, et al. Ann Rheum Dis. 2016;75:481-9.

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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 $\pm$ 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