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THU0596

MEASUREMENT OF SERUM CALPROTECTIN MRP8/14 IN PAEDIATRIC PATIENTS DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS AND AUTOINFLAMMATORY DISEASES

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Background: There is evidence of the correlation between serum levels of calprotectin MRP8/14 and disease activity in Juvenile Idiopathic Arthritis (JIA), but the same correlation with other rheumatic diseases in children such as autoinflammatory diseases has not been studied as much.

Objectives: To analyse calprotectin MRP8/14 in serum of patients with juvenile idiopathic arthritis (JIA) and various autoinflammatory diseases with different degrees of activity. To check if there is a correlation between serum MRP8/14 and disease activity.

Methods: Study in two phases: 1) Initial, transversal, in JIA and/or autoinflammatory disease patients, determining serum MRP8/14 (by ELISA test) and collecting clinical data: number of active joints, Visual Analogue Scale parents/patients (VASp), VAS physician (VASph); and analytical: C-Reactive Protein (CRP) and white cells blood count (WBC) (among others). 2) Second prospective phase, repeating the same analysis 3–6 months later. Disease activity was assessed by Juvenile Arthritis Disease Activity Score (JADAS) in AIJ; and by VASp, VASph and CRP in autoinflammatory diseases.

Results: The sample included 90 patients (25 males) between the ages of 1 and 21 years (median 11.1); 61 diagnosed with JIA (excluding systemic category), and 29 with different autoinflammatory diseases (including systemic JIA). 69 patients (20 males, with median age 11.2, 48 AIJ, 21 autoinflammatory) participated in the prospective phase. The main results are shown in table 1.

MRP=myeloid related proteins. JADAS=Juvenile arthritis disease activity score. ACJ=active joints count. VASm=visual analogue scale–physician. VASp=visual analogue scale–parents/patient. CRP=C reactive Protein.

Conclusions: In patients with non-systemic JIA, a positive correlation was found between serum MRP8/14 and JADAS, VASph, VASp, CRP, WBC, neutrophilia and (inversely) haemoglobin.

In autoinflammatory diseases positive correlation has been found with VASm, CRP, leukocytosis, neutrophilia, thrombocytosis and (inversely) haemoglobin. MRP8/14 seems to behave as a marker of activity in both JIA and autoinflammatory diseases, although with a stronger association in the latter.

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THU0597

PULMONARY MANIFESTATIONS IN MIXED CONNECTIVE TISSUE DISEASE WITH JUVENILE AND ADULT ONSET – ARE THERE ANY DIFFERENCES?

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Background: Mixed connective tissue disease (MCTD) presents in childhood in 7%–23% of cases, but there is limited knowledge about the comparability of juvenile and adult onset of the disease. A common and serious manifestation is interstitial lung disease (ILD), possibly more common in adult MCTD according to a retrospective report.¹

Objectives: To compare disease variables in juvenile and adult onset MCTD, particularly regarding pulmonary manifestations, after long-term follow-up.

Methods: Two cohorts consisting of, respectively, 52 patients with juvenile onset MCTD and 90 patients with adult onset MCTD from all regions of Norway were compared. Inclusion criteria were fulfilment of the Kasukawa- or the Alarcon-Segovia criteria. Patients with onset of symptoms before the age of 18 years were considered to have juvenile onset. All patients were clinically examined, including high resolution CT and pulmonary function tests.

Results: Mean age at examination was 28.0 (SD 10.3) in juvenile onset, and 54.3 (SD 13.0) in adult onset MCTD (p<0.001). Age at disease onset was 14.4 (SD4.4) and 37.9 (SD 15.1) years, respectively. Patient and disease characteristics are shown in table 1.

	Juvenile onset	Adult onset	p-value
Male gender, n (%)	8 (15)	28 (24)	0.192
Disease duration from symptom onset, mean (SD)	16.2 (10.3)	17.0 (8.9)	0.766
Anti-RNP levels, median (IQR)	180 (36.0–240.0)	44.0 (7.0–237.0)	0.002
ESR, median (IQR)	8.0 (5.0 to 16.0)	11.0 (7.0–18.5)	0.048
CRP, median (IQR)	0.7 (0.5–2.5)	2.0 (0.7–4.9)	<0.001
ILD, n (%)	14 (27)	39 (43)	0.051
ILD% of TLV, median (IQR)	4.0 (1.0–8.3)	5.0 (1.8–20.0)	0.258
ILD in >20% of TLV, n (%)	1 (2)	10 (11)	0.048
DLCO% pred, mean (SD)	73.0 (12.5)	72.0 (19.4)	0.598
FVC% pred, mean (SD)	89.2 (14.7)	89.2 (20.8)	0.711
FEV1% pred, mean (SD)	89.4 (13.7)	81.2 (20.0)	0.016

Juvenile patients had higher levels of anti-RNP, but lower ESR and CRP compared to adult onset patients. ILD was found in 27% of juvenile and 43% of adult patients (p=0.051), and more adult onset patients had ILD in >20% of total lung volume (TLV). Adult onset patients had lower forced expiratory volume in 1 s (FEV1), but similar diffusing capacity (DLCO) and forced vital capacity (FVC) as the juvenile patients.

Conclusions: ILD tended to be more frequent in patients with adult onset MCTD than in those with juvenile onset, although not statistically significant. More patients with adult onset had affection of >20% of TLV. Juvenile and adult patients

	JIA (n=61)		Autoinflammatory diseases (n=29)	
	1 st determination (n=61)	2nd determination (n=48)	1 st determination (n=29)	2nd determination (n=21)
JADAS	r=0.270* p=0.035	r=0.054 p=0.717		
ACJ	r=0.053 p=0.685	r=0.042 p=0.779		
VASph	r=0.308* p=0.016	r=0.041 p=0.784	r=0.304 p=0.108	r=0.622** p=0.003
VASp	r=0.329* p=0.010	r=-0.023 p=0.877	r=0.341 p=0.082	r=0.341 p=0.141
CRP	r=0.212 p=0.107	r=0.349* p=0.018	r=0.579** p=0.001	r=0.102 p=0.688
WBC	r=0.296* p=0.022	r=-0.071 p=0.633	r=0.749** p=0.000	r=0.693** p=0.000
Neutrophiles	r=0.389* p=0.002	r=0.421** p=0.002	r=0.281 p=0.140	r=0.710** p=0.000
Haemoglobin	r=-0.255* p=0.049	r=-0.023 p=0.828	r=-0.454* p=0.013	r=-0.552** p=0.009
Platelets	r=-0.033 p=0.802	r=0.001 p=0.993	r=0.659** p=0.000	r=0.208 p=0.366

with similar disease duration had comparable degree of ILD. Juvenile MCTD patients showed higher levels of anti-RNP, but lower ESR and CRP than patients with adult MCTD.

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THU0598

SAFETY OF TOCILIZUMAB IN PATIENTS AGED <2 YEARS WITH ACTIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS TREATED FOR ONE YEAR

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Background: Intravenous (IV) tocilizumab (TCZ) was approved in the, US (2011), EU (2013) and other countries for the treatment of systemic juvenile idiopathic arthritis (sJIA) patients (pts) ≥2 years of age, based on a phase 3 study WA18221.¹ US Food and Drug Administration approval resulted in postmarketing requirement to investigate TCZ in pts with sJIA <2 years of age (study NP25737; ClinicalTrials.gov, NCT01455701). Results from the 12 week main evaluation period (MEP) have been reported.²

Objectives: Report safety results after completion of the optional extension period (OEP) of NP25737 (until 52 weeks from baseline or 2 years of age, whichever was longer).

Methods: NP25737 was a multicenter, open-label, single-arm study to evaluate the pharmacokinetics and safety of IV TCZ, 12 mg/kg every 2 weeks, for 12 weeks in pts aged <2 years with active sJIA for ≥1 month who failed corticosteroid and nonsteroidal anti-inflammatory drug treatment and received stable background therapy during the MEP. After the 12 week MEP, pts could participate in the OEP and continue TCZ treatment (without requirement for stable background therapy). Cumulative adverse events (AEs) over the entire study period are reported.

Results: Seven of 11 pts enrolled in the MEP continued to the OEP and received ≥1 dose of TCZ. Over the entire study period (n=11), the median number of TCZ doses was 11 (range, 2–26) and the median duration of TCZ exposure was 22 weeks (range, 4–58). Most pts (10/11; 91%) had ≥1 AE; most were mild or moderate in intensity and unrelated to study drug. The most common AEs were upper respiratory tract infection (6/11 pts, 55%), hypersensitivity, neutropenia, rash, viral upper respiratory tract infection, and vomiting (each in 3/11 pts; 27%). Seven serious AEs occurred in 5 of 11 pts (46%): 2 in the OEP (transaminases increased and histiocytosis hemophagocytic), 3 in the MEP (3 hypersensitivity events), and 2 in the safety follow-up of the MEP (sJIA flare and hand-foot-and-mouth disease). AEs leading to dose modification occurred in 5 of 11 pts (1 in the MEP, 4 in the OEP) mostly because of infections, neutropenia, and elevated liver enzymes, all mild or moderate in intensity. AEs leading to withdrawal occurred in 5 of 11 pts (46%): 1 in the OEP because of serious increased transaminases, 3 in the MEP because of serious hypersensitivity reactions to TCZ, and 1 in the MEP because of thrombocytopenia. No deaths were reported during the study. AE rates per 100 pt-years of exposure are reported in the table 1.

Abstract THU0598 – Table 1. Rates of AEs

Table. Rates of AEs	TCZ 12 mg/kg IV Every 2 Weeks		
	Main Evaluation Period n = 11	Optional Extension Period n = 7	Entire Study Period n = 11
Total patient-years at risk	2.3	5.1	7.4
Number of events (AE rate per 100 patient-years at risk)			
All AE	32 (138.4)	47 (926.5)	79 (1072.7)
Serious AE	5 (218.2)	2 (39.6)	7 (95.1)
AE with fatal outcome	0	0	0
AE leading to withdrawal	4 (174.6)	1 (19.7)	5 (67.9)
AE leading to dose interruption	1 (43.6)	12 (236.5)	13 (176.5)

Conclusions: During the OEP of the study, long-term treatment with TCZ was well tolerated in sJIA pts aged <2 years, and no additional safety signals were reported in the OEP beyond those reported in the MEP or observed previously for pts with sJIA aged ≥2 years.

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THU0599

EVALUATION OF EFFICACY AND SAFETY OF CANAKINUMAB IN JAPANESE PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN PHASE III CLINICAL TRIAL, COMPOSED PREDOMINANTLY OF PATIENTS WITH PRIOR USE OF TOCILIZUMAB

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Background: Systemic juvenile idiopathic arthritis (SJIA) is a distinct form of juvenile idiopathic arthritis (JIA), accounting for approximately 4% to 17% of JIA¹. In Japan, a higher frequency of SJIA, 41.7% of JIA² has been reported compared to Europe and United States. Tocilizumab (TCZ) is the only approved biologic for SJIA treatment in Japan. However, some patients (pts) demonstrate persistently high disease activity and/or drug intolerance. Therefore, new treatment options are required. Here, we evaluated the efficacy and safety of canakinumab (CAN), a human anti-interleukin-1β monoclonal antibody, in Japanese SJIA pts.

Objectives: To report the results of a 28 week (Wk) interim whole analysis of Phase III data (NCT02396212) of CAN, and the subgroup analysis of pts with or without prior use of TCZ.

Methods: Patients (age ≥2–<20 years) received open-labelled CAN 4 mg/kg (max 300 mg) every 4Wks (q4w) subcutaneously (s.c.). The primary objective was to evaluate the proportion of pts who achieved 30% improvement from baseline of adapted ACR Paediatric criteria (aACR 30) at Wk8 and who achieved corticosteroid tapering at Wk28. Steroid reduction was allowed from Wk8. We also analysed the data with or without prior use of TCZ.

Results: The trial enrolled 19 pts who had insufficient response to prior treatment; the majority (15/19, 78.9%) had received TCZ (table 1). Of the 19 pts, 3 discontinued CAN due to lack of efficacy or adverse events (AE) by Wk28 and 16 completed the assessment of Wk28. All pts (19/19) achieved aACR 30/50/70 at Wk8 (figure 1). Overall, 73.7% (14/19) pts achieved corticosteroid tapering at Wk28 and 2 pts (10.5%) achieved "steroid free". Of 15 pts with prior use of TCZ, 12 pts (80.0%) achieved aACR 100 at Wk8 and 11 pts (73.7%) achieved corticosteroid tapering (26.3%, 5/19). Serious AE (SAE) was seen in 41.1% (8/19) pts, and the most frequent SAE was JIA (flare or worsening of SJIA, 21.1%, 4/19). One macrophage activation syndrome (MAS) but no death was reported.

Abstract THU0599 – Table 1. Patient Characteristics

Characteristic	G1301 trial n=19
Male (%)	6 (31.6)
Age (mean)	9.9
BMI (kg/m ²) (mean)	19.59
Time from SJIA diagnosis to study entry (years) (mean)	6.1
CRP at baseline (standardised in mg/L) (mean)	357.79
Oral prednisone equivalent dose (mg/kg/day) (mean)	0.309
Oral steroid use at baseline - n(%)	19 (100)
Number of active joints (mean)	6.3
Number of joints with limitation of motion (mean)	4.4
Prior use of tocilizumab (%)	15 (78.9)