THU0569

A RANDOMISED, DOUBLE-BLIND, PARALLEL STUDY TO COMPARE RATES OF REMISSION (INACTIVE DISEASE) IN PATIENTS WITH JIA ON MTX TREATMENT ALONE VERSUS A COMBINATION OF MTX AND ETANERCEPT

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Background: Remission is the major goal of treatment of juvenile idiopathic arthritis (JIA). Advances in treatment options allowed achievement of remission to come into reach. Timing for initiating intensive treatment in a treat to target approach to early reach remission is still a debate.

Objectives: Multi-centre, double-blind, randomised study in polyarticular JIA patients (pts) receiving either Etanercept+Methotrexate (cohort 1) or Placebo +Methotrexate (cohort 2) for 24 weeks followed by 24 week open label phase. Escape to open-label ETN and MTX for pts not achieving paedACR30 at week 12 or not achieving inactive disease at week 24.

Results: 35 pts were randomised to cohort 1 and 33 to cohort 2. Baseline demographic and clinical characteristics were comparable between the groups except mean tender joint count, physician assessment of global disease activity and JADAS10 which all were higher in cohort 1. At week 12, 12 pts randomised to cohort 2 did not reach paedACR30. At week 24, further 10 pts of cohort 2 not reaching inactive disease escaped to ETA and MTX. 5 pts of cohort 1 and 4 pts of cohort 2 dropped out. At week 12, significantly more pts on ETA and MTX (33 (94%)/27 (79%)) than on PLC and MTX (17 (52%)/15 (47%)) reached paedACR30/50 ($p<0.001/0.01$). At week 24, inactive disease was reached by 10 pts on ETA and MTX vs. 6 on PLC and MTX. Inactive disease at week 48 was achieved by 5 pts of cohort 2 on MTX alone while 22 patients (67%) escaped to open label ETA and MTX. 15 (43%) pts of cohort 1 and 16 (49%) of cohort 2 reached inactive disease at week 48. At week 48, paedACR30/50/70/90 was reached by 100%/97%/97%/77% in cohort 1 compared to (97%/93%/93%/73%) in cohort 2. The number of visits with inactive disease in cohort 1 (87 (24%)) was comparable to that of cohort 2 (79 (21%)) while the number of visits with no active joint was significantly higher in cohort 1 (178(48%) vs. 146 (39%); OR 1.45 (1.08–1.94); $p=0.012$). 44 (74/100 y) adverse events (AE) were noted leading to discontinuation in 6 patients. 3 serious AE occurred, two first uveitis events and one diagnosis of dermatomyositis, all in the placebo group. No new safety signal arose from our observation.

Conclusions: Early combination of ETA and MTX proved to be highly effective with a high rate of patients reaching high paediatric ACR response and 50% reaching inactive disease. Pre-defined targets to treat to, paediatric ACR30 at week12, defining minimal response or inactive disease at week 24/48 were more often reached upon ETA and MTX than with MTX alone. Compared to immediate intense antirheumatic combination treatment with ETA and MTX, a comparable rate of patients on targeted therapy reached the final endpoint of inactive disease at week 48 but numbers of visits with active arthritis were higher in patients receiving delayed combination therapy.

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THU0570

LONG-TERM EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FMF (CRFMF), TRAPS AND HIDS/MKD: RESULTS FROM THE PIVOTAL PHASE 3 CLUSTER TRIAL

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Background: Canakinumab (CAN), a selective, human anti-interleukin (IL)–1 β mAb, has demonstrated efficacy and safety in patients (pts) with colchicine-resistant familial Mediterranean fever (crFMF), TNF receptor-associated periodic syndrome (TRAPS), and hyper-IgD syndrome (HIDS)/mevalonate kinase deficiency (MKD) in the epoch 2 and 3 (E2 and E3) of the CLUSTER study (NCT02059291).¹

Objectives: To evaluate the long-term maintenance of optimal control of disease activity (median of no or 1 flare, and no upitration) and safety on every 4 weeks (q4w) and every 8 weeks (q8w) dosing regimens of CAN in pts with crFMF, TRAPS or HIDS/MKD from the epoch 4 (E4; 112 weeks) of the CLUSTER study.

Methods: The study comprised 4 epochs (E1–E4). Study design for E2 and E3 have been reported earlier.¹ After lead-in E1, in E2, a 16 wk randomised, double-blind, placebo (PBO)-controlled epoch, efficacy of CAN 150/300 mg q4w to induce complete response (absence of flares) was assessed. E3 (24 wks) evaluated whether responders to CAN 150/300 mg q4w in E2 could maintain clinical efficacy on 150/300 mg q8w or PBO. In E4, a 72 wk, open-label epoch, the long-term maintenance of efficacy and safety of CAN 150/300 mg q4w or q8w in pts with crFMF, TRAPS or HIDS/MKD was evaluated. Pts who did not maintain clinical response on q8w could be uptitrated to 150/300 mg q4w. Safety assessments included adverse events (AEs) and serious AEs.

Results: At the end of E4 (Wk 112), a substantial proportion of pts maintained optimal control of disease activity following treatment with 150/300 mg q4w or q8w in all 3 cohorts (figure 1). HIDS/MKD pts more often required upitration to 300 mg q4w. Majority of pts in all 3 cohorts had 1 or no new flare (crFMF: 96.6%, TRAPS: 94.3%, HIDS/MKD: 83.3%) and physician global assessment <2 (no or minimal disease activity). In all 3 cohorts, the median SAA levels decreased rapidly from baseline and remained suppressed through E4 (crFMF: 618 to 21 mg/L, TRAPS: 243 to 12 mg/L and HIDS/MKD: 2061 to 16 mg/L). No new safety findings were reported in CAN-treated pts through E4.

*Optimal control of disease activity was defined as median of no or 1 flare, and no upitration.

Abstract THU0570 – Figure 1 Proportion of responders who maintained optimal control of disease activity* at the end of epoch 4 (Week 112; following treatment with canakinumab 150/300 mg q4w or q8w)

Conclusions: Epoch 4 of the CLUSTER study demonstrated that optimal control of disease activity in the crFMF, TRAPS and HIDS/MKD patients can be maintained following long-term treatment with canakinumab 150/300 mg q4w. For all 3 cohorts, patients requiring 150/300 mg q8w in epoch 3 to maintain disease control were less likely to control disease during epoch 4 and therefore a substantial number of these patients were up-titrated to q4w regimen by the end of epoch 4. No new or unexpected safety issues were reported over 112 weeks of canakinumab treatment.

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THU0571 PROTEOMIC IDENTIFICATION OF SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS PHENOTYPIC BIOMARKERS

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Background: Systemic juvenile idiopathic arthritis (SJIA) is a childhood rheumatic auto-inflammatory disorder of largely unknown pathogenesis. The presence of fever, rash and arthritis support a diagnosis of SJIA, though early in disease arthritis may be minimal, complicating the exclusion of alternative diagnoses such as infection. Furthermore, two clinical phenotypes of SJIA can be identified, a chronic articular-dominant (ART_SJIA) and a classical auto-inflammatory phenotype (AID_SJIA).

Objectives: To identify novel serum protein biomarkers that may discriminate ART_SJIA from AID_SJIA and distinguish AID_SJIA from infection.

Methods: Patients with active SJIA (joint activity plus or minus fever and elevated laboratory inflammation markers) were sub-grouped into the two clinical phenotypes (ART_SJIA and AID_SJIA). Serum from patients with SJIA or confirmed infection was analysed for the standard laboratory markers: C-reactive protein (CRP), white cell count (WCC) and erythrocyte sedimentation rate (ESR). A "discovery cohort" (n=10 per group) of patient serum samples was subjected to unbiased label-free proteomics using liquid chromatography mass spectrometry (LC-MS/MS) and in a separate "verification cohort" (AID_SJIA, n=48; ART_SJIA, n=29; infection, n=32) candidate biomarkers were measured by multiple reaction monitoring MS (MRM-MS; Agilent 6490 and 6495) and microsphere bead-based immunoassay (Luminex). Serum concentrations of S100A12 and MRP8/14 were also measured in all samples using enzyme linked immunoabsorbant assays (ELISAs).

Results: The routine laboratory markers CRP, WCC, ESR, as well as ELISA-measured S100A12 and MRP8/14 serum concentrations were highest in AID_SJIA, followed by infection and were lowest in patients with ART_SJIA. Proteins identified and quantified by LC-MS/MS could differentiate patients with ART_SJIA from those with AID_SJIA (area under the curve, AUC: 0.97). The discrimination between AID_SJIA and infection performed less well, AUC: 0.58. Targeted MRM measurement of novel protein candidate biomarkers verified the discovery cohort data. A combined biomarker panel consisting of MRM, ELISA and Luminex analysis which was evaluated using a Random forest model, indicated the correct

overall identification of the clinical groups to be as follows: ART_SJIA: 24/29 (83%), AID_SJIA: 37/45 (82%) and infection: 20/32 (63%).

Conclusions: Significant differences in the serum protein signature between two phenotypes of SJIA suggest that different immunological processes may underlie these phenotypes. Serum protein profiles also distinguished patients with SJIA and infection. Distinguishing these two groups remains an important goal of research and therefore this study could help inform future prospective studies.

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THU0572 ORGANISED SPORTS IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): A COMPARISON OF PATIENT AND GENERAL POPULATION PARTICIPATION

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Background: Despite the well-established physical, social and mental health benefits of physical activity (PA) in childhood, a substantial proportion of children and adolescents with JIA seem to be not active enough to achieve their age-appropriate fitness level.¹ Previous research revealed that organised sports (OS)¹ is associated with greater health benefits compared to non-organised sporting activities, as intensity and net exercise duration are usually higher,² has a strong predictive value in improving leisure time PA, and³ has a positive influence on mental well-being and life satisfaction.²

Objectives: This study was aimed at comparing OS prevalence in JIA with the general population and at determining correlates associated with OS participation.

Methods: Data from the German National Paediatric Rheumatologic Database (NPRD) were considered for the analyses. The outcome variable 'OS participation' was analysed in patients aged 3 to 17 and compared to a population-based nationwide sample (German Health Interview and Examination Survey for Children and Adolescents; KIGGS). Correlates of OS participation were analysed using data of the year 2014.

Results: 5,056 children and adolescents with JIA (mean disease duration 4.5 ± 3.6 years) provided information about their exercise habits, of which 36% stated to be involved in OS (34% of girls, 41% of boys). The prevalence was higher in the age groups 7 to 10 and 11 to 13 years with almost 50% than in the age groups 3 to 6 and 14 to 17 years with 35% and 42%, respectively. In KIGGS participants, almost 60% reported to be physically active in OS (54% aged 3 to 6, 65% aged 7 to 10, 60% aged 11 to 13% and 49% aged 14 to 17). Non-participation in OS was associated with active disease status (cJADAS), functional disability (C-HAQ), low parental education, higher body mass index (BMI) and worse patient-reported pain, fatigue and overall well-being.

Conclusions: The prevalence of OS participation in JIA was considerably lower compared to the general population and varied with increasing age, parental education and functional ability. Considering that low levels of PA might even be more dangerous for young patients with JIA, as they also have signs of inflammation, it is all the more important to create opportunities and incentives in the future to improve young rheumatic's exercise habits.

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