NORMAL VERSUS ELEVATED ACUTE PHASE REACTANTS IN PATIENTS WITH POLYMYALGIA RHEUMATICA: ARE THESE DIFFERENT SUBSETS?

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Background: Systemic signs of inflammation such as raised CRP or ESR are a classical feature of PMR, but some patients present with normal acute phase reactants (APR). It is not known whether these patients represent milder forms of PMR or another pathophysiological subset of PMR or another disease. Data on demographic and clinical characteristics between PMR patients with normal versus elevated APR might provide some answers.

Objectives: To explore baseline differences in demographics and clinical characteristics in PMR patients with and without elevated APR.

Methods: We conducted a retrospective cohort study of clinical characteristics of newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic between April 2012 and September 2017. Patient with concomitant inflammatory rheumatic disease were excluded. Data on patient-, disease-, and treatment-related characteristics were extracted from the electronic health record. Descriptive statistics were used (using mean (SD), median (p25-p75) or n (%) as appropriate), and differences between patients with high APR (CRP>10 mg/L and/or ESR >30mm/hour) were tested using Fischer's exact test for categorical data, t-test for normally and Wilcoxon test for non-normally distributed data.

Results: 454 patients were included (table 1). Sixty-two patients had normal, and 392 had elevated APR. In the group with normal APR, fewer patients had peripheral arthritis (2 versus 9%; p=0.044) and fewer had anemia at diagnosis (17 versus 39%; p=0.0014) and differences between patients with high APR (CRP>10 mg/L and/or ESR >30mm/hour) were tested using Fischer's exact test for categorical data, t-test for normally and Wilcoxon test for non-normally distributed data.

Disclosure of Interests: None declared


OP0146

EFFICACY OF APEXPLAST FOR ORAL ULCERS ASSOCIATED WITH ACTIVE BEHÇET’S SYNDROME OVER 64 WEEKS: RESULTS FROM A PHASE III STUDY

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Background: Behçet’s syndrome is a chronic, relapsing, multi-system inflammatory disorder characterized by recurrent oral ulcers (OU) that can impact quality of life (QoL).

Objectives: To assess apexlila (APR) efficacy and safety for the treatment of OU associated with Behçet’s syndrome in the phase III RELIEF study for up to 64 wks and at 4-wk follow-up (after APR discontinuation).

Methods: Adult patients (pts) with active Behçet’s syndrome (defined by >3 OU at randomization or >2 OU at screening and at randomization without active major organ involvement) were randomized (1:1) to placebo (PBO) or APR 30 mg twice daily for 12 wks. All pts then received APR through Wk 64. Pts who completed the Wk 64 visit or discontinued treatment at any time and for any reason in the study entered a 4-wk posttreatment observational follow-up. The primary endpoint was area under the curve for the number of OU (AUCWk0-12), which reflects the number of OU over time and accounts for the recurring-relenting course of OU. Other outcomes included change from baseline in OU pain VAS, complete response (percentage of pts with no OU) and partial response (percentage of pts with >50% reduction in number of OU), disease activity (Behçet’s Disease Current Activity Index [BDCAI], Pt’s and Clinician’s Perception of Disease Activity and Behçet’s Syndrome Activity Score [BSAS]), and QoL (Behçet’s Disease QoL [BDQoL]).

Results: A total of 207 pts were randomized and received ≥1 dose of study medication (PBO: n=103; APR: n=104); 178 pts entered the active treatment phase (PBO/APR: n=83; APR: n=95) and 143 pts (PBO/APR: n=68; APR: n=75) completed Wk 64. The primary endpoint of AUCWk0-12 was achieved; significantly lower AUCWk0-12 was observed for APR vs PBO (P<0.0001). Significantly lower OU counts (P<0.0015) and OU pain (P<0.0035) were observed with APR vs PBO from Wks 1 through 12; APR efficacy was sustained up to 64 wks (Figure). Significantly greater improvements with APR were observed in complete and partial response of OU at Wk 12 (P<0.0001); effects were maintained through Wk 64 (53.3% and 76.0%, respectively). Pts initially randomized to PBO and switched to APR at Wk 12 showed comparable benefits through Wk 64 (Figure). Improvements in disease activity (BDCAI: P<0.0335; BSAS: P<0.0001) and QoL (BDQoL: P<0.0003) were significant in pts receiving APR vs PBO at Wk 12 and maintained at Wk 64. Comparable effects in pts who switched from PBO to APR were observed at Wk 64. After APR was discontinued before or at Wk 12, the improvements in OU persisted through Wk 64 (Figure). Disease activity measures and BDQoL similarly indicated recurrence of symptoms at the 4-wk follow-up. Incidence of any adverse event (AE) was comparable for pts initially randomized to APR vs PBO during the PBO-controlled period (78.8% vs 71.8%) and through Wk 64 for pts who continued APR vs pts who switched from PBO to APR (84.3% vs 88.5%). The most common AEs with APR were diarrhea, nausea, headache and upper respiratory tract infection; most AEs were mild/moderate in severity, and no new safety concerns were identified.

Disclosure of Interests: None declared

Conclusion: APR demonstrated efficacy in the treatment of OU in pts with active Behçet’s syndrome. Benefits were sustained for up to 64 weeks with continued treatment. APR was well tolerated, and safety was consistent with the known safety profile of APR.


OP0147

KAWAKINRA: A PHASE IIA MULTICENTER TRIAL TO ASSESS THE EFFICACY, AND SAFETY OF ANAKINRA IN PATIENTS WITH INTRAVENTRICAL IMMUNOGLOBULIN-RESISTANT KAWASAKI DISEASE

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Background: The development of more potent therapeutic approaches of KD is an urgent need because intravenous immunoglobulin (IVig) treatment is not effective in 20% of patients, increasing the risk of coronary dilatations/aneurysms. The combination of genetic and transcriptomic data revealed the key role of interleukin-1 receptor antagonist (IL-1RA, IL-1 receptor antagonist) could prevent the development of vascular aneurysms.

Objectives:
- To assess as primary objective, the efficacy of anakinra in patients with KD who fail to respond to at least one infusion of 2g/kg of IVig.
- To assess its safety and tolerability and its effect on disease activity, systemic inflammation and coronary lesions.

Methods: A 45-day, phase IIa proof of concept study open labeled with anakinra dose escalation, with a target of at least 12 patients completing the study. Eligible patients had KD according to the AHA criteria, duration of fever ≤ 14 days, and were > 3 months and 5 Kg. They had persistent (or relapsing) fever (>38°C) within 48h of the last IVig infusion, had not received other alternative treatment including steroids, and had no other exclusion criteria. After informed consent, they received a starting dose of 2mg/kg (patients <10kg and/or <3 months: 4mg/ kg) of anakinra, which could be increased every 24h of 2mg/kg until a maximum of 6mg/kg (patients <10kg and/or >8 months: 8mg/kg), in case of persistent fever. Anakinra treatment duration was 15 days. Outcome measures were fever, KD symptoms, blood inflammation and cardiac echography. Total study duration was 45 days. Clinical trials: NCT02390596. The study is supported by a grant from the French ministry of health, APHP, national PHRC 2014. IRB approval was obtained and all patients (parents) gave informed consent.

Results: 18 patients were screened and 16 were included and 13 have completed the study. Anakinra was started in 16 patients (14 boys, 2 girls) at a median age 2 years (3 months to 6 years) and at a median of 9.5 days after the onset of fever. 4 patients escaped early for SAE, and 1 had sJIA final diagnosis. The maximum dose of anakinra was 6mg/kg in 6 patients, 4mg/kg in 6, and 2mg/kg in 4. Mean PGA decreased from 7.80 (4-10) to 1.2 (0-3) at D14. Median temperature was 37.6°C (36.7-39.7)° at day 3 and 37.2°C at D7 (36.7-37.9). Median CRP was 135mg/L at screening and decreased to 9.5 mg/L at D7. 8/14 evaluated patients had coronary dilatation (Z score max >2±5mm) at inclusion, 5/14 at D14 and 3/14 at D45. 3/14 patients who increased Z score at D14 decreased it at D45. We observed 3 severe adverse events (SAE) where treatment was discontinued: anakinra overdose. MAS in a patient evolving to sJIA and increase of coronary dilatation. Others AE included cytolytic hepatitis (2 patients), hypereosinophilia (1), injection site reactions (4), and pancreatitis (1) without treatment discontinuation.

Conclusion: We have realized the first experimental study assessing IL-1 block- ade in severe refractory KD. 15 days duration of anakinra treatment, given early in the course of IVIG-resistant KD, was rapidly effective on KD symptoms, biologic inflammation and coronary dilatations in almost all patients, with a good tolerability.

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Journeys from bench to bedside in paediatric rheumatology.

OP0148

METABOLICOMICS IN JUVENILE-ONSET SLE: IDENTIFYING NEW BIOMARKERS TO PREDICT CARDIOVASCULAR RISK

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Background: Juvenile-onset systemic lupus erythematosus (JSLE) is an autoimmune disorder characterised by immune dysregulation, chronic inflammation and increased cardiovascular risk (CVR). Cardiovascular disease is the leading cause of mortality in JSLE not attributable to lupus flare. Our findings in adult-onset SLE link immune cell dysregulation with dyslipidaemia but little is known about the immune profile or whether abnormal lipid metabolism contributes to disease pathogenesis in JSLE.

Objectives: The objective of this study was to investigate dyslipidaemia and CVR in a cohort of JSLE patients using in depth metabolomics and relate this to clinical arterial, immune cell profiles and to identify novel biomarkers to predict CVR in these patients.

Methods: Metabolic biomarker analysis (NMR) and in-depth immune cell phenotyping (30 subsets by flow cytometry) was performed on serum and PBMCs respectively from a discovery cohort of 35 JSLE patients (median age 19 (14-25), 12 males, 23 females) compared with 39 age/sex matched healthy donors (HCs) (median age 18 (16-25), 17 males, 22 females). Data was analysed using cluster and correlation-correlation and receiver operating characteristic (ROC) analysis. Results were validated in a second cohort of 31 JSLE patients.

Results: Patient stratification by metabolic profile using unbiased hierarchical clustering revealed 3 groups that each had a unique lipidprotein profile, immune cell phenotype and clinical presentation. Group-1 had decreased atheroprotective high density lipoproteins (HDL) and increased atherogenic very low and low density lipoproteins (VLDL/LDL) and Group-2 had elevated HDL but reduced VLDL/ LDL indicating that these groups could be at high and low CVR respectively. This hypothesis was validated by previously recognised markers of CVR including the atherogenic index of plasma, ApoB:A1 ratios and lipid biomarkers we previously identified to be associated with pre-clinical atherosclerotic plaque in adult SLE patients. Patients in Group-1 had a significant increase in plasmablasts and activated T-cells compared to HCs and had clinical features associated with increased disease activity. These immunopathogenic properties were not seen in