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


OP0147 KAWAKIRNA: A PHASE IIA MULTICENTER TRIAL TO ASSESS THE EFFICACY, AND SAFETY OF ANAKINRA IN PATIENTS WITH INTRAVENTRICULAR IMMUNOGLOBULIN-RESISTANT KAWASAKI DISEASE

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Background: The development of more potent therapeutic approaches to 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 (IL-1) signaling in KD vasculitis and mouse model of KD has shown that anakinra (IL1RA: IL-1R1 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 IVIg/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 others exclusion criteria. After informed consent, they received a starting dose of 2mg/kg (patients < 10kg and/or < 8 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 153mg/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 reaction (1) and pancreatitis (1) without treatment discontinuation.

Conclusion: We have realized the first experimental study assessing IL-1 blockade 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. This study calls for further investigation of IL-1 blockade in KD.

Disclosure of Interests: Isabelle Koné-Paut Grant/research support from: SOBI has supported drug product (anakinra) for the presented study, Consultant for: SOBI, Novartis, Pfizer, Abbvie, UCB, CHUGAI, ROCHE, stephanie tellier: None declared, virginie Lambert: None declared, Corinne Guitton: None declared, alexandre belot: None declared, Perrine Dusser: None declared, Linda Rossi-Semerano Grant/research support from: Roche, Isabelle Marie: None declared, gregory allain: None declared, helene agostini: None declared, celine piedvache: None declared DOI: 10.1136/annrheumdis-2019-eular.5633

OP0148 METABOLOMICS 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 and 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 protein 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 plasma blasts and activated T-cells compared to HCs and had clinical features associated with increased disease activity. These immunopathogenic properties were not seen in

Thursday, 13 June 2019 Journeys from bench to bedside in paediatric rheumatology.