OP0145

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

diane marsman1*, Aatke van der Maas 1, Alfons den Broeder1, Frank van den Hoogen2,3, Nathan den Broeder4, Nadine Boers1. 4Nijmegen, Sint Maartenskliniek, Rheumatology, Utrecht, Netherlands; 2Radboud University Medical Center, Rheumatology, Nijmegen, Netherlands

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).1,2 It is not known whether these patients represent milder forms of PMR, or represent a different pathophysiological subset of PMR.

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 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 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 anaemia at diagnosis (17 versus 43%; p= 0.001). Furthermore, patients had a longer median duration of symptoms before diagnosis (13 versus 10 weeks; p= 0.0196) and were more likely to have a history of PMR (16 versus 8%; p= 0.057). No significant differences were found in other clinical characteristics.

Conclusion: The results of this cohort indeed suggest that patients with normal APR are a different subset of PMR patients. Fewer cases have peripheral arthritis and anaemia at diagnosis, suggesting a milder form of PMR. Secondly, our results do not support the hypothesis that PMR of those with normal APR is not yet fully expressed, as they have a longer symptom duration prior to diagnosis.

REFERENCES:

Disclosure of Interests: None declared


OP0146

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

Gülen Hateres1, Alfred Mahf3, Mitsuhiro Takeno2, Doyoung Kim4, Haner Direskeneli5, Sue Cheng6, Shannon McCue7, Maria Parisi3, Mindy Chen7, Yusuf Yazici3, 8
1Istanbul University – Cerrapahsa, School of Medicine, Istanbul, Turkey; 2Hospital Saint-Louis, University Paris Diderot, Paris, France; 3Nippon Medical School, Tokyo, Japan; 4Yersin University College of Medicine and Severance Hospital, Seoul, Korea, Rep. of (South Korea); 5Groupe Hospitalier Pitie Salpêtrière, Paris, France; 6Marmara University, School of Medicine, Turkey; 7Celgene Corporation, Summit, United States of America; 8New York University School of Medicine, New York, United States of America

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 apremilast (APR) efficacy and safety for the treatment of OU associated with Behçet’s syndrome in the phase III RELIEF study for up to 64 weeks and at 4-week 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 over 12 wks (AUCWk0-12), which reflects the normal course of OU over time and accounts for the recurring/remitting course of OU. Other outcomes included change in baseline in OU pain VAS, complete response (pts with no OU) or partial response (pts with ≥50% reduction in number of OU), disease activity (Behçet’s Disease Current Activity Form [BDCAF]), composed of the Behçet’s Disease Current Activity Index [BDCAI]. Pts’ 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=0.0353; 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 Wk 12 or at Wk 64, the improvements in OU assessments decreased within 4 wks. 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 86.5%). 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.

Table 1: Baseline characteristics of patients with normal versus elevated APR.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal APR</th>
<th>Elevated APR</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>50±10</td>
<td>52±10</td>
<td>0.065</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>55%</td>
<td>51%</td>
<td>0.457</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>24±12</td>
<td>30±15</td>
<td>0.012</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>3±2</td>
<td>12±5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>12±5</td>
<td>24±10</td>
<td>&lt;0.0001</td>
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Scientific Abstracts
KAWAKINRA: A PHASE IIA MULTICENTER TRIAL TO ASSESS THE EFFICACY, AND SAFETY OF ANAKINRA IN PATIENTS WITH INTRAVENTRIOUS IMMUNOGLOBULIN-RESISTANT KAWASAKI DISEASE

Isabelle Koné-Paut1, Stephanie Tellier2, Virginie Lambert3, Corinne Guittori4, Alexandre Belot5, Perrine Dusser6, Linda Rossi-Semerano4, Nathalie Marie5, Gregory Allain3, Helene Agostini3, Celine Piedvache1, CHU de Bicêtre, university of Paris sud Caydat, Pediatric rheumatology and CEREMAIA, Le Kremlin Bicêtre, France; 2Hopital Purpan, Pediatrics, Toulouse, France; 3Institut Mutualiste Montsouris, pediatric cardiology, Paris, France; 4CHU de Bicêtre, university of Paris sud Caydat, Pediatrics, Le Kremlin Bicêtre, France; 5CHU de Lyon, Pediatric rheumatology and RAISE, Lyon, France; 6CHU de Bicêtre, university of Paris sud Caydat, clinical research unit, Le Kremlin Bicêtre, France

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 coronary lesions in almost all patients, with a good tolerability profile.

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 <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 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 J45. 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 profile. 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, UCBI, CHUGAI, ROCHE, stephanie tellier: None declared, virginie lambert: None declared, Corinne Guittor: None declared, alexandre belot: None declared, Perrine Dusser: None declared, Linda Rossi-Semerano: None declared, Nathalie Marie: None declared, gregory allain: None declared, helene agostini: None declared, celine piedvache: None declared