

Macrophage Activation Syndrome/Systemic JIA Working Party

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MACROPHAGE ACTIVATION SYNDROME/SYSTEMIC JIA WORKING PARTY e-Congress PReS 2020 - 25 September 2020

The 2020 MAS/sJIA WP meeting was a fully virtual live meeting during the E-Congress PReS 2020, attended by 134 participants (62 pediatric rheumatologists are active members of the group).

Presentation of the current core team, elected during the 2018 PReS meeting according to the new mission of the PReS WPs (2.0):

- Chair:
Claudia Bracaglia, Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy; claudia.bracaglia@opbg.net
- Secretary and lead of clinical care:
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- Lead of science and research:
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- Lead of education and training:
Sebastian Vastert, Pediatric Rheumatology and Immunology, University Medical Center Utrecht, the Netherlands; b.vastert@umcutrecht.nl

The core team closely collaborate with:

- **EMERGE representative:** Merav Heshin-Bekenstein, Dana Children's Hospital, Tel Aviv Medical Center, Tel Aviv, Israel; meravheshin@gmail.com
- **Patient/Parent representative:** Wendy Costello, ENCA President, ICAN Chair (Ireland); icanireland@gmail.com

The aim of WP is to:

- promote knowledge and international multidisciplinary collaboration among experts in the field of MAS and systemic JIA ;
- foster translational research in order to improve care and outcome of patients with MAS and patients with systemic JIA.

Update of current research projects:

1. ***“Validation of risk score for MAS in sJIA patients”***. The aim of this study is to define a risk score of MAS for sJIA patients using routine laboratory parameters of disease activity and severity. Claudia Bracaglia presented the preliminary results of this project. The project was conducted in two steps: 1) development of the score on 69 sJIA patients, with or without history of MAS, followed at Ospedale Bambino Gesù in Rome; 2) validation of the score on a multicentre international cohort of sJIA patients with the involvement of many MAS/sJIA WPs centers. In this second phase the score was validated on 132 patients collected from 10 paediatric rheumatologic centres around the world with 81.3% of sensitivity and 60.0% of specificity (NPV 90.9%). The study is concluded and the manuscript is in preparation.
2. ***“MAS patients with systemic thrombotic microangiopathy (TMA)”***. The aim of this study is to describe clinical and laboratory features, therapeutic choices and outcome of a multinational cohort of pediatric patients with MAS/sHLH and TMA. The data collection phase has just completed and Francesca Minoia presented the preliminary results of this study: a total of 28 patients with MAS/sHLH (22 MAS and 6 sHLH) and TMA were collected from 18 centres in 9 countries, with the involvement of many MAS/sJIA WPs centers. The association between TMA and MAS/sHLH is likely still under-recognized, however if not promptly detected and treated might severely impact on mortality and morbidity of MAS patients. The study is concluded and the manuscript is in preparation.
3. ***“Current treatment in sJIA and MAS/sHLH: a PReS/PRINTO survey”***. The aim of this project, led by Francesca Minoia and Bas Vastert for the MAS/sJIA WP, is to capture the real-life treatments strategies currently available for sJIA and MAS/sHLH. The survey aims to involve the pediatric rheumatology centers of the PReS/PRINTO network and (for MAS/sHLH section) also pediatric hematologists and intensive care physicians. Furthermore, a section of the survey specifically addressed to parent/patients, in collaboration with ENCA., will be developed. The project was submitted for the 2019 PReS/PRINTO grant and received 2nd rank. During the meeting the core team proposed to re-submit the project for the 2020 PReS/PRINTO grant, unless other projects from the MAS/sJIA WP are received. The possibility to considerate also a grant from the Histiocyte Society was discussed.
4. ***“ReSyst study”***. The aim of this study is to set up an international research infrastructure, collecting biosamples and clinical data, to better understand disease mechanisms that lead to refractory sJIA (recurrent MAS, patients refractory to IL-1 and IL-6 treatments, sJIA-associated ILD). Bas Vastert presented the last update of the project, which is endorsed by ERN-RITA and currently involve Rome, Utrecht and Leuven but will be open to all interested centers. Biosample collection will follow the UCAN SOP's protocols. Regional biobank will be settled up in Europe (Utrecht, Rome) linked to US-Cincinnati, Toronto. In June 2020 the project received a funding from the sJIA Foundation and by December 2020, once approved by ethical committee, the collection phase will start.
5. ***“Analysis of type I IFN score and IL-18 expression in MAS and MAS risk patients”***. Christoph Kessel and Claas Hinze presented the preliminary results of a translations research project aimed to evaluate the correlation between type I IFN score and IL-

18 gene expression in MAS and MAS risk patient. A panel containing IL-1 β , INF α and INF γ -driven genes has been tested on a preliminary cohort of patients with active/inactive sJIA, pre-MAS and MAS followed in Rome and Munster. The project is open for multicentre collaboration.

Proposal of new collaborative research projects:

1. **“International registry on COVID-19 related Hyperinflammation in children (HyperPED-COVID)”**

Francesca Minoia and Claudia Bracaglia, on behalf of the WP core team, presented a PReS/PRINTO/ISSAID/ESID and ERN-RITA joined effort aimed to develop a common Registry to collect standardized clinical data on the hyperinflammatory conditions related to COVID19 in childhood. The primary endpoints of the projects are to 1) capture the burden of the spectrum of pediatric hyperinflammatory conditions related to COVID19; 2) to analyze different clinical phenotypes in relation to age and geographical location; 3) to identify clinical predictors of severity and outcome; 3) to evaluate the availability of biosamples in different centers.

Educational proposal

1. **“1st PReS ACADEMY COURSE on sJIA and MAS”**

Claudia Bracaglia, on behalf of the WP core team, presented the proposal of the first PReS Academy Course focused on sJIA and MAS. The course will address the most relevant new clinical and basic updates in sJIA and MAS and will involve young investigators to discuss difficult cases in a dedicated session in collaboration with EMERGE. The course was initially planned for November 2020, but actually postponed due to COVID19 pandemic.