pediatric rheumatology european society

MAS/sJIA Working Party

Chair: Claudia Bracaglia (claudia.bracaglia@opbg.net)
Secretary: Francesca Minoia (francesca.minoia@policlinico.mi.it)
Lead of science and research: Christoph Kessel (christoph.kessel@uni-muenster.de)
Lead of education and training: Sebastiaan Vastert (b.vastert@umcutrecht.nl)

MACROPHAGE ACTIVATION SYNDROME/SYSTEMIC JIA WORKING PARTY
e-Congress PReS 2021 - 22 September 2021

The 2021 MAS/sJIA WP meeting was a fully virtual live meeting during the E-Congress PReS 2021, attended by 82 participants (73 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:
  Francesca Minoia, Clinica De Marchi Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; francesca.minoia@policlinico.mi.it
- Lead of science and research:
  Christoph Kessel, Department of Pediatric Rheumatology and Immunology, University Hospital Muenster, Germany; christoph.kessel@uni-muenster.de
- 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.

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Update on recent publications:

1. Minoia F, Tibaldi J, Muratore V, Gallizzi R, Bracaglia C, Arduini A, et a; MAS/sJIA Working Group of the Pediatric Rheumatology European Society (PReS). *Thrombotic Microangiopathy Associated with Macrophage Activation Syndrome: A Multinational Study of 23 Patients.* J Pediatr. 2021 Aug;235:196-202.

2. *The Risk score for MAS in sJIA patients*. Bracaglia C et al, manuscript in preparation

Update of current research projects:

1. ***Systemic JIA-associated Lung Disease in Europe***. Lung disease is increasingly recognized as a severe life-threatening complication of sJIA, especially in North America. The aim of this project, led by Claudia Bracaglia, is to capture the burden of this emerging condition in Europe. The first step of the project, a retrospective collection of patients with sJIA-associated LD, is ongoing and enrolment is open. The second step will be a prospective study which will include also standardized biosampling.
   PI: Claudia Bracaglia (claudia.bracaglia@opbg.net)

2. ***HyperPED-COVID: International registry on COVID-19 related hyperinflammation in children and young adults***
   Francesca Minoia, on behalf of the MAS/sJIA core team presented the update of the 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 analyse 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. So far, data of almost 300 patients have been collected worldwide. The registry is now open to enrolment and available at PRINTO website (www.printo.it)
   PI: Marco Gattorno (printo@gaslini.org)

3. ***Analysis of type I IFN score and IL-18 expression in MAS and MAS risk patients.*** Claas Hinze presented an update of a translational research project aimed to evaluate the correlation between type I IFN score and IL-18 gene expression in MAS and sJIA patients. A panel containing IL-1β, INFα and INFγ-driven genes has been tested in a cohort of patients with active/inactive sJIA, pre-MAS and MAS followed in Rome and Munster. The project is open for multicenter collaboration.

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PIs: Christoph Kessel, Claas Hinze
(christoph.kessel@uni-muenster.de, claas.hinze@ukmuenster.de)

4. ***Comparability of MAS biomarker assays (CoMASBA study).*** This project, led by Christoph Kessel, is aimed to evaluate the variance of current MAS biomarker quantification among different centers. This will lead to a better understanding of assay variability/handling and of the comparability of assay results. The project includes: 1) preparation phase, in which centers will be asked regarding type of biomarkers and assay's methods; 2) quantification phase, in which patients and control samples will be distributed to the centers for quantification; 3) data collection phase, in which results from different centers will be analysed to determine biomarker variability. Currently 9 centers in Europe and 3 in North America are involved; the project is still open for multicenter collaboration.
   PI: Christoph Kessel (christoph.kessel@uni-muenster.de)

5. ***Current treatment in MAS/sHLH: a PReS/PRINTO survey***. The aim of this project, led by Francesca Minoia and Bas Vastert, is to capture the real-life treatments strategies currently available for MAS/sHLH. The survey aims to involve the pediatric rheumatology centers of the PReS/PRINTO network and also pediatric hemato-oncologists. Furthermore, a specific section of the survey in collaboration with patient/parent organizations, will be developed. The project has been already submitted for the PReS/PRINTO grant in 2019 and 2020, ranked 2nd and 4th respectively.
   PIs: Francesca Minoia, Bas Vastert
   (francesca.minoia@policlinico.mi.it, b.vastert@umcutrecht.nl)

6. ***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 will be open to all interested centers. Biosample collection will follow the UCAN SOP's protocols. In 2020-2021 the study received funds from the sJIA Foundation and Utrecht Institution with potential connection with other already ongoing projects (UCAN CAN DU, Permidriar, PReS-CARRA).
   PI: Bas Vastert (b.vastert@umcutrecht.nl)

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Proposal of new collaborative research projects:

1. ***Development of clinical definitions of refractory disease trajectories in systemic JIA***. Bast Vastert presented this new proposal, linked to ReSyst, aimed to develop a widely accepted definition of refractory disease in sJIA, in order to enable collaborative research and foster targeted therapeutic strategies. The project will follow 3 different steps: 1) literature review; 2) international Delphi survey; 3) expert consensus meeting.
   PI: Bas Vastert (b.vastert@umcutrecht.nl)

2. ***An international consensus core dataset for sJIA.*** This proposal, led by Francesca Minoia and Claudia Bracaglia on behalf of the WP core team, is aimed to develop an internationally agreed dataset for sJIA, feasible in clinical practice, to guide collaborative research and foster comparison of data between international centres. This project will include 4 steps: 1) selection of items from sJIA existing registries and from literature review; 2) international Delphi survey; 3) data analysis; 4) expert consensus meeting, and could be a potential collaboration with CARRA.
   PIs: Francesca Minoia, Claudia Bracaglia
   (francesca.minoia@policlinico.mi.it, claudia.bracaglia@opbg.net)

3. ***NLRC4-GoF Clinical Trial***. Fabrizio De Benedetti presented a three-period multicenter study, with a randomized-withdrawal, double blinded, placebo-controlled design in Period 2 to evaluate the efficacy, safety and tolerability of MAS825 in NLRC4-GoF patients (NCT04641442). MAS825 is a cytokine capture bispecific novel antibody that builds upon canakinumab an anti-IL18 antibody. This study currently involves 7 countries (Italy, USA, Japan, France, Czech Republic, Spain and Turkey) and 13 centers (5 active for recruitment).
   Lead PI: Fabrizio De Benedetti (fabrizio.debenedetti@opbg.net)

Ongoing collaboration with Vaccination WP:

1. ***Influenza vaccine uptake among JIA patients in COVID-19 era.*** Despoina Maritsi presented an update of this multicenter cross-sectional project, aimed to evaluate the current practice in influenza vaccination in patients with JIA, with a particular focus on sJIA and on the impact of COVID19 pandemic.
   PI: Despoina Maritsi (dmaritsi@gmail.com)

2. ***Prospective MMR vaccination study.*** The aim of this project, presented by Masa Bizjak, is to prospectively evaluate safety and long-term immunogenicity of 2nd dose of MMR vaccine. Inclusion criteria include: patients with immune-mediated disease, who have

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stable disease and are treated with DMARDs/bDMARDs or JAK-inhibitors and are scheduled to receive the 2nd dose of MMR vaccine according to national vaccination programme. So far 22 patients have already been included in 4 active centers (2 more centers with recent ethical approval). The project is ongoing with active enrolment and multicenter participation is welcome.
PI: Natasa Toplak (natasa.toplak@kclj.si)

3. ***Safety and immunogenicity of COVID-19 vaccination.*** This project, led by Merav Heshin, is aimed to evaluate safety and immunogenicity of COVID19 vaccination in children with rheumatic disease treated with immunomodulatory medications. So far the study involves 4 centers in 2 countries (Israel and Slovenia) but further multicenter participation is welcome.
   PI: Merav Heshin Beckenstein (meravheshin@gmail.com)

4. ***Current approach to COVID19 and other vaccinations in previous MIS-C/PIMS.*** Francesca Minoia presented, on behalf of both MAS/sJIA and Vaccination WP core teams, a collaborative effort aimed to evaluate the current approach, in different international centers, on COVID19 and other vaccinations in children with previous MIS-C/PIMS. A web-survey has been developed and is addressed to the international pediatric rheumatology community, but also to the other physicians involved in the care of MIS-C/PIMS patients.
   The survey is available online at the following link:
   https://www.surveymonkey.com/r/KJCGVZP
   PI: Francesca Minoia (francesca.minoia@policlinico.mi.it)

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 is planned for March 17-18th, 2022. More information will be soon available on the PReS website.