pediatric rheumatology european society

Paediatric MAS Working Party

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October 8, 2017

To all MAS Working Party members

Dear Colleague,

Here is a short report of the MAS Working Party meeting that we had on September 14, from 16:00 to 17:30, during PReS congress in Athens

1. Claudia Bracaglia, Sebastiaan Vastert: RESYST (Resistant SYstemic juvenile idiopathic arthritis STudy): Identification of pathogenic pathways in resistant systemic juvenile idiopathic arthritis.

This project is focused on resistant sJIA. These patients are challenging, no curative treatment is available, and therefore accumulate significant morbidity and have unacceptably high mortality. Collection of an adequate number of samples by means of a collaborative study is necessary to allow for molecular stratification by genetic/molecular factors in these patients and to subsequently develop and apply appropriate novel targeted treatments.

The project will involve patients with resistant sJIA defined as diagnosis of sJIA according to the ILAR classification criteria and at least one of the following:

- No response to IL-1 or IL-6 inhibitors (defined as glucocorticoids dependency > 0.2 mg/Kg at 6 months from onset)
- Interstitial lung disease (pulmonary hypertension or alveolar proteinosis)
- Recurrent macrophage activation syndrome (>1 episode)
- Resistant arthritis (persistent > 2 yrs duration, destructive with evidence of structural damage).

Specific Operational Procedures (SOPs) will be used for collecting, handling and storing samples from peripheral blood.

Samples will be collected at recruitment and at time of flare and/or change in therapies.
All patients with sJIA enrolled in the sJIA/MAS Italian Pediatric Rheumatology Study Groups (STEERING), and in the Netherlands nationwide study (ESTIS) will be used as controls. This initiative is also linked to the FROST sJIA prospective cohort study of the CARRA.

Sample analysis will be performed as follow:

- **Genetic analysis** based on whole genome sequencing and mosaicism
- **Inflammatory proteins** (immune mediators, including cytokines, chemokines and serum proteins) will be quantified by Luminex tech

- **Phenotypic and functional assays** by FACS, RNAseq in sorted cell populations and stimulation assays to identify differences in immune mediated pathways

UCAN will provide starting funds to set up the biobank and contribute in shipment costs and other funding will be requested from PReS/EULAR/CARRA.

PI: Fabrizio de Benedetti, Sebastiaan Vastert

2. Francesca Minoia: "A diagnostic score for early detection of macrophage activation syndrome in systemic juvenile idiopathic arthritis based on an improper linear model method

Aim: To develop and validate a diagnostic score for timely detection of MAS in patients with sJIA
Patients and Methods: 362 patients with sJIA-associated MAS and 404 patients with active sJIA without evidence of MAS, collected in the multinational collaborative project that led to the development of the 2016 classification criteria.
80% of the population was used to develop the score and 20% as a validation sample.

Results: The MS score

Variables	OR	β	Points in MS score
CNS involvement	17.3	2.9	3
Hemorrhagic manifestations	10.2	2.3	3
Platelet count ≤ 340 x 10^9/l	4.7	1.6	2
Triglycerides ≥ 145 mg/dl	4.5	1.5	2
Ferritin ≥ 1550 ng/ml	4.1	1.4	2
Lactic dehydrogenase ≥ 640 U/l	3.3	1.2	2
Albumin ≤ 3.3 g/dl	2.2	0.8	1
White blood cell count ≤ 14 x 10^9/l	2.2	0.8	1
Aspartate transaminase ≥ 48 U/l	1.9	0.7	1
Hepatomegaly	1.9	0.6	1
Absence of skin rash	0.4	- 1.0	1
Absence of arthritis	0.2	- 1.4	2

The final score was made up with the sum of each single score and range from 0 to 21

MS score > 7 revealed the best performance in discriminating MAS from active sJIA.

Conclusion: The MS score is a powerful and feasible tool for the early detection of MAS in patients with active sJIA. Notably, the use of an improper linear model method may allow the application of the score also in different settings. The MS score deserve validation in a prospective cohort of patients with sJIA-associated MAS.

3. Masterpiece initiative

- the first multi-disciplinary collaborative project to improve MAS/sHLS diagnostics in adults.

We had disscusion about participation of the MAS Working Party in the Masterpiece initiative.

Sincerely yours

A. V. Ramanan, Chair

Marija Jelusic, Secretary