

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.4075

OP0034

A NOVEL SERUM CALPROTECTIN (MRP8/14) PARTICLE ENHANCED IMMUNO-TURBIDIMETRIC ASSAY (SCAL TURBO) HELPS TO DIFFERENTIATE SJIA FROM OTHER DISEASES IN ROUTINE CLINICAL LABORATORY SETTINGS

Keywords: Innate immunity, Diagnostic Tests, Biomarkers

D. Foell¹, M. Saers¹, C. Park¹, N. Brix², M. Glerup³, C. Kessel¹, H. Wittkowski¹, C. Hinze¹, L. Bernntson⁴, A. Fasth⁵, S. Nielsen⁶, E. Nordal^{7,8}, M. Rygg^{9,10}, H. Hasle³, T. Herlin³, D. Holzinger^{11,12}, C. Niederberger¹³, B. Schlüter¹⁴.

¹University Hospital Children's Muenster, Department of Pediatric Rheumatology and Immunology, Muenster, Germany; ²Aalborg University Hospital, Department of Paediatric and Adolescent Medicine, Aalborg, Denmark; ³Aarhus University Hospital, Department of Pediatrics and Adolescent Medicine, Aarhus, Denmark; ⁴Uppsala University, Department of Women's and Children's Health, Uppsala, Sweden; ⁵University of Gothenburg, Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg, Sweden; ⁶Copenhagen University Hospital, Department of Pediatrics, Copenhagen, Denmark; ⁷University Hospital of North Norway, Department of Pediatrics, Tromsø, Norway; ⁸Arctic University of Norway, Department of Clinical Medicine, Tromsø, Norway; ⁹St. Olavs Hospital, Department of Pediatrics, Trondheim, Norway; ¹⁰Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway; ¹¹University of Duisburg-Essen, Department of Pediatric Hematology- Oncology, Essen, Germany; ¹²University of Applied Sciences Bochum, Department of Applied Health Sciences, Bochum, Germany; ¹³BÜHLMANN Laboratories, BÜHLMANN AG, Schönenbuch, Switzerland; ¹⁴University Hospital Muenster, Central Laboratory, Muenster, Germany

Background: Differential diagnosis in children with signs of unprovoked inflammation can be challenging. In particular, differentiating systemic-onset juvenile idiopathic arthritis (SJIA) from other diagnoses is difficult in individuals presenting with fever of unknown origin. We have recently validated myeloid-related protein 8/14 (MRP8/14, S100A8/A9, calprotectin) serum analyses as a helpful tool supporting the diagnosis of SJIA. The results could be confirmed with a commercial ELISA. However, further optimization of the analytical technology will be important to enable large-scale use in routine laboratory settings.

Objectives: To evaluate the accuracy in identifying children with SJIA, the performance of an immunoturbidimetric assay for measurements of serum-calprotectin (BÜHLMANN sCAL turbo) on an automated laboratory instrument was tested in serum samples of children with various conditions.

Methods: Samples from 650 children were available with diagnoses SJIA (n=99), non-systemic JIA (n=169), infections (n=51), other inflammatory diseases (n=161), and acute lymphatic leukemia (ALL, n=147). In addition, samples from 23 healthy controls were included. The patients with systemic inflammatory diseases were collected at Muenster University as reported before.[1] Patients with non-systemic JIA were from the Nordic JIA cohort as previously described in detail.[2] The ALL cohort included consecutive cases from Aalborg and Aarhus University Hospitals.[3] The BÜHLMANN sCAL turbo test is a particle enhanced immuno-turbidimetric assay (PETIA) and was compared to the established MRP8/14 ELISA from BÜHLMANN (EK-MRP8/14). The sCAL PETIA has a range of 230-15,000ng/mL (extended range up to 225,000ng/ml by dilution of 1:15) in sample volumes of only 2-3 µl and was implemented into the automated laboratory setting at the central clinical laboratory of the University Hospital Muenster as a rapid test available on demand.

Results: The sCAL turbo assay showed an excellent correlation to the MRP8/14 ELISA used in the previous validation studies ($r=0.99$, $p<0.001$). It could reliably differentiate SJIA from all other diagnoses with significant accuracy (cut-off at 9,100ng/ml, sensitivity 93%, specificity 87%, ROC area under curve 0.961, $p<0.001$). Results are shown in Table 1 and Figure 1.

Table 1. Accuracy (ROC analyses) of sCAL turbo measurements in differentiating groups of patients

	SJIA vs all groups	SJIA vs infections	SJIA vs ALL	SJIA vs others
AUC (95%CI)	0.961 (0.943-0.978)	0.908 (0.862-0.953)	0.992 (0.985-0.999)	0.958 (0.934-0.981)
Cut-Off (ng/ml)	9,100	10,500	9,100	9,100
Sensitivity (%)	93	82	99	93
Specificity (%)	87	84	87	86

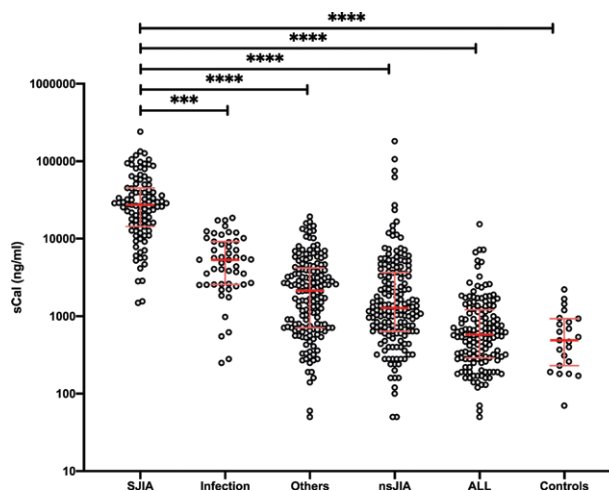


Figure 1. Results of sCAL turbo measurements in different groups of patients (red line showing median, error bars showing interquartile range; * $p<0.001$, **** $p<0.0001$)**

Conclusion: MRP8/14 (S100A8/A9, calprotectin) serum analyses have been validated as a helpful tool supporting the diagnosis of SJIA in children with prolonged fever or inflammatory disease. Here we show that an immunoturbidimetric assay for detection of serum-calprotectin on an automated laboratory instrument can be implemented in clinical laboratory settings to facilitate its use as a diagnostic routine test in clinical practice.

REFERENCES:

- [1] Park C, Miranda-Garcia M, Berendes R, et al. MRP8/14 serum levels as diagnostic markers for systemic juvenile idiopathic arthritis in children with prolonged fever. *Rheumatol*. 2022;61(7):3082-3092.
- [2] Glerup M, Rypdal V, Herlin T et al. Long-Term Outcomes in Juvenile Idiopathic Arthritis: Eighteen Years of Follow-Up in the Population-Based Nordic Juvenile Idiopathic Arthritis Cohort. *Arthritis Care Res*. 2019;72(4):507-516.
- [3] Brix N, Kessel C, Foell D et al. Phagocyte-related S100 proteins and cytokines in Acute Lymphoblastic Leukemia at diagnosis and follow-up and their prognostic value may improve prediction of minimal residual disease. *Leuk Lymphoma* 2022 (in print)

Acknowledgements: The authors thank all patients, families and physicians who helped collecting samples and data. Samples from non-systemic JIA patients were provided by the Nordic Study Group of Pediatric Rheumatology (NoSPeR). ALL samples were collected by the Nordic Society of Pediatric Oncology and Hematology (NOPHO). All other samples were provided by the University Hospital Muenster from existing and reported repositories.

Disclosure of Interests: Dirk Foell Speakers bureau: Novartis, Sobi, Biontech, Werfen, Consultant of: Novartis, Sobi, Boehringer, Grant/research support from: Novartis, Sobi, Boehringer, Melanie Saers: None declared, Carolin Park: None declared, Ninna Brix: None declared, Mia Glerup: None declared, Christoph Kessel Speakers bureau: Sobi, Consultant of: Sobi, Grant/research support from: Novartis, Helmut Wittkowski: None declared, Claas Hinze: None declared, Lillemor Bernntson: None declared, Anders Fasth: None declared, Susan Nielsen: None declared, Ellen Nordal: None declared, Marite Rygg: None declared, Henrik Hasle: None declared, Troels Herlin: None declared, Dirk Holzinger: None declared, Christian Niederberger Employee of: BÜHLMANN Diagnostics AG, Bernhard Schlüter: None declared.

DOI: 10.1136/annrheumdis-2023-eular.854

OP0035

THE USE OF CHILDHOOD LLDAS: FIRST RESULTS IN A REAL-LIFE LONGITUDINAL CHILDHOOD LUPUS COHORT SHOW GOOD FEASIBILITY BUT DIFFICULT ATTAINMENT

Keywords: Treat to target, Systemic lupus erythematosus

S. Bergkamp¹, T. Kanagasabapathy¹, M. Gruppen¹, T. Kuijpers¹, A. Nassar-Sheikh Rashid¹, J. M. Van den Berg¹, D. Schonenberg-Meinema¹. ¹Amsterdam UMC, locatie AMC, Pediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam, Netherlands

Background: Almost half of childhood-onset SLE (cSLE) patients show damage within 5 years after disease onset, which is partially disease- and partially