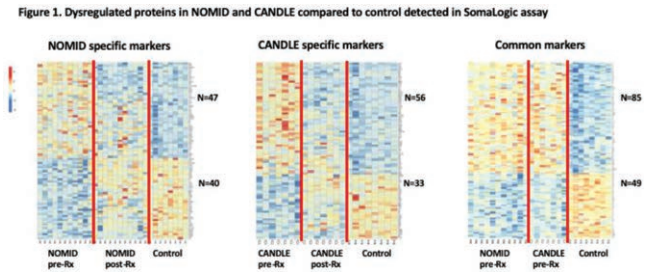

Figure 1. Dysregulated proteins in NOMID and CANDLE compared to control detected in SomaLogic assay

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OP0287 A MACHINE LEARNING APPROACH FOR PRECISION STRATIFICATION OF JUVENILE-ONSET SLE

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Background: Juvenile-onset systemic lupus erythematosus (JSLE) is a complex and heterogeneous disease characterised by diagnosis and treatment delays. An unmet need exists to better characterise the immunological profile of JSLE patients and investigate its links with the disease trajectory over time.
Objectives: A machine learning (ML) approach was applied to explore new diagnostic signatures for JSLE based on immune-phenotyping data and stratify patients by specific immune characteristics to investigate longitudinal clinical outcome.
Methods: Immune-phenotyping of 28 T-cell, B-cell and myeloid-cell subsets in 67 age and sex-matched JSLE patients and 39 healthy controls (HCs) was performed by flow cytometry. A balanced random forest (BRF) ML predictive model was developed (10,000 decision trees). 10-fold cross validation, Sparse Partial Least Squares-Discriminant Analysis (sPLS-DA) and logistic regression was used to validate the model. Longitudinal clinical data were related to the immunological features identified by ML analysis.
Results: The BRF-model discriminated JSLE patients from healthy controls with 91% prediction accuracy suggesting that JSLE patients could be distinguished from HCs with high confidence using immunological parameters. The top-ranked immunological features from the BRF-model were confirmed using sPLS-DA and logistic regression and included CD19+ unswitched memory B-cells, naïve B-cells, $CD14^+$ monocytes and total $CD4^+$, $CD8^+$ and memory T-cell subsets.
K-mean clustering was applied to stratify patients using the validated signature. Four groups were identified, each with a distinct immune and clinical profile. Notably, $CD8^+$ T-cell subsets were important in driving patient stratification while B-cell markers were similarly expressed across the JSLE cohort. JSLE patients with elevated effector memory $CD8^+$ T-cell frequencies had more persistently active disease over time, and this was associated with increased treatment burden and prevalence of lupus nephritis. Finally, network analysis identified specific clinical features associated with each of the top JSLE immune-signature variables.
Conclusion: Using a combined ML approach, a distinct immune signature was identified that discriminated between JSLE patients and HCs and further stratified patients. This signature could have diagnostic and therapeutic implications. Further immunological association studies are warranted to develop data-driven personalised medicine approaches for JSLE.
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OP0288 ANTI-IL1 TREATMENT IN COLCHICINE RESISTANT PEDIATRIC FMF PATIENTS-REAL LIFE DATA FROM THE HELIOS REGISTRY

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Background: FMF is a prototype of autoinflammatory diseases associated with excess IL1 production. Anti-IL1 treatments are the first-line alternatives in colchicine resistant/intolerant FMF patients.
Objectives: We aimed to investigate the efficacy and safety of anti-IL1 treatment in pediatric FMF patients in our local (HELIOS) registry.
Methods: HELIOS (Hacettepe univErsity eLectronIc research fOrmS) is a web-based biological drug registry for pediatric rheumatology patients (helios.hacettepe.edu.tr). Data were recorded at biological treatment onset (month 0), at month 6 and yearly thereafter in patients. We have analysed the clinical features, disease activity parameters, treatment responses and safety outcomes in FMF patients treated with anti-IL1 agent.
Results: Forty pediatric FMF patients were included to the study group (67% female).
Thirty-four patients received continous anti-IL1 treatment. The mean age at the start of the colchicine was 5.55±3.87 years. Age at onset of the anti-IL1 treatment was 11.47±5.41 with a mean follow-up duration of 3.87±1.96 years. Apart from two patients, all of them had biallelic exon-10 mutations.
We have also given anti-IL1 treatment on an on-demand basis in six adolescent patients. Five of them were having very severe attacks during menstrual periods and one was having attacks during extreme stress periods along with very high CRP levels. The quality of life has markedly improved and these patients no longer reveal any CRP elevation.
Anakinra was used as the first-line anti-IL1 treatment. During the last visit, six patients were treated with anakinra and 28 patients were treated with canakinumab. Anti-IL1 treatment decreased the CRP levels, number and severity of the attacks. (Figure 1.) There were three hospitalizations reported due to mild infections. Eleven patients had local skin reactions, two patients had leukopenia with anakinra and one patient had thrombocytopenia with canakinumab. We have discontinued anti-IL1 treatment until the cytopenia subsided. We have switched to on-demand therapy in one patient, started the same treatment and gradually increased the dose in the other two patients. There were no malignancy or other severe adverse reactions.

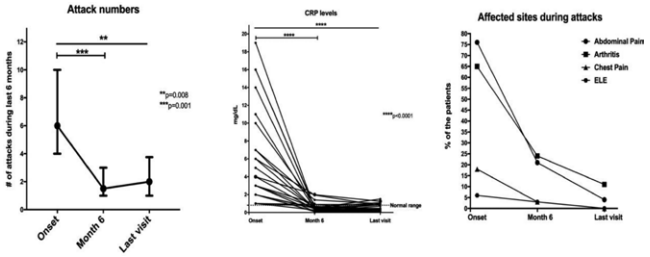

Figure 1.

Conclusion: Anakinra and canakinumab are efficient and safe alternatives in colchicine resistant and intolerant pediatric FMF patients. We also for the first time, report on-demand use of anti-IL1 in pediatric FMF patients. We suggest that on-demand treatment should be considered under certain circumstances where the trigger is known and short-lasting (such as menstruation and periods of extreme stress)
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Disclosure of Interests: Erdal Sag Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Fuat Akal Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Erdal Atalay Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Ummusen Kaya Akca Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Selcan Demir Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Dilara Demirel Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during the establishment of infrastructure, Ezgi Deniz Batu Grant/research support from: Novartis and SOBI financially supported the HELIOS registry during