Methods: Five biologic registries are currently being mapped to the OMOP CDM: 1) the Czech biologics register (ATTRA), 2) Registro Español de Acontecimientos Adversos de Terapias Biológicas en Enfermedades Reumáticas (BIOBADASER), 3) British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA), 4) German biologics register 'Rheumatoid arthritis observation of biologic therapy' (RABBIT), and 5) Swiss register 'Swiss Clinical Quality Management in Rheumatic Diseases' (SCQM). Data collected at baseline are being mapped first. Details that uniquely identify individuals are mapped to the person table, with the observation_period table defining the time a person may have had clinical events recorded. Baseline comorbidities are mapped to the condition_occurrence CDM table, while baseline medications are mapped to the drug_exposure CDM table. This mapping is summarised in Figure 1.

Figure 1. Overview of initial mapping

Results: A total of 64,901 individuals are included in the 5 registries being mapped to the OMOP CDM, see table 1. The number of unique baseline conditions being mapped range from 17 in BSRBR-RA to 108 in RABBIT, while the number of baseline medications range from 26 in ATTRA to 802 in BSRBR-RA. Those registries which captured more comorbidities or medications generally allowed for these to be inputted as free text.

Table 1. Summary of initial code mapping

Registry	Number of individuals	Number of mapped baseline conditions	Number of mapped baseline medications
ATTRA	5,326	26	26
BIOBADASER	6,496	30	51
BSRBR-RA	21,695	17	802
RABBIT	13,062	108	78
SCQM	18,322	26	33

Conclusion: Due to differences in study design and data capture, the baseline information captured on comorbidities and drugs across registries varies greatly. However, these data have been mapped and mapping biologic registry data to the OMOP CDM is feasible. The adoption of the OMOP CDM will facilitate collaboration across registries and allow for multi-database studies which include data from both biologic registries and other sources of health data which have been mapped to the CDM.

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Novel diagnostic and therapeutic approaches in paediatric rheumatic diseases

OP0286 **PROTEOMICS AND RNA SEQUENCING APPROACHES HIGHLIGHT THE ROLE OF ENDOTHELIAL CELL DYSREGULATION IN IL-1 AND IFN MEDIATED AUTOINFLAMMATORY DISEASES, NOMID AND CANDLE**

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Background: Systemic Autoinflammatory diseases present with sterile inflammation. NOMID (Neonatal-Onset Multisystem Inflammatory Disease) is caused by gain-of-function mutations in *NLRP3* and excess IL-1 production, presents with fever, neutrophilic dermatosis, aseptic meningitis, hearing loss and eye inflammation; CANDLE (Chronic Atypical Neutrophilic Dermatitis, Lipodystrophy and Elevated Temperature) is caused by loss-of-function mutations in proteasome genes that lead to type-1 interferon signaling, characterized by fever, panniculitis, lipodystrophy, cytopenia, systemic and pulmonary hypertension and basal ganglia calcification. IL-1 blockers are approved for NOMID and JAK-inhibitors show efficacy in CANDLE treatment.

Objectives: We used proteomic analysis to compare differentially expressed proteins in active NOMID and CANDLE compared to healthy controls before and after treatment, and whole blood bulk RNA seq to identify the immune cell signatures.

Methods: Serum samples from active NOMID (n=12) and CANDLE (n=7) before and after treatment (table 1) and age matched healthy controls (HC) (n=7) were profiled using the SomaLogic platform (n=1125 proteins). Differentially expressed proteins in NOMID and CANDLE were ranked after non-parametric tests for unpaired (NOMID $p < 0.05$, CANDLE, $p < 0.1$) and paired ($p < 0.05$) analysis and assessed by enriched Gene Ontology pathways and network visualization. Whole blood RNA seq was performed (NOMID=7, CANDLE=7, Controls=5) and RPKM values were used to assess immune cells signatures.

Results: Compared to control, 205 proteins (127 upregulated, 78 downregulated) were significantly different at baseline in NOMID, compared to 163 proteins (101 upregulated, and 62 downregulated) in CANDLE. 134 dysregulated proteins (85 upregulated, 49 downregulated) overlapped in NOMID and CANDLE (Figure 1). Pathway analysis identified neutrophil and monocyte chemotaxis signature in both NOMID and CANDLE. NOMID patients had neutrophilia and active neutrophils. CANDLE patients exhibited active neutrophils in whole blood RNA. Endothelial cell activation was the most prominent non-hematopoietic signature and suggest distinct endothelial cell dysregulation in NOMID and CANDLE. In NOMID, the signature included neutrophil transmigration (SELE) endothelial cell motility in response to angiogenesis (HGF, VEGF), while in CANDLE the endothelial signatures included extracellular matrix protein deposition (COL8A) suggesting increased vascular stiffness. CANDLE patients had higher expression of Renin, 4 out of 7 had hypertension, NOMID patients did not have hypertension. Treatment with anakinra and baricitinib normalized 143 and 142 of dysregulated proteins in NOMID and CANDLE respectively.

Conclusion: Differentially expressed proteins in NOMID and CANDLE are consistent with innate immune cell activation. Distinct endothelial cell signatures in NOMID and CANDLE may provide mechanistic insight into differences in vascular phenotypes. Treatment with anakinra and Baricitinib in NOMID and CANDLE leaves 30% and 13% of the dysregulated proteins unchanged.

Table 1. Patient's characteristics

	NOMID N=12, Male =6	CANDLE N=7, Male =6		
Age	12 (2, 28)	16 (3, 20)		
Median (range)				
Ethnicity	80 (20)	100 (30)		
%White (Hispanic)				
Genetics	<i>NLRP3</i> mutation (2 Somatic, 10 Germline)	mutations in proteasome compo- nent genes (1 digenic, 6 Homozygous/com- pound Heterozygous)		
	Before treatment	After treatment	Before treatment	After treatment
CRP	52 (16-110)	5 (0-23)	5 (0-101)	1 (0-4)
Median (range) mg/L				
IFN score	0	NA	328 (211-1135)	3 (0-548)
median (range)				

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 continuous 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 cytopoenia 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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