oligonucleotide-tagged antibodies (CITE-Seq) performed, allowing us to generate a proteogenomic dataset of 35,609 NK cells. Antibody-derived-tags were used to delineate whether cells were isolated from PB or SF, and a community detection algorithm was used to cluster neighbours of cells for differential gene expression.

Results: We identified 468 differentially expressed genes (>0.2 log2 fold change) between peripheral and synovial NK cells, among which were CD56bright- and CD56dim-specific genes, and a synovia-specific signature. Antibody-tag measurements confirmed the majority of synovial NK cells to be phenotypically CD56bright, with a spectrum of modified gene expression patterns compared of those in the periphery. 6 distinct synovial clusters were identified by community detection, among which were a large number of proliferating cells, a transitionary CD56bright population, and 2 uniquely activated signatures.

Conclusion: Synovial NK cells possess a significantly different transcriptomic identity compared with those in the periphery. However, though they share a gene signature that is most comparable to blood CD56bright NK cells, it is not identical. Uniquely activated subpopulations also provide the first evidence of NK cell activation during oligo-JIA pathogenesis, suggesting that these cells could hold therapeutic potential.

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POS0168 NON-INVASIVE IMAGING IN JUVENILE LOCALISED SCLERODERMA: HIGH-FREQUENCY ULTRASOUND, THERMOGRAPHY, LASER DOPPLER & MULTISPECTRAL IMAGING

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Background: Outcome measures which can differentiate activity (inflammation) from damage (fibrosis/atrophy) would facilitate development of new treatment strategies in juvenile localized scleroderma (JLS) to target the inflammatory phase of the disease.

Objectives: To evaluate whether in JLS, non-invasive imaging modalities (high frequency ultrasounds (HFUS), multispectral imaging (MSI), laser doppler imaging (LDI) & infra-red thermography (IRT)) can detect differences between affected & non-affected skin, as a next step in developing these as outcome measures. Our hypothesis was that blood flow (and therefore temperature & oxygenation) would be increased in lesional skin.

Methods: Participants aged 4-17 were recruited from 3 paediatric rheumatology centres in the UK. For each participant, a single lesion was selected. HFUS (30MHz), MSI (bespoke camera and tuneable liquid crystal filter, coupled to custom analysis software, 500nm/710nm wavelengths), LDI and IRT imaging were performed at four sites relating to each lesion: two of affected skin (centre & inner edge of lesion) and two of non-affected skin (one cm from edge of lesion ('outer') & contralateral unaffected side). Imaging was performed at 4 visits at 3 monthly intervals. Mean values were compared between the four sites using data from all visits by mixed-effects linear regression to account for individual-level clustering.

Results: 24 participants completed all 4 visits and 1 attended 3. 20 participants were female (80%) & 5 male (20%). Mean age at diagnosis was 7.6 years & disease duration 4.9 years. Subtype of disease was linear head in 5/25 (20%), linear limb 12/25 (48%), generalised morphea 1/25 (4%), mixed 5/25 (20%) and superficial plaque in 2/25 (8%).

Table 1 shows a subset of data. All 4 imaging techniques could detect differences between healthy (outer/contralateral) & affected skin (centre/inner edge). For HFUS, there was strong evidence of a difference between affected & unaffected skin (p<0.001) indicating affected skin is thinner than unaffected. Higher mean values of oxygenation, perfusion & temperature were observed in affected compared to non-affected skin in MSI, LDI and IRT respectively. There was no statistical difference seen between inner edge and centre of the lesion in any of the methods.

Table 1. Mean differences between different locations for each imaging technique

Imaging technique	Location	Overall mean difference (95% CI)	p-value
HFUS	Centre - Contralateral	-0.34 (-0.46, -0.22)	<0.001
	Inner edge - Contralateral	-0.30 (-0.40, -0.20)	<0.001
(mm)	Centre - Outer	-0.35 (-0.46, -0.24)	<0.001
	Inner edge - Outer	-0.31 (-0.40, -0.21)	<0.001
	Centre - Inner edge	-0.04 (-0.10, 0.02)	0.168
MSI	Centre - Contralateral	0.06 (0.03, 0.10)	<0.001
	Inner edge - Contralateral	0.06 (0.03, 0.09)	<0.001
(rel units)	Centre - Outer	0.04 (0.01, 0.07)	0.012
	Inner edge - Outer	0.03 (0.00, 0.06)	0.028
	Centre - Inner edge	0.01 (0.00, 0.02)	0.251
LDI	Centre - Contralateral	44.8 (24.4, 65.2)	<0.001
	Inner edge - Contralateral	47.9 (21.0, 74.8)	<0.001
Relative perfusion units	Centre - Outer	19.1 (1.0, 37.1)	0.039
	Inner edge - Outer	24.8 (6.7, 42.9)	0.007
	Centre - Inner edge	-3.5 (-20.3, 13.2)	0.679
IRT	Centre - Contralateral	0.58 (0.24, 0.91)	0.001
	Inner edge - Contralateral	0.44 (0.13, 0.75)	0.005
°C	Centre - Outer	0.44 (0.22, 0.66)	<0.001
	Inner edge - Outer	0.30 (0.09, 0.52)	0.006
	Centre - Inner edge	0.14 (-0.05, 0.32)	0.153

The overall mean difference is the measurement of the first location minus the measurement from the second location (e.g. centre minus contralateral), averaged across the four visits.

Conclusion: Our results suggest non-invasive imaging can detect differences between healthy & unaffected skin in JLS. Whether each technique is only measuring activity & not damage requires further evaluation. The leading edge of lesions has historically been considered as most active compared to the centre. However, no difference was seen between centre & inner edge measurements suggesting that in future studies, imaging protocols can be simplified.

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POS0169 OPEN-LABEL, LONG-TERM (10-YEAR) STUDY OF THE SAFETY OF ETANERCEPT IN CHILDREN AND YOUNG ADULTS WITH EXTENDED OLIGOARTICULAR, ENTHESITIS-RELATED, OR PSORIATIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: CLIPPER2 was an 8-year, open-label extension of the phase 3b, multicenter, 2-year CLIPPER study of the safety and efficacy of etanercept (ETN) in the treatment of patients (pts) with juvenile idiopathic arthritis (JIA) categorized as extended oligoarticular arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA).

Objectives: The objective of this analysis was to describe the safety of ETN in this population after 10 years of follow up.

Methods: Pts (n=127) with eoJIA (2-17 years), ERA, or PsA (each 12-17 years) who received ≥1 ETN dose (0.8 mg/kg once weekly [max, 50 mg]) in CLIPPER were eligible to enter CLIPPER2. The primary outcome measure was the occurrence of malignancy. Long-term safety was assessed as the total incidence of events from CLIPPER baseline (BL) to month (mth) 120, frequency of events per 100 patient-years (EP100PY), and frequency of events in each study year.

Results: A total of 109/127 (86%) pts entered CLIPPER2; 99 (78%) continued in the active treatment period. At mth 120, 84 (66%) pts had completed the study; 27 (21%) while actively taking ETN; 7 (6%) had withdrawn from treatment due to low/inactive disease; 5 (4%) had re-started ETN following an earlier withdrawal from treatment; and 45 (35%) had stopped ETN (but remained under observation); 25 (20%) pts permanently discontinued from the CLIPPER2 study. In CLIPPER/CLIPPER2, 1 case of malignancy (Hodgkin's disease) was reported (1 pt with eoJIA in Year 3). There was 1 case of uveitis (1 pt with eoJIA in Year 8) and 3 of Crohn's disease (2 pts with ERA, Year 1/Year 6; 1 pt with eoJIA, Year 5). There were 2 cases of opportunistic infections (both herpes zoster), and no deaths. Overall, there were 559 (81.82 EP100PY) treatment-emergent adverse events

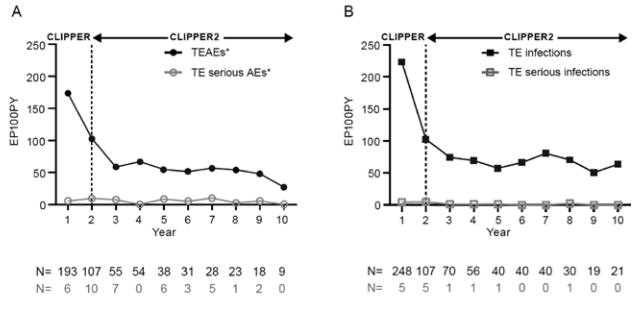
(TEAEs) excluding infections and injection-site reactions (ISRs). The overall rate of TE serious infections was low (N=14; 2.05 EP100PY) (Table 1), with the most common TE serious infection being gastroenteritis (N=2; 0.29 EP100PY). The most frequently reported TEAEs (N [EP100PY]) were headache (28 [4.10]), arthralgia (24 [3.51]), pyrexia (21 [3.07]), diarrhea (14 [2.05]), and leukopenia (12 [1.76]). Overall, 39 patients reported serious AEs (excluding infections/ISRs). The number and frequency (N [EP100PY]) of TEAEs (excluding infections/ISRs) decreased over the 10-year study period from 193 [173.81] in Year 1 to 9 [27.15] in Year 10. The number and frequency of TE infections and TE serious infections also decreased over the 10-year study period. There was no clear trend of a decrease over time for the incidence of TE serious AEs (Figure 1).

Table 1. ETN Safety Summary (from CLIPPER BL to mth 120), N (EP100PY) (FAS)*

	eoJIA, n=60 (EXP=313.667 PY)	ERA, n=38 (EXP=206.971 PY)	PsA, n=29 (EXP=162.576 PY)	Total, n=12 (EXP=683.214 PY)
TEAEs†	269 (85.76)	176 (85.04)	114 (70.12)	559 (81.82)
TE serious AEs†	16 (5.10)	17 (8.21)	7 (4.31)	40 (5.85)
TE ISRs	23 (7.33)	29 (14.01)	12 (7.38)	64 (9.37)
TE infections	418 (133.26)	99 (47.83)	155 (95.34)	672 (98.36)
TE serious infections‡	5 (1.59)	4 (1.93)	5 (3.08)	14 (2.05)
Opportunistic infections§	0	1 (0.48)	1 (0.62)	2 (0.29)
TEAEs causing withdrawal†	7 (2.23)	9 (4.35)	2 (1.23)	18 (2.63)
TE infections causing withdrawal	2 (0.64)	0	1 (0.62)	3 (0.44)

*While on active ETN treatment or within 30 days of last dose†Excluding infections/ISRs‡Gastroenteritis, 2 (0.29); acute tonsillitis, anal abscess, bronchopneumonia, gastrointestinal infection, helicobacter gastritis, influenza, peritonitis, pharyngitis, pyelocystitis, sepsis, urinary tract infection, viral infection, all 1 (0.15)§Both herpes zosterEXP, exposure to ETN; FAS, full analysis set; n, number of patients; N, number of events

Figure. Incidence of TEAEs (A) and TE Infections (B) in CLIPPER/CLIPPER2 by Study Year, N (EP100PY)



*Excluding infections/ISRs

Conclusion: ETN treatment to mth 120 was well tolerated in this patient population and consistent with the known safety profile. Frequency of TEAEs and TE infections decreased over time. Over 10 years, there was 1 reported event of malignancy and the overall rate of TE serious infections was low.

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POS0170 EXPERIENCES WITH COVID-19 INFECTIONS IN GERMAN PEDIATRIC RHEUMATOLOGY CENTERS

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Background: Although the risk for severe COVID-19 progression in children is low, this may be aggravated by the underlying disease and/or immunosuppressive drugs.

Objectives: We analyzed clinical data of COVID-19 cases among paediatric patients with rheumatic diseases reported to the BIKER registry.

Methods: The main task of the German BIKER (Biologics in Pediatric Rheumatology) registry is to monitor the safety of biologics therapies in JIA. After the onset of the COVID-19 pandemic, the survey was expanded with a standardized form to proactively interview all participating centers about the occurrence, presentation, and outcome of SARS-CoV-2- infections in children with rheumatic diseases. Interviews were conducted with 68 centers initially weekly and later biweekly.

Results: A total of 68 centres participated in the survey. Clinical data from 194 COVID-19 cases reported to the BIKER registry from 41 German and 1 Austrian pediatric rheumatology institutions between February 2020 and December 2021 were analyzed. Juvenile idiopathic arthritis (JIA, n=144) was the most common diagnosis followed by genetic autoinflammation (n=18; i.e. FMF, TRAPS, CAPS, HIDS, DADA2), systemic autoimmune diseases (n=11; i.e. SLE, dermatomyositis, vasculitis) and 16 with other rheumatic diseases (i.e. CRMO, Uveitis). 5 patients with no rheumatic disease were excluded. 104 (54%) patients were receiving conventional DMARDs, 81 (43%) received biologics, mainly TNF inhibitors (n=66 (35%)). Of the 189 rheumatic patients with SARS-CoV2 infection, 123 (63%) were female. The mean age was 12.4+/-4.4 years in females and 13.2+/-4.1 in males. The duration of SARS-Co2 infection associated symptoms was 13.8+/-15.3 days (max. 113 days), in 35 (43%) patients they lasted for > 12 days. 46 (24%) were asymptomatic. Patients with autoinflammation and systemic autoimmunopathies reported more symptoms such as fever, head and throat ache. 4 patients only complained about dyspnea. Only 3 patients were hospitalized and received Oxygen-supplementation. The only patients admitted to ICU, received ventilation but succumbed. This 3½-year-old patient, initially diagnosed with systemic JIA, developed fatal disease with intracranial edema and respiratory failure, as well as typical pulmonary texture changes. Prior to her SARS-CoV-2 infection, the patient was treated with MTX and low-dose steroids. Genetic testing revealed a so far unrecognized congenital immunodeficiency. In the total JIA cohort, treatment with corticosteroids, conventional DMARDs, biologics or combinations did not influence the number of reported symptoms or the favorable outcome of the cohort. However, the duration of symptoms was lower in the TNF-treated cohort (10.4+/-6.4 days vs. 15.7 +/- 19.7 days). In the cohort with autoinflammation, fever was observed in 11 (61%). Those 6 who received IL-1-inhibitors did not show a different outcome than those 12 who did not. No case of PIMS/MISC in children with rheumatic diseases was reported.

Conclusion: Except for one patient with congenital immunodeficiency who died from her COVID-19 infection, no case of severe COVID-19 was reported in our cohort. At the time of infection, over 80% of patients in our cohort had been treated with conventional DMARDs and/or biologics. This did not appear to have a negative impact on the severity or outcome of SARS-CoV2 infection. Interestingly, no case of PIMS/MISC was observed.

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