resolved or improved over time and this was associated with improvements in SF-36 summary scores for peripheral neuropathy and mononeuropathy.

Conclusion: PNS disease is an important component of total NPSLE and has a significant negative impact on health related quality of life. The outcome is favourable for most patients, but several factors associated with longer time to resolution were identified.

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OP0253

WORLDWIDE TRENDS IN MORTALITY OF SYSTEMIC LUPUS ERYTHEMATOSUS BETWEEN 2000 AND 2015: ANALYSIS OF THE WORLD HEALTH ORGANIZATION DATABASE

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Background: Although diagnosis, treatment and prevention strategies of Systemic Lupus Erythematosus (SLE) have further improved during the last two decades, the net benefit in term of global SLE-related mortality remains unknown.

Objectives: To describe the worldwide trends in SLE mortality between 2000 and 2015 using data of 125 countries from the World Health Organization (WHO) mortality database. To modelize SLE-related deaths taking into account temporal changes, geographical localization and country wealth.

Methods: We analyzed the WHO mortality database containing cause-specific mortality of participating countries. SLE-related deaths were identified using the international classification of disease 10 (ICD-10, code M32). In all countries which provided data between 2000 and 2015, sex-specific mortality rate was calculated for each year using the WHO reference population database. To have a better understanding of mortality fluctuations, countries were grouped geographically by continents and their nominal gross domestic product (GDP) per capita

were retrieved from the United Nation database. A mixed regression model for repeated measures was used to take into account the time factor, GDP per capita and continent in SLE-related death.

Results: Between 2000 and 2015, a total of 97,008 SLE-related deaths occurred in 125 countries, which accounted for 0.021% of all deaths during the same period. World-wide, the overall mortality rate attributed to SLE remained stable ($p=0.86$) over the study years. However, we detected significant differences between continents ($p=0.0006$) with the mortality rate of Africa being significantly higher than that of Europe ($p=0.004$). There was a significant interaction between the continents and the study years ($p=0.01$) revealing a strong increase in the mortality rate attributed to SLE in Africa. We found a very strong association between SLE-attributed mortality and the GDP per capita ($p<0.0001$).

Conclusion: We observed drastic differences in the evolution of SLE-related mortality due to country geographic localization, wealth and ethnic factors. SLE-related remained stable as a whole but strongly increased in the African continent.

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Tackling the challenges of autoimmune/ autoinflammatory conditions in children and young people

OP0254

CANAKINUMAB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RECURRENT FEVER SYNDROMES: RESULTS FROM A PHASE 3 TRIAL (CLUSTER)

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Background: Recurrent fever syndromes have a significant impact on health-related quality of life (HRQoL).¹ Canakinumab (CAN) has demonstrated efficacy and safety in patients with colchicine-resistant familial Mediterranean fever (crFMF), hyper-immunoglobulin D syndrome/mevalonate kinase deficiency (HIDS/MKD) and tumour necrosis factor receptor-associated periodic syndrome (TRAPS) in the pivotal, Phase 3, CLUSTER trial (NCT02059291),² but there are limited published data on the impact of CAN on the HRQoL, work/school and social life of these patients.

Objectives: To evaluate effect of CAN on HRQoL, work/school and social life of patients in the 3 disease cohorts (crFMF, HIDS/MKD, and TRAPS) in a double blinded randomised study.

Methods: The detailed study design was reported previously.² The HRQoL of patients treated with CAN was assessed at Baseline (BL), Week 17 (Wk17) and Week 41 (Wk41) in patients who fully responded (absence of flares), either to 150 mg q4w CAN, or to 300 mg q4w CAN after up dosing. Methods used were the Child Health Questionnaire (CHQ)-PF50 physical (PhS) and psychosocial (PsS) summary scores (children >5–<18 years), Short-Form health survey (SF-12) physical component summary (PCS) and mental component summary (MCS; adults ≥18 years) scores. An increase from baseline of 2, 5, and 8 points in the CHQ-PF50 physical and psychological component summary scores corresponds to a small, moderate and large treatment effect, respectively. Functional impairment related to work/school, social life and family life/home responsibilities was assessed by Sheehan Disability Scale (SDS). A score of 5 or higher in SDS is associated with significant impairment.

Results: Patients showed a high impairment of HRQoL at baseline in all 3 cohorts (crFMF n=31, HIDS/MKD n=37 and TRAPS n=22). At Wk17, a moderate to large

treatment effect, either with 150 mg or 300 mg q4w CAN, was observed by an improvement in the CHQ-PF50 PHS and Pss (increased >5), SF-12 PCS (increased >5) and SDS scores (decreased below 2). At Wk41, the number of patients on CAN was limited (crFMF n=9, HIDS/MKD n=6 and TRAPS n=4) due to the design of the trial (randomised withdrawal part). For the patients who remained on CAN, the improvement in HRQoL, work/school and social life was sustained.

Conclusion: Treatment with CAN led to sustained improvement of HRQoL, work/school and social life in patients with crFMF, HIDS/MKD and TRAPS.

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- [2] De Benedetti, et al. *NEJM* 2018;378:1908–1990.

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OP0255

MICROBIOTA TRANSPLANT TO CONTROL INFLAMMATION IN A NLR4-RELATED DISEASE PATIENT WITH RECURRENT HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Background: The NLR4 inflammasome activation is essential in host defence, particularly against enteric pathogens. Gain-of-function mutations in *NLR4* are associated with a distinct autoinflammatory syndrome characterized by enterocolitis and recurrent HLH.

Objectives: To report safety and efficacy of faecal microbiota transplantation (FMT) in a patient carrying a *de novo* missense mutations in *NLR4*, with gut inflammation and gut colonization by multi-drug resistant (MDR) pathogens.

Methods: Subject and donors were screened for potential FMT according to Cammarota *et al.* (1) with modifications introduced by Ospedale Pediatrico Bambino Gesù Committee for paediatric FMT procedures. Culture-based and NGS-based microbiota profiling were performed to address MDR persistence and microbial associated communities coupled to inflammatory profiling. After wide donor screening, a universal adult donor was selected and infusion performed twice by colonoscopy from fresh and frozen faeces, respectively. A one year FMT follow up was ensured to address clinical outcomes.

Results: A Caucasian 16 months old boy presented, from 1 month of life, with recurrent HLH, diarrhoea and vasculitic skin lesions, secondary to a *de novo* missense mutation in *NLR4* (I343N). His disease was not controlled despite treatment with repeated high dose of intravenous methylprednisolone pulses and chronic daily glucocorticoid therapy, cyclosporine-A (5 mg/kg) and anakinra (ranging from 5 to 25 mg/kg/day). Because of recurrent HLH episodes, the patient was treated with emapalumab (anti-IFN γ antibody) for three months, with HLH control. However, the patient presented persistent diarrhoea with gut inflammation and colonization by MDR pathogens (*Enterobacter cloacae* and *Enterococcus faecalis*), leading by translocation to systemic infections and, hence, HLH reactivation. Moreover, he developed severe intestinal meteorism with subsequent paralytic-ileus that required ileostomy. Based on the hypothesis that his intestinal dysbiosis concurred in the persistent gut inflammation related to his underlying disease, he received a first FMT with initial clinical improvement. Therefore, ileal anastomosis was performed with recanalization, and a second FMT was performed a month later. The patient did not develop any complication. The stool cultures no longer showed the presence of enteropathogenic germs and since the last FMT (12 months of follow-up) he did not present any symptom of gut inflammation or HLH reactivations.

Conclusion: *NLR4*-related disease is typically characterized by enterocolitis and *NLR4*, highly expressed in intestinal macrophages, is critical for pathogen restriction by phagocytes in the gut lamina propria. The chronic gut inflammation of *NLR4*-patients is a stimulus for systemic inflammation. Moreover, pathogens

present in the gut can trigger HLH episodes. A presence of a selected microbiota from appropriate donor can decrease gut inflammation. FMT may represent a valid and safe therapeutic option in *NLR4*-patients in order to reduce chronic inflammatory stimuli.

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OP0256

IN MEDIUM TO LONG-TERM JUVENILE DERMATOMYOSITIS, PROINFLAMMATORY AND PROFIBROTIC CYTOKINES ARE DIFFERENTLY ASSOCIATED WITH PULMONARY INVOLVEMENT IN ACTIVE VS INACTIVE DISEASE

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Background: Knowledge about associations between cytokines and lung involvement in juvenile dermatomyositis (JDM) is scarce.

Objectives: To examine associations between cytokines and pulmonary involvement in JDM assessed after medium to long-term follow-up.

Methods: 58 JDM patients examined median 17y after disease onset were stratified in active and inactive disease by the updated PRINTO criteria (Ref 1). Serum levels of cytokines were analyzed by Luminex or ELISA. Pulmonary function tests (PFT) included forced vital capacity (FVC), total lung capacity (TLC) and diffusing capacity for carbon monoxide (DLCO) (hgb adjusted). PFT variables are expressed as% of predicted. High resolution computed tomography (HRCT) scans were scored for interstitial lung disease (ILD), calcinosis in chest wall and airway disease. Associations between lung involvement and cytokines are presented as Spearman's correlation coefficient (r_s).

Results: Table 1. Characteristics, PFT, HRCT findings and cytokines

	Total (n=58)	Active (n=37)	Inactive (n=21)
Age, y, median (IQ range)	21 (15-34.8)	20 (14-34)	26 (17-37)
Female, n (%)	35 (60)	25 (68)	10 (48)
Disease duration, y (IQ range)	17 (7-27)	16 (6-26)	17 (8-28)
TLC ^a	93 (11)	91 (10)	94 (11)
FVC ^a	96 (12)	94 (12)	99 (12)
DLCO ^a	82 (15)	79 (13)	87 (16)
Any HRCT findings, n (%)	21 (36)	15 (40)	6 (29)
HRCT ILD, n (%)	8 (14)	6 (16)	2 (10)
HRCT calcinosis, n (%)	8 (14)	6 (16)	2 (10)
HRCT airways disease, n (%)	9 (15)	7 (18)	2 (10)
TGFb1 ^b	29252 (8868)	29698 (9623)	28467 (7513)
PDGF ^b	9083 (2799)	8990 (2979)	9248 (2511)
IP-10 ^b	1448 (1281)	1491 (1438)	1371 (972)
MCP-1 ^b	34 (21)	34 (19)	34 (26)
Eotaxin ^b	138 (103)	142 (108)	132 (95)
IL-17 ^b	15 (14)	15 (15)	15 (10)
IL-5 ^b	1.4 (1.3)	1.6 (1.6)	1.2 (0.5)
MIP1a ^b	2.5 (1.4)	2.7 (1.5)	2.3 (1.1)

Numbers are mean (SD) if not stated otherwise; ^aPFT variables are% of predicted; ^b unit: pg/ml

No significant differences were found between active and inactive patients in tbl. 1.

Associations between cytokines and PFT/HRCT findings

Numbers are r_s , all p 's < 0.05

In patients total, TGFb1 and PDGF correlated with TLC and FVC (- 0.38 - -0.30). For TGFb1 correlations with TLC and FVC were - 0.62 and -0.59 in the inactive group, whereas PDGF correlated with FVC in the active group (- 0.48). IP-10 correlated with TLC in active patients only (- 0.35).