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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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).