OP0144

INTRAVENOUS VERSUS ORAL CYCLOPHOSPHAMIDE (CYC) FOR THE TREATMENT OF INTERSTITIAL LUNG INVOLVEMENT (ILD) AND SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS (SSC): SAFETY AND EFFICACY EVALUATION IN A LARGE MULTI-CENTRE SCLERODERMA COHORT

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Background: In the last decade, oral CYC has shown modest but significant effect on SSc-ILD and skin thickness in two large randomised controlled trials, with superiority to placebo and similar efficacy to mycophenolate. However, many centres give priority to monthly IV CYC for expected milder toxicity.

Objectives: To compare efficacy and safety of oral versus iv CYC for treating ILD and/or skin involvement in SSC.

Methods: SSc patients treated with oral or iv CYC for at least 6 months were followed for 1 year from the last administration. Data were obtained from the EUSTAR database and the Scleroderma Lung Studies I and II regarding safety [both serious (SAEs) and non-serious adverse events (AEs)] and efficacy (%FVC, %DLCO, mRSS) at end of treatment and after one-year follow-up were analysed [mean $\pm$ SD or median (IQR) as appropriate].

Results: 322 patients were eligible: 149 patients received oral CYC with median daily dose 106(93–134) mg, treatment duration 365(364–366) days, while 153 patients received IV CYC median monthly dose 1000(700–1200) mg, treatment duration 335(291–374) days. Ethnicity, previous DMARD exposure, previous and concomitant steroid exposure and dosage, current/previous smoking exposure, prevalence of digital ulcers and arterial hypertension were different between the two groups (see table 1 for further details).

For efficacy: despite different baseline %FVC and %DLCO, adjusted changes in pulmonary measures from end of treatment (EOT) vs baseline and follow-up visit (FU) vs EOT were, respectively: %FVC [0 (–5–5) vs 0 (–7–7) and 1 (–6–4) vs –2 (–7–4), p=NS], %DLCO [–4 (–9–3) vs –3 (–9–6), 1 (–6–5) vs –1 (–9–6), p=NS] and mRSS [–3 (–5–0) vs –1 (–5–0), –1 (–4–1) vs 0 (–3–1), p=NS]. In a multivariate analysis, no independent variable significantly influenced %FVC change at any visit. %DLCO change was influenced by baseline %DLCO and history of SSc-related cardiomyopathy at EOT assessment and by history of SSc-muscle involvement at FU visit. Baseline mRSS was the only variable having a significant impact on mRSS change.

For safety: in the oral group, there were more leukopenia (WBC $<2500 \times 10^9/\text{mm}^3$ at least once – 21.6% vs 1.2%, p<0.001), haemorrhagic cystitis [5.5% (8 instances) vs 0%, p=0.011] at EOT visit. In contrast, there were more SAEs (9% vs 19%, p=0.025), need for oxygen supplementation (5% vs 14%, p=0.016) and SSc-related cardiomyopathy onset (2% vs 9%, p=0.024) during follow-up in the IV group.

Abstract OP0144 – Table 1 Baseline significant differences between study population groups.

	Oral CYC (149 pts)	Intravenous CYC (153 pts)	P
Caucasian race, n(%)	104 (69.8)	146 (95.4)	<0.001
Afro-american race, n(%)	23 (15.4)	0 (0)	<0.001
Previous steroid exposure, n(%)	42 (28.4)	70 (46.7)	0.001
Previous DMARD exposure, n(%)	35 (23.5)	62 (41.3)	0.001
Steroid treatment at baseline, n(%)	51 (34.6)	111 (72.5)	<0.001
CYC treatment duration (days), mean	365 (365–366)	343 (194–514)	0.035
CYC daily dose (mg), mean (IQR)	106.6 (93.1–132.3)	33.3 (23.3–40)	0.001
Smoking history, n(%)	21 (14.6)	10 (6.6)	0.035
%FVC at baseline, mean (IQR)	69 (60–75)	83 (68–96)	<0.001
%DLco at baseline, mean (IQR)	51 (40–63)	56 (42–71)	0.022
History/presence of digital ulcers, n(%)	40 (26.8)	64 (42.1)	0.008
History/presence of arterial	40 (26.8)	25 (16.3)	0.035

CYC=cyclophosphamide, DMARD=disease modifying ant rheumatic drug, FVC=forced vital capacity, DLco=lung diffusion of carbon oxide.

Conclusions: In this hypothesis generating study, similar efficacy of one year of oral and iv CYC were seen. In contrast, a different safety profile for AE time courses and types of AEs were seen in the two groups. Although significantly higher dosage of steroids at all visits and prevalence of DMARDs use were

present in the IV CYC group (as a post-treatment maintenance), these did not have an impact on either safety or efficacy. Case-control or randomised studies are warranted to extend and confirm our data.

Disclosure of Interest: None declared

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OP0145

SCLERODERMA RELATED INTERSTITIAL LUNG DISEASE AND MYCOPHENOLATE : LONG TERM OUTCOMES

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Background: Interstitial lung disease [ILD] is a leading cause of mortality in scleroderma. ¹ Scleroderma lung study-II clearly illustrates the equivalent efficacy and a better side-effect profile of mycophenolate mofetil [MMF] as compared to cyclophosphamide.

Objectives: To study the long term outcomes of mycophenolate mofetil in scleroderma related interstitial lung disease (SSc-ILD) in terms of change in forced vital capacity (FVC)

To determine the effect of MMF on longitudinal high resolution computed tomography (HRCT) scores.

Methods: All patients of SSc-ILD from 2013 till date who had a baseline FVC and follow up FVC were taken for analysis. All patient received an average dose of 2 g/day of MMF for a median duration of 2 years and were tapered as per the standard protocol. FVC was measured using standard protocols. The FVC change was computed as percentage relative change from baseline FVC value. According to American Thoracic society recommendations, improvement is defined as an increase in FVC $\geq 10\%$, stabilisation by change in FVC $<10\%$ and worsening by a reduction in FVC $\geq 10\%$.

Results: We had 88 patients with a baseline and followup FVC data. Of these 66 patients had a 1 year follow up; 46 patients had a 2 year followup and 29 patients had a 3 year followup data. The absolute median (IQR) increase in the FVC value at the end of 1 year, 2 years, 3 years were 4.15 (–2.3 to 10.5), 2.85 (–3.4 to 7.2) and 3.8 (–0.6 to 10.4) respectively. At the end of 1 year, 2 years and 3 years 89.4%; 82.6% and 75.9% respectively had a stable or improved relative FVC change from baseline.

Of the 52 individuals who had a baseline as well as repeat HRCT, stable/improved scores in ground glass opacity, fibrosis and honey combing was seen in 80.8%, 86.5% and 86.5% respectively. There was no difference in the extent of FVC change between those with limited vs extensive disease.

Abstract OP0145 – Table 1

Baseline Characteristics	Value
Age, yr. mean(SD)	33.8 (± 11.3)
Female sex, n (%)	75 (85.2%)
Type of SSc	5
Limited	71
Diffuse	6
Sine scleroderma	
Disease duration, months, mean (SD)	46.6 (± 42.1)
Antibodies	70
Scl-70	1
Anti centromere	
MRSS, mean (SD) n=52	20.4 (± 13.2)
FVC% predicted, mean (SD)	61.2 (± 17.9)
HRCT pattern [n=85]	68
NSIP (cellular)	11
NSIP (fibrotic)	6
UIP	
HRCT determined disease extent [median(IQR)] ; n=52	0.33 (0–1.3)
Maximum fibrosis score (0–4)	1 (0–1.5)
Maximum ground glass opacity (0–4)	0 (0.08)
Maximum honeycombing (0–4)	
Maximum fibrosis score n=52	29 (55.8%)
1%–25%	23 (44.2%)
26%–100%	
HRCT change over 2 years	Frequency (Percentage)
Ground Glass opacity	42 (80.8%)
Stable/Improved	10 (19.2%)
Worsened	
Fibrosis	45 (86.5%)
Stable/Improved	7 (13.5%)
Worsened	
Honey combing	45 (86.5%)
Stable/Improved	7 (13.5%)
Worsened

Abstract OP0145 – Figure 1 Relative change in FVC from base line at different time points

Conclusions: A vast majority of individuals of scleroderma ILD patients on MMF in our cohort had a stable disease or improvement over short and long term followup both in terms of FVC change from baseline as well as HRCT scoring.

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OP0146 IDIOPATHIC INFLAMMATORY MYOPATHIES & INTERSTITIAL LUNG DISEASE

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Background: Idiopathic inflammatory myopathies (IIM) is associated with interstitial lung disease (ILD). IIM associated ILD ranges from subclinical disease, to rapidly progressive ILD (RPILD). Early recognition of these patients is essential for determining treatment.

Objectives: A retrospective case-control study in a tertiary referral centre to identify: a) Clinical features associated with ILD in IIM.

b) Whether antibodies e.g. anti-ENA and myositis specific antibodies (MSA), may aid recognition of ILD or RPILD.

c) Whether intensive immunosuppressants have implication on prognosis of ILD.

Methods: The clinical records of IIM patients who were followed up in rheumatology clinic or admitted into our hospital from Jan 2013 to Dec 2016 were reviewed. We analyse the clinical characteristics (*rash, arthritis, myositis, Raynaud's phenomenon, mechanic hands, and cutaneous ulcers with blood tests*), antibody profile (*anti-ENA: anti-Jo1, Ro, La, Sm, RNP, Scl 70 and MSA: anti-OJ, EJ, PL7, PL12, SRP, PM-Scl75, PM-Scl100, Ku, SAE1, NXP2, TIF1γ, MDA5, Mi2*), treatment and survival. We compare these parameters in IIM-ILD patients against those without ILD. Chi-squared and Mann-Whitney U tests were used to analyse categorical and continuous variables. Log rank test was used to compare survivals.

Results: Among the 101 IIM patients, the mean age was 62 years old with 71% female. 74 patients (73%) had dermatomyositis, 17 (17%) had polymyositis and 10 (10%) clinical amyopathic dermatomyositis. 53 patients (52%) had ILD; 48 (48%) had no ILD. In ILD group, 11/53 patients (21%) were RPILD.

All patients had anti-ENA checked. 59/101 patients (58%) had MSA profile.

Significantly more ILD patients had arthritis, mechanic hands, anti Jo1, anti Ro and anti MDA5 than those without ILD. 21/101 patients had cancers associated with IIM, but cancers were less common in ILD group. Subgroup analyses revealed arthritis, mechanic hands and anti MDA5 were again significantly more common in RPILD compared to other ILD patients (table 1). Anti MDA5 were more commonly found in deceased versus alive patients (40% vs 8.2%, $p=0.02$; OR=7.5). Deceased patients also had significantly higher median peak ferritin (2475 vs 553 pmol/L, $p=0.008$), so did the ILD group (2332 vs 484 pmol/L, $p=0.02$).

ILD patients received more intensive immunosuppressants (high dose steroid, cyclophosphamide, MMF, tacrolimus, IVIg or even rituximab) than non ILD group. The survival was not significantly different between ILD and non ILD groups. However despite intensive immunosuppressants, RPILD patients' survival was still much worse than the other ILD patients (figure 1).

Abstract OP0146 – Table 1 Features with $P<0.05$ and the odds ratios (OR)/relative risks (RR)

	ILD (%)	Non ILD (%)	P value	OR/ RR	RPILD (%)	Other ILD (%)	P value	OR/ RR
Arthritis	53	21	0.001	4.3	73	33	0.02	5.3
Mechanic hands	17	0	0.003	2.1	36	6	0.008	9.7
Carcinoma	8	35	0.001	0.2				
Anti Jo1	20	5	0.03	5				
Anti MDA5	24	0	0.02	2	50	8	0.008	11.8
Anti Ro	40	17	0.01	3.3

Abstract OP0146 – Figure 1 Kaplan Meier curves of RPILD & ILD groups

Conclusions: Certain clinical features and MSA aid recognition of IIM-ILD. Anti MDA5 is related to ILD, RPILD and mortality. Ferritin may be a disease activity and prognostic marker for IIM-ILD. With immunosuppressants, survival of IIM patients with or without ILD is similar. For RPILD patients, the survival is significantly worse despite active treatment.

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OP0147 ABERRANT ACTIVATION OF TYPE I INTERFERON SYSTEM IN ANTI-MDA5 DERMATOMYOSITIS PATIENTS

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Background: Anti-melanoma differentiation-associated gene 5 (MDA5) DM patients have an increased risk of interstitial lung disease (ILD), with a potentially fatal course.¹ Viral infection has been speculated to be the putative trigger for anti-MDA5 DM.^{2,3} The molecular pathogenesis remains largely unknown.

Objectives: In this study, we aimed to explore the role of type I interferon (IFN) system in the pathogenesis of anti-MDA5 DM.

Methods: We studied 20 anti-MDA5 DM patients and compared them with anti-aminoacyl-tRNA synthetase (ARS) DM patients (n=10) and seronegative DM patients (n=30). The levels of IL-1b, IL-4, IL-6, IL-8, IL-10, IL-12, IL-18, TNF-a, IFN-a, IFN-b, IFN-g, B cell activating factor (BAFF), Krebs von den Lungen-6 (KL-6) in blood were tested by enzyme-linked immunosorbent assay and multiplex assay. Expressions of mRNA for sensor molecules (TLR3, TLR4, TLR7, TLR9, MDA5, RIG-1) and type I IFN inducible genes (IRF7, STAT1, MxA, ISG15) in peripheral blood mononuclear cell (PBMC) were detected by real-time polymerase chain reaction analysis. Expressions of STAT1, MxA, ISG15 proteins in skin lesions from anti-MDA5 DM were analysed by immunohistochemistry technique.

Results: Anti-MDA5 DM patients had higher levels of plasma type I IFN (IFN-a, IFN-b), IL-6, IL-10 and TNF-a than seronegative-DM patients. In comparison to anti-ARS DM patients, IFN-a alone displayed heightened level in anti-MDA5 DM patients. Among these 3 subsets of patients, PBMC from anti-MDA5 DM patients