EULAR review

Annual European Congress of Rheumatology

2 - 4 JUN 2023

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Sociedad Española de Reumatología

Enfermedades Autoinmunes Sistémicas: LES, Sjögren y Esclerodermia

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OP0141

Long Term Safety and Efficacy of CAR-T Cell treatment in refractory SLE- Data from the first seven patients

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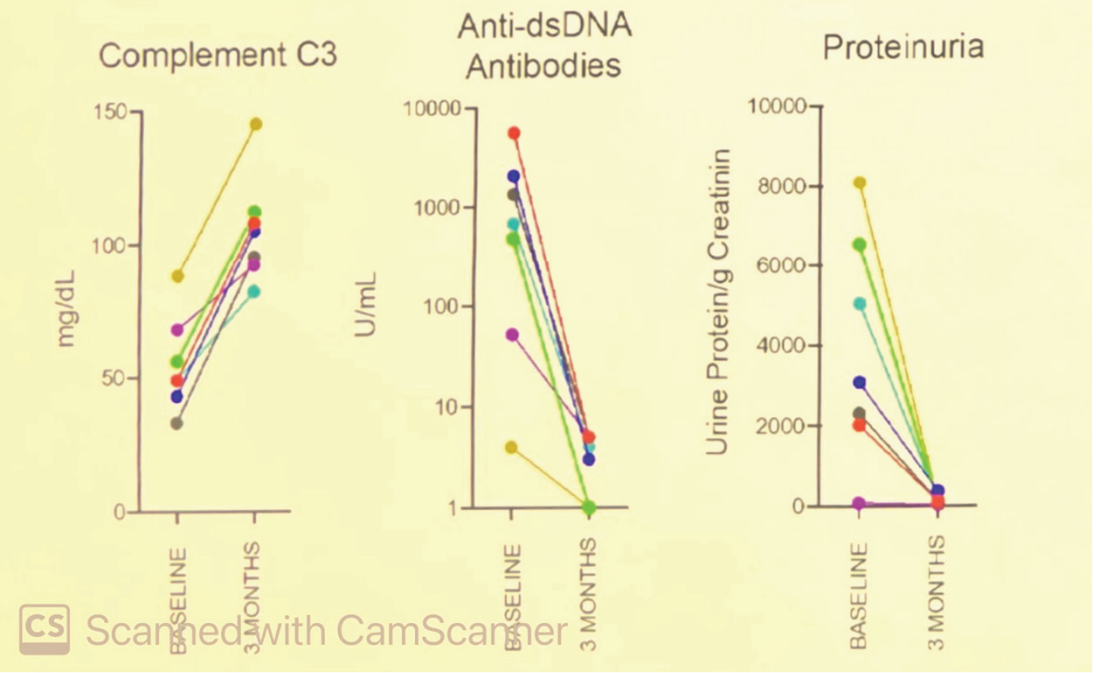
Schett G et al.

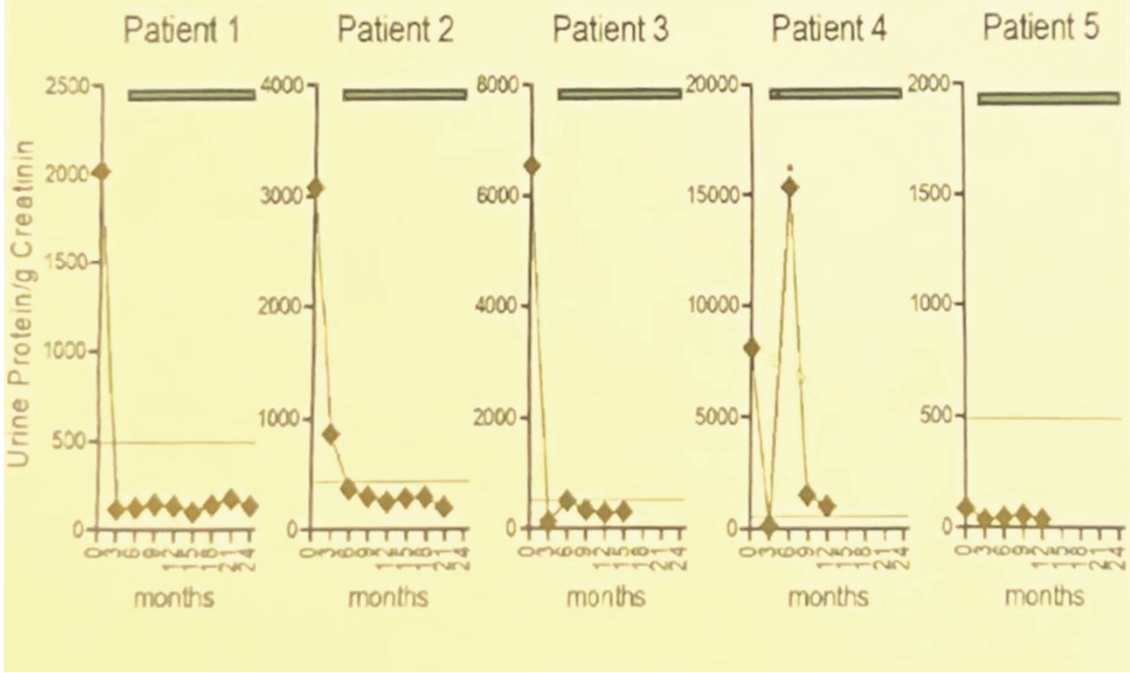
	Pat #1	Pat #2	Pat #3	Pat #4	Pat #5	Pat#6	Pat#7
Age (ys)	22	23	22	24	18	33	33
Sex (F/M)	F	M	F	F	F	F	F
Disease Duration (ys)	4	1	6	9	3	18	1
N organs involved	4	3	5	6	4	6	3
N failed treatments	7	5	4	7	5	15	7
Baseline SLEDAI (score)	16	16	10	8	9	16	10
Baseline C3 (mg/dl)	49	43	56	88	68	33	49
Baseline anti-dsDNA (IE/ml)	5600	2060	479	4	52	1335	680
Baseline Proteinuria (mg/g crea)	2015	3080	6539	8096	88	2025	5044
Conditioning Dose (%)	100	100	100	100	100	100	50
Peak CAR T (cells/µl)	167	461	33	697	146	24	117
Peak CAR T (% of T cells)	27	41	11	59	26	13	12
Duration of B cell Aplasia (days)	148	196	120	93	63	205	58
Follow-up (months)	22	16	14	13	11	8	4
Seroconversion	+	+	+	+	+	+	+
SLEDAI (last follow-up)	0	0	0	0	0	0	0
LLDAS (last follow-up)	+	+	+	+	+	+	+
DORIS Remission (last follow-up)	+	+	+	+	+	+	+
CRS (grade 0-4)	0	1	0	1	0	1	1
ICANS (grade 0-4)	0	0	0	0	0	0	0

Table 1 contains baseline demographic data from seven SLE patients treated with CD19 CAR T-cell therapy. Patient number one to seven, age in years (ys), sex in female (F) and male (M). Disease duration in years (ys). Number (N) of organs involved and number (N) of failed treatments, disease activity at baseline presented with SLE disease activity index (SLEDAI). Conditioning dose referred to 1x cyclophosphamide 1g/m2 and 3x fludarabine 25mg/m2. Maximum of CAR-T cell expansion after administration of 1 million CAR-T cells /kg body weight given as peak of CAR-T cells absolute and percent CAR+ of CD3+ T-cells. Efficacy criteria listed as seroconversion, disappearance of SLE specific antibodies (antidsDNA), Lupus Low Disease Activity State (LLDAS), definitions of remission in systemic lupus erythematosus (DORIS) remission. Adverse events listed at Cytokine-release syndrome (CRS) and Immune-related effector Cell Neurotoxicity Syndrome (ICANS) in grade 0-4.

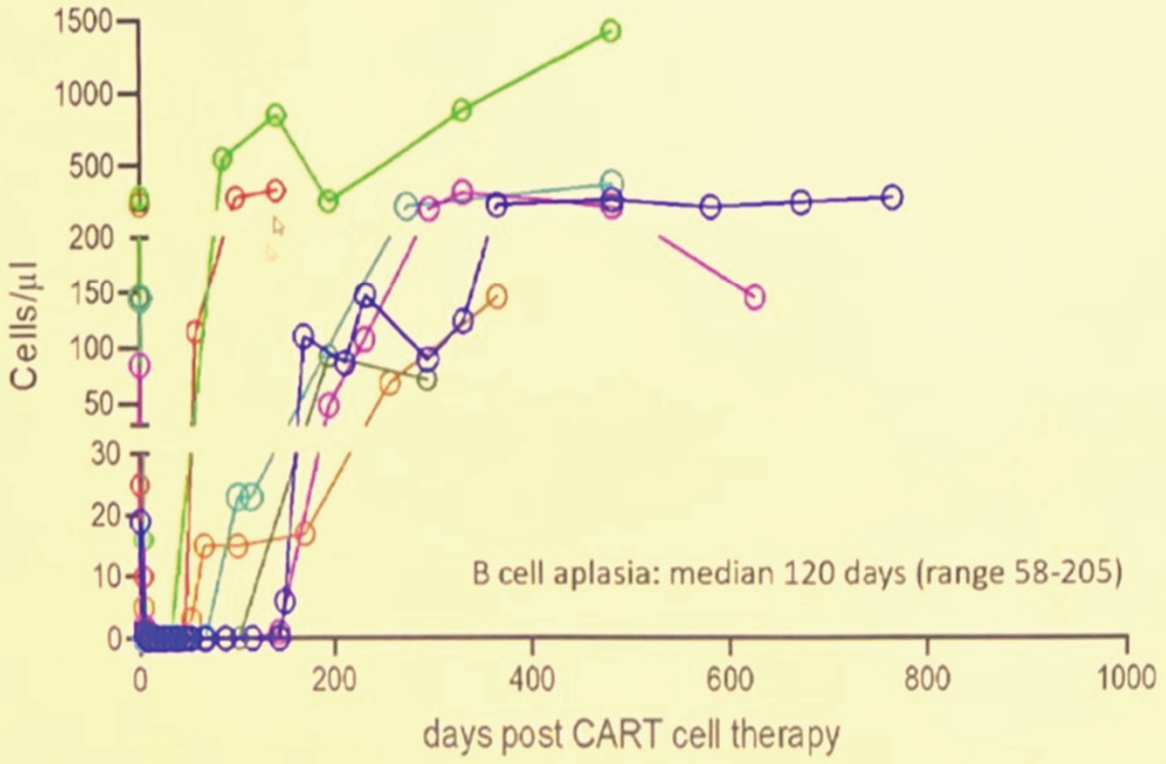
Rapid improvement of signs of SLE



Proteinuria (long-term follow-up)



Reappearance of B cells (long-term follow-up)



Infections after CD19 CAR T cell therapy in SLE

	0-3 months	4-6 months	6-12 months	>12 months
Patient 1	Urogential	0	0	Flu-Like
Patient 2	0	0	COVID19	0
	0	0	Rhinitis	0
Patient 3	COVID19	0	Tonsillitis	COVID19 (P)
				Herpes Zoster(A)
Patient 4	0	0	0	0
Patient 5	0	COVID19 (P)	0	
Patient 6	0	COVID19 (P)	COVID19 (P)	
	0	RSV	Conjunctivitis*	
Patient 7	0	0		

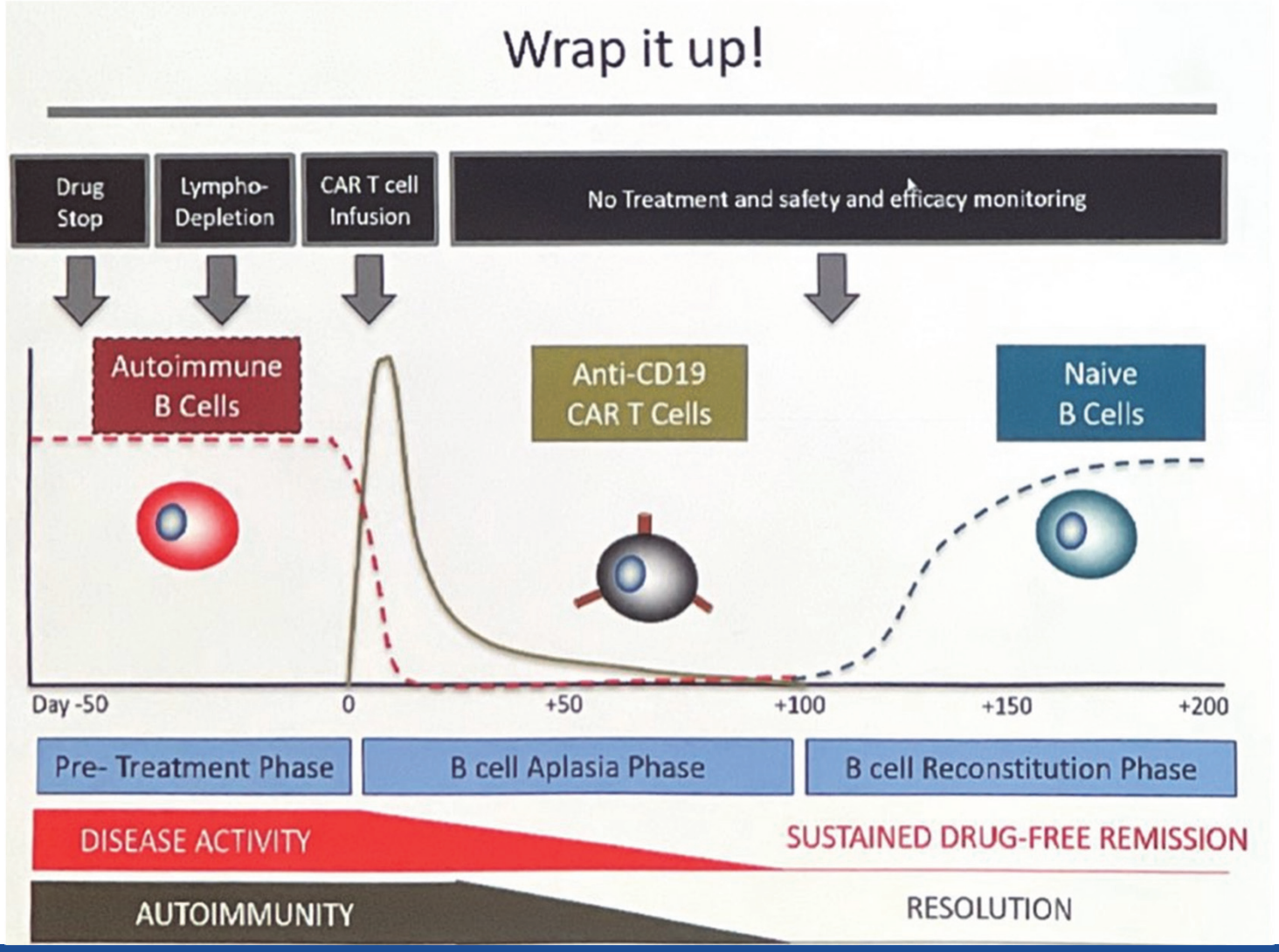
RSV, respiratory syncytial virus; (P) paxlovid treatment; (A) acylcovir treatment

mild course moderate course severe course

Safety and Efficacy of CD19 CAR T Cells in SLE

	#1	#2	#3	#4	#5	#6	#7
Follow-Up Months	24	21	15	12	12	10	5
SLEDAI	0	0	0	0	0	0	0
DORIS Remission	+	+	+	+	+	+	+
Drug-free State	+	+	+	+	+	+	+
CRS (grade 0-4)	0	1	0	1	0	1	0
ICANS (grade 0-4)	0	0	0	0	0	0	0

Wrap it up!


Drug Stop
Lympho-Depletion
CAR T cell Infusion
No Treatment and safety and efficacy monitoring
Autoimmune B Cells
Anti-CD19 CAR T Cells
Naive B Cells
Day -50
0
+50
+100
+150
+200
Pre- Treatment Phase
B cell Aplasia Phase
B cell Reconstitution Phase
DISEASE ACTIVITY
SUSTAINED DRUG-FREE REMISSION
AUTOIMMUNITY
RESOLUTION

OP0222 (2023)

TRAJECTORIES OF ANTIMALARIAL ADHERENCE AMONG NEWLY DIAGNOSED RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A POPULATION-BASED COHORT STUDY

Objectives

- To identify the groups of patients with similar patterns or trajectories of antimalarial adherence over time and evaluate the baseline determinants of the group membership of adherence trajectories.

Methods:

- All patients with incident RA/SLE and incident antimalarial use in British Columbia, Canada, between January 1997 and March 2021
- We calculated a measure of adherence, the proportion of days covered (PDC) for all patients each month. Then, we used group-based trajectory model (GBTM) analysis on monthly PDC values to identify the latent groups of antimalarial adherence trajectories

Results:

- We identified **27,510** patients with incident antimalarial use (**23,997** RA and **3,513** SLE patients, mean ± SD age 56.8 ± 15.5 years, 74.8% female

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Figure 1: Antimalarial adherence trajectory groups from group-based trajectory model analysis

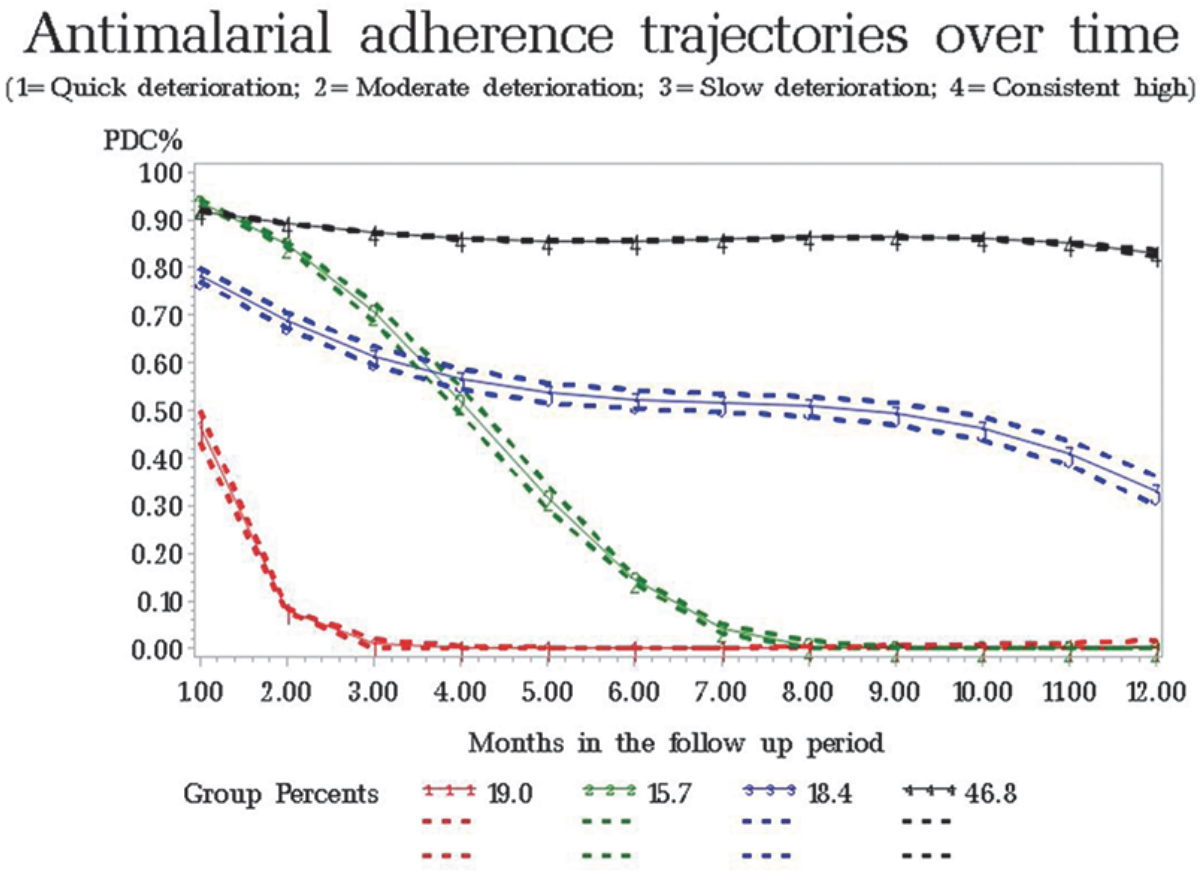

Table 1. Determinants of belonging into better adherence trajectory groups: results from an ordinal logistic regression model including only significant factors.

Factors	Adjusted OR(95% CI)
Age	1.009 (1.008-1.011)
Neighborhood income quartile(Ref: 3)	
1	0.914 (0.854-0.978)
2	0.963 (0.899-1.032)
4	1.075 (1.002-1.153)
5	1.041 (0.969-1.117)
SLE vs RA	1.551 (1.444-1.665)
Have hypertension	1.068 (1.002-1.138)
Have angina	0.878 (0.776-0.995)
Have COPD	0.861 (0.761-0.975)
Rheumatologist visits	1.035 (1.022-1.048)
Glucocorticoids use	1.082 (1.033-1.134)
Immunosuppressives use	1.177 (1.117-1.239)
Cox-2 selective NSAIDs use	1.080 (1.017-1.147)
Biologics use	0.559 (0.426-0.734)

Among incident RA/SLE incident antimalarial users from a population-based cohort, **53.2%** did not continuously adhere to the antimalarial regimen in the first year of treatment

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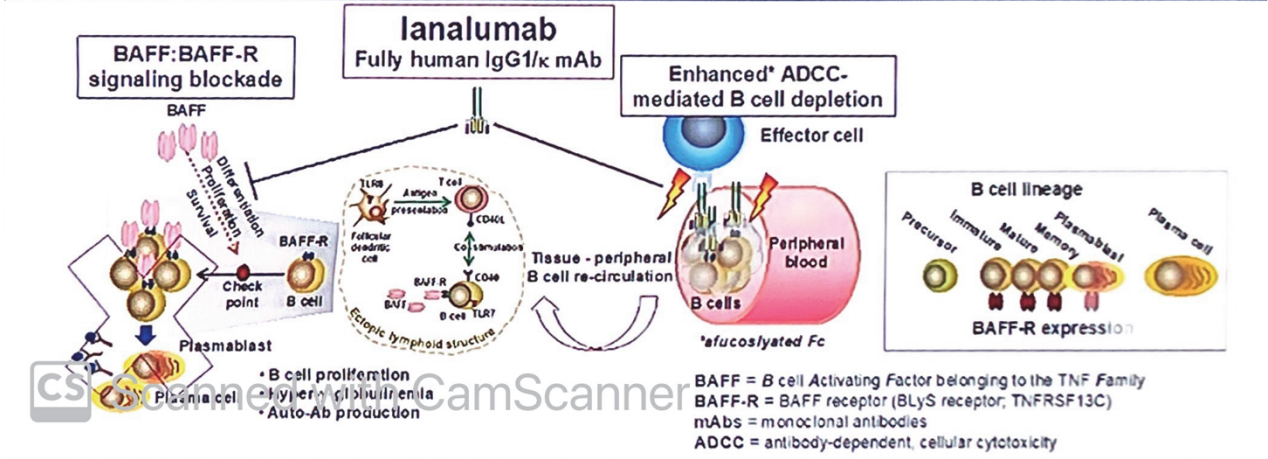
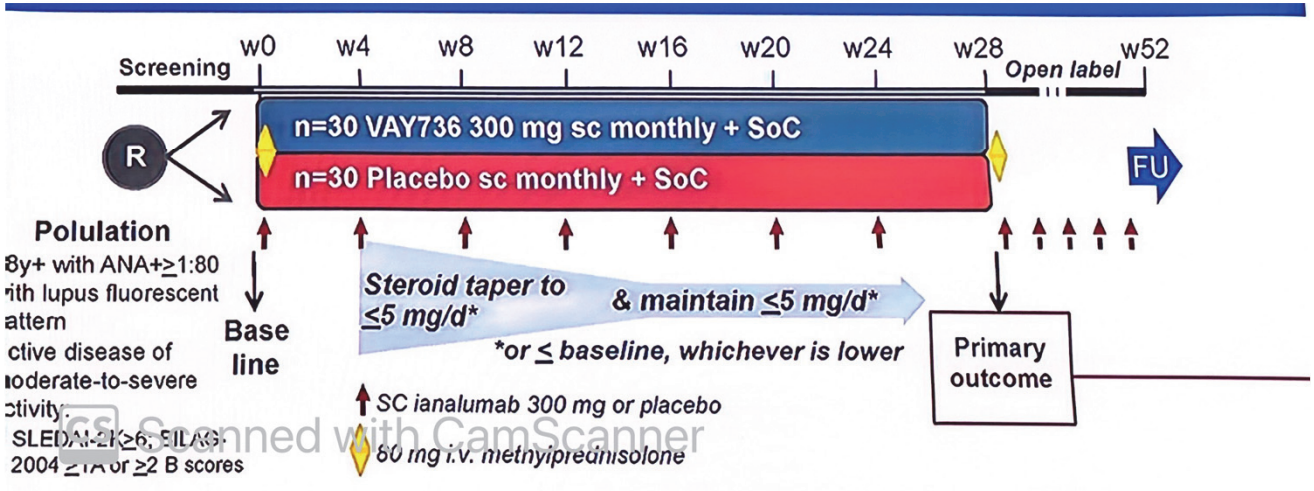
POS0120 (2023)

SAFETY AND EFFICACY OF SUBCUTANEOUS (S.C.) DOSE IANALUMAB (VAY736; ANTI-BAFFR mAb) ADMINISTERED MONTHLY OVER 28 WEEKS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

J. Cortés-Hernández[1], S. Ignatenko[2], A. Gordienko[3], N. Agmon-Levin[4], P. Narongroeknawin[5], K. Romanowska -Prochnicka[6], N. Shen[7], H. Ciferská[8], M. Kodera[9], J. C. C. Wei[10], P. Leszczynski[11], J. L. Lan[12], R. Wojciechowski[13], T. Tarr[14], E. Vishneva[15], Y. H. Chen[16], Y. Kaneko[17], S. Finzel[18], A. Hoi[19], M. Okada[20], A. Koolvisoot[21], S. S. Lee[22], L. Dai[23], H. Kaneko[24], B. Rojkovich[25], L. Sun[26], E. Zotkin[27], B. Magallares[28], T.

INTRODUCTION





Baseline patient characteristics		VAY736 *n* = 34	Placebo *n* = 33
Age (years)	Median (*range*)	42.0 (*25-70*)	39.0 (*18-57*)
Sex - *n* (%)	Female	32 (94.1)	27 (81.8)
Race *n* (%)	White	25 (73.5)	21 (63.6)
	Asian	9 (26.5)	12 (36.4)
ENA Status - *n* (%)	Positive	29 (85.3)	27 (81.8)
SLEDAI-2K score	Median (*range*)	10.0 (*6-32*)	10.0 (*4-18*)
BILAG 2004 score	Median (*range*)	20.5 (*9-37*)	17.0 (*9-34*)
Physician globall assesment score (*mm*)	Median (*range*)	59.0 (*37-81*)	58.0 (*34-85*)
Predinso(lo)ne mg/day	Median (*range*)	10.0 (*0-30*)	10.0 (*0-27.5*)

Figure: Proportion of patients with SRI-4 and achieving Week 28 composite endpoint

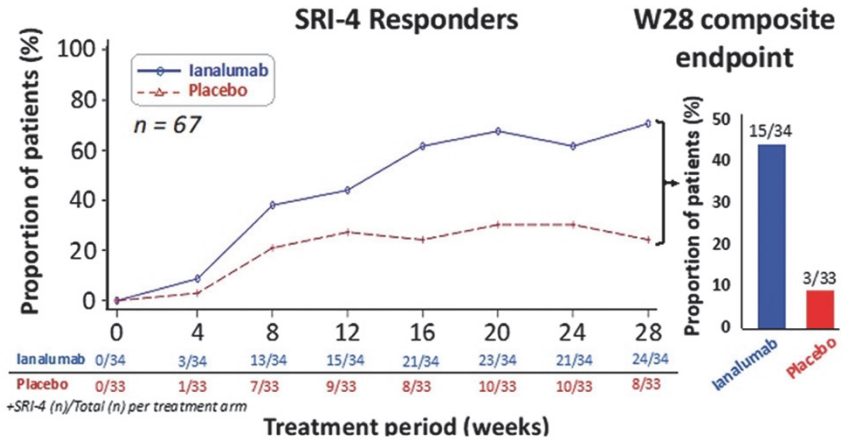
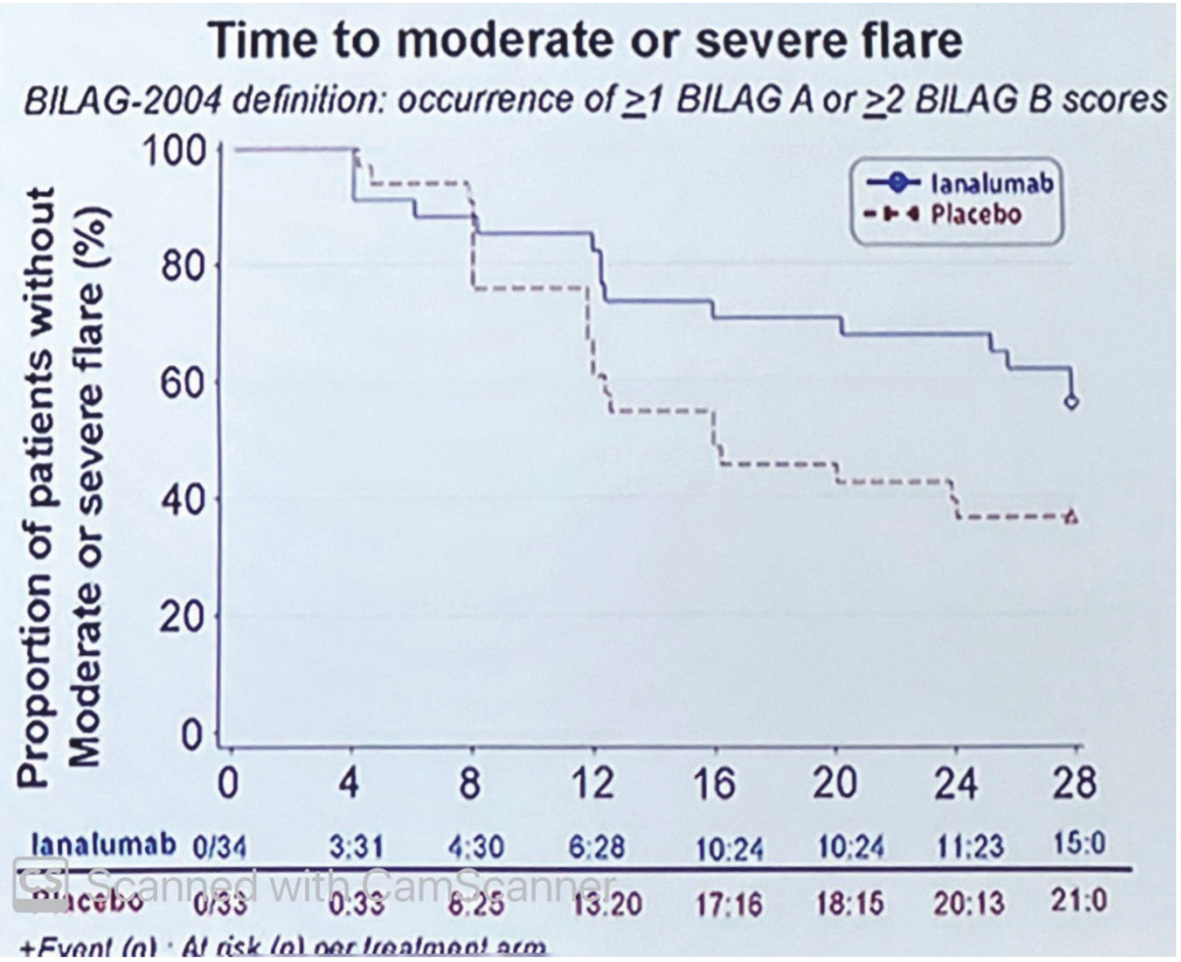
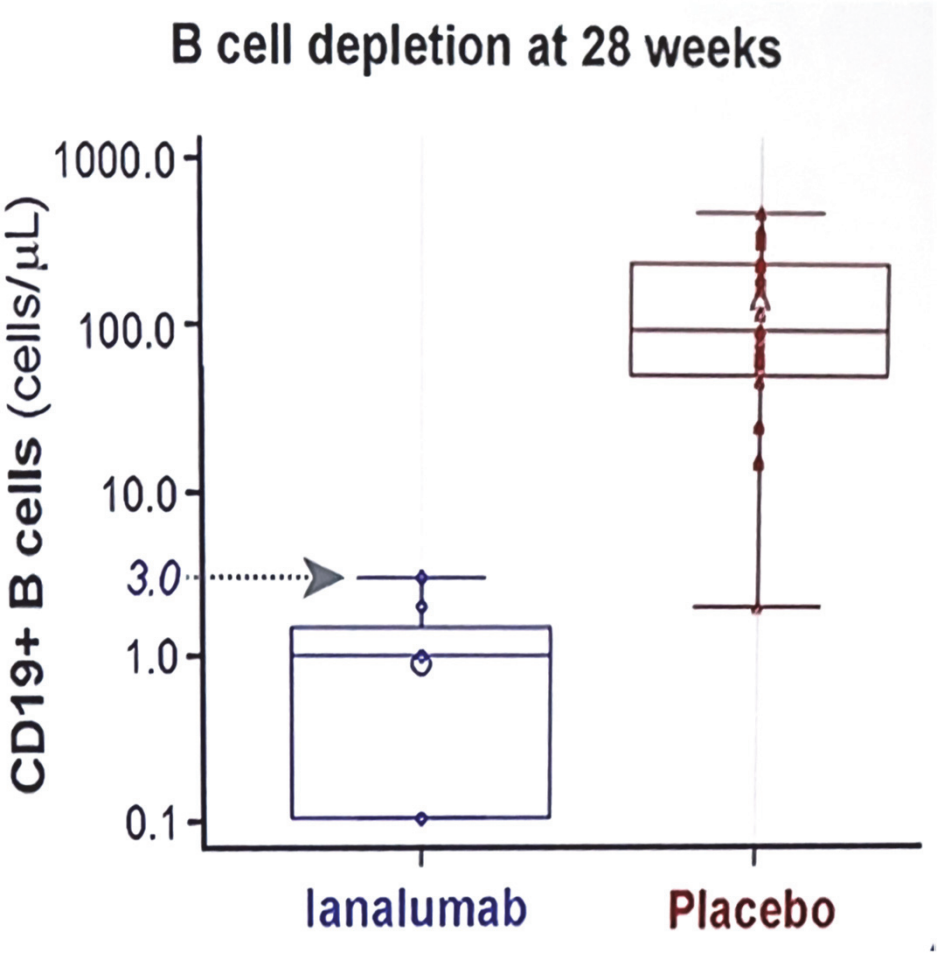


Table 1. Selected secondary and exploratory outcomes

Outcomes		Ianalumab (n=34)	Placebo (n=33)
Incidence of flare*	n (%)	15 (44)	21 (64)
Time to first flare* (Days)	Mean (SD)	108 (73)	87 (39)
	Median (range)	87 (29-276)	84 (30-170)
Week 28 LLDAS	n (%)	9 (27)	3 (9)
Ratio BL at Week 28			
Serum C3	Geo-mean(95% CI)	1.13 (1.05, 1.22)	0.95 (0.88, 1.03)
Serum C4		1.44 (1.24, 1.67)	1.01 (0.90, 1.13)
Anti-dsDNA		0.52 (0.39, 0.70)	0.88 (0.73, 1.06)
Anti-CXCL13		0.50 (0.37, 0.67)	0.83 (0.68, 1.02)
Anti-C1q		0.70 (0.56, 0.87)	0.85 (0.71, 1.02)

*Moderate or severe: post-BL BILAG 2004 domain activity ≥1 'A' or ≥2 'B'





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OP0238 (2023)

IMMUNOSUPPRESSION WITH TARGETED DMARDS REDUCES MORBIDITY AND MORTALITY IN PRE-CAPILLARY PULMONARY HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS: A EUSTAR ANALYSIS

C. Bruni[1,2], L. Tofani[3], H. Fretheim[4], Y. Weber[1], E. Hachulla[5], P. Carreira[6], D. Giuggioli[7], P. Airò[8], E. Siegert[9], U. Müller-Ladner[10], M. Matucci-Cerinic[2,11], G. Riemekasten[12], C. P. Simeon Aznar[13], J. De Vries-Bouwstra[14], L. A. Saketkoo[15], J. Distler[16], A. Balbir-Gurman[17], I. Castellví[18], E. Zanatta[19], V. Smith[20,21,22], C. P. Denton[23], B. Maurer[24], A. Giollo[19,25], F. Iannone[26], L. Dagna[11], M. E. Truchetet[27], M. Kuwana[28], Y. Allanore[29], Y. Tanaka[30], M. Martin[31], E. Rosato[32], A. M. Gheorghiu[33], F. Del Galdo[34], K. Solanki[35], A. Vacca[36], C. Resende[37], S. Vieira[38], L. Czirják[39], M. Baresic[40], F. P. Cantatore[41], V. Riccieri[42], K. Andréasson[43], L. Chung[44], C. Souza Muller[45], D. Opris-Belinski[46], S. Rednic[47], P. Sfikakis[48], Y. Levy[49], V. Hsu[50], S. Heitmann[51], J. Henes[52], G. Moroncini[53], M. Iudici[54], E. De Langhe[55], A. Herrick[56], C. Montecucco[57], A. M. Hoffmann-Vold[1,4], O. Distler[1]

Background: Pre-capillary pulmonary hypertension (precapPH) affects 9-**15%** of patients with systemic sclerosis (SSc) and may be associated with interstitial lung disease (ILD) of variable extent.

Immunosuppressants (IMS) are standard of care for treating ILD, skin or musculoskeletal manifestations in SSc. However, their beneficial effect on precapPH remains unclear.

Objectives: To determine whether **exposure to IMS** in SSc-precapPH affects morbidity and mortality in the EUSTAR cohort.

Methods: We considered exposure to a drug if it was ongoing at or prescribed after precapPH diagnosis and administered for at least 30 days. **Patients were clustered into group 1 or group 3** precapPH based on ILD presence on HRCT and FVC <70%, as proposed in the INCREASE trial.

Bruni C et al.

Results 755 SSc-precapPH patients from 54 EUSTAR centers were included (18% males, age 63±11 years, disease duration 11±9 years, 29% diffuse skin subset, 60% ILD on HRCT): **377 (50%)** received IMS [365 (47%) csDMARDs, **68 (9%**) targeted therapies] and **642 (85%)** PAH medications

In 2.9 (1.2-5.4) years median follow-up, **546 (70%) patients developed a morbidity-mortality event**. While overall IMS exposure did not associate with the outcome, targeted therapies were associated with reduced risk of morbidity-mortality [HR 0.59 (95% CI 0.36-0.96), p=0.04].

When clustering into group 1 [n=561, 40% IMS, n=32 (6%) targeted therapies] or group 3 [n=194, 80% IMS, n=36 (19%) targeted therapies], less morbidity-mortality events were recorded for group 1 (69% vs 81%). Despite the rarer use, the protective effect of targeted therapies for morbidity-mortality was confirmed in group 1 (HR 0.24, 95% CI 0.02-0.64, p=0.01,) but not in group 3

Conclusion In this large EUSTAR SSc-precapPH cohort, targeted therapies are associated with a significantly **reduced risk of mortality and precapPH worsening over time**. This is the first large study adjusted for confounders supporting a potential effect of targeted therapies on SSc-precapPH

OP0240 (2023)

A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF TACROLIMUS WITH MYCOPHENOLATE MOFETIL IN PATIENTS WITH SYSTEMIC SCLEROSIS - INTERSTITIAL LUNG DISEASE (INSIST TRIAL)

Objectives: To compare the safety and efficacy of Tacrolimus with MMF in patients with progressive SSc-ILD.

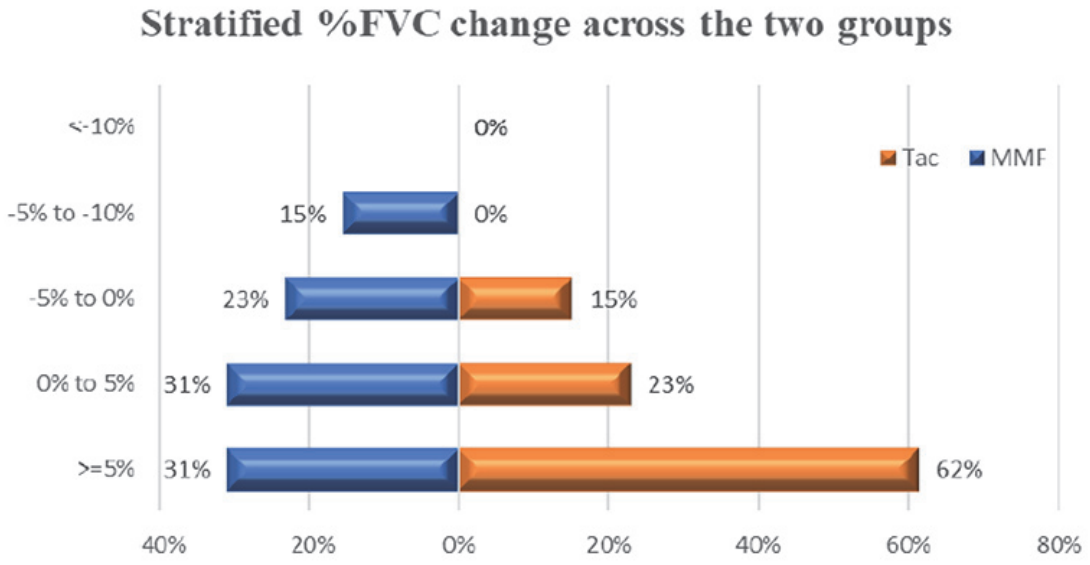
Methods: In this single center open labelled, prospective, two-arm parallel group, randomized controlled pilot study (INSIST) conducted between November 2021 to December 2022, patients with progressive ILD (FVC decline >10%) due to SSc, aged between 18-65 years.

- The primary endpoint was the **difference in change in FVC% at 24 weeks**; secondary outcomes included absolute change in FVC, skin scores, 6-minute walk distance.

Mathew J et al.

Results:

- 25 out of 26 patients (13 in each group) completed 24 weeks follow up. Majority had Anti-Scl 70 positivity (73%) and limited skin disease.
- At 24 weeks, the mean change in FVC was 4.4% (10.6) and 6.92%(8.4) in the MMF and tacrolimus groups respectively (difference 2.52%, 95% CI (-10.3 to 5.18); p-0.500).
- All patients on tacrolimus and 85% of patients on MMF had stabilization (ΔFVC% -5% TO 5%) or improvement (ΔFVC%>10%) in lung function.



Conclusions: Tacrolimus resulted in comparable improvement to MMF across primary and secondary outcome measures at 24 weeks with a favorable safety profile in patients with SSc ILD

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