PT72

PROSPECTIVE EVALUATION OF LOW DISEASE ACTIVITY STATE AS TREATMENT ENDPOINT IN A LARGE COHORT OF ADOLESCENTS AND YOUNG ADULTS WITH CHILDHOOD ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction

- ✓ Treat-to-target (T2T) strategies aim to facilitate tight disease control to improve outcomes.
- ✓ T2T outcome definitions in childhood-onset SLE (cSLE) include Childhood Lupus Low Disease Activity State (cLLDAS), cSLE clinical remission on-corticosteroids (cCR) and cSLE clinical remission off-corticosteroids (cCR-0)
- ✓ No previous studies evaluated prospectively the feasibility and impact of active implementation of T2T strategy in routine practice in a cohort of adolescents and young adults (AYA) with cSLE.

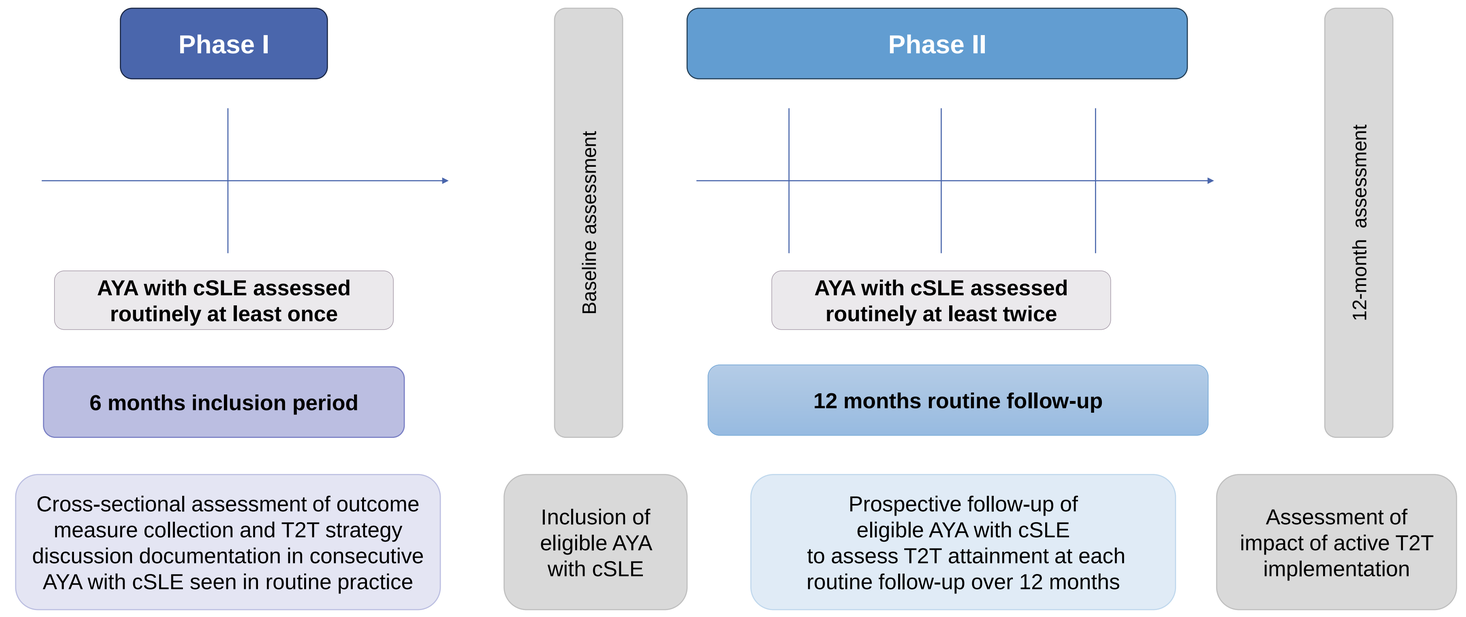
Objectives

This study aimed to:

- ✓ Assess the feasibility of agreeing and documenting a treatment target in a large cohort of AYA with cSLE
- ✓ Explore the impact of setting cLLDAS as therapeutic target on disease states over a12-month routine follow-up period

Method

- We used a prospective real-life cSLE quality improvement evaluation cohort study design.
- The study had two phases: **a recruitment phase (Phase 1)** and **an evaluation phase (Phase 2)**



Inclusion criteria

AYA with cSLE

- *classified based on:*
- ✓ the Systemic Lupus International Collaborating Clinics (SLICC) 2012 criteria and/or
- ✓ the European Alliance of Associations of Rheumatology/ American College of Rheumatology (ACR) 2019 criteria

- *reviewed consecutively* in routine clinics during the ***Phase 1*** of the study

- *with complete data collected longitudinally at each routine appointment* during ***Phase 2*** of the study, pertaining to the following:
- ✓ cumulative organ involvement
- ✓ serological markers
- ✓ cumulative treatment, including steroid dose
- ✓ paediatric British Isles Lupus Assessment Group (pBILAG) score
- ✓ SLE Disease Activity Index (SLEDAI)- 2K score
- ✓ paediatric SLICC/ACR Damage Index score (pedSDI)
- ✓ physician global assessment on a 0-3 VAS (PGA)

Cohort characteristics (N=135)

Median age (years)	**26.5±5.1 years**
Mean disease duration ± SD (years)	13.5 ±4.8 years
Median age at onset	12.3
Ethnicity (%)	
White	40 (29.6%)
Black	38 (28.1%)
Asian	40 (29.6%)
Other	17 (12.5%)
Cumulative Clinical Features	Number (%)
Renal Involvement	60 (44%)
Constitutional Involvement	96 (71.1%)
Neuropsychiatric Involvement	24 (17.8%)
Mucocutaneous Involvement	116 (86%)
Musculoskeletal Involvement	89 (66%)
Haematological Involvement	101 (75%)
Cardiorespiratory Involvement	21 (15.5%)
Gastrointestinal Involvement	5 (3.7%)
Ophthalmic Involvement	0 (0%)
Cumulative Serological Features	Number (%)
ANA positivity ever	135 (100%)
Current ANA positive	113 (83.7%)
Anti-dsDNA positivity ever	72 (53.3%)
Current Anti-dsDNA positivity	54 (40%)
APS screening positive twice (ever)	11 (8.1%)
Cumulative classification criteria fulfilled	Number (%)
2012 SLICC classification criteria	135 (100%)
2019 ACR/EULAR classification criteria	132 (97.7%)

Current Treatment (unless specified otherwise)	**Number (%)**
None	10 (7.4%)
Current B-cell targeted therapy	15 (11.1%)
B-cell targeted therapy ever	45 (33.3%)
Hydroxychloroquine	115 (85.2%)
Methotrexate	14 (10.3%)
Azathioprine	27 (20%)
Mycophenolate Mofetil	74 (54.8%)
Cyclophosphamide in the past year	5 (3.7%)
Cyclophosphamide ever	26 (19.2%)
Current Prednisolone dose ≤ 5mg daily	73 (54%)
Current Prednisolone dose >5 mg but ≤7.5 mg/day	6 (14%)
Current Prednisolone dose > 8 mg daily	36 (26.6%)
Not on Prednisolone	20 (14.8%)
Disease activity/damage scores (within 6 months of inclusion, N=135)	Number (%)
Average SLEDAI	1.6 (0-18)
SLEDAI = 0	60 (44.4%)
SLEDAI ≤4	66 (48.8%)
SLEDAI = 5-9	6 (4.4%)
SLEDAI ≥10	3 (2.2%)
PedSDI ≥ 1	50 (37%)
PGA VAS = 0	90 (66.6%)
PGA VAS ≤ 1/3	36 (26.6%)
PGA VAS >1	9 (6.65)

Results 1: Implementing routine outcome measure collection in clinical practice was feasible:

- ✓ Only 13/135 (9.8%) AYA with cSLE had incomplete assessments/no therapeutic target discussed/recorded
- ✓ The SLEDAI)-2K, PedSDI and PGA, were recorded in 122/135 (91.2%) AYA with cSLE
- ✓ The pBILAG score was systematically recorded only in 92/135 (68.1%) of clinical letters (significantly less frequently, P<0.00001)
- ✓ Median SLEDAI-2K = 0 (IQR=2), mean SLEDAI-2K = 1.6 ± 2.79 (N=122)
- ✓ Median global pBILAG score = 0 (IQR=1) and mean global pBILAG score = 0.96 ± 2.97 (N=92)
- ✓ The median PedSDI was 0 (IQR=1), with 47 (38.5%) overall having already acquired damage: mild damage (PedSDI = 1 or 2) in 37/47 and severe damage (PedSDI≥3) in 10/47 AYA with Csle (N=122)

Conclusion:

- ✓ T2T strategy implementation was achievable and associated with improved cSLE control.
- ✓ Spending at least 3/12 months in cLLDAS led to less damage.

Results 2: Agreeing with AYA with cSLE on a treatment target was achievable:

- ✓ 122/135 (90.4%) had a therapeutic target initially agreed and assessed against at least at two, and
- ✓ 82/122 (67.2%) at least at three different time points over 12-months routine follow-up

(338 routine clinical assessments for the whole cohort during ***Phase 2*** of the study).

The reasons for not agreeing on a target in 13/135 cases were the following:
- ✓ 5/13 (38.5%) AYA were experiencing cSLE flares at baseline, and setting a target was not feasible
- ✓ 8/13 (62.5%) cases, the assessment against a feasible treatment target was not consistently documented, potentially because of time constraints.

Results 3: Setting cLLDAS as minimum therapeutic target in cSLE was associated with improved disease outcomes after 12 months follow-up

Treatment target achieved	**Baseline N=122**	**Last assessment N=122**	**P value**
	100/122 in target	**112/122 in target**	
Complete remission off steroid treatment	13 (10.6%)	17 (13.9%)	0.43
Complete remission on steroid treatment*	34 (27.8%)	32 (26.2%)	0.77
Clinical remission off steroid treatment (cCR-0)	5 (4.1%)	13 (10.7%)	**0.048**
Clinical remission on steroid treatment (cCR)*	29 (23.8%)	39 (31.9%)	0.158
cLLDAS**	19 (15.5%)	11 (9%)	0.121
Not on target because of moderate flare	5 (4.1%)	2 (1.6%)	0.24
Not on target because of severe flare	5 (4.1%)	5 (4.1%)	0.99
Not on target despite no clinical activity	12 (9.8%)	3 (2.5%)	0.017
AYA with cSLE in target (minimum cLLDAS)	100 (81.9%)	112 (91.8%)	**0.022**

Achieving minimum cLLDAS for longer than 3 months was associated with reduced damage accrual (HR=1.7; 95%CI=1.1-2.5; P<0.0001) at 12 months.

Key messages:

This is the first large prospective study in AYA with cSLE to evaluate the impact of active T2T implementation.
T2T strategies were feasible to implement in 122/135 (91.2%) AYA with cSLE in routine practice.
T2T approach was associated with improved disease control and decreased damage accrual at 12 month.

References:
1. Gotch R, Ahmed Y, Wilson R, Hawkins E, Ciurtin C (2024); Impact of active implementation of low disease activity state as treatment endpoint in childhood onset systemic lupus erythematosus, *Clinical Rheumatology, in press*
2. Smith EMD, Aggarwal A, Ainsworth J, Al-Abadi E, Avcin T, Bortey L, Burnham J, Ciurtin C, Hedrich CM, Kamphuis S, et al.. (2024), Defining Remission in Childhood Lupus: An International cSLE T2T Task Force Collaborative Effort endorsed by the Paediatric Rheumatology European Society (PReS), *Clinical Immunology*, https://doi.org/10.1016/j.clim.2024.110214