Cluster Analysis of Patients with SLE in the Adelphi Lupus Disease Specific Programme

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Introduction

- Better understanding of the patterns of symptom and organ involvement in patients with systemic lupus erythematosus (SLE) may facilitate individualized management and evaluation of new interventions against more specific unmet needs
- The Adelphi Real World cross-sectional survey, Lupus Disease Specific Programme (DSP) was conducted in 2015 to describe physician- and patient-reported treatment satisfaction, and to assess functional and clinical outcomes in a large real-world cohort of patients with SLE[1]
- This analysis utilized the DSP data to categorize patients with SLE into different groups (clusters) according to their organ system involvement

Objectives

- To categorize patients with SLE into clusters according to the presence and type of organ system involvement
- To describe and compare the clinical and treatment characteristics and patient-reported outcomes of each cluster

Box 1. Results of cluster analysis based on organ system involvement

Cluster 1 (n=250, 18.2%)
Lowest overall organ system burden, predominantly mucocutaneous involvement

Cluster 2 (n=670, 48.7%)
Predominantly mucocutaneous and musculoskeletal, with limited renal and hematologic involvement (i.e., cutaneous-articular)

Cluster 3 (n=150, 10.9%)
High burden across multiple organ systems, with the highest rates of hematologic and renal involvement compared with other clusters

Cluster 4 (n=306, 22.2%)
High burden across multiple organ systems; all patients had mucocutaneous and musculoskeletal disease, with the highest rates of constitutional, cardiorespiratory, neuropsychiatric and ophthalmic involvement compared with other clusters, high rates of hematologic involvement, and no renal involvement

Methods

Study design

- This was a post-hoc, multivariate, cross-sectional analysis (GSK study 208683) of survey data collected from physicians and patients enrolled in the Adelphi Real World 2015 Lupus DSP (GSK study 205086; United States and Europe; August–September)

Analyses

- Latent class modeling, a statistical technique for identifying unobservable (latent) subgroups within a population, was used to generate clusters of patients based on the presence or absence of activity in each organ system at the time of the survey as reported by the physician
- Characteristics of each cluster were compared using the chi-square test for categorical variables and Kruskal-Wallis test for ordered/numeric outcomes

Study population

Rheumatologists
- Actively involved in the management of ≥5 patients with SLE/month
- Agreed to complete patient record forms (PRFs), describing the clinical and treatment characteristics of their next five eligible patients

Patients
- ≥18 years of age
- Confirmed diagnosis of SLE
- Those who had submitted patient self-completion forms (PSCs) were included in the analysis

Results

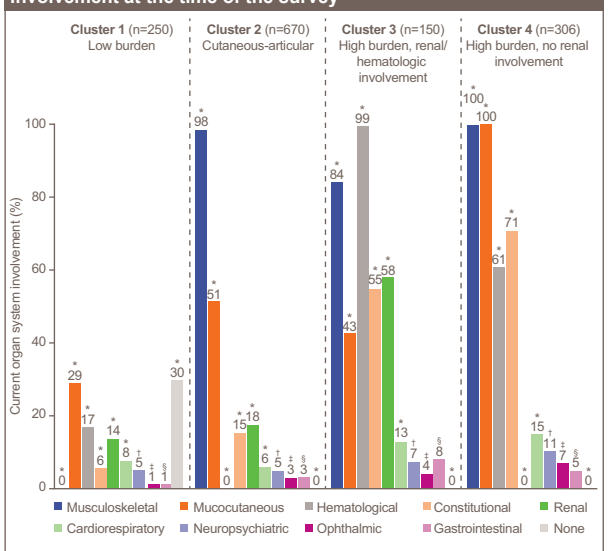
Overall study population

- Overall, 250 rheumatologists completed PRFs for 1376 patients, all of whom were included in the analyses described here; 859 of these patients completed PSCs
- Patients were predominantly white/Caucasian and female, and had a mean (standard deviation [SD]) age of 42.1 (13.6) years

Generation of clusters

- Based on organ system involvement at the time of the survey, four patient clusters were generated (**Figure 1** and **Box 1**)

Figure 1. Clusters of patients with SLE defined by organ system involvement at the time of the survey



P values represent differences across the clusters
*p<0.0001; †p=0.0092; ‡p=0.0019; §p=0.0022

Demographic characteristics of patient clusters (Table 1)

- Significant differences were observed between the clusters in terms of patient ethnicity (p=0.001), with the highest proportions of black and Hispanic/Latino patients in Cluster 3

Table 1. Patient demographic characteristics at the time of the survey

	Cluster 1 Low burden n=250	Cluster 2 Cutaneous-articular n=670	Cluster 3 High burden, renal/ hematologic involvement n=150	Cluster 4 High burden, no renal involvement n=306
Female, n (n (%))	250 (209 (83.6))	670 (579 (86.4))	150 (134 (89.3))	304 (274 (90.1))
Age (years), n (Mean (SD))	249 (41.0 (14.0))	670 (42.6 (13.5))	150 (40.9 (14.0))	306 (42.4 (13.3))
Ethnicity* (n [%]), n	247	666	149	304
White/Caucasian	170 (68.8)	520 (78.1)	84 (56.4)	229 (75.3)
Black	42 (17.0)	86 (12.9)	40 (26.8)	46 (15.1)
Hispanic/Latino	9 (3.6)	23 (3.5)	11 (7.4)	11 (3.6)
Asian, other	6 (2.4)	13 (2.0)	5 (3.4)	5 (1.6)
Asian, Indian subcontinent	9 (3.6)	2 (0.3)	2 (1.3)	3 (1.0)
Chinese	4 (1.6)	9 (1.4)	1 (0.7)	2 (0.7)
Other	7 (2.8)	13 (2.0)	6 (4.0)	8 (2.6)
Unemployed†, n (n (%))	250 (22 (8.8))	670 (69 (10.3))	150 (24 (16.0))	306 (45 (14.7))

P values represent differences across the clusters
*p=0.001; †p<0.05

Clinical characteristics of patient clusters

- Significant between-cluster differences were observed for physician-assessed disease severity and progression (both p<0.0001)
  - SLE was least severe in Cluster 1 and most severe in Cluster 3 (**Figure 2**)
  - Disease progression status was most compromised in Cluster 3 (i.e., highest renal involvement), with a higher proportion of patients exhibiting unstable or deteriorating disease compared with other clusters (**Table 2**)
  - Flare rate and symptom burden were highest among Clusters 3 and 4 (**Table 2**)

Figure 2. Disease severity at the time of the survey

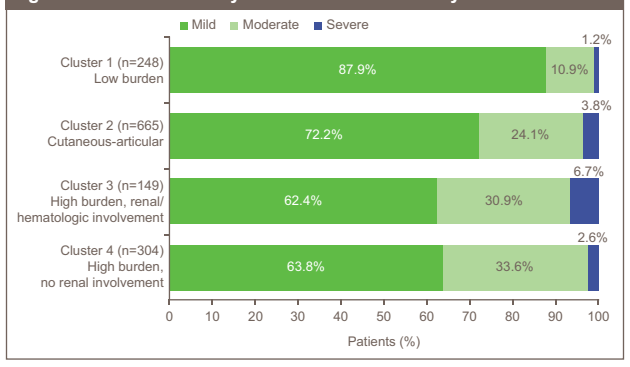


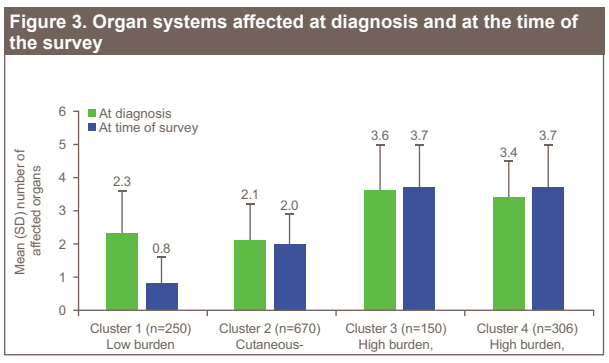
Table 2. Patient clinical characteristics at the time of the survey (physician-reported)

	Cluster 1 Low burden n=250	Cluster 2 Cutaneous-articular n=670	Cluster 3 High burden, renal/ hematologic involvement n=150	Cluster 4 High burden, no renal involvement n=306
Time since diagnosis* (weeks), n (Mean (SD))	245 (307.6 (334.3))	655 (256.6 (307.0))	149 (348.4 (351.5))	302 (300.8 (308.8))
Disease progression† (n [%]), n	250	669	150	306
Improving	86 (34.4)	184 (27.5)	35 (23.3)	67 (21.9)
Stable	149 (59.6)	381 (57.0)	79 (52.7)	179 (58.5)
Deteriorating slowly	9 (3.6)	78 (11.7)	25 (16.7)	48 (15.7)
Deteriorating rapidly	3 (1.2)	7 (1.0)	4 (2.7)	1 (0.3)
Unstable	3 (1.2)	19 (2.8)	7 (4.7)	11 (3.6)
SLE symptoms, n (%)				
Pain/inflammation†	27 (10.8)	533 (79.6)	108 (72.0)	262 (85.6)
Skin†	62 (24.8)	326 (48.7)	79 (52.7)	228 (74.5)
Neuropsychiatric†	22 (8.8)	120 (17.9)	41 (27.3)	99 (32.4)
Cardiovascular†	32 (12.8)	108 (16.1)	45 (30.0)	64 (20.9)
Renal†	25 (10.0)	74 (11.0)	60 (40.0)	6 (2.0)
Fatigue†	40 (16.0)	279 (41.6)	95 (63.3)	197 (64.4)
Number of patients experiencing a flare in the last 12 months†, n (n (%))	250 (44 (17.6))	667 (181 (27.1))	150 (69 (46.0))	304 (136 (44.7))
Number of flares in the last 12 months†, n (Mean (SD))	181 (0.5 (1.2))	484 (0.8 (1.5))	107 (1.3 (1.2))	219 (1.4 (1.5))

P values represent differences across the clusters
*p<0.001; †p<0.0001

- The number of organs affected at diagnosis, compared with at the time of the survey, remained stable in Clusters 2, 3, and 4, thus suggesting that in patients with more severe SLE, organ system involvement may be permanent (**Figure 3**)
  - Conversely, the number of organs affected in Cluster 1 decreased over time

Figure 3. Organ systems affected at diagnosis and at the time of the survey



Treatment history and patient-reported outcomes

- Patients in Clusters 3 and 4 had the highest mean number of prior treatments, treatment classes, and highest use of corticosteroids, immunosuppressants, and biologic disease modifying antirheumatic drugs (p=0.003, p=0.003, and p<0.0001 across clusters, respectively; **Table 3**)

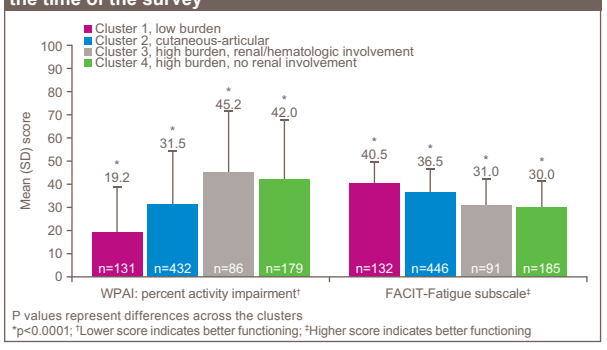
Table 3. Patient treatment history

	Cluster 1 Low burden n=250	Cluster 2 Cutaneous-articular n=670	Cluster 3 High burden, renal/ hematologic involvement n=150	Cluster 4 High burden, no renal involvement n=306
Number of prior treatments*, n (Mean (SD))	177 (3.0 (2.3))	422 (3.1 (2.5))	122 (3.8 (2.6))	221 (3.8 (3.2))
Number of prior treatment classes*, n (Mean (SD))	177 (2.9 (2.2))	422 (3.0 (2.3))	122 (3.6 (2.5))	221 (3.5 (2.9))
Current treatment class (n [%]), n	250	670	150	306
Corticosteroid†	133 (53.2)	464 (69.3)	118 (78.7)	242 (79.1)
Anti-malarial‡	168 (67.2)	377 (56.3)	88 (58.7)	193 (63.1)
Immunosuppressant†	110 (44.0)	364 (54.3)	100 (66.7)	193 (63.1)
NSAID§	20 (8.0)	105 (15.7)	22 (14.7)	56 (18.3)
Biologic DMARD†	25 (10.0)	59 (8.8)	32 (21.3)	54 (17.6)

P values represent differences across the clusters
*p=0.0030; †p<0.0001; ‡p=0.0141; §p=0.0056
DMARD, disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug

- Patient-reported Work Productivity and Activity Impairment (WPAI) percent activity impairment and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scores deteriorated across the clusters (both p<0.0001); both were worse in Clusters 3 and 4 (**Figure 4**)

Figure 4. WPAI: percent activity impairment and fatigue scores at the time of the survey



P values represent differences across the clusters
*p<0.0001; †Lower score indicates better functioning; ‡Higher score indicates better functioning

Conclusions

- **This analysis of international real-world cross-sectional cohort data identified distinct and potentially clinically meaningful subsets of SLE**
- **A similarly high disease burden was found in Clusters 3 and 4, confirming the extensive impact of SLE regardless of the presence or absence of renal involvement**
- **Analysis of organ system involvement over time confirms that once an organ system is involved, it remains affected in patients with more severe SLE**
- **Limitations included the absence of serological findings or disease activity indices for cluster formation or comparison**
- **The current study utilized data from an aggregate global sample; thus, it could not identify subtle differences in the management approach between clusters. Future studies may address this topic**
- **Patients were included in the study with varying lengths of time since diagnosis. As time since diagnosis differed significantly between the clusters, it is possible that differences in the clusters' characteristics were influenced by different stages of SLE**

References

1. Pascoe K, *et al. Clin Ther.* 2017;39(9):1811–26.

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Disclosures

- **JA**, **KG**, and **AL** are employees of GSK and hold shares in the company. **BH**, **DB**, and **OM** are employees of Adelphi Group.

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