

Supplemental Figure legends

Supplemental Figure S1. Proportion of SLE patients who achieved remission (DORIS) and low disease activity (LLDAS) over specific duration of follow-up time

(A) Proportion of patients who achieved the treatment targets according to increasing cut-offs of cumulative follow-up time. (B) Proportion of patients who achieved the treatment targets according to increasing cut-offs of sustained cumulative follow-up time

Supplemental Figure S2. Effect of increasing cut-offs of cumulative time in treatment targets on the risk for organ damage accrual and severe flares in active moderate-to-severe SLE patients

Generalized linear models were performed assessing the effect of different thresholds ($\geq 30\%$, $\geq 40\%$, $\geq 50\%$, $\geq 60\%$, $\geq 70\%$) of observation time in LLDAS (A, C) and DORIS (B, D) against accrual of organ damage (A, B) and severe flares (C, D). Dots with blue-coloured error bars represent the relative risk (compared to not meeting each threshold) and 95% confidence intervals.

Supplemental Figure S3. Attainment of treatment targets above specific exposure thresholds results in significant reduction of severe flares

(A-B) Survival plot of new severe flare-free time according to achievement of (A) DORIS $\geq 50\%$ of observation time or not (hazard ratio[HR] 0.13; [95% confidence interval] 0.10–0.24, multiple-failures Cox-proportional hazards), and (B) LLDAS $\geq 60\%$ of time or not (HR 0.15; 0.10–0.22). Banded areas represent 95% CI. (C-D) Survival plot of new severe flare-free time according to sustained attainment of (C) DORIS ≥ 24 months or not (HR 0.15; 0.08–0.27, multiple-failures Cox-proportional hazards) and (D) LLDAS ≥ 36 months or not (HR 0.11; 0.06–0.19). Banded areas represent 95% CI. **I** The same plot as above according to accomplishment of DORIS $\geq 50\%$ of time

(with or without LLDAS $\geq 60\%$ of time), LLDAS $\geq 60\%$ /DORIS $< 50\%$, and LLDAS $< 60\%$ /DORIS $< 50\%$. Using the latter condition as reference, LLDAS $\geq 60\%$ /DORIS $< 50\%$ had reduced hazard for organ damage accrual (HR 0.22; 0.14–0.35, $p < 0.001$). **(F)** The same plot as above according to sustained attainment of DORIS ≥ 24 months (with or without LLDAS ≥ 36 months), LLDAS ≥ 36 months/DORIS < 24 months, and LLDAS < 36 months. The survival plots of the first two conditions are overlapping due to identical hazard ratios.

Supplemental Figure S4. Survival plots of time-to-first occurrence of organ damage accrual and severe flare according to attainment of the treatment targets in active moderate-to-severe SLE patients

(A-B) Cox-regression survival plots for time-to-first damage in patients who experienced (A) LLDAS $< 60\%$ (left panel) or $\geq 60\%$ (right panel) of time, and (B) DORIS $< 50\%$ (left panel) or $\geq 50\%$ (right panel) of time. **(C-D)** Cox-regression survival plots for time-to-first severe flare in patients who experienced (C) LLDAS $< 60\%$ (left panel) or $\geq 60\%$ (right panel) of time, and (D) DORIS $< 50\%$ (left panel) or $\geq 50\%$ (right panel) of time. Dotted lines represent 95% confidence intervals. The number of at-risk individuals was obtained from each corresponding life table analysis.

Supplemental Figure S5. Silhouette method to define the optimal number of patient clusters

Silhouette width (y-axis) was calculated for each object of the classification thus indicating how well they fit into their respective cluster. X-axis represents the number of possible clusters.

Supplemental Figure S6. Modified versions of DORIS and LLDAS and their attainment across the three patient clusters (A, B) Comparison of (A) DORIS and modified DORIS, (B)

LLDAS and modified LLDAS attainment across the three SLE patient clusters. Dots with error bars represent the median (interquartile range) percentage of follow-up time with target attainment. Median values are shown in red color. Statistical analysis was performed with Kruskal-Wallis test followed by post-hoc Dunn's test for pairwise comparisons. **(C-E)** Time-adjusted average (C) clinical SLEDAI-2K, modified clinical SLEDAI-2K, (D) PGA and (E) glucocorticoid (prednisone equivalent) dose intake across the three clusters. Statistical analysis was performed with the Kruskal-Wallis test followed by post-hoc Dunn's test for pairwise comparisons. **(F)** Comparison of the modified DORIS and modified LLDAS attainment (% of follow-up time) in Cluster 1, 2 and 3 patients. Dotted connecting lines correspond to paired-samples statistical analysis performed with the Wilcoxon signed ranks test. ns= not significant; * $p<0.05$; ** $p<0.01$; *** $p<0.001$; **** $p<0.0001$.