

### **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  $\geq 24$  months or not (HR 0.15; 0.08–0.27, multiple-failures Cox-proportional hazards) and (D) LLDAS  $\geq 36$  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  $\geq 24$  months (with or without LLDAS  $\geq 36$  months), LLDAS  $\geq 36$  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; \*  $p<0.05$ ; \*\*  $p<0.01$ ; \*\*\*  $p<0.001$ ; \*\*\*\*  $p<0.0001$ .