26 COMPARISON OF EFFECTS OF DORIS REMISSION AND LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) ON DISEASE OUTCOMES IN A MULTINATIONAL PROSPECTIVE STUDY

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Background The Definitions of Remission in SLE (DORIS) group has proposed multiple definitions of remission, but these are infrequently attained and have not previously been evaluated in relation to protection from damage accrual. In contrast, the Lupus Low Disease Activity State (LLDAS) is more attainable, and has been shown to be associated with improved patient outcomes. The objective of this study was to compare the attainability and effect of LLDAS and remission on outcomes in a prospective multicenter study.

Methods A prospective multinational cohort study was undertaken in 13 centres between 2013–2017. Time dependent Cox proportional hazards models were used to compare LLDAS and DORIS definitions of remission in terms of impact on disease flares and damage accrual.

Results 1735 SLE patients were recruited, and followed for (mean $\pm$ SD) 2.2 ± 0.9 years. LLDAS was achieved in 6922 visits (54.6%). In contrast, remission was achieved in 1.1%–15.4% of visits. LLDAS attainment at any visit was associated with significantly reduced subsequent flare (HR 0.65, 95% CI 0.56–0.76, $p < 0.001$) and damage accrual (HR 0.55, 95% CI 0.43–0.70, $p < 0.001$). In contrast, only the least stringent remission definition was associated with reduced damage accrual (HR 0.58, 95% CI 0.39–0.88, $p = 0.01$). Only remission definitions including serological remission were significantly associated with reduction in subsequent flares. Patients who spent 50% of their observed time in LLDAS had two-fold reduction in risk of damage accrual (HR 0.53, 95% CI 0.41–0.68, $p < 0.001$), while only the least stringent remission definition, or the related definition excluding serology, were significantly protective against damage (HR 0.59, 95% CI 0.42–0.83, $p = 0.003$; HR 0.69, 95% CI 0.48–0.99, $p = 0.05$, respectively).

Conclusions LLDAS was markedly more attainable than any remission definition, whilst still conferring significant protection against flares and damage accrual. Only the least stringent remission definitions could be shown to be associated with significant reduction in damage accrual, likely reflecting a low frequency of remission attainment overall; and normal serology was required for protection from flare. LLDAS is a valid treatment target for SLE and is more achievable than remission.

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27 COMBINATION TREATMENT WITH LACTOBACILLUS ACIDOPHILUS AND TACROLIMUS HAVE POTENT THERAPEUTIC EFFICACY AND IMPROVES TACROLIMUS INDUCED TH17/TREG CELL IMBALANCE IN ANIMAL MODEL OF LUPUS

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Background Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by tissue-binding autoantibodies and immune complexes. Tacrolimus, also known as FK506, is an immunosuppressant that has been used for the treatment of lupus as well as for the prevention of graft rejection after organ transplantation. It achieves immunosuppressive activity by inhibiting IL-2, a molecule that promotes the development and proliferation of T cells. However, tacrolimus induces T cell imbalance because IL-2 is also known to promote Treg cells and inhibit proinflammatory Th17 cells. Recently, there have been reports showing that SLE is associated with gut microbiota. *Lactobacillus acidophilus*, one of the typical intestinal bacteria, is reported to have therapeutic efficacy through T cell regulation in immune-mediated inflammatory diseases including SLE.

Methods The present study was undertaken to investigate whether combination therapy of *Lactobacillus acidophilus* and tacrolimus improves the therapeutic efficacy and T cell imbalance in animal model of SLE (MRL/lpr mice). The 8-week-old MRL/lpr mice were orally administered with 5 mg/kg tacrolimus and/or 50 mg/kg *Lactobacillus acidophilus* daily.

Results The results showed that spleen size was markedly decreased in tacrolimus and *Lactobacillus acidophilus* combination group compared with tacrolimus alone group, and that DNT cells, which is a pathogenic immune cell subset, of MRL/lpr mice, were profoundly decreased in peripheral blood (PB) and spleens of mice treated with combination therapy. In addition, serum levels of ds-DNA and IgG2a were decreased, and renal pathology score was markedly alleviated by combination treatment. *In vitro* experiments using spleen cells from MRL/lpr mice revealed that treatment with *Lactobacillus acidophilus* and tacrolimus induces Treg cells and decreases Th17 cells.

Conclusions In conclusion, we demonstrated that addition of *Lactobacillus acidophilus* can augment the therapeutic effect of tacrolimus while improving the T cell imbalance in SLE.

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28 VISCERAL PSEUDO-OBSTRUCTION (VPO): A NEW TERMINOLOGY OF SYSTEMIC LUPUS ERYTHEMATOSUS GASTROINTESTINAL INVOLVEMENT AND A CT SCORING SYSTEM

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Background To identify the relevant parameters for SLE-VPO evaluation on computed tomography (CT), and try to develop a CT image based evaluation system for SLE-VPO.

Abstract 28 Figure 1 Anatomical distribution of SLE-VPO involvement.

2a CT Scoring System	
Anatomical sites affected	Score (total score= 6)
Thickness of bowel walls	≤3.0mm, 0; 3.1-7.9mm, 1; ≥8.0mm, 2
Small intestine (duodenum, jejunum and ileum)	0/1/2
Colon	0/1/2
Bile-pancreatic system	0/1
Urinary system	0/1

Abstract 28 Figure 2 CT scoring system and illustration. A CT image based scoring system was developed, taken into consideration of both the extent of VPO multi-compartment involvement and the severity of intestinal wall thickness(a). Give an example of how to perform CT scoring (b-d), c: arrow refers to ureterohydronephrosis (1-point) and intestinal edema (8.4 mm, 2-point); d: arrow refers to colonic edema (10.2 mm, 2-point). The patient had a CT score of 5 points and the time to PO50 was 49 days. The measurements of gastric and rectum wall thickness are excluded from the scoring system to avoid food/fecal contents-induced inaccuracy. Thickness of bowel walls refers to the thickest bowel wall measured of each GI segment. Bile-pancreatic system involvement includes gallbladder edema, bile duct dilatation, pancreatic duct dilatation, pancreatic edema/exudation without mechanical obstruction. Urinary system involvement includes ureterohydronephrosis and interstitial cystitis without mechanical obstruction.

Methods Patients with SLE gastrointestinal involvement from two independent retrospective cohorts were included in our study. All patients fulfilled the ACR 1997 revised classification criteria for SLE. CT scan at least once is necessary prior to glucocorticoid treatment in all enrolled

patients. The primary endpoint was set to time to GI functional recovery, defined as intake 50% ideal calories POPO50. A new CT scoring system for SLE-VPO was established in the derivation cohort and validated in the validation cohort.

Abstract 28 Figure 3 CT scores predict GI functional outcome. CT score for VPO is positively correlated with patients' time to PO50 ($r=0.47$, $p<0.0001$ in derivation cohort, $r=0.44$, $P=0.0018$ in validation cohort, a-b). CT score for VPO is lesser extent correlated with the length of hospital stay ($r=0.27$, $p=0.01$ in derivation cohort, $r=0.21$, $P=0.1577$ in validation cohort, c-d). Patients with a CT score ≤ 2 tend to have a more rapid reversible course with an average time to PO50 of 5.72 and 7.44 days in the derivation cohort and the validation cohort, respectively; while patients with a CT score > 2 have a significantly prolonged recovery with an average time to PO50 of 14.55 ($p<0.0001$) and 18.45 ($P=0.0064$) days, respectively (e). Kaplan-Meier curve presenting the cumulative percent of patients not reaching PO50 with different CT scores over the follow-up period ($P=0.0002$ in derivation cohort, f; $P=0.134$ in validation cohort, g; $P=0.0018$ in pooled cohort, h). Comparison was performed using log-rank (Mantel-Cox) test

Results A total of 90 and 47 patients with SLE gastrointestinal involvement were enrolled in the derivation cohort and the validation cohort, respectively. The time to PO50 was significantly correlated with extent of anatomical involvement ($P \leq 0.0015$) and thickness of the intestinal wall ($P=0.0008$) in the derivation cohort. A CT scoring system was developed with the combination of extent of anatomical involvement and thickness of the intestinal wall. CT score for VPO was positively correlated with patients time to PO50

($r=0.47$, $p<0.0001$ in derivation cohort, $r=0.44$, $p=0.0018$ in validation cohort), and to a lesser extent correlated with the length of hospital stay ($r=0.27$, $p=0.01$ in derivation cohort, $r=0.21$, $p=0.1577$ in validation cohort). Patients with a CT score ≤ 2 tend to have a more rapid reversible course with an average time to PO50 of 5.72 and 7.44 days in the derivation cohort and the validation cohort, respectively; while patients with a CT score > 2 have a significantly prolonged recovery with an average time to PO50 of 14.55 ($p<0.0001$)

Abstract 28 Figure 4 A flow chart of SLE-VPO dietary recovery and TPN use based on CT scoring system

and 18.45 ($p=0.0064$) days, respectively. More TPN was prescribed in the high CT score group in both cohorts (74.47% vs 51.16%, $p=0.0289$ in the derivation cohort; 80% vs 40.74%, $p=0.0089$ in the validation cohort). And the proportions of patients underwent TPN ≥ 7 days were also much higher in the high CT score group in both cohorts ($p<0.05$).

Conclusions The terminology of VPO and a CT-based scoring system may facilitate more accurate assessment and individualized management for SLE patients with GI involvement. It also meant to be helpful in terms of future clinical trial design and in-depth mechanistic research for this unique complication of lupus.

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SEROSITIS, HEMATOLOGIC INVOLVEMENT, AND STEROID DOSE ARE RISK FACTORS FOR SERIOUS INFECTIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Infection occurs frequently in patients with systemic lupus erythematosus (SLE) and has been a major cause

of morbidity and mortality. However, no large-scale comprehensive studies have estimated the effect of clinical characteristics on serious infections in actual clinical practice yet. We investigated the influence of clinical characteristics on serious infections using electronic medical record data.

Methods We conducted a nested case-control study. Patients with SLE who developed serious infections needing hospitalization or intravenous antibiotic administration were matched to controls who did not. Odds ratios (ORs) and 95% confidence intervals (CIs) for infection associated with the clinical characteristics were obtained using logistic regression analyses.

Results Among the total of 120 cases with infection, 93 (77.5%) were bacterial infections with 40 (25%) upper respiratory tract infections, 26 (21.7%) pneumonia, 24 (20%) sepsis, and 22 (18.3%) urinary tract infections. The patients with serious infections had lower hemoglobin and C3 levels and less frequent hydroxychloroquine administration. In addition, they had more frequent nephritis, serositis, and hematologic involvement and took higher than the low dose of glucocorticoids (GCs; >7.5 mg/d prednisolone-equivalent). The conditional logistic regression analysis with adjustment showed that serositis (OR, 2.76; 95% CI, 1.33–5.74), hematologic involvement (OR, 2.53; 95% CI, 1.32–4.87), and use of higher than the low dose of GCs (OR, 2.65; 95% CI, 1.31–5.34) were related to serious infections in SLE.

Conclusions Serositis, hematologic involvement, and use of higher than the low dose of GCs are risk factors for serious infections in patients with SLE.