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Systemic lupus erythematosus

Evaluation and prediction of relapse risk in stable systemic lupus erythematosus patients after glucocorticoid withdrawal (PRESS): an open-label, multicentre, non-inferiority, randomised controlled study in China

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<INTRODUCTION>

- SLE再燃率は8-45%と報告されている。
- EULARはGCをPSL 5mg以下の維持で、可能なら中止と推奨。
- SLE寛解達成後のGC減量中止方法や、どのような患者が中止可能かは不明。
- HCQの再燃抑制やDamage蓄積抑制効果は複数の報告がある
- **寛解かLLDASを維持できている安定したSLE患者において、GC中止後再燃リスクを明らかにするために、またHCQの再燃抑制効果を確認するために、多施設共同、非盲検RCTを非劣勢デザインで行った**

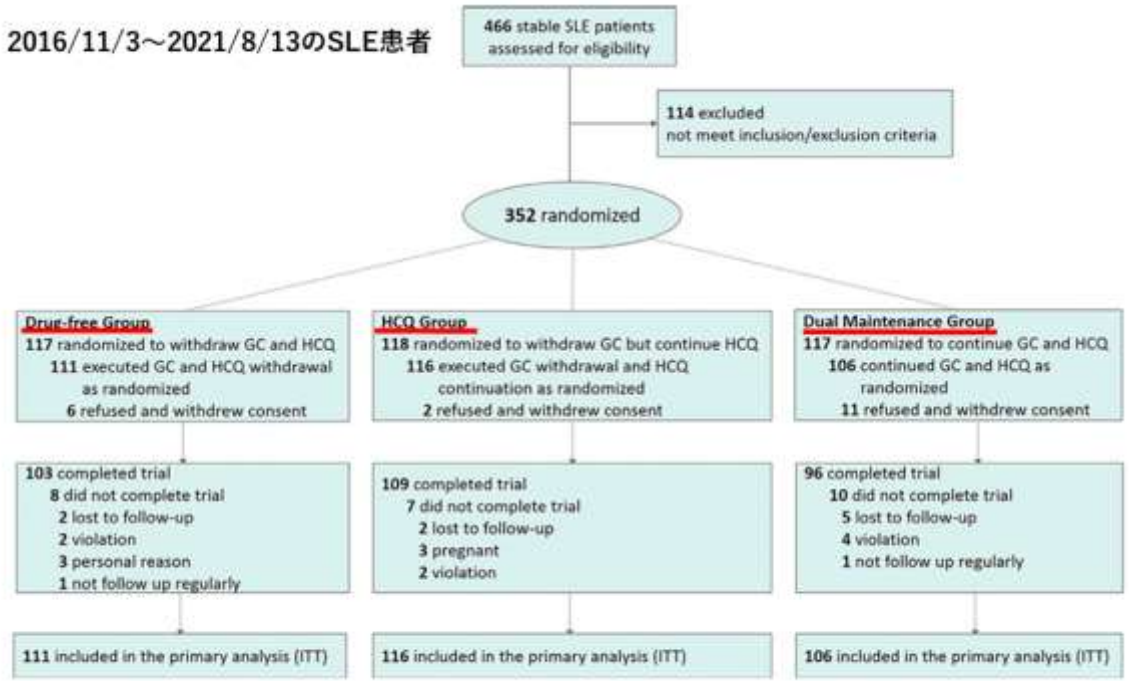


Figure 1. Study flow diagram. GC, glucocorticoids; HCQ, hydroxychloroquine; ITT, intention-to-treat analysis; SLE, systemic lupus erythematosus.

Inclusion Criteria

- 18-60歳
- **1年以上SELENA-SLEDAIが３以下を維持**し、新規の臓器障害なし
- DNA抗体ほぼ正常（免疫蛍光法で陰性、ELISAで正常２倍以下）
- C3正常下限の0.5倍以上でC3のfluctuationが最近1年間で10%以内
- 尿蛋白量≦0.5g/日
- **PSL ≦7.5mg/日を６か月以上維持**
- **HCQ以外の免疫抑制薬を最近６か月は使用していない**
- 生物学的製剤の使用歴なし
- ２年以内に重篤な臓器障害がないこと

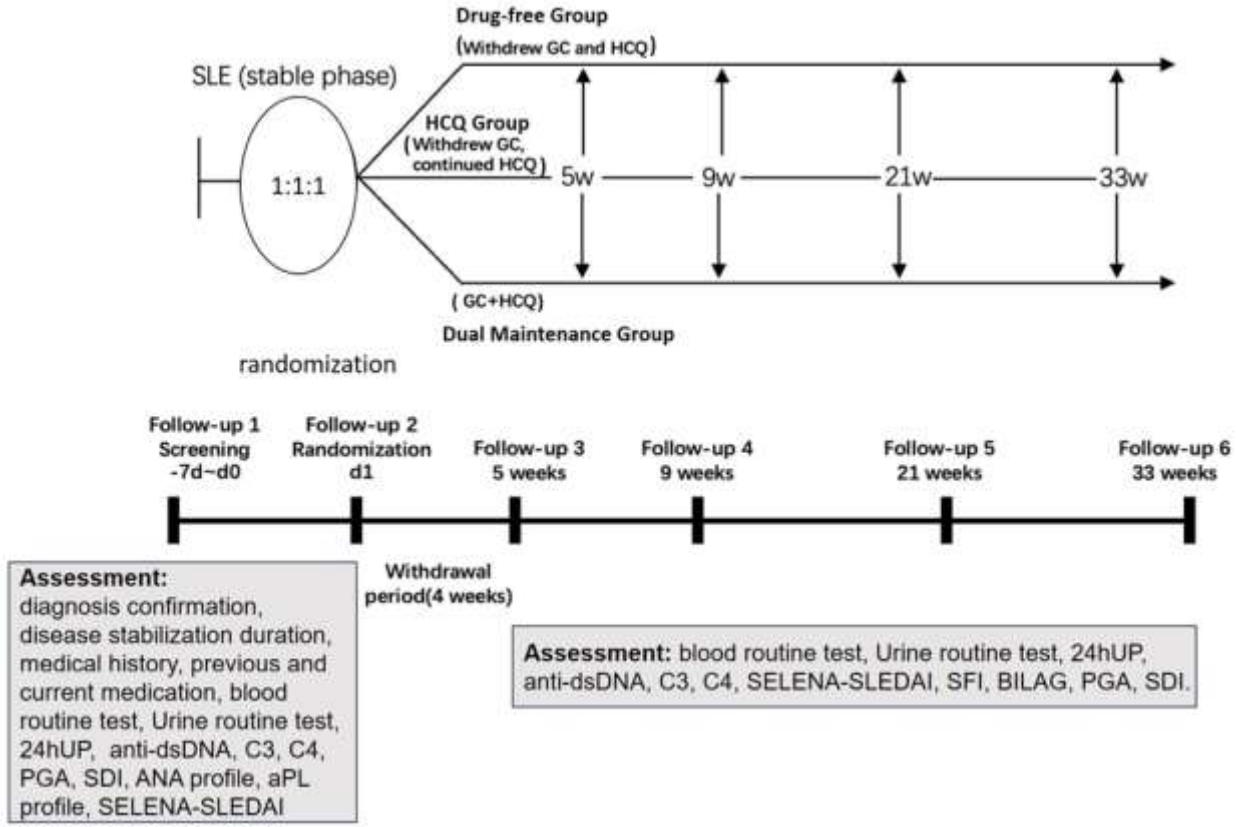
Supplementary Figure 1.

Study Protocol

Drug freeとHCQグループは
GCをベースラインの1/4ずつ1週毎に減量し４週間で中止する

Drug free グループでは
HCQを即座に中止

Dual Maintenanceグループでは
GCとHCQをそのまま続ける



Flareの定義： SFI (以下)とBILAG

Table 6. SELENA-SLEDAI flare index.

Mild/moderate flare	Severe flare
□ Change in SLEDAI > 3 points or	□ Change in SLEDAI > 12 or
□ New/worse discoid, photosensitive, profundus, cutaneous vasculitis, bullous lupus, Nasopharyngeal ulcers, Pleuritis, Pericarditis, Arthritis, or Fever (SLE) or	□ New/worse CNS-SLE; Vasculius; Nephritis; Myositis; PLT < 60.000; Hemolytic anemia: Hb <7mg/dl or decrease in Hb > 3mg/dl; Requiring: double prednisone or Prednisone>0.5 mg/kg/day or hospitalization
□ Increase in Prednisone, <0.5 mg/kg/day or	□ Prednisone >0.5 mg/kg/day
□ Added NSAID or Plaquenil	□ New Cytoxan, Azathioprine, Methotrexate, Hospitalization (SLE)
□ ≥1.0 Increase in PGA, but not to more than 2.5	□ Increase in PGA to > 2.5

Primary Endpoint

SFIで定義した再燃率

Secondary Endpoint

SLEDAI<4の割合
PGA変化の平均
BILAG Bを1以上もつ患者割合
SFI or BILAGによるsevere flareの割合
SFI or BILAGによるmild/moderate flareの割合

Drop-outした患者はBOCF (baseline-observation carried forward)法およびWOCF (worst observation carried forward)法で補完。

Statistical Analysis

Sample size calculation:

Dual maintenance group のrelapse rate 15% (at 33wk),
HCQ/drug-free groupのrelapse rate も同様と想定
significance level を片側 0.025、80%のpowerで設定すると各群89例
drop-outを20%と想定し**各群111例必要と計算した**

Two-parallel non-inferiority tests:

Drug-free vs dual maintenance group
HCQ group vs dual maintenance group
non-inferiority marginを15%の違いとした

すべての解析はITTを基本としている

Primary Endpointに関しては、Newcombe hybrid score interval methodを適用

Secondary Endpointの差に関しては、
Student t-test or Mann-Whitney U tests for continuous data
$\chi 2$ test or Fisher's exact tests for categorical data

Subgroup analysisではforest plotsで提示
Breslow-Day testでp値を各因子で算出
多変量解析はlogistic regressionを用いた

各グループの背景

Table 1

Baseline demographic and clinical characteristics of different groups

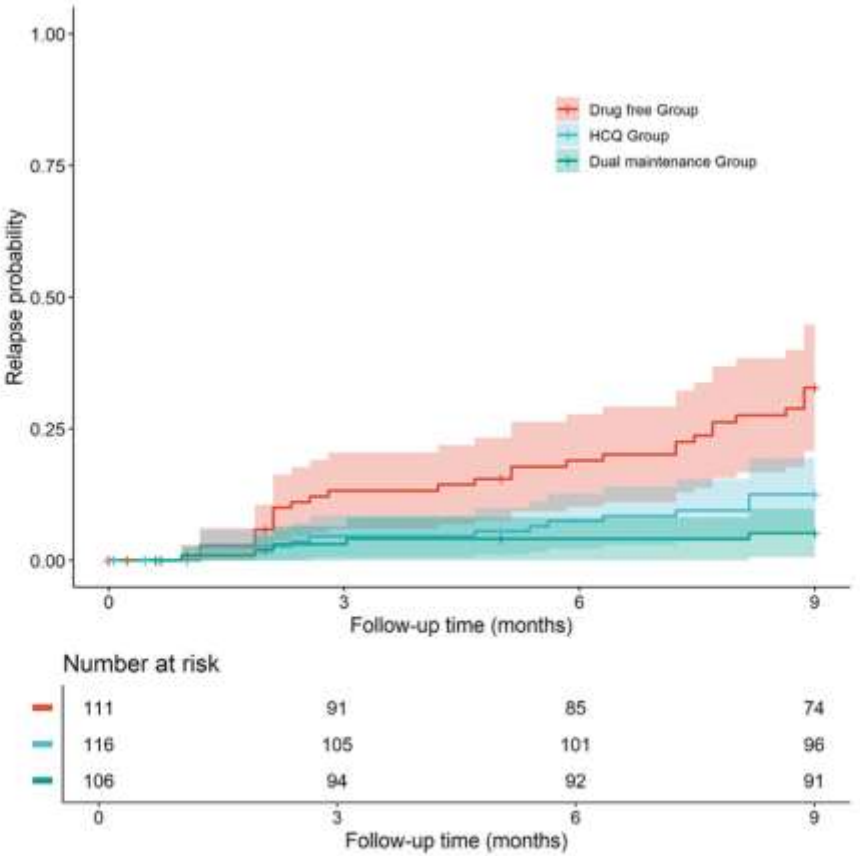
	Drug-free group (n = 111)	HCQ group (n = 116)	Dual maintenance group (n = 106)
Sex (female:male)	104:7	113:3	101:5
Average onset age (mean±SD, years)	35.3±10.1	34.7±10.3	34.4±10.7
Disease duration at enrolment (mean±SD, years)	8.0±5.6	7.2±4.5	7.4±4.5
SELENA-SLEDAI at enrolment (median, IQR)	0 (0, 2.0)	0 (0, 2.0)	0 (0, 2.0)
SELENA-SLEDAI at enrolment (mean±SD)	0.67±0.94	0.56±0.93	0.58±0.91
SELENA-SLEDAI at diagnosis (median, IQR)	9.0 (7.0, 11.0)	9.0 (6.0, 11.5)	9.0 (7.0, 12.0)
SELENA-SLEDAI at diagnosis (mean±SD)	9.86±4.14	9.16±3.93	10.37±5.01
GC dose at enrolment (mean±SD, mg)	4.37±1.98	4.06±1.97	4.13±2.01
Low-dose GC maintenance time (mean±SD, months)*	47.07±34.77	38.67±25.99	41.55±30.80
DORIS remission at enrolment (%)	57 (53.3)	72 (62.6)	59 (56.2)
History of Relapse (%)	21 (18.9)	26 (22.4)	23 (21.7)
System involvement and serological positivity in history			
Renal involvement (%)	49 (44.1)	44 (37.9)	42 (39.6)
Central nervous system involvement (%)	8 (7.2)	5 (4.3)	9 (8.5)
Haematological involvement (%)	62 (55.9)	54 (46.6)	57 (53.8)
Arthritis (%)	51 (45.9)	64 (55.2)	53 (50.0)
Rashes or mucosal ulceration (%)	77 (69.4)	80 (69.0)	78 (73.6)
Gastrointestinal tract involvement (%)	4 (3.6)	4 (3.4)	2 (1.9)
Hypocomplementaemia (%)	90 (81.1)	93 (80.2)	79 (74.5)
Anti-dsDNA positivity (%)	69 (62.2)	61 (52.6)	54 (50.9)
Antiphospholipid positivity† (%)	6/105 (5.7)	9/108 (8.4)	2/102 (2.0)
Anti-ribosomal P positivity‡ (%)	29 (26.1)	28/115 (24.3)	25 (24.0)

Primary Endpoint

各群におけるSLE再燃率と、その差の検定

Figure 2

すべての再燃by SFI



26.1%
11.2%
4.7%

p= <0.001
p= 0.077

$P_{noninferiority}$= 0.238
$P_{noninferiority}$= 0.034

Table 2の一部

Primary and secondary endpoints in two parallel non-inferiority analyses at 33 weeks

	Drug-free group vs dual maintenance group (N = 111:106)	P value	HCQ group vs dual maintenance group (N = 116:106)	P value
Cumulative relapse (%)	29 (26.1): 5 (4.7)	0.238 for non-inferiority	13 (11.2): 5 (4.7)	0.034 for non-inferiority
Median relapse time points (months)	4.7±3.0: 3.0±2.8	0.335	3.4±2.7: 3.0±2.8	0.997
Relapse by SFI (%)	29 (26.1): 5 (4.7)	**<0.001**	13 (11.2): 5 (4.7)	0.077
Mild/moderate relapse (%)	26 (23.4): 4 (3.8)	**<0.001**	10 (7.8): 4 (3.8)	0.207
Severe relapse (%)	3 (2.7): 1 (0.9)	0.622	3 (2.6):1 (0.9)	0.623

Secondary Endpoints

各群におけるSLE再燃率と、その差の検定

Table 2

Primary and secondary endpoints in two parallel non-inferiority analyses at 33 weeks

	Drug-free group vs dual maintenance group (N = 111:106)	P value	HCQ group vs dual maintenance group (N = 116:106)	P value
Cumulative relapse (%)	29 (26.1): 5 (4.7)	0.238 for non-inferiority	13 (11.2): 5 (4.7)	0.034 for n
Median relapse time points (months)	4.7±3.0: 3.0±2.8	0.335	3.4±2.7: 3.0±2.8	0.997
Relapse by SFI (%)	29 (26.1): 5 (4.7)	**<0.001**	13 (11.2): 5 (4.7)	0.077
Mild/moderate relapse (%)	26 (23.4): 4 (3.8)	**<0.001**	10 (7.8): 4 (3.8)	0.207
Severe relapse (%)	3 (2.7): 1 (0.9)	0.622	3 (2.6):1 (0.9)	0.623
Relapse by BILAG index (%)	29 (26.1): 5 (4.7)	**<0.001**	13 (11.2): 5 (4.7)	0.077
Mild relapse (%) New BILAG C	21 (18.9): 4 (3.8)	**<0.001**	7 (6.0): 4 (3.8)	0.438
Moderate relapse (%) New BILAG B	2 (1.8): 0 (0.0)	0.498	3 (2.6): 0 (0.0)	0.248
Severe relapse (%) New BILAG A	6 (5.4): 1 (0.9)	0.120	3 (2.6): 1 (0.9)	0.623
Moderate/severe (%)	8 (7.2): 1 (0.9)	**0.036**	6 (5.2): 1 (0.9)	0.122
Patients experiencing an increase in the SDI (%)	0 (0.0): 0 (0.0)	–	2 (1.7): 0 (0.0)	0.499
Mean change in PGA				
PGA≥1 and <2.5 (%)	24 (21.6): 4 (3.8)	**<0.001**	10 (8.6): 4 (3.8)	0.138
PGA≥2.5 (%)	2 (1.8): 1 (0.9)	1.000	2 (1.7): 1 (0.9)	1.000
Relapse organs				
Nephritis (%)	7 (6.3): 0 (0)	**0.014**	2 (1.7): 0 (0)	0.499
Central nervous system (%)	0 (0): 0 (0)	–	1 (0.9): 0 (0)	1.000
Leucopenia (%)	3 (2.7): 0 (0)	0.247	6 (5.2): 0 (0)	**0.030**
Thrombocytopaenia (%)	1 (0.9): 1 (0.9)	1.000	1 (0.9): 1 (0.9)	1.000
Skin/mucosa (%)	10 (9.0): 2 (1.9)	**0.022**	2 (1.7): 2 (1.9)	1.000
Arthritis (%)	5 (4.5): 1 (0.9)	0.213	1 (0.9): 1 (0.9)	1.000
Myositis (%)	0 (0): 0 (0)	–	1 (0.9): 0 (0)	1.000
Digestive system (%)	1 (0.9): 0 (0)	1.000	0 (0): 0 (0)	–

Severe relapseは
Drug freeでも稀

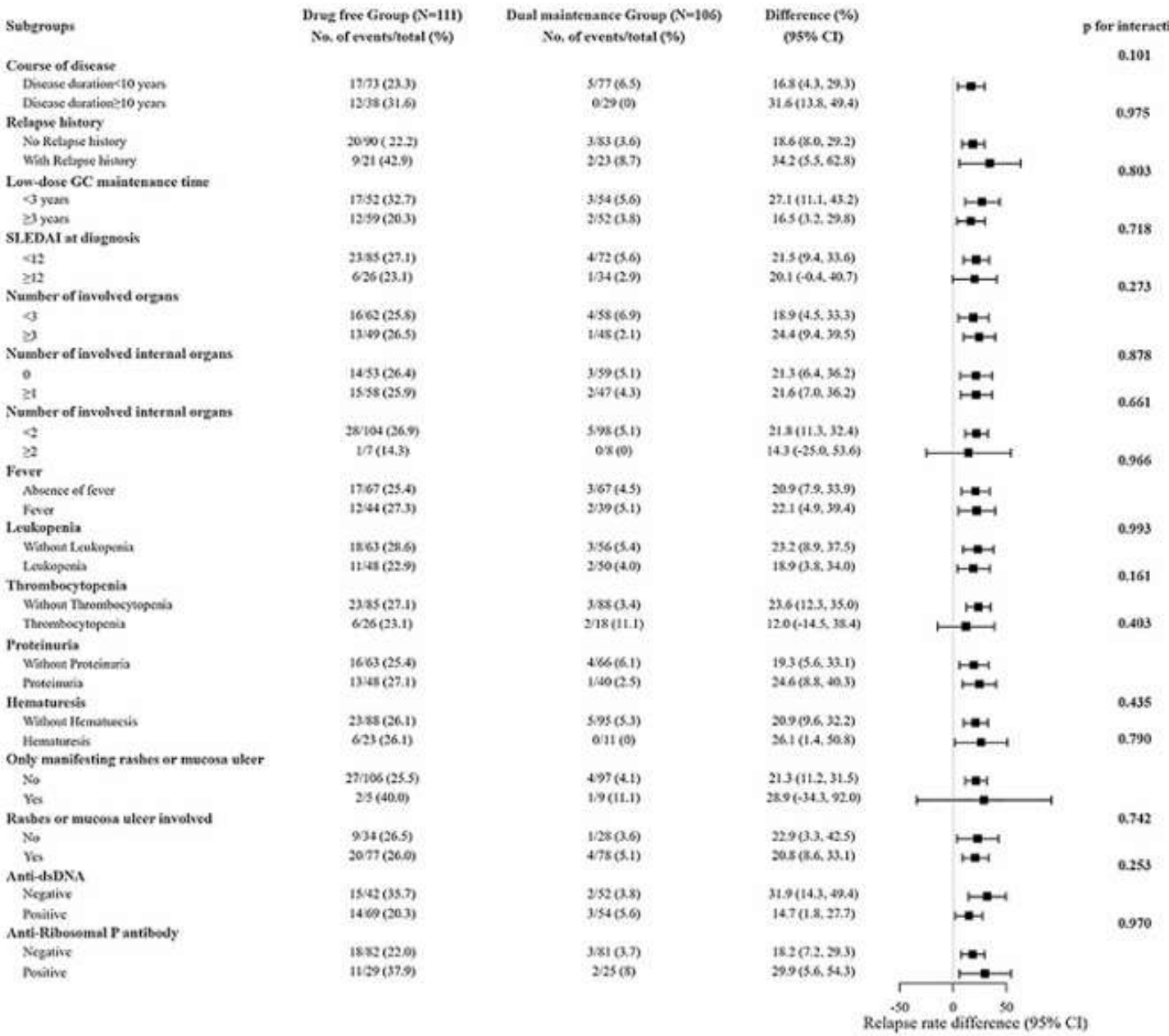
BILAGによる
再燃も同じ傾向

軽度のPGA変化
がdrug-freeで差

HCQ群では白血球減少でのみ
対照群と差。
Drug-free群では腎症と皮疹で
対照群と差。
（HCQが腎、皮疹を抑制？）

サブグループ解析（ベースラインの特徴で再燃リスクを予想できるか？）

(A)
Drug-free
vs
対照群



Subgroups	Drug free Group (N=111) No. of events/total (%)	Dual maintenance Group (N=106) No. of events/total (%)	Difference (%) (95% CI)	p for interaction
Course of disease				0.101
Disease duration<10 years	17/73 (23.3)	5/77 (6.5)	16.8 (4.3, 29.3)	
Disease duration≥10 years	12/38 (31.6)	0/29 (0)	31.6 (13.8, 49.4)	
Relapse history				0.975
No Relapse history	20/90 (22.2)	3/83 (3.6)	18.6 (8.0, 29.2)	
With Relapse history	9/21 (42.9)	2/23 (8.7)	34.2 (5.5, 62.8)	
Low-dose GC maintenance time				0.803
<3 years	17/52 (32.7)	3/54 (5.6)	27.1 (11.1, 43.2)	
≥3 years	12/59 (20.3)	2/52 (3.8)	16.5 (3.2, 29.8)	
SLEDAI at diagnosis				0.718
<12	23/85 (27.1)	4/72 (5.6)	21.5 (9.4, 33.6)	
≥12	6/26 (23.1)	1/34 (2.9)	20.1 (-0.4, 40.7)	
Number of involved organs				0.273
<3	16/62 (25.8)	4/58 (6.9)	18.9 (4.5, 33.3)	
≥3	13/49 (26.5)	1/48 (2.1)	24.4 (9.4, 39.5)	
Number of involved internal organs				0.878
0	14/53 (26.4)	3/59 (5.1)	21.3 (6.4, 36.2)	
≥1	15/58 (25.9)	2/47 (4.3)	21.6 (7.0, 36.2)	
Number of involved internal organs				0.661
<2	28/104 (26.9)	5/98 (5.1)	21.8 (11.3, 32.4)	
≥2	1/7 (14.3)	0/8 (0)	14.3 (-25.0, 53.6)	
Fever				0.966
Absence of fever	17/67 (25.4)	3/67 (4.5)	20.9 (7.9, 33.9)	
Fever	12/44 (27.3)	2/39 (5.1)	22.1 (4.9, 39.4)	
Leukopenia				0.993
Without Leukopenia	18/63 (28.6)	3/56 (5.4)	23.2 (8.9, 37.5)	
Leukopenia	11/48 (22.9)	2/50 (4.0)	18.9 (3.8, 34.0)	
Thrombocytopenia				0.161
Without Thrombocytopenia	23/85 (27.1)	3/88 (3.4)	23.6 (12.3, 35.0)	
Thrombocytopenia	6/26 (23.1)	2/18 (11.1)	12.0 (-14.5, 38.4)	
Proteinuria				0.403
Without Proteinuria	16/63 (25.4)	4/66 (6.1)	19.3 (5.6, 33.1)	
Proteinuria	13/48 (27.1)	1/40 (2.5)	24.6 (8.8, 40.3)	
Hematuresis				0.435
Without Hematuresis	23/88 (26.1)	5/95 (5.3)	20.9 (9.6, 32.2)	
Hematuresis	6/23 (26.1)	0/11 (0)	26.1 (1.4, 50.8)	
Only manifesting rashes or mucosa ulcer				0.790
No	27/106 (25.5)	4/97 (4.1)	21.3 (11.2, 31.5)	
Yes	2/5 (40.0)	1/9 (11.1)	28.9 (-34.3, 92.0)	
Rashes or mucosa ulcer involved				0.742
No	9/34 (26.5)	1/28 (3.6)	22.9 (3.3, 42.5)	
Yes	20/77 (26.0)	4/78 (5.1)	20.8 (8.6, 33.1)	
Anti-dsDNA				0.253
Negative	15/42 (35.7)	2/52 (3.8)	31.9 (14.3, 49.4)	
Positive	14/69 (20.3)	3/54 (5.6)	14.7 (1.8, 27.7)	
Anti-Ribosomal P antibody				0.970
Negative	18/82 (22.0)	3/81 (3.7)	18.2 (7.2, 29.3)	
Positive	11/29 (37.9)	2/25 (8)	29.9 (5.6, 54.3)	

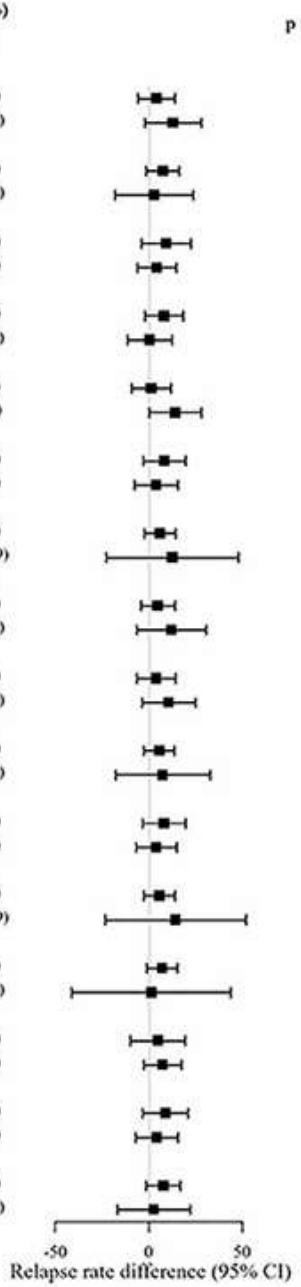
Figure 3. Forest plot of relapse in subgroups analysis with factors at baseline. (A) Forest plot of comparison of relapse with subgroup factors at baseline between drug-free group and dual maintenance Group. (B) Forest plot of comparison of relapse with subgroup factors at baseline between HCQ group and dual maintenance group. Breslow-Day test was used for subgroup analysis and p values were presented to indicate the interaction between subgroup factors and treatment groups. GC, glucocorticoid; HCQ, hydroxychloroquine; SELENA-SLEDAI, the Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index.

Drug-freeにして再燃しやすさを
ベースラインの特徴で予想することは
できなかった

サブグループ解析（ベースラインの特徴で再燃リスクを予想できるか？）

(B)
HCQ群
vs
対照群

Subgroups	HCQ Group (N=116) No. of events/total (%)	Dual maintenance Group (N=106) No. of events/total (%)	Difference (%) (95% CI)	p for interaction
Course of disease				0.145
Disease duration<10 years	9/85 (10.6)	5/77 (6.5)	4.1 (-5.7, 13.9)	
Disease duration≥10 years	4/31 (12.9)	0/29 (0.0)	12.9 (-2.2, 28.0)	
Relapse history				0.444
No Relapse history	10/90 (11.1)	3/83 (3.6)	7.5 (-1.3, 16.3)	
With Relapse history	3/26 (11.5)	2/23 (8.7)	2.8 (-18.1, 23.8)	
Low-dose GC maintenance time				0.788
<3 years	8/54 (14.8)	3/54 (5.6)	9.3 (-3.9, 22.4)	
≥3 years	5/62 (8.1)	2/52 (3.8)	4.2 (-6.1, 14.5)	
SLEDAI at diagnosis				0.585
<12	12/87 (13.8)	4/72 (5.6)	8.2 (-2.0, 18.5)	
≥12	1/29 (3.4)	1/34 (2.9)	0.5 (-11.4, 12.4)	
Number of involved organs				0.094
<3	6/73 (8.2)	4/58 (6.9)	1.3 (-9.3, 11.9)	
≥3	7/43 (16.3)	1/48 (2.1)	14.2 (0.2, 28.2)	
Number of involved internal organs				0.742
0	9/67 (13.4)	3/59 (5.1)	8.3 (-3.1, 19.8)	
≥1	4/49 (8.2)	2/47 (4.3)	3.9 (-7.8, 15.6)	
Number of involved internal organs				0.495
<2	12/108 (11.1)	5/98 (5.1)	6.0 (-2.3, 14.3)	
≥2	1/8 (12.5)	0/8 (0.0)	12.5 (-22.9, 47.9)	
Fever				0.604
Absence of fever	8/87 (9.2)	3/67 (4.5)	4.7 (-4.4, 13.9)	
Fever	5/29 (17.2)	2/39 (5.1)	12.1 (-6.3, 30.5)	
Leukopenia				0.458
Without Leukopenia	7/75 (9.3)	3/56 (5.4)	4.0 (-6.4, 14.4)	
Leukopenia	6/41 (14.6)	2/50 (4.0)	10.6 (-3.7, 25.0)	
Thrombocytopenia				0.704
Without Thrombocytopenia	8/89 (9.0)	3/88 (3.4)	5.6 (-2.6, 13.8)	
Thrombocytopenia	5/27 (18.5)	2/18 (11.1)	7.4 (-17.8, 32.7)	
Proteinuria				0.969
Without Proteinuria	10/70 (14.3)	4/66 (6.1)	8.2 (-3.3, 19.7)	
Proteinuria	3/46 (6.5)	1/40 (2.5)	4.0 (-6.9, 15.0)	
Hematuresis				0.388
Without Hematuresis	12/109 (11.0)	5/95 (5.3)	5.7 (-2.6, 14.1)	
Hematuresis	1/7 (14.3)	0/11 (0.0)	14.3 (-23.3, 51.9)	
Only manifesting rashes or mucosa ulcer				0.557
No	12/108 (11.1)	4/97 (4.1)	7.0 (-1.1, 15.1)	
Yes	1/8 (12.5)	1/9 (11.1)	1.4 (-41.2, 44.0)	
Rashes or mucosa ulcer involved				0.956
No	3/36 (8.3)	1/28 (3.6)	4.8 (-9.8, 19.3)	
Yes	10/80 (12.5)	4/78 (5.1)	7.4 (-2.6, 17.4)	
Anti-dsDNA				0.539
Negative	7/55 (12.7)	2/52 (3.8)	8.9 (-3.2, 21.0)	
Positive	6/61 (9.8)	3/54 (5.6)	4.3 (-7.1, 15.7)	
Anti-Ribosomal P antibody				0.440
Negative	10/87 (11.5)	3/81 (3.7)	7.8 (-1.3, 16.8)	
Positive	3/28 (10.7)	2/25 (8.0)	2.7 (-16.7, 22.1)	



HCQ群の再燃しやすさを
ベースラインの特徴で予想
することもできなかった

多変量解析（ベースラインの特徴で再燃リスクを予想できるか？）

Supplementary Table: Logistic regression of factors associated with the primary endpoint

	Odds Ratio	95% Confidence Limits		P
Drug-free Group vs Dual Maintenance Group	6.71	2.33	19.31	***<0.001***
HCQ Group vs Dual Maintenance Group	2.55	0.82	7.88	0.967
Sex: female vs male	3.91	0.42	36.76	0.234
Onset age	0.95	0.90	1.00	***0.046***
Age at enrolment	1.05	0.99	1.11	0.085
Duration (years)	1.022	0.953	1.097	0.534
SLEDAI at enrolment	1.13	0.75	1.72	0.553
SLEDAI at diagnosis	0.96	0.85	1.09	0.509
Fever	2.25	1.00	5.02	***0.049***
Renal involvement	0.96	0.39	2.38	0.935
Central nervous system	0.45	0.05	4.26	0.489
Skin/mucosa	1.21	0.53	2.79	0.650
Arthritis	0.89	0.39	2.02	0.783
Leukopenia	0.67	0.31	1.49	0.329
Haemolytic anaemia	1.23	0.22	6.95	0.817
Thrombocytopenia	1.33	0.54	3.27	0.537
Low-dose GC maintenance time (months)	0.992	0.979	1.004	0.185
Coombs test	0.17	0.02	1.75	0.135
Anti-ribosomal P positivity	2.26	1.00	5.09	0.050
Prednisone (or equivalent) at enrolment （>5mg/d vs ≤5mg/d）	2.86	1.12	7.30	***0.029***

若いほど再燃しやすい

熱があると再燃しやすい

発症時の
障害臓器、DNA抗体、
低補体は再燃リスクに
ならなかった（本文）

組み入れ時のPSLが多い
方が再燃しやすい

有害事象

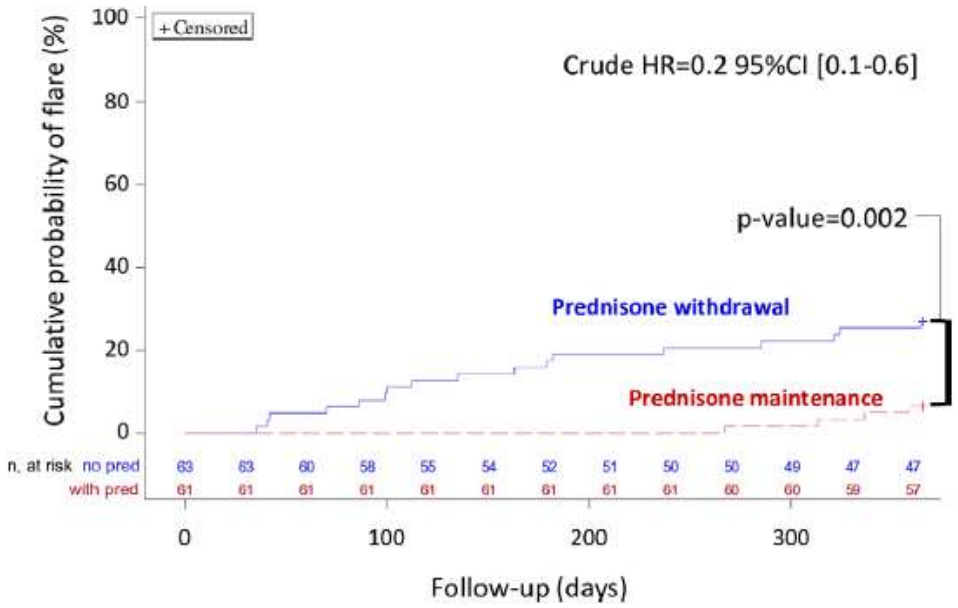
スタディ期間中に重篤な有害事象は全体で１例のみ（HCQ群の心筋梗塞）
ドロップアウトした患者にも有害事象関連はなかった

Discussion

＜過去の類似報告＞ **GC中止不可**

Withdrawal of low-dose prednisone in SLE patients with a clinically quiescent disease for more than 1 year: a randomised clinical trial

Mathian A et al., ARD 2020; 79: 339



PSL 5mgで１年以上安定したSLE患者をRCTでPSL突然中止群（hydrocortisone 20mg/d 1カ月後）と維持群に分け
１年間の再燃率を比較。サブ解析でもRisk予測因子なし（HCQ含め）

本研究とよく似た試験。上記試験の4人に１人はIS使用されていた
しかし、本研究のHCQ群の方がrelapse rateが低い

GC中止可能

Gradual Glucocorticosteroid Withdrawal Is Safe in Clinically Quiescent Systemic Lupus Erythematosus

Tselios K et al., ACR Open Rheumatol 2021; 3: 550

Table 2. Flare rates at 12 and 24 months and damage accrual at 24 months

	Maintenance Group (n = 102)	Withdrawal Group (n = 102)	*P* Value
Flares at 12 months			
Flare (first definition)[a]	30 (29.4)	18 (17.6)	0.023
Flare (second definition)[b]	14 (13.7)	11 (10.8)	0.467
Flare (third definition)[c]	12 (11.8)	7 (6.9)	0.197
Flares at 24 months			
Flare (first definition)[a]	51 (50)	34 (33.3)	0.01
Flare (second definition)[b]	28 (27.5)	15 (14.7)	0.024
Flare (third definition)[c]	27 (26.5)	13 (12.7)	0.013
Damage accrual at 24 months			
Related to glucocorticosteroids	12 (11.8)	3 (2.9)	0.02
Not related to glucocorticosteroids	7 (6.9)	4 (3.9)	0.317
Increase in SDI	18 (17.6)	7 (6.9)	0.022

Abbreviation: SDI, Systemic Lupus International Collaborating Clinics Damage Index; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index-2000; SMD, standardized mean difference.
Data are given as n (%).
[a] Any increase in clinical SLEDAI-2K (excluding serology).
[b] Any increase in clinical SLEDAI-2K plus treatment escalation (for glucocorticosteroids, antimalarials or immunosuppressives).
[c] Any increase ≥4 in clinical SLEDAI-2K.

PSL 5mgで安定したSLE患者を後ろ向きに維持群と２年以内の中止群に分け、Propensity scoreをmatchさせて再燃率の差をみた。
GC中止群の方が再燃率が低かった。
サブ解析でもリスク予測因子なし（HCQ at baseline含め）

＜過去の類似報告（続き）＞

Risk factors of flare in patients with systemic lupus erythematosus after glucocorticoids withdrawal. A systematic review and meta-analysis

Lanlan Ji et al., Lupus Sci Med 2022; 9: e000603

SACQ

GC中止不可

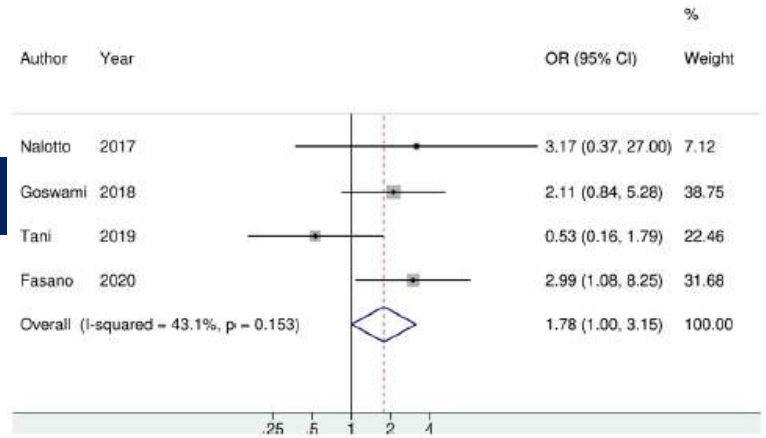
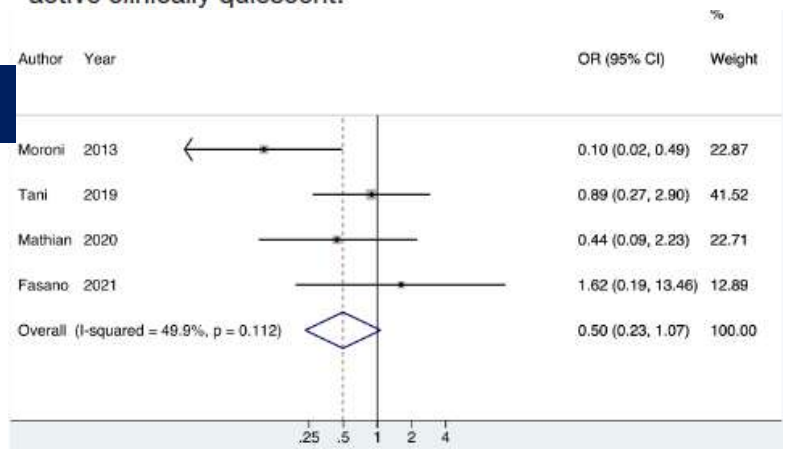


Figure 4 Forest plots of the OR for the risk of flare in patients who stopped glucocorticoids regarding serologically active clinically quiescent.

HCQ

GC中止可能



GC中止論文のsystematic review.
SACQ, ageがflare risk。HCQ(-)はflare傾向

引用されていない重要論文

GC減量可能

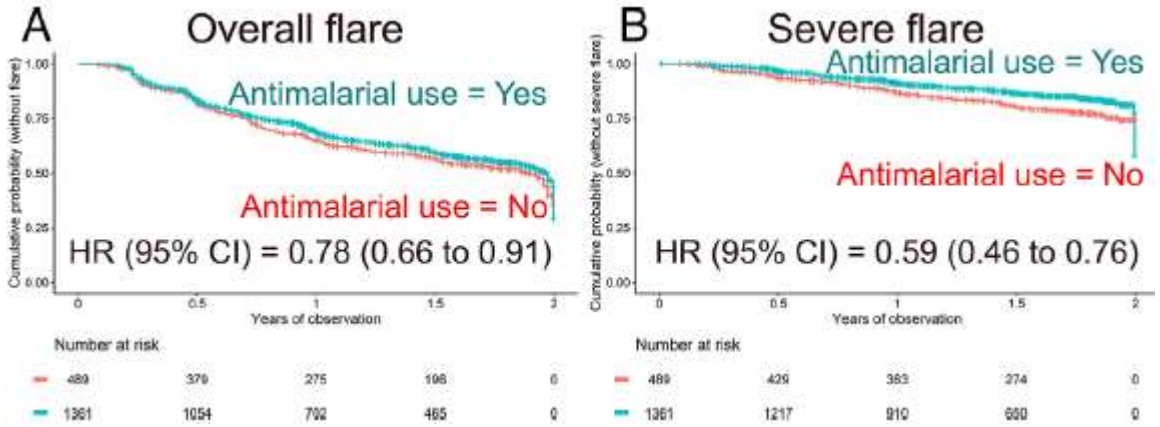
Risk of flare and damage accrual after tapering glucocorticoids in modified serologically active clinically quiescent patients with systemic lupus erythematosus: a multinational observational cohort study

Katsumata Y et al., ARD 2024; 83: 998

Table 2 The risk of subsequent flare or damage accrual per 1 mg decrease of prednisolone in mSACQ patients with SLE assessed using Cox proportional hazard models

Initial prednisolone-equivalent GC dosage (mg/day)	Overall flare HR (95% CI)	Severe flare HR (95% CI)	Damage accrual HR (95% CI)
0≤ and ≤7.5	1.02 (0.99 to 1.05)	0.98 (0.96 to 1.004)	0.97 (0.96 to 0.99)
	P value=0.27	P value=0.11	P value=0.007
	742 events	271 events	180 events
0≤ and ≤5	1.02 (0.98 to 1.06)	0.98 (0.96 to 1.01)	0.98 (0.96 to 1.01)
	P value=0.41	P value=0.28	P value=0.25
	555 events	197 events	133 events
5< and ≤7.5	1.01 (0.96 to 1.06)	0.98 (0.92 to 1.03)	0.96 (0.93 to 0.99)
	P value=0.84	P value=0.41	P value=0.007
	187 events	74 events	47 events

Cox proportional hazard models were used to assess the risk of subsequent flare or damage accrual per 1 mg decrease of prednisolone, adjusting for other covariates listed in table 3. Factors/covariates except 'initial prednisolone-equivalent GC dosage' were those at subsequent visits.
GC, glucocorticoid; mSACQ, modified serologically active clinically quiescent; SLE, systemic lupus erythematosus.



Asia-Pacific Lupus Collaborationの前向き収集データ解析
PSL 1mgずつ減量のflare riskでみるとFlare risk上昇しない
HCQはflare riskを下げる

Discussion続き

- どのような患者がGC freeを達成できるかのrisk因子はより大きなスタディが必要。
- 本研究でもリスク因子検索を試みたが、皮膚粘膜症状のみの患者がHCQでGC freeで再燃抑制できるとわかったのみ。

＜Limitation＞

1. Short follow up period
2. Sample size
3. Not a multiethnic study
4. 主解析で行ったImputationの方法（BOCF)。十分バイアスリスクを回避できない。