IMPACT OF LUPUS NEPHRITIS FLARES ON HEALTHCARE UTILIZATION: A RETROSPECTIVE COHORT STUDY IN THE UNITED STATES BETWEEN 2016 AND 2025

EE186

Jiying Zou,[1] Huong Trinh,[1] Jesse Sussell,[1] Shu Wang,[2] Anisha M. Patel,[1] William F. Pendergraft III,[1] Lisa Lindsay[1]

[1]Genentech, Inc., South San Francisco, CA, USA; [2]Genesis Research, Hoboken, NJ, USA.

To access this poster, scan the QR code or go to the following URL: https://go.roche.link/02zwy33f

BACKGROUND

- Systemic lupus erythematosus (SLE) is a chronic progressive autoimmune condition characterized by periods of unpredictable disease flares[1]
- Approximately 50% of individuals with SLE will develop lupus nephritis (LN), caused by immune complex deposition, inflammation, and glomerular damage in the kidneys[2]
- Declining kidney function over time can lead to severe clinical outcomes such as end-stage kidney disease, dialysis, transplant, and death[2,3]
- LN flares are associated with irreversible nephron loss. Therefore, prevention of LN flares is an important treatment goal[2,4]
- Characterizing the impact of LN flares on healthcare utilization (HCU) will provide additional evidence regarding the societal burden of LN flares

OBJECTIVE

- This real-world study assessed incremental HCU by encounter type (inpatient, outpatient, and emergency room visits) due to LN flares among individuals receiving routine care

METHODS

Retrospective matched cohort study design: De-identified patient electronic health record (EHRs) from a US-based network of healthcare organizations representing approximately 118 million individuals

Study period: January 1, 2016, to May 31, 2025

Index date: date on which the initial criteria for LN were met, between January 1, 2018, and May 31, 2024

Study population: adults with LN (based on diagnosis in ≥1 inpatient or ≥2 outpatient encounters separated by ≥7 days) who had:
- evidence of presence in the EHR in each of the two years pre-index; baseline (index ±90 days) urine protein-to-creatinine ratio (UPCR) ≥0.5 g/g and estimated glomerular filtration rate (eGFR) results;
- >1 additional post-baseline UPCR and eGFR result;
- no prior dialysis or kidney transplant

LN flares identified if any of the following occurred:
- eGFR decrease >20% compared with baseline
- Increase in UPCR >1 if UPCR <0.2 g/g; or UPCR >2.0 g/g if UPCR ≥0.2 and ≤1.0 g/g; or doubling if UPCR >1 g/g compared with baseline UPCR value
- Receipt of IV methylprednisolone ≥100 mg AND a SLE/LN diagnostic code (International Classification of Diseases, Ninth Revision [ICD-9] 710 or 580-583 [excluding 581.2, 582.2, 583.2, 583.6 and 583.7] or Tenth Revision [ICD-10] M32) occurring in the patient's record ±14 days of the injection

Risk set matching with propensity scores:
- Individuals with LN flares were matched 1:1 without replacement to patients without an LN flare within comparable 365-day periods post-index using a propensity score (PS) derived from the likelihood of experiencing a flare from a logistic model that included demographic and clinical characteristics[a,b]

LN flare date: Date when an individual first met the criteria for an LN flare within 90 days post-index

Flare date assignment:
- Flare date: the date an individual first met flare criteria >90 days post-index (provided they had 365 days of continuous follow-up after the flare)
- Pseudo-flare date: a reference date assigned to matched "control" patients who did not flare in the time period that mirrors the time post-index of the individual who had an LN flare

HCU analyses: HCU rate for inpatient, outpatient, and emergency room encounters in the 365 days post-LN flare and pseudo-flare date were tallied, and the HCU rate ratio and rate difference by flare status was estimated using negative binomial modeling with a cluster-robust variance estimator

Description of HCU encounters post-LN flare: Top diagnosis, symptom, and procedure codes were ranked by post-LN flare frequency (within 365 days) and displayed using Pareto charts and a table for procedures to identify key contributors to the post flare encounters

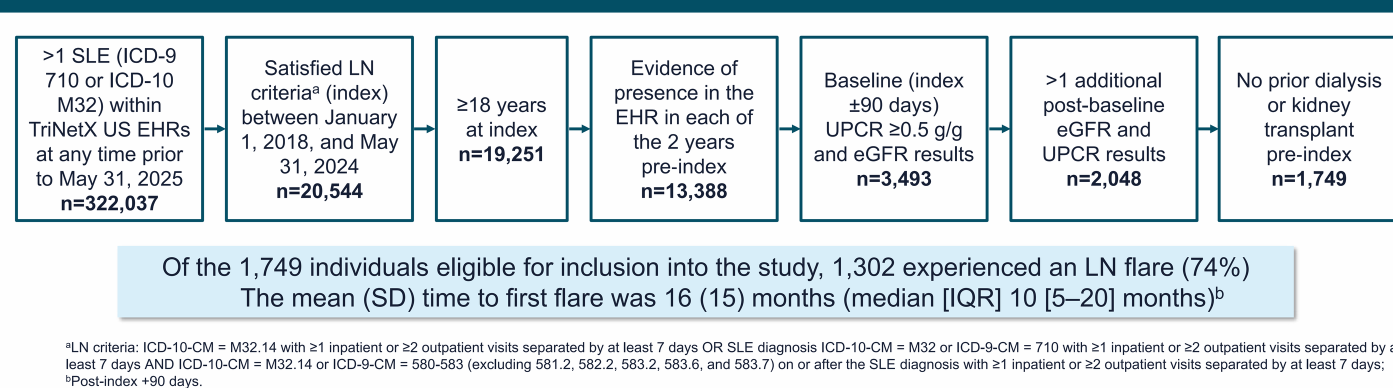
[a]Age, race, incident vs prevalent LN, evidence of kidney biopsy, baseline chronic kidney disease (CKD) stage 3+, hypertension, diabetes; [b]Controls matched at the time of flare were required to be flare-free for ≥365 days beyond the match date and have quarterly alignment in their matched follow-up periods, in addition to being within a 0.2 standard deviation (SD) caliper PS range; one-way cross-over was allowed for patients who were flare negative but subsequently flared; covariate balance was assessed using standardized mean differences post-matching; variables with an absolute standardized mean differences <0.1 were considered well-balanced.

CONCLUSIONS

- LN flares significantly increased the annual rate of inpatient, outpatient, and emergency room visits compared with matched individuals who did not experience an LN flare, demonstrating the importance of sustained disease control for both patients and society
- LN flares affect multiple bodily systems beyond the kidneys. Among the most commonly affected are the cardiovascular, hematologic, esophageal/gastrointestinal, musculoskeletal, metabolic/endocrine and respiratory systems

RESULTS

Figure 1. Patient Attrition



Of the 1,749 individuals eligible for inclusion into the study, 1,302 experienced an LN flare (74%)
The mean (SD) time to first flare was 16 (15) months (median [IQR] 10 [5–20] months)[b]

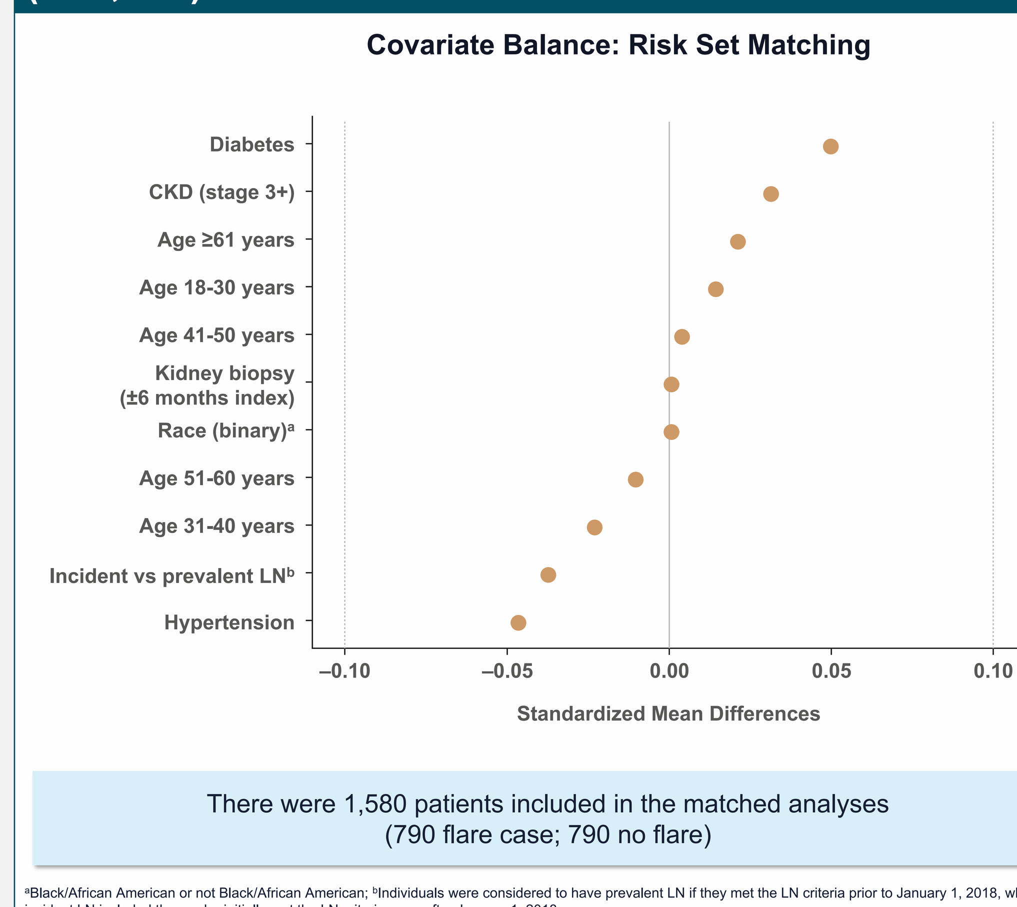
[a]LN criteria: ICD-10-CM = M32.14 with ≥1 inpatient or ≥2 outpatient visits separated by at least 7 days OR SLE diagnosis ICD-10-CM = M32 or ICD-9-CM = 710 with ≥1 inpatient or ≥2 outpatient visits separated by at least 7 days AND ICD-10-CM = M32.14 or ICD-9-CM = 580-583 (excluding 581.2, 582.2, 583.2, 583.6, and 583.7) on or after the SLE diagnosis with ≥1 inpatient or ≥2 outpatient visits separated by at least 7 days; [b]Post-index +90 days.

Table 1. Description of Study Population (Pre-Matched) Overall and According to Subsequent Lupus Nephritis Flare

	Overall (N=1,749)	LN Flare (N=1,302)	No LN Flare (N=447)	p-value[a]
Follow-up, months, mean (SD)	58 (24)	62 (23)	48 (23)	<0.001
Age, years, mean (SD)	40 (15)	41 (15)	39 (15)	0.042
Sex, n (%)				
Female	1,459 (84)	1,087 (84)	372 (83)	0.826
Male	281 (16)	207 (16)	74 (17)	
Race, n (%)				
Asian	141 (8)	101 (8)	40 (9)	0.001
Black/African American	729 (42)	578 (44)	151 (34)	
White	559 (32)	390 (30)	169 (38)	
Other/Unknown	320 (18)	233 (18)	87 (19)	
Ethnicity, n (%)				
Hispanic or Latino	318 (18)	236 (18)	82 (18)	0.902
Non-Hispanic or Latino	1,177 (67)	874 (67)	303 (68)	
Unknown	254 (15)	192 (15)	62 (14)	
LN status, n (%)				
Incident	942 (54)	635 (49)	307 (69)	<0.001
Prevalent	807 (46)	667 (51)	140 (31)	
Kidney biopsy pre-index to 6 months post-index, n (%)	1,008 (58)	725 (56)	283 (63)	0.006
Baseline CKD stage 3+, n (%)	934 (53)	770 (59)	164 (37)	<0.001
Baseline hypertension, n (%)	1,470 (84)	1,123 (86)	347 (78)	<0.001
Baseline diabetes, n (%)	242 (14)	208 (16)	34 (8)	<0.001
Baseline medication (±90 days of index), n (%)				
ACE/ARB/SGLT2i	703 (40)	525 (40)	178 (40)	0.896
Antimalarial	888 (51)	635 (49)	253 (57)	0.005
Systemic glucocorticoid steroids	1,095 (63)	796 (61)	299 (67)	0.035
Immunosuppressant (any of following):	1,093 (62)	797 (61)	296 (66)	0.067
MMF/MPA	843 (48)	606 (47)	237 (53)	0.021
MTX	25 (1)	20 (2)	5 (1)	0.681
AZA	120 (7)	90 (7)	30 (7)	0.971
CyC	114 (7)	88 (7)	26 (6)	0.558
CNI	143 (8)	102 (8)	41 (9)	0.429
Belimumab	93 (5)	59 (5)	34 (8)	0.017
Rituximab	70 (4)	51 (4)	19 (4)	0.865

[a]p-values calculated using Wilcoxon rank-sum test for continuous variables and Chi-squared and Fisher's Exact test for categorical/binary variables.

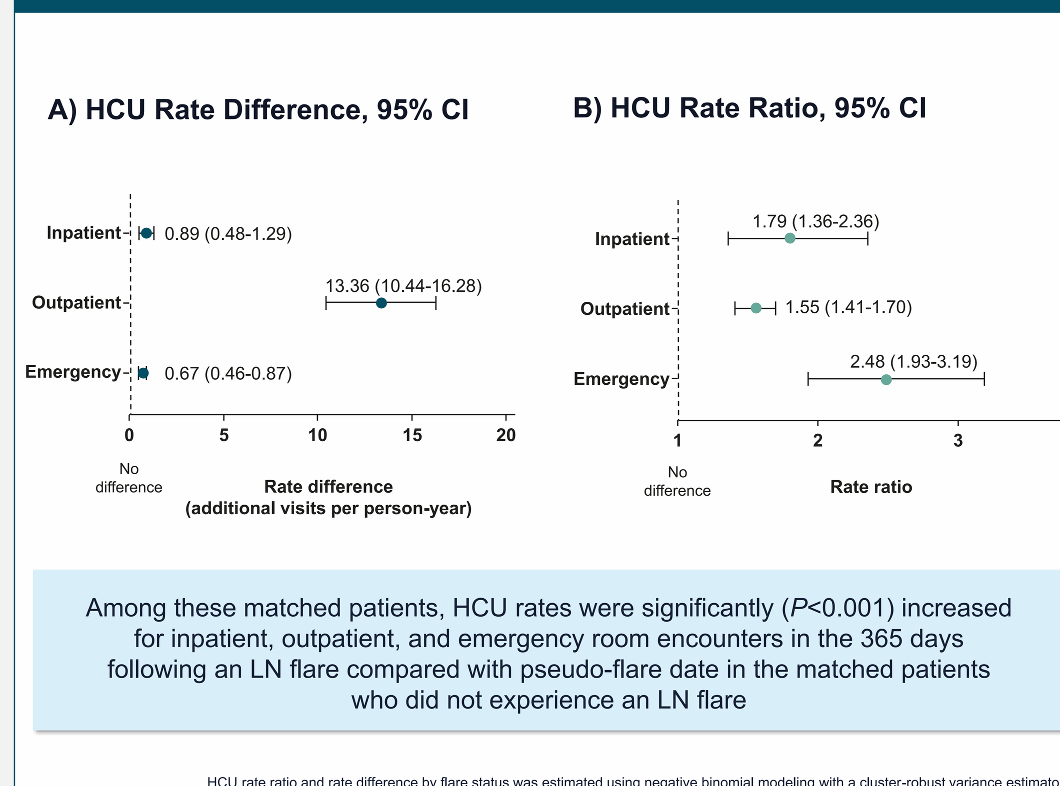
Figure 2. Standardized Mean Difference for Covariates Following Propensity Score Matching (n=1,580)



There were 1,580 patients included in the matched analyses (790 flare case; 790 no flare)

[a]Black/African American or not Black/African American; [b]Individuals were considered to have prevalent LN if they met the LN criteria prior to January 1, 2018, whereas incident LN included those who initially met the LN criteria on or after January 1, 2018.

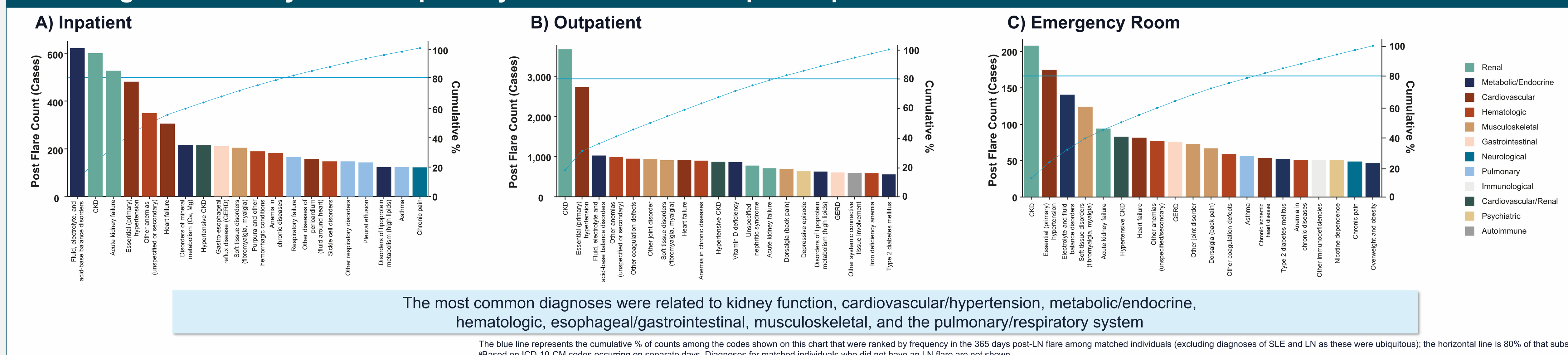
Figure 3. Inpatient, Outpatient, and Emergency Room Healthcare Utilization Among Individuals Who Experience a Lupus Nephritis Flare Compared with Matched Non-Flare Patients



Among these matched patients, HCU rates were significantly ($P<0.001$) increased for inpatient, outpatient, and emergency room encounters in the 365 days following an LN flare compared with pseudo-flare date in the matched patients who did not experience an LN flare

HCU rate ratio and rate difference by flare status was estimated using negative binomial modeling with a cluster-robust variance estimator.

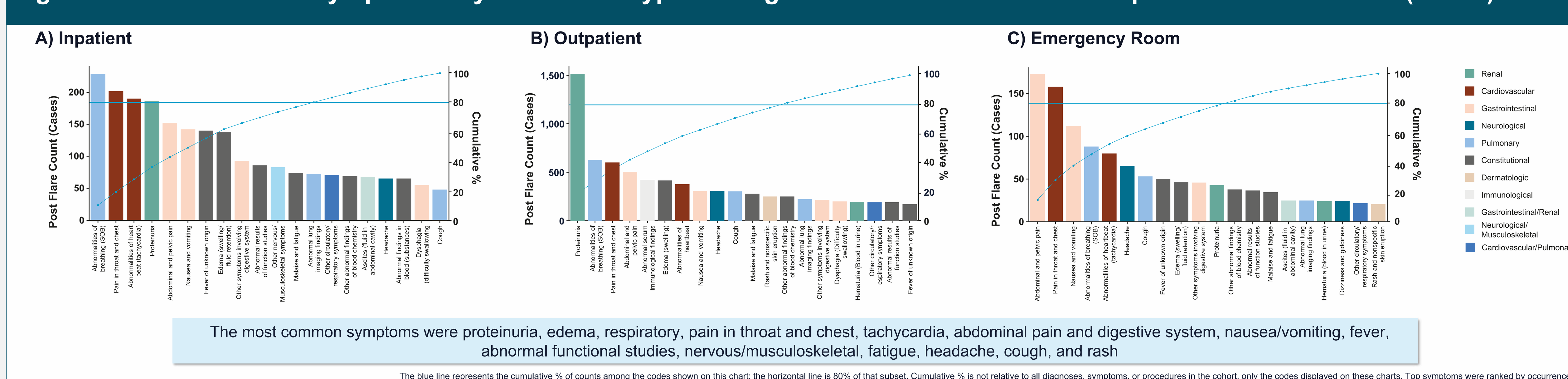
Figure 4. Most Common Diagnoses by Encounter Type Among Matched Individuals Who Experienced an LN Flare (n=790),[a] Excluding Codes for Systemic Lupus Erythematosus and Lupus Nephritis



The most common diagnoses were related to kidney function, cardiovascular/hypertension, metabolic/endocrine, hematologic, esophageal/gastrointestinal, musculoskeletal, and the pulmonary/respiratory system

The blue line represents the cumulative % of counts among the codes shown on this chart that were ranked by frequency in the 365 days post-LN flare among matched individuals (excluding diagnoses of SLE and LN as these were ubiquitous); the horizontal line is 80% of that subset. [a]Based on ICD-10-CM codes occurring on separate days. Diagnoses for matched individuals who did not have an LN flare are not shown.

Figure 5. Most Common Symptoms[a] by Encounter Type Among Matched Individuals Who Experienced an LN Flare (n=790)



The most common symptoms were proteinuria, edema, respiratory, pain in throat and chest, tachycardia, abdominal pain and digestive system, nausea/vomiting, fever, abnormal functional studies, nervous/musculoskeletal, fatigue, headache, cough, and rash

The blue line represents the cumulative % of counts among the codes shown on this chart; the horizontal line is 80% of that subset. Cumulative % is not relative to all diagnoses, symptoms, or procedures in the cohort, only the codes displayed on these charts. Top symptoms were ranked by occurrence in 365 days post flare and displayed using Pareto charts to identify key contributors to the post flare encounters. [a]Based on ICD-10-CM "R" codes occurring on separate days among matched individuals who had an LN flare. Symptoms for matched individuals who did not have an LN flare are not shown.

Table 2. Frequency of Most Common Procedures[a] in 365 Days Post Flare/Pseudo Flare in Matched Individuals by Health Encounter Type

Procedure Category	Inpatient			Outpatient			Emergency Room		
	Flare	No Flare	p<0.05	Flare	No Flare	p<0.05	Flare	No Flare	p<0.05
Pathology and Laboratory	19,846	2,775	*	47,223	20,773	NS	5,162	1,218	*
Immunization and injection/Infusions	2,147	324	NS	7,173	2,535	*	1,239	271	NS
Imaging and Radiology	1,649	435	*	3,189	1,737	*	902	325	*
Cardiovascular	958	202	*	1,914	569	*	587	153	NS
Biopsy/Surgery	627	194	*	1,552	678	NS	152	29	NS
Pulmonary	458	61	NS	570	267	NS	131	29	NS
Anesthesiology	70	18	NS	117	59	NS	31	13	NS
Dialysis	79	3	*	330	2	*	8	0	NS

LN flares significantly increased the need for procedures in the 365 days post flare compared with matched patients who did not experience an LN flare, including pathology/laboratory tests, imaging, cardiovascular, surgery and dialysis

[a]Based on current procedural terminology and Healthcare Common Procedure Coding System codes occurring in the 365 days post flare and post-pseudo-flare date. P value based on Fisher's exact test. Procedures were counted only once per patient day; thus, procedures occurring >1 time per day may be undercounted.

Presented at ISPOR 2026; May 17–20, 2026; Philadelphia, USA

REFERENCES

1. Piga M, et al. *Best Practice & Res Clin Rheum.* 2023;101938;
2. Anders HJ, et al. *Nat Rev Dis Primers.* 2020;6:7;
3. Mahajan A, et al. *Lupus.* 2020;29:1011–1020;
4. Kidney Disease: Improving Global Outcomes (KDIGO) Lupus Nephritis Work Group. *Kidney Int.* 2024;105:S1–S69.

ABBREVIATIONS

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; AZA, azathioprine; CI, confidence interval; CKD, chronic kidney disease; CM, clinical modification; CNI, calcineurin inhibitor; CyC, cyclophosphamide; EHR, electronic health record; eGFR, estimated glomerular filtration rate; GERD, gastro-esophageal reflux disease; HCU, healthcare utilization; ICD-9 or ICD-10, International Classification of Diseases, Ninth or Tenth Revision; IQR, interquartile range; IV, intravenous; LN, lupus nephritis; MMF, mycophenolate mofetil; MPA, mycophenolic acid; MTX, methotrexate; NS, not significant; PS, propensity score; RD, rate difference; RR, rate ratio; SGLT2i, sodium-glucose transport 2; SLE, systemic lupus erythematosus; SOB, shortness of breath; UPCR, urine protein-to-creatinine ratio.

DISCLOSURES

J. Zou, H. Trinh, J. Sussell, A.M. Patel, W. F. Pendergraft III, and **L. Lindsay** are employees of Genentech, Inc. and shareholders of F. Hoffmann-La Roche Ltd.
S. Wang is an employee of Genesis Research Group LLC.

ACKNOWLEDGMENTS

We thank all study participants, the staff, and the study investigators.

This study was funded by F. Hoffmann-La Roche Ltd.
Editorial assistance was provided by Nucleus Global and funded by F. Hoffmann-La Roche Ltd.