Supplemental Material

METHODS

Exclusion criteria

Key exclusion criteria were severe, active lupus nephritis (as assessed by the investigator or urine protein/creatinine ratio of >200 mg/mmol or estimated creatinine clearance <30 mL/min); severe, active central nervous system (CNS) or peripheral neurologic disease; use of oral prednisone >40 mg/day (or equivalent); change in antimalarial or immunosuppressant dose within 30 days of baseline; initiation of immunosuppressants within 90 days of baseline; intravenous immunoglobulin treatment within 180 days of baseline; previous treatment with any B-cell targeted therapies; or previous treatment with any biologic therapy within 90 days or 5 half-lives of baseline. Recipients of plasmapheresis or a live vaccine within 90 days of baseline and patients with any infection or serious infection within 30 days of screening or 90 days of baseline, respectively, or who had any recent surgery, malignancy, or any condition or event that, in the investigator's opinion, would pose an unacceptable risk to the patient were excluded. Patients with active hepatitis B, hepatitis C, human immunodeficiency virus (HIV), or evidence of active or untreated latent tuberculosis and women who were pregnant or breastfeeding were also excluded.

Pharmacodynamic and safety assessments

Blood samples were collected for determination of serum tabalumab concentrations and pharmacodynamic markers of biologic activity (eg, changes in total B cells, B-cell subsets, mean B-cell activating factor [BAFF] level, and immunoglobulins [IgG, IgM, and IgA]). B cells and B-cell subsets were assessed by flow cytometry. BAFF levels were assessed by an assay that detected total BAFF and did not differentiate between free and tabalumab-bound BAFF. Safety assessments were conducted at every visit. These included all adverse events (AEs), serious AEs (SAEs), treatment-emergent AEs (TEAEs), adverse events of special interest, the Columbia-Suicide Severity Rating Scale (C-SSRS), vital signs, and clinical laboratory data. AEs of special interest included infection, major adverse cardiovascular events (MACE), malignancies, injection-site reactions, allergic/hypersensitivity reactions, and depression-associated events. Infections could be further classified as serious or severe. Serious infections were defined as events resulting in hospitalization, a congenital anomaly or death, or an event that is persistently

incapacitating, life threatening, or significant for any other reason. Severe infections were rated as such by investigators on a mild, moderate, or severe scale. MACE events were adjudicated in a blinded manner by an external committee to ensure all events were judged uniformly by the same group using the same definition. The Quick Inventory of Depressive Symptomatology (QIDS-SR16) was assessed every 6 months. Anti-drug antibodies (ADAs) were assessed approximately every 3 months.

Supplemental Table 1. SELENA-SLEDAI Organ Improvement at Week 52

	120 Q2W n=381	120 Q4W n=378	Placebo n=379
CNS	n=6	n=3	n=6
	0	2 (66.7)	4 (66.7)
Vascular	n=28	n=29	n=30
	17 (60.7)	13 (44.8)	17 (56.7)
Musculoskeletal	n=315	n=294	n=305
	175 (55.6)	161 (54.8)	156 (51.1)
Renal	n=35	n=40	n=42
	18 (51.4)	23 (57.5)	19 (45.2)
Mucocutaneous	n=342	n=344	n=346
	126 (36.8)	103 (29.9)	108 (31.2)
Cardiovascular and respiratory	n=27	n=24	n=25
	13 (48.1)	16 (66.7)	15 (60.0)
Immunologic	n=268	n=282	n=271
	43 (16.0)	48 (17.0)	23 (8.5)
Constitutional	n=5	n=4	n=5
	2 (40.0)	3 (75.0)	4 (80.0)
Hematologic	n=39	n=40	n=46
	19 (48.7)	21 (52.6)	21 (45.7)

Abbreviations: CNS, central nervous system; Q2W, every 2 weeks; Q4W, every 4 weeks; SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index.

FIGURE CAPTION

Supplemental Figure 1. Pharmacodynamic outcomes. **A)** Mean change in total B cells over the 52-week treatment period. **B-D)** Mean change in serum immunoglobulin G, M, and A, respectively, over the 52-week treatment period. *p≤0.05 vs. placebo; **p≤0.001 vs. placebo. Abbreviations: Q2W: every 2 weeks; Q4W: every 4 weeks.