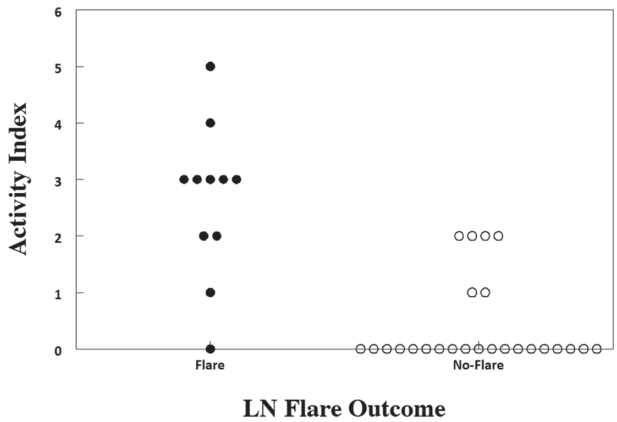
patients in histologic remission are candidates for withdrawal of therapy.
Trial registration ClinicalTrial. gov, NCT02313974



Abstract CT-02 Figure 1 Persistent histologic activity on repeat biopsy after clinical remission is associated with renal flare after withdrawal of maintenance immunosuppression

CT-03 PHASE 2 TRIAL OF INDUCTION THERAPY WITH ANTI-CD20 (RITUXIMAB) FOLLOWED BY MAINTENANCE THERAPY WITH ANTI-BAFF (BELIMUMAB) IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS

[1]Cynthia Aranow*, [2]Maria Dall'Era, [3]Margie Byron, [4]Linna Ding, [5]Dawn Smilek, [1]Betty Diamond, [2]David Wofsy, on behalf of the CALIBRATE investigators and Lupus Nephritis Trials Network. *[1]Feinstein Institute for Medical Research, Manhasset; [2]University of California, San Francisco; [3]Rho Federal Systems, Inc, Chapel Hill; [4]National Institute of Allergy and Infectious Diseases, Bethesda; [5]Immune Tolerance Network (ITN), San Francisco, USA*

10.1136/lupus-2018-lsm.75

Background Despite case series suggesting efficacy, controlled trials of anti-CD20 in lupus nephritis (LN) did not confirm benefit (*Arthritis Rheum* 2012;64:1215 and 2013;65:2368).
Objectives One possible explanation for this failure stems from the fact that B cell depletion stimulates production of B cell activating factor (BAFF) which, in turn, facilitates maturation of autoreactive B cells in lymphoid organs or during B cell repopulation. The CALIBRATE study (NCT 02260934) was designed to test this hypothesis, to determine whether addition of anti-BAFF could enhance the clinical effects of anti-CD20, and to assess safety of the combination.
Methods Forty-three patients with active LN despite conventional treatment enrolled in a prospective randomized open-label trial that compared two treatment strategies. All subjects received iv rituximab (1000 mg), CTX (750 mg), and methylprednisolone (100 mg) at wks 0 and 2, followed by 40 mg/d prednisone tapered to 10 mg/d by wk 12. At wk 4, subjects received either belimumab (10 mg/kg iv at wks 4, 6, 8 and then every 4 wks) plus prednisone (n=21) or prednisone alone (n=22). Complete response (CR) was defined as: (i) urine protein:creatinine ratio (UPCR) <0.5; (ii) eGFR >120 or, if <120, eGFR >80% of screening; and (iii) prednisone tapered to 10 mg/d. The definiton of partial response (PR) differed only in the UPCR criterion (>50% reduction).
Results The clinical outcome at wk 24 was similar in both groups (table 1). The CR rate was 24% in the belimumab group (RCB) and 23% in the control group (RC). Three subjects in each group withdrew (WD) prior to wk 24 (two withdrawals in each group due either to progressive nephritis or an infusion reaction, and one in each group for reasons unrelated to SLE or its treatment). B cell depletion from blood was virtually absolute in both groups at wk 12, but the pace of recovery differed. Six subjects experienced serious adverse events between wks 0 and 24; three subjects in the RC group (pneumonia followed by LN flare; deep vein thrombosis; SLE flare); and three subjects in the RCB group (anti-CD20 infusion reaction; soft-tissue abscesses prior to anti-BAFF treatment; quadriceps tendon rupture).
Conclusions An interim analysis of data from CALIBRATE shows: (i) anti-BAFF following anti-CD20 for LN did not improve clinical outcome at week 24; (ii) anti-BAFF delayed blood B cell reconstitution following B cell depletion; and (iii) anti-BAFF following anti-CD20 was not associated with hypogammaglobulinemia or an increase in serious infections. Further analyses at 48 weeks and beyond will address how anti-BAFF therapy affects quantitative and qualitative recovery of B cells as well as long-term clinical outcome.

Abstract CT-03 Table 1

					Median B Cell Count			Median IgG Level	
	CR	PR	NR	WD	Wk0	Wk12	Wk24	Wk0	Wk24
RC Group	23%	23%	41%	14%	105	1	31	1050	1100
RCB Group	24%	24%	38%	14%	143	1	3	984	837

Acknowledgements Conducted by ITN with support from NIAID (UM1AI109565) and Genentech.
Trial registration NCT02260934

CT-04 SAFETY AND EFFICACY OF ALLOGENEIC UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS (MSCS) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS OF AN OPEN-LABEL PHASE I STUDY

Diane L Kamen*, Paul J Nietert, Hongjun Wang, Tara Duke, Colleen Cloud, Angela Robinson, Gary S Gilkeson. *Medical University of South Carolina, Charleston SC, USA*

10.1136/lupus-2018-lsm.76

Background Mesenchymal stem cells (MSCs) are known to possess significant immunosuppressive properties, and their use in refractory SLE is supported by promising safety and efficacy in autoimmune animal models and human trials. We conducted this phase I open-label study to test the hypothesis that a single infusion of human allogeneic umbilical cord-derived MSCs (IND 16377) is safe when added to standard-of-care therapy for active SLE. The primary safety outcome is frequency of Grade 3 or higher adverse events (AEs) by Week 24. The primary efficacy outcome is change in SLE disease activity between Baseline and Week 24 measured by SLEDAI score and prednisone dose.

Abstract CT-04 Table 1

		SLEDAI Score						
Subject	Baseline Age, Race/Ethnicity, Sex	Baseline	Week 4	Week 8	Week 12	Week 24	Non-Serious AEs (#)	SAE (#)
1	32 yo Black Female	6	4	2	0	0	3 Grade 1 5 Grade 2 0 Grade≥3	0
2	38 yo Caucasian Female	8	8	8	2	2	0 Grade 1 2 Grade 2 0 Grade≥3	0
3	33 yo Caucasian Female	6	12	8	Dropped out	Dropped out	2 Grade 1 2 Grade 2 0 Grade≥3	1
4	26 yo Hispanic Female	10	8	15	10	6	0 Grade 1 3 Grade 2 0 Grade≥3	0
5	48 yo Caucasian Female	8	2	0	2	0	1 Grade 1 1 Grade 2 0 Grade≥3	0
6	38 yo Black Female	11	5	8	8	5	1 Grade 1 1 Grade 2 0 Grade≥3	0

Methods Patients (n=6) with active SLE (SLEDAI ≥6) who signed informed consent and met all inclusion and exclusion criteria sequentially received 1×10^6 cells/kg umbilical cord-derived MSCs given as an IV infusion in Plasma-Lyte A solution. Post-infusion, Week 1 and 2 safety data from each participant was reviewed by the Data Safety Monitoring Board prior to enrolling the next patient. Primary safety and efficacy endpoints were determined at Week 24. Each patient is followed for a total of 52 weeks.

Results Table 1 summarizes the demographics, visit SLEDAI scores, number of serious and non-serious adverse events (SAEs, AEs). The 6th participant completed their Week 24 visit on April 11, 2018. To date, there has been 1 SAE, deemed not unexpected and not attributed to investigational product. No non-serious AEs higher than Grade 2 by NCI-CTCAE scoring were reported. The SAE was prolonged hospitalization following a partial dose infusion of rituximab IV leading to anaphylaxis. Rituximab was started for persistent SLE disease activity (patient dropped out of the study after Week 8) and was given in the hospital ICU setting due to her prior history of anaphylaxis to Tween (polyethoxylated surfactant found in IV and SQ medications). Anaphylaxis resulted in a prolonged hospital stay of 2 days, resolving with treatment without sequelae. The SAE was attributed to her known allergy to ingredients in the rituximab infusion and deemed unrelated to the MSCs that she received several months earlier. The AEs 'possibly' attributable to the investigational product were Grade 2 nausea, Grade 2 tachycardia, and Grade 1 flushing with Grade 1 toe paresthesias – all of which resolved without sequelae.

Among the 5 patients who completed their Week 24 evaluations, all showed improved SLE activity (mean SLEDAI score 8.6 ±1.9 at Baseline improved to 2.6±2.8 at Week 24) with stable or lower doses of prednisone and stable background immunosuppressants. Mean physician global assessment (PGA) scores also improved from 1.71±0.48 at Baseline to 0.32±0.17 at Week 24.

Conclusions A single-dose of umbilical cord-derived MSCs was safe and well-tolerated in this open-label phase I trial for 6 patients with active SLE. Initial efficacy data for MSCs in SLE appears promising and will be further tested in a larger controlled trial.

Acknowledgements We would like to thank all of the study participants for their time and commitment to the study. This research study was supported by grants from the Lupus Foundation of America and the National Institutes of Health: National Institute of Allergy and Infectious Diseases (R34 AI114453) and the South Carolina Clinical and Translational Research (SCTR) Institute at the Medical University of South Carolina (UL1 RR029881).

Trial registration NCT 03171194

CT-05 ALTERNATIVE AVAILABLE DRUG DEVELOPMENT PATHWAYS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Lee S Simon*. *SDG LLC, Cambridge, USA*

10.1136/lupus-2018-lsm.77

Background Development of drugs in SLE is difficult for many reasons including the heterogeneity of the disease, the outcome measures used to define responsiveness which are cumbersome, poorly responsive to change and have little relationship to clinical practice. The drugs targets are potentially immunosuppressive in an immunologically compromised host. Regulatory agencies require large safety databases associated with the development programs. Consideration of alternate pathways for approval may be warranted. In Europe and the US the Orphan Drug Designation allows for therapies to be approved on far smaller data bases, at typically less cost and patient burden.