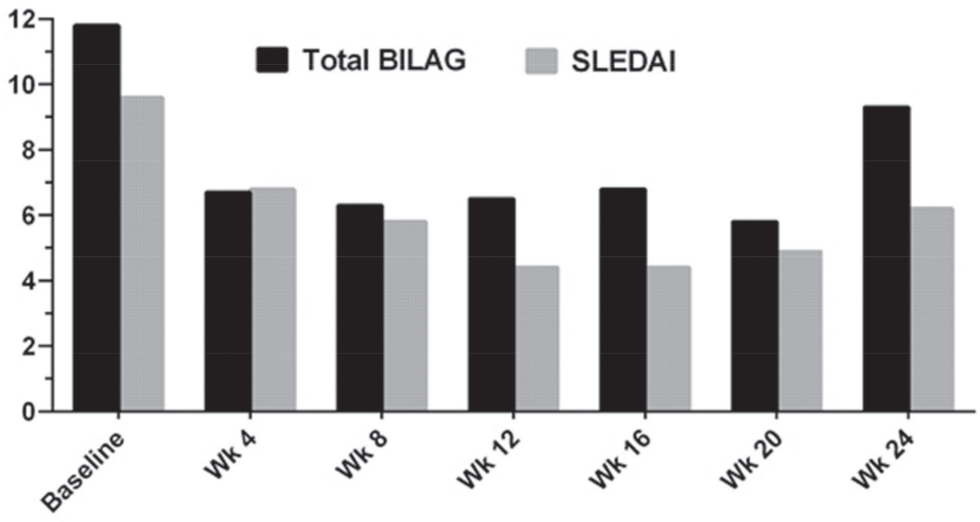

Abstract CT-01 Figure 1 Mean total BILAG and mean SLEDAI at baseline and then every 4 weeks until week 24

was suspended with patients currently being randomised under double-blind conditions to receive treatment with 250 mg doses, a reduced dose of 100 mg, or placebo control.

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Trial Registration Clinicaltrials.gov identifier: NCT01845740

CT-02 FEATURES OF PATIENTS SCREENED FOR CALIBRATE (RITUXIMAB PLUS CYCLOPHOSPHAMIDE FOLLOWED BY BELIMUMAB FOR THE TREATMENT OF LUPUS NEPHRITIS); HYPOGAMMAGLOBULINEMIA IS FREQUENT IN PATIENTS WITH MARKED ELEVATION OF URINARY PROTEIN

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Background Treatment options for lupus nephritis (LN) are limited by imperfect efficacy and multiple toxicities; new approaches are needed. Autoreactive B cells are attractive therapeutic targets given their pathogenic role in LN. However, a prospective randomised LN trial of B cell depletion with rituximab did not demonstrate improved efficacy. It is likely that the high levels of BAFF that exist following B cell depletion facilitate the maturation of autoreactive B cells. This autoreactivity may contribute to the limited clinical response. We have hypothesised that administration of an anti-BAFF reagent following B cell depletion will result in an enhanced, sustained clinical response.

Materials and methods CALIBRATE is a trial assessing the safety of belimumab following B cell depletion in patients with non-naïve LN (relapsed LN or LN that is resistant to therapy). Forty subjects will receive treatment with rituximab and cyclophosphamide; 20 will be randomised to receive belimumab for up to 1 year, 20 will receive no other therapy except for glucocorticoids. Efficacy and mechanistic outcomes at 1 and 2 years will also be evaluated. Given the ability of both rituximab and belimumab to depress serum IgG levels, levels of IgG are determined at screening in order to follow the combined effect of rituximab and belimumab on IgG and risk of infection during the CALIBRATE trial. We now present the characteristics of subjects screened for this study.

Results CALIBRATE has screened 27 patients. Demographic and clinical features at screening are shown in Table 1. Patients with a Up/c ratio >3 were 16 times (95% CI: 1.4, 767.3) more likely to have IgG levels ≤450 mg than patients with Up/c ≤3. Furthermore Up/c correlated inversely with serum IgG ($r = -0.524$, $p = 0.0050$).

Abstract CT-02 Table 1 Demographic and clinical features of patients screened for the CALIBRATE study

Age, years mean (SD)	30.2 (8.29)
Gender N (%)	
Male	4 (14.8)
Female	23 (85.2)
Race N (%)	
White	10 (37.0)
Black	7 (25.9)
Other/Unknown	10 (37.0)
ISN Class N (%)	
Class III	2 (7.4)
Class IV	5 (18.5)
Class V + III	5 (18.5)
Class V + IV	15 (55.6)
Up/c r ratio mean (SD)	3.99 (3.333)
Up/c ratio > 3 N (%)	14 (51.9)
Up/c ratio ≤ 3 N (%)	13 (48.1)
Serum IgG mean (SD)	938.26 (547.684)
Hypogammaglobulinemia (IgG ≤ 450) N (%)	9 (33.3)
IgG ≤ 450 with Up/c ratio > 3 N (%)	8 (57.1)
IgG ≤ 450 with Up/c ratio ≤ 3 N (%)	1 (7.7)

Conclusions Physicians caring for lupus patients do not routinely measure IgG, even when considering initiation of rituximab or belimumab, therapies known to reduce serum IgG levels . We report that 33% of patients with non-naïve LN and >50% of patients with Up/c >3 are hypogammaglobulinemic. Transient

hypogammaglobulinemia was previously demonstrated in almost 1/3 of LN subjects participating in a study of abatacept and cyclophosphamide (ACCESS study) and did not associate with serious infections. Proteinuria correlated inversely with serum IgG. Our preliminary findings demonstrate that a considerable number of patients with active, non-naïve LN are hypogammaglobulinemic, and confirm an inverse association between IgG levels with proteinuria. The CALIBRATE trial will follow levels of serum IgG and urinary protein prospectively and will monitor patients for the potential development of infectious events.

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Trial Registration ClinicalTrials.gov Identifier: NCT02260934

CT-03 ANIFROLUMAB REDUCES DISEASE ACTIVITY IN MULTIPLE ORGAN DOMAINS IN PATIENTS WITH MODERATE TO SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Anifrolumab was evaluated in a Phase IIb study of adults with moderate to severe systemic lupus erythematosus (SLE), in which 305 patients received intravenous infusions of anifrolumab (300 mg, 1000 mg) or placebo for 48 weeks. Global disease activity was reduced in both dose groups compared with placebo, although a more favourable risk-benefit profile was observed with the 300-mg dose. This analysis of the Phase IIb study compared the impact of anifrolumab on individual organ domains in patients.

Materials and methods Changes from baseline in organ domain activity were assessed at Week 52 using the SLE Disease Activity Index 2000 (SLEDAI-2K) and British Isles Lupus Assessment Group (BILAG). SLEDAI domain improvement required a lower score compared with baseline in at least one of its components. BILAG organ domain improvement was defined as the transitioning from "A" or "B" to a lower score.

Results The majority of patients had baseline involvement of the mucocutaneous and/or musculoskeletal domains of SLEDAI-2K and BILAG. A greater percentage of anifrolumab-treated patients demonstrated improvement in these frequently involved domains compared with placebo (Table 1). Potential benefits were observed in most of the other less frequently active domains, including SLEDAI-2K cardiorespiratory, vascular, haematological, and constitutional; and BILAG cardiorespiratory and constitutional domains. In patients with baseline involvement in the SLEDAI-2K immunological domain (positive anti–double-stranded DNA [anti-dsDNA] and/or low complement level), normalisation of anti-dsDNA and/or hypocomplementemia were seen more frequently at Day 365 in patients receiving anifrolumab compared with placebo (Table 1). However, among patients who had a normal anti-dsDNA and/or normal complements at baseline, a slightly greater number of patients in the 300-mg anifrolumab group had an increase in the score representing the development of a new anti-dsDNA or hypocomplementemia compared with baseline (Table 1).

Conclusions Treatment with anifrolumab resulted in greater rates of improvement in multiple organ domains compared with placebo. The greatest impact was seen with 300-mg anifrolumab.

Abstract CT-03 Table 1 Changes from baseline in organ domain activity at Day 365

	Placebo	Anifrolumab 300 mg*	*P*-Value	Anifrolumab 1000 mg*	*P*-Value
Organ domain improvement at Day 365					
BILAG, n (%)					
Mucocutaneous	24/87 (27.6)	49/84 (58.3)	<0.001	33/82 (40.2)	0.069
Musculoskeletal	47/95 (49.5)	64/94 (68.1)	0.005	54/91 (59.3)	0.149
SLEDAI-2K, n (%)					
Mucocutaneous	38/100 (38.0)	61/99 (61.6)	<0.001	51/102 (50.0)	0.082
Musculoskeletal	42/99 (42.4)	55/97 (56.7)	0.032	50/98 (51.0)	0.197
Immunological	4/53 (7.5)	9/43 (20.9)	0.068	18/59 (30.5)	0.004
Organ domain worsening at Day 365					
SLEDAI-2K, n (%)					
Immunological	7/79 (8.9)	11/82 (13.4)	–	6/79 (7.6)	–

*Every 28 days from Day 1 to Day 337. BILAG, British Isles Lupus Assessment Group; SLEDAI-2K, SLE Disease Activity Index 2000

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CT-04 USING THE AMERICAN COLLEGE OF RHEUMATOLOGY AND SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS CRITERIA TO MEASURE DISEASE SEVERITY IN DISCOID LUPUS ERYTHEMATOSUS

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Backgroun d Discoid lupus erythematosus (DLE) progresses to systemic lupus erythematosus (SLE) in up to 28% of cases. The 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria were developed to improve the American College of Rheumatology (ACR) criteria. So far, the SLICC criteria have not been evaluated in DLE.

Methods This is a case-control study comparing patients with DLE who meet ACR and/or SLICC criteria for SLE against patients with DLE-only disease. The data was obtained from an ongoing database with 142 DLE patients at Penn and from their respective medical records.

Results Using the ACR criteria, 75 (53%) patients were classified as DLE/SLE and 67 (47%) as DLE-only, compared with 66 (47%) DLE/SLE and 76 (53%) DLE-only patients using the SLICC criteria ($p = 0.08$). This net increase of eight patients meeting ACR criteria was due to the presence of the photosensitivity criterion and fewer immunologic criteria under ACR. Due to the