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

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

CT-02

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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).

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
Background Anifrolumab was evaluated in a Phase Ib 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 trial compared the impact of anifrolumab on individual organ domains.

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 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.