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TREATMENT OF SLE WITH THE IMMUNOPROTEASOME INHIBITOR KZR-616: RESULTS FROM THE FIRST 4 COHORTS OF THE MISSION STUDY, AN OPEN-LABEL PHASE 1B DOSE ESCALATION TRIAL

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Background Subcutaneous (SC) administration of KZR-616 (30 and 45 mg weekly [QW]) was demonstrated as safe and well-tolerated, and successfully achieved target levels of immunoproteasome inhibition in healthy volunteers.^{1,2}

Methods SLE patients in this open-label multicenter dose escalation trial received KZR-616 at doses of 45 mg (Cohort 1), 60 mg (Cohort 2), or 30 mg with escalation to 60 mg (Cohorts 2a and 2b) subcutaneously weekly through Week 13 (W13) with 12 weeks of follow-up.

Results As of 16 January 2020, 33 patients had enrolled and received at least 1 dose of KZR-616. The majority of TEAEs have been mild or moderate with no reported peripheral neuropathy, prolonged GI-related AEs, and no clinically significant laboratory AEs. When compared to baseline, improvement in measures of disease activity were seen at W13 and beyond. A single patient with active class IV/V nephritis who failed prior treatment with tacrolimus was enrolled on prednisone 10 mg, leflunomide 10 mg, and hydroxychloroquine 200 mg/day; nephrotic-range proteinuria at baseline (3.85 g/day) decreased to 0.6 g/day 4 weeks after the last dose of KZR-616.

Conclusions Weekly SC administration of KZR-616 at 45 and 60 mg was safe and well-tolerated. Evidence of disease suppression at W13 was observed, and 94% of evaluable patients had improvements on at least 2 measures/assessments of disease activity. In addition, one study participant with active proliferative nephritis (LN) was enrolled with significant reduction in proteinuria. The Phase 2 portion of this study in active proliferative LN is open for enrollment.

REFERENCES

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BELIMUMAB IN THE TREATMENT OF 38 PORTUGUESE SLE PATIENTS: A REAL-LIFE MULTICENTRIC STUDY

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Background Belimumab, an anti-BLyS monoclonal antibody, is the first biologic available for SLE treatment. We studied its effectiveness and safety in clinical practice.

Abstract P131 Table 1 Evolution of SLEDAI, anti-dsDNA antibodies and C3 levels at 6, 12 and 24 months of belimumab and its significance compared to baseline values.

	Baseline	6 months	12 months	24 months
SLEDAI - mean±SD	8.2±3.9	3.8±2.2 (p<0.001)	4.1±3.2 (p<0.001)	3.1±1.6 (p=0.002)
Anti-dsDNA antibodies (UI/mL) - mean±SD	231.6 ±238.3	155.3±198.7 (p=0.025)	157.9±341.1 (p=0.031)	107.4±132.2 (p=0.003)
C3 (mg/dL) - mean±SD	82.6±28.8	89.6±27.1 (p=0.223)	94.6±25.8 (p=0.018)	100.9±36.9 (p=0.139)

Methods Multicentric cohort study of SLE patients, fulfilling the 2012 SLICC classification criteria, treated with belimumab in rheumatology departments and registered in the Portuguese registry *Reuma.pt*.

Results Thirty-eight patients were included: 37 (97.4%) female, aged 46.2±13.9 years, mean disease duration of 11.9±8.6 years. The reasons for prescribing belimumab were: multiorgan involvement in 20 (52.6%), haematologic disorders in 9 (23.7%), cutaneous manifestations in 5 (13.0%), arthritis in 3 (7.9%), necrotizing vasculitis in 1 (2.6%). Belimumab was administered intravenously for a mean of 22.3±20.3 months.

SRI response was achieved in 14/27 (51.9%), 12/20 (60%) and 11/12 (91.7%) at 6, 12 and 24 months of belimumab treatment, respectively. Mean SLEDAI significantly decreased from 8.2±3.9 at baseline to 3.8±2.2, 4.1±3.2 and 3.1±1.6 at 6, 12 and 24 months, respectively.

Anti-dsDNA antibodies significantly decreased at 6, 12 and 24 months and C3 increased at 12 months of belimumab (table 1). We found a significant reduction in mean daily prednisolone dosage (p<0.001) from baseline (10.8±5.1 mg) to the last evaluation under belimumab (5.5±3.0 mg).

Eleven (28.9%) patients discontinued belimumab: loss of effectiveness in 4, lost to follow-up in 4, adverse events in 3 (urinary tract infections, acute myocardial infarction, breast cancer). Three presented infections related to belimumab.

Conclusions We confirmed belimumab effectiveness and safety in real-life active SLE patients.

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DESIGN OF AN ADAPTIVE, PHASE 2, PLACEBO-CONTROLLED, DOSE-RANGING STUDY TO ASSESS THE EFFICACY AND SAFETY OF AMG 570 IN SUBJECTS WITH ACTIVE SLE AND INADEQUATE RESPONSE TO STANDARD OF CARE THERAPY

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Background/Purpose Current SLE treatment options have limited efficacy and potential toxicities that impede an individual's ability to remain on therapy. AMG 570 is a bispecific antibody inhibiting both ICOSL and BAFF that engages ICOSL on antigen-presenting cells (dendritic cells and B cells) and reduces circulating naïve B cells in healthy subjects. This phase 2 study will employ SLE drug screening and response-adaptive randomization (RAR) to optimize dose selection of AMG 570 in subjects with active SLE and