Cohort 2a (n=5 to date), there has been 1 SAE of localized herpes zoster. In pts, PK and PD were similar to that achieved for the same doses in HV¹. Efficacy data for evaluable pts are shown in the table. Two (33%) and 2 (67%) evaluable pts in Cohorts 1 and 2, respectively, had a SLEDAI improvement of ≥ 4 points from BL at W13.

Conclusion: KZR-616 dosed at 45 mg SC QW appears to be safe and well tolerated and showed evidence of disease suppression at W13 in active SLE pts on stable background therapy. The Ph 2 doses in the first randomized placebo-controlled trial with KZR-616 in active LN pts on mycophenolate and prednisone will be 30 and 45 mg. Efforts are ongoing to evaluate KZR-616 doses ≥ 60 mg using step-up dosing.

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FRI0197

EFFICACY DATA OF MC2-03 (CICLOSPORIN 0.03% AND 0.06% EYEDROPS) IN SJÖGREN'S PATIENTS WITH SEVERE KERATITIS: OUTCOMES OF THE NORTHERN LIGHTS PHASE 2B TRIAL

Frederic Gomez¹, Johan Selmer¹, Morten Præstegaard¹, Miguel Teus², Luis Pablo³, Maite Sainz de la Maza⁴, Steffen Heegaard⁵. ¹MC2 Therapeutics, Hørsholm, Denmark; ²University of Alcalá, Madrid, Spain; ³University Hospital Miguel Servet, Zaragoza, Spain; ⁴Institute Clinic of Ophthalmology, Hospital Clinic of Barcelona, Barcelona, Spain; ⁵Department of Ophthalmology/University Hospital Rigshospitalet, Copenhagen, Denmark

Background: Sjögren's syndrome is one of the most common rheumatic autoimmune disorders (1). It is a chronic systemic autoimmune disease in which immunomediated inflammation, characterized by lymphocytic infiltration of exocrine glands and epithelia, causes secretory gland dysfunction leading to dryness of the main mucosal surfaces (2) including dry eye with severe keratitis. Ciclosporin is a well-known immunosuppressant with anti-inflammatory properties through inhibition of cell-mediated reactions (inhibit the release of cytokines including IL-2).

Objectives: To report the clinical efficacy of MC2-03 (ciclosporin 0.03% and 0.06% eyedrops) in Sjögren's patients with severe keratitis from a 6-month clinical trial.

Methods: The NORTHERN LIGHTS trial is a randomized, double masked, controlled multicentre European trial that assessed MC2-03 0.03%, MC2-03 0.06%, vehicle and best-standard-of-care (BSC) for the treatment of moderate-to-severe dry eye disease (patients having baseline corneal fluorescein staining (CFS) score 3 or 4). The full analysis set consisted of a total of 255 patients with 66 patients having a documented history of Sjögren's syndrome. The objective of the trial was to evaluate safety and efficacy of MC2-03 after treatment once daily for 6 months followed by a 3 month safety follow-up. The primary efficacy endpoint was the proportion of patients achieving 2-grade improvement in CFS. CFS was evaluated using the modified Oxford grading system: a 7-point ordinal scale (0, 0.5, and 1 to 5), where grade 0 represents complete corneal clearing (absence of staining dots).

Results: The 66 patients with documented history of Sjögren's syndrome constituted 25.9% of the trial population with 90.9% of the patients being females (n=60). Among the Sjögren patients, 58% (n=38) had severe dry

eye (CFS 4) at baseline. Data analyzed for observed cases showed that the proportion of Sjögren's patients achieving 2-grade improvement of CFS (baseline CFS 3 and CFS 4) was higher in MC2-03 groups compared to the control groups (Table 1). When patients treated with any active were compared to patients treated with any control, a 2-grade improvement of the CFS was observed in 51.9% patients in the combined active group vs. 26.7% for the combined control group (p=0.0620).

Table 1. Sjögren patients with 2-grade reduction in CFS

MC2-03 0.06%	MC2-03 0.03%	vehicle	BSC	Combined active	Combined control	Significance
7/16 (43.8%)	7/11 (63.6%)	4/14 (28.6%)	4/16 (25%)	14/27 (51.9%)	8/30 (26.7%)	p=0.0620

Using the same approach, the most severe patients, having CFS 4 at baseline, had a statistically significantly higher responder rate of 64.3% in the combined active group versus 21.1% in the combined control group (p=0.0286).

Table 2. Severe Sjögren patients with 2-grade reduction in CFS

Combined active	Combined control	Significance
9/14 (64.3%)	4/19 (21.1%)	p=0.0286

Conclusion: Data from the NORTHERN LIGHTS trial show that MC2-03 ciclosporin eyedrops has the potential to be a safe, well-tolerated and efficient treatment in Sjögren's patients.

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ANTIMALARIAL AGENTS DIMINISH WHILE METHOTREXATE, AZATHIOPRINE AND MYCOPHENOLIC ACID INCREASE BAFF LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Borja Hernández-Breijo¹, Alvaro Gomez^{2,3}, Sofia Soukka^{2,3}, Petter Johansson^{2,3}, Ioannis Parodis^{2,3}. ¹La Paz University Hospital, Immuno-Rheumatology Research Group, IdiPaz, Madrid, Spain; ²Karolinska Institutet, Division of Rheumatology, Department of Medicine, Stockholm, Sweden; ³Karolinska University Hospital, Rheumatology, Stockholm, Sweden

Background: Elevated levels of the B cell activating cytokine BAFF (also known as BLyS) have been associated with active systemic lupus erythematosus (SLE), and the anti-BAFF monoclonal antibody belimumab has been approved as an add-on to standard-of-care SLE treatment, the latter mainly comprising glucocorticoids, antimalarial agents (AMA) and other immunosuppressive treatments.

Objectives: To investigate the effect of AMA and three other commonly used in SLE immunosuppressive agents (methotrexate, azathioprine, mycophenolate mofetil/sodium) on serum BAFF levels.

Methods: Access to data from the phase III clinical trials of belimumab BLISS-52 (n=865; NCT00424476) and BLISS-76 (n=819; NCT00410384) was granted by GlaxoSmithKline (Uxbridge, UK); a total of 1684 SLE patients were analysed. Serum samples obtained prior to belimumab initiation were stored at -80°C until BAFF level determination by ELISA. The non-parametric Mann-Whitney U test was used to compare BAFF level distributions between treatment groups. Linear regression models were applied to determine independence.