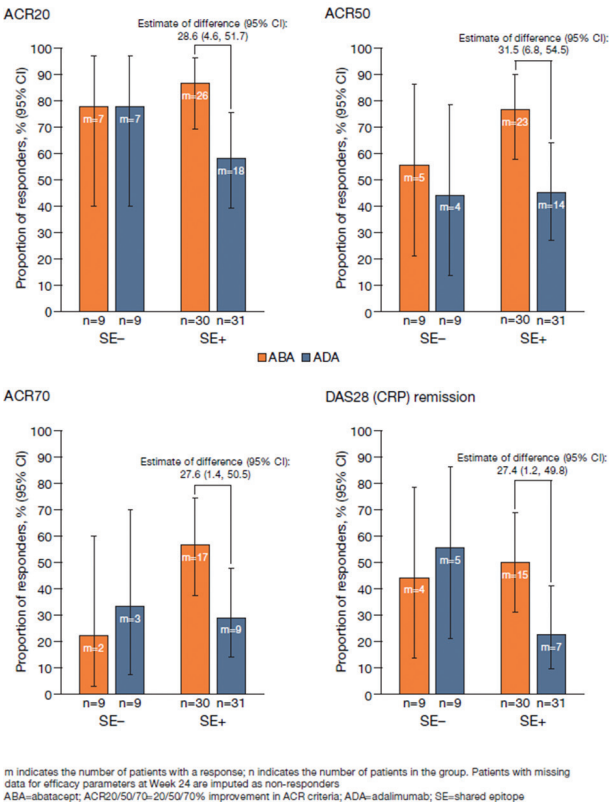
Figure 1. Clinical outcomes in ABA- vs ADA-treated pts at Wk 24 by SE genotype: as-treated analysis population



m indicates the number of patients with a response; n indicates the number of patients in the group. Patients with missing data for efficacy parameters at Week 24 are imputed as non-responders
ABA=abatacept; ACR20/50/70=20/50/70% improvement in ACR criteria; ADA=adalimumab; SE=shared epitope

study in which greater efficacy was seen with abatacept, but not TNF inhibitors, in anti-CCP2+ vs anti-CCP2- pts with RA (Harrold *et al. J Rheumatol* 2018).

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LB0009 FIRST-IN-HUMAN STUDY OF NOVEL IMPLANTED VAGUS NERVE STIMULATION DEVICE TO TREAT RHEUMATOID ARTHRITIS

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Background: The inflammatory reflex plays a role in regulating innate and adaptive immunity through cellular and molecular pathways[1]. Activation of this neuroimmune reflex by electrical vagus nerve stimulation (VNS) reduced systemic inflammation and improved disease activity in a 17 subject rheumatoid arthritis (RA) proof-of-concept study using a reprogrammed epilepsy stimulator[2]. A novel miniaturized neurostimulator, the "MicroRegulator" (MR), was developed for a first-in-human pilot study in multi-drug refractory RA.

Objectives: To assess the safety and efficacy of the MR in a double-blind study in active RA patients.

Methods: The MR was implanted in 14 patients with active RA and prior insufficient response to =2 bDMARDS or JAK inhibitors with =2 different modes of action; all patients remained on stable background of methotrexate. Three weeks after implantation, the first 3 subjects were stimulated 1 min QD and, following safety review board approval, the remaining 11 patients were implanted with the MR and randomized to 1 min of sham, QD, or QID stimulations for 12 weeks. Patients, rheumatologists, joint assessors and monitors were fully blinded to treatment arm. Subjects randomized to sham had their devices activated after the primary endpoint at 12 weeks. Clinical efficacy was measured by DAS28-CRP response and contrast-enhanced MRI (RAMRIS OMERACT). The pharmacodynamic response to VNS was assessed in blood using cytokine production in an ex-vivo bioassay (TruCulture).

Results: 14 patients were enrolled (mean prior bDMARDs= 4.8, mean DAS28-CRP= 5.94). Implantation and stimulation were generally well tolerated. There were no device or treatment-related SAEs and 2 surgery related adverse events (left vocal cord paralysis, Horner's syndrome) that resolved without clinically significant sequelae. DAS28-CRP change at week 12 was (mean ± SEM): Open label QD= -1.44 ± 0.64, QD= -1.24 ± 0.88, QID= 0.38 ± 0.71, Sham=0.16 ± 0.21. Of QD stimulated patients, 4 of 6 had a EULAR good or moderate response. MRI measures of synovitis or osteitis did not change after 12 weeks of stimulation. RAMRIS erosion scores correlated with EULAR response (change ± SEM in erosion scores in EULAR responders = -2.2 ± 1.4 vs. 2.4 ± 0.96 in EULAR non-responders). The pharmacodynamic response to VNS was confirmed in actively stimulated groups with >30% decrease from baseline in bioassay levels of IL-1β, IL-6, and TNF-a at week 12.

Conclusion: The novel MR device and stimulation was well tolerated independent of the two surgery-related events. MR associated stimulation reduced signs and symptoms of RA in a meaningful number of highly drug-refractory subjects. No clinical improvement was observed in the sham group. These initial pilot data support the use of the MR in a larger blinded sham-controlled study in patients who have failed biologics or targeted oral therapies as a novel approach for treatment of RA and other chronic inflammatory diseases.

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LB0010 ULTRA-LOW DOSES OF RITUXIMAB OR RETREATMENT OF RHEUMATOID ARTHRITIS: A RANDOMISED CONTROLLED NON-INFERIORITY TRIAL

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Background: Rituximab (RTX) is an effective treatment for patients with Rheumatoid Arthritis (RA). 1000mg (1 × 1000mg or 2 × 500mg) has similar 6-month efficacy as the registered dose of 2 × 1000mg. Based on several case reports and a