Table. Efficacy and safety outcomes at Week 12

	Placebo (N=62)	LY3337641		
		5-mg (N=63)	10-mg (N=62)	30-mg (N=63)
Efficacy, n (%)				
ACR	n=54	n=56	n=52	n=55
ACR20 ^a	26 (48.1)	31 (55.4)	23 (44.2)	28 (50.9)
ACR50 ^a	15 (27.8)	14 (25.0)	8 (15.4)	16 (29.1)
ACR70 ^a	9 (16.7)	5 (8.9)	1 (1.9)	9 (16.4)
DAS28-CRP	n=62	n=63	n=62	n=63
Low disease activity ^b	15 (24.2)	18 (28.6)	11 (17.7)	16 (25.4)
Remission ^b	11 (17.7)	11 (17.5)	4 (6.5)	14 (22.2)
Change from baseline, observed, mean (SD) ^c	n=44	n=49	n=47	n=43
Safety, n (%) ^d				
Treatment emergent adverse events	31 (50.0)	22 (34.9)	37 (59.7)	34 (54.0)
Serious adverse events	2 (3.2)	0	0	3 (4.8)
Deaths	0	0	0	1 (1.6)
Adverse events leading to discontinuation	2 (3.2)	1 (1.6)	3 (4.8)	3 (4.8)

ACR=American College of Rheumatology; ACR20/50/70=20%/50%/70% improvement according to the criteria of the ACR; DAS28-CRP=Disease Activity Score for 28 joints based on C-reactive protein.

^aIncludes patients who completed through Week 12 at time of study discontinuation by sponsor.

^dIncludes all patients who received study drug.

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SAT0090

GUT MICROBIOTA COMPOSITION IS CONTINGENT WITH DISEASE PHASES IN RHEUMATOID ARTHRITIS

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Background: Increasing evidences suggest that alterations in the gut microbiota may contribute to the pathogenesis and influence the clinical outcome of Rheumatoid arthritis (RA).

Objectives: To characterize the gut microbiota composition in RA patients in different disease phases contingently to therapeutic regimens.

Methods: Forty-four RA patients (7 naïve to treatment, 13 MTX-IR and 24 in sustained clinical and ultrasound remission under conventional and bDMARD combination therapy, respectively) (age 55.2±11.4 years, 79.5% female and 59.1% positive for ACPA and/or RF) and 20 age/sex matched healthy controls (HC) were enrolled in the study. At study entry, RA specific data set were collected and dietary habits were recorded using the 14-items Mediterranean Diet Adherence Screener (MeDAS) questionnaire. DNA was extracted from stool samples of each patient, amplified and 16S rRNA gene V3-V4 region was sequenced using an Illumina MiSeqTM platform. For downstream sequence analysis, a combination of software packages QIIME (v1.9.1) and VSEARCH (v1.1) was used and a biological observation matrix (BIOM) at different taxonomic

levels (from phylum to genus) was produced. The BIOM was analysed using the Web-based program MicrobiomeAnalyst. Statistical analyses were performed using the R phyloseq software package. Differences in the relative abundance of individual bacterial taxa between a priori defined groups were assessed by LEfSe analysis.

Results: Microbiota composition analysis showed that RA patients had a decrease in the gut microbial species richness compared to HC ($p<0.01$). In particular, the principal coordinate analysis (PCoA) visualization of UniFrac distances and analysis of group similarities (ANOSIM) showed that faecal microbiota composition differs between RA and HC ($p<0.01$) confirmed by the LEfSe analysis showing that RA microbiota is enriched of *Bacteroidetes* and *Proteobacteria*, whereas HC were enriched of *Verrucomicrobia* and *Firmicutes*. Considering the RA cohort, no significant differences in microbiota composition were found stratifying patients based on autoantibody profile, disease duration and BMI category. However, considering the disease phase, RA patients with active disease (DAS>3.7) showed significant differences in α -diversity compared to RA patients in LDA or in sustained clinical and ultrasound remission ($p=0.01$) with a relative abundance of *Haemophilus parainfluenzae* in high disease activity patients ($p<0.01$). A slightly higher α -diversity in RA patients with the highest adherence to Mediterranean diet ($p=0.10$).

Conclusion: Despite limited sample size, this study strengthen the concept of significant microbiota differences in RA, contingently with disease phases, compared to HC. The evaluation of microbiota composition in the patients follow-up according to response to therapies is ongoing.

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SAT0091

INCREASED FREQUENCY AND DEFECTIVE SUPPRESSIVE CAPACITY OF CD4⁺CD25⁺FOXP3⁺ TREG CELLS IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Conflicting evidence exists regarding the proportion and function of CD4⁺CD25⁺Foxp3⁺ Treg Cells in the peripheral blood (PB) of patients with rheumatoid arthritis (RA)¹⁻⁶.

Objectives: The aim of our study was to determine whether Treg cells are defective in Chinese RA patients.

Methods: Levels of CD4⁺CD25⁺Foxp3⁺ Treg cells in the peripheral blood of 224 patients with RA and 38 healthy controls were detected by flow cytometry. The expression of CTLA-4, GITR, Helios and ICOS was also evaluated in order to gain insight into the regulatory function of Treg cells. The production of IFN- γ , IL17 and IL10 cytokines by Treg cells was also evaluated. Clinical parameters, including DAS28_ESR, the levels of serum Anti-CCP, IgG and IgM were tested. Correlations with Treg cells were systematically analyzed.

Results: Compared to the healthy controls, active RA patients had significantly higher frequency of CD4⁺CD25⁺Foxp3⁺ Treg cells ($P < 0.01$). Furthermore, the CD4⁺CD25⁺Foxp3⁺ Treg cells expressed lower CTLA4 ($P < 0.01$) and produced higher IL17 ($P < 0.05$) and lower IL10 ($P < 0.05$) in RA patients compared with healthy controls in vitro stimulation assay. We also found the proportions of CD4⁺CD25⁺Foxp3⁺ Treg cells were significantly higher in Anti-CCP ⁺patients compared Anti-CCP patients ($P < 0.01$). The frequency of CD4⁺CD25⁺Foxp3⁺ Treg cells in RA patients was positively correlated with DAS28_ESR ($r = 0.135$, $P = 0.043$), the levels of serum Anti-CCP ($r = 0.239$, $P < 0.001$), IgG ($r = 0.239$, $P < 0.001$) and IgM ($r = 0.168$, $P = 0.015$).

Conclusion: We showed higher frequency of CD4⁺CD25⁺Foxp3⁺ Treg cells in PB of RA patients, of which the suppressive capacity was defective.

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