Conclusions: This indirect comparison of different studies in cs/bDMARD-naïve RA patients, after adjusting for differences in baseline characteristics, suggest a greater pain reduction and improved physical function for BARI monotherapy vs. TCZ and ADA monotherapy. There is suggestion of greater pain reduction for BARI monotherapy vs. TOFA monotherapy, but no differences in improved physical function between the JAK inhibitors. A H2H clinical trial would be needed to confirm these results.

REFERENCES:

- 1 Fleischmann, et al. Arthritis Rheumatol 2017.
- 2 Breedveld, et al. Arthritis Rheumatol 2006.
- 3 Lee, et al. N Engl J Med 2014.
- 4 Jones, et al. Ann Rheum Dis 2010.
- 5 Burmester, et al. Ann Rheum Dis 2016.
- 6 Signorovitch, et al. Pharmacoeconomics 2010.
- 7 Bucher, et al. J Clin Epi 1997.

Disclosure of Interest: B. Fautrel Grant/research support from: AbbVie, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, SOBI, UCB, B. Zhu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Taylor Grant/research support from: Celgene, Eli Lilly and Company, Galapagos, UCB, Abide Therapeutics, Consultant for: AbbVie, Eli Lilly and Company, Galapagos, GlaxoSmithKline, Pfizer, UCB, Biogen, Sandoz, Novartis, and Janssen, M. van de Laar Grant/research support from: AbbVie; BMS; Grunenthal; Pfizer; Janssen; MSD, Lilly, Consultant for: AbbVie, Grunenthal; Pfizer, Janssen, MSD, Lilly, Speakers bureau: Pfizer; Janssen, Eli Lilly, P. Emery Consultant for: Pfizer, MSD, AbbVie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, F. De Leonardi Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C. Gaich Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C. Nicolay Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Z. Kadziola Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, I. De La Torre Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, R. Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Genetech, GlaxoSmithKline, Janssen, Eli Lilly and Company, Merck, Pfizer, Regeneron, Roche, Sanofi, Aventis, UCB, Consultant for: AbbVie, Akros, Amgen, Bristol-Myers Squibb, Celgene, Genetech, GSK, Janssen, Eli Lilly and Company, Pfizer, Sanofi-Aventis, UCB

DOI: 10.1136/annrheumdis-2018-eular.1997

SAT0226

A PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE- AND MULTIPLE-RISING DOSE STUDY OF THE BTK INHIBITOR TAK-020 IN HEALTHY VOLUNTEERS

E. Esfandiari¹, H. Gevorkyan², H. Faessel³, Z. Zhao⁴, K. Hanna⁵, G. Smithson³, J. Wagner³, E. R. Fedyk³, L. Mclean⁶. ¹Takeda, London, United Kingdom, ²Parexel, Glendale CA, ³Takeda, Boston, ⁴Takeda, ⁵PRA, Deerfield IL, ⁶Takeda, San Diego, United States

Background: TAK-020 is a highly selective covalent inhibitor of the Btk enzyme. Btk is involved both in B cell receptor and FcR signaling. TAK-020 showed anti-inflammatory and disease-modifying efficacy in a rat collagen-induced arthritis model and is in clinical development, with potential for immune disorders including RA and SLE.

Objectives: To assess the safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) properties of TAK-020.

Methods: The study population comprised healthy volunteers aged 18 to 55 years. The SRD had 9 cohorts and the MRD, each randomized 6 active- to 2 placebo-treated subjects. 72 subjects were enrolled in the SRD, with 6 each receiving 0.1 mg, 0.5 mg, 2.5 mg, 4.4 mg, 8.8 mg, 17.5 mg, 35 mg, 70 mg, or 105 mg of TAK-020; and 18 subjects received placebo. 48 subjects were in the MRD, six

each receiving 7 once-daily (OD) doses of 3.75 mg, 5.75 mg, 13 mg, 25 mg, 45 mg, or 60 mg. A total of 30 subjects received placebo.

The PD effects of TAK-020 were assessed by measuring Btk occupancy and the inhibition of FcεR1-mediated activation of basophils, a Btk-dependent process resulting in increased CD63 expression.

Results: In the SRD the same percentage of subjects (11.1%) in the pooled placebo group and the overall TAK-020 group experienced treatment-emergent adverse events (TEAE). All TEAEs were of mild intensity. Abdominal distension, upper abdominal pain, nausea, and headache were reported as drug-related TEAEs in 3 subjects in the TAK-020 group. In the MRD a lower percentage of subjects receiving TAK-020 had TEAEs than with placebo (30.6 vs 41.7%). In 4 subjects (11.1%) these were considered drug-related and included nausea, diarrhea, dizziness and headache.

There were no serious AEs or AEs leading to study drug discontinuation. No subject had clinically significant changes in laboratory tests, vital signs, or ECGs.

TAK-020 was rapidly absorbed (median Tmax 45- 60 min), and had a mean elimination half-life of approximately 3- 9 hr after single and multiple dosing. Plasma exposure was in general proportional to dose up to 70 mg administered as a single dose and up to 60 mg after 7d of OD dosing.

Single doses of TAK-020 were associated with rapid binding of Btk, with occupancy >80% and maintained for 72 hours. Sustained binding of Btk was associated with >80% reduction from baseline in the proportion of CD63-positive basophils. This PD effect was sustained throughout the entire 24 hr dosing interval after administration of the 2 highest repeat doses of TAK-020 (45 and 60 mg) but fully reversed 1 week after the last dose.

Conclusions: TAK-020 was well tolerated in healthy volunteers after single and multiple doses, and demonstrated target engagement and biological activity. The PD effects outlasted PK exposures, as expected for a covalent inhibitor.

Disclosure of Interest: E. Esfandiari Shareholder of: Takeda, Employee of: Takeda, H. Gevorkyan Employee of: Parexel, H. Faessel Shareholder of: Takeda, Employee of: Takeda, Z. Zhao Shareholder of: Takeda, Employee of: Takeda, K. Hanna Employee of: PRA, G. Smithson Shareholder of: Takeda, Employee of: Takeda, J. Wagner Shareholder of: Takeda, Employee of: Takeda, E. Fedyk Shareholder of: Takeda, Employee of: Takeda, L. Mclean Shareholder of: Takeda, Employee of: Takeda

DOI: 10.1136/annrheumdis-2018-eular.2813

SAT0227

RHEUMATOID ARTHRITIS PATIENTS TREATED WITH A LOW-DOSE AND SHORT-TERM GLUCOCORTICOID WERE SATISFIED WITH EARLIER IMPROVEMENT AND REPORTED DECREASED ANXIETY REGARDING ADVERSE EVENTS.

E. Torikai¹, D. Suzuki¹, M. Suzuki², Y. Matsuyama². ¹Department of Rheumatology, Iwata city hospital, Iwata, ²Department of Orthopaedic surgery, Hamamatsu university school of medicine, Hamamatsu, Japan

Background: At EULAR 2017, we reported that the treatment of early rheumatoid arthritis (RA) patients by a low-dose and short-term glucocorticoid therapy (low and short GC) enabled earlier improvement and didn't worsen the rate of new complications. Currently, in RA treatment, subjective assessment of patients as well as objective assessment of doctors is gaining more importance⁽¹⁾. What do patients think about the risks of low and short GC? Does low and short GC improve patients' satisfaction?

Objectives: In this study, we investigated the change in each factor of the disease activity index (DAI) and patients' expectation of and anxiety regarding low and short GC through a questionnaire.

Methods: We include 96 Japanese patients with RA and <2-years disease duration. Patients were treated with a T2T strategy; if the disease activity was not improved within 3 months, their DMARDs were replaced with alternatives or additional DMARDs were added. We classified patients into two groups: those treated with DMARDs alone (N group; 35 females, 10 males) and those treated with ≤5 mg/day GC for a maximum of 1 year along with DMARDs (GC group; 40 females, 11 males). The mean ages of the N and GC groups were 56.3 and 60.9 years, respectively. In the GC group, the mean GC dose was 2.46 mg/day. No significant differences were observed between the groups regarding MTX or Biologics agent use rates. We evaluated changes in the number of swollen joints and tender joints, DAS28-CRP score, CRP and VAS of pain for 3 years and compared each factor of DAI between both groups. We then asked them by a questionnaire what was beneficial from the therapies and how much paid attention to the adverse events.

Results: There were no significant differences in all factors of DAI at baseline between the groups. At 1 month after treatment, there were significant differences in the improvement rate of VAS, CRP and DAS28-CRP score in the GC group compared with the N group. However, no significant difference was observed between the groups at ≥3 months after treatment (figure 1). In the questionnaire (figure 2), pain improvement was the most expected effect from the treatment (89%), and early therapeutic effect was the second (80%) in the GC group. The pain improvement and the early therapeutic effect were significantly higher in the