Methods: In RA-BEGIN, 588 pts (mean disease duration 1.4 years) were randomized 4:3:4 to MTX, bari 4-mg once-daily, or combination MTX and bari 4-mg. At Wk 52, pts could enter a long-term extension study in which all pts received open-label bari 4-mg. Pts initially randomized to bari 4-mg monotherapy were defined as early-start and MTX pts who switched to bari 4-mg at Wk 52 were defined as delayed-start for this analysis. Change from baseline using mixed model repeated measures and mean scores were assessed for the Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Disease Activity Score 28-joints-high-sensitivity C-reactive protein (DAS28-hsCRP), Disease Activity Score 28-joints-erythrocyte sedimentation rate (DAS28-ESR), Health Assessment Questionnaire-Disability Index (HAQ-DI), and modified Total Sharp Score (mTSS) to compare early- vs delayed-start groups between Wks 0 and 100 (Wks 52-100 for mTSS). Percent of pts achieving low disease activity (LDA, SDAI ≤ 11) and remission (SDAI ≤ 3.3) were also assessed.

Results: LDA and remission response rates in the delayed-start group increased from 60% to 78% and 18% to 31%, respectively, within 4 wks after switching to bari 4-mg. Remission rates reached 47% within 1 year after switching, but were not different from the group that initiated bari (Figure 1). Similar results were seen for CDAI, DAS28-ESR, and DAS28-hsCRP (only up to Wk 40 for DAS28-ESR) (data not shown). Pts initially randomized to bari 4-mg had significantly greater change from baseline, observed as early as Wk 1 and up to Wk 52, for HAQ-DI than pts treated with MTX (Figure 2). After switching to bari, the delayed-start group showed a rapid improvement in HAQ-DI with similar improvement at Wk 56 – 4 wks after switching to bari. Upon initiating bari, there was a reduction in the rate of structural damage; however, delaying initiation of bari for 1 year resulted in numerically higher mTSS.

Conclusion: In early MTX-naïve pts, improved clinical, functional, and radiographic efficacy with bari 4-mg vs MTX was observed in most outcome measures up to 52 wks. Switching from MTX to bari at Wk 52 provided a rapid clinical response, allowing the majority of pts to achieve similar results 4 wks post-switch. However, if the goal of therapy is to achieve rapid and sustained control of disease activity, the differences noted here for HAQ-DI and especially structural progression support earlier switch to bari for pts who do not obtain disease control with MTX. Further analysis may be needed to explore prognostic factors, such as hsCRP and disease duration (< or >6 months), baseline erosion, or anticitrullinated protein antibody positivity, which may help clinicians identify pts who may benefit from earlier treatment with bari.

REFERENCES:

- [1] Fleischmann, et al. Arthritis & Rheumatism. 2017;69:506-517

Figure 1. Percent of patients achieving low disease activity (SDAI ≤ 11) or remission (SDAI ≤ 3.3) in the early (baricitinib group) and delayed (MTX group) start patients *P-value ≤ 0.05 , ** ≤ 0.01 , *** ≤ 0.001 vs MTX. Note: Dashed lines indicate that at Week 52 all MTX patients who entered the LTE were switched to baricitinib 4-mg. MTX=methtexate; SDAI=Simplified Disease Activity Index.

Abstract THU0075 – Figure 1

Figure 2. Efficacy outcomes in the early (baricitinib group) and delayed (MTX group) start patients *P-value ≤ 0.05 , ** ≤ 0.01 , *** ≤ 0.001 vs MTX. Note: Dashed lines indicate that at Week 52 all MTX patients who entered the LTE were switched to baricitinib 4-mg. HAQ-DI=Health Assessment Questionnaire-Disability Index; LSM=least squares mean; MTX=methtexate; mTSS=modified Total Sharp Score

Abstract THU0075 – Figure 2

Disclosure of Interests: Roy Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Michael Schiff Consultant for: AbbVie, BMS, Eli Lilly and Company, JJ, UCB, Speakers bureau: AbbVie, BMS, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Cem Gabay Grant/research support from: Roche, Pfizer, AB2 Bio Ltd, Consultant for: Roche, Pfizer, Lilly, AbbVie, Sanofi, Regeneron, Bristol-Myers Squibb, Novartis, UCB, AB2 Bio Ltd, Debiopharm, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celltrion, Anabela Cardoso Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jinglin Zhong Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Yun-Fei Chen Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Jennifer Workman Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Tsutomu Takeuchi Grant/research support from: Astellas Pharma Inc, Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., AbbVie GK, Asahikasei Pharma Corp., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Eisai Co., Ltd., AYUMI Pharmaceutical Corporation, Nipponkayaku Co. Ltd., Novartis Pharma K.K., Grant/research support from: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Grant/research support from: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., AbbVie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., GlaxoSmithKline K.K., UCB Japan Co. Ltd., Consultant for: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol Myers Squibb, and Nipponkayaku Co. Ltd., Speakers bureau: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK., Bristol-Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Astellas Pharma Inc, Daiichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K.

DOI: 10.1136/annrheumdis-2019-eular.975

THU0076 THE IMPACT OF VARYING EXCLUSION CRITERIA ON TREATMENT RESPONSE: REAL-WORLD EVIDENCE TO GUIDE THE DESIGN OF FUTURE CLINICAL TRIALS

Thomas Frisell¹, Scott Jelinsky², Mark Peterson², Johan Askling¹. ¹Karolinska Institutet, Solna, Sweden, ²Pfizer Research Technology Center, Cambridge, United States of America

Background: Clinical trials of novel pharmaceuticals in Rheumatoid Arthritis routinely use strict inclusion/exclusion criteria aimed at selecting a defined homogeneous population and producing a non-confounded demonstration of the agent's clinically relevant pharmacologic effect. However, the act of strictly defining numerous individual criteria has the potential

for impacting the observed response rates, while the effect upon limiting the pool of eligible subjects is often poorly understood. Unnecessarily narrow criteria may limit the generalizability of trial results to real world patient populations. Conversely, certain patient characteristics may be associated with high or low probabilities of response to active treatment or to placebo.

Objectives: To assess the impact of applying a range of different exclusion criteria on the proportion eligible subjects, and on the observed treatment response rates, in a large real-world patient population.

Methods: Data on RA characteristics, demographics, and co-morbidities among RA patients were identified by linking the Swedish Rheumatology register (SRQ) to the nationwide and virtually complete Swedish census and healthcare registries. Representing an early RA trial scenario, we identified patients starting methotrexate monotherapy as first ever DMARD (N=8981) between 2007 and 2016. The cohort was assessed overall and stratified by baseline DAS28. Treatment outcome was defined as the proportions reaching (1) EULAR Good Response and (2) Low Disease Activity, and the change in (3) HAQ and (4) CDAI at 3 and 6 months. Exclusions were made based on age, baseline disease activity, sex, RF, predefined comorbidities, degree of healthcare utilization history, education, and taxed income level (cut-offs for continuous variables were based on distributions from recent clinical trials of tofacitinib). In total, 165 different definitions of exclusion criteria were evaluated.

Results: Within the entire cohort, 50% of patients achieved EULAR DAS28 good response at 3 months. Exclusions based on age, sex, RF status, or duration of RA symptoms before RA diagnosis generally lead to large reductions in number of eligible subjects but did not appreciably affect (< 5% change) the proportion of EULAR good responders. Exclusions based on HAQ had a noticeable drop in the proportion of EULAR good response (~10%, see Figure), although exclusions above 80% was necessary to observe an effect. A similar pattern was observed for TJC, patient's global health and ESR but exclusions based on SJC or CRP did not impact EULAR response.

Exclusions of specific comorbidities, such as history of myocardial infarction, history of joint replacement, generally had no or modest impact on the observed response rate. Exclusions based on health care use (total number of drugs, hospitalizations), affected response rates (+/- around 5%), while exclusions based on educational level, work ability, or income did not.

The impact of exclusions was very similar on the 3 and 6 month responses.

Conclusion: Exclusions in a range of criteria commonly used in clinical trials had only a modest impact on observed treatment outcome, while impacting on the enrollment pool – sometimes dramatically. More extreme restrictions (excluding well above half the potentially eligible patients) were generally necessary to shift the proportion EULAR Good Response by more than 5 percentage points. This should not be a surprise given the lack of identified strong predictors of treatment outcome in RA, but may raise the question of whether the lowered generalizability and impacts on enrollment rates caused by strict inclusion criteria in clinical trials is warranted by the aspiration to increase chances of demonstrating clinically meaningful effects.

Abstract THU0076– Figure 1

Disclosure of Interests: Thomas Frisell: None declared, Scott Jelinsky Shareholder of: Pfizer, Employee of: Pfizer, Mark Peterson Shareholder of: Pfizer, Employee of: Pfizer, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer.

DOI: 10.1136/annrheumdis-2019-eular.1022

THU0077

RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS CLINICAL TRIALS: HOW TO ENCOURAGE PATIENT PARTICIPATION? RESULTS FROM A REAL-WORLD STUDY CONDUCTED VIA CARENITY, A WORLDWIDE ONLINE PATIENT COMMUNITY

remi gauchoux, Anthony Boisbouvier, Roman Dos Santos, Lise Radoszycki. CARENITY, Paris, France

Background: Involving patients affected with rheumatoid arthritis or ankylosing spondylitis in clinical trials may be highly challenging: in a worldwide context of competitive rheumatoid arthritis and ankylosing spondylitis clinical research, patient engagement is key to optimize medical research and increase participation rates.

Objectives: The aim of this study was to identify patients' motivations for and hindrances to joining a trial in order to increase participation rate by implementing tailored services and information.

Methods: An online questionnaire was submitted from August 2017 to October 2017 to Carenity's French members affected with rheumatoid arthritis or ankylosing spondylitis.

Results: 136 patients affected with rheumatoid arthritis (n = 55, 40%, mean age = 55 y/o, 71% of women) or ankylosing spondylitis (n = 81, 60%, mean age = 48 y/o, 80% of women) participated in the study. 10 patients (7%) already participated in a clinical trial.

Non-participants (n=126) exposed the incentives that may increase participation rate: reimbursing the expenses related to the clinical trial can improve their motivation (median weight on motivation to join a trial = 10/10) as well as a better medical follow-up (8.0/10) or leveraging the trial's investigator notoriety (8.0/10). Patients' healthcare practitioners could be leveraged as well: their favorable opinion turns patients on to clinical trials (7.0/10). On the contrary, a doctor's negative opinion may strongly deter patients from joining a trial (median weight on reluctance to join a trial = 8.0/10). Communication should aim at reassuring them about side effects (9.0/10), potential risks for their health (8.0/10) and more generally the risk that the new treatment would not be better than their current one (8.0/10). Logistic challenges should also be taken into account: the trip between patients' home and the site of the clinical trial is perceived as an important burden (8.0/10).

Implementing tailored services and information would be an efficient way to reassure patients and increase their willingness to participate. 81% of non-participants would be enticed to participate if they had access to a website to exchange with healthcare professionals or to follow the results of the trial. 79% would be interested in participants' testimonials and 74% in a 24-hour phone helpline. Spreading and clarifying information before the trial is also critical: 6/10 patients who participated in a clinical trial did not understand clearly if they will have out-of-pocket costs and 5/10 patients were also unclear on the terms and conditions for leaving the clinical trial. Informing patients via convenient channels is key: 88% of participants and non-participants think that an online patient community is a relevant medium to convey information about clinical trials and 81% of non-participants would like to have access to an information brochure about the trial process.

Conclusion: This real-world study allowed to identify concrete levers to reassure patients affected with rheumatoid arthritis or ankylosing spondylitis about the benefits/constraints balance and to clarify information at each stage of the trial (before, during, after), which is essential to accelerate clinical trial recruitment.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6922

THU0078

SAFETY PROFILE OF BARICITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS UP TO 7 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS

Mark C. Genovese¹, Josef S. Smolen², Tsutomu Takeuchi³, Gerd Rüdiger Burmester⁴, Dennis Brinke⁵, Terence Rooney⁶, Jinglin Zhong⁶, Daojun Mo⁵, Chadi Saifan⁵, Anabela Cardoso⁵, Maher Issa⁵, Wen-Shuo Wu⁵, Kevin Winthrop⁷. ¹Stanford University Medical Center, Palo Alto, United States of America; ²Medical University of Vienna, Vienna, Austria; ³Keio University, Tokyo, Japan; ⁴Charité – University Medicine Berlin, Berlin, Germany; ⁵Eli Lilly and Company, Indianapolis, United States of America; ⁶IQVIA, Rockville, United States of America; ⁷Oregon Health Sciences University, Portland, United States of America

Background: Baricitinib (bari), is an oral, selective inhibitor of Janus kinase (JAK) 1/JAK 2, to treat moderately to severely active RA in adults.

Objectives: To update bari's safety profile with data from an additional Phase (Ph) 3 trial and on-going long-term extension (LTE) study.

Methods: Long-term safety of once-daily bari was evaluated in the All-Bari-RA dataset: all patients (pts) exposed to any bari dose from 9