JAK/STAT signaling and inflammation genes. No significant changes in the expression of DAGs were observed in PBO-treated patients. FIL also broadly reversed DAGs and DAPs, and ongoing research is exploring the relationship between changes in gene and pathway modulation across a range of clinical endpoints.

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Disclosure of Interests: Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Bryan Downie Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Luting Zhuo Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Rachael E. Hawtin Shareholder of: Gilead, Employee of: Gilead, Jinfeng Liu Shareholder of: Gilead Sciences, Inc., Roche, Employee of: Gilead Sciences, Inc., Amer M. Mirza Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc.

DOI: 10.1136/annrheumdis-2019-eular.2509

THU0195

ULTRASOUND EVALUATION FOR MONITORING RESPONSE TO BARICITINIB IN RHEUMATOID ARTHRITIS PATIENTS AT EARLY STAGE AFTER TREATMENT

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Background: Baricitinib (bari) is approved for treating moderate-severe RA in many countries including Japan. Bari, an oral Janus kinase (JAK1)/JAK2 selective inhibitor, has shown the efficacy in patients with rheumatoid arthritis (RA) and in adequate response to conventional synthetic DMARDs in some clinical trials. Thanks to technological improvement in Ultrasound (US) equipment and the use of internationally approved scanning techniques and definitions for normal findings and pathology, US monitoring are widely used to assess inflammatory and structural lesions in daily clinic.

Objectives: To monitor the short-term response to baricitinib therapy in bilateral wrist and finger joints of RA patients by US and to evaluate correlation between US findings and clinical assessments.

Methods: We included 23 Japanese patients with RA who have inadequate response to csDMARDs or bDMARDs (biologics-naïve 19 cases and biologics-experience 4 cases). Patients were scheduled to receive bari 4mg or 2mg once daily dose as monotherapy or in combination with other csDMARDs. They were allowed to be decreased prednisolone when their disease activity was improved. Clinical evaluation was performed blinded to the results of the US assessment that had been carried out on the same day. Swollen joint counts on 28 joints (SJC), tender joint counts on 28 joints (TJC) and Clinical Disease Activity Index (CDAI) were registered for each patient. Each parameter was evaluated at baseline, after 1 month and 3 months. Four sonographers, experiences in musculoskeletal US, who were blinded to the clinical and laboratory data, performed the US examination. The US assessment and scanning technique included evaluation of synovial sites in 26 joints (wrist- radiocarpal, midcarpal, radiocarpal joints, 1 - 5 MCP joints and 1 - 5 PIP joints). Gray scale (GS) and power doppler (PD) were graded according to a 0 - 3 semi-quantitative score depending on their severity [1]. We calculated total scores for each patient in GS (GS score) and PD (PD score) differently. We compared the change of GS score and PD score. In addition, we evaluated the correlation between the changes in GS score or PD score and the variations in clinical evaluation items.

Results: Patient's backgrounds were provided in Table 1. All clinical parameters were significantly improved at each follow-up periods after treatment. Mean SJC, TJC and CDAI decreased from 7.52 ± 3.89 , 8.26 ± 3.82 and 26.89 ± 9.48 at baseline to 1.52 ± 1.75 , 1.82 ± 1.89 and 6.40 ± 5.17 at 1 month and to 1.27 ± 1.39 , 1.27 ± 1.38 and 3.99 ± 3.49 at 3 months respectively (Table 2). GS and PD score at each follow-up periods after treatment were also significantly improved. Mean GS and PD decreased from 8.11 ± 3.41 and 12.42 ± 4.45 at baseline to 3.63 ± 2.45 and 7.73 ± 4.70 at 1 month and to 2.10 ± 1.49 and 4.21 ± 2.70 at 3 months respectively (Table 2). GS score significantly correlated with SJC ($r = 0.586$, $p < 0.01$), TJC ($r = 0.602$, $p < 0.01$) and CDAI ($r = 0.656$, $p < 0.01$). PD score significantly correlated with SJC ($r = 0.606$, $p < 0.01$), TJC ($r = 0.624$, $p < 0.01$) and CDAI ($r = 0.658$, $p < 0.01$).

Conclusion: Baricitinib therapy had significantly improved disease activity of RA patients at early stage after the treatment. GS and PD score were also significantly improved and correlated with clinical parameters.

These data confirm that the use of US evaluation is very useful method for evaluating the monitoring the response of treatment and feasible method complementary to clinical assessment for guiding the clinician in the appropriate therapeutic decision.

Abstract THU0195 –Table 1.

Age (years)	66.6 $\pm$ 9.4	RF positive (%)	73.9
Disease duration (years)	3.91 $\pm$ 5.07	ACRA positive (%)	78.2
MTX dose (mg/week)	7.65 $\pm$ 8.82	Stage (I/II/III/IV)	6/10/7/0
PSL dose (mg/day)	1.28 $\pm$ 1.80	Class (I/II/III/IV)	3/8/10/2

	baseline	1 month	3 months
SJC	7.52 $\pm$ 3.89	1.52 $\pm$ 1.75*	1.27 $\pm$ 1.39*
TJC	8.26 $\pm$ 3.82	1.82 $\pm$ 1.89*	1.27 $\pm$ 1.38*
CDAI	26.89 $\pm$ 9.48	6.40 $\pm$ 5.17*	3.99 $\pm$ 3.49*
GS score	8.11 $\pm$ 3.41	3.63 $\pm$ 2.45*	2.10 $\pm$ 1.49*
PD score	12.42 $\pm$ 4.45	7.73 $\pm$ 4.70*	4.21 $\pm$ 2.70*

*p < 0.05 vs baseline

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.4508

THU0196

EFFICACY AND SAFETY UP TO 24 WEEKS OF BARICITINIB FOR JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL WORLD MULTICENTER CLINICAL DATA

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Background: Baricitinib (bari) is approved for treating moderate-severe rheumatoid arthritis (RA) in many countries, including Japan. Bari is an oral Janus kinase (JAK1)/JAK2 selective inhibitor that has shown good efficacy in patients with RA and adequate response to conventional synthetic DMARDs in some clinical trials. However, there have been few reports about the efficacy and safety of bari in real-world clinical data.

Objectives: We evaluated the efficacy and safety of bari for Japanese RA patients who have an inadequate response to DMARDs in real-world multicenter clinical data.

Methods: We included 32 Japanese patients with RA who show an inadequate response to csDMARDs or bDMARDs (biologics-naïve (BN group): 19 cases and biologics-experience (BE group): 13 cases). Patients were scheduled to receive bari 4 or 2 mg once daily dose as a monotherapy or in combination with other csDMARDs. If the disease activity was not improved within 3 months in patients treated with bari 2 mg, the bari dose was increased to 4 mg. Patients were allowed to decrease their prednisolone treatment if their disease activity improved. First, we evaluated changes in the number of swollen joints and tender joints, CRP (mg/dL), visual analog scale of pain (0–100 mm), patient's global assessment (0–100 mm), Clinical Disease Activity Index, and HAQ-DI for 24 weeks. Second, we evaluated the proportion of patients with adverse events (AEs) and progress after these AEs.

Results: Patients' backgrounds are provided Table 1. Many patients felt the early effect of bari. At 1 month after treatment, ACR20/50/70 were 84.2%/63.2%/21.1% in the BN group and 53.8%/23.1%/7.7% in the BE group, respectively. All measurement items of disease activity and patient-reported outcomes were significantly improved after treatment. This tendency continued until the final evaluation (Table 2). At 24 weeks, remission and low disease activity rates were 47.4% and 78.9% in the BN group and 15.4% and 61.5% in the BE group, respectively. One case in the BE group discontinued bari treatment due to no response. These data were better than clinical trial data (Japanese subpopulation data from RA-BEAM and RA-BUILD studies^[1]). We determined that we could take an aggressive treatment course according to treat to target strategies in real-world clinics. Greater early improvements in HAQ-DI were seen. HAQ-DI was improved significantly at each evaluation time point after bari treatment (Table 2).

We had two cases of mild pneumonia and one case of herpes zoster. These cases were improved after 1–2 weeks of antibiotic therapy or antiviral drug therapy. One case discontinued bari. Although the other two cases withdrew from bari treatment, we could restart it. We think that the most important reason why they did not advance in severe because we were able to diagnose and treat these cases earlier. No patient showed malignancies, cardiovascular events, or deep vein thrombosis. No patient discontinued bari treatment due to AEs. Also, increases in blood pressure and d-dimer were not observed during the follow-up period. Other mild AEs, including upper respiratory tract infection, nasopharyngitis, and laboratory data abnormalities occurred in 62.5% of patients (Table 3). A small increase in lymphocyte count and small decrease in neutrophil count

were seen at 1 month after bari treatment. These either remained flat or improved 3 months after treatment. An increase from baseline in creatinine was also seen. These tendencies continued to the final observation. Moving forward, these items should be monitored for long-term evaluation.

Abstract THU0196 –Table 1.

Table 1. Patients' background		(mean ± SD)	
	Bio naïve	Bio experienced	
Age (years old)	66.4 ± 9.0	69.8 ± 11.2	
Disease duration (years)	3.81 ± 3.80	4.57 ± 3.13	
Male / Female	3 / 16	4 / 9	
RF positive / ACPA positive (%)	68.4 / 73.7	84.6 / 76.9	
Stage (I/II/III/IV) / Class (I/II/III/IV)	(10/5/4/0) / (4/8/4/3)	(5/4/3/1) / (2/5/4/2)	
MTX dose (mg/week)	8.94 ± 9.23	6.67 ± 7.10	
PSL dose (mg/day)	1.41 ± 1.87	1.33 ± 2.06	

Table 2. Change of clinical assessments		(mean ± SD)		
(Bio naïve)	baseline	1 month	3 months	6 months
SJC	7.06 ± 2.54	1.68 ± 1.70 [§]	0.75 ± 1.29 [§]	0.66 ± 0.85 [§]
TJC	7.68 ± 3.18	2.19 ± 1.94 [§]	1.13 ± 1.50 [§]	0.98 ± 1.05 [§]
CRP (mg/dl)	2.00 ± 1.50	0.67 ± 0.93 [§]	0.17 ± 0.25 [§]	0.15 ± 0.24 [§]
CDAI	24.92 ± 7.26	7.11 ± 4.84 [§]	3.87 ± 4.31 [§]	2.94 ± 3.13 [§]
Pain VAS	50.3 ± 21.4	21.4 ± 16.8 [§]	15.3 ± 13.8 [§]	12.0 ± 9.8 [§]
PGA	49.9 ± 18.6	21.2 ± 17.6 [§]	11.5 ± 13.8 [§]	9.8 ± 12.5 [§]
HAQ-DI	0.76 ± 0.33	0.43 ± 0.24 [§]	0.30 ± 0.18 [§]	0.28 ± 0.17 [§]

Table 2. Change of clinical assessments		(mean ± SD)		
(Bio experienced)	baseline	1 month	3 months	6 months
SJC	7.78 ± 5.65	2.22 ± 1.92 [*]	0.78 ± 1.09 [*]	0.75 ± 1.49 [*]
TJC	8.67 ± 4.82	2.22 ± 1.79 [*]	1.78 ± 1.72 [*]	1.62 ± 1.84 [*]
CRP (mg/dl)	4.40 ± 4.51	0.82 ± 1.45 ^{**}	0.78 ± 1.00 [*]	0.72 ± 1.10 [*]
CDAI	28.77 ± 12.30	9.06 ± 6.82 [*]	6.23 ± 6.16 [*]	6.28 ± 6.50 [*]
Pain VAS	59.0 ± 28.0	29.1 ± 27.5 [*]	23.8 ± 25.0 [*]	21.3 ± 27.9 [*]
PGA	66.6 ± 25.2	25.4 ± 24.3 [*]	20.6 ± 26.3 [*]	21.6 ± 25.4 [*]
HAQ-DI	1.04 ± 0.56	0.68 ± 0.57 [*]	0.56 ± 0.47 [*]	0.50 ± 0.54 [*]

Table 3. Adverse events		(mean ± SD)	
Barigroup + TNFi group	N (%)		
Pneumonia	2 (6.3)		
Herpes zoster	1 (3.1)		
upper respiratory tract infection	5 (15.6)		
nasopharyngitis	3 (9.3)		
Laboratory data abnormality	15 (46.9)		

[§]p < 0.01 vs baseline

^{*}p < 0.01 vs baseline

[§]p < 0.01 vs baseline

^{*}p < 0.01 vs baseline

Conclusion: These data showed that bari has a favorable benefit-risk balance in a real-world clinic and thus may be considered as a good treatment option for Japanese RA patients who have an inadequate response to csDMARDs or bDMARDs.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.4496

THU0197

MONOTHERAPY WITH UPADACITINIB IN MTX-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-EARLY STUDY

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, was efficacious as monotherapy upto 24 weeks (wks) in MTX-naïve patients (pts) with active RA.¹

Objectives: To assess safety and efficacy of UPA through 48 wks in an ongoing extension of the ph 3 SELECT-EARLY RCT.

Methods: SELECT-EARLY had a 48-wk double-blind active comparator-controlled period. Pts were initially randomized to monotherapy (mono) with UPA 15 or 30 mg or MTX (titrated up to Wk8). Rescue therapy was offered if pts met the following: (1) From Wk 12-24, pts without ≥20% improvement from BL (Δ) in both TJC and SJC at 2 consecutive visits continued blinded study drug with optimized background RA medications. (2) At Wk26, pts with CDAI ≤2.8 continued their original study drug; in pts with CDAI >2.8 and <20% Δ in TJC and SJC, for those on MTX, UPA15/30mg was added; for those on UPA15/30mg, MTX was added. For pts with CDAI ≤2.8 but ≥20%Δ in TJC and SJC, background medications were optimized. Background csDMARDs could be initiated after Wk26. After Wk48, pts could continue in a long-term extension. Efficacy data up to the Wk48 visit are reported based on initial randomized treatment. For binary non-radiographic endpoints, NRI was used for missing data and rescue handling; for continuous non-radiographic endpoints, LOCF was used for rescue handling. Radiographic analyses are based on linear extrapolation for missing data imputation and rescue handling. Adverse events (AE) per 100 pt yrs (PY) are summarized up to a cut-off date of Aug 16 2018.

Results: Of 945 pts randomized and treated, 747(79%) completed Wk48 treatment, 163 (17.2%) discontinued (D/C) study drug prior to Wk48, 35

pts (4%) had not completed the Wk48 treatment as of this analysis. Primary reasons for D/C were AEs for 62 pts (6.5%), and lack of efficacy in 20 pts (2.1%). At Wk26, UPA15/30 was added for 37 (12%) of pts on MTX; MTX was added for 19 (6%) and 9 (3%) of pts on UPA15 and UPA30, respectively. Cumulative exposures to MTX mono, UPA15 mono and UPA30 mono were 314.4, 343.1 and 336.7 PYs, respectively. Through Wk48, pts on UPA15 and 30 vs MTX continued to have significantly greater improvements in clinical, functional and pt-reported outcomes (except FACIT-F for UPA15, p=.058 vs MTX) (Table 1). At Wk 48, CDAI Remission (REM) was achieved by 33% and 40% of pts on UPA15 and 30 respectively vs 17% on MTX; 28% and 33% vs 13% achieved Boolean REM. At Wk48, ΔmTSS were significantly less on UPA15 and UPA30 vs MTX. The safety profile of UPA15 and UPA30 mono was generally similar to MTX, except for total AEs and herpes zoster, which were higher with UPA15 and 30 vs MTX (Table 2). There were 11 deaths (including 3 non-treatment emergent deaths) due to varied causes.

Abstract THU0197 –Table 1.

Table 1. Efficacy Endpoints at Week 48			
	MTX N=314	UPA 15 MG N=317	UPA 30 MG N=314
ACR20, %	57	74***	75***
ACR50, %	43	63***	68***
ACR70, %	29	51***	53***
DAS28-CRP LDA (≤3.2), %	39	59***	66***
DAS28-CRP <2.6, %	29	49***	53***
CDAI LDA, (≤10), %	43	60***	64***
CDAI REM, (≤2.8), %	17	33***	40***
Boolean REM, %	13	28***	33***
Change in HAQ-DI	-0.74	-0.96***	-1.04***
Change in FACIT-F	8.5	10.1*	11.6***
Change in mTSS [§]	1.00	0.03***	0.14***

Results are based on NRI (binary endpoints), LOCF for rescue (change in HAQ-DI, FACIT-F), or linear extrapolation (change in mTSS); ***, p<.001 vs MTX; *, p=.058;

Boolean REM: TJC ≤1, SJC ≤1, CRP ≤1 mg/dl, PGA ≤1 (0–10 scale)

[§]mTSS from 2nd reading session of radiographs at Wk48

Abstract THU0197 –Table 2.

Table 2. Treatment emergent adverse event (AE) summary; E/100PY in Patients on monotherapy (censored at time of change to combination exposure of UPA+MTX/csDMARD)			
	MTX MONO N=314, PYs=314.4	UPA 15 MONO N=317 PY=343.1	UPA 30 MONO N=314 PY=336.7
Any Adverse Event	303.1	345.4	358.2
Serious AE	11.8	14.3	15.4
AE Leading To D/C Of Study Drug	8.9	11.4	10.7
Serious Infection	2.9	4.1	5.0
Herpes Zoster [†]	1.3	6.4	4.8
Hepatic disorder [‡]	19.7	18.7	15.7
Any Malignancy (excluding NMSC) [§]	1.0	1.2	0.6
MACE (adjudicated) [¶]	0.6	0.9	1.2
VTE (adjudicated) [¶]	0.6	0	0.3
Deaths [‡]	0.3	1.2	1.8

[†]Herpes zoster: most involved a single dermatome and were non-serious. No cases of CNS involvement.

[‡]Hepatic disorders: majority were asymptomatic transaminase elevations.

[§]Malignancies excl. NMSC: MTX: 1 malignant neoplasm of ovary, 1 pt with gall bladder adenocarcinoma and hepatic cancer;

UPA15: 1 malignant neoplasm progression, 1 metastatic malignant melanoma, 1 squamous cell carcinoma of lung, 1 uterine carcinoma in situ;

UPA30: 1 cervix cell carcinoma, 1 uterine cancer

[¶]MACE (includes cardiovascular [CV] death, non-fatal Myocardial infarction [MI], non-fatal stroke):

MTX: 1 CV death, 1 non-fatal stroke; UPA15: 1 CV death, 1 pt had 2 adjudicated events: a non-fatal MI, followed by CV death (due to hypoxic encephalopathy, not MI); UPA30: 3 CV deaths, 1 non-fatal MI

[‡]VTE: MTX: 1 pt with PE; 1 pt with DVT and PE; UPA30: 1 DVT

[‡]Deaths (includes non-treatment emergent [NTE] deaths): MTX: 1 due to acute MI; UPA15: 2 due to MI (1 was NTE), 1 due to malignant melanoma and malignant neoplasm (NTE), 1 non-CV death; UPA30: 1 due to pneumonia/sepsis, 1 fatal MI, 2 CV deaths, 1 due to peritonitis, 1 CV death due to other causes (NTE); 1 death due to meningitis was reported on combination of UPA30+csDMARDs

Conclusion: UPA15 and 30 monotherapy continued to show significant improvements in RA signs and symptoms and inhibition of structural damage vs MTX through 48 wks. Only a small proportion of pts required MTX addition to UPA mono at Wk26 to achieve and maintain response. The safety profile based on all exposure remained consistent with ph 2 and 3 RCTs in RA, although an integrated safety analysis of UPA across the full ph 3 RA program will provide a more comprehensive understanding of the benefit:risk profile of UPA in RA.

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Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto of AbbVie, Inc.

Disclosure of Interests: Ronald van Vollenhoven Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, GlaxoSmithKline, Pfizer, Roche, and UCB, Consultant for: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex., Speakers bureau: