events or malignancies were reported in the study through Week 24 for PBO and through Week 52 for BARI group. No unexpected safety signals were observed.

Table 1. Study RA-BALANCE efficacy measures

	Week 12		Week 24		Week 52 [†]
	PBO (N=145)	BARI (N=145)	PBO (N=145)	BARI (N=145)	BARI (N=145)
ACR20, n (%)	41 (28.3)	85 (58.6)***	47 (32.4)	93 (64.1)***	91 (62.8)
ACR50, n (%)	12 (8.3)	44 (30.3)***	17 (11.7)	56 (38.6)***	68 (46.9)
ACR70, n (%)	2 (1.4)	14 (9.7)***	6 (4.1)	27 (18.6)***	36 (24.8)
DAS28-hsCRP ≤3.2, n (%)	13 (9.0)	36 (24.8)***	15 (10.3)	51 (35.2)***	67 (46.2)
DAS28-hsCRP <2.6, n (%)	4 (2.8)	17 (11.7)***	10 (6.9)	21 (14.5)***	48 (33.1)
CDAI ≤10, n (%)	13 (9.0)	26 (17.9)***	13 (9.0)	39 (26.9)***	67 (46.2)
SDAI ≤11, n (%)	12 (8.3)	30 (20.7)***	14 (9.7)	40 (27.6)***	67 (46.2)
HAQ-DI MCID ≥0.22, n (%)	89 (61.4)	102 (70.3)	51 (35.2)	94 (64.8)***	89 (61.4)
HAQ-DI MCID ≥0.3, n (%)	67 (46.2)	90 (62.1)***	45 (31.0)	85 (58.6)***	83 (57.2)
LS mean Δ Patient's Assessment of Pain (0-100 mm VAS) [‡]	-17.7	-31***	-20.1	-34.8***	-40.2
LS mean Δ Patient's Global Assessment of Disease Activity (0-100 mm VAS) [‡]	-20.0	-31.3***	-18.5	-33.4***	-37.8

PBO, placebo; BARI, baricitinib; MCID, minimum clinically important difference; VAS, visual analogue scale. Patients received stable background MTX throughout the study. Data are % patients (NRI), unless otherwise stated. *Data are least squares (LS) mean change from baseline; †Initially randomized to baricitinib. **p<0.05, ***p<0.001, ****p<0.0001 vs PBO.

Conclusions: Compared to PBO, BARI provided significant improvements in control of signs and symptoms, including pain and physical function with an acceptable safety profile.

Disclosure of Interest: Z. Li Consultant for: Advisory board member of baricitinib, J. Hu: None declared, C. Bao Consultant for: Advisory board member of baricitinib, X. Li Consultant for: Advisory board member of baricitinib, X. Li Consultant for: Advisory board member of baricitinib, J. Xu: None declared, A. Spindler: None declared, X. Zhang Consultant for: Advisory board member of baricitinib, J. Xu Consultant for: Advisory board member of baricitinib, Z. Li Consultant for: Advisory board member of baricitinib, G. Wang Consultant for: Advisory board member of baricitinib, J. Sun Shareholder of: Eli Lilly and company, Employee of: Eli Lilly and company, F. Ji Shareholder of: Eli Lilly and company, Employee of: Eli Lilly and company, H. Tao Shareholder of: Eli Lilly and company, Employee of: Eli Lilly and company, L. Zhan Employee of: Eli Lilly and company, T. Rooney Shareholder of: Eli Lilly and company, Employee of: Eli Lilly and company, C. Zerbini Grant/research support from: Grants for research received by my research center CEPIC, for teriparatide and baricitinib protocols, Consultant for: Advisory board member of baricitinib

DOI: 10.1136/annrheumdis-2018-eular.1983

SAT0219

UPADACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS: A PHASE 3 RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY OF A SELECTIVE JAK1 INHIBITOR

M. C. Genovese¹, R. Fleischmann², B. Combe³, S. Hall⁴, Y. Zhang⁵, Y. Zhou⁵, M. F. Mohamed⁵, S. Meerwein⁶, A. L. Pangan⁵. ¹Stanford Univ, Palo Alto, ²Univ of Texas Southwestern, Dallas, United States, ³Montpellier Univ, Montpellier, France, ⁴Monash Univ, Cabrini Health & Emeritus Res, Malvern, Australia, ⁵AbbVie, N Chicago, United States, ⁶AbbVie Deutschland, Ludwigshafen, Germany

Background: Upadacitinib (UPA), an oral, selective JAK1 inhibitor was effective in ph 2 trials in rheumatoid arthritis (RA) pts with inadequate response (IR)/intolerance to csDMARDs and bDMARDs.

Objectives: To evaluate safety and efficacy of UPA in bDMARD-IR pts on stable background csDMARDs.

Methods: Pts with active RA (TJC≥6, SJC≥6; hsCRP≥3 mg/L) were randomized 2:2:1:1 to receive UPA 15 mg or 30 mg once daily (QD) or PBO for 12 wks followed by UPA 15 mg or 30 mg QD starting at Wk 12. The primary endpoints were the proportion of pts achieving ACR20 (for FDA) and the proportion achieving DAS28CRP≤3.2 (for EMA) at Wk 12 (NRI).

Results: Of 499 randomized pts, 498 received study drug; 451 (90.6%) and 419 (84.1%) completed Wks 12 and 24 respectively. BL disease characteristics

indicated long-standing severe, refractory disease: (means) duration since diagnosis 13 yrs; DAS28CRP, 5.8; TJC68, 27.9; SJC66, 16.8; 53% experienced ≥2 prior bDMARDs. At Wk 12, more pts (p<0.001) on UPA 15 and 30 vs PBO achieved the primary endpoints (ACR20: 64.6% and 56.4% vs 28.4%; DAS28CRP≤3.2: 43.3% and 42.4% vs 14.2%) and other secondary endpoints (Table). Among pts with IR to multiple bDMARDs/MOAs, and pts with lack of efficacy for α-IL-6, the proportions achieving ACR20 on UPA vs PBO were comparable to the overall treated population. By Wk 1, more pts achieved ACR20 on UPA 15 and 30 vs PBO (27.4% and 24.8% vs 10.7%, p<0.001). At Wk 12, significant improvements were observed on UPA 15 and 30 vs PBO for HAQ-DI (LSM change -0.39 and -0.42 vs -0.17, p<0.001). At Wk 24, responses were similar or greater for pts originally on UPA and comparable for pts who switched to UPA after 12 wks of PBO.

Up to wk 12, the frequency of AEs was comparable for PBO and UPA 15, but higher for UPA 30 (table 1). Overall AE rates (E/100 PY) through Wk 24 for UPA 30 were similar or slightly higher vs UPA 15; more AEs led to study drug discontinuation in UPA 30. Occurrence of infections was similar in all arms, but there were more serious infections and herpes zoster cases in UPA 30. Malignancies were reported in 3 pts over 12 wks with 1 additional case through Wk 24. Through Wk 12, pulmonary embolism (PE) was reported in 2 pts (1 each on UPA 15 and 30), none with DVT; through Wk 24, PE were reported in 4 more pts (UPA 15: 3, 1 of whom also had a DVT; UPA 30:1). All had risk factors for DVT/PE. 2 deaths were reported (UPA30: 1 before Wk 12; UPA 15:1 after Wk12).

Efficacy Measures [†] ; Percentage of Patients with a Response	Week 12			Week 24			
	PBO N=169	UPA 15 N=164	UPA 30 N=165	PBO→ UPA 15 N=85	PBO→ UPA 30 N=84	UPA 15 N=164	UPA 30 N=165
ACR20	28.4	64.6***	56.4***	61.2	60.1	61.6	59.4
DAS28-CRP≤3.2	14.2	43.3***	42.4***	38.8	36.0	52.4	51.5
ACR50	11.8	34.1***	35.8***	35.3	38.1	42.7	43.0
ACR70	6.5	11.6	23.0***	22.4	21.4	22.0	24.2
CDAI ≤10	14.2	31.7***	33.9***	34.1	30.6	47.0	43.6
CDAI ≤8	4.7	7.9	11.5*	12.9	14.3	10.4	15.2
DAS28-CRP <2.6	9.5	28.7***	23.6***	28.2	34.5	32.3	34.5
ACR20 in pts who failed ≥2 bDMARDs and/or ≥3 MOA	23.1	70.8	50.0	-	-	-	-
ACR20 in pts with LoE for anti-IL6	20.0	55.6	58.1	-	-	-	-
Summary of AEs, n (%)							
	Week 0-12			Week 12-24			
	PBO N=169	UPA 15 N=164	UPA 30 N=165	PBO→ UPA 15 N=72	PBO→ UPA 30 N=75	UPA 15 N=156	UPA 30 N=168
AEs	95 (56.2)	91 (55.5)	111 (67.3)	30 (41.7)	50 (66.7)	82 (52.6)	83 (56.1)
AE Leading To D/C	9 (5.3)	4 (2.4)	15 (9.1)	2 (2.8)	3 (4.0)	5 (3.2)	5 (3.4)
Serious AEs	0	8 (4.9)	12 (7.3)	5 (6.9)	5 (6.7)	5 (3.2)	5 (3.4)
Patients with Adverse Events of Special Interest, n (%)							
Infection	51 (30.2)	54 (32.9)	55 (33.3)	16 (22.2)	31 (41.3)	43 (27.6)	47 (31.8)
- Serious Infection	0	1 (0.6)	4 (2.4)	2 (2.8)	1 (1.3)	1 (0.6)	2 (1.4)
- Opportunistic Infection [‡]	0	1 (0.6)	2 (1.2)	0	0	0	1 (0.7)
- Herpes Zoster [§]	1 (0.6)	1 (0.6)	4 (2.4)	0	1 (1.3)	2 (1.3)	2 (1.4)
- Tuberculosis	0	0	0	0	0	0	0
Malignancy (exc NMSC) [¶]	0	1 (0.6)	2 (1.2)	0	0	1 (0.6)	0
NMSC	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0
Hepatic Disorder	2 (1.2)	2 (1.2)	3 (1.8)	0	2 (2.7)	4 (2.6)	4 (2.7)
GI Perforation	0	0	0	0	0	0	1 (0.7)
PE	0	1 (0.6)	1 (0.6)	2 (2.8) [§]	1 (1.3)	1 (0.6)	0
CV Events adjudicated [§]	0	1 (0.6)	0	0	1 (1.3)	2 (1.3)	0
Deaths [§]	0	0	1 (0.6)	0	0	1 (0.6)	0

D/C, discontinuation; LoE, lack of efficacy; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; GI, gastrointestinal; CV, cardiovascular

[†]Opportunistic infections: oral candidiasis, one case of mucocutaneous candidiasis

[‡]Herpes Zoster: most were mild and all but one were single dermatome; 2 serious cases

[§]Malignancies through Wk 12-UPA 15: 1 malignant melanoma; UPA 30: 2 pts with prostate cancer. Wk 12-24, UPA 15: 1 pt with bladder cancer

[¶]1 pt also had DVT; [§]Adjudicated CV events through Wk 12-UPA 15 mg: 1 pt with ischemic stroke. Wk 12-24, UPA 15: 1 pt with CV procedure, 1 pt with cardiac arrest adjudicated to undetermined/unknown cause of death; UPA 30: 1 pt with myocardial infarction; Deaths through Wk 12-UPA 30: 1 due to cardiac failure & PE. Wk 12-24, UPA 15: 1 unwitnessed death adjudicated as undetermined/unknown cause of death

Conclusions: In this treatment-refractory, bDMARD-IR RA population, rapid, significant improvements were observed with UPA at both doses vs PBO during 12 wks of treatment, and maintained through 24 wks. Overall safety was consistent with ph2 and other ph3 studies with UPA. The rates of PE and DVT observed in this study have not been reported for the other ph3 studies that have been unblinded to date. Overall data from the ph3 program will allow a comprehensive evaluation of the benefit:risk profile of UPA in RA.

Acknowledgements: AbbVie sponsored study design, data collection, analysis & interpretation, writing, review, approval of final. Med writing:Naina Barretto of AbbVie

Disclosure of Interest: M. Genovese Grant/research support from: AbbVie, Lilly, Pfizer, Galapagos, Gilead, Consultant for: AbbVie, Lilly, Pfizer, Galapagos, Gilead, R. Fleischmann Grant/research support from: AbbVie, Consultant for: AbbVie, B. Combe Consultant for: AbbVie, BMS, Jansen, Lilly, MSD, Pfizer, Roche Chugai, UCB, S. Hall: None declared, Y. Zhang Shareholder of: AbbVie, Employee of: AbbVie, Y. Zhou Shareholder of: AbbVie, Employee of: AbbVie, M. Mohamed Shareholder of: AbbVie, Employee of: AbbVie, S. Meerwein Shareholder of: AbbVie, Employee of: AbbVie, A. Pangan Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2018-eular.4180