Figure. Change from baseline in SF-36 at 16 weeks in (A.) biologic naïve patients and (B.) TNFi-experienced patients

*p<0.05, **p<0.01, ***p<0.001, compared to PBO.

SF-36=Short Form-36 Questionnaire; PCS=physical component summary; MCS=mental component summary; LSM=least squares mean; PBO=placebo; ADA=adalimumab 40 mg every 2 weeks; IXE Q4W= 80 mg IXE every 4 weeks; IXE Q2W=80 mg IXE every 2 weeks

Results: Biologic naïve and TNFi-experienced patients treated with IXE reported significantly greater improvement than PBO patients in SF-36 Physical Component Summary and the physical functioning, bodily pain, general health, and vitality domains. No changes between treatments groups were reported in Mental Component Summary scores. The greatest numerical improvements with IXE were observed in the bodily pain domain. Similar improvements were reported in the IXE Q4W, IXE Q2W, and ADA groups.

Conclusion: IXE improved self-reported HRQoL, as measured by the SF-36 questionnaire, at Week 16 in patients with active AS/r-axSpA who were naïve or experienced with biologic treatments.

REFERENCES:

- [1] Yang, et al. (2016). Qual Life Res. 25:2711-23.
- [2] van der Heijde, et al. (2018). Lancet. 392(10163):2441-51.
- [3] Deodhar, et al. (2018). *Arthritis Rheumatol*. Doi: 10.1002/art.40753.

Disclosure of Interests: Jessica A. Walsh Grant/research support from: Abbvie, Pfizer, Consultant for: Abbvie, Celgene, Lilly, Novartis, Uta Kiltz Grant/research support from: AbbVie, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB., Consultant for: AbbVie, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB., James Cheng-Chung Wei Grant/research support from: Abbvie, BMS, Celgene, Janssen, Novartis, Pfizer, and UCB pharma, Consultant for: TSH Taiwan, Speakers bureau: Janssen, Novartis, Pfizer and TSH, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB., Theresa Hunter Employee of: Eli Lilly and Company, Yan Dong Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Xiaoqi Li Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Luis Leon Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Vibeke Strand Consultant for: AbbVie, Amgen, Bayer, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmedix, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Sam-sung, Sandoz, Sanofi, Servier, UCB.

DOI: 10.1136/annrheumdis-2019-eular.1237

FRI0421

IXEKIZUMAB SIGNIFICANTLY REDUCED PAIN, INFLAMMATION, AND FATIGUE IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLARTHROSIS (R-AXSPA)/ANKYLOSING SPONDYLITIS (AS)

James Cheng-Chung Wei¹, Xenofon Baraliakos², Theresa Hunter³, Baojin Zhu³, Rebecca Bolce³, Fangyi Zhao³, Philip J. Mease⁴. ¹Chung Shan Medical University Hospital, Taichung City, Taiwan, Republic of China; ²Rheumazentrum Ruhrgebiet Herne, Ruhr University Bochum, Herne, Germany; ³Eli Lilly and Company, Indianapolis, United States of America; ⁴Swedish Medical Center/Providence St. Joseph Health, Seattle, United States of America

Background: Chronic pain, inflammation, and fatigue are among the most common symptoms of radiographic axial spondyloarthritis (r-axSpA)/ankylosing spondylitis (AS).^{1,2} Efficacy data for ixekizumab (IXE), a high affinity monoclonal antibody that selectively targets interleukin-17A, compared to placebo (PBO) in patients with r-axSpA have been reported.^{3,4}

Objectives: The purpose of this analysis was to evaluate the impact of IXE on pain, inflammation, and fatigue in patients with r-axSpA treated with IXE versus PBO over 16 weeks.

Methods: This was a prespecified analysis from two Phase 3, multicenter, randomized, placebo-controlled studies comparing the efficacy and safety of IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) to PBO or reference, adalimumab (ADA), over 16 weeks in biologic-naïve (COAST-V; NCT02696785) and to PBO in tumor necrosis factor inhibitor (TNFi)-experienced (COAST-W; NCT02696798) patients with active r-axSpA per Assessment of Spondyloarthritis (SpA) international Society (ASAS) criteria (sacroiliitis modified New York criteria and ≥ 1 SpA feature). Patient global, spinal pain, spinal pain at night, and inflammation (average of BASDAI Q5&6) data were collected at baseline and Weeks 1, 2, 4, 8, 12, and 16. Fatigue Numeric Rating Scale data were collected at baseline, Week 8, and Week 16. Changes from baseline were analyzed using mixed-effects model of repeated measures.

Results: In biologic-naïve (COAST-V) and TNFi-experienced (COAST-W) patients, significant improvements from baseline in patient global, spinal pain, spinal pain at night, and inflammation were observed as early as Week 1 (Table 1, Figure 1). Significant reductions in fatigue as early as Week 8 (first measurement) were seen in patients receiving IXE Q2W and Q4W and maintained up to Week 16 (Table 1; $P<0.05$).

Table 1. Change from baseline in patient global, inflammation, and fatigue in patients with r-axSpA with IXE, ADA, and PBO in biologic-naïve (COAST-V) and TNFi-experienced (COAST-W) patients

Parameter	Study	Week	Least Squares Mean (Standard Error)			
			IXE Q2W	IXE Q4W	ADA	PBO
Patient Global	COAST-V	1	-1.3 (0.17)	-1.3 (0.18)	-1.4 (0.17)	-0.6 (0.17)
		16	-2.8 (0.25)*	-2.5 (0.25)	-2.6 (0.24)*	-1.4 (0.24)
	COAST-W	1	-1.3 (0.18)*	-1.1 (0.16)	-	-0.4 (0.16)
		16	-2.1 (0.24)*	-2.4 (0.22)*	-	-0.7 (0.23)
	COAST-V	1	-1.5 (0.18)*	-1.6 (0.18)*	-1.4 (0.17)*	-0.4 (0.18)
		16	-2.9 (0.23)*	-3.2 (0.24)*	-2.7 (0.22)*	-1.3 (0.23)
Inflammation (average of BASDAI Q5/Q6)	COAST-W	1	-1.4 (0.17)*	-1.3 (0.15)*	-	-0.4 (0.16)
		16	-2.4 (0.25)*	-2.4 (0.23)*	-	-0.7 (0.24)
	COAST-V	8	-1.7 (0.23)*	-2.0 (0.23)	-2.1 (0.22)*	-0.9 (0.22)
		16	-2.1 (0.24)*	-2.5 (0.24)	-2.2 (0.23)*	-1.4 (0.23)
	COAST-W	8	-1.5 (0.23)	-1.8 (0.21)*	-	-0.5 (0.22)
		16	-1.7 (0.25)	-2.0 (0.23)*	-	-0.7 (0.24)
Fatigue NRS	COAST-V	8	-1.7 (0.23)*	-2.0 (0.23)	-2.1 (0.22)*	-0.9 (0.22)
		16	-2.1 (0.24)*	-2.5 (0.24)	-2.2 (0.23)*	-1.4 (0.23)
	COAST-W	8	-1.5 (0.23)	-1.8 (0.21)*	-	-0.5 (0.22)
		16	-1.7 (0.25)	-2.0 (0.23)*	-	-0.7 (0.24)

*p<0.001 vs PBO; p<0.01 vs PBO; †p<0.05 vs PBO.

ADA, adalimumab; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IXE, ixekizumab; NRS, Numeric Rating Scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

Figure 1. Change from baseline in pain over 16 weeks in A) biologic-naïve patients (COAST-19) and B) TNF-experienced patients (COAST-20)

*p<0.001 vs PBO; **p<0.01 vs PBO

ADA, anti-adalimumab; IXE, ixekizumab; LSM, least squares mean; NRS, Numeric Rating Scale; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

Conclusion: IXE significantly improved pain, inflammation, and fatigue in patients with r-axSpA.

REFERENCES:

- [1] Sieper J, et al. *Lancet*. 2017;390:73–84.
- [2] Stebbings SM, et al. *Clin Rheumatol*. 2014;33:1467–74.
- [3] Van der Heijde D, et al. *Lancet*. 2018;392:2411–51.
- [4] Deodhar A, et al. *Arthritis Rheumatol*. 2018 Oct 20. Doi: :10.1002/art.40753.

Disclosure of Interests: James Cheng-Chung Wei Grant/research support from: Abbvie, BMS, Celgene, Janssen, Novartis, Pfizer, and UCB pharma, Consultant for: TSH Taiwan, Speakers bureau: Janssen, Novartis, Pfizer and TSH, Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Theresa Hunter Employee of: Eli Lilly and Company, Baojin Zhu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Rebecca Bolce Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Fangyi Zhao Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Philip J Mease Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun and UCB., Consultant for: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, Sun, UCB., Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer, and UCB.

DOI: 10.1136/annrheumdis-2019-eular.1236

FRI0422

HS016, A PROPOSED ADALIMUMAB BIOSIMILAR, SHOWED EQUIVALENT PHARMACOKINETICS AND SIMILAR SAFETY, IMMUNOGENICITY AND TOLERABILITY TO CHINA-LICENSED ADALIMUMAB IN HEALTHY MALE SUBJECTS, ACCORDING TO A 2.3-MONTHS PHASE I STUDY

Guoying Cao¹, Jicheng Yu¹, Jingjing Wang¹, Xiaoli Yang¹, Yu Xue², Jufang Wu¹, Xiaojie Wu¹, Jing Zhang¹. ¹Phase I Clinical Trial Center, Huashan Hospital Fudan University, Shanghai, China; ²Department of Rheumatology, Huashan Hospital Fudan University, Shanghai, China

Background: HS016, a biosimilar to China-licensed adalimumab, has an identical amino acid sequence, similar physicochemical and in vitro functional properties to China-licensed adalimumab.

Objectives: The primary objective of this study was to demonstrate PK equivalence between HS016 and China-licensed adalimumab. PK characteristics, safety, tolerability and immunogenicity were investigated as secondary objectives.

Methods: The first-in-human study was a randomized, double-blind, parallel-control, single-dose study conducted in 136 healthy male subjects at 1 site in China. Subjects were randomized to receive a 40 mg subcutaneous injection of either HS016 or China-licensed adalimumab and were followed up for 70 days. Blood samples were taken pre-dose and at multiple intervals to day 70.

The primary outcomes were area under the concentration-time curve from time zero to time t (AUC_{0-t}) area under the concentration-time curve from time zero to infinity (AUC_{0-∞}), and maximum concentration (C_{max}). The secondary endpoints were the time taken to reach the maximum concentration (T_{max}), elimination half-life (T_{1/2}) etc. Equivalence for the primary outcomes were to be concluded if the 90% confidence intervals (CIs) for

the ratio of geometric least squares means (LS Means) of the groups compared were completely contained within the pre-defined equivalence margin of 0.8 to 1.25 using analysis of variance (ANOVA).

Safety indicators mainly included physical examination, vital signs, laboratory examination, electrocardiogram, chest X-ray, etc. Immunogenicity evaluation explored kinetics and magnitude of anti-drug antibody (ADA) and its neutralizing ability of Neutralizing ADA.

Results: The 90% confidence intervals of geometric least squares means ratios (GMR) of C_{max}, AUC_{0-∞} and AUC_{0-t} between HS016 and China-licensed adalimumab arms were (0.9855, 1.1359), (0.8743, 1.0841) and (0.8724, 1.0605). The 90% confidence intervals of all GMRs fell within pre-specified confidence bounds of 80% to 125%.

Table 1. Statistical Analysis of Bioequivalence-Pharmacokinetic Analysis Set

	Statistic	Ismeans	95% CIs	GLSM	95% CIs	HS016 compare with adalimumab 90% CIs
HS016 (N=68)	AUC _{0-t} (hr·ng/mL)	14.66	(14.58, 14.74)	2326562.38	(2142491.09, 2526448.09)	(0.8724, 1.0605)
	AUC _{0-∞} (hr·ng/mL)	14.73	(14.63, 14.82)	2484615.56	(2268102.44, 2721797.02)	(0.8743, 1.0841)
	C _{max} (ng/mL)	8.3	(8.24, 8.36)	4034.86	(3799.95, 4284.29)	(0.9855, 1.1359)
adalimumab (N=68)	AUC _{0-t} (hr·ng/mL)	14.7	(14.62, 14.78)	2418702.15	(2227341.01, 2626504.01)	
	AUC _{0-∞} (hr·ng/mL)	14.75	(14.66, 14.84)	2552064.12	(2331241.56, 2793803.70)	
	C _{max} (ng/mL)	8.25	(8.19, 8.31)	3813.61	(3591.58, 4049.36)	

Of the 136 subjects, 128 had adverse events (AEs) with 63 (92.6%) and 65 (95.6%) AEs occurring in the HS016 and China-licensed adalimumab, respectively. Among these AEs, 172 from 50 subjects (73.5%) in HS016 group and 148 from 55 subject (80.9%) in China-licensed adalimumab were treatment emergent adverse event.

The proportion of confirmed anti-drug antibody responses in the 2 study arms were, 25.0% (17 cases) and 22.1% (15 cases) at day 14, 50.0% (34 cases) and 42.6% (29 cases) at day 42, for the HS016 and China-licensed adalimumab arms, respectively. Neutralizing antibodies were all negative at day 14 for both groups, except 2 cases (3.7%) and 1 case (1.6%) at day 42, for the HS016 and China-licensed adalimumab arms, respectively.

Conclusion: It is concluded that HS016 have shown a similar PK to china -licensed adalimumab in healthy male subjects, and no meaningful differences in safety of immunogenicity were observed.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3883

Psoriatic arthritis

FRI0423

NAIL ULTRASONOGRAPHY FINDINGS IN GRAYSCALE AND POWER DOPPLER TO DIFFERENTIATE PSORIATIC ARTHRITIS, PSORIASIS AND CONTROL INDIVIDUALS

Samanta DE Rossi^{1,2}, José Alexandre Mendonça³, Penelope Palominos¹, Charles Kohem¹, Tania Cestari², Rafael Chakr¹. ¹Hospital de Clínicas de Porto Alegre – Universidade Federal do Rio Grande do Sul, Rheumatology, Porto Alegre, Brazil; ²Hospital de Clínicas de Porto Alegre – Universidade Federal do Rio Grande do Sul, Dermatology, Porto Alegre, Brazil; ³Pontifical Catholic University of Campinas, Rheumatology, Campinas, Brazil

Background: The early diagnosis of psoriatic arthritis (PsA) on patients with psoriasis (PsO) is challenging, but may prevent functional impairment. Patients with nail psoriasis have an odds ratio of nearly 3.0 of developing psoriatic arthritis. Ultrasonography is a replicable, radiation-free method that could be used to identify nail changes before clinical manifestations.

Objectives: To verify if nail changes identified via ultrasonography can differentiate between PsA and PsO patients as well as between PsA/PsO patients and a control group.