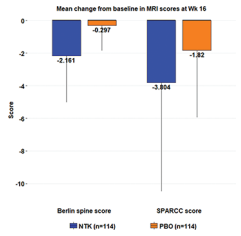

Figure 1. Change from baseline in MRI scores

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FRI0413 EFFICACY, PHARMACOKINETICS, SAFETY AND IMMUNOGENICITY OF THE BIOSIMILAR HS016 IN COMPARISON WITH ADALIMUMAB IN CHINESE PATIENTS WITH ANKYLOSING SPONDYLITIS: A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PARALLEL-GROUP, PHASE 3 TRIAL

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

Objectives: To assess the efficacy, pharmacokinetic (PK) equivalence, safety and immunogenicity of HS016 compared with adalimumab in Chinese patients with ankylosing spondylitis (AS).

Methods: In a multicenter, randomized, double-blind, parallel-controlled phase 3 study, patients with AS fulfilled with the Modified New York Criteria in 1984 in China were randomized 2:1 to receive HS016 or adalimumab with a dose of 40mg every other week for 24 weeks. Blood samples for PK analyses were collected in about half of AS patients pre-dose every other week and during week 12 and week 14. Samples for anti-drug antibodies (ADA) and neutralizing antibodies (NAb) were analyzed in all patients. The primary endpoint was the proportion of patients achieving 20% improvement in Assessment in SpondyloArthritis International Society (ASAS 20) at week 24. Equivalent efficacy was concluded if 90% confidence interval (CI) of the difference in ASAS 20 response rate was between -15% and 15%. The secondary endpoints included the ASAS 20 response rate at week 12, ASAS 40, 50% improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI 50), ASAS5/6 response rate at week 12 and week 24, PK, safety and immunogenicity.

Results: 416 patients were randomly assigned to receive HS016 and 232 to receive adalimumab. The ASAS 20 response rates at week 24 were 87.50% and 90.09% in HS016 and adalimumab groups, respectively, and the difference was -2.59% (90%CI, -6.77% to 1.60%), demonstrating clinical equivalence between HS016 and adalimumab. No significant difference of the proportion of ASAS 40, BASDAI 50 and ASAS 5/6 between the two groups were detected at week 12 or week 24 (table 1).

Table 1. Response rates (%) at week 12 and week 24.

	Week 12			Week 24		
	HS016 (N=416)	Adalimumab (N=232)	P value	HS016 (N=416)	Adalimumab (N=232)	P value
ASAS 20	79.57	81.03	0.65	87.50	90.09	0.32
ASAS 40	58.65	61.64	0.35	71.15	75.43	0.18
BASDAI 50	61.78	61.21	0.96	76.44	78.45	0.52
ASAS 5/6	57.45	58.62	0.86	62.98	67.24	0.37

ASAS, the Assessment in SpondyloArthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

Pharmacokinetic values from 188 AS patients in HS016 group and 109 in adalimumab group were analyzed. The geometric means for steady-state maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from time zero to infinity (AUC_{inf}) were similar between HS016 group and adalimumab group. The proportions of treatment-emergent adverse events, serious adverse events and injection site reactions were similar between the two groups (table 2).**Table 2**. Adverse events in AS patients with HS016 or adalimumab.

Adverse events N (%)	HS016 (N=416)	Adalimumab (N=232)
TEAEs	352 (84.62)	200 (86.21)
TEAEs related to study drug	267 (64.18)	154 (66.38)
TEAEs leading to discontinuation	22 (5.29)	15 (6.47)
SAEs	18 (4.33)	6 (2.59)
Injection site reactions	21 (5.05)	11 (4.74)

TEAE, treatment-emergent adverse event; SAE, serious adverse event.

The frequencies of ADA and NAb positive were similar between the two groups at different time points. Through week 24, 79.13% of 412 patients in HS016 and 79.91% of 229 patients in adalimumab group developed ADAs, and 17.48% of 412 in HS016 and 18.78% of 229 in adalimumab group developed NAbs.

Conclusion: The results of efficacy, PK, safety, immunogenicity from the study conducted in Chinese AS patients support a high similarity between HS016 and the adalimumab.

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FRI0414 SECUKINUMAB PROVIDES RAPID AND SIGNIFICANT IMPROVEMENT IN THE SIGNS AND SYMPTOMS OF ANKYLOSING SPONDYLITIS: PRIMARY (16-WEEK) RESULTS FROM A PHASE 3 CHINA-CENTRIC STUDY, MEASURE 5

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Background: Secukinumab (SEC), a fully human monoclonal antibody to IL-17A, has demonstrated significant and sustained efficacy in patients (pts) with ankylosing spondylitis (AS) across several phase 3 studies.[1-3] MEASURE 5 (NCT02896127) is a placebo (PBO)-controlled phase 3 China centric 1-year study in pts with active AS.

Objectives: To present the primary efficacy and safety results of the MEASURE 5 study.

Methods: Pts were randomised (2:1) to receive subcutaneous (s.c.) SEC 150 mg or PBO at baseline (BL), Weeks (Wks) 1, 2, 3, and 4, and then every 4 wks (q4w) thereafter through Wk 52. All PBO pts were switched to s.c. SEC 150 mg q4w starting at Wk 16. Primary endpoint was ASAS20 at Wk 16. Key secondary endpoints were ASAS40, hsCRP, ASAS5/6, BASDAI, SF-36 PCS, ASQoL and ASAS partial remission (PR). Randomisation was stratified by geographic location (China vs. non-China). Statistical analyses used non-responder imputation (NRI) for binary and mixed-effect model repeated measures (MMRM) for continuous variables. A pre-defined hierarchical testing strategy was used for overall population to adjust multiplicity. Safety analysis included all pts who received $\geq$1 dose of SEC.

Results: A total of 458 pts were randomised; 327 (71.4%) from China and 131 (28.6%) from Czech Republic, South Korea and UK. Overall, 97.7% (298/305) and 97.4% (149/153) pts in the SEC and PBO groups, respectively, completed 16 wks. BL characteristics were comparable between groups. Approximately 24% of pts were anti-TNF-inadequate responders/intolerant. The primary endpoint was met; SEC (58.4%) significantly improved ASAS20 response at Wk 16 vs. PBO (36.6%; $P < 0.0001$); corresponding rates were 56.0% vs. 38.5% ($P < 0.01$) in the Chinese population. Improvements were demonstrated in all secondary

endpoints at Wk 16 for SEC vs. PBO (overall and Chinese populations; Table). Serious AE rates were reported in 3.3% and 2.0% of SEC and PBO pts, respectively. Uveitis was reported in 1.0% (SEC) and 0.7% (PBO) of pts. No MACE, IBD or deaths were reported.

Conclusion: SEC demonstrated rapid and significant improvement in the signs and symptoms of AS in both the overall and Chinese populations. Secukinumab was well tolerated with no new safety signals identified.

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Table. Wk 16 data

	Overall		Chinese	
	SEC 150 mg (N=305)	PBO (N=153)	SEC 150 mg (N=218)	PBO (N=109)
ASAS20[1]	58.4*	36.6	56.0§	38.5
ASAS40[1]	43.9*	17.0	41.7*	16.5
hsCRP[2,3]	0.39*	1.05	0.33*	0.97
ASAS5/6[1]	47.2*	17.6	45.9*	17.4
BASDAI[2]	-2.79*	-1.50	-2.63*	-1.37
SF-36 PCS[2]	7.43*	4.60	7.18*	4.07
ASQoL[2]	-4.83*	-2.93	-4.50†	-2.50
ASAS PR[1]	16.7§	6.5	15.1‡	6.4

*$P < 0.0001$; †$P < 0.001$; §$P < 0.01$; ‡$P < 0.05$ vs. PBO (P-values are adjusted for overall and un-adjusted for Chinese populations). NRI for binary and MMRM for continuous variables.

[1]% responders; [2]LS mean change from BL; [3]ratio of post-BL/BL; LS, least squares; N, total number of randomised pts

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FRI0415

BIOSIMILAR BAT1406 VERSUS ADALIMUMAB THERAPY ON ACTIVE ANKYLOSING SPONDYLITIS: A RANDOMIZED, DOUBLE-BLINDED, MULTICENTER, CONTROLLED PHASE 3 TRIAL

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Background: Adalimumab has been proved to be effective and safety in management of ankylosing spondylitis (AS) in several clinical trials. In China, small proportion of AS patients had ever used TNF inhibitors and most of them discontinued because of expensive cost. BAT1406 and ADA have demonstrated comparable in protein structure, physicochemical properties, biological activity and immunological characteristics.

Objectives: To compare the effects, safety and immunogenicity of biosimilar BAT1406 vs adalimumab (ADA) in patients with active AS.

Methods: A multicenter, randomized, non-inferiority, double-blinded, ADA controlled clinical trial with 24 weeks of follow-up was conducted in China. Participants with active AS defined as BASDAI $\geq$4 and average back pain score (VAS 0-10) $\geq$4 were eligible for participation. Participants were randomly assigned to receive BAT1406 (40mg q2w) or adalimumab (40mg q2w) at a ratio of 2:1 for 24 weeks. Primary outcome was the proportion of patients achieving ASAS20 response at 12 weeks. Inclusion of the 95% CI of the ASAS20 response difference within a ± 15% margin was required for equivalence. Secondary outcomes included ASAS40, ASAS5/6, BASDAI50 response, patient reported outcomes, safety and immunogenicity. This trial is approved by China Food and Drug Administration (number 2015L05751).

Results: 554 eligible patients were enrolled from Jan 2017 to Aug 2017 and randomly assigned to receive BAT1406 (n=363) or Adalimumab (n=191) participants, 514 completed the study. Patients (86.5% of whom were male and whose mean age was 31.6 years) had a mean disease duration was 5.82 years. Over 12 weeks, 75.69% of patients in BAT1406 group and 73.68% in ADA group (between group difference 1.6%, 95% CI [-6.82% to 10.03%]) achieved ASAS20 response (per-protocol set; adjusted treatment difference 2.16%, 95% CI [-6.9% to 11.22%]). Outcomes for secondary end points were consistent with the primary efficacy findings. The frequency of adverse events (AEs) was comparable between groups ((BAT1406 316[87.1%] vs ADA 162 [85.3%]), as well as serious AEs, adverse drug reactions and discontinuations due to AEs. Similar positive rate was found in two groups for anti-drug antibodies up to week 24.

Conclusion: The study met the primary endpoint of demonstrating equivalent efficacy of BAT1406 and ADA. BAT1406 was comparable in tolerance, safety and immunogenicity with ADA in active AS patients.

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