


Abstract N°: 669
safety, pharmacokinetics, pharmacodynamics effects and immunogenicity of jyb194, a novel half-life extended anti-ige monoclonal antibody: a randomized, double-blind, placebo and positive controlled study in healthy participants

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Introduction & Objectives:

Immunoglobulin E (IgE)-mediated pathways drive multiple inflammatory disease, including urticaria, asthma and food allergy. JYB1904 is a novel recombinant humanized half-life extended anti-IgE monoclonal antibody. The objective of this first-in-human study was to characterize the safety, pharmacokinetics (PK), pharmacodynamics (PD) and immunogenicity of JYB1904 in healthy participants.

Materials & Methods:

This was a randomized, double-blind, placebo and positive-controlled phase I study with single ascending doses. 8 participants were enrolled in 75 mg group and receive JYB1904 or the placebo in a 3:1 ratio. 10 participants were enrolled in each of ascending dose groups (150, 300, 450, 600 mg) to receive JYB1904 or the placebo in a 4:1 ratio. 8 participants were enrolled in the 150 mg omalizumab group as active control in non-blinded manner. All the participants were followed-up until Day 168. Safety was assessed by ECG, vital signs, physical examination, laboratory assessments and adverse events (AEs). PD endpoints included serum free and total IgE.

Results:

Demographic Characteristics: A total of 56 participants were enrolled with 38 participants receiving JYB1904, 10 participants receiving placebo and 8 participants receiving 150 mg omalizumab. 20 (35.7%) participants were female. The mean age was 30.9 years old, ranging from 18 to 48 years old.

Safety: All treatment-emergent AEs (TEAEs) were Grade 1-2 in severity. No SAEs were reported.

No consistent, clinically relevant abnormalities were identified in safety laboratory, vital sign or 12-lead ECG data.

Table 1. Summary of TEAE (SS)

	JYB1904 75 mg (N=6)	JYB1904 150 mg (N=8)	JYB1904 300 mg (N=8)	JYB1904 450 mg (N=8)	JYB1904 600 mg (N=8)	JYB1904 Total (N=38)	Omalizumab 150 mg (N=8)	Pla (N=2)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n
All TEAEs	2 (33.3)	6 (75.0)	6 (75.0)	5 (62.5)	5 (62.5)	24 (63.2)	4 (50.0)	6 (100)
TEAEs related to study drug	0	1 (12.5)	2 (25.0)	0	4 (50.0)	7 (18.4)	1 (12.5)	1 (100)
Grade 1	1 (16.7)	6 (75.0)	4 (50.0)	4 (50.0)	5 (62.5)	20 (52.6)	4 (50.0)	4 (100)
Grade 2	1 (16.7)	1 (12.5)	3 (37.5)	2 (25.0)	5 (62.5)	12 (31.6)	0	1 (100)
Grade 3	0	0	0	0	0	0	0	1 (100)
Grade 4	0	0	0	0	0	0	0	
Grade 5	0	0	0	0	0	0	0	
Adverse reactions at injection site	0	1 (12.5)	0	0	0	1 (2.6)	0	
TEAEs leading to early withdrawal	0	0	0	0	0	0	0	

Pharmacokinetics: Approximately dose-proportional exposure (AUC and C_{max}) increase was observed. Median terminal half-life ranged from 32 to 67 days. The half-life of JYB1904 was about 2.3-fold longer than omalizumab at 150 mg dose level, 60 days and 26 days respectively.

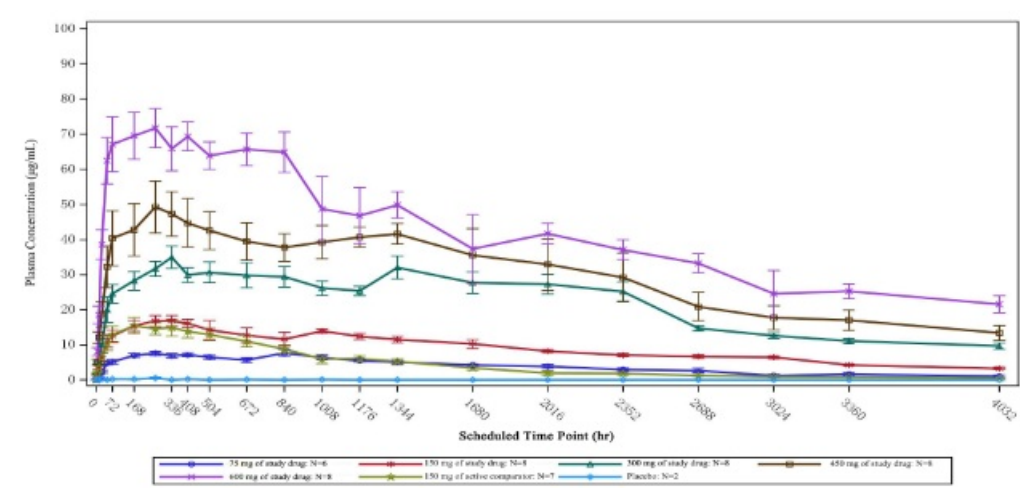


Figure 1. Mean Serum Concentration-Time Curve (PKCS)

Pharmacodynamics: JYB1904 demonstrated dose- and time-dependent suppression of free IgE. JYB1904 150 mg showed more inhibition on free IgE and accumulation of total IgE compared with omalizumab 150 mg.

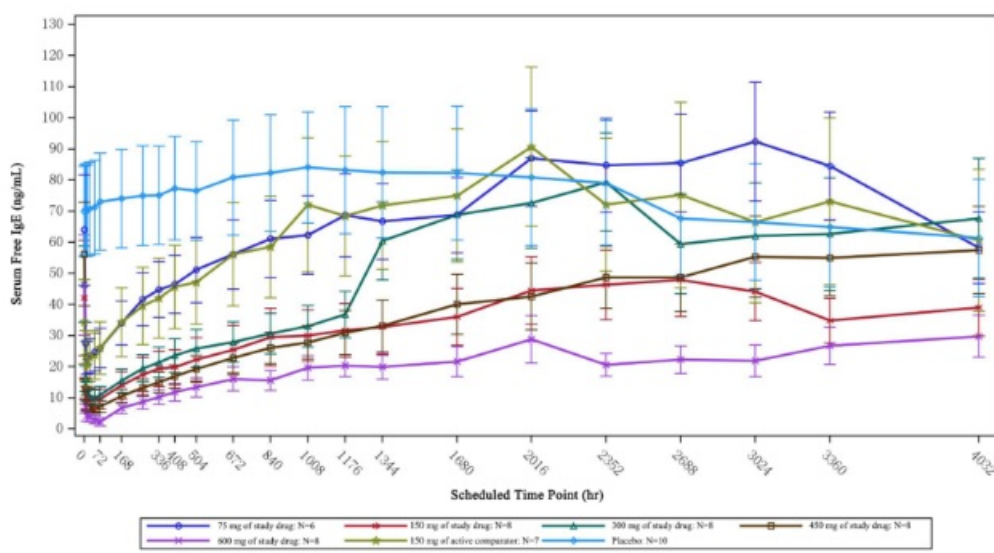


Figure 2. Mean Concentration-Time Curve of Serum Free IgE (PDCS)

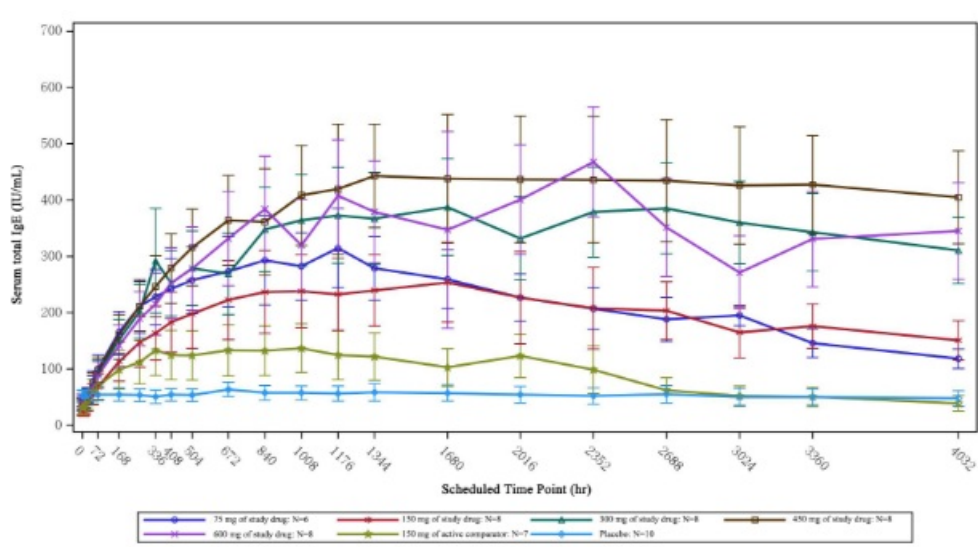


Figure 3. Mean Concentration-Time Curve of Serum Total IgE (PDCS)

Immunogenicity: The positive rate of anti-drug antibodies (ADAs) for JYB1904 was 10.5% (4/38) at JYB1904 75 mg and 150 mg dose level. The titers were all 1:1 and the neutralizing antibody tests were all negative.

Conclusion:

JYB1904 was well tolerated. No additional significant safety risks were observed compared with omalizumab. JYB1904 exhibited favorable PK/PD characteristics supporting longer treatment interval, such as every 8 or 12 weeks, for further clinical studies.

