Xeligekimab, an interleukin-17A antagonist for Active Radiographic Axial Spondyloarthritis in Chinese Patients: 16- and 48-Week Results from a Phase III, Randomized, Double-Blind, Placebo-Controlled Study

Supplementary Materials
BioDrugs

Author

Shangzhu Zhang, MD[1], Dong Xu, MD [1], Shengyun Liu, MD [2], Shujie Li, MS[3], Xiaoxia Wang, MS[4], Fenghong Yuan, MS[5] , Wei Gou, MS [6], Baijie Xu, BS [7], Lingyun Sun, MD [8], Jieruo Gu, MS [9], Dongmei Zhou, MD [10], Xiaomei Li, MS [11], Ning Kong, MD [12], Yi Zhao, MD [13], Jie Hao, MS [14], Tianwang Li, MD [15], Xiaoyun Fan, PhD [16], Qiang Shu, MD [17], Hua Wei, MD [18], Tao Jiang, MD [19], Jing Yang, MS[20], Long Qian, MS [21], Hongsheng Sun, MD [22], Xiaoyan Cai, MD [23], Zhenyu Jiang, MD [24], Guohua Yuan, MD [25], Li Qin, BS [26], Min Yang, MS [27], Jian Xu, MD [28], Wenqiang Fan, MS [29], Li Sun, MS [30], Hua Zhang, MS [31], Chunyan Zhang, MD [32], Ning Zhang, MD [33], Zhanyun Da, MS [34], Jiankang Hu, BS [35], Jingchun Jin, MD [36], Ju Liu, BS [37], Lie Dai, MD [38], Lingli Dong, PhD [39] ,Wei Wang, MS [40] and Xiaofeng Zeng, PhD [1]

Affiliations

[1]Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China; National Clinical Research Center for Dermatologic and Immunologic Diseases(NCRC-DID), Ministry of Science & Technology, Beijing, China; State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Beijing, China; Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, Beijing, China

Corresponding author details:

Full name: Xiaofeng Zeng

Postal address: No. 1 Shuaifuyuan Wangfujing Dongcheng District, Beijing 100730, China

Email address (preferably institutional): xiaofeng.zeng@cstar.org.cn

ORCID: 0000-0002-3883-2318

Protocol

This is a randomized, double-blind, placebo-controlled multicenter clinical study to evaluate the efficacy, safety, and immunogenicity characteristics of GR1501 injection in radiographic positive axial spondyloarthritis patients。

Randomization stratification factors include previous biological therapy history (yes or no); weight (≥70 kg or <70 kg).

Participants originally in the placebo group will be randomized 1:1 to either the 100 mg GR1501 injection group or the 200 mg GR1501 injection group in W16.

Main Study Objectives：

To evaluate whether the proportion of subjects achieving ASAS20 response at Week 16 with GR1501 injection treatment is superior to placebo in radiographic positive axial spondyloarthritis patients.

Primary Endpoint: Proportion of patients achieving ASAS20 at Week 16.

Secondary Endpoints: Proportions of patients achieving ASAS20, ASAS40, ASAS5/6 during the trial. Changes in ASDAS, BASDAI, BASFI, etc. compared to baseline.

Inclusion Criteria

1.Age ≥18 years.

2.Diagnosis of axial spondylarthritis (axSpA) according to the ASAS criteria, with imaging changes of sacroiliitis meeting the modified New York criteria: bilateral sacroiliitis grade ≥2 or unilateral sacroiliitis grade 3-4.

3.Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 and spinal pain score ≥4 prior to screening and randomization.

4.Poor response to previous treatment with non-steroidal anti-inflammatory drugs (NSAIDs); or contraindications to NSAIDs or inability to tolerate them.

5.If the subject is currently taking NSAIDs or oral corticosteroid, the dose must have been stable for ≥2 weeks prior to randomization; if not stable, they must have stopped the medication for at least 2 weeks prior to randomization.

6.If the subject is on methotrexate, sulfasalazine, they must have been on stable doses for ≥3 months

prior to randomization; if not stable, they must have stopped the medication for at least 4 weeks prior to randomization.

7.Must voluntarily sign the informed consent form and be capable of adhering to the protocol and completing related procedures.

Main Exclusion Criteria：

1. Complete spinal ankylosis.
2. Active inflammatory bowel disease.
3. Other systemic inflammatory diseases or other chronic pain conditions that may affect efficacy evaluation.
4. History of lymphoproliferative disease; current malignancy or history of malignancy.
5. History of significant organ transplantation or hematopoietic stem cell/bone marrow transplantation.
6. Positive hepatitis B surface antigen, positive hepatitis B core antibody (except those with negative HBV DNA); positive hepatitis C antibody, positive human immunodeficiency virus (HIV) antibody, positive syphilis antibody (but negative RPR or TRUST).
7. Clinical symptoms, signs, laboratory tests, CT scans, or medical history indicating active tuberculosis at screening.
8. History of two or more drug allergies or severe allergies, or any allergies to biologics that the investigator determines may pose a risk.
9. Significant abnormalities laboratory results.
10. Clinically significant ECG abnormalities.
11. History of serious herpes virus infections such as herpes encephalitis, ocular herpes, disseminated herpes.
12. Presence of active infections or medical history indicating infection.
13. Recent use of the following biologics or their biosimilars.
14. Use of ≥2 tumor necrosis factor α (TNF-α) inhibitors or receipt of any biologic targeting IL-17.
15. Use of any JAK inhibitors within 4 weeks before randomization.
16. Intra-articular corticosteroid injections affecting efficacy assessments within 4 weeks before randomization.
17. Use of traditional disease-modifying antirheumatic drugs.
18. Spinal surgery or joint surgery within 8 weeks before randomization.
19. Presence of unstable extra-articular clinical manifestations as determined by the investigator within 4 weeks before randomization (e.g., uveitis, enteritis, psoriasis).

Study Intervention Description

Trial Drug: GR1501 injection/Placebo for GR1501 injection

Dosing: 100 mg or 200 mg

Dosing Frequency: Every two weeks for the first 4 weeks (W0, W2, W4), followed by every four weeks (W8, W12, W16, W20, W24, W28).
Administration Route: Subcutaneous injection
Number of Cases： 465
Visit Duration： Approximately 48 weeks

Supplementary Table 1 Change from baseline of secondary endpoint at Week 16(the Estimand Population)

	Placebo (n=156)	Xeligekimab 100mg (n=155)	Xeligekimab 200mg (n=154)
BASDAI50	28 (19.7)	58 (38.4)	62 (41.3)
ASDAS-CRP < 2.1	32 (24.2)	73 (52.1)	83 (58.5)
ASDAS-CRP < 1.3	5 (3.8)	21 (15.0)	32 (22.5)
BASFI	-0.97±1.39	-1.42±1.51	-1.60±1.52
Spinal pain NRS	-1.5±1.86	-2.6±1.95	-2.4±1.76
ASQoL	-3.4±4.02	-4.8±4.23	-5.1±4.25
WAPI[a]	-7.10±17.04	-13.03±17.0	-13.83±19.0
FACIT-F	6.1±8.42	9.6±8.50	8.6±8.93
hs-CRP (mg/L)	-0.51±15.76	-10.07±16.75	-9.08±18.6

ASDAS-CRP Ankylosing Spondylitis Disease Activity Score based on C-reactive protein, ASQoL Ankylosing Spondylitis Quality of Life, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, BASFI Bath Ankylosing Spondylitis Functional Index，EP， FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue, hs-CRP hypersensitive C-reactive protein， WPAI, Work Productivity and Activity Impairment.

[a] Percent overall work impairment due to health.