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LETTER TO THE EDITOR Open Access

Firsekibart in acute gouty arthritis

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To the Editor,

Gout is a painful and disabling disease that constitutes the most common inflammatory arthritis [1]. Current treatments, such as non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids, are ineffective, poorly tolerated, or contraindicated for a significant proportion of patients. There is an urgent need to explore alternative therapies for those patients with limited options.

IL-1β is a key initiation factor for gout flare and anti-IL-1β therapy has been recommended for gout patients in guidelines [2, 3]. Firsekibart is a novel fully human monoclonal antibody, characterized by high affinity for IL-1β [4]. Here, we introduce the efficacy and safety data of Firsekibart for the treatment of acute gouty arthritis, representing the first phase III clinical trial of an IL-1β monoclonal antibody for acute gout flares conducted in China.

We conducted a randomized, active-controlled, double-blind, multicentre phase III trial between 2022 and 2024 in China. Patients who met the 2015 ACR preliminary criteria for the classification of acute arthritis of primary gout (GA) and contraindicated for, intolerant of, or unresponsiveness to NSAIDs and/or colchicine, with ≥ 2 episodes in the preceding year were screened for eligibility. Patients stratified by baseline visual analog scale (VAS) pain score of the target joint (50 mm ≤ VAS < 70 mm and 70 mm ≤ VAS ≤ 100 mm) were randomized with a 1:1 ratio to receive a single dose of Firsekibart 200 mg (subcutaneous administration) or Compound betamethasone (CB) 7 mg (intramuscular injection). The trial included a 48-week treatment period (24 weeks for double-blind phase and 24 weeks for open-label intervention). The co-primary endpoints were the reduction in pain intensity from baseline to 72 h in the most affected joint measured by VAS (non-inferiority testing), and the time to first new flare over 12 weeks (superiority testing). Secondary endpoints included time to first achieving 50% pain reduction in the target joint, percentage of patients with at least one new flare (12weeks, 24weeks), mean number of new flares per patient, median time to first new flare (24weeks), and the safety evaluation. All efficacy endpoints were analyzed with the full analysis set (FAS) (i.e. all randomized patients who received study drugs had at least one post-baseline efficacy assessment), and safety assessments were based on the safety analysis set (SS) (i.e. all randomized patients who received study drugs and had at least one post-baseline safety assessment).

A total of 313 patients were randomized, one patient in the Firsekibart group did not receive the study drug,

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Table 1 Baseline characteristics and efficacy of Firsekibart /Compound betamethasone treated patients(FAS)

	Firsekibart (*N* = 156)	**Compound betamethasone (*N* = 155)**
Baseline		
Male (%)	100	97.4
Age (years) (mean (SD))	45.7 (13.73)	44.1 (12.16)
BMI (kg/m^2) (mean (SD))	27.45 (3.89)	27.55 (3.79)
≥ 3 flares reported during prior one year N(%)	143 (91.7)	135 (87.1)
Percentage of patients with tophus N(%)	61 (39.1)	65 (41.9)
Efficacy		
Change in pain intensity from baseline to 72 h (mm) (Least Squares mean (95%CI))	-57.09 (-60.08, -54.10)	-53.77 (-56.77, -50.77)
Median time to first new flare (24 weeks)	Not estimable	45 days
Time to First Achieving 50% Pain Reduction in the target joint (median (95CI%))	24.5 h (24.10, 48.00)	24.3 h (24.03, 48.00)
Percentage of patients with ≥ 1 new flare		
12 weeks	10.9%	65.2%
24 weeks	14.7%	66.5%
Mean number of new flares per patient (mean (SD))		
12 weeks	0.2 (0.52)	1.2 (1.27)
24 weeks	0.2 (0.79)	1.6 (1.79)

and another in the CB group lacked valid efficacy data, with final 311 included in the FAS analysis. The baseline characteristics and efficacy were detailed in Table 1. Compared with CB, Firsekibart showed a non-inferiority effect on the reduction in pain intensity from baseline to 72 h (-57.09 mm [95% CI: -60.08, -54.10] vs. -53.77 mm [95% CI: -56.77, -50.77]) (Least Squares Mean), significantly delayed median time to first new flare (Not estimable vs. 45 days) and reduced risk of new flare by 90% (HR 0.10; 95% CI: 0.06, 0.17; p<0.0001) over the first 12 weeks, 87% (HR 0.13; 95% CI: 0.08, 0.21; p<0.0001) over the 24 weeks. Time to first achieving 50% pain reduction in the target joint was similar (24.5 h [95% CI: 24.10, 48.00] vs. 24.3 h [95% CI: 24.03, 48.00]) (median). Besides, fewer patients treated with Firsekibart experienced at least one new flare over 12 weeks and 24 weeks (10.9% vs. 65.2%, p < 0.0001, 14.7% vs. 66.5%, p < 0.0001), and the mean number of new flares per patient was lower in patients treated with Firsekibart over 12 and 24 weeks (0.2 (0.52) vs. 1.2 (1.27), 0.2 (0.79) vs. 1.6 (1.79))(mean(SD)).

The total adverse events and treatment-related adverse events were 365 and 146 in the Firsekibart-treated group, versus 471 and 188 in the CB-treated group, respectively. Treatment-related serious adverse events were reported in 3 patients and all in CB-treated group.

In this study, Firsekibart demonstrated significant efficacy and safety in the treatment of acute gouty arthritis. Compared with Compound betamethasone, Firsekibart was non-inferior in short-term pain relief and significantly superior in the prevention of new flares. Besides, fewer adverse events occurred in patients treated with Firsekibart and no infection-related serious adverse events were observed. Firsekibart was the first IL-1 inhibotor completing its phase III study in China, and data showed it had the potential to be a new choice for gout patients.

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Not applicable.

Authors' contributions
Hejian Zou conceived and designed the experiments. Yu Xue, Tianshu Chu, Jiankang Hu, Wei Gou, Ning Zhang, Juan Li, Jing Yu, Rongping Li, RongbinLi, Long Qian, Xinwang Duan, and Lihua Duan performed the experiments and analyzed the data. Yu Xue wrote the paper.

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Data availability
The datasets generated and/or analysed during the current study are not publicly available due [Firsekibart is currently under review at the Center for Drug Evaluation for NDA] but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval was obtained from the Ethics Review Committee of Huashan Hospital Affiliated to Fudan University, Number: 2022 (976). Informed consent was obtained from all individual participants included in the study.

Consent for publication
All authors approved the publication of the manuscript.

Competing interests
The authors declare that they have no competing interests.

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