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# A Post-Hoc Analysis of the 48-Week Data from Study 301 of Firsekibart for Acute Gouty Arthritis: Evaluation of Number of Doses and Switching-to-Firsekibart Efficacy

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**Abstract:** *Objective:* This post-hoc analysis aimed to evaluate the number of Firsekibart administrations over 48 weeks in patients with acute gout and the efficacy of switching to Firsekibart treatment during the open-label period in patients who had recurrent flare recurrence on compound betamethasone. *Methods:* We performed a post-hoc analysis on the 48-week treatment data from the 301 study (a multicenter, randomized, double-blind, active-controlled Phase III clinical trial) of Firsekibart for acute gout. A total of 312 patients with acute gout were randomized to receive either Firsekibart 200 mg subcutaneously or compound betamethasone 7 mg intramuscularly during the 24-week double-blind period, followed by a 24-week open-label period. After the initial dose, patients could receive additional doses upon gout flare; those with an inadequate response could receive oral prednisone as rescue therapy. During the open-label period, patients in the betamethasone group who experienced gout flares could switch to Firsekibart treatment. Differences in the number of doses between the two groups over 48 weeks, differences in the number of doses before and after switching to Firsekibart treatment in the betamethasone group, and the proportion of patients experiencing at least one gout flare after switching were analyzed. *Results:* Over 48 weeks, the median number of doses in the Firsekibart group was 1.0 (Q1, Q3: 1.0, 2.0), which was significantly lower than that in the compound betamethasone group (2.0 [1.0, 3.0]), $P < 0.0001$. For patients who switched from compound betamethasone to Firsekibart treatment, the median number of doses after switching was 1.0 (1.0, 1.0), markedly lower than the 2.0 (1.0, 3.0) before switching ($P < 0.0001$). During the open-label period, 69 patients (44.2%) in the betamethasone group switched to Firsekibart treatment, of whom only 2 (2.9%) experienced a gout flare. This recurrence rate was significantly lower than that observed during the double-blind period while receiving compound betamethasone (2.9% vs. 82.6%, $P < 0.001$). *Conclusion:* The median annual number of doses of Firsekibart for treating acute gout flares is one dose per year. For patients with inadequate response to corticosteroid therapy, Firsekibart demonstrates favorable efficacy and dosing convenience in controlling gout flares, representing a valuable new option for long-term gout management.

**Keywords:** Firsekibart; Acute gout; Post-hoc analysis; Compound betamethasone

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## 1. Introduction

Gout is the most common inflammatory arthritis, with a growing global burden. A recent Global Burden of Disease (GBD) study reported that the global prevalence of gout reached 55.8 million in 2020 and is projected to increase to 95.8 million by 2050, an increase of over 70% [1]. The prevalence of gout in China has increased particularly significantly, with disability-adjusted life years (DALYs) due to gout increasing by 172.35% between 1990 and 2019, and the number of affected individuals rising from 5.86 million to 16.16 million [2]. Gout not only causes severe joint pain and functional impairment but is also strongly associated with cardiovascular disease (87% increased risk), chronic kidney disease (4.61-fold increased risk), and all-cause mortality (58% increased risk) [3]. It is estimated that the total number of patients with gout in China is approximately 38.4 million. Among patients diagnosed with gout, 17.4% experience at least one acute flare within 1 year, suggesting that approximately 6.682 million patients in China suffer a gout flare each year. However, the overall healthcare-seeking rate among patients with gout in China remains low, with annual consultation rates of 59.67% in rural areas and 64.56% in urban areas, yielding an average consultation rate of 61.1%. Based on this estimate, approximately 4.082 million patients with gout flares seek medical care each year.

Current first-line treatments for acute gout flares include nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids. However, these conventional treatments have significant limitations. A study shows that 1.9% of gout patients have contraindications or intolerance to standard anti-inflammatory treatments, and 1.8% respond inadequately to conventional therapies [4]. Together, these two groups account for 3.7% of patients, indicating that an estimated 151,000 patients with acute gout flares in China may require novel anti-inflammatory therapies such as interleukin-1 (IL-1) inhibitors each year. Furthermore, the side effects of conventional drugs, such as hepatotoxicity, nephrotoxicity, gastrointestinal reactions, and metabolic disturbances, limit their use in patients with multiple comorbidities. In a commentary, Professor Richette, an author of the EULAR gout guidelines, noted that gout management extends far beyond urate-lowering; it is a complex inflammatory process ignited by multiple factors, requiring long-term, precise anti-inflammatory therapy until monosodium urate crystals are completely dissolved to fundamentally prevent gout flares [5]. Therefore, there is an unmet clinical need in gout management for a long-acting anti-inflammatory drug with reliable efficacy, convenient administration, and a low adverse reaction profile.

The core mechanism of gout flares involves the activation of the NLRP3 inflammasome by urate crystals, promoting the maturation and release of IL-1β and triggering an inflammatory cascade. IL-1β levels correlate positively with gout severity, and its sustained presence can lead to multiple organ damage, including bone erosion, chronic kidney disease, and atherosclerosis. Firsekibart, the first anti-IL-1β fully human monoclonal antibody approved in China, has been shown in its Phase III 24-week core treatment period data [6,7] to rapidly control gout flares in patients with acute gout who have contraindications, intolerance, or inadequate response to NSAIDs and colchicine. It significantly reduces the risk of gout recurrence at 12 and 24 weeks by up to 90% and 87%, respectively, and markedly reduces levels of the inflammatory marker high-sensitivity C-reactive protein (hs-CRP) at Day 8 and Week 4. These results indicate that during acute gout flares, Firsekibart treatment precisely binds IL-1β, blocking the IL-1β

inflammatory cascade pathway, exerting a long-acting anti-inflammatory effect, thereby significantly reducing the risk of gout recurrence and related organ damage. This post-hoc analysis aims to further evaluate the number of doses of long-term Firsekibart therapy in gout patients and its efficacy in patients with inadequate response to corticosteroids by analyzing the complete 48-week treatment data from Study 301. This will help understand drug exposure in acute gout patients treated with Firsekibart and provide evidence for pharmacoeconomic evaluations.

## 2. Methods

### 2.1. Study design

This study is a post-hoc analysis of Study 301 investigating Firsekibart for acute gout. Study 301 was a multicenter, randomized, double-blind, double-dummy, active-controlled Phase III clinical trial (NCT05983445) conducted across 51 centers in China from January 2023 to June 2024. The study comprised two phases: a double-blind period (0–24 weeks), where patients were randomized 1:1 to receive either Firsekibart 200 mg subcutaneously plus compound betamethasone placebo, or compound betamethasone 7 mg intramuscularly plus Firsekibart placebo; and an open-label period (24–48 weeks). After the double-blind period, patients in the Firsekibart group who experienced a gout flare could continue receiving Firsekibart, while patients in the betamethasone group who experienced a gout flare could switch to Firsekibart treatment. Data from the 24-week core treatment period have been published in the journal *Innovation* [6].

### 2.2. Patient population

Study 301 enrolled 313 patients who met the 2015 ACR gout classification criteria, had contraindications, intolerance, or lack of efficacy to NSAIDs and/or colchicine, had at least 2 gout flares in the past year, and had a baseline target joint pain VAS score ≥50 mm during an acute gout flare. Baseline characteristics were balanced between groups, with a mean age of 44.9 years, 98.7% male, and a median gout history of 84.0 months. One patient in the betamethasone group did not receive the study drug after randomization, leaving 312 patients in the safety set, with 156 patients in each group.

### 2.3. Outcome measures

Assessment included drug exposure duration and the mean number of doses administered over 48 weeks for patients in the Firsekibart and betamethasone groups. Additionally, drug exposure duration, mean number of doses, and the proportion of patients experiencing at least one gout flare were evaluated before and after switching to Firsekibart treatment in patients from the betamethasone group who switched upon recurrence.

### 2.4. Statistical analysis

All statistical analyses were performed using SAS software. The number of doses data were right-skewed; minimum, Q1, median, Q3, and maximum values were calculated to describe central tendency and dispersion, with mean ± standard deviation (SD) also presented. Recurrence rates were expressed as percentages. Comparisons of the number of doses between two groups were performed using the signed-rank test, and comparisons of recurrence rates were performed using Fisher's exact test. All statistical tests were two-sided, with $P < 0.05$ considered statistically significant.

# 3. Results

## 3.1. Drug exposure analysis

Over 48 weeks, the mean drug exposure duration after the first dose was 339.00 ± 44.00 days in the Firsekibart group and 325 ± 67.62 days in the betamethasone group. During the open-label period, 69 patients (44.2%) in the betamethasone group who experienced gout flares switched to Firsekibart treatment and completed follow-up. Their mean exposure duration before and after switching was 215.7 ± 45.64 days and 129.0 ± 36.40 days, respectively.

## 3.2. Number of doses analysis

Over 48 weeks, the median number of doses in the Firsekibart group was 1.0 (Q1, Q3: 1.0, 2.0), which was significantly lower than that in the betamethasone group (2.0 [1.0, 3.0]) (**Table 1**), $P < 0.001$. Over the 48-week treatment period, the mean number of doses was 1.6 ± 1.18 in the Firsekibart group and 2.5 ± 1.55 in the betamethasone group.

During the open-label period following the first 24 weeks, patients in the betamethasone group who switched to Firsekibart treatment after recurrence had a median of 1.0 dose (1.0, 1.0) after switching, markedly lower than the 2.0 doses (1.0, 3.0) before switching (**Table 1**), $P < 0.001$. The mean number of doses before switching was 2.6 ± 1.42, compared to 1.0 ± 0.77 after switching to Firsekibart treatment.

**Table 1.** Comparison of number of doses over 48 weeks: Firsekibart group vs. betamethasone group, and betamethasone group patients before and after switching to Firsekibart treatment

| | **Firsekibart group (*n* = 156)** | **Betamethasone group (*n* = 156)** | **Betamethasone group patients before switching (*n* = 69)** | **Betamethasone group patients after switching (*n* = 69)** |
|---|---|---|---|---|
| | | Number of doses | | |
| Median (Q1, Q3) | 1.0 (1.0, 2.0)* | 2.0 (1.0, 3.0) | 2.0 (1.0, 3.0) | 1.0 (1.0, 1.0)# |
| Range | 1,10 | 1,7 | 1,6 | 1,2 |
| Mean ± SD | 1.6 ± 1.18 | 2.5 ± 1.55 | 2.6 ± 1.42 | 1.0 ± 1.17 |
| Number of doses – *n* (%) | | | | |
| 1 dose | 90 (57.7) | 51 (32.7) | 19 (27.5) | 67 (97.1) |
| 2 dose | 54 (34.6) | 38 (24.4) | 19 (27.5) | 2 (2.9) |
| 3 dose | 5 (3.2) | 31 (19.9) | 15 (21.7) | 0 |
| 4 dose | 3 (1.9) | 15 (9.6) | 8 (11.6) | 0 |
| 5 dose | 2 (1.3) | 12 (7.7) | 5 (7.2) | 0 |
| 6 dose | 0 | 6 (3.8) | 3 (4.3) | 0 |
| 7 dose | 0 | 3 (1.9) | 0 | 0 |
| 9 dose | 1 (0.6) | 0 | 0 | 0 |
| 10 dose | 1 (0.6) | 0 | 0 | 0 |

*$P < 0.0001$ vs. betamethasone group; #$P < 0.0001$ vs. before switching.

## 3.3. Recurrence rate before and after switching to Firsekibart treatment

During the open-label period after 24 weeks, among the 69 patients in the betamethasone group who switched to Firsekibart treatment, only 2 experienced one gout flare each. The recurrence rate was significantly lower than before switching (2.9% vs. 82.6%, $P < 0.0001$, **Figure 1**). Furthermore, after retreatment with

Firsekibart, no further gout flares occurred through week 48.

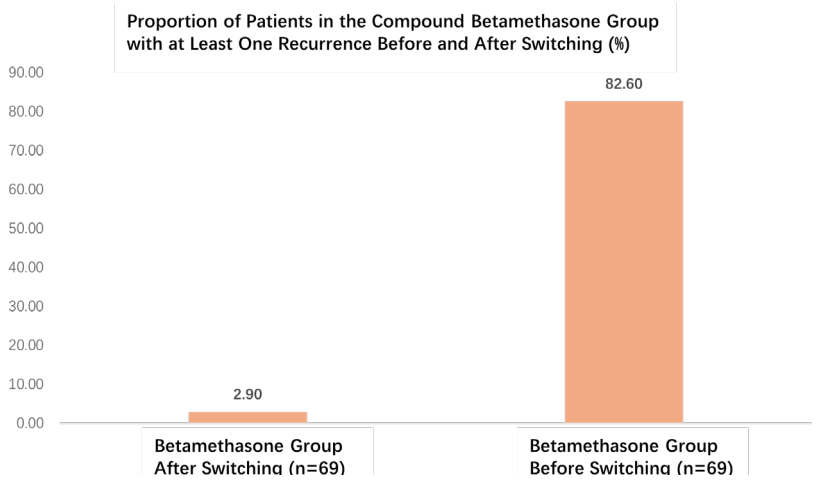


**Figure 1.** Significant reduction in gout flare rate after switching to Firsekibart treatment in patients previously treated with compound betamethasone

## 4. Discussion

Gout, a prevalent inflammatory arthritis, significantly impacts patients' quality of life and long-term health due to the severe pain of acute gout flares and the characteristic of chronic, recurrent episodes [8]. While conventional first-line treatments such as NSAIDs, colchicine, and corticosteroids (e.g., compound betamethasone) can control inflammation in the short term, they often face challenges in long-term management, including diminished efficacy over time, high recurrence rates, and potential side effects (e.g., metabolic disturbances, immunosuppression) [9], making them unsuitable for sustained anti-inflammatory therapy. Therefore, there is a clinical need for a therapeutic strategy that provides highly effective, durable inflammation control with an improved safety profile. Firsekibart, which targets IL-1β—the core inflammatory cytokine in gout flares—offers a compelling solution, as demonstrated by the results of Study 301. Firsekibart treatment not only markedly reduced the risk of gout recurrence at 12 and 24 weeks by up to 90% and 87%, respectively [6], but the 48-week drug exposure data from this study show that the number of doses in the Firsekibart group was significantly lower than that in the betamethasone group, which could substantially improve treatment adherence. Furthermore, Firsekibart demonstrates a revolutionary therapeutic advantage in gout patients with an inadequate response to corticosteroids.

The most direct finding of this study is the substantial advantage of Firsekibart in terms of dosing convenience. The presence of refractory gout patients in both groups, who experienced more frequent gout flares and received more doses throughout the study, contributed to the right-skewed distribution of dosing data. Over the 48-week treatment period, the median number of doses in the Firsekibart group was only 1, with an interquartile range of 1, significantly lower than the 2 doses in the betamethasone group ($P < 0.0001$). This indicates that 75% of patients in the Firsekibart group required no more than 2 doses per year. This finding profoundly demonstrates that, unlike the conventional model requiring repeated corticosteroid dosing to manage frequent gout flares, Firsekibart, through its long-acting pharmacological properties, preliminarily achieves the ideal goal of maintaining long-term inflammation control with "no more than two

injections per year." When patients in the betamethasone group who experienced gout flares during the open-label period switched to Firsekibart treatment, their median number of doses dropped dramatically from 2.0 to 1.0 ($P < 0.0001$), further supporting the clinical advantage of Firsekibart's long-acting anti-inflammatory effect. This drastic reduction in the number of doses not only signifies a significant decrease in patient treatment burden (including clinic visits, injection discomfort, and time costs) but also reflects that Firsekibart achieves more durable and fundamental suppression of the core inflammatory pathways in gout, thereby reducing the reliance on "on-demand" therapy. This paradigm shift represents a critical step towards more precise and convenient chronic gout management.

Another key finding of this study is the clear confirmation of Firsekibart's prominent efficacy in patients who responded inadequately to corticosteroid therapy. Among patients who later switched to Firsekibart treatment, the recurrence rate during the betamethasone treatment period was as high as 82.6%, reflecting a real-world clinical scenario where a considerable proportion of patients respond poorly to conventional corticosteroid therapy or cannot effectively prevent recurrence, posing a challenge in clinical management. The open-label study design provides compelling evidence for this patient population. Sixty-nine patients (44.2% of the original corticosteroid group) who experienced gout flares switched to Firsekibart treatment during the open-label period. During the subsequent 24-week follow-up, only 2 patients experienced a gout flare, yielding a recurrence rate as low as 2.9%. This represents a statistically significant and clinically striking reduction compared to the 82.6% recurrence rate observed during the preceding compound betamethasone treatment period ($P < 0.0001$). This comparative data powerfully demonstrates that Firsekibart can exert robust anti-inflammatory effects in gout inflammation not adequately controlled by corticosteroids, effectively halting acute gout flares and preventing recurrences. It also establishes a clear clinical application scenario for IL-1β antibodies: as an effective step-up therapy after failure or intolerance to conventional anti-inflammatory treatments, particularly corticosteroids. The recently published *Guideline for Anti-inflammatory Therapy in Gout (2025 Edition)* recommends IL-1 inhibitors for anti-inflammatory treatment in gout patients with multiple comorbidities or tophi [10]; the results of this study provide new clinical evidence supporting this recommendation.

Limitations of this study include the potential bias introduced by the open-label design and the limited sample size, underscoring the need for large-scale, long-term real-world evaluations of Firsekibart's anti-inflammatory efficacy and organ-protective benefits. Future research should focus on the efficacy of Firsekibart in patients with moderate-to-severe renal impairment or cardiovascular disease and explore its synergistic value when combined with urate-lowering therapy.

## 5. Conclusion

Firsekibart provides long-acting, precise anti-inflammatory therapy with an ultra-low number of doses—"no more than two injections per year"—fundamentally changing the paradigm of anti-inflammatory treatment for gout and greatly enhancing treatment convenience and patient adherence. For patients who do not respond adequately to corticosteroids, Firsekibart also demonstrates excellent anti-inflammatory effects, significantly reducing the rate of gout recurrence.

## Disclosure statement

The authors declare no conflict of interest.

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