# Clinical Safety and Pharmacokinetics of FMX101 4% Topical Minocycline Foam in Pediatric Patients for the Treatment of Moderate-to-Severe Acne Vulgaris

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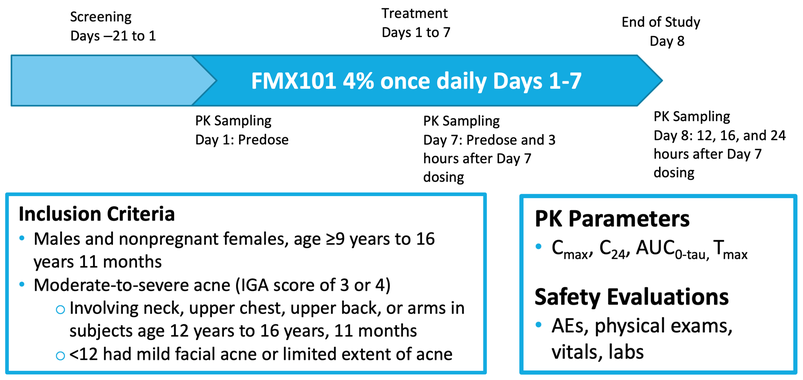
## Introduction

- Acne vulgaris (AV) typically first manifests in adolescence and affects most of the population at some point during their life[1,2]
  - Approximately 95% to 100% of boys and 83% to 85% of girls are affected by AV by the time they reach 17 years of age[3]
  - Patients under the age of 18 represent 38% of the overall AV population[3]
- Although oral minocycline and doxycycline are considered first-line therapy for moderate-to-severe acne, their use can be limited by potentially serious systemic side effects such as headache, fatigue, dizziness, and pruritus, as well as serious dermal adverse effects, including photosensitivity and pigmentation of the skin, mucous membranes, and teeth[4]
- FMX101 4% is the first stable, topical foam formulation of minocycline
- FMX101 4% has been shown in 3 Phase 3 studies with 2445 enrolled patients to be an effective and well-tolerated treatment for moderate-to-severe AV in patients ≥9 years of age[5]
- The overall safety and pharmacokinetic (PK) profile of FMX101 4% in younger patients with AV would be important to understand
  - The PK and relative bioavailability of FMX101 4% have been previously evaluated in adult subjects with moderate-to-severe acne
  - That study compared multiple-dose topical administration of FMX101 4% vs single-dose oral administration of minocycline HCl extended-release tablets[6]
- This report describes the clinical safety and PK profile for subjects 9-17 years of age treated with FMX101 4% for AV. The data are sourced from:
  - Three Phase 3 clinical trials (FX2014-04, FX2014-05, and FX2017-22)
  - A single-center, active-controlled PK study (FX2016-21) in subjects age 9 years to 16 years, 11 months

## Methods

- A single-center, nonrandomized, open-label, (FX2016-21) study was conducted to characterize minocycline bioavailability and to evaluate safety and tolerability under maximum-use conditions in pediatric subjects with moderate to severe AV (**Figure 1**)
  - Subjects 9-17 years of age; 20 subjects
    - 9-11 years (N=6)
    - 12-14 years (N=8)
    - 15-16 years, 11 months (N=6)
  - Maximum-use conditions were 4 g once-daily topical application of FMX101 4% for 7 days

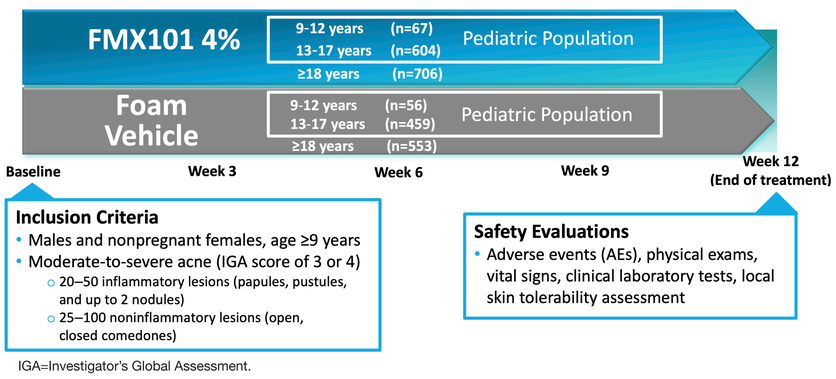
**Figure 1. Study design of the PK study**




$C_{max}$=maximum observed plasma concentration (ng/mL); $C_{24}$=plasma minocycline concentration 24 hours after FMX101 4% application (ng/mL); $AUC_{0\text{-}tau}$=area under the concentration-time curve (ng/mL*hours) from time zero (predose) through 24 hours; $T_{max}$=time to maximum measured plasma concentration (hours).

- Three Phase 3 randomized, multicenter, double-blind, vehicle-controlled, 2-arm studies (FX2014-04, FX2014-05, and FX2017-22) were used for the analysis (**Figure 2**)
- The studies evaluated the efficacy, safety, and tolerability of topical FMX101 4% in the treatment of moderate-to-severe AV
  - Subjects were randomized 2:1 (FX2014-04, FX2014-05) or 1:1 (FX2017-22) to FMX101 4% or foam vehicle
  - Foam was self-applied daily for 12 weeks
  - 1186 of 2445 (48.5%) subjects comprised the pediatric population (age 9-17 years)

**Figure 2. Study design of the Phase 3 trials**




IGA=Investigator's Global Assessment.

## Results

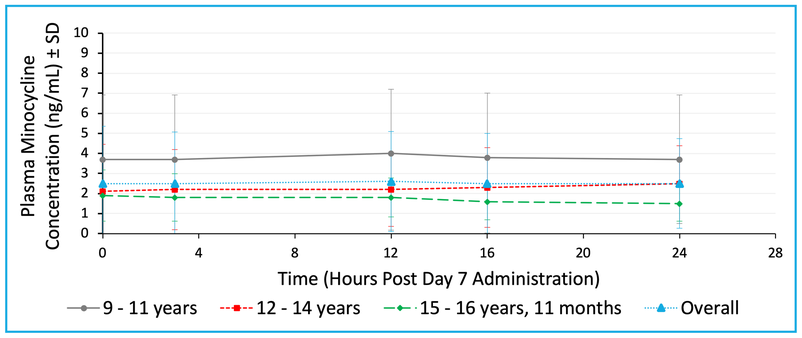
### Pharmacokinetics

- Baseline characteristics for the PK study are shown in **Table 1**
- Overall plasma levels of minocycline were relatively constant throughout, following the application of FMX101 4% once daily for 7 days (**Figure 3**)
  - $C_{24}$ value was 2.5 ng/mL

**Table 1. Baseline demographics and subject characteristics**

| | FX2016-21 (N=20) |
|---|---|
| **Mean age (range), yr** | 13.2 (10-16) |
| **Gender, n (%)**<br>Male<br>Female | <br>9 (45)<br>11 (55) |
| **Race, n (%)**<br>White<br>Black or African American | <br>7 (35)<br>13 (65) |
| **Ethnicity, n (%)**<br>Hispanic/Latino<br>Non-Hispanic/Latino | <br>2 (10)<br>18 (90) |
| **IGA Severity, n (%)**<br>2 – Mild<br>3 – Moderate<br>4 – Severe | <br>2 (10)<br>18 (90)<br>0 |

**Figure 3. Mean plasma concentrations of minocycline following application of FMX101 4% once daily for 7 days in pediatric subjects**




SD = standard deviation.

- There were no substantial differences in mean PK parameters of minocycline among the 3 pediatric cohorts treated with FMX101 4% for 7 days (**Table 2**)
  - Mean overall Cmax value was ~3.1 ng/mL
  - Mean overall AUC0-tau value was ~61 ng*hr/mL

**Table 2. PK Parameters of minocycline in plasma in pediatric subjects**

| Age group | Geometric mean $C_{max}$ (ng/mL) | Geometric mean $AUC_{0\text{-}tau}$ (ng*hr/mL) | Geometric mean $C_{24}$ (ng/mL) | $T_{max}$[a] (hours) |
|---|---|---|---|---|
| **9-11 years (N=6)** | 3.52 | 68.18 | 2.93 | 12 (0,24) |
| **12-14 years (N=8)** | 2.25 | 42.17 | 2.00 | 20 (0,24) |
| **15-16 years, 11 months (N=6)** | 1.74 | 35.07 | 1.30 | 6 (0,24) |
| **Overall (N=20)** | 2.38 | 46.09 | 1.97 | 12.1 (0,24) |

[a]Median (minimum, maximum) shown for $T_{max}$.

### Safety summary

- Daily application of FMX101 4% was found to be safe and well tolerated in maximum-use conditions
- A single pediatric subject experienced 2 unrelated TEAEs (nausea and vomiting)
- Among the 20 subjects enrolled, no serious TEAEs or TEAEs resulting in subject discontinuation were reported

### Clinical safety

- Overall incidence of treatment-emergent AEs (TEAEs) was similar across all age groups (**Table 3**)
- No serious treatment-related TEAEs were reported

**Table 3. Summary of TEAEs in safety population[a]**

| | FMX101 4%<br>9-12 years (n=67)<br>13-17 years (n=604)<br>≥18 years (n=706) | Foam Vehicle<br>9-12 years (n=56)<br>13-17 years (n=459)<br>≥18 years (n=553) |
|---|---|---|
| **Subjects with any TEAE, n (%)** | 359 (26.1) | 261 (24.4) |
| **Number of TEAEs**<br>9-12 years<br>13-17 years<br>≥18 years | <br>18 (26.9)<br>158 (26.2)<br>183 (25.9) | <br>11 (19.6)<br>110 (24.0)<br>140 (25.3) |

[a]Safety population includes all randomized subjects who received at least 1 dose of study drug.

- Noncutaneous and cutaneous TEAEs were similar in incidence and frequency across all age groups (**Table 4**)
  - A slightly higher incidence of URTI was observed in the age group 9-12 years (6.5%) vs the age group 13-17 years (1.8%) and ≥18 years (3.1%); however, the data may be influenced by the difference in sample sizes between age groups

**Table 4. Noncutaneous and cutaneous AEs in ≥2% of subjects**

| | FMX101 4% (N=1377) | | | Foam Vehicle (N=1068) | | |
|---|---|---|---|---|---|---|
| | 9-12 years (n=67) | 13-17 years (n=604) | ≥18 years (n=706) | 9-12 years (n=56) | 13-17 years (n=459) | ≥18 years (n=553) |
| Overall AEs, n (%) | 18 (26.9) | 158 (26.2) | 183 (25.9) | 11 (19.6) | 110 (24.0) | 140 (25.3) |
| **Noncutaneous AEs in ≥2 subjects, n (%)** | | | | | | |
| Viral upper respiratory tract infection | 1 (1.5) | 28 (4.6) | 18 (2.5) | 0 (0.0) | 16 (3.5) | 20 (3.6) |
| Headache | 1 (1.5) | 12 (2.0) | 29 (4.1) | 1 (1.8) | 10 (2.2) | 14 (2.5) |
| Upper respiratory tract infection | 5 (7.5) | 12 (2.0) | 22 (3.1) | 3 (5.4) | 7 (1.5) | 17 (3.1) |
| Increased creatine phosphokinase | 1 (1.5) | 9 (1.5) | 14 (2.0) | 1 (1.8) | 8 (1.7) | 5 (0.9) |
| Ligament sprain | 2 (3.0) | 4 (0.7) | 4 (0.6) | 0 (0.0) | 4 (0.9) | 0 (0.0) |
| **Cutaneous AEs in ≥2 subjects, n (%)** | | | | | | |
| Worsening Acne | 1 (1.5) | 11 (1.8) | 10 (1.4) | 0 (0.0) | 5 (1.1) | 21 (3.8) |

URTI=upper respiratory tract infection.

## Conclusions

### Pharmacokinetics

- In pediatric subjects with moderate-to-severe AV, there was low systemic exposure to minocycline following maximum-use daily application of FMX101 4%
  - There is no difference in systemic exposure between age groups within the pediatric population
  - All 3 age cohorts had similar levels of minocycline (~2.5 ng/mL) across the dosing interval with daily application of FMX101 4% in maximum-use conditions (4g/day) for 7 days
  - This was comparable to results seen in adults following exposure to FMX101 4% (Cmax 1.1-1.5 ng/mL), in whom the levels were 730-765 times lower than with oral minocycline[4]
  - No serious TEAEs and no discontinuations secondary to a TEAE were reported

### Clinical safety

- The clinical safety profile for FMX101 4% in pediatric subjects was favorable and similar to that reported in adult subjects across 3 Phase 3 studies
  - Safe and well-tolerated in pediatric subjects with moderate-to-severe AV
  - No serious treatment-related TEAEs were reported
  - Overall incidence of TEAEs was similar across all age groups, ranging from 23.6% to 25.7%
  - The most common noncutaneous TEAE (≥1%) across all groups was URTI

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## Disclosures/Acknowledgment

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