Pharmacokinetic Evaluation of Once-Daily Topical 4% Minocycline Foam in Adult and Pediatric Subjects With Moderate-to-Severe Acne in Two Phase 1 Studies

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Background
- Acne vulgaris (AV) is a common skin disease that affects adolescents and can persist into adulthood.
- The mainstay of treatment for AV is systemic tetracyclines, such as doxycycline and minocycline.
- FMX101 4% is a novel topical foam formulation of minocycline. It has been shown to be an effective and well-tolerated treatment for moderate-to-severe AV in a Phase 2 clinical trial.
- Two Phase 1 studies were conducted to characterize minocycline pharmacokinetics (PK) and safety following multiple-dose administration of FMX101 4% minocycline foam in adult (Study FX2014-03) and pediatric (Study FX2016-21) patients with moderate-to-severe AV.

Methods
- 2 Phase 1, single-center, nonrandomized, open-label studies (Figure 1, Table 1).
- Adults (age 18 to 35 years) or pediatric subjects (age 9 years to 16 years, 11 months) with moderate-to-severe AV.

Adolescents (9-16 years, n=9)
- All subjects received FMX101 4% foam on days 1, 2, 4, 6, 9, 10, 11, 16.
- Subjects received a once-daily topical application of 4 g FMX101 4% for 21 days in comparison with remaining 96-hour sample period.

Pediatric subjects (9-16 years, n=9)
- Subjects received a once-daily topical application of 4 g FMX101 4% for 21 days.

Results

Baseline Demographics
- Table 2. Table 2. Baseline characteristics are shown in Table 2.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Adult Study (FX2014-03)</th>
<th>Pediatric Study (FX2016-21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>12 (40)/80 (n=18)</td>
<td>8 (27)/60 (n=12)</td>
</tr>
<tr>
<td>Race</td>
<td>27 (90)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>3 (10)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>11 (36.7)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Non-Hispanic/Latino</td>
<td>19 (63.3)</td>
<td>18 (90)</td>
</tr>
</tbody>
</table>

Table 2. Baseline Characteristics

Pharmacokinetics – Adults
- The mean plasma concentration of oral minocycline in adult subjects reached Cmax by 3 hours after administration, followed by a log-linear decrease in concentration for the remaining 96-hour sample period. (Figure 2).
- The mean plasma minocycline concentration of FMX101 4% increased until 8–14 hours (median Tmax) value on days 1, 12, and 21. (Figure 2).
- Figure 2 shows a comparison of mean plasma minocycline concentrations during the first 24 hours after a single dose of oral minocycline and after topical applications of FMX101 4% at 3 timepoints in adult subjects. (Figure 2).
- In adult subjects, oral minocycline treatment had a geometric mean Cmax of 850 ng/mL, while topical application of 4 g FMX101 4% in adults had a geometric mean Cmax ranging from 1.109–1.539 ng/mL (days 1–2, days 12–13, and days 21–25). (Figure 2).
- Steady state was achieved on day 6 of treatment. (Figure 2).

Pharmacokinetics – Pediatrics
- In pediatric subjects, the overall plasma concentrations of minocycline following the application of FMX101 4% once daily for 7 days were relatively constant over day 7 (~2.5 ng/mL) (Figure 3).

Figure 3. Mean Plasma Concentrations of Minocycline Following Application of FMX101 4% Once Daily for 7 Days in Pediatric Subjects (Study FX2016-21)

Safety
- In both adult and pediatric subjects, daily application of FMX101 4% was found to be safe and well tolerated. (Table 5).
- No adult or pediatric subjects experienced a serious treatment-emergent adverse event (TEAE), treatment-related TEAEs, or a TEAE leading to withdrawal from the study.
- 9 adult subjects in the FMX101 4% group reported 1 or more TEAEs; all were mild or moderate in intensity (FX2014-03).
- A single pediatric subject experienced 2 unrelated TEAEs (nausea and vomiting) (FX2016-21).

Table 5. Overall Summary of TEAEs Following Administration of Oral Minocycline and Topical Application of FMX101 4% in Adult and Pediatric Subjects

Conclusions
- In adult subjects, mean minocycline AUC and Cmax values were substantially lower following the daily topical application of 4 g FMX101 4% for 21 days in comparison with a single dose of oral minocycline (~1 mg/kg).
- There was no evidence of accumulation in adult subjects receiving daily topical application of FMX101 4% for up to 21 days.

Disclosure: Foamix Pharmaceuticals, Inc., sponsored this study.

References