Pharmacokinetics of Minocycline Foam FMX103 in Subjects With Moderate-to-Severe Facial Papulopustular Rosacea Under Maximum-Use Conditions: Results of a Phase 1 Study

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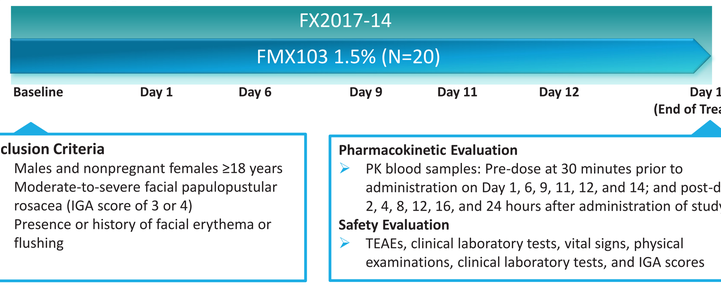
Introduction

- Rosacea is a chronic, inflammatory, facial skin condition affecting approximately 16 million people in the United States[1,2]
- Topical therapies such as metronidazole and azelaic acid are considered first-line options for the treatment of papulopustular rosacea[2-5]
- Oral tetracyclines, doxycycline and minocycline, are mainstays of treatment; however, they are associated with significant systemic side effects[2,4]
- FMX103 1.5% is a topical minocycline foam that was developed for the treatment of moderate-to-severe papulopustular rosacea. Efficacy and safety have been established in:
  - A Phase 2 clinical trial
  - 2 pivotal, identical, Phase 3, double-blind, vehicle-controlled studies (Study FX2016-11 and Study FX2016-12)
- A Phase 1 open-label study (FX2017-14) was conducted to evaluate minocycline's pharmacokinetic (PK) and safety profile following multiple-dose topical administration of FMX103 1.5% minocycline foam for moderate-to-severe facial papulopustular rosacea
  - Single-center, nonrandomized trial
  - 14 days, maximum-use conditions
- This report presents data from the completed PK and safety study

Methods

- FX2017-14, a Phase 1, single-center, nonrandomized, single-period, PK and safety evaluation study of FMX103 1.5% topical minocycline foam in the treatment of moderate-to-severe facial papulopustular rosacea (**Figure 1**)
  - FMX103 1.5% foam applied daily to full face for 14 days
  - 20 subjects
  - Approximately 2 grams of FMX103 1.5%

Figure 1. Study design



IGA=Investigator's Global Assessment; TEAE=treatment-emergent adverse event.

Results

- 20 subjects enrolled in the study
- Baseline demographics and disease characteristics are shown in **Table 1**

Table 1. Baseline demographics and disease characteristics

	FMX103 1.5% (N=20)
Mean age, years	47.3
Male, n (%) **Female, n (%)**	6 (30.0) 14 (70.0)
Race, n (%) White	 20 (100)
IGA score, n (%) 3 – Moderate 4 – Severe	 18 (90.0) 2 (10.0)

Table 2. Summary of PK parameters

	FMX103 1.5% (N=19)*	
PK Parameter	**Day 1** Mean (SD)	**Day 14** Mean (SD)
C_{max} (ng,mL)	1.30 (0.92)	0.75 (0.54)
T_{max} (h)	11.8 (4.07)	9.5 (3.82)
$AUC_{0\text{-}tldc}$ (ng*h/mL)	21.3 (16.2)	23.1 (34.1)
C_{24} (ng/mL)	0.86 (0.64)	0.57 (0.42)
$AUC_{0\text{-}tau}$ (ng*h/mL)	22.5 (16.2)	15.8 (11.4)
R_{ACC}	NA	0.77 (0.34)

*1 subject had all plasma concentrations below the limit of quantification.
$AUC_{0\text{-}tau}$ = area under the concentration-time curve from time zero (predose) through 24 hours; $AUC_{0\text{-}tldc}$ = area under the concentration-time curve from time zero (pre-dose) to the time of last determinable concentration; C_{24} = plasma minocycline concentration 24 hours after FMX103 1.5% application; C_{max} = maximum observed plasma concentration; R_{ACC} = accumulation ratio; SD = standard deviation; T_{max} = time to maximum measured plasma concentration.

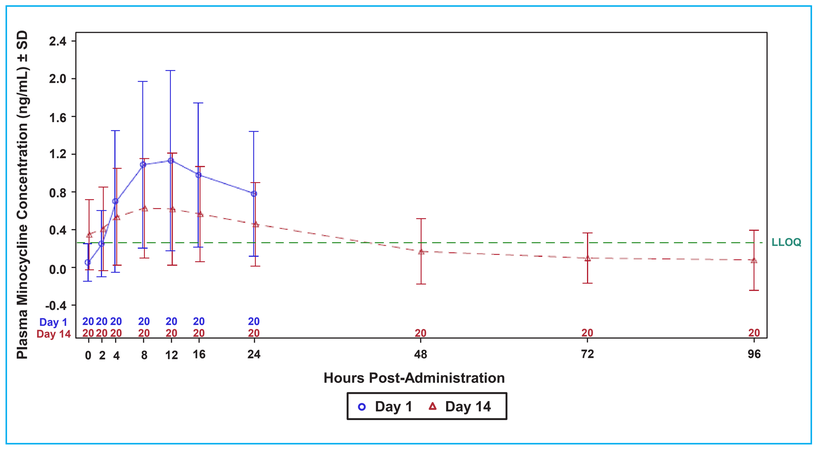
Table 3. Study drug concentrations by time points in PK population, day 1 to day 14

Visit	Time Point	FMX103 1.5% (N=20) Mean (SD)
Day 1	Pre-dose	0.05 (0.20)
	2 hours post-dose	0.24 (0.36)
	4 hours post-dose	0.70 (0.75)
	8 hours post-dose	1.09 (0.89)
	12 hours post-dose	1.13 (0.96)
	16 hours post-dose	0.98 (0.77)
Day 2	24 hours post-dose	0.78 (0.66)
Day 6	Pre-dose	0.38 (0.40)
Day 9	Pre-dose	0.37 (0.38)
Day 11	Pre-dose	0.44 (0.37)
Day 12	Pre-dose	0.40 (0.33)
Day 14	Pre-dose	0.34 (0.37)
	2 hours post-dose	0.40 (0.45)
	4 hours post-dose	0.53 (0.51)
	8 hours post-dose	0.62 (0.53)
	12 hours post-dose	0.61 (0.60)
	16 hours post-dose	0.56 (0.51)

Table 4. Study drug concentrations by time points in PK population, 24 to 96 hours after final treatment with FMX103 1.5%

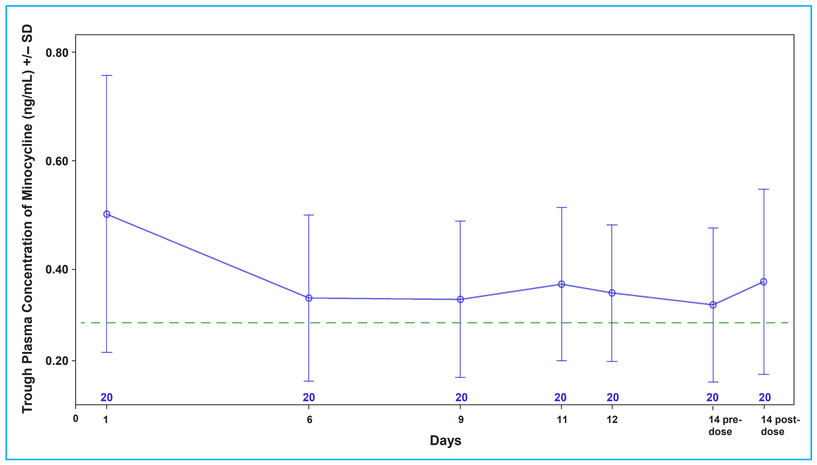
Visit	Time Point	FMX103 1.5% (N=20) Mean (SD)
Day 15	24 hours post-dose	0.45 (0.44)
Day 16	48 hours post-dose	0.16 (0.35)
Day 17	72 hours post-dose	0.09 (0.27)
Day 18	96 hours post-dose	0.07 (0.32)

Figure 2. Linear plot of mean plasma minocycline concentration, day 1 and day 14 following application of FMX103 1.5%



LLOQ=lower limit of quantification.

Figure 3. Linear plot of mean plasma trough concentrations of minocycline



Pharmacokinetics Summary

- After daily application of FMX103 1.5%, PK parameters of minocycline were generally similar for day 1 and day 14. Plasma concentrations of minocycline were low across the study (**Table 2**)
- Day 1 and day 14 plasma concentrations demonstrated a PK profile consistent with the dosing of FMX103 1.5%. The mean (SD) values for the maximum observed plasma concentration (C_{max}) were approximately 1.30 ng/mL on day 1 and 0.75 ng/mL on day 14 (**Tables 2-4; Figure 2**)
- Trough levels were approximately 0.5 ng/mL overall, from 24 hours after the first dose through 24 hours after the day 14 dose; mean (SD) values ranged from 0.34 (0.37) ng/mL to 0.78 (0.66) ng/mL (**Table 3; Figure 3**)
- Steady-state appeared to be achieved within 1 day

Table 5. Summary of TEAEs in the all-treated population

	FMX103 1.5% (N=20)
Subjects with any TEAE, n (%) Number of TEAEs	1 (5.0) 2[a]
Subjects with any treatment-related TEAE, n (%) Number of treatment-related TEAEs	1 (5.0) 1[b]
Subjects with any serious TEAE, n (%) Number of serious TEAEs	0 0
Subjects with any severe TEAE, n (%) Number of severe TEAEs	0 0
Subjects with any TEAE leading to discontinuation of study, n (%) Number of TEAEs leading to discontinuation	0 0

[a]Arthralgia, headache.
[b]Headache.

Table 6. TEAEs in the all-treated population

	FMX103 1.5% (N=20)
One or more TEAEs, n (%)	1 (5.0)
Adverse events, n (%)	
Arthralgia	1 (5.0)
Headache	1 (5.0)

Safety Summary

- FMX103 1.5% was generally safe and well tolerated
- All 20 subjects completed the study
- There were no serious TEAEs, no severe TEAEs, and no TEAEs that resulted in the study drug being withdrawn or requiring a dose reduction (**Table 5**)
- 1 subject reported 2 TEAEs: arthralgia, which was thought to be unrelated to the study drug, and a mild headache, considered possibly related to the study drug (**Table 6**)

Conclusions

- The results of the Phase 1 PK and safety evaluation study showed that FMX103 1.5% was safe and well tolerated by subjects with moderate-to-severe facial papulopustular rosacea
- Once-daily topical application of approximately 2 grams of FMX103 1.5% for 14 days yielded low plasma concentrations of minocycline over time and a PK profile consistent with dosing
- TEAEs were reported in 1 subject, but there were no serious or severe TEAEs, and no subjects discontinued or required dose reductions secondary to a TEAE

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Disclosures

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