FMX101 4% Topical Minocycline Foam for the Treatment of Moderate-to-Severe Acne Vulgaris: Efficacy and Safety From a Phase 3 Randomized, Double-Blind, Vehicle-Controlled Study

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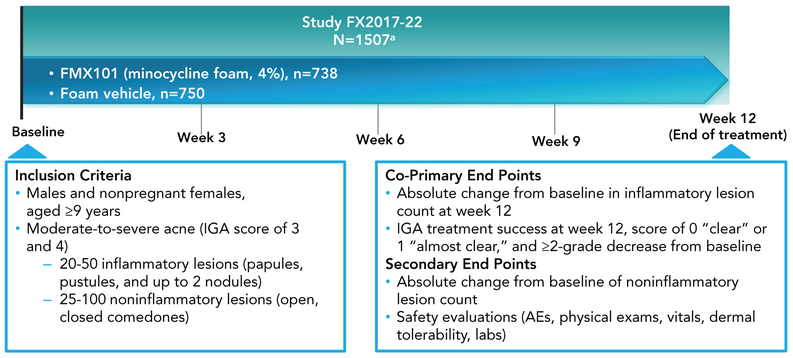
Introduction

- Acne vulgaris is a prevalent chronic, inflammatory skin disorder that affects most of the population at some point in their life[1]
- Oral minocycline and doxycycline are considered first-line therapy for the treatment of moderate-to-severe acne but are associated with potentially serious systemic side effects[2]
- FMX101 4% is the first stable topical foam formulation of minocycline that has been shown to be an effective and well-tolerated treatment for acne
  - Phase 2 clinical trial
  - 2 double-blind Phase 3 pivotal studies, Study FX2014-04 and Study FX2014-05[3,4]
- A third Phase 3 study (FX2017-22) was conducted to further evaluate the efficacy and safety of daily topical administration of FMX101 4% vs vehicle foam for a period of 12 weeks in the treatment of moderate-to-severe acne vulgaris
  - Multicenter, randomized, double-blind, vehicle-controlled, 2-arm study

Methods

- FX2017-22, a Phase 3 multicenter (89 sites), randomized, double-blind, vehicle-controlled, 2-arm study, further evaluated the efficacy and safety of topical FMX101 4% in the treatment of moderate-to-severe acne vulgaris (**Figure 1**)
  - Subjects were randomized 1:1 to receive either FMX101 4% or vehicle foam
  - Foam was self-applied once-daily for 12 weeks

Figure 1. Study design



AE=adverse event; IGA=Investigator's Global Assessment.
[a]Due to quality issues identified at one center, 19 subjects were prospectively removed from the intent-to-treat (ITT) population.

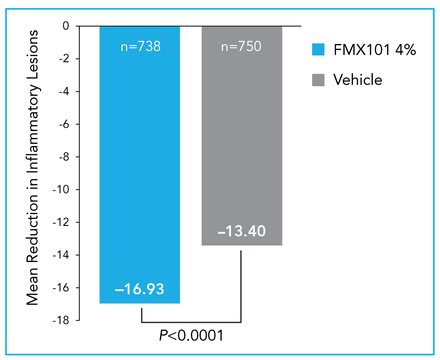
Results

- 1507 subjects were enrolled in the study
- Baseline demographics and disease characteristics are shown in **Table 1**

Table 1. Baseline demographics and disease characteristics

	FMX101 4% (n=738)	Vehicle Foam (n=750)
Mean age, years	20.2	20.6
Age distribution, n (%)		
9-12 yr	42 (5.7)	41 (5.5)
13-17 yr	321 (43.5)	309 (41.2)
>18 yr	375 (50.8)	400 (53.3)
Male, n (%)	278 (37.7)	281 (37.5)
Female, n (%)	460 (62.3)	469 (62.5)
Ethnicity, n (%)		
White	571 (77.4)	560 (74.7)
Black	125 (16.9)	144 (19.2)
Other	42 (5.7)	46 (6.1)
Inflammatory lesion count, mean (SD)	30.7 (8.89)	30.8 (8.27)
Noninflammatory lesion count, mean (SD)	49.7 (19.70)	49.6 (19.47)
Total lesion count, mean (SD)	80.4 (22.7)	80.3 (22.4)
IGA score, n (%)		
3 – Moderate	620 (84.0)	626 (83.5)
4 – Severe	118 (16.0)	124 (16.5)

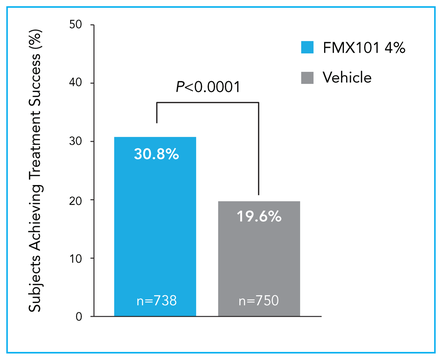
Figure 2. Absolute change in inflammatory lesion count from baseline at week 12



ANCOVA, ITT population, MI.
ANCOVA=analysis of covariance.

- At week 12, subjects treated with FMX101 4% had a statistically significantly greater reduction in the number of inflammatory lesions from baseline as compared with the vehicle treatment group, *P*<0.0001 (**Figure 2**)

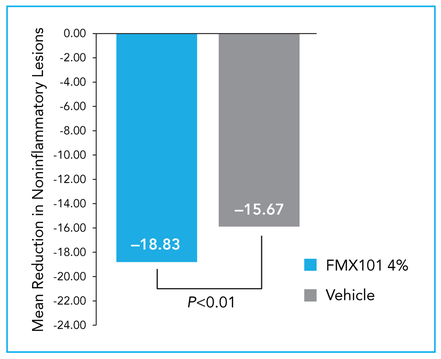
Figure 3. IGA treatment success at week 12



Cochrane Mantel-Haenszel test, stratified by analysis center, ITT population, MI.

- At week 12, the proportion of subjects achieving IGA treatment success in the FMX101 4% treatment group was statistically significantly higher than in the vehicle treatment group, *P*<0.0001 (**Figure 3**)

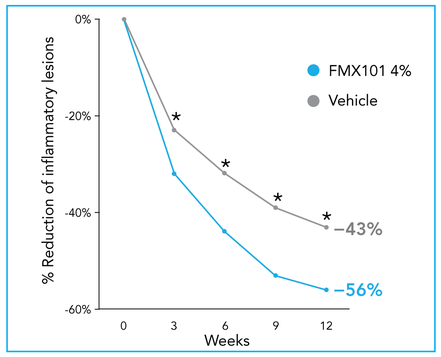
Figure 4: Absolute change of noninflammatory lesion count at week 12



ANCOVA, ITT population, MI.

- At week 12, the absolute change in noninflammatory lesion count in the FMX101 4% treatment group was statistically significantly greater than in the vehicle treatment group, *P*<0.01 (**Figure 4**)

Figure 5. Percentage change from baseline to week 12 in inflammatory lesions by visit



ANCOVA, ITT population, observed cases.
*$P \leq .0001$.

- The percentage reduction in inflammatory lesions was statistically significantly greater for FMX101 4% vs vehicle at all visits – week 3, 6, 9, and 12 (**Figure 5**)

Table 2. Summary of treatment-emergent adverse events (TEAEs) in safety population[a]

	FMX101 4% (n=737)	Vehicle (n=747)
Subjects with any TEAE, n (%)	193 (26.2)	183 (24.5)
Number of TEAEs	255	235
Subjects with any serious TEAE, n (%)	1 (0.1)	4 (0.5)
Number of serious TEAEs	1[b]	5[c]

[a]Safety population includes all randomized subjects who used at least 1 dose of study drug.
[b]Spontaneous abortion.
[c]Gastrointestinal disorders, spontaneous abortion, cholecystitis.

Table 3. Summary of subject discontinuation

	FMX101 4%	Vehicle
Subjects discontinued, n (%)	89 (12.1)	106 (14.1)
Reason for discontinuation		
Adverse event	3 (0.4)	2 (0.3)
Abnormal laboratory result	1 (0.1)	0 (0.0)
Lost to follow-up	34 (4.6)	39 (5.2)
Subject request	36 (4.9)	53 (7.1)
Protocol deviation	6 (0.8)	4 (0.5)
Other	9 (1.2)	8 (1.1)

Table 4. Nondermal and dermal AEs

	FMX 101 4%	Vehicle
One or more, n (%)	193 (26.2)	183 (24.5)
Nondermal AEs in ≥1% of subjects, n (%)		
URTI	31 (4.2)	26 (3.5)
Viral URTI	16 (2.2)	22 (2.9)
Headache	14 (1.9)	11 (1.5)
CK increased	14 (1.9)	6 (0.8)
Influenza	11 (1.5)	4 (0.5)
Dermal AEs in ≥1% of subjects, n (%)		
Acne	22 (3.0)	26 (3.5)

CK=creatine phosphokinase; URTI=upper respiratory tract infection; UTI=urinary tract infection.

Table 5. Facial local tolerability assessments at week 12, scale 0 (none) to 3 (severe)

Facial Local Tolerability Assessment,[a] n (%)	FMX101 (n=737)				Vehicle Foam (n=747)			
	0=None	1=Mild	2=Moderate	3=Severe	0=None	1=Mild	2=Moderate	3=Severe
Erythema	515 (82.7)	100 (16.0)	11 (1.8)	0 (0.0)	514 (82.5)	98 (15.7)	11 (1.8)	0 (0.0)
Dryness	568 (90.7)	53 (8.5)	5 (0.8)	0 (0.0)	550 (88.3)	68 (10.9)	4 (0.6)	1 (0.2)
Hyperpigmentation[b]	536 (85.6)	75 (12.0)	14 (2.2)	1 (0.2)	515 (82.7)	90 (14.4)	17 (2.7)	1 (0.2)
Skin Peeling	607 (97.0)	18 (2.9)	1 (0.2)	0 (0.0)	587 (94.2)	33 (5.3)	2 (0.3)	1 (0.2)
Itching	588 (93.9)	30 (4.8)	7 (1.1)	1 (0.2)	577 (92.6)	40 (6.4)	6 (1.0)	0 (0.0)

[a]Based on safety population.
[b]The term hyperpigmentation was most commonly used to describe localized post-inflammatory darkening of the affected skin.

Safety Summary

- FMX101 4% was generally safe and well tolerated
- Treatment-emergent adverse events (TEAEs) were few in type and frequency; most were mild in severity
- The most common adverse event in the study was upper respiratory tract infection, with similar frequency in the treatment arm (4.2%) and vehicle arm (3.5%)
- There were no treatment-related serious adverse events, and there was low subject discontinuation due to a TEAE (**Tables 2 and 3**)
- Cutaneous TEAEs were comparable in frequency in the FMX101 4% treatment group and vehicle group; the most common cutaneous AE (≥1% of subjects) was acne (**Table 4**)
  - >95% of subjects had none or mild signs and symptoms at week 12 assessment of dermal tolerability (**Table 5**)
- In total, 5 subjects discontinued from Study 22 due to a TEAE
  - 3 subjects for FMX101 4% 2 subjects for vehicle group

Conclusions

- The results of the Phase 3 study showed that FMX101 4% was safe and effective for the treatment of moderate-to-severe acne
- The study met both co-primary end points of absolute change from baseline in inflammatory lesion count and proportion with IGA treatment success at week 12
  - Significant reduction in number of both inflammatory and noninflammatory lesions at week 12 from baseline in FMX101 4% treatment group vs vehicle treatment group
  - Significant improvement in IGA treatment success at week 12 in FMX101 4% treatment group vs vehicle treatment group
- The safety profile of FMX101 was found to be consistent with that determined from the 2 prior Phase 3 studies (FX2014-04 and FX2014-05)

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Disclosures
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