Efficacy and Safety of FMX103 (1.5% Minocycline Foam) in the Treatment of Moderate-To-Severe Papulopustular Rosacea: Results from two Phase 3 Randomized, Multicenter, Double-Blind, Vehicle-Controlled Studies

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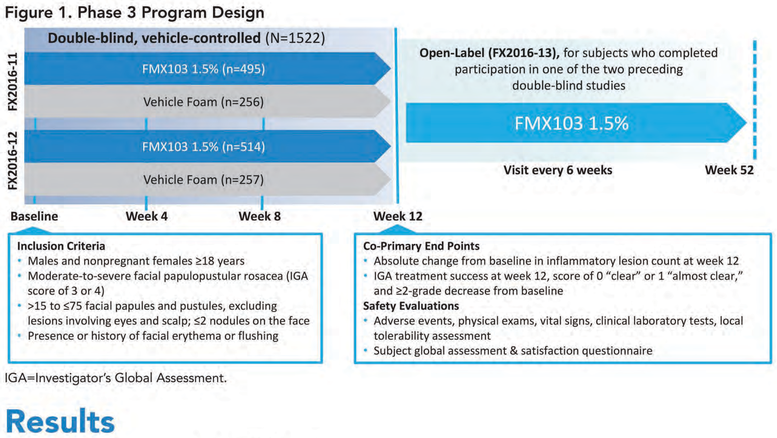
Introduction

- Rosacea is a common, chronic, inflammatory cutaneous disorder involving the face that affects approximately 16 million individuals in the United States[1,2]
- Rosacea is typically characterized by cutaneous signs such as flushing, erythema, edema, papules, and pustules[1-5]
- Topical therapies such as metronidazole and azelaic are considered first-line therapies for papulopustular rosacea[2-5]
  - Oral tetracyclines, specifically doxycycline and minocycline, are mainstays of treatment for moderate-to-severe disease; however, they are associated with significant systemic side effects[2,4]
- FMX103 1.5% topical minocycline foam was developed for the treatment of moderate-to-severe papulopustular rosacea; efficacy and safety have been established in:
  - Phase 2 clinical trial
  - Phase 1 pharmacokinetic study
- Two pivotal, identical, Phase 3, double-blind, vehicle-controlled studies, FX2016-11 and FX2016-12, were conducted to determine the efficacy, safety, and tolerability of FMX103 1.5% topical minocycline foam in subjects with facial papulopustular rosacea
  - Multicenter, randomized, 12 weeks
- This report presents data from the completed Phase 3 studies

Methods

- FX2016-11 and FX2016-12 were identical Phase 3, double-blind, multicenter, randomized, vehicle-controlled, 2-arm studies of FMX103 1.5% topical minocycline foam in the treatment of moderate-to-severe facial papulopustular rosacea (**Figure 1**)
  - FMX103 1.5% or vehicle foam was applied once daily to the face for 12 weeks
  - Randomized 2:1

Figure 1. Phase 3 Program Design



Inclusion Criteria
- Males and nonpregnant females ≥18 years
- Moderate-to-severe facial papulopustular rosacea (IGA score of 3 or 4)
- >15 to ≤75 facial papules and pustules, excluding lesions involving eyes and scalp; ≤2 nodules on the face
- Presence or history of facial erythema or flushing

Co-Primary End Points
- Absolute change from baseline in inflammatory lesion count at week 12
- IGA treatment success at week 12, score of 0 "clear" or 1 "almost clear," and ≥2-grade decrease from baseline

Safety Evaluations
- Adverse events, physical exams, vital signs, clinical laboratory tests, local tolerability assessment
- Subject global assessment & satisfaction questionnaire

IGA=Investigator's Global Assessment.

Results

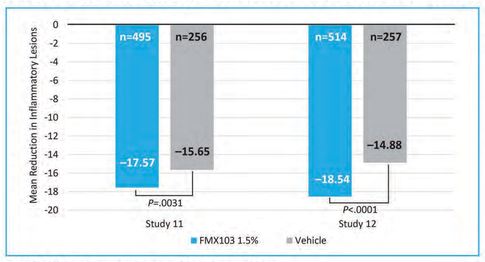
- 1522 subjects were enrolled in the 2 studies
- Baseline demographics and disease characteristics are shown in **Table 1**

Table 1. Baseline demographics and disease characteristics

	FX2016-11		FX2016-12	
	FMX103 1.5% (n=495)	Vehicle Foam (n=256)	FMX103 1.5% (n=514)	Vehicle Foam (n=257)
Mean age, years (range)	48.9 (18-82)	49.7 (22-86)	50.9 (18-85)	50.9 (18-82)
Male, n (%)	140 (28.3)	70 (27.3)	149 (29.0)	89 (34.6)
Female, n (%)	355 (71.7)	186 (72.7)	365 (71.0)	168 (65.4)
Ethnicity, n (%)				
White	474 (95.8)	241 (94.5)	499 (97.3)	250 (97.7)
Other	21 (4.2)	15 (5.5)	15 (2.7)	7 (2.3)
Inflammatory lesion count, mean (SD)	28.5 (12.05)	29.0 (12.13)	30.0 (12.84)	30.2 (12.99)
IGA score, n (%)				
3 – Moderate	444 (89.7)	222 (86.7)	443 (86.2)	213 (82.9)
4 – Severe	51 (10.3)	34 (13.3)	71 (13.8)	44 (17.1)

SD=standard deviation.

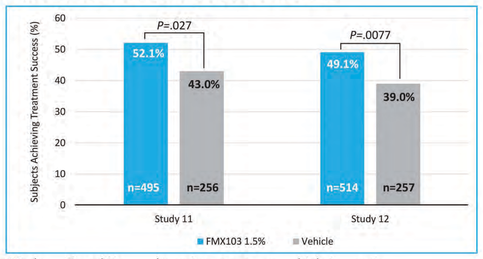
Figure 2. Absolute change in inflammatory lesion count from baseline at week 12



*ANCOVA, Intent-to-treat, multiple imputation.

- At week 12, subjects in both studies treated with FMX103 1.5% had statistically significant reductions in the number of inflammatory lesions from baseline as compared with vehicle (**Figure 2**)

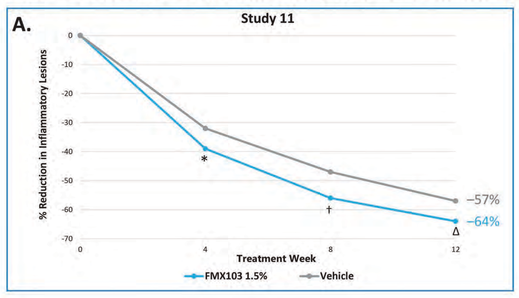
Figure 3. IGA treatment success at week 12



*Cochran-Mantel-Haenszel test, Intent-to-treat, multiple imputation.

- The proportion of subjects achieving IGA treatment success in both FMX103 1.5% treatment groups was statistically significant as compared with vehicle at week 12 (**Figure 3**)

Figure 4. Percentage change from baseline to week 12 inflammatory lesions by visit‡



- The percentage reduction in inflammatory lesions was statistically significant for FMX103 1.5% at all visits in both studies – weeks 4, 8, and 12 (**Figure 4**)

*P=.025; †P<.0001; $^{\Delta}P$=.002
‡ANCOVA, Intent-to-treat, observed cases.

Table 2. Summary of treatment-emergent adverse events (TEAEs, safety population)

	FX2016-11		FX2016-12	
	FMX103 1.5% (n=494)	Vehicle Foam (n=256)	FMX103 1.5% (n=514)	Vehicle Foam (n=257)
Subjects with any TEAE, n (%)	91 (18.4)	54 (21.1)	124 (24.1)	67 (26.1)
Number of TEAEs	132	70	159	88
Subjects with any serious TEAE, n (%)	2 (0.4)	3 (1.2)	1 (0.2)	2 (0.8)
Number of serious TEAEs*	7[a]	5[b]	1[c]	3[d]
Subjects with any TEAE leading to discontinuation, n (%)	5 (1.0)	2 (0.8)	2 (0.4)	0 (0.0)
Number of TEAEs leading to study discontinuation	5[e]	2[f]	2[g]	0
Subjects with any treatment-related TEAEs, n (%)	8 (1.6)	7 (2.7)	13 (2.5)	6 (2.3)
Number of treatment-related TEAEs	8[h]	7[i]	13[j]	6[k]
Subjects with a TEAE resulting in death, n (%)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Number of TEAEs resulting in death	0	1[l]	0	0

[a]Nausea, chest discomfort, fatigue, seasonal allergy, dehydration, syncope, dyspnea. [b]Myocardial infarction, tachycardia, gastrointestinal hemorrhage, chest pain, hypertension. [c]Hypertension. [d]Asthma, dyspnea, pyrexia. [e]Influenza, urinary tract infection, dermal cyst, dermatitis, pruritus, bladder mass. [f]Rash pustular, myocardial infarction. [g]Pruritus, telangiectasia. [h]Application-site pain, facial pain, ophthalmic herpes simplex, dysgeusia, migraine, dermatitis contact, pruritus, skin hyperpigmentation. [i]Facial pain, cellulitis, urine odor abnormal, nail discoloration, rosacea, skin exfoliation. [j]Eye irritation, aphthous ulcer, cheilitis, application-site erythema, nodule, sunburn, dizziness, dermatitis, hair color changes, nail discoloration, pruritus, rash. [k]Application-site pain, headache, nail discoloration. [l]Myocardial infarction.
*There were no treatment-related serious adverse event in either study.

Table 3. Noncutaneous TEAEs in the safety population

	FX2016-11		FX2016-12	
	FMX103 1.5% (n=494)	Vehicle Foam (n=256)	FMX103 1.5% (n=514)	Vehicle Foam (n=257)
Noncutaneous AEs in ≥1 subjects, n (%)				
Viral upper respiratory tract infection	9 (1.8)	4 (1.6)	15 (2.9)	8 (3.1)
Hypertension	6 (1.2)	2 (0.8)	3 (0.6)	1 (0.4)
Urinary tract infection	5 (1.0)	4 (1.6)	3 (0.6)	3 (1.2)
Upper respiratory tract infection	4 (0.8)	5 (2.0)	15 (2.9)	8 (3.1)
Sinusitis	4 (0.8)	0 (0.0)	7 (1.4)	2 (0.8)
Diarrhea	4 (0.8)	0 (0.0)	6 (1.2)	2 (0.8)
Influenza	3 (0.6)	1 (0.4)	5 (1.0)	3 (1.2)
Headache	3 (0.6)	4 (1.6)	11 (2.1)	6 (2.3)
Vomiting	------	------	5 (1.0)	1 (0.4)

Table 4. Cutaneous TEAEs in the safety population

	FX2016-11		FX2016-12	
	FMX103 1.5% (n=494)	Vehicle Foam (n=256)	FMX103 1.5% (n=514)	Vehicle Foam (n=257)
Cutaneous AEs, n (%)				
Pruritus	4 (0.8)	0 (0.0)	3 (0.6)	1 (0.4)
Dermatitis	2 (0.4)	0 (0.0)	2 (0.4)	1 (0.4)
Dermatitis contact	2 (0.4)	0 (0.0)	------	------
Rash	1 (0.2)	1 (0.4)	4 (0.8)	1 (0.4)
Actinic keratosis	1 (0.2)	1 (0.4)	------	------
Dermal cyst	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)
Hyperpigmentation	1 (0.2)	0 (0.0)	------	------
Hand dermatitis	1 (0.2)	0 (0.0)	------	------
Nail discoloration	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.4)
Erythema	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
Hair color change	------	------	1 (0.2)	0 (0.0)
Telangiectasia	------	------	1 (0.2)	0 (0.0)
Ingrowing nail	------	------	1 (0.2)	0 (0.0)
Skin exfoliation	0 (0.0)	1 (0.4)	------	------
Skin irritation	------	------	------	------
Onycholysis	------	------	0 (0.0)	1 (0.4)
Rosacea	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.4)
Seborrheic dermatitis	------	------	0 (0.0)	1 (0.4)

Figure 5. Facial local tolerability assessments at week 12 in FMX103 1.5% treatment group safety population (pooled analysis, n=1008)

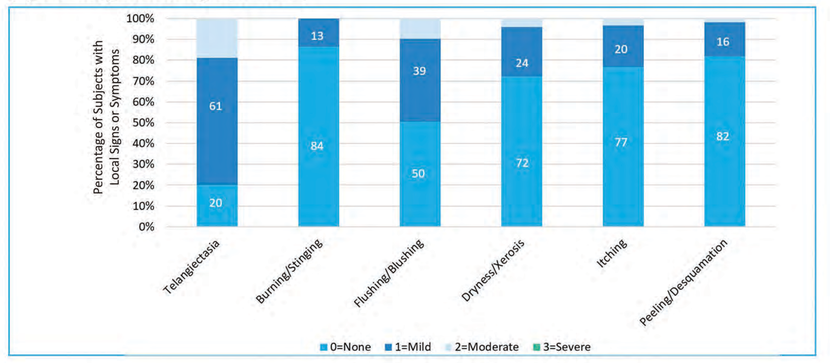


Figure 6. Erythema assessments from baseline to week 12 by visit in FMX103 1.5% treatment group safety population (pooled analysis, n=1008)

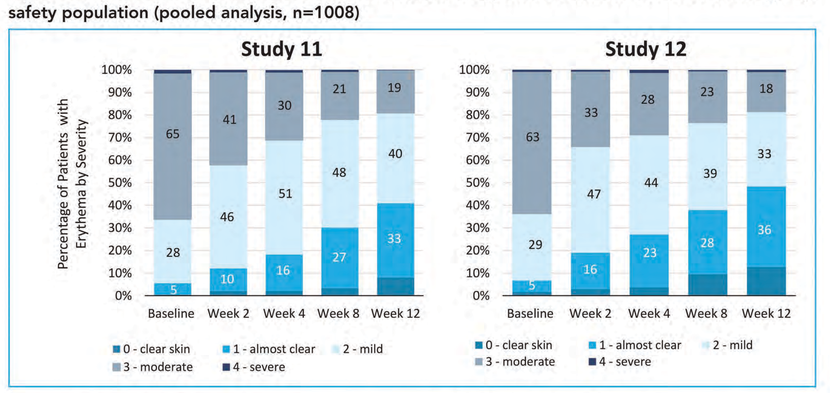
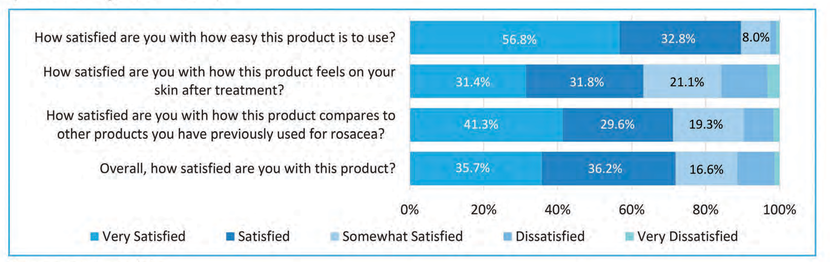


Figure 7. Subject satisfaction questionnaire results of FMX103 1.5% treatment group (pooled analysis, n=1009*)



*Intent-to-treat population.

Safety Summary

- FMX103 1.5% appeared to be generally safe and well tolerated
- Treatment-emergent adverse events (TEAEs) were few in frequency, and most were mild in severity
- The most common TEAE across both studies was viral upper respiratory tract infection (**Table 3**)
- There were no serious treatment-related TEAEs, and there was low subject discontinuation due to a treatment-related TEAE (**Table 2**)
- In total, 9 subjects across both studies discontinued due to a TEAE
  - 7 subjects in FMX103 treatment group
  - 2 subjects in the vehicle group
- Cutaneous TEAEs in the FMX103 1.5% treatment groups were few and comparable across both studies. Most were mild and included erythema, telangiectasia, and flushing (**Table 4** and **Figure 5**)
  - >80% of signs and symptoms were classified as "none" or "mild"
  - Severity of erythema decreased during the treatment period (**Figure 6**)
- Overall, >85% of subjects were satisfied with FMX103 1.5% (**Figure 7**)

Conclusions

- The results of the Phase 3 study demonstrated that FMX103 1.5% topical minocycline foam was effective, safe, and well tolerated for the treatment of moderate-to-severe facial papulopustular rosacea
- The study met both co-primary end points of absolute change in inflammatory lesion count from baseline and proportion of IGA treatment success at week 12
  - Significant reduction at week 12 in the number of inflammatory lesions from baseline, as compared with vehicle
  - Significant reduction in inflammatory lesion count seen as early as week 4 across both studies
  - Significant proportion of subjects achieving IGA treatment success, as compared with vehicle, at week 12
- FMX103 1.5% appeared to be safe and well tolerated, with cutaneous AEs occurring in <1% of subjects in the FMX103 1.5% treatment groups across both studies
- FMX103 1.5% significantly reduced overall clinical erythema severity over the treatment course
- There was high satisfaction with FMX103 1.5%

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Disclosures

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