The Efficacy and Safety of FMX101, Minocycline Foam 4%, for the Treatment of Acne Vulgaris: A Pooled Analysis of 2 Phase 3 Studies

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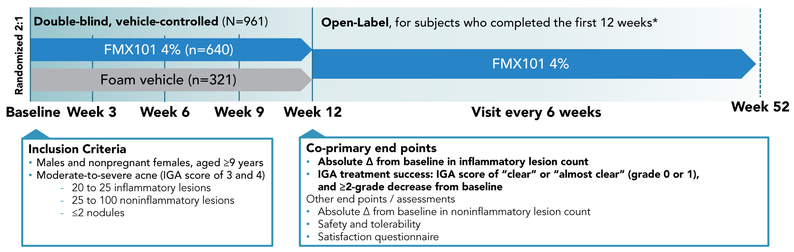
Background

- Acne vulgaris (AV) is a chronic inflammatory disease that affects approximately 85% of adolescents and can also present in pre- and post-adolescents[1]
- Oral antibiotics of the tetracycline class, including doxycycline and minocycline, are first-line therapies for moderate-to-severe acne; however, there are concerns with systemic side effects (eg, hyperpigmentation, phototoxicity, autoimmune disorders)[2,3]
- FMX101, minocycline foam 4%, is a novel, stable foam formulation of minocycline that has been previously demonstrated in a Phase 2 study to be an effective and well-tolerated treatment for moderate-to-severe acne[4]
- Two identical Phase 3, randomized, double-blind studies were conducted to evaluate the efficacy and safety of the topical administration of FMX101 4% in the treatment of moderate-to-severe AV
  - The 2 studies consisted of a 12-week double-blind phase followed by a 9-month open-label phase
- This report presents data from the completed double-blind phase

Methods

- Two Phase 3 (Study 04 and Study 05), randomized, double-blind, vehicle-controlled trials evaluated the safety and efficacy of FMX101 4% in the treatment of moderate-to-severe AV (**Figure 1**)
  - Patients were randomized 2:1 to receive either FMX101 4% or a foam vehicle
  - Foam was self-applied once daily for 12 weeks

Figure 1. Study Design



*Subjects with ≥1-grade IGA improvement. IGA=Investigator's Global Assessment.

Results

- 961 subjects (Study 04: N=466; Study 05: N=495) were enrolled in the studies
- Baseline demographics and disease characteristics are shown in **Table 1**

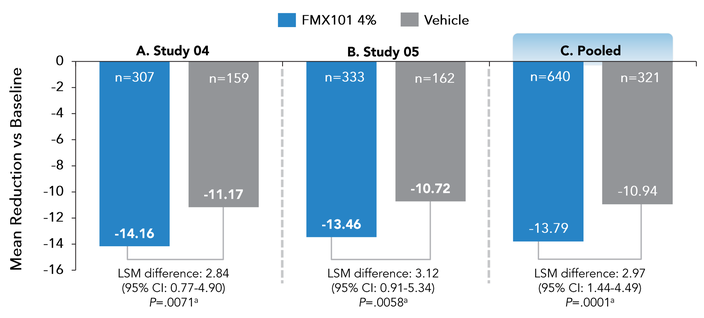
Table 1. Baseline Demographics and Disease Characteristics

	Study 04		Study 05	
	FMX101 4% (n=307)	Vehicle (n=159)	FMX101 4% (n=333)	Vehicle (n=162)
Demographics				
Mean age (range), years	20.5 (11-52)	20.0 (10-57)	20.5 (10-55)	20.8 (11-54)
Male/Female, %	45.3 / 54.7	38.4 / 61.6	40.8 / 59.2	42.6 / 57.4
Ethnicity (white, black, other), %	62.5, 28.0, 9.5	62.9, 25.2, 11.9	73.0, 21.9, 5.1	76.5, 18.5, 5.0
Inflammatory lesions, n				
Mean (range)	32.2 (20-50)	31.6 (20-76)	31.6 (20-69)	32.3 (20-50)
Noninflammatory lesions, n				
Mean (range)	49.5 (25-100)	46.5 (25-98)	50.0 (25-100)	50.9 (26-104)
IGA score, n (%)				
3 – Moderate	255 (83.1)	137 (86.2)	296 (88.9)	148 (91.4)
4 – Severe	52 (16.9)	22 (13.8)	37 (11.1)	14 (8.6)

Efficacy

- After 12 weeks of treatment, subjects treated with FMX101 4% had a significantly greater reduction in inflammatory lesion count from baseline vs vehicle in both studies (**Figure 2A, B**)
- FMX101 4% was superior to vehicle for the first co-primary end point in the pooled analyses (all 961 subjects) (**Figure 2C**)

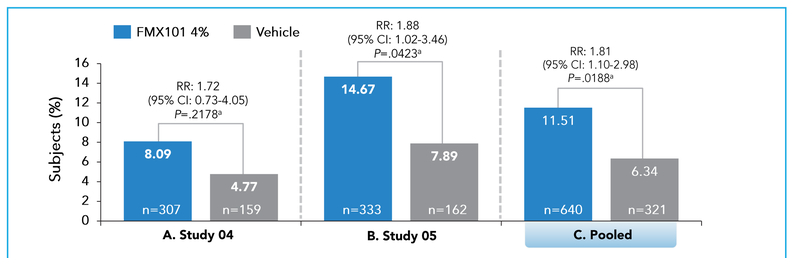
Figure 2. Co-primary End Point – Absolute Change in Inflammatory Lesion Count From Baseline at Week 12



[a]ANCOVA, ITT population, multiple imputation.
ANCOVA=analysis of covariance; CI=confidence interval; ITT=intention to treat; LSM=least squares means.

- A greater proportion of subjects in both studies achieved IGA treatment success with FMX101 4% vs vehicle at week 12 (**Figure 3A, B**)
  - However, a statistically significant difference was achieved only in Study 05; a numerical superiority was achieved in Study 04
- In the pooled analysis of the 2 studies, FMX101 4% was significantly superior to vehicle for the second co-primary end point of IGA treatment success (**Figure 3C**)

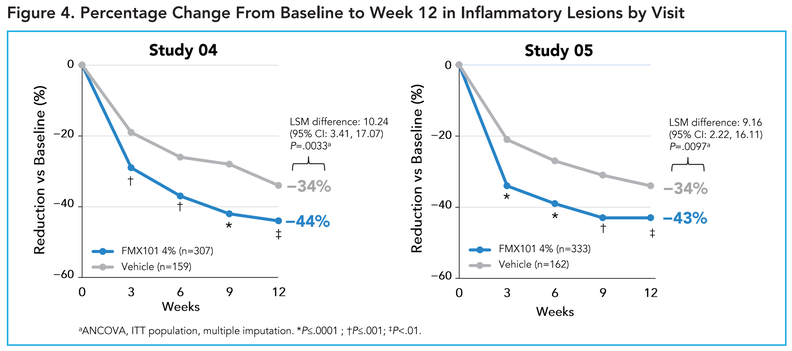
Figure 3. Co-primary End Point – IGA Treatment Success at Week 12



[a]Cochrane-Mantel-Haenszel test (RR=FMX101 4%/vehicle foam), ITT population, multiple imputation.
RR=risk ratio.

- The percentage reduction in inflammatory lesions was significantly greater for FMX101 4% vs vehicle in both studies (**Figure 4**)
  - A significantly greater reduction was observed as early as week 3 with FMX101 4%

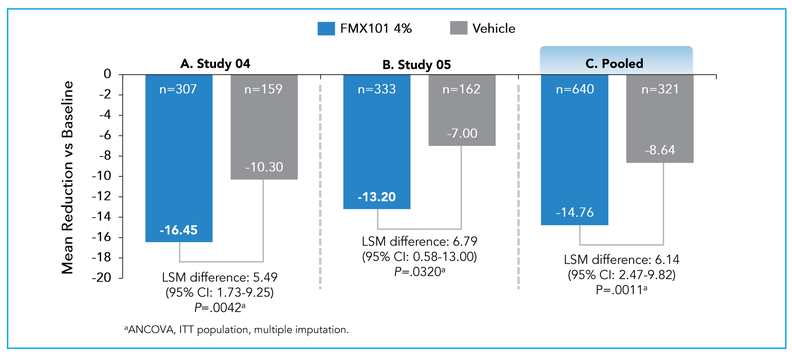
Figure 4. Percentage Change From Baseline to Week 12 in Inflammatory Lesions by Visit



[a]ANCOVA, ITT population, multiple imputation. *P≤.0001 ; †P≤.001; ‡P<.01.

- Subjects treated with FMX101 4% had a significantly greater reduction in noninflammatory lesion count from baseline at week 12 vs vehicle in both studies (**Figure 5A,B**), as well as in the pooled analysis (**Figure 5C**)

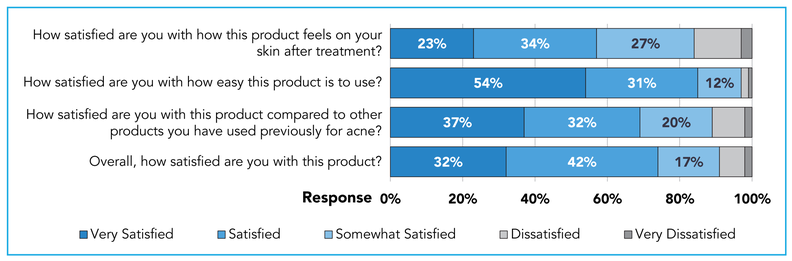
Figure 5. Absolute Change in Noninflammatory Lesion Count From Baseline at Week 12



[a]ANCOVA, ITT population, multiple imputation.

- There were high rates of subject satisfaction with using FMX101 4% (**Figure 6**)
  - Overall, 90% of subjects were satisfied with FMX101 4%
  - The majority of subjects were satisfied with FMX101 4% in comparison with previous acne products (ie, gels and creams), with its ease of use, and with the feel of the product on their skin

Figure 6. Patient Satisfaction Questionnaire Results (Pooled analysis, n=534)



Safety

- FMX101 4% was generally safe and well tolerated in both Study 04 and Study 05
- Across the 2 studies, the percentage of subjects reporting treatment-emergent adverse events (TEAEs) ranged between 16.9% and 33% for FMX101 4%, vs 18.2% to 26.5% for vehicle (**Table 2**)
  - 1 subject receiving FMX101 4% discontinued treatment in Study 05 (ectopic pregnancy; not related to treatment), as compared with 4 subjects for vehicle across the 2 studies
  - 7 subjects reported 9 serious TEAEs across the 2 studies; all were considered not related to treatment
  - Few treatment-related TEAEs were reported in both studies
- The most common TEAEs in ≥2% of subjects were nasopharyngitis and headache (**Table 3**)
  - Dermal TEAEs were reported in <1% of all subjects in the FMX101 4% treatment groups; their severity was mostly mild
- The majority (>95%)[a] of FMX101 4% subjects reported none or mild signs and symptoms for tolerability assessment parameters at week 12 (**Table 4**)

[a]Based on observed cases.

Table 2. Summary of Treatment-Emergent AEs (TEAEs)

	Study 04		Study 05	
	FMX101 4% (n=307)	Vehicle (n=159)	FMX101 4% (n=333)	Vehicle (n=162)
Subjects with any TEAE, n (%)	52 (16.9)	29 (18.2)	110 (33.0)	43 (26.5)
Number of TEAEs	78	35	169	80
Subjects with any serious TEAE, n (%)	1 (0.3)	0	4 (1.2)	2 (1.2)
Number of serious TEAEs	1[a]	0	5[b]	3[c]
Subjects with any TEAE leading to study discontinuation, n (%)	0	3 (1.9)	1 (0.3)	1 (0.6)
Number of TEAEs leading to study discontinuation	0	4[d]	1[e]	1[f]
Subjects with any treatment-related TEAE, n (%)	6 (2.0)	4 (2.5)	9 (2.7)	3 (1.9)
Number of treatment-related TEAEs	7	6	10	4

[a]Suicide attempt. [b]Intestinal obstruction, intestinal perforation, facial bones fracture, ectopic pregnancy; asthma. [c]Biliary dyskinesia, cholecystitis, pneumonia. [d]Application-site acne, application-site burn, application-site erythema, application-site pruritus. [e]Ectopic pregnancy. [f]Hepatic enzyme increased.

Table 3. Nondermal and Dermal AEs Profile

Adverse Event	Study 04		Study 05	
	FMX101 4% (n=307)	Vehicle (n=159)	FMX101 4% (n=333)	Vehicle (n=162)
Nondermal AEs in ≥1% of subjects, %				
One or more	16.9	18.2	33.0	26.5
Nasopharyngitis	2.0	3.8	7.2	3.7
Headache	2.3	3.1	6.0	5.6
Upper respiratory tract infection	–	–	1.8	1.2
CK increased	1.0	0.6	1.5	2.5
Ligament sprain	0.3	1.3	1.8	0.6
Nausea	–	–	1.2	0.6
Vomiting	–	–	1.2	0.6
Administration-site dermal AEs, %				
Acne worsening	–	0.6	0.3	–
Burn	–	1.3	–	–
Dermatitis	–	–	0.3	–
Discoloration[a]	0.7	1.3	0.9	–
Discomfort	0.3	–	–	–
Erythema	–	0.6	–	–
Pruritus	–	0.6	–	–
Rash	–	–	0.3	0.6

[a]Several terms were coded to "discoloration" including discoloration, yellow discoloration and, in 1 case, hyperpigmentation.
CK=creatinine phosphokinase.

Table 4. Tolerability Assessment Results at Week 12 (Based on Observed Cases)

Tolerability Assessment, n (%)						
	0=None	1=Mild	2=Moderate	0=None	1=Mild	2=Moderate
Study 04	FMX 101 4% (n=267)			Vehicle (n=128)		
Erythema	248 (92.9)	19 (7.1)	–	124 (96.9)	4 (3.1)	–
Dryness	250 (93.6)	17 (6.4)	–	120 (93.8)	8 (6.3)	–
Hyperpigmentation[a]	233 (87.3)	28 (10.5)	6 (2.2)	110 (85.9)	14 (10.9)	4 (3.1)
Skin Peeling	259 (97.0)	8 (3.0)	–	125 (97.7)	3 (2.3)	–
Itching	254 (95.1)	12 (4.5)	1 (0.4)	124 (96.9)	3 (2.3)	1 (0.8)
Study 05	FMX101 4% (n=294)			Vehicle (n=136)		
Erythema	238 (81.0)	49 (16.7)	7 (2.4)	102 (75.0)	29 (21.3)	5 (3.7)
Dryness	281 (95.6)	11 (3.7)	2 (0.7)	124 (91.2)	11 (8.1)	1 (0.7)
Hyperpigmentation[a]	237 (80.6)	44 (15.0)	13 (4.4)	118 (86.8)	15 (11.0)	3 (2.2)
Skin Peeling	281 (95.6)	12 (4.1)	1 (0.3)	131 (96.3)	5 (3.7)	–
Itching[b]	274 (93.2)	18 (6.1)	2 (0.7)	123 (90.4)	12 (8.8)	–

[a]Hyperpigmentation was most commonly used to describe localized post-inflammatory darkening of the affected skin.
[b]A case of severe itching in the vehicle group.

Conclusions

- The results of the 2 Phase 3 studies showed that FMX101 4% was effective for the treatment of moderate-to-severe acne
  - There was significantly greater reduction of both inflammatory and noninflammatory lesions at week 12 from baseline with FMX101 4% vs vehicle in both Study 04 and Study 05, as well as in the pooled analysis (a co-primary end point)
    - A significant reduction in inflammatory lesions was observed as early as week 3 for FMX101 4%
  - The rate of IGA treatment success was significantly greater for FMX101 4% vs vehicle in Study 05, but not Study 04 (a co-primary end point)
    - Pooled analysis of IGA treatment success was statistically significant for FMX101 4%
- >95% of subjects had none or mild signs and symptoms at the week 12 assessment of dermal tolerability
- FMX101 4% appeared to be safe and well tolerated, with dermal AEs occurring in <1% of FMX101 4% subjects and no serious drug-related AEs reported
- There was high satisfaction with FMX101 4%
- The FMX101 4% open-label phase is currently ongoing to determine long-term safety

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