An Open-Label Extension of Two Phase 3 Studies Evaluating Long-Term Efficacy of FMX101 4% Minocycline Foam for the Treatment of Acne Vulgaris

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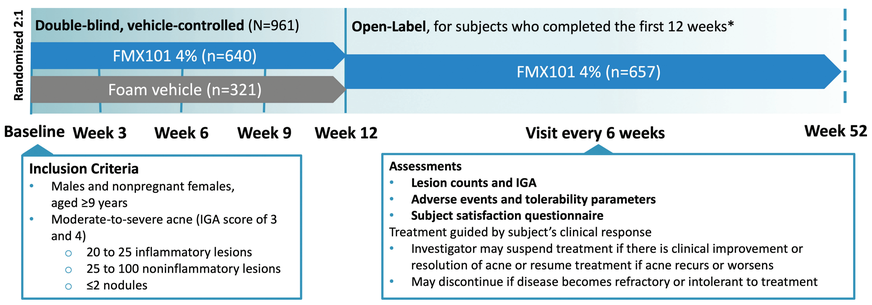
Introduction

- Acne vulgaris is a chronic inflammatory disease that affects approximately 85% of adolescents and can persist into adulthood[1]
- FMX101 4% is a topical foam formulation of minocycline under development for the treatment of moderate-to-severe acne vulgaris
- The efficacy and safety of FMX101 4% in treating moderate-to-severe acne have been previously reported in 3 Phase 3 studies (Study 04, Study 05, and Study 22)[2,3]
  - In all 3 studies, FMX101 4% demonstrated statistically significant reductions in both inflammatory and noninflammatory lesions from baseline to week 12 compared to vehicle
  - During the 12-week double-blind phase, FMX101 4% appeared to be effective, safe, and well tolerated for the treatment of moderate-to-severe acne
- To assess the long-term safety of FMX101 4% topical minocycline foam, an open-label extension phase of Study 04 and Study 05 was conducted in which FMX101 4% was applied daily over the course of an additional 40 weeks
  - Safety assessments were carried out at all visits (weeks 16, 22, 28, 34, 40, 46 and 52) including adverse events, vital signs, dermal tolerability and lab testing (weeks 28 and 52)
  - Efficacy assessments were carried out at all visits during the open-label phase, allowing for an evaluation of the continuation of effects of FMX101 4% in subjects with moderate-to-severe acne over a total of 52 weeks of treatment

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 acne vulgaris (**Figure 1**)
  - Patients were randomized 2:1 to receive either FMX101 4% or vehicle foam
  - Foam was self-applied once daily for 12 weeks
  - Eligible patients from both groups moved to the open label phase and continued for 40 weeks with FMX101 4%

Figure 1. Study Design

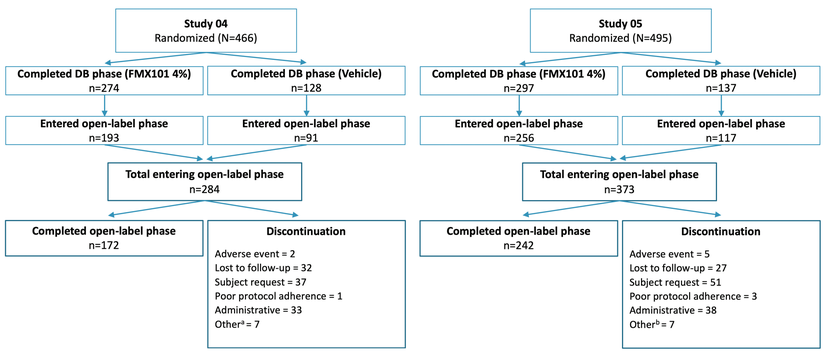


*Subjects with ≥1-grade IGA improvement. IGA=Investigator's Global Assessment.

Results

- 961 subjects (Study 04: N=466; Study 05: N=495) were enrolled in the studies (**Figure 2**)
  - At the end of Week 12, 657 subjects (Study 04: N=284; Study 05: N=373) were rolled over into the open label phase
  - 414 subjects completed the open-label extension (Study 04, n=172; Study 05, n=242).

Figure 2. Subject Disposition



[a]Other reasons that subjects discontinued included sponsor's request, the subject was not qualified for the study, subject moved away from the site, and positive pregnancy test.

[b]Other reasons that subjects discontinued included positive pregnancy test, subject noncompliance, subject withdrew consent, lack of efficacy, subject did not meet eligibility criteria, subject moved, site closure.

- Baseline demographics and disease characteristics are shown in **Table 1**

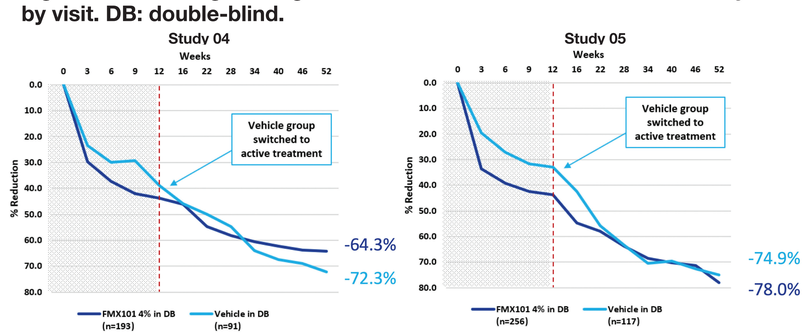
Table 1. Baseline Demographics and Disease Characteristics (double-blind phase)

	Study 04 (N=284)	Study 05 (N=373)
Mean age, yr 9 to >18 yr	20.3	19.8
Gender, n (%) Male Female	 126 (44.4) 158 (55.6)	 167 (44.8) 206 (55.2)
Race, n (%) White Black Other	 196 (69.0) 55 (19.4) 33 (11.7)	 285 (76.4) 72 (19.3) 16 (4.3)
Mean lesion count, n (SD) Inflammatory lesions Noninflammatory lesions	 32.2 (8.4) 49.7 (17.4)	 32.0 (8.4) 50.0 (19.4)
IGA score, n (%) 3 – Moderate 4 – Severe	 238 (83.8) 46 (16.2)	 335 (89.8) 38 (10.2)

IGA: Investigator's Global Assessment; SD: standard deviation.

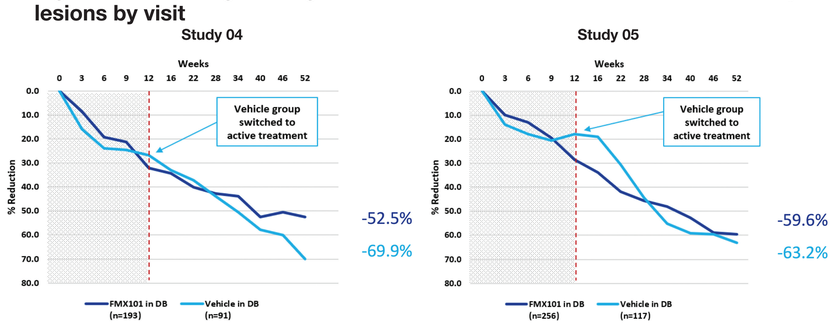
- Throughout the OLE treatment period, both studies demonstrated ongoing reduction in inflammatory and noninflammatory lesion counts from baseline and an increase in the proportion of subjects achieving IGA treatment success
  - For the inflammatory lesion count, the week 52 assessment showed reductions from baseline in both studies for subjects treated with FMX101 4% (Study 04, 64.3%; Study 05, 78.0%) (**Figure 3**)

Figure 3. Percentage change from baseline to week 52 in inflammatory lesions by visit. DB: double-blind.



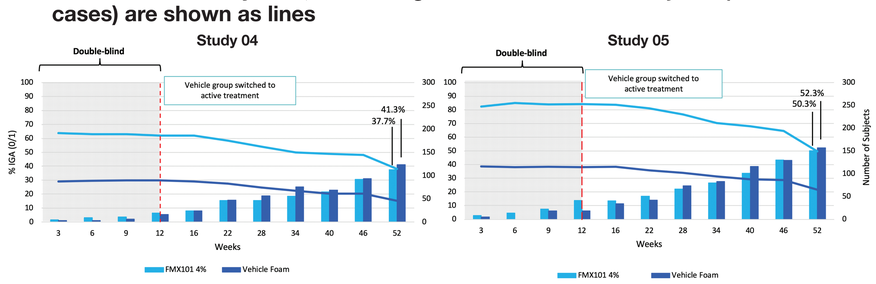
- The reduction from baseline in noninflammatory lesion count was also maintained throughout the OLE phase (Study 04, 52.5%; Study 05, 59.6%) (**Figure 4**)

Figure 4. Percentage change from baseline to week 52 in noninflammatory lesions by visit



- Through week 52, there was an increase in the proportion of subjects achieving IGA treatment success defined as a score of "clear" (0) or "almost clear" (1) and at least 2-grade improvement from baseline (Study 04, 37.7%; Study 05, 50.3%) (**Figure 5**)

Figure 5. Percentage of patients achieving IGA treatment success at week 52. IGA is shown by bars, and changes in the number of subjects (observed cases) are shown as lines



- More than 99% of the TEAEs that occurred were mild or moderate in severity (**Table 2**)
  - No serious TEAEs leading to subject discontinuation were reported in either study
  - Three TEAEs leading to discontinuation (application-site acne, application-site edema, application-site dermatitis) were potentially related to treatment but were not regarded as serious in nature
  - In the OLE, there were 3 SAEs (pneumonia, fatigue, head injury from falling); all resolved prior to study completion and were deemed not to be related to treatment

Table 2. Summary of TEAEs in the safety population and rates of discontinuation

	Study 04 (N=284)	Study 05 (N=373)
Subjects with any TEAE, n (%)	65 (22.9)	120 (32.2)
Number of TEAEs	132	207
Subjects with any serious TEAE, n (%)	1 (0.4)	1 (0.3)
Number of serious TEAEs	1[a]	2[b]
Subjects with treatment-related TEAEs, n (%)	5 (1.8)	8 (2.1)
Number of treatment-related TEAEs	7[c]	11[d]
Subjects discontinued due to TEAE, n (%)	2 (0.7)	5 (1.3)
Number of TEAEs leading to discontinuation	2[e]	5[f]

[a]Pneumonia.
[b]Fatigue, head injury from fainting.
[c]Increased alanine aminotransferase, increased aspartate aminotransferase, increased gamma-glutamyltransferase, application-site acne, headache.
[d]Headache, migraine, sunburn, application-site dermatitis, application-site discoloration, application-site edema, pharyngeal erythema, seborrheic dermatitis, lymphadenopathy.
[e]Application-site acne.
[f]Application-site edema, upper abdominal pain, flank pain, application-site dermatitis.
TEAE: treatment-emergent adverse event.

- Similar to the double-blind phase, the most frequently observed TEAEs in the OLE were nasopharyngitis (5.0%), headache (3.2%), and elevated creatinine phosphokinase (2.3%)

Table 3. Common TEAEs in ≥1% of Subjects During the Open-Label Phase (Week 52)

	Study 04	Study 05
Subjects with one or more, n (%)	65 (22.9)	120 (32.2)
Noncutaneous AEs, n (%)		
Nasopharyngitis	10 (3.5)	23 (6.2)
Influenza	6 (2.1)	5 (1.3)
CK increased	5 (1.8)	10 (2.7)
Cough	4 (1.4)	----------
Headache	4 (1.4)	17 (4.6)
URTI	4 (1.4)	----------
Back pain	3 (1.1)	----------
Pharyngitis streptococcal	3 (1.1)	----------
Pyrexia	3 (1.1)	----------
UTI	3 (1.1)	----------
Sinusitis	----------	8 (2.1)
ALT increased	----------	5 (1.3)
Abdominal pain	----------	4 (1.1)
AST increased	----------	4 (1.1)
Gastroenteritis	----------	4 (1.1)
Cutaneous AEs, n (%)		
Application-site acne	3 (1.1)	----------

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine phosphokinase; TEAE: treatment-emergent adverse event; URTI: upper respiratory tract infection; UTI: urinary tract infection.

- At the week 52 assessment of facial local tolerability (erythema, dryness, hyperpigmentation, skin peeling, itching), >95% of subjects evaluated in the open-label phase of both studies reported none, or only mild, signs and symptoms

Table 4. Dermal Tolerability Assessment at Week 52 (Scale: 0=none to 3=severe)

Assessment	Study 04 (N=284)[a] n (%)[c]				Study 05 (N=373)[b] n (%)[c]			
	0=None	1=Mild	2=Moderate	3=Severe	0=None	1=Mild	2=Moderate	3=Severe
Erythema	155 (96.9)	5 (3.1)	0 (0.0)	0 (0.0)	188 (88.3)	23 (10.8)	2 (0.9)	0 (0.0)
Dryness	146 (91.3)	13 (8.1)	1 (0.6)	0 (0.0)	209 (98.1)	4 (1.9)	0 (0.0)	0 (0.0)
Hyperpigmentation[d]	153 (95.6)	5 (3.1)	2 (1.3)	0 (0.0)	193 (90.6)	18 (8.5)	2 (0.9)	0 (0.0)
Skin peeling	155 (96.9)	4 (2.5)	1 (0.6)	0 (0.0)	212 (99.5)	1 (0.5)	0 (0.0)	0 (0.0)
Itching	159 (99.4)	1 (0.6)	0 (0.0)	0 (0.0)	210 (98.6)	3 (1.4)	0 (0.0)	0 (0.0)

[a]160 respondents at week 52.
[b]213 respondents at week 52.
[c]Percentages based on observed cases.
[d]Hyperpigmentation was considered a characteristic of inflammatory and post-inflammatory changes associated with acne.

Limitations

- Due to the nature of the open-label trial design, a comparator analysis of efficacy was not feasible
  - However, the results of this study suggest that the safety and efficacy of FMX101 4% were sustained from week 12 through week 52
- During the OLE period, subjects were permitted to use concomitant medications (prescription or over-the-counter) and were able to discontinue or recommence participation in the study at any time
  - Although this may confound interpretation of the long-term clinical effect attributed to FMX101 4%, it may be more representative of real-world practice

Conclusions

- The results of this OLE study extend prior findings demonstrating the safety and efficacy of FMX101 4% beyond 12 weeks of use
- The safety profile for an additional 40 weeks of daily application was similar to that seen after 12 weeks of use in the double-blind phase of these studies
- Through week 52, inflammatory and non-inflammatory lesion counts continued to decrease while the portion of subjects achieving IGA treatment success continued to increase
- Overall, FMX101 4% during the open label extension phase of Study 04 and Study 05 appeared to be safe, effective and well tolerated for the long-term treatment of acne

Disclosures
This study was funded by Foamix Pharmaceuticals. Dr. Stein Gold is an advisor and investigator for Foamix, Galderma, LEO, Novartis, and Valeant, and is an investigator for Janssen, AbbVie, and Solgel and an advisor and investigator for Novartis.
Dr. Dhawan is an investigator for Foamix, AbbVie, Galderma, Lilly, Moberg, Solgel, Incyte, Valeant, Novartis, and Dermira, and a speaker for Pfizer and Dermira.
Dr. Weiss is a principal investigator for AbbVie, Aclaris, Endo, Foamix, Galderma, LEO, Moberg, Promius, and Valeant; he is a speaker for AbbVie and Ortho Dermatologics and a consultant for Aclaris and LEO, as well as an advisor for Foamix, Galderma, and Valeant.
Dr. Draelos is a principal investigator and advisor for Foamix.
Dr. Ellman is a former employee and stockholder of Foamix.
Dr. Stuart is an employee and stockholder of Foamix.

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