XP-23829, a novel fumaric acid ester, is efficacious in reducing psoriatic lesions: Results from a phase 2 randomized controlled study

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Introduction

- Dimethyl Fumarate (DMF) is a fumaric acid ester (FAE) approved in Germany for the treatment of moderate to severe chronic plaque psoriasis. Monomethyl fumarate (MMF) is the active moiety of DMF.
- XP-23839 is an extended release FAE that is being developed for the treatment of moderate to severe plaque psoriasis.
- Here, we examine a phase 2 study to evaluate the safety and efficacy of 3 doses and 2 dosing regimens at 12 weeks.

Methods

- Randomized, double-blind, placebo-controlled, dose-finding efficacy and safety study in 33 US sites.
- Patients with chronic plaque psoriasis > 6 months, PASI (Psoriasis Area and Severity Index) ≥ 12, sPGA (static Physician Global assessment) ≥ 3, and psoriasis BSA (Body Surface Area) ≥ 10%.
- 200 subjects randomized in a 1:1:1:1 ratio into 4 arms: 400 mg QD, 400 mg BID, 800 mg QD, Placebo.
- A 3-week titration phase was followed by 9 weeks of treatment.
- The primary endpoint was the percentage change in PASI score from baseline to the end of week 12.

Results

- Primary efficacy analysis (mITT population) included 194 subjects: 400 mg QD (48), 800 mg QD (53), 400 mg BID (46), and placebo (47).
- Least squares mean percent change from baseline was statistically significant compared with placebo for the 800 mg QD group (-48.2% vs -25.0%; *P*=.001) and the 400 mg BID group (-50.7% vs -25.0%; *P*<.001); the difference between 400 mg QD and placebo did not reach statistical significance (-38.1% vs -25.0%; *P*=.066) (Table 1) (Figure 1).
- Diarrhea was the most common TEAE, reported in 22.4%, 40.0%, 39.6%, and 14.6% of subjects in the XP-23829 400 mg QD, 800 mg QD, 400 mg BID, and placebo groups, respectively. Most cases of diarrhea were mild to moderate in severity (Table 2).
- Nausea and abdominal pain were reported in more than 10% of the overall XP-23829 population (Table 2).
- Flushing was reported in 5.9% of XP-23829 subjects and 6.3% of placebo subjects (Table 2).
- No subject demonstrated grade 3 or 4 lymphopenia (Table 2).
- No new or unexpected adverse events related to XP-23829 were reported compared to what is known for the FAE class (Table 2).

Conclusions

- In this study XP-23829 in 400 mg BID and 800 mg QD doses demonstrated significant efficacy over 12-week of treatment and efficacy did not appear to have plateaued at the end of the study.
- Efficacy and safety is being further assessed in a 24-week phase 2 study.

Table 1. Least Squares Mean for Percentage Change in Total PASI Score

	XP-23829 400 mg QD (N=48)		XP-23829 800 mg QD (N=53)		XP-23829 400 mg BID (N=46)		Placebo (N=47)
Overall mITT Population	LSM (SE)	*P* Value vs Placebo	LSM (SE)	*P* Value vs Placebo	LSM (SE)	*P* Value vs Placebo	LSM (SE)
Week 12	-38.1 (5.07)	0.066	-48.2 (5.06)	.001	-50.7 (5.50)	< .001	-25.0 (5.06)

LSM = least squares mean; SE = standard error

Table 2. Frequent Treatment-Emergent Adverse Effects (≥10%)

	XP-23829 400 mg QD (N=49)	XP-23829 800 mg QD (N=55)	XP-23829 400 mg BID (N=48)	XP-23829 (N=152)	Placebo (N=48)
Any TEAE	36 (73.5)	42 (76.4)	37 (77.1)	115 (75.7)	29 (60.4)
Diarrhea	11 (22.4)	22 (40.0)	19 (39.6)	52 (34.2)	7 (14.6)
Nausea	6 (12.2)	4 (7.3)	10 (20.8)	20 (13.2)	6 (12.5)
Abdominal pain	1 (2.0)	7 (12.5)	11 (22.9)	19 (12.5)	2 (4.2)
Flushing	4 (8.2)	3 (5.5)	2 (4.2)	9 (5.9)	3 (6.3)
Headache	2 (4.1)	3 (5.5)	5 (10.4)	10 (6.6)	2 (4.2)
Vomiting	3 (6.1)	7 (12.7)	1 (2.1)	11 (7.2)	1 (2.1)

Figure 1. Least Squares Mean % Change From Baseline in PASI Score Over Time PPN-06 vs Fumaderm

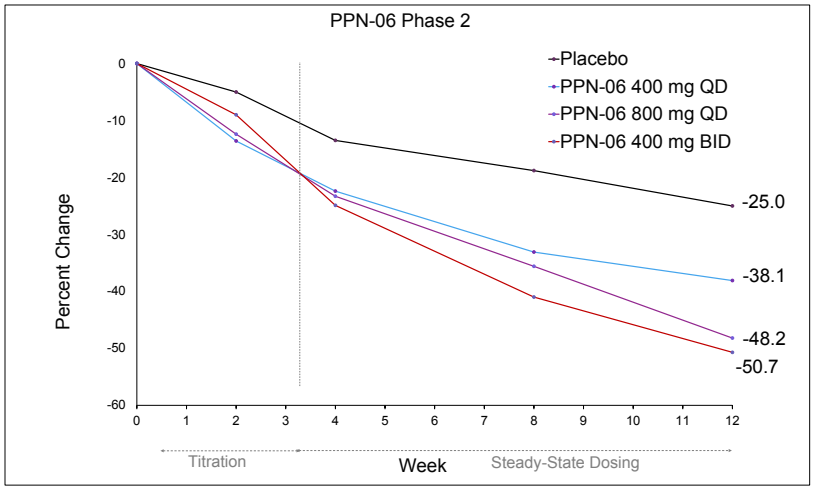

Table 3. Maximum Lymphocyte Grades at Any Given Visit

	400 mg QD (N=49)	800 mg QD (N=55)	400 mg BID (N=48)	Placebo (N=48)
Grade 1	3 (6.1%)	5 (9.1%)	7 (14.6%)	2 (4.2%)
Grade 2	2 (4.1%)	2 (3.6%)	1 (2.1%)	0
Grade 3 or 4	0	0	0	0

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