EFFICACY AND SAFETY OF MICROENCAPSULATED BENZOYL PEROXIDE 3% AND MICROENCAPSULATED TRETINOIN 0.1% (E-BPO/E-ATRA) IN ACNE VULGARIS: RESULTS FROM TWO RANDOMIZED CONTROLLED CLINICAL TRIALS

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INTRODUCTION

- Benzoyl peroxide (BPO) is recommended for treatment of acne of all severities.[1] It is bactericidal against *C. acnes* on the skin and within hair follicles with no risk for development of resistance,[1,2] and it also has sebostatic and keratolytic effects.[3]
- BPO is widely used as a single agent in many different vehicles,[4] and in combination with other medications.[3,5] Multiple analyses have indicated that the efficacy of BPO is enhanced when used in combination with topical retinoids, such as tretinoin (ATRA).[6,7] However, BPO causes degradation of tretinoin, reducing its effectiveness.[8]
- BPO and ATRA can also result in significant skin irritation when applied to the face of patients with acne,[9,10] and there is some evidence suggesting that their irritative effects may be additive.[11]
- E-BPO/E-ATRA is an investigational, antibiotic-free, fixed-dose combination of microencapsulated tretinoin 0.1% and microencapsulated BPO 3% cream. The use of Sol-Gel's microencapsulation technology platform provides a stable combination of BPO and ATRA, extending drug delivery time, and reducing potential irritation caused by direct application of the drugs to the skin.

METHODS

2x trials / 12 weeks / 63 sites across US

Design

- Two multicenter, randomized, double-blind, parallel-group vehicle-controlled trials (SGT-65-04 and SGT-65-05) carried out at 63 sites across the United States (**Figure 1**).

Figure 1. Study design

E-ATRA, microencapsulated tretinoin; E-BPO, microencapsulated benzoyl peroxide; IGA, Investigator's Global Assessment; QD, once daily.

Endpoints

Co-Primary Efficacy Endpoints

- Proportion of patients who achieved a two-grade reduction from baseline and grade 0 (Clear) or grade 1 (Almost Clear) at Week 12 on a 5-point IGA scale.
- Absolute change in inflammatory lesion counts from baseline at Week 12.
- Absolute change in non-inflammatory lesion counts from baseline at Week 12.

Safety Endpoints

- Safety was assessed through cutaneous safety assessment, local tolerability assessment, adverse event (AE) reporting, physical examination, and vital signs.

Data Analysis

- All efficacy analyses were carried out using the intent-to-treat population. Safety analyses were carried out using the safety population.

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Table 1. Baseline patient characteristics

	Study 65-04		Study 65-05	
Number of sites	32		31	
	E-BPO/E-ATRA (n=281)	Vehicle (n=143)	**E-BPO/E-ATRA (n=290)**	Vehicle (n=144)
Age, years				
Mean (SD)	20.9 (8.48)	21.4 (8.62)	20.1 (6.96)	20.3 (6.67)
Median (range	18.0 (11-67)	18.0 (10-57)	18.0 (10-51)	18.5 (9-42)
Sex, n (%)				
Male	106 (37.7%)	60 (42.0%)	117 (40.3%)	67 (46.5%)
Female	175 (62.3%)	83 (58.0%)	173 (59.7%)	77 (53.5%)
Ethnicity, n (%)				
Hispanic/Latino	102 (36.3%)	44 (30.8%)	85 (29.3%)	56 (38.9%)
Not Hispanic or Latino	178 (63.3%)	98 (68.5%)	204 (70.3%)	87 (60.4%)
Unknown/Not Reported	1 (0.4%)	1 (0.7%)	1 (0.3%)	1 (0.7%)
IGA severity				
Moderate	251 (89.3%)	132 (92.3%)	262 (90.3%)	133 (93.0%)
Severe	30 (10.7%)	11 (7.7%)	28 (9.7%)	10 (7.0%)
Inflammatory lesion count				
Mean (SD)	33.5 (14.62)	33.5 (14.69)	28.2 (8.70)	27.5 (8.52)
Median (range)	28.0 (20-97)	78 0 (20-90)	25.0 (20-62)	75 (20-75)
Non-inflammatory lesion count				
Mean (SD)	48.6 (20.24)	47.1 (19.97)	44.6 (18.03)	44.9 (18.82)
Median (range)	42.0 (30-148)	41.0 (30-140)	39.0 (23-149)	38.0 (30-123)

Table 2. Skin tolerability for E-BPO/E-ATRA and vehicle

	E-BPO/E-ATRA (n=274) %				Vehicle (n=139) %			
Study 65-04	None	Mild	Moderate	Severe	None	Mild	Moderate	Severe
Erythema	62.0%	33.2%	4.4%	0.4%	65.9%	25.8%	8.3%	0
Scaling	78.8%	19.6%	1.6%	0	83.3%	15.9%	0.8%	0
Pigmentation	61.6%	32.8%	4.8%	0.8%	67.4%	27.3%	5.3%	0
Dryness	71.2%	22.0%	6.0%	0.8%	78.0%	18.9%	3.0%	0
Itching	86.0%	12.8%	1.2%	0	89.4%	7.6%	3.0%	0
Burning	92.4%	6.0%	1.6%	0	95.5%	3.8%	0.8%	0
Stinging	92.4%	7.2%	0.4%	0	94.7%	3.8%	1.5%	0
Study 65-05								
Erythema	57.8%	32.8%	9.4%	0	64.4%	28.0%	7.6%	0
Scaling	83.2%	13.1%	3.7%	0	89.4%	9.8%	0.8%	0
Pigmentation	70.5%	21.7%	7.8%	0	70.5%	25.8%	3.8%	0
Dryness	73.0%	22.5%	4.5%	0	84.1%	14.4%	1.5%	0
Itching	88.1%	9.4%	2.5%	0	87.9%	9.8%	2.3%	0
Burning	91.4%	5.7%	2.9%	0	96.2%	30%	0.8%	0
Stinging	96.7%	3.3%	0.0%	0	99.2%	0.0%	0.8%	0

Figure 2. Success in IGA at week 12

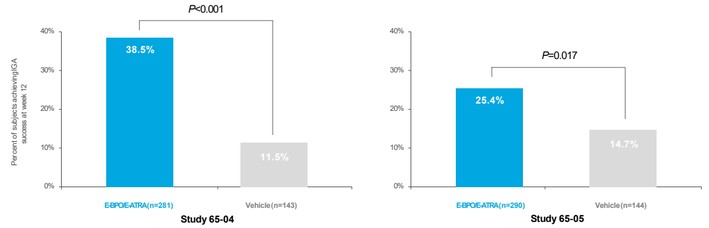


Figure 3. Improvement in IGA and reduction in lesion count with E-BPO/E-ATRA

Although this patient did not achieve success as defined by the trial protocol, this represents a real-world clinical success and the authors note the improvement is unusual for topical monotherapy

Figure 4. Reduction in inflammatory lesion count at week 12

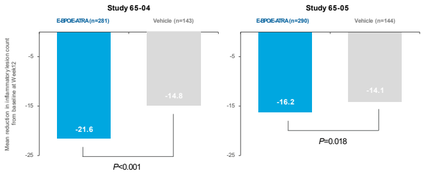
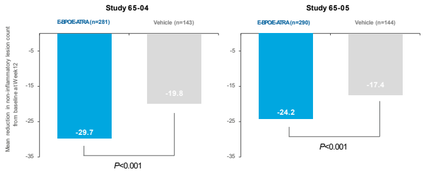


Figure 5. Reduction in non-inflammatory lesion count at week 12



RESULTS

Patients

- In Study 65-04, 281 patients were randomized to E-BPO/E-ATRA and 143 to Vehicle; 249 (88.6%) and 131 (91.6%) completed the trial. In Study 65-05, 290 patients were randomized to E-BPO/E-ATRA and 144 to Vehicle; 242 (83.4%) and 131 (91.6%) completed the trial. Baseline patient characteristics were balanced across groups in both trials (**Table 1**)

Efficacy

IGA

- In each of the two trials, E-BPO/E-ATRA was significantly superior to Vehicle for the percentage of patients achieving IGA success (**Figures 2 and 3**).

Lesions

- Results from both trials indicated that E-BPO/E-ATRA was significantly superior to Vehicle for decreasing the number of inflammatory lesions (**Figure 4**) and non-inflammatory lesions (**Figure 5**) from baseline at week 12.

Safety

- Nearly all AEs were mild or moderate in severity.
- A total of 18 subjects discontinued from Studies 65-04 and 65-05 due to a treatment-emergent AE: 18 (2%) in E-BPO/E-ATRA and 0 in Vehicle.
- No treatment-related serious AEs (SAEs) were identified in either study.
- 2 subjects reported SAEs in Study 65-05; (1) E-BPO/E-ATRA subject reported depression.
- Prospective evaluations indicated very good skin tolerability for E-BPO/E-ATRA (**Table 2**).

CONCLUSIONS

E-BPO/E-ATRA successfully met all primary efficacy endpoints demonstrating statistically significant improvements over Vehicle. There were no treatment-related SAEs. E-BPO/E-ATRA was well tolerated, with results similar to Vehicle at 12 weeks.