ADAPALENE-BENZOYL PEROXIDE, A UNIQUE FIXED-DOSE COMBINATION GEL FOR ACNE TREATMENT : A RANDOMIZED, DOUBLE-BLIND, CONTROLLED TRIAL IN 1668 PATIENTS

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INTRODUCTION

International guidelines recommend combination therapy with a topical retinoid and antimicrobials for the treatment of mild to moderate inflammatory acne, thus targeting three of the four major pathophysiologic features of acne[1]. However, in the context of increasing bacterial resistance attributable to the widespread use of antibiotics, reduction in their usage has been recommended[2].

A new antibiotic-free fixed-dose combination of adapalene 0.1% and benzoyl peroxide 2.5% (adapalene-BPO combination) has been recently marketed in several countries. Adapalene possesses anticomedogenic, comedolytic, and anti-inflammatory properties whereas BPO is more effective than topical antibiotics against *P. acnes* with no evidence of bacterial resistance to its effects.

Several recently published clinical studies have demonstrated the efficacy and tolerability of this combination and its early onset of action[3-6].

METHODS

- Randomized, multicenter, double-blind, parallel group, controlled study
- 60 participating centers in the United States, Puerto Rico and Canada

Patient selection

- Facial acne vulgaris rated 3 (moderate) on the Investigator's Global Assessment (IGA) of acne severity scale (ranging from 0: Clear to 4: Severe), 20 to 50 inflammatory lesions (IL), 30 to 100 non-inflammatory lesions (NIL), no cysts and no more than 1 nodule

Treatment

- Randomisation in a 1:1:1:1 ratio to adapalene-BPO combination gel, adapalene gel, BPO gel, or gel vehicle (adapalene gel and BPO gel, used as monotherapies in this study, were formulated in the same vehicle as the combination)
- Application of study treatments to the face (and trunk, if applicable), once daily in the evening, for 12 weeks
- In case of dry skin, use of a moisturizer, daily throughout the study

Outcomes

- Success Rate : percentage of patients rated "clear" or "almost clear" on the IGA scale
- Percent change in IL, NIL and total lesion counts
- Change in IGA
- Patient's assessment of acne improvement
- Signs and symptoms (erythema, scaling dryness, stinging/ burning) of facial tolerability rated on a scale ranging from 0 (none) to 3 (severe)
- Adverse events
- Patient's appreciation questionnaire

RESULTS

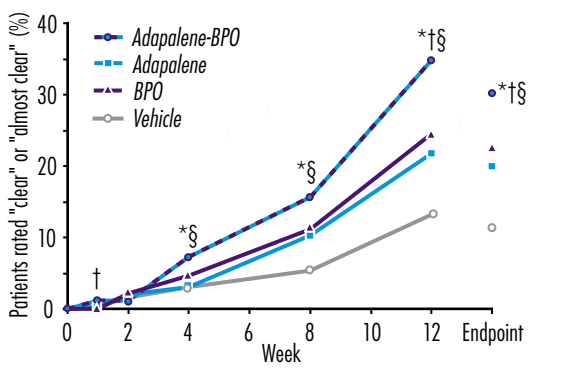
PATIENT DISPOSITION AND BASELINE DEMOGRAPHICS

	Adapalene-BPO	Adapalene	BPO	Vehicle	Total
Enrolled	415	420	415	418	1668
Completed, n (%)	347 (93.3)	363 (88.5)	372 (93.3)	347 (88.7)	1429 (85.7)
Discontinued,n (%)	68 (16.4)	57 (13.6)	43 (10.4)	71 (17.0)	22 (1.3)
- Due to AE, n (%)	11 (2.7)	4 (1.0)	5 (1.2)	2 (0.5)	239 (14.3)
Gender, n (%)					
- Male	205 (49.4)	203 (48.3)	208 (50.1)	196 (46.9)	812 (48.7)
- Female	210 (50.6)	217 (51.7)	207 (49.9)	222 (53.1)	856 (51.3)
Age (Year)					
- Mean	18.7	17.9	18.4	18.0	18.2
- Min, Max	12 - 58	12 - 41	12 - 56	12 - 50	12 - 58
Race, n (%)					
- Caucasian	273 (65.8)	281 (66.9)	258 (62.2)	270 (64.6)	1082 (64.9)
- Black	66 (15.9)	64 (15.2)	81 (19.5)	66 (15.8)	277 (16.6)
- Asian	4 (1.0)	4 (1.0)	4 (1.0)	5 (1.2)	17 (1.0)
- Hispanic	67 (16.1)	66 (15.7)	65 (15.7)	72 (17.2)	270 (16.2)
- Other	5 (1.2)	5 (1.2)	7 (1.7)	5 (1.2)	22 (1.3)
Baseline lesion counts (median)					
- IL	27	27	27	27	27
- NIL	44	47	46	46	46
- Total	76	79	76	76	76
IGA at baseline, n (%)					
3 = Moderate	415 (100)	420 (100)	414 (99.8)	414 (99.5)	1663 (99.8)
4 = Severe	0	0	1 (0.2)	2 (0.5)	3 (0.2)

IGA : Investigator's Global Assessment
IL : Inflammatory lesions
NIL : Non-inflammatory lesions

- Patient disposition, demographics and baseline acne characteristics were similar between the treatment groups.
- The rates for discontinuation due to adverse events were low for all of the study groups.

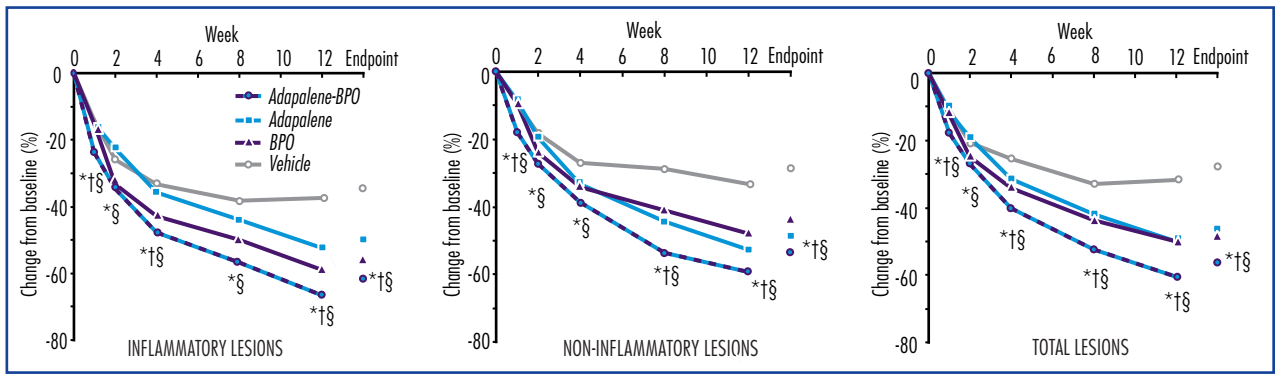
SUCCESS RATES OVER TIME (ITT POPULATION)



**Statistical significant difference between adapalene-BPO combination and adapalene monotherapy (at least P<.05)*
†Statistical significant difference between adapalene-BPO combination and BPO monotherapy (at least P<.05)
§Statistical significant difference between adapalene-BPO combination and vehicle (at least P<.05)

- At endpoint, the Success Rate reached 30.1% with adapalene-BPO combination, compared to 19.8%, 22.2%, and 11.3% with adapalene monotherapy, BPO monotherapy, and vehicle, respectively.
- At endpoint comparisons of adapalene-BPO combination to the monotherapies and vehicle were significant.
- A significant early treatment effect of adapalene-BPO combination compared to vehicle (P=.004) and to adapalene monotherapy (P=.008) was observed starting at week 4 and sustained until the end of the study.

AT WEEK 12, ADAPALENE-BPO COMBINATION WAS SIGNIFICANTLY MORE EFFECTIVE THAN EACH INDIVIDUAL COMPONENT AND THE VEHICLE IN LESION COUNT PERCENT CHANGE (ITT POPULATION)



** Statistical significant difference between adapalene-BPO combination and adapalene monotherapy (at least P<.05) - † Statistical significant difference between adapalene-BPO combination and BPO monotherapy (at least P<.05) - § Statistical significant difference between adapalene-BPO combination and vehicle (at least P<.0*

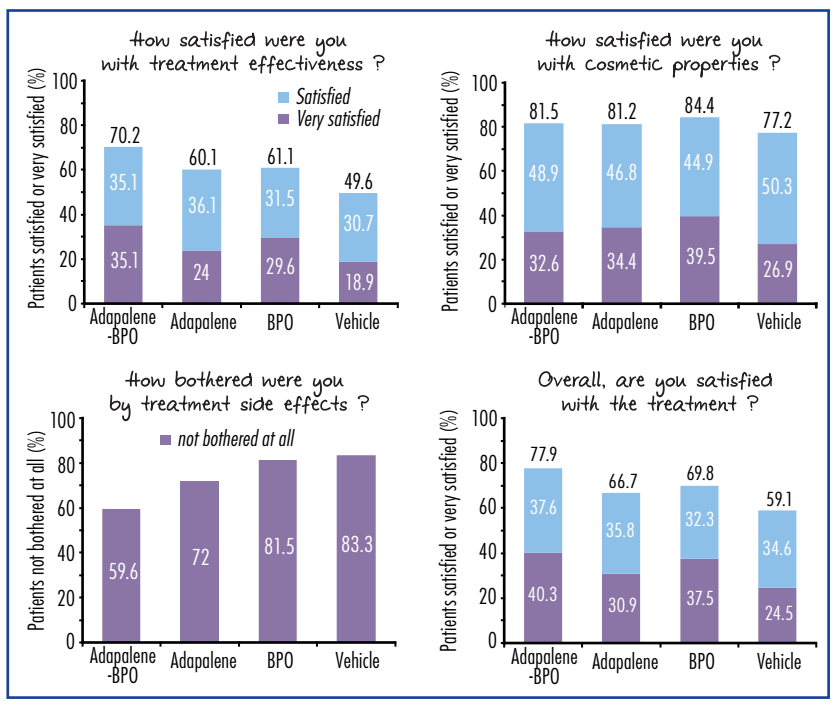
Change in IGA and Patient's assessment of acne improvement at Week 12

- The percentage of patients who showed improvement in IGA was greater in the adapalene-BPO combination group compared to the adapalene and BPO monotherapies and the vehicle: 67.8%, 61.1%, 59.1%, and 45.7%, respectively.
- Per the patient's assessment, moderate, marked, or complete improvement was reported for 73.5%, 65.6%, 66.7%, and 55.0% of the adapalene-BPO combination, adapalene and BPO monotherapies, and the vehicle treated patients, respectively.

Safety

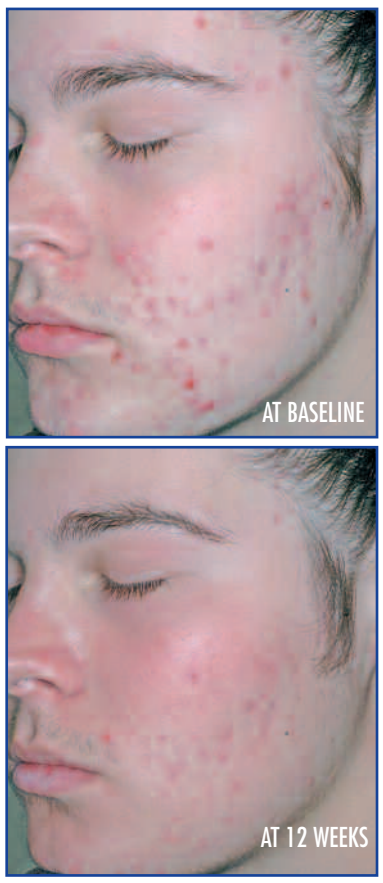
- Slightly more patients treated with the adapalene-BPO combination experienced local tolerability signs and symptoms compared to the other arms. However, those were transient, occurred at the beginning of treatment and were mostly mild or moderate in severity.
- Mean worst scores for all tolerability signs and symptoms were all below grade 1 (mild).
- The safety of adapalene-BPO combination was found to be comparable to that of the monotherapies or the vehicle.

PATIENT APPRECIATION QUESTIONNAIRE



- A lower percentage of patients in the adapalene-BPO combination group stated they were not bothered at all by treatment side effects as compared to the other treatment groups.
- However, appreciation of treatment effectiveness and overall satisfaction with treatment favored adapalene-BPO combination.
- Cosmetic properties were equally appreciated among all treatment groups.

EFFECT OF ADAPALENE-BPO FIXED-DOSE COMBINATION GEL



CONCLUSION

Adapalene-BPO fixed-dose combination gel :

- is superior to the adapalene and BPO monotherapies and the corresponding vehicle,
- provides an early onset of efficacy starting from Week 1,
- has a good tolerability and safety profile.

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