Sub-group Analyses from a Trial of a Fixed Combination of Clindamycin Phosphate 1.2% and Benzoyl Peroxide 3.75% Gel for the Treatment of Moderate-to-severe Acne Vulgaris

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ABSTRACT

Background: Acne vulgaris is commonplace and can be difficult to manage. Providing an effective and well-tolerated treatment may lead to improved adherence, increased patient satisfaction, and improved clinical outcomes. **Methods:** A review of efficacy, safety, and cutaneous tolerability of clindamycin phosphate 1.2%-benzoyl peroxide 3.75% gel in 498 patients with moderate-to-severe acne vulgaris enrolled in a multicenter Phase III study randomized to receive active or vehicle once daily for 12 weeks, including the most recent *post-hoc* analyses. **Results:** Significantly superior reductions in lesion counts were observed with clindamycin phosphate 1.2%-benzoyl peroxide 3.75% gel from Week 4, with median percent reductions in inflammatory and noninflammatory lesions from baseline of 68.4 and 57.9 percent, respectively (both $p<0.001$ versus vehicle). More than half (55.1%) of the severe acne vulgaris patients treated with clindamycin phosphate 1.2%-benzoyl peroxide 3.75% gel achieved ≥2-grade improvement from baseline in their Evaluator's Global Severity Score, and almost a third of the adolescent acne vulgaris patients (32.4%) achieved at least a marked improvement in their acne vulgaris as early as Week 2. In adult female acne overall treatments success was achieved in 52.7 percent of patients treated with clindamycin phosphate 1.2%-benzoyl peroxide 3.75% gel. Overall, and in the specific subpopulations, clindamycin phosphate 1.2%-benzoyl peroxide 3.75% gel was well-tolerated with a similar adverse event profile to vehicle. **Limitations:** *Post-hoc* analyses from a single clinical trial with demographic imbalances that could potentially confound the results. **Conclusion:** Clindamycin phosphate 1.2%-benzoyl peroxide 3.75% gel appears to be effective in treating acne across various clinically relevant sub-groups.
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Acne vulgaris remains very common in dermatology practice. It affects almost 85 percent of people aged 12 to 24 years,[1] and published lifetime prevalence rates have ranged from 73.3 to almost 100 percent.[2,3] Although often considered a teenager's disease, a significant percentage of patients (especially women) continue to be affected by acne vulgaris well into adulthood.[2] In addition, we are increasingly seeing patients who were clear in their teenage years, but have developed acne vulgaris later in life.

Effective treatment of acne vulgaris is important to reduce both severity and potential recurrence of the disease. Topical therapies remain the most common and effective treatment option for mild-to-moderate acne vulgaris and also for maintenance therapy for all levels of acne vulgaris severity.[4] In addition, fixed combinations have been studied in moderately severe disease.[5,6]

Although it has been recognized that therapy is best tailored to individual patient circumstance, it is also

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TABLE 1. Treatment of moderate and severe acne vulgaris with clindamycin (clin)-BP 3.75% aqueous gel. Comparison with vehicle, intention-to-treat population

	MODERATE ACNE (N=412)			SEVERE ACNE (N=86)		
	Clin-BP 3.75% gel (N=212)	Vehicle (N=200)	*P*-value	Clin-BP 3.75% gel (N=41)	Vehicle (N=45)	*P*-value
Mean age (years)	18.1	19.0	0.148	18.6	20.8	0.038
Gender (male/female, %)	48.6%/51.4%	53.0%/47.0%	0.274	65.9%/34.1%	44.4%/55.6%	0.073
LESION REDUCTION AT WEEK 12						
Mean percent reduction in inflammatory lesions	61.9%	34.3%	<0.001	52.6%	18.0%	<0.001
Mean percent reduction in noninflammatory lesions	52.1%	28.3%	<0.001	50.5%	24.8%	0.001
TREATMENT SUCCESS AT WEEK 12						
Subjects with ≥2 grade reduction in EGSS	31.3%	16.7%	0.001	55.1%	18.3%	0.002
Subjects clear/almost clear (subject self-assessment)	35.7%	19.2%	<0.001	30.6%	8.3%	0.042

becoming clear through *post-hoc* analyses and practical experience that some products may be more effective in certain patient populations. Acne vulgaris both in adolescents and adult women can be a challenge to treat successfully. In addition, we need effective topical treatments for moderately severe disease.

Here, the authors review the clinical data on a new fixed combination product for the treatment of moderate-to-severe acne vulgaris, clindamycin phosphate 1.2%-benzoyl peroxide 3.75% (clindamycin-BP 3.75%) gel. They also look specifically at data in important subpopulations.

EFFICACY AND TOLERABILITY OF CLINDAMYCIN-BP 3.75% AQUEOUS GEL

The efficacy and safety of once-daily clindamycin-BP 3.75% gel has been evaluated in a Phase III vehicle-controlled study of 498 patients with moderate-to-severe acne vulgaris and reported elsewhere.[5,6] Briefly, after 12 weeks daily treatment, inflammatory and noninflammatory lesion counts were reduced by a median of 68.4 and 57.9 percent, respectively, with clindamycin-BP 3.75% gel, compared to 35.5 and 32.5 percent with vehicle gel (both $p<0.001$).[5]

Treatment success (defined as at least a 2-grade improvement in Evaluator's Global Severity Score [EGSS] at Week 12) was achieved in more than one-third of patients (34.3%) on clindamycin-BP 3.75% gel compared to 15.6 percent on vehicle gel ($p<0.001$).[5] In addition, in 25.9% of patients, acne vulgaris was considered "clear" or "almost clear" compared to 12.2 percent with vehicle.[5]

EFFICACY AND TOLERABILITY OF CLINDAMYCIN-BP 3.75% AQUEOUS GEL IN SPECIAL POPULATIONS

The efficacy of clindamycin-BP 3.75% gel in special populations has been assessed in *post-hoc* analyses of the pivotal clinical study.

Moderate or severe acne vulgaris populations. The relatively high number of patients with severe acne vulgaris (17.3%) in the pivotal study is probably unique in clinical practice, as this is not a group normally selected for dual therapy without a retinoid.[6,7] In addition, it is perhaps counterintuitive that patients with more severe disease would show clinically significant improvement to topical

TABLE 2. Treatment of adolescent acne vulgaris with clindamycin (clin)-BP 3.75% aqueous gel. Comparison with vehicle, intention-to-treat population population

	ADOLESCENT ACNE (≤12 TO <18 YEARS) (N=289)		
	Clin-BP 3.75% gel (N=155)	Vehicle (N=134)	*P*-value
Mean age (years)	14.8	15.1	0.101
Gender (male/female, %)	61.3%/38.7%	59.0%/41.0%	0.592
Baseline severity (moderate/severe, %)	85.2%/14.8%	85.5%/14.2%	0.805
LESION REDUCTION AT WEEK 12			
Mean percent reduction in Inflammatory lesions	59.9%	22.6%	<0.001
Mean percent reduction in noninflammatory lesions	50.5%	21.3%	<0.001
TREATMENT SUCCESS AT WEEK 12			
Subjects with ≥2 grade reduction in EGSS	33.1%	8.5%	<0.001
Subjects clear/almost clear (subject self-assessment)	34.7%	12.8%	<0.001

therapy, but a comparison study of topical retinoids showed that moderately inflamed subjects had a greater percentage improvement than those with milder disease, although this could be simply because in mild disease there is less room for improvement than in moderate disease.[8]

More than half of the patients (55.1%) with severe acne vulgaris in the pivotal study met the criteria for treatment success (at least a 2-grade improvement in the EGSS) at Week 12 with clindamycin-BP 3.75% gel, suggesting that topical therapy may indeed be more valuable than often assumed in patients with severe acne vulgaris (see Table 1). However, it is important to note that among the severely afflicted subset of this trial, the treatment groups were imbalanced with respect to gender and age, with a greater proportion of female patients and younger patients being treated with clindamycin-BP 3.75% gel. The potential impact of these differences in demographics is unknown.

Adolescent acne vulgaris. Acne vulgaris is commonplace in adolescents and can be difficult to manage at a time when these patients are undergoing significant psychological, social, and physical change. It is the most common dermatological condition we see in adolescents, with teenagers comprising 36.5 percent of all acne vulgaris patients.[9,10] The impact of acne vulgaris on any one individual teenager is difficult to judge. Even mild acne vulgaris can cause significant emotional distress for some, diminishing their quality of life and social functioning.[11,12] Severe disease (seen in about 16% of cases[13]) can leave permanent scarring, especially if left untreated.[14–16]

In a *post-hoc* analysis of 289 adolescent subjects (12 to <18 years of age) with moderate-to-severe acne vulgaris, once-daily clindamycin-BP 3.75% gel was found to be superior to vehicle at Week 12 for all primary and supportive endpoints.[17] Overall treatment success (≥2 grade reduction in EGSS from baseline) with clindamycin-BP 3.75% gel was achieved in 33.1 percent of patients compared to 8.5 percent with vehicle (p<0.001, Table 2).[17] The difference between the two treatment arms was significant from Week 4. Almost a third of patients (32.4%) reported at least "marked improvements" in their acne vulgaris with clindamycin-BP 3.75% as early as two weeks after treatment initiation.[17]

Acne vulgaris in adult females. Although acne vulgaris tends to resolve in the majority of patients by the third decade of life, up to 20 percent of adolescents can have acne vulgaris that persists into adulthood, with a majority of these patients being female. It has been suggested that the prevalence of acne vulgaris in adulthood is due to undertreated acne vulgaris in adolescence or late-onset disease. Thought of traditionally as an inflammatory condition affecting the lower face and jawline, postadolescent acne vulgaris in females has been shown to have a similar facial distribution to teenage acne vulgaris and characterized not only by inflammatory lesions, but also comedones.[18,19] Disease burden can be significant, with three

TABLE 3. Treatment of adult female acne vulgaris with clindamycin (clin)-BP 3.75% aqueous gel. Comparison with vehicle, intention-to-treat population

	ADULT FEMALE ACNE (≥25 YEARS) (N=72)		
	Clin-BP 3.75% gel (N=29)	Vehicle (N=43)	*P*-value
Mean age (years)	14.8	15.1	0.101
Baseline severity (moderate/severe, %)	79.3%/20.7%	74.4%/25.6%	NS
LESION REDUCTION AT WEEK 12			
Mean percent reduction in inflammatory lesions	68.7%	39.7%	0.019
Mean percent reduction in noninflammatory lesions	60.4%	34.0%	0.020
TREATMENT SUCCESS AT WEEK 12			
Subjects with ≥2 grade reduction in EGSS	52.7%	30.4%	0.074
Subjects clear/almost clear (subject self-assessment)	44.0%	13.5%	0.026

quarters of women in a recent survey indicating their acne vulgaris was "moderately-to-very severely" troublesome.[19]

In a *post-hoc* analysis of 79 adult women (aged ≥25 years) with moderate-to-severe acne vulgaris, once-daily clindamycin-BP 3.75% gel was found to be superior to vehicle at Week 12 for all primary and supportive endpoints.[20] Overall treatment success (≥2-grade reduction in EGSS from baseline) with clindamycin-BP 3.75% gel was achieved in 52.7 percent of adult female patients, compared to 30.4 percent with vehicle. Although numerically greater, it was not statistically different from vehicle, perhaps due to the small number of patients (p=0.074, Table 3).[20] Almost 20 percent of adult female patients reported at least "marked improvements" in their acne vulgaris with clindamycin–BP 3.75% gel as early as Week 2, and more than 70 percent at Week 12.[20]

Clindamycin-BP 3.75% gel was well-tolerated with a similar AE profile to vehicle, with only one AE in each group (burning sensation, contact dermatitis) related to study medication. Local signs and symptoms of erythema, scaling, itching, burning, or stinging were rare and generally were mild when present.[20] There were no study discontinuations because of AEs.

DISCUSSION

Acne vulgaris is a very common skin disease that usually presents in adolescence, but frequently continues into adulthood. Late-onset acne vulgaris is also becoming more prevalent, especially in adult women; although there are few data to explain why it begins or persists into adulthood or why adult women are affected by acne vulgaris significantly more than men.

It remains a challenge to treat successfully, both in teenagers and postadolescent patients. Unrealistic expectations of acne vulgaris therapy or poor tolerability can lead to low adherence and poor clinical outcomes.[21–23] Patient education is an important component of successful treatment, especially in adolescents.[24] It has been reported that as many as 16 percent of adolescents with acne vulgaris consider their condition to be severe.[13] They tend to prefer topical drugs[13]; however, data of their use in severe acne vulgaris are limited.

In women who often cosmetically camouflage acne vulgaris with makeup, medication tolerability and the lack of skin irritation are paramount. However, little is known about a medication's cosmetic compatibility. New data have recently been reported showing clindamycin-BP 3.75% gel to have excellent cosmetic compatibility with facial foundation.[24]

Providing an effective and well-tolerated acne vulgaris treatment may lead to improved adherence, increased patient satisfaction, and improved clinical outcomes. Clindamycin-BP 3.75% gel is an effective, safe, well-tolerated treatment for moderate-to-severe acne vulgaris.

Post-hoc analyses suggest that clindamycin-BP 3.75% gel may be particularly helpful in treating acne vulgaris in adolescents, adult female patients, and those with moderately severe disease. However, these analyses have limitations. They present data from subgroups within a single clinical trial, and experience in clinical practice may be quite different. Also, an imbalance in some of the resultant demographics may confound the results.

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