Randomized, Observer-blind, Split-face Compatibility Study with Clindamycin Phosphate 1.2%/Benzoyl Peroxide 3.75% gel and Facial Foundation Makeup

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ABSTRACT

Background: Cosmetic compatibility in the treatment of acne is an important issue significantly impacting quality of life, but often overlooked, as dermatologists commonly recommended avoidance of cosmetic foundations when treating adult female patients. Fixed combinations of clindamycin/benzoyl peroxide are widely used in the treatment of acne, but little is known about the impact of their concomitant use with facial foundation. **Objective:** To assess the compatibility of clindamycin phosphate 1.2%/benzoyl peroxide 3.75% gel with foundation makeup for up to six hours after application. **Methods:** Twenty-nine female subjects applied makeup to their face after randomly applying clindamycin phosphate 1.2%/benzoyl peroxide 3.75% gel to one side of the face. Investigator and subject self-assessment included facial skin attributes, facial tolerability, and cosmetic compatibility post-application and at Hour 6; as well as cutaneous tolerability. **Results:** No statistical difference was noted between the treated and untreated side of the face in terms of coverage, blotchiness, appearance, skin tone, or visual smoothness. Tolerability was excellent, with no erythema, edema, dryness, and peeling post-makeup application. For both the treated and untreated side, there was a slight lack of improvement in cosmetic appearance six hours post-makeup application. **Conclusion:** Clindamycin/benzoyl peroxide 3.75% gel was shown to have excellent cosmetic compatibility with facial foundation.
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Dermatology is a unique specialty in that the majority of therapeutic approaches are topical. Topical medications present advantages in that they avoid many of the systemic side effects encountered with oral products, but they introduce other challenges. Irritation, in the form of peeling, xerosis, and erythema, is frequently encountered, affecting patient adherence and treatment outcomes.[1,2]

Monotherapies for mild-to-moderate acne remain the most common and topical effective treatment option, and also as maintenance therapy for all levels of acne severity.[3] In addition, fixed combinations have been shown to be effective, even in moderate-to-severe disease.

Fixed combination therapy (e.g., benzoyl peroxide [BP] and antibiotic, retinoid and antibiotic or BP) is now considered standard of care for patients with both comedonal and inflammatory acne, simplifying treatment regimen and reducing dosing frequency.[4–7] However, little is known about their cosmetic compatibility; the ability of topical acne medication to perform optimally in the presence of skin care products, such as moisturizers, toners, sunscreens, and facial foundations.

Clindamycin phosphate 1.2%/BP 3.75% gel is a new fixed combination treatment for moderate-to-severe acne vulgaris. Results from the pivotal phase 3 trial showed it to be effective, generally safe, and well-tolerated.[7]

This study assesses the cosmetic compatibility of clindamycin phosphate 1.2%/BP 3.75% gel with foundation makeup, utilizing a split-face technique.

DISCLOSURE: Dr. Bhatia is a consultant and/or speaker for Actavis, Allergan, Aqua, Bayer, Dusa, Exeltis, Ferndale, Galderma, Leo, Nerium, Novartis, PharmaDerm, Promius, and Valeant. Dr. Pillai is an employee of Valeant.

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TABLE 1A. Investigator assessment of local cutaneous tolerability (scale 0–3)

	ERYTHEMA	EDEMA	DRYNESS	PEELING
0=None	No erythema in treatment area	No edema/swelling in treatment area	No dryness in treatment area	No peeling in treatment area
1=Mild	Slight, but definite redness	Slight, but definite edema	Slight, but definite dryness	Slight, but definite peeling
2=Moderate	Definite redness	Definite edema	Definite dryness	Definite peeling
3=Severe	Marked redness	Marked edema	Marked dryness	Marked peeling

TABLE 1B. Subject assessment of local cutaneous tolerability (scale (0–3)

	BURNING	STINGING	ITCHING
0=None	No burning in treatment area	No stinging in treatment area	No itching in treatment area
1=Mild	Slight burning sensation, not really bothersome	Slight stinging sensation, not really bothersome	Slight itching sensation, not really bothersome
2=Moderate	Definite warm, burning sensation somewhat bothersome	Definite stinging somewhat bothersome	Definite itching somewhat bothersome
3=Severe	Hot burning sensation causing definite discomfort and may interrupt daily activities and/or sleep	Marked stinging sensation causing definite discomfort and may interrupt daily activities and/or sleep	Marked itching sensation causing definite discomfort and may interrupt daily activities and/or sleep

METHODS

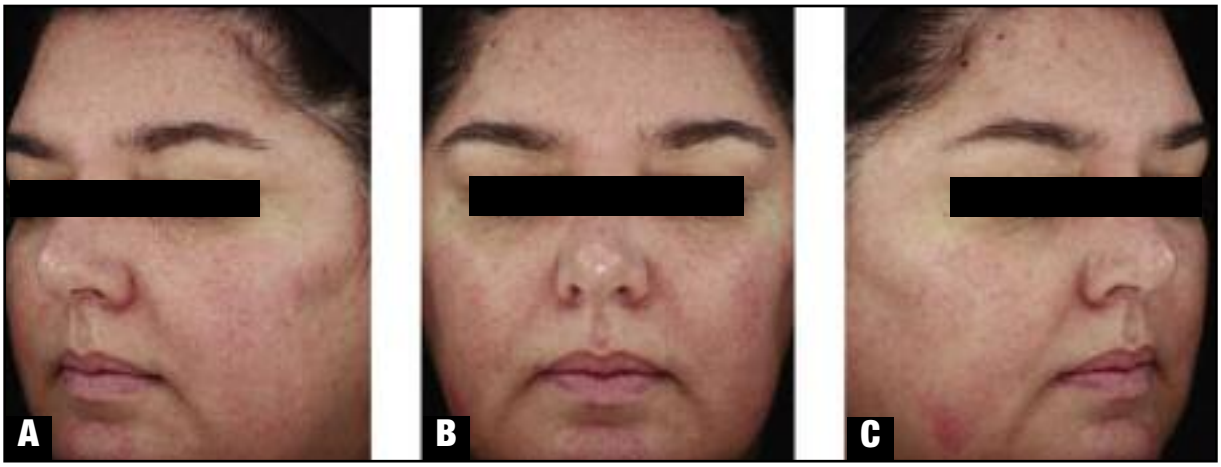
Female patients who were frequent users of foundation and facial makeup were enrolled in a single-center, evaluator-blinded, randomized, controlled, cosmetic compatibility study following completion of an Institutional Review Board (IRB)-approved informed consent and photographic release documents (IntegReview, Austin, Texas). Exclusion criteria included patients with known allergies to facial skin products, users of tanning beds/sun lamps, and individuals having a health condition and/or pre-existing or dormant dermatologic disease (such as psoriasis, rosacea, acne, eczema), or a previous history or other condition that the investigator deemed inappropriate for participation or could interfere with the study outcome.

Prior to the initial clinic visit, patients were instructed to remove existing makeup. Their face was washed with mild soap in clinic, rinsed, and dried before any subsequent application. Clindamycin phosphate 1.2%/BP 3.75% gel (Onexton® Gel, Valeant Pharmaceuticals, Bridgewater, New Jersey) was applied randomly to one side of the face in accordance with the manufacturer's instructions. Usually worn foundation makeup was then applied as normal to the untreated side of the face prior to applying to that side of the face pre-treated with clindamycin phosphate 1.2%/BP 3.75% gel to avoid any cross-contamination.

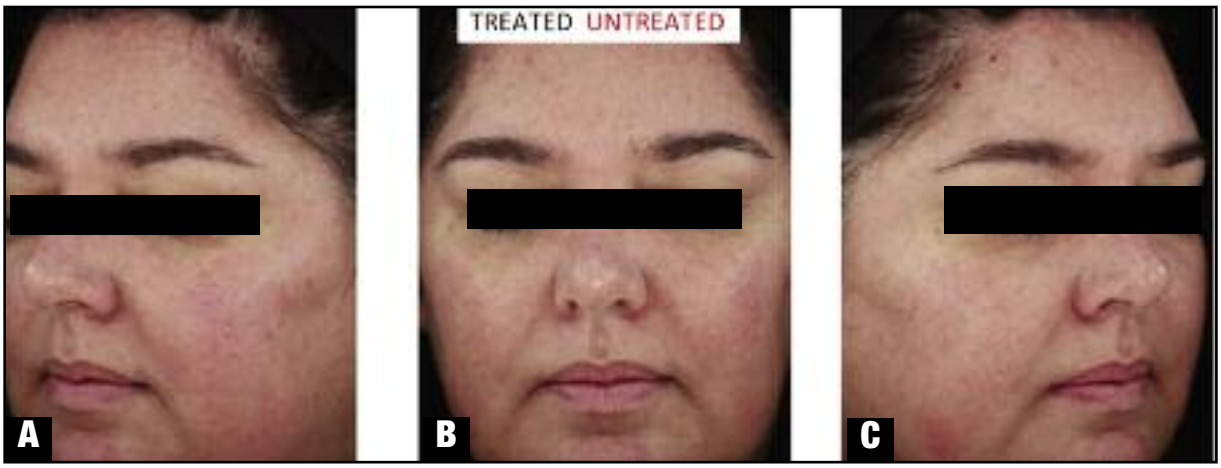
Patients were evaluated at baseline, post-application of clindamycin phosphate 1.2%/BP 3.75% gel, post-makeup application, and six hours later (Hour 6).

Investigator assessment. Investigator assessments included clinical grading of the foundation on the right and left side of the patient's face using a modified Griffiths 10-point scale to evaluate overall coverage, blotchiness, appearance of foundation, evenness of skin tone, and visual smoothness; where 0=none (best possible condition), 1–3=mild, 4–6=moderate, and 7–9=severe (worst possible condition).[8]

Local cutaneous tolerability was also assessed separately on both sides of the face at each evaluation point. The investigator assessed signs and symptoms of erythema, edema, dryness, and peeling on a 4-point scale (where 0=none and 3=severe), and patients reported the degree of burning, itching, or stinging (Tables 1A and 1B).



Figures 1A–1C. Photographs from a representative patient example under standard light conditions at baseline



Figures 2A–2C. Photographs from a representative patient example under standard light conditions post-product application. Figure 2B shows which side of the face was treated.

Digital images were taken of each patient using the VISIA CR photo-station (Canfield Imaging Systems, Fairfield, New Jersey) with a Canon Mark II 5D digital SLR camera (Canon Incorporated, Tokyo, Japan) at baseline, immediately post-product application, immediately post-makeup application, and at Hour 6. For each patient, three full-face images were taken (right side, left side, and center view) using standard (bright/visible) and cross-polarized lighting. Adverse events (AEs) were recorded throughout the study.

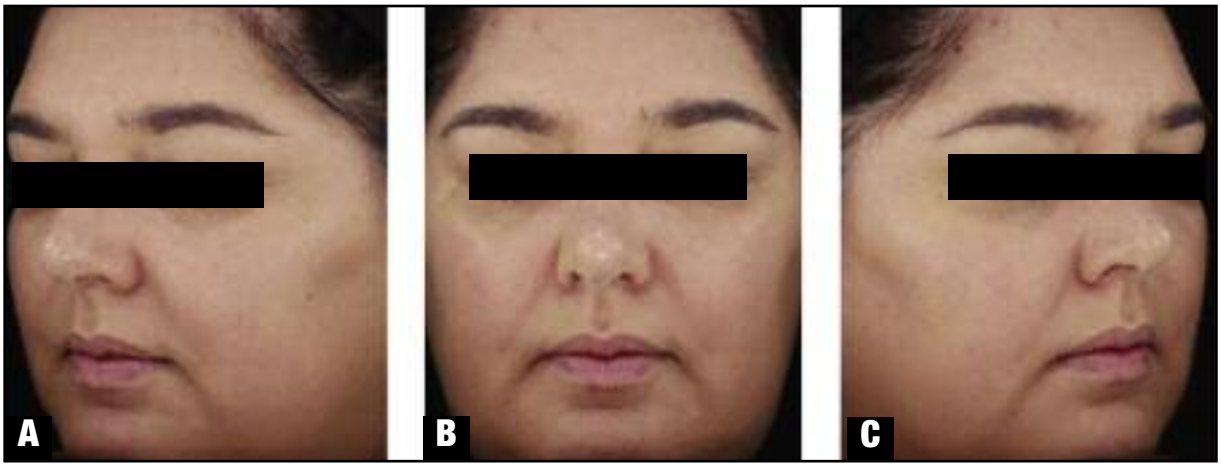
Subject assessment. Patient evaluations included facial skin attributes, including skin smoothness and tone; and cosmetic compatibility assessment including evenness/fullness of application, and its overall natural-looking appearance on a 4-point scale, where 1=strongly disagree and 4=strongly agree, immediately post makeup application and at Hour 6. Patients also reported the degree of burning, itching, or stinging on a 4-point scale (Table 1B).

Statistical analysis. A paired *t*-test was used to compare the individual scores at Hour 6 relative to their respective immediately post-makeup application time point for treated and untreated separately. No statistical testing was performed on the Subject's Self-Assessment.

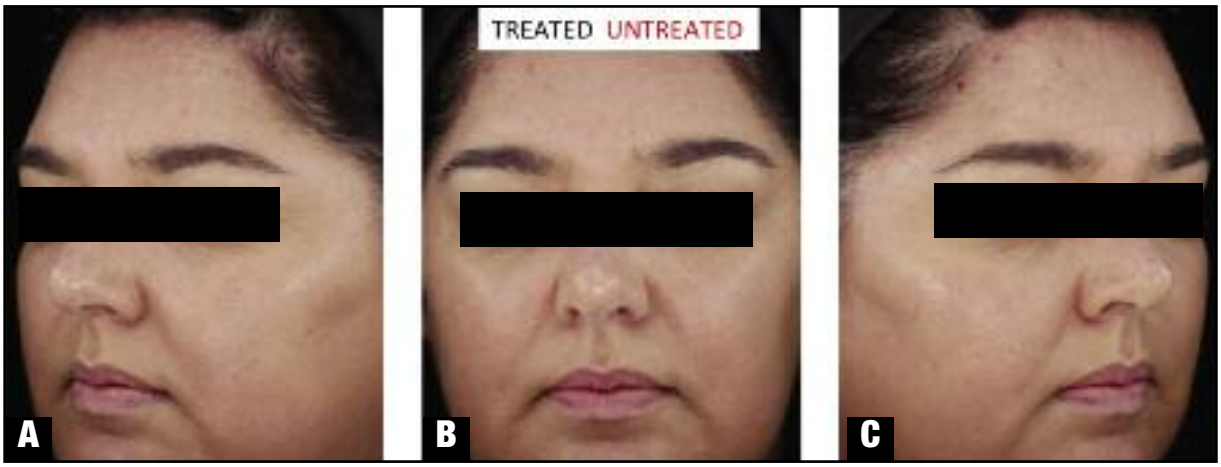
RESULTS

Twenty-nine female patients (25–45 years of age, mean 34.8 years) were enrolled in the study. In all, 28 patients completed the study without any adherence issues or AEs. One subject requested withdrawal from the study after post-application grading and is included in the Intent-to-Treat (ITT) population.

Investigator assessment. A typical baseline presentation is shown in Figure 1, using standard lighting conditions, and in Figure 2 following application of clindamycin phosphate 1.2%/BP 3.75% gel to the left side of the face (patient's right). Clindamycin phosphate 1.2%/BP 3.75% gel demonstrated excellent cosmetic compatibility. No statistical difference was noted between the treated and untreated side of the face in terms of coverage, blotchiness,



Figures 3A–3C. Photographs from a representative patient example showing makeup compatibility under standard light conditions post-makeup application



Figures 4A–4C. Photographs from a representative patient example showing makeup compatibility in standard light conditions at Hour 6. Figure 4B shows which side of the face was treated.

appearance, skin tone, or visual smoothness. Post-makeup application all mean scores were <1 (range 0.21–0.86, Table 2. See Figure 3 for a typical patient presentation post-makeup application). Six hours after makeup application, all scores increased, with the exception of visual smoothness, but still remained in the "mild" range (0.21–2.46). The change was significant in terms of percent coverage (P<0.001), overall coverage, and appearance of foundation (P<0.001) and skin tone (P<0.015), but not in terms of blotchiness or visual smoothness (Table 2. See Figure 4 for a typical patient presentation six hours post-makeup application). A comparison of baseline and Hour 6 effect is shown in Figure 5.

Tolerability was excellent, with an absence of erythema, edema, and peeling post-makeup application or at Hour 6. There was one report of mild dryness at Hour 6 on the treated face and one report of mild erythema post-makeup application on the untreated face (Table 3).

Subject self-assessment. Overall cosmetic compatibility was excellent with clindamycin phosphate 1.2%/BP 3.75% gel. Mean scores ranged from 3.46 to 3.57 post-makeup application (where 3=agree somewhat and 4=strongly agree), with no significant changes by Hour 6 (Table 4). There was no significant difference between treated and untreated areas of the face, although there was a significant worsening at Hour 6 in the untreated face in terms of natural-looking appearance and full evenness of coverage (P=0.031, Table 4).

There were no reports of burning at any assessment point. There were two reports of mild stinging post-application and three reports of mild itching at Hour 6 on the treated side of the face (Table 5).

DISCUSSION

Cosmetic compatibility is an important concept in dermatology and has a significant influence on quality of life in acne sufferers who wish to combine topical prescription medications with facial colored cosmetics.[9] Although

TABLE 2. Investigator assessment of cosmetic compatibility using Modified Griffiths Skin Grading Scale, post-makeup application and at Hour 6 (N=28)

PARAMETER	TIME POINT	TREATED		UNTREATED		TREATED/ UNTREATED
		MEAN (±SD)	*P*-VALUE	MEAN (±SD)	*P*-VALUE	*P*-VALUE
% Coverage	Post-makeup application	0.32 (0.72)	–	0.25 (0.52)	–	–
	Hour 6	2.46 (1.40)	<0.001	2.46 (1.40)	<0.001	0.537
Blotchiness	Post-makeup application	0.21 (0.83)	–	0.21 (0.83)		
	Hour 6	0.54 (1.14)	0.059	0.43 (1.10)	0.161	0.184
Overall coverage/ appearance of foundation	Post-makeup application	0.32 (0.72)	–	0.25 (0.52)	–	–
	Hour 6	2.46 (1.40)	<0.001	2.29 (1.38)	<0.001	0.621
Skin tone (color) evenness	Post-makeup application	0.86 (1.35)	–	0.86 (1.35)	–	–
	Hour 6	1.25 (1.38)	0.009	1.21 (1.34)	0.015	0.326
Visual smoothness	Post-makeup application	0.21 (0.57)	–	0.21 (0.57)	–	–
	Hour 6	0.21 (0.57)	1.000	0.21 (0.57)	1.000	–

Figure 5. Post-makeup comparison (Hour 0 and Hour 6) under standard light conditions

dermatologists commonly discourage patients from using cosmetics when treating their acne in a belief that cosmetics and makeup may aggravate acne eruptions, it has been shown that the number and severity of acne eruptions can decrease even though patients were applying makeup, with a corresponding improvement in quality of life.[10] This finding highlights the importance of treating acne and the need to incorporate compatible cosmetic agents without the potential for causing irritation.[9] Adolescent female acne patients may consider using facial foundation to camouflage underlying healing acne lesions. Older female acne patients, with an increased incidence of hormonal acne, may also wish to use facial cosmetics. Instructions for using skin care and cosmetics should complement conventional acne

TABLE 3. Investigator assessment of cutaneous tolerability at baseline, post-application, post-makeup and Hour 6 (4-point scale). There were no reports of moderate or severe scores/grades

PARAMETER	TIME POINT	TREATED (N/%)			UNTREATED (N/%)		
		0=NONE	0.5	1=MILD	0=NONE	0.5	1=MILD
Erythema	Baseline	27 (93.1)	1 (3.4)	1 (3.4)	26 (89.7)	1 (3.4)	2 (6.9)
	Post-application	27 (93.1)	1 (3.4)	1 (3.4)	26 (89.7)	1 (3.4)	2 (6.9)
	Post-makeup application	28 (100.0)		–	27 (96.4)	–	1 (3.6)
	Hour 6	28 (100.0)		–	28 (100.0)	–	–
Edema	Baseline	29 (100.0)	–	–	29 (100.0)		–
	Post-application	29 (100.0)	–	–	28 (100.0)		–
	Post-makeup application	28 (100.0)	–	–	29 (100.0)		–
	Hour 6	28 (100.0)		–	28 (100.0)		–
Dryness	Baseline	29 (100.0)	–	–	28 (96.6)	1 (3.4)	–
	Post-application	29 (100.0)	–	–	28 (96.6)	1 (3.4)	–
	Post-makeup application	28 (100.0)	–	–	28 (100.0)	–	–
	Hour 6	27 (96.4)		1 (3.6)	28 (100.0)	–	–
Peeling	Baseline	29 (100.0)	–	–	29 (100.0)		–
	Post-application	29 (100.0)	–	–	28 (100.0)		–
	Post-makeup application	28 (100.0)	–	–	28 (100.0)		–
	Hour 6	28 (100.0)		–	28 (100.0)		–

TABLE 4. Subject self-assessment of makeup appearance post-makeup application and at Hour 6 (N=28)

PARAMETER	TIME POINT	TREATED		UNTREATED		TREATED/ UNTREATED
		MEAN (±SD)	*P*-VALUE	MEAN (±SD)	*P*-VALUE	*P*-VALUE
My makeup foundation has a natural looking appearance	Post-makeup application	3.54 (0.74)	–	3.57 (0.74)	–	–
	Hour 6	3.43 (0.79)	0.326	3.36 (0.78)	0.031	0.184
My makeup foundation appears to have an even full coverage	Post-makeup application	3.57 (0.69)	–	3.57 (0.69)	–	–
	Hour 6	3.46 (0.79)	0.326	3.36 (0.78)	0.031	0.184
My skin appears to be smooth with my makeup foundation applied	Post-makeup application	3.50 (0.69)	–	3.50 (0.69)	–	–
	Hour 6	3.50 (0.75)	1.000	3.39 (0.74)	0.083	0.083
With my makeup foundation my skin tone appears to be even	Post-makeup application	3.46 (0.74)	–	3.46 (0.74)	–	–
	Hour 6	3.43 (0.74)	0.713	3.32 (0.72)	0.103	0.184

TABLE 5. Investigator reports of cutaneous tolerability at baseline, post-application, post-makeup and Hour 6 (4-point scale) based on subject self-assessment. There were no reports of moderate or severe scores/grades

PARAMETER	TIME POINT	TREATED (N/%)			UNTREATED (N/%)		
		0=NONE	0.5	1=MILD	0=NONE	0.5	1=MILD
Burning	Baseline	29 (100.0)	–	–	29 (100.0)	–	–
	Post-application	29 (100.0)	–	–	29 (100.0)	–	–
	Post-makeup application	28 (100.0)	–	–	28 (100.0)	–	–
	Hour 6	28 (100.0)	–	–	28 (100.0)	–	–
Stinging	Baseline	29 (100.0)	–	–	29 (100.0)		–
	Post-application	27 (93.1)	–	2 (6.9)	29 (100.0)		–
	Post-makeup application	26 (92.9)	–	2 (7.1)	28 (100.0)		–
	Hour 6	28 (100.0)		–	28 (100.0)		–
Itching	Baseline	29 (100.0)	–	–	29 (100.0)	–	–
	Post-application	27 (93.1)	2 (6.9)	–	29 (100.0)	–	–
	Post-makeup application	27 (96.4)	1 (3.6)	–	28 (100.0)	–	–
	Hour 6	25 (89.3)	–	3 (10.7)	28 (100.0)	–	–

treatments.[11] As improvement in quality of life has been shown to be related to patient satisfaction and adherence, makeup applied at the onset of treatment may help increase patient satisfaction and yield improved clinical outcomes.[9] Facial foundation may also be helpful to cover up scarring from previous acne or dyschromia secondary to acne that may not have been treated thoroughly.[9]

Acne medications should not influence the application of a facial foundation. If the acne medication film is not even, the facial foundation applied on top will streak, clump, and not distribute evenly over the skin leading to an unattractive, unnatural appearance. Uneven dyschromia is often aggravated when there is more desquamation, a common finding with concomitant use of BP-containing acne therapies. Medications should also discourage facial foundation migration, commonly observed in oily-skinned acne patients, where the sebum floats the facial foundation, and underlying acne medication, off the skin surface destroying the film. The facial foundation pigment tends to migrate to the follicular ostia and up the hair shaft.

Cosmetic compatibility embodies the characteristics of avoiding facial foundation color shift, application problems, cosmetic streaking, and migration difficulties, yet provides confirmation that a topical prescription may be successfully used on the face simultaneously with a pigmented facial foundation. In our study, there were no significant differences in terms of cosmetic compatibility or skin attributes when makeup was applied to a treated or untreated face. It is not surprising that slight changes were seen six hours post-makeup application; however, as demonstrated, there were

no statistical differences between the treated and untreated face, suggesting these changes were more a function of time rather than treatment. Interestingly, from a patient's perspective, changes in makeup appearance at Hour 6 were no different to those post-makeup application, and it was only on the untreated side of the face where significant changes were reported at Hour 6.

Clindamycin phosphate 1.2%/BP 3.75% gel is a new fixed combination treatment for moderate-to-severe acne vulgaris. It has been shown to have superior results compared to vehicle, with both co-primary and co-secondary efficacy outcomes, including measures of inflammatory and noninflammatory lesion reduction, treatment success, patient satisfaction, and reduction in facial skin oiliness.[7] It is also generally safe and well-tolerated. Treatment-emergent adverse events (TEAEs) occurred in less than two percent of patients (compared with 3.0% with vehicle).[7] There were no discontinuations because of TEAEs.[7] For most patients treated with clindamycin phosphate 1.2%/BP 3.75% gel, no local signs and symptoms of erythema, scaling, itching, burning, or stinging were reported.[7] When they did occur, the vast majority were mild, not bothersome, and usually occurred early in the study, disappearing by Week 12.

In our study, tolerability was excellent with no reports of erythema, edema, and peeling post-makeup application or at Hour 6, and only one report of mild dryness at Hour 6 on the treated face.

There are limitations to our study. No patient suffered from acne and although it is not expected that differences would be seen, further study in a female acne population may be helpful. Clindamycin phosphate 1.2%/BP 3.75% gel was only administered once, to one side of the face. Acne is a chronic condition requiring weeks, and in some cases months of treatment. Again it is not anticipated that long-term use of makeup in acne sufferers treated with clindamycin phosphate 1.2%/BP 3.75% gel would create any untoward effect, but a longer term study would provide these details. In addition, our results may not apply to different clindamycin phosphate/BP combinations or other acne medications in which the vehicle is different from the one studied.

In conclusion, clindamycin phosphate 1.2%/BP 3.75% gel was shown to have excellent cosmetic compatibility with facial foundation.

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