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The Efficacy and Tolerability of Dapsone 5% Gel in Female Versus Male Patients With Facial Acne Vulgaris: Gender as a Clinically Relevant Outcome Variable

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ABSTRACT

Background: Two identical phase 3, randomized, double-blind, and vehicle-controlled trials (DAP0203 and DAP0204) demonstrated the superior efficacy and tolerability of dapsone 5% gel over vehicle gel in patients with facial acne vulgaris. At week 12, dapsone gel–treated patients achieved greater mean reductions in inflammatory, noninflammatory, and total lesion counts, and a higher incidence of clinical success as indicated by the Global Assessment of Acne Severity (GAAS), than patients receiving vehicle. Some investigators noted greater acceptance and efficacy of dapsone gel in female versus male patients. We performed an analysis of data pooled from these 2 trials to evaluate the effect of gender on dapsone 5% gel efficacy and tolerability.

Methods: A total of 2898 patients were included in the pooled analysis; an additional 112 patients were enrolled in the phase 3 trials but were excluded from the analysis due to an absence of post-treatment efficacy data. Among the included patients, 1453 (753 female; 700 male) received dapsone 5% gel twice daily, and 1445 (767 female; 678 male) received vehicle twice daily. Patient assessments were performed at baseline and at weeks 2, 4, 6, 8, and 12. Mean percentage reduction from baseline in acne lesion counts (inflammatory, noninflammatory, and total), the proportion of patients achieving treatment success (GAAS score of 0 [clear skin] or 1 [almost clear skin]), and the proportion of patients without erythema, oiliness, dryness, or peeling were analyzed and compared in female versus male patients.

Results: In dapsone-treated patients, the mean percentage reduction in lesion counts from baseline to 12 weeks was significantly greater in females than males for inflammatory (–56.8% vs –43.2%; $P < 0.0001$), noninflammatory (–39.8% vs –28.5%; $P < 0.0001$), and total lesion counts (–46.6% vs –35.8%; $P < 0.0001$). In vehicle-treated patients, the mean percentage reduction in lesion counts from baseline to 12 weeks was also significantly greater in females than males (inflammatory: –52.9% vs –35.7% [$P < 0.0001$]; noninflammatory: –33.9% vs –17.8% [$P < 0.0001$]; total: –41.1% vs –26.1% [$P < 0.0001$]). The within-gender treatment differences (dapsone 5% gel – vehicle) in percentage lesion reduction at 12 weeks were also significant for all lesion types in both female patients (inflammatory: –4.83, $P = 0.0138$; noninflammatory: –5.90, $P = 0.0154$; total: –5.51, $P = 0.0029$) and in male patients (inflammatory: –7.56, $P = 0.0002$; noninflammatory: –10.69, $P < 0.0001$; total: –9.72, $P < 0.0001$). Similarly, the clinical success rate based on GAAS score was significantly higher in females than in males in both dapsone-treated (48.6% vs 34.4%; $P = 0.0003$) and vehicle-treated patients (39.4% vs 28.0%; P = 0.0013). The proportion of patients with erythema, dryness, peeling, or oiliness was low (≤10% at 12 weeks) in both treatment arms and did not differ significantly by gender.

Conclusions: Gender outcomes have been largely ignored in acne clinical trials. In these 2 identical pivotal trials, the results appear to be influenced by gender, with female patients experiencing a significantly greater reduction than male patients in acne lesion counts, and a significantly higher proportion of female patients than male patients achieving clinical success (GAAS ≤1), following 12 weeks of treatment with dapsone 5% gel. These data suggest that gender is a novel predictor of outcome that should be considered in acne clinical trial design.

BACKGROUND

- Dapsone 5% gel has demonstrated superior efficacy and excellent tolerability compared with vehicle gel in 2 identical phase 3, randomized, double-blind trials in patients with facial acne vulgaris (DAP0203 and DAP0204).[1]
  - Percentage reductions in mean inflammatory, noninflammatory, and total lesion counts were significantly greater with dapsone gel compared with vehicle gel at 12 weeks (inflammatory: –32% vs –24%; noninflammatory: –39% vs –32%; total: –48% vs –42%, respectively; $P < 0.001$ for all).
  - At 12 weeks, patients receiving dapsone had a significantly higher incidence of clinical success, as indicated by a GAAS score of 0 (none) or 1 (minimal), than patients receiving vehicle (41% vs 33%; $P < 0.001$).
  - Rates of overall and application-site adverse events were similar between the 2 treatment groups.
  - Local signs and symptoms of acne and cutaneous irritation (erythema, oiliness, dryness, and peeling) were similar in both groups and declined in both groups over the course of treatment.
- Some investigators noted greater acceptance and efficacy of dapsone gel in female versus male patients.
- In order to explore the effect of gender on the efficacy and tolerability of dapsone 5% gel, we performed a gender subanalysis of the pooled data from these 2 trials.

METHODS

- Patients in DAP0203 and DAP0204 were randomized to receive either dapsone 5% gel or vehicle gel twice daily.
  - Both trials were identical in design.
  - Patient assessments were performed at baseline and at weeks 2, 4, 6, 8, and 12.
- Data were included in this subanalysis for all patients who were dispensed treatment kits and who had at least 1 post-dose measurement (n = 2898).
  - 112 patients enrolled in the trials were excluded from the analysis due to an absence of post-treatment efficacy data.
- The following parameters were analyzed and compared in female versus male patients:
  - The mean percentage reduction from baseline in acne lesion counts (inflammatory, noninflammatory, and total)
  - The proportion of patients achieving treatment success (GAAS score of 0 [none] or 1 [minimal])
  - The proportion of patients with erythema, oiliness, dryness, or peeling
- A modified last-observation-carried-forward (LOCF) approach was used to imputate missing data.
  - Continuous parameters: for week 2 missing data, the average between baseline and week 4 data was used; for all other weeks of measurement, LOCF was used.
  - Discrete parameters: LOCF was used for all weeks.

RESULTS

- 1453 patients (753 female; 700 male) who received dapsone 5% gel twice daily, and 1445 patients (767 female; 678 male) who received vehicle twice daily were included in the analysis.
- Baseline lesion counts and GAAS scores are presented in Table 1.

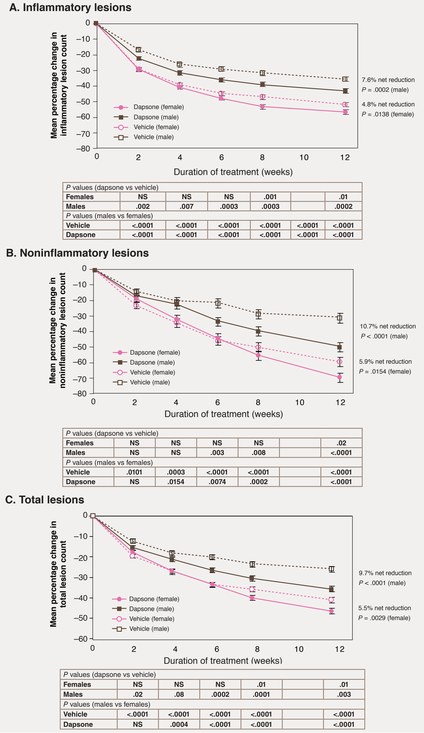
Table 1. Demographics and Baseline Characteristics

	Vehicle gel (n = 1445)	Dapsone gel (n = 1453)
Sex, n (%)		
Female	767 (53.1)	753 (51.8)
Male	678 (46.9)	700 (48.2)
Lesion counts, mean ± SE		
Inflammatory		
Female	28.17 ± .30	28.18 ± .31
Male	32.95 ± .43	33.61 ± .41
Noninflammatory		
Female	45.89 ± .81	46.07 ± .86
Male	50.06 ± .93	50.40 ± .94
Total		
Female	74.06 ± .92	74.25 ± .98
Male	83.00 ± 1.10	84.01 ± 1.08
GAAS scores, n (%)		
0 or 1		
Female	55 (7.2)	43 (5.7)
Male	22 (3.2)	32 (4.6)
≥ 2		
Female	712 (92.8)	710 (94.3)
Male	656 (96.8)	668 (95.4)

Lesion Counts

- In dapsone-treated and in vehicle-treated patients, the mean percentage reduction in lesion counts from baseline to 12 weeks was significantly greater in females than males for inflammatory, noninflammatory, and total lesion counts (Figure 1).
- Within-gender treatment differences (dapsone gel – vehicle gel) in percentage lesion reduction were significant at 12 weeks for all 3 lesion counts in both female and male patients.

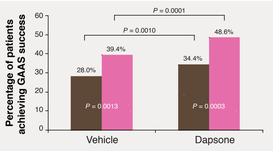
Figure 1. Lesion counts. Female patients experienced a significantly larger percentage decrease in inflammatory (A), noninflammatory (B), and total (C) lesion counts than male patients in both the dapsone gel and vehicle gel treatment arms. The net reduction was calculated as the difference between dapsone gel and vehicle gel, and was significant in both male and female patients.



GAAS Incidence of Treatment Success

- In both dapsone-treated and vehicle-treated patients, the treatment success rate based on GAAS score was significantly higher in female than in male patients (Figure 2).
- The within-gender treatment difference (dapsone gel –vehicle gel) in the proportion of patients achieving treatment success was 9.2% in females ($P = 0.0001$) and 6.4% in males ($P = 0.0010$).
- The odds ratio for treatment success in dapsone-treated versus vehicle-treated patients was similar in female and male patients (females: 1.61 [95% CI, 1.26-2.06]; males: 1.56 [95% CI, 1.20-2.03]).

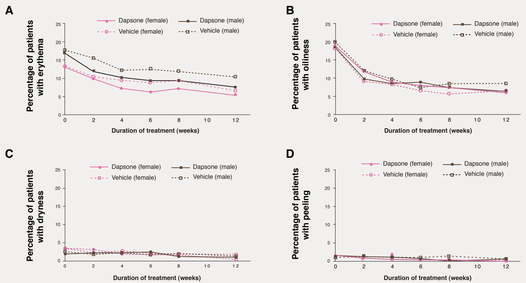
Figure 2. GAAS incidence of treatment success. A significantly greater proportion of female patients achieved treatment success at 12 , as indicated by a GAAS score of 0 or 1, compared with male patients in both treatment arms.



Tolerability

- The proportion of patients with erythema, dryness, peeling, or oiliness was low and decreased over the course of treatment.
- At all time points, the occurrence of erythema, dryness, peeling, or oiliness was similar between males and females and did not significantly differ by treatment arm (Figure 3).

Figure 3. Tolerability. The proportion of patients with erythema (A), oiliness (B), dryness (C), or peeling (D) did not significantly differ between male and female patients.



CONCLUSIONS

- Female patients experienced a significantly greater reduction from baseline in acne lesion counts than male patients in response to dapsone gel at 12 weeks.
- A significantly higher proportion of female patients than male patients achieved clinical success (GAAS ≤1) following 12 weeks of treatment with dapsone gel.
- Female patients had smaller differences between vehicle and active dapsone response.
- These data suggest that patient gender may influence the outcome of acne treatment.
- Patient gender should be considered when designing acne clinical trials.

REFERENCE

1. Draelos ZD, Carter E, Maloney JM, et al. Two randomized studies demonstrate the efficacy and safety of dapsone gel, 5% for the treatment of acne vulgaris. *J Am Acad Dermatol.* 2007;56:439-410.

AUTHOR DISCLOSURES: Dr. Harper is a consultant, advisor, and speaker for Allergan, an advisor and speaker for Coria Laboratories and Galderma Laboratories, a speaker and investigator for Intendis, an investigator for Medicis, and a consultant and speaker for Stiefel Laboratories. Dr. Oefelein is an employee of Allergan. Dr. Tanghetti is an investigator and speaker for Allergan and Stiefel Laboratories, and is a consultant and speaker for Galderma Laboratories. Third-party medical writing assistance supported by Allergan, Inc., was used in the preparation of this poster.

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