

# Cortexolone 17 $\alpha$ -propionate 1% cream, a new potent antiandrogen for topical treatment of acne vulgaris. A pilot randomized, double-blind comparative study vs. placebo and tretinoin 0.05% cream

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## Summary

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### Conflicts of interest

L.M. is an employee at Cosmo S.p.A., Lainate (MI), Italy. G.C. is a consultant at Cosmo Research & Development S.p.A., Lainate (MI), Italy.

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**Background** Acne vulgaris is a disorder of the pilosebaceous unit in which the androgens contribute to its onset and persistence. The use of antiandrogens is therefore potentially effective; however, antiandrogens for topical use are not available on the market. Cortexolone 17 $\alpha$ -propionate (CB-03-01; Cosmo S.p.A, Lainate, Italy) is a new potent topical antiandrogen potentially useful in acne vulgaris.

**Objectives** To evaluate the safety and the topical efficacy of CB-03-01 1% cream in acne vulgaris as compared with placebo and with tretinoin 0.05% cream (Retin-A<sup>®</sup>; Janssen-Cilag).

**Methods** Seventy-seven men with facial acne scored 2–3 according to Investigator's Global Assessment (IGA) were randomized to receive placebo cream (n = 15), or CB-03-01 1% cream (n = 30), or tretinoin 0.05% cream (n = 32) once a day at bedtime for 8 weeks. Clinical efficacy was evaluated every 2 weeks including total lesion count (TLC), inflammatory lesion count (ILC), acne severity index (ASI) and IGA. Safety assessment included local irritancy score, laboratory tests, physical examination, vital signs and recording of adverse events.

**Results** CB-03-01 1% cream was very well tolerated, and was significantly better than placebo regarding TLC (P = 0.0017), ILC (P = 0.0134) and ASI (P = 0.0090), and also clinically more effective than comparator. The product also induced a faster attainment of 50% improvement in all the above parameters. **Conclusions** This pilot study supports the rationale for the use of topical antiandrogens in the treatment of acne vulgaris. CB-03-01 1% cream seems to fit with the profile of an ideal antiandrogen for topical use.

Acne vulgaris is a chronic disorder of the pilosebaceous unit in which genetic predisposition, endocrine factors, follicular hyperkeratinization and bacterial infection contribute to its onset and persistence. As sebaceous glands and sebum production are undoubtedly stimulated by the androgen hormones, antiandrogens appear to offer a rational approach to the management of acne vulgaris.<sup>1,2</sup> Nevertheless, the use of antiandrogens could be hampered by the potential occurrence of endocrine side-effects also when applied locally.<sup>3</sup> Thus the profile of an ideal antiandrogen for topical use should include strong activity confined to skin, absence of systemic effects

and good tolerability. However, antiandrogens for topical use, endowed with all the above characteristics, are not available on the market.

Cortexolone 17 $\alpha$ -propionate (CB-03-01; Cosmo S.p.A, Lainate, Italy) is a new steroidal antiandrogen endowed with strong topical antiandrogenic activity associated with mild anti-inflammatory properties.<sup>4,5</sup> CB-03-01 competes at the human androgen-receptor level<sup>6</sup> without inhibiting the skin 5 $\alpha$ -reductase.<sup>7</sup> The steroid easily penetrates human skin<sup>8</sup> and is quickly and extensively metabolized to free inactive cortexolone, thus being devoid of systemic antiandrogenic

effects. The toxicological profile showed that CB-03-01 is well tolerated in rat and rabbit in repeated subcutaneous and dermal toxicities, is not mutagenic, and is not a skin sensitizer.

In adult male volunteers a single skin application of various volumes of CB-03-01 1% cream was very well tolerated with negligible absorption in the bloodstream.<sup>9</sup> All these preclinical and clinical results prompted us to evaluate, in a pilot clinical study, the potential efficacy and the safety of CB-03-01 1% cream in acne vulgaris compared with placebo and with topical tretinoin 0.05% cream (Retin-A<sup>®</sup>; Janssen-Cilag).

## Materials and methods

### Study aim and objectives

The study aim was to evaluate the clinical efficacy and tolerability of CB-03-01 1% cream vs. its vehicle alone (placebo) and vs. local tretinoin 0.05% cream in acne vulgaris of mild-to-moderate severity. The primary objective was to demonstrate the clinical and statistical superiority of CB-03-01 1% cream against placebo in improving total lesion count (TLC), inflammatory lesion count (ILC), acne severity index (ASI), and in the proportion of subjects with 'success' outcome at Investigator's Global Assessment (IGA). The secondary objective was to assess the efficacy of CB-03-01 1% cream compared with tretinoin 0.05% cream regarding the same parameters, and evaluating the effect regarding time in days to reach improvement of 50% in TLC, ILC and ASI.

### Ethical considerations

The trial was performed in compliance with the ethical principles stated in the Declaration of Helsinki and its subsequent revisions. Study protocol and all other relevant documentation were approved by the Romanian National Authorities and by the relevant local Ethical Committees. The trial was conducted in agreement with Good Clinical Practice and with the applicable European and Romanian regulatory requirements. Prior to participation in the trial, each subject gave his written, informed and witnessed consent.

### Participants

Between January and July 2009, three dermatological hospital centres and one outpatient dermatological centre in Bucharest, Romania, screened 83 white-skinned men (age range 18–45 years), 77 of whom were randomized to the treatments. The subjects were affected by acne vulgaris of the face of mild-to-moderate severity, with a score of 2 or 3 on IGA, and with TLC between 20 and 100, and ILC between 10 and 50. Exclusion criteria were: women, presence of facial lesions other than acne vulgaris, use of systemic antiacne medications or any kind of light treatment in the month before starting the study, or topical application of acne medications in the last

2 weeks, history of hypersensitivity to any ingredient of the trial drugs, severe liver or renal impairment, presence of diabetes, glaucoma, psychoses, or severe diseases in other organs including viral or bacterial infections.

### Study design and treatment

This pilot clinical study (EudraCT no. 2008-004335-37) was a randomized, double-blind, parallel-group, comparative trial. After completion of screening, the 77 eligible subjects were randomly assigned to three parallel groups. Each group received CB-03-01 1% cream ( $n = 30$ ), or tretinoin 0.05% cream ( $n = 32$ ), or placebo ( $n = 15$ ) constituted by the same excipients of CB-03-01 1% cream (cetyl alcohol, glyceryl monostearate, liquid paraffin, propylene glycol, tocopherol, sodium edetate, polysorbate 80, water). The treatments were thereafter shortly indicated as CB-03-01, tretinoin and placebo, respectively. The products were self-applied in adequate amounts only to the affected areas of the face, once a day at bedtime for 8 weeks. The products were assigned to the subjects in tubes totally indistinguishable according to a blinded randomization list, stratified every six subjects, generated by the sponsor and undisclosed to the investigators and the subjects. Throughout the study duration no additional local or systemic antiacne treatments were allowed, and the subjects were discouraged from starting any new medication without consulting the investigator.

### Treatment compliance

Subjects were requested to return, at each visit, all used/non-used medication tubes. The investigator weighed the returned medication tubes, and recorded the returned amounts on drug accountability logs.

### Efficacy assessment

The following four variables were assessed at the screening visit and at the end of weeks 2 (visit 1), 4 (visit 2), 6 (visit 3) and 8 (visit 4) of treatment:

TLC and ILC.<sup>10</sup> The count was performed on the right and left sides of the face including the chin, forehead, left and right cheeks. No other regions were considered. TLC included both noninflammatory (comedones) and inflammatory (papules, pustules and nodules) lesions, whereas ILC included only inflammatory lesions. At the screening visit both TLC and ILC values were considered as 100%, and any decrease in the following visits was calculated and regarded as percentage improvement.

ASI.<sup>11</sup> The severity of acne was assessed considering, for each type of lesion, the following correction factors: comedones  $\times 0.5$ , papules  $\times 1$ , pustules  $\times 2$ , and nodules  $\times 3$ . The total individual severity score was obtained by multiplying the number of each type of lesion with its correction factor, and adding them together. At the screening visit the ASI value obtained was considered as 100%, and any decrease in the

following visits was calculated and regarded as percentage improvement.

IGA.<sup>12</sup> The assessment was made on an ordinal scale with five severity grades, as follows: grade 0, clear skin without inflammatory or noninflammatory lesions; grade 1, almost clear, with rare noninflammatory lesions and no more than one small inflammatory lesion; grade 2, mild severity greater than grade 1, with some noninflammatory lesions and no more than a few inflammatory lesions (papules/pustules only, no nodular lesions); grade 3, moderate severity greater than grade 2, up to many noninflammatory lesions and may have some inflammatory lesions, but no more than one small nodular lesion; grade 4, severe, greater than grade 3, up to many noninflammatory and inflammatory lesions, but no more than a few nodular lesions. The 'success' outcome at IGA was defined as grade  $\leq 1$  with a grade 0 or 1 for the subjects whose baseline score was 3, and grade 0 for the subjects with baseline score 2.

### Safety assessment

The local tolerability was evaluated at weeks 2, 4, 6 and 8 applying an irritancy score (IS) considering redness, peeling, dryness, swelling, itching and burning, each scored from 0 to 3 according to the severity. Systemic tolerability was evaluated by mean of standard haematology, clinical laboratory, urinalysis, physical examination and vital signs performed at screening and at the end of treatment. Occurrence of adverse events (AEs) was recorded and monitored throughout the study, and during 2 weeks after treatment discontinuation.

### Statistical analysis

Data management and statistical analysis were performed by an independent contract research organization (InnoPharma s.r.l., Desio, Italy). The following analysis populations were used: intent to treat (ITT) population, including all randomized subjects who were dispensed study medication with at least one postbaseline assessment, and safety population including all subjects randomized and treated at least once. Main and secondary variables in the comparison between treatments were analysed at a two-sided significance level of  $P = 0.05$ . Treatment differences in the percentage improvement of TLC, ILC and ASI at various weeks, and compared with the screening visit, were assessed by analysis of variance with repeated measures together with a 95% confidence interval (CI). The proportion of subjects with IGA 'success' outcome at various weeks was assessed by the Cochran–Mantel–Haenszel method. The Kaplan–Meier method was used in the survival analysis to analyse the time in days to reach 50% improvement in TLC, ILC and ASI using the two-sided log-rank test. Safety was assessed by the incidence of AEs and by evaluation of vital signs, physical examination, laboratory values and local tolerability. Index of tolerability to the medications was assessed by the same methodology as primary efficacy endpoints or, if the necessary assumptions were not satisfied, in a nonparametric way.

## Results

### Subject disposition, characteristics and compliance

Subject disposition, characteristics and compliance are reported in Table 1. Eighty-three subjects were screened. Six screen failures occurred, so that 77 subjects were randomized. Of the 77 randomized, 10 subjects did not complete the study as per protocol (four consent withdrawal, six lack of compliance). Seventy-two subjects were analysed both as ITT and safety population (14 in placebo group, 30 in tretinoin group, and 28 in CB-03-01 group). The groups were well balanced regarding demographic characteristics, severity of clinical parameters and proportion of subjects with IGA grade 2 and IGA grade 3. Good and comparable compliance was detected among the groups regarding exposure duration, amount of study drug used, and daily amount of medication self-applied. No concomitant medication potentially interfering with acne outcome or its evaluation was reported.

### Efficacy assessment

#### Total lesion count

The results are reported in Figure 1. Starting from week 2 onwards, the mean reduction of TLC was greater in the CB-03-01 group than in the placebo group, whereas tretinoin showed a profile of activity intermediate between CB-03-01 and placebo groups. The mean  $\pm$  SD percentage improvement at the final visit was  $65.70 \pm 31.42$  in the CB-03-01 group,  $52.51 \pm 25.70$  in the tretinoin group, and  $37.0 \pm 33.31$  in the placebo group. Considering the improvement at the different visits, CB-03-01 was significantly more active than placebo at weeks 2 (17.9%, 95% CI 0.42–35.37%,  $P = 0.0447$ ), 4 (19.9%, 95% CI 2.49–37.44%,  $P = 0.0254$ ), 6 (22.4%, 95% CI 4.89–39.85%,  $P = 0.0124$ ) and 8 (28.3%, 95% CI 10.75–45.82%,  $P = 0.0017$ ). In the comparison with tretinoin, CB-03-01 was always clinically more effective without reaching a statistically significant level. No significant differences, at any time point, were noticed between placebo and tretinoin groups. The time to reach 50% improvement showed significant differences among the groups (log rank test:  $P = 0.0199$ ) with a median time of 43.5 days for CB-03-01, 57.0 days for tretinoin, and 58.0 days for placebo (data not shown).

#### Inflammatory lesion count

The results are reported in Figure 2. Starting from week 2 onwards, the mean  $\pm$  SD reduction of ILC was greater in the CB-03-01 group than in the placebo and tretinoin groups. The percentage improvement at final visit was  $67.26 \pm 32.03$  in the CB-03-01 group,  $50.71 \pm 34.46$  in the tretinoin group and  $38.98 \pm 33.22$  in the placebo group. Considering the improvement at the different visits, CB-03-01 was significantly more effective than placebo at weeks 4 (22.7%, 95% CI 0.78–44.62%,  $P = 0.0424$ ), 6 (22.2%, 95% CI 0.27–44.10%,

Table 1 Disposition, characteristics of subjects and compliance

	Placebo	Tretinoin	CB-03-01
Randomized subjects	15	32	30
Subjects completing the study per protocol	14	26	27
Subjects not completing the study	1	6	3
Consent withdrawal	–	3	1
Lack of compliance	1	3	2
Subjects analysed as ITT population	14	30	28
Subjects analysed as safety population	14	30	28
Age (years), mean $\pm$ SD	20.4 $\pm$ 1.7	21.2 $\pm$ 3.4	20.6 $\pm$ 3.5
Weight (kg), mean $\pm$ SD	72.9 $\pm$ 10.2	77.5 $\pm$ 11.9	74.8 $\pm$ 9.8
Height (cm), mean $\pm$ SD	175.9 $\pm$ 7.7	179.5 $\pm$ 8.1	178.1 $\pm$ 7.5
TLC, mean $\pm$ SD	50.6 $\pm$ 15.9	48.5 $\pm$ 17.2	46.2 $\pm$ 15.0
ILC, mean $\pm$ SD	33.5 $\pm$ 11.4	29.1 $\pm$ 10.4	28.5 $\pm$ 11.1
ASI, mean $\pm$ SD	51.4 $\pm$ 19.0	48.2 $\pm$ 17.1	45.7 $\pm$ 17.4
IGA grade 2, %	57	43	50
IGA grade 3, %	43	57	50
Exposure duration (days), mean $\pm$ SD (range)	50.9 $\pm$ 3.6 (39–55)	46.8 $\pm$ 13.5 (13–55)	51.9 $\pm$ 1.8 (46–56)
Total amount of cream used (g), mean $\pm$ SD (range)	97.3 $\pm$ 48.8 (23.2–203.2)	100.9 $\pm$ 65.6 (2.3–221.9)	116.4 $\pm$ 65.1 (13.2–221.0)
Daily dose (g), mean $\pm$ SD (range)	1.9 $\pm$ 0.9 (0.5–3.9)	2.1 $\pm$ 1.2 (0.2–4.4)	2.2 $\pm$ 1.2 (0.3–4.2)
Concomitant medications	0	0	0

ITT, intent to treat; TLC, total lesion count; ILC, inflammatory lesion count; ASI, acne severity index; IGA, Investigator's Global Assessment.

$P = 0.0472$ ) and 8 (27.9%, 95% CI 5.85–49.82%,  $P = 0.0134$ ). When compared with tretinoin, CB-03-01 was superior at each observation time, and also statistically better at week 6 (19.2%, 95% CI 1.13–37.32%,  $P = 0.0374$ ). No significant differences, at any time point, were noticed between the placebo and tretinoin groups. The time to reach 50% improvement showed significant differences among the groups (log rank test:  $P = 0.0490$ ) with a median time of 36.5 days for CB-03-01, 44.0 days for tretinoin and 58.0 days for placebo (data not shown).

#### Acne severity index

The results are reported in Figure 3. Starting from week 2 onwards, mean ASI improvement was more evident in the CB-03-01 group than in the placebo group. The improvement in the tretinoin group was intermediate between that observed in the CB-03-01 and placebo groups. The mean  $\pm$  SD percentage improvement at the end of treatment was 68.35  $\pm$  30.58 in the CB-03-01 group, 53.07  $\pm$  33.49 in the tretinoin group and 39.52  $\pm$  31.63 in the placebo group. Considering the

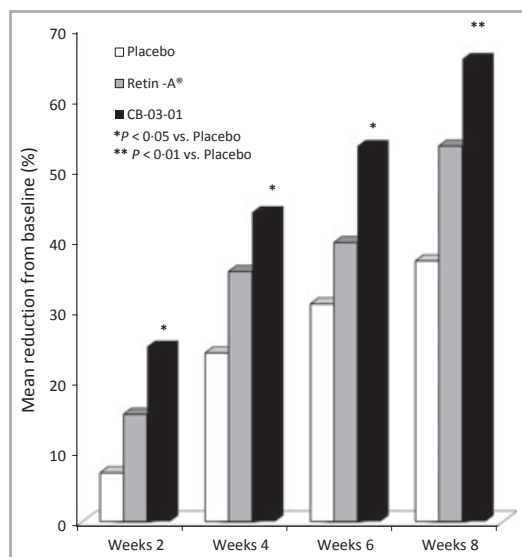


Fig 1. Improvement in total lesion count.

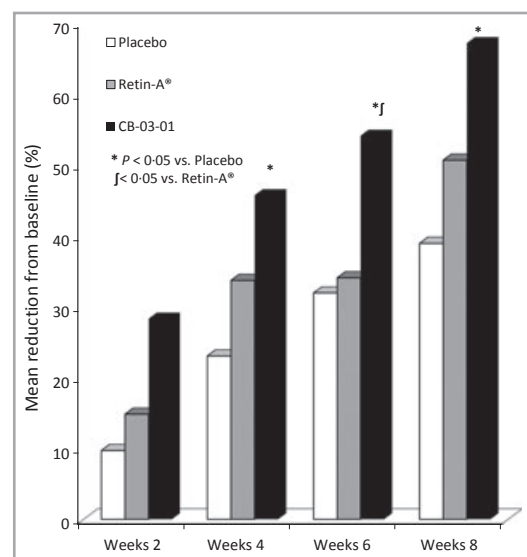


Fig 2. Improvement in inflammatory lesion count.

improvement at the different visits, CB-03-01 was always better than placebo, and this was statistically significant at weeks 2 (22.2%, 95% CI 5.08–39.37%,  $P = 0.0113$ ), 6 (22.3%, 95% CI 1.19–43.50%,  $P = 0.0385$ ) and 8 (23.4%, 95% CI 7.17–49.62%,  $P = 0.0090$ ). When compared with tretinoin, CB-03-01 was clinically but not statistically more effective at each observation time. No significant differences at any time

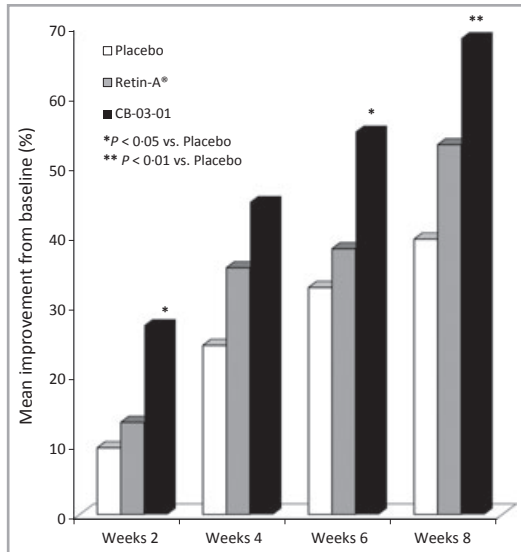


Fig 3. Improvement in acne severity index.

Table 2 Effect on Investigator's Global Assessment

Treatment	Subjects achieving 'success', n (%)	Subjects shifted from score 2–3 to score 0–1, n (%)
Placebo (n = 14)	1 (7)	2 (14)
Tretinoin (n = 26)	3 (12)	7 (27)
CB-03-01 (n = 27)	6 (22)	11 (41)

point were noticed between the placebo and tretinoin groups. The time to reach 50% improvement showed significant differences among the groups (log rank test:  $P = 0.0438$ ) with a median time of 42.5 days for CB-03-01, 44.0 days for tretinoin and 57.0 days for placebo (data not shown).

### Investigator's Global Assessment

The results are reported in Table 2. The statistical analysis applied to IGA 'success' did not show significant differences among the treatments. Nevertheless, in the CB-03-01 group a higher proportion of 'success' was detected (22%) as compared with the tretinoin (12%) and placebo (7%) groups. In agreement with these findings, the proportion of subjects reducing to IGA grade between 0 and 1 was notably higher in the CB-03-01 group (41%) than in the tretinoin (27%) and placebo (14%) groups.

### Safety assessment

The local tolerability of CB-03-01 was good. In contrast, in the groups treated with tretinoin and placebo an evident worsening of IS was observed within the first 2 weeks. This effect gradually abated to near normal value ( $\leq 1$ ) at the end of the treatment period (Table 3). An exploratory analysis showed a statistically significant difference between the CB-03-01 and placebo groups at visit 1 ( $P = 0.0412$ ). Regarding systemic tolerability, no clinically important abnormalities were detected in any treated group in haematology, clinical laboratory, urinalysis, vital signs and other observations related to safety. A total of eight subjects (11%) experienced 14 AEs which were distributed as follows: five in the placebo group, six in the tretinoin group, and three in the CB-03-01 group (Table 4). The most frequently reported AEs were laryngitis, herpes simplex, pruritus and acne worsening. All AEs were mild or moderate, and none was judged as either serious or requiring withdrawal from the study or treatment discontinuation.

Table 3 Irritancy score improvement

Treatment	Visit 1 (2 weeks)	Visit 2 (4 weeks)	Visit 3 (6 weeks)	Visit 4 (8 weeks)
<b>Placebo</b>				
n	14	14	14	14
Mean $\pm$ SD	2.14 $\pm$ 2.18	2.14 $\pm$ 3.92	1.79 $\pm$ 4.46	0.86 $\pm$ 2.14
Range	0–8	0–15	0–17	0–8
<b>Tretinoin</b>				
n	30	26	26	26
Mean $\pm$ SD	2.20 $\pm$ 3.17	1.04 $\pm$ 2.13	0.73 $\pm$ 1.43	0.62 $\pm$ 1.20
Range	0–13	0–10	0–6	0–5
P-value vs. placebo	0.3809	0.2834	0.5257	0.8261
<b>CB-03-01</b>				
n	28	28	28	27
Mean $\pm$ SD	1.29 $\pm$ 2.42	0.75 $\pm$ 1.48	0.57 $\pm$ 1.03	0.30 $\pm$ 0.61
Range	0–11	0–6	0–3	0–2
P-value vs. placebo	0.0412	0.1015	0.2772	0.6046

**Table 4** Adverse events (AEs) by system organ class

AEs	Placebo (n = 14)		Tretinoin (n = 30)		CB-03-01 (n = 28)	
	Events, n	Patients with AEs, n (%)	Events, n	Patients with AEs, n (%)	Events, n	Patients with AEs, n (%)
AEs and patients with any AEs	5	3 (21)	6	2 (7)	3	3 (11)
AEs by system organ class						
Infection and infestations	2	2 (14)	1	1 (3)	1	1 (4)
Metabolism and nutrition disorders	0	0	1	1 (3)	0	0
Musculoskeletal and connective tissue disorders	0	0	1	1 (3)	0	0
Skin and subcutaneous tissue disorders	3	3 (21)	3	2 (7)	2	2 (7)

## Discussion

CB-03-01 is a new potent steroidal antiandrogen, with additional anti-inflammatory properties, which was demonstrated in animal models to act selectively at the skin level without systemic effects.<sup>4,5</sup>

The present study was a pilot, randomized, double-blind, comparative trial evaluating the efficacy and the tolerability of CB-03-01 1% cream in acne vulgaris of mild-to-moderate severity, compared with placebo and topical tretinoin. As this trial was the first experience of repeated administration of CB-03-01 to humans, it was deemed prudent to enrol only a limited number of adult males, and not to expose them for too long a period of treatment exceeding 8 weeks. Considering the concerns raised from some Ethical Committees about the need to treat patients only with placebo, the size of the placebo group was reduced.

CB-03-01 was significantly more effective than placebo in improving TLC, ILC and ASI. Worthy of interest is the effect particularly evident on the inflammatory lesions, probably due to the ancillary anti-inflammatory activity of the molecule. All the above effects had already become evident after 2–4 weeks of treatment and increased proportionally thereafter. The faster effect of CB-03-01, as compared with that of placebo and tretinoin, has been also confirmed by the survival analyses showing an evident reduction of number of days required to reach 50% improvement in all parameters. Also in the comparison with tretinoin, CB-03-01 was globally more effective in all above parameters. This finding is of particular interest as topical retinoids have a well-established clinical efficacy in the treatment of acne vulgaris.<sup>13</sup> In our study the clinical activity of tretinoin was very similar to that described in other clinical trials<sup>14–16</sup> but, surprisingly, it was found not significantly better than placebo. This inconsistency could be attributed to the small and unbalanced groups of patients, thus preventing detection of statistically significant differences between tretinoin and placebo despite evident differences of activity. The study did not show statistically significant differences among treatments regarding the ‘success’ achievement in the IGA at the end of the treatment. Nevertheless, CB-03-01 induced a higher proportion of IGA ‘success’ than placebo and tretinoin, and also induced

a notably higher proportion of subjects in whom the IGA grade 2–3 at screening was reduced to grade 0–1 at the end of the treatment period.

During the study, no concerns were raised regarding the local and systemic safety of CB-03-01. Worthy of interest is the better tolerability of CB-03-01 as compared with tretinoin, already evident at visit 1. This is of practical importance considering that one of the main concerns in using topical retinoids is the appearance of skin irritation in the first weeks of treatment, frequently leading to discontinuation or reduction of the number of applications. No serious AEs were detected through the study, no drop-outs occurred for safety reasons, and no differences among the groups were noticed concerning the nature and the incidence of AEs.

In conclusion, the data provided by this pilot study support the rationale for the use of topical antiandrogens in the treatment of acne vulgaris of mild-to-moderate severity. CB-03-01 was found to be significantly more effective than placebo, clinically better than tretinoin, very quick in onset of clinical effect, and mostly well tolerated.

Considering the preliminary nature of this trial, additional studies including more patients and more international study centres are needed to evaluate the potential of CB-03-01 1% cream in the treatment of acne vulgaris.

### What’s already known about this topic?

- Antiandrogens are considered potentially effective in treatment of acne vulgaris; nevertheless, antiandrogens for topical use are not yet on the market.

### What does this study add?

- This study demonstrated, for the first time, that the topical antiandrogen cortexolone 17 $\alpha$ -propionate 1% cream is safe and effective in the treatment of acne vulgaris, as compared with vehicle and topical tretinoin. These data contribute to support the use of topical antiandrogens in the treatment of acne vulgaris.

## References

- 1 Simpson NB, Cunliffe WJ. Disorders of the sebaceous glands. In: Rook's Textbook of Dermatology (Burns DA, Breathnach SM, Cox NH, Griffiths CEM, eds), 7th edn, Vol. 3. Oxford: Blackwell Science, 2004; 43.1–43.75.
- 2 Thiboutot D, Chen WC. Update and future of hormonal therapy in acne. *Dermatology* 2003; **206**:57–67.
- 3 Chen C, Puy LA, Simarg J *et al.* Local and systemic reduction by topical finasteride or flutamide of hamster flank organ size and enzyme activity. *J Invest Dermatol* 1995; **105**:678–82.
- 4 Celasco G, Moro L, Bozzella R *et al.* Biological profile of cortexolone 17 $\alpha$ -propionate (CB-03-01), a new topical and peripherally selective androgen antagonist. *Arzneimittelforschung* 2004; **54**:881–6.
- 5 Celasco G. Compound profile CB-03-01, September 2010. Data on Cosmo file.
- 6 Neliat G. *In vitro* pharmacology: human androgen receptor – study of CB-03-01 and CB-03-04. Cerep Study Report 10631, January 2006. Data on Cosmo file.
- 7 Juhaux F. Effect of the compound CB-03-01 on testosterone metabolism in reconstructed human epidermis. Bioalternatives Study Report GT050709, December 2005. Data on Cosmo file.
- 8 Ford G. CB-03-01: *in vitro* dermal penetration studies. BioDynamics Research Ltd Study Report CPS/01, October 2007. Data on Cosmo file.
- 9 Müller M. First dose in man of CB-03-01; a new topical anti-androgen drug. Cross S.A. Study Report CRO-07-89, September 2008. Data on Cosmo file.
- 10 Burke BM, Cunliffe WJ. The assessment of acne vulgaris – the Leeds technique. *Br J Dermatol* 1984; **111**:83–92.
- 11 Tucker SB, Tausend R, Cochran R *et al.* Comparison of topical clindamycin phosphate, benzoyl peroxide, and a combination of the two for the treatment of acne vulgaris. *Br J Dermatol* 1984; **110**:487–92.
- 12 Center for Drug Evaluation and Research. Guidance for Industry. *Acne Vulgaris: Developing Drugs for Treatment*. Rockville, MD: CDER, 2005.
- 13 Thieliz A, Abdel-Naser MB, Fluhr JW *et al.* Topical retinoids in acne – an evidence-based overview. *J Dtsch Dermatol Ges* 2010; **8** (Suppl. 1):S15–23.
- 14 Berger R, Barba A, Fleischer A *et al.* A double-blinded, randomized, vehicle-controlled, multicenter, parallel-group study to assess the safety and efficacy of tretinoin gel microsphere 0.04% in the treatment of acne vulgaris in adults. *Cutis* 2007; **80**:152–7.
- 15 Nighland M, Grossman R. Tretinoin microsphere gel in facial acne vulgaris: a meta-analysis. *J Drugs Dermatol* 2008; **8** (Suppl.):S2–8.
- 16 Webster G, Cargill DI, Quiring J *et al.* A combined analysis of 2 randomized clinical studies of tretinoin gel 0.05% for the treatment of acne. *Cutis* 2009; **83**:146–54.