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Official Journal of the Italian Acne Board

Official Journal of the Mediterranean Acne Board



# EJAD

**Efficacy of combining Micronized Silver, Zinc Acetate  
and Lauric Acid in mild-moderate acne**

**Antonia Gimma, Carla Cardinali**

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**Antonia Gimma, Carla Cardinali**

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## Efficacy of combining Micronized Silver, Zinc Acetate and Lauric Acid in mild-moderate acne



Gimma - Cardinali

### SUMMARY

*Acne is a multifactorial inflammatory disease in which *P. acnes* assuredly plays a key role.*

*Though it is not an infectious disease, antibiotics are used to reduce the *P. acnes* load and for their anti-inflammatory action. The common use of oral antibiotics concurrently with topical antibiotics has increased the phenomenon of antibiotic resistance. This problem occurs both with the pathogenic agent of acne and also with infectious agents, such as certain strains of *S. aureus*, coagulase negative *Staphylococci* and *A* group *Streptococci*, that cause serious infections, such as MRSA and infections in the upper airways. Hence, therapeutic failure does not only occur in the case of acne but also towards other important infections in other organs. This has encouraged studies to seek anti-inflammatory*

*therapies that do not develop resistances, such as the combination of Micronized Silver, Zinc Acetate and Lauric Acid, and which have an anti-inflammatory and antibacterial action.*

*In our study we administered this combination as treatment to a group of 20 patients (Group A) presenting slight-moderate acne + a specific cleansing agent for acneic skin containing Taurates, Silver Citrate and microspheres of Silicon, and treated Group B made up of 20 patients presenting slight-moderate acne with the same combination + a non-specific cleansing agent for acneic skin.*

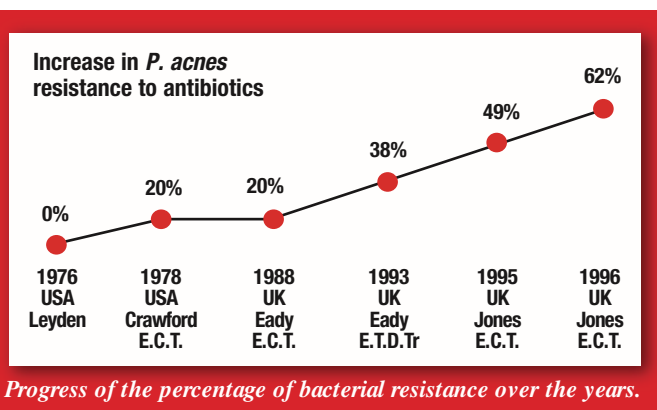
*The combination of Micronized Silver + Zinc Acetate + Lauric Acid is effective in reducing acneic lesions, both inflammatory and non-inflammatory, in both treated groups. The statistically significant reduction is more enhanced for inflammatory lesions.*

**Key words:** Acne, Micronized Silver, Zinc Acetate, Lauric Acid.

### Introduction

Antibiotic therapy has been extensively used for the treatment of acne to reduce the *P. acnes* load and for its anti-inflammatory action. The widespread use of oral antibiotics started in 1960 but signs of antibiotic resistance occurred only in the mid-70s after topical antibiotics were introduced for slight-moderate acne therapy<sup>1</sup>. In 1979 Crawford *et al.* described early signs of resistance shown by *P. acnes* towards erythromycin and clindamycin. In 1983 Leyden *et al.* were the first to report resistance to tetracyclines<sup>2</sup>. Several other studies followed between 1992 and 2001, proving that resistance to erythromycin and to clindamycin was more frequent than to tetracyclines, and the concurrent use of topical and systemic antibiotics increases the possibility of developing antibiotic-resistance<sup>3</sup>. Resistance does not only develop

against the pathogenic agent of acne but also against certain strains of *S. aureus*, coagulase negative *Staphylococci* and infections in the upper airways. Hence, the therapeutic failure in cases of acne and, especially, towards other important infections of other organs<sup>4</sup>.



*International guidelines for the prevention of bacterial resistance.***CONSENSUS: Strategies to limit antibiotic resistance are important in acne management***Level of evidence: V*

- Treatment regimens that limit, or even reduce, the incidence of bacterial antibiotic resistance are recommended.
  - Selection pressure can affect other, more pathogenic bacteria in addition to *P. acnes*.
  - High rates of resistance have been correlated with high outpatient use of antibiotics.
- Use of oral antibiotics can lead to resistance in commensal flora at all body sites; topical antibiotics lead to resistance largely confined to skin of treated site.
  - Oral antibiotics are recommended for moderate to moderately severe acne.
  - Topical antibiotics may be used in mild to moderate acne as long as they are combined with benzoyl peroxide (BPO) and a topical retinoid.
  - Limit the duration of antibiotic use and assess response to antibiotics and continuing need at 6 or 12 weeks.
  - Some countries have regulatory guidance limiting the duration of use of topical antibiotics (alone and in fixed-dose combination products) to 11 to 12 weeks.
- Use BPO concomitantly as a leave-on or as a wash.
  - BPO for 5 to 7 days between antibiotic courses may reduce resistant organisms on the skin; however, BPO does not fully eradicate potential for resistant organisms.
- Avoid using antibiotics (either oral or topical) as a monotherapy either for the acute treatment or maintenance therapy.
- Avoid the simultaneous use of oral and topical antibiotics without BPO, particularly if chemically different.

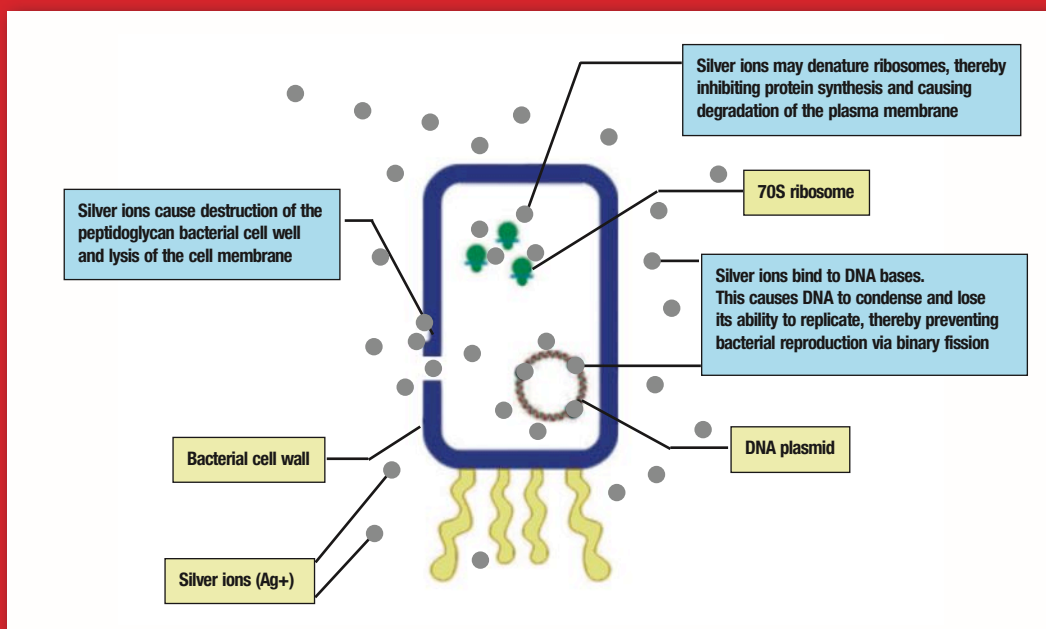
	Comedonal acne	Mild-to-moderate papulopustular acne	Severe papulopustular/moderate nodular acne	Severe nodular/conglobate acne
High strength of recommendation	-	Adapalene + BPO (f.c.) or BPO + clindamycin (f.c.)	Isotretinoin	Isotretinoin
Medium strength of recommendation	Topical retinoid	Azelaic acid or BPO or topical retinoid or systemic antibiotic + adapalene	Systemic antibiotics + adapalene or systemic antibiotics + azelaic acid or systemic antibiotics + adapalene + BPO (f.c.)	Systemic antibiotics + azelaic acid
Low strength of recommendation	Azelaic acid or BPO	Blue light or oral zinc or topical erythromycin + isotretinoin (f.c.) or topical erythromycin + tretinoin (f.c.) or systemic antibiotic + BPO or systemic antibiotic + azelaic acid or systemic antibiotics + adapalene + BPO (f.c.)	Systemic antibiotics + BPO	Systemic antibiotics + BPO or systemic antibiotics + adapalene or systemic antibiotics + adapalene + BPO (f.c.)
Alternatives for female patients	-		Hormonal antiandrogens + topical treatment or hormonal antiandrogens + systemic antibiotics	Hormonal antiandrogens + systemic antibiotics

*European Guidelines to "discourage" bacterial resistance.*

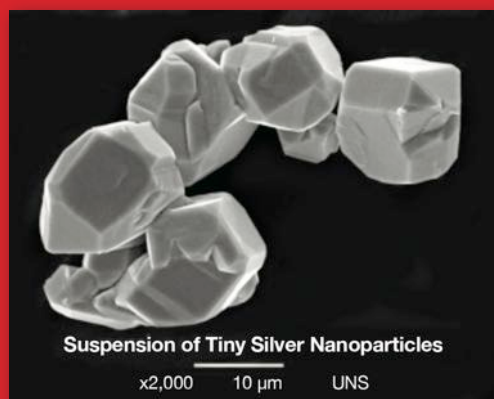
Said resistance might reach 80% in 2015!

The phenomenon of antibiotic resistance has led to seek anti-inflammatory therapies that do not develop resistance against pathogens that are not only the cause of acne but also, and especially, of

other infectious diseases. The combination of Micronized Silver, Zinc Acetate and Lauric Acid meets these requirements for the antiseptic, anti-inflammatory properties of their components. Particularly, Micronized Silver has an antimicro-



*Antimicrobial activity of Micronized Silver.*

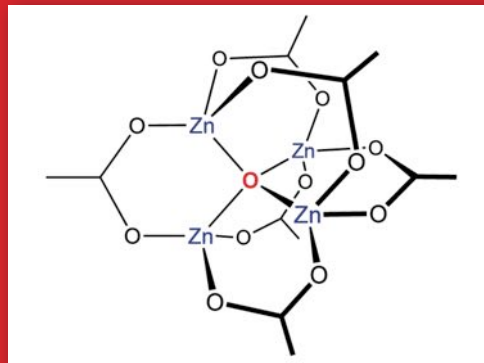


*Micronized Silver.*

bial action also against two Gram negative bacterial strains (e.g. *Escherichia coli*), and Gram positive strains (e.g. *Staphylococcus aureus*). The antimicrobial action is directly correlated with the quantity of silver that is released, and which has a scarce tendency to develop bacterial resistance. Micronized Silver increases the absorption of silver, strengthening its antimicrobial action<sup>5</sup>. Hence, the use of compounds that contain silver

ensures the availability of scarcely toxic products that possess broad spectrum antiseptic properties without developing bacterial resistance<sup>6</sup>.

Zinc is a vital element for humans since it is an essential component of more than 300 metalloenzymes and of more than 2,000 transcription factors that are necessary to regulate the metabolism of lipids, proteins and nucleic acids. The mean content in humans is 1.5-2.5 g, and it is especially found in



*Zinc Acetate.*

*The zinc content of foods (mg/100 g).*

Atlantic Oysters	74.7
Wheat germ	14.3
Beef	6.2
Cocoa powder	5.6
Cheese	4.0
Oats	3.4
Durum wheat	3.4
Dried peas	3.2
Lentils	3.1
Walnuts*	3.1
Almonds*	3.0
Black-eyed beans	2.9
Peanuts	2.9
Ham	2.8
Beans	2.8
Veal	2.8
Soft wheat	2.7
Chickpeas	2.7
Whole-wheat flour	2.4
Chicken	2.4
Wholemeal bread	1.8
Brown rice	1.8
Rye bread	1.6
Semi-whole wheat flour	1.5
2 Eggs, 50 g each	1.0
Spinach, raw	0.8
Fish	0.7
White bread	0.6
Common pasta, cooked	0.5
Tomato, ripe	0.2

(N. Valerio, da Krause & Mahan 1984 e \*USA Dept. Agr.)

the prostate gland, seminal fluid, uveal tract tissue and skin. The recommended daily dose for adults is 11 mg, which can be increased in women during pregnancy and breast-feeding. It circulates in the blood bound to albumin and alpha-2-macroglobulin, and is, especially, excreted in faeces. One third of the world population presents zinc deficiency in South East Asia and in Saharan Africa <sup>7</sup>.

Zinc has antioxidant properties.

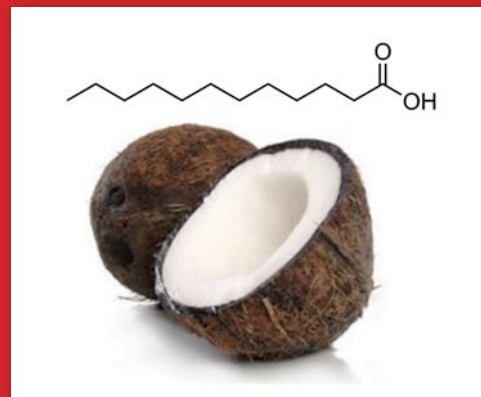
It reduces UV-induced damages and the incidence of malignant tumours. It is involved in the maintenance of reproductive and immune function, and in the wound repair process. It has anti-androgenic and sebum-suppressive properties by inhibiting 5-alpha-reductase <sup>8</sup>.

The anti-inflammatory properties of zinc are the reason for its use in several inflammatory dermatoses, such as acne, rosacea, eczema, ulcers and wounds. In 1974 G. Michaelsson reported the improvement of acneic lesions in a patient presenting acrodermatitis enteropathica treated with zinc salts. The mechanism of its efficacy in the treatment of acne has still not been entirely explained. Topical zinc alone or combined with other agents may be effective in the case of acne for its anti-inflammatory action and the capacity to reduce the *P. acnes* load by inhibiting lipase and free fatty acid levels. Moreover, it facilitates the absorption of the antibiotic when used in combination with it <sup>8</sup>.

Lauric Acid (LA) is a medium chain saturated fatty acid that is made up of 12 carbon atoms, and which is found in dairy products, animal fats and tropical oils, such as coconut oil.

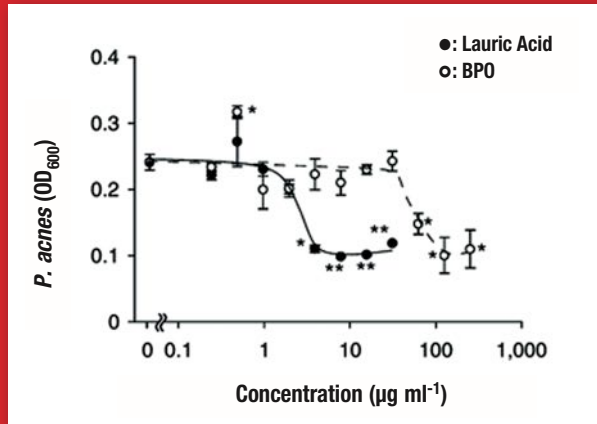
The cell membrane is permeable to LA, which forms 1-2% of free fatty acids (FFA) of sebum with a higher antimicrobial action than all other FFAs by exerting an inhibitory effect on the growth of *P. acnes*, *S. aureus* and *S. epidermidis* at a concentration that is 15 times lower than benzoyl peroxide. Lauric acid determines a significant suppression of IL-8 induced by *P. acnes* and of IL-6 induced by sebocytes <sup>9</sup>.

The combination of LA with other local antimicrobial therapies can increase the capacity to cross the bacterial membrane, thus enhancing the antimicrobial action. Hence, LA is a potential alternative therapeutic option for antibiotic-therapy in the



*Lauric Acid.*





Micronized Silver + Zinc Acetate + Lauric Acid + a specific cleansing agent for acneic skin containing Taurates, Silver Citrate and microspheres of Silicon twice a day. Sixteen of these patients presented a family history of acne. A Group B of 20 subjects with slight-moderate acne, 8 males and 12 females, with mean age 16 years, treated with the same topical combination + a non-specific cleansing agent for acneic skin containing acyl-glutamates and mallow twice a day. Sixteen patients presented a family history of acne.

treatment of acne<sup>10</sup>. The problem with LA is its precipitation in high concentrations as a result of its insolubility in water. The problem has been solved by encapsulating LA into liposomes with a subsequent increase in bioavailability and, therefore, a greater antimicrobial action<sup>11</sup>.

## Our study

We recruited two patient groups.

A Group A of 20 subjects with slight-moderate acne, 10 females and 10 males, with mean age 16.5 years, treated with the topical combination of

## Results

### Group A

- First visit
- 1<sup>st</sup> follow-up visit after 4 weeks (T1)
- 2<sup>nd</sup> follow-up visit after 8 weeks (T2)
- 3<sup>rd</sup> follow-up visit after 12 weeks (T3)

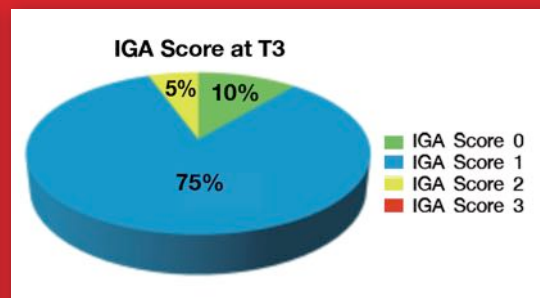
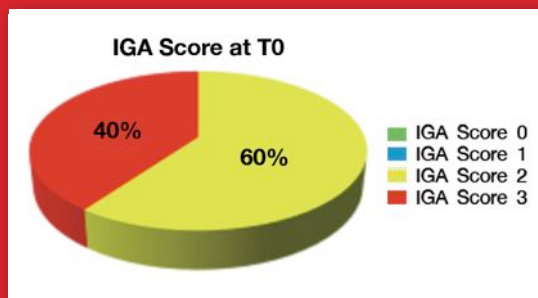
The third visit was only attended by 13 patients because 7 of them had achieved “clinical healing” already at the second follow-up visit.

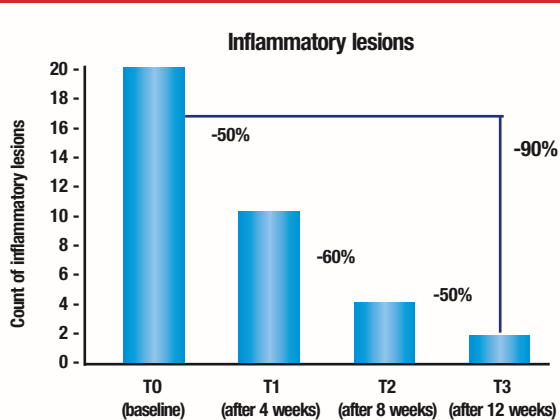
None of the patients presented side-effects, such as dry skin, desquamation, itching and rash, during all the follow-up visits.

All products were highly tolerated.

### GROUP A

*The IGA Score of patients diminishes significantly at the end of treatment. The assessment of the IGA Score of 20 patients at T0, T3 revealed a progressive improvement in the clinical condition with a reduction in the score and a result of mild/absent.*



**GROUP A**

*Highly significant reduction in the number of lesions, inflammatory (especially) .*

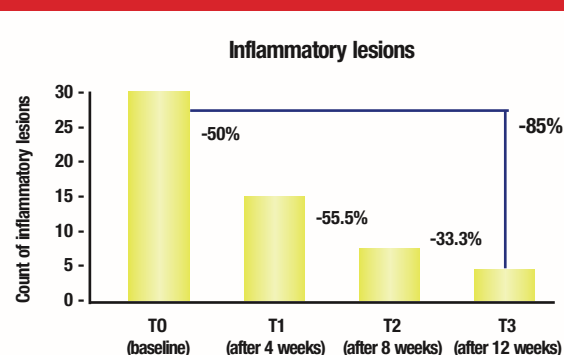
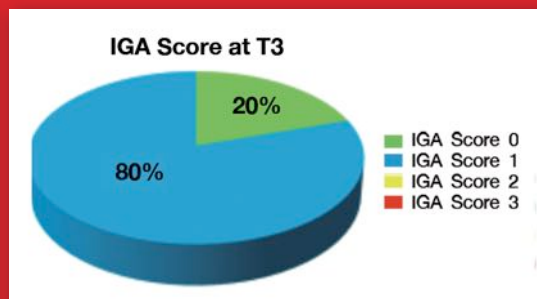
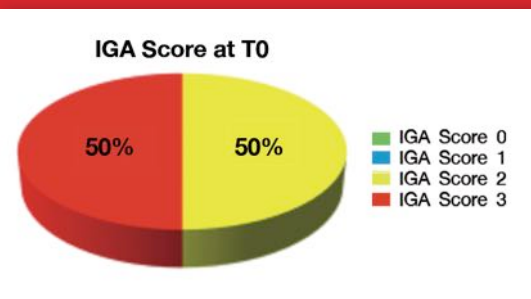
*T3\* visit performed only on 13 patients.*

**Group B**

- First visit
- 1<sup>st</sup> follow-up visit after 4 weeks (T1)
- 2<sup>nd</sup> follow-up visit after 8 weeks (T2)
- 3<sup>rd</sup> follow-up visit after 12 weeks (T3)

**GROUP B**

- The IGA Score of patients diminishes significantly at the end of treatment.
- The assessment of the IGA Score of 20 patients at T0, T3 revealed a progressive improvement in the clinical condition with a reduction in the score and a result of mild/absent.



The third visit was only attended by 10 patients because 10 of them had achieved “clinical healing” already at the second follow-up visit.

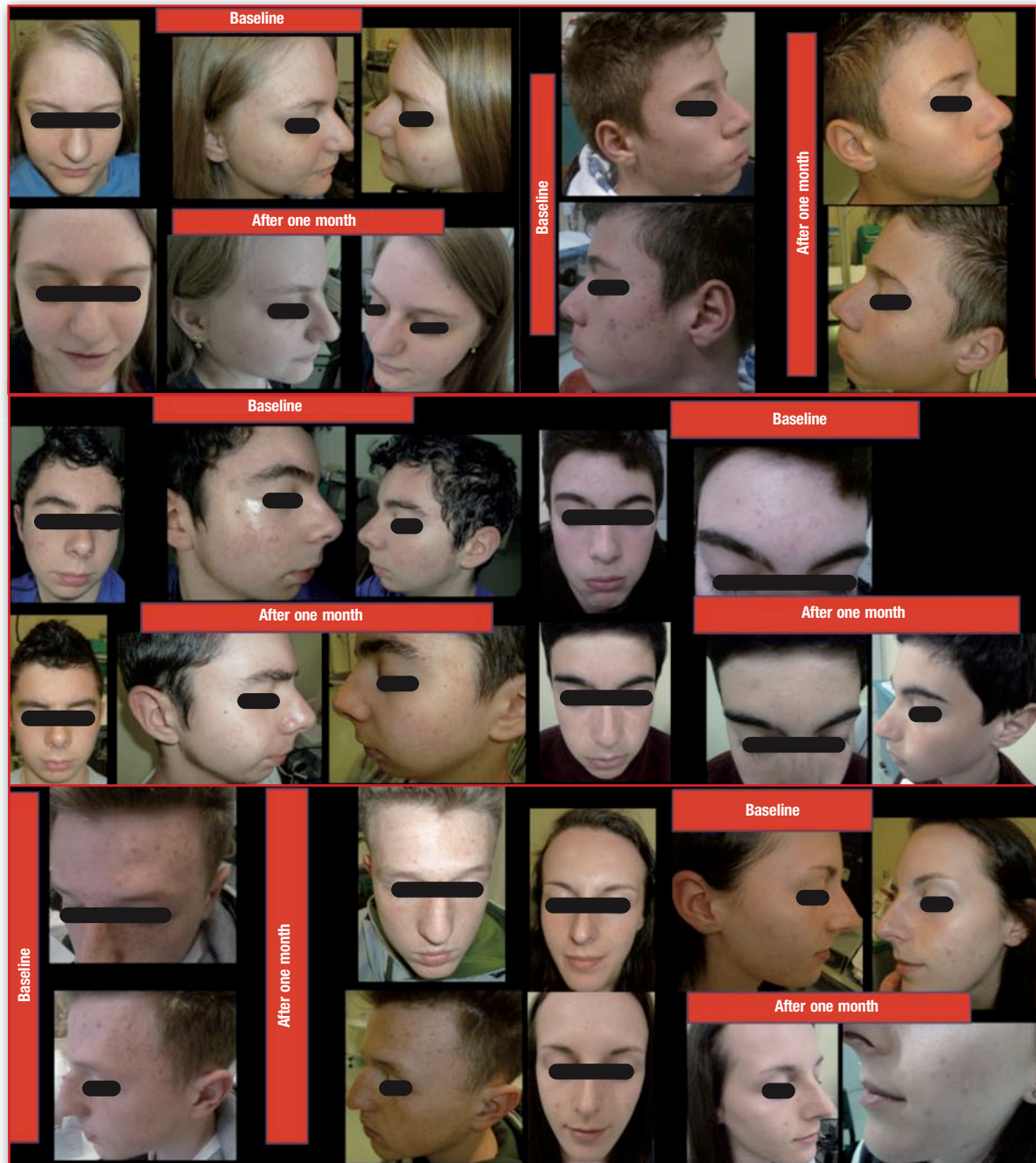
**GROUP B**

*Highly significant reduction in the number of lesions, inflammatory (especially).*

*T3\* visit performed only on 13 patients.*



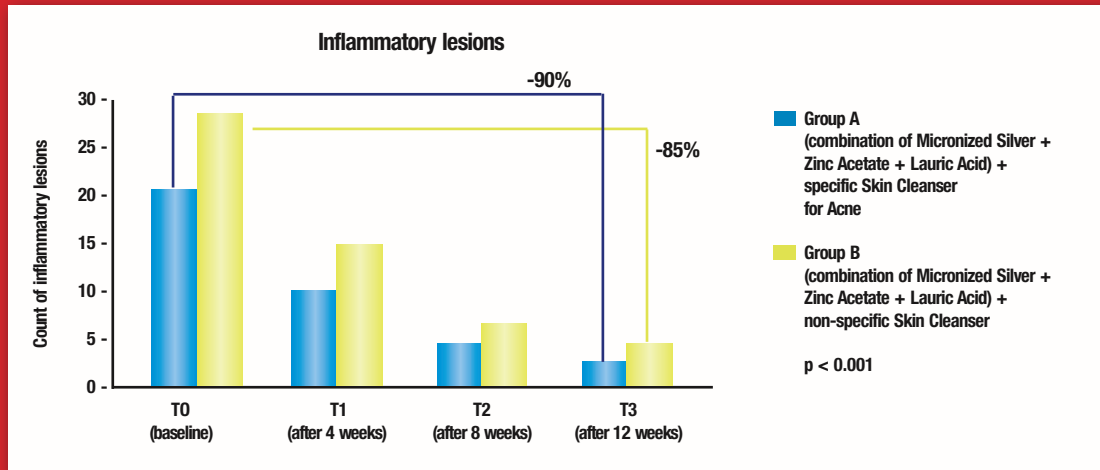
### *Clinical pictures*



### **Conclusions**

The combination of Micronized Silver + Zinc Acetate + Lauric Acid is effective in reducing acneic lesions, both inflammatory and non-inflammatory, in both treated groups.

The statistically significant reduction is more enhanced for inflammatory lesions and, however slightly, said reduction is more pronounced in the group combined with the specific cleansing agent



*T3\* visit performed only on 13 patients, Group A.  
T3\* visit performed only on 10 patients, Group B.*

for acneic skin (Group A). Sebum reduction is not highly significant in any of the two groups.

The IGA score is significantly reduced in both groups from the initial visit to the last follow-up visit. Treatment tolerability was excellent. The combination of Micronized Silver + Zinc Acetate + Lauric Acid might also be used in combination with a topical keratolytic/retinoid agent to boost its effi-

cacy in moderate acneic forms with an important comedo component. We can conclude that, considering its anti-inflammatory efficacy and excellent tolerability, the combination of Micronized Silver + Zinc Acetate + Lauric Acid might be an effective therapeutic option for slight-moderate acne vulgaris presenting an inflammatory component, without the onset of bacterial resistance!

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