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March 26-28, 1998

Tropical Dermatology Update, Acapulco, Mexico,  
June 2-4, 1998 (Rescheduled)

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## Clinical trial

# Clarithromycin versus doxycycline in the treatment of rosacea

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### Drug names

clarithromycin: Biaxin  
doxycycline: Vibramycin

Forty patients with rosacea were entered into a study comparing clarithromycin with doxycycline in the systemic treatment of mild and severe rosacea. The patients, 25 women and 15 men, aged from 26 to 62 years, were subdivided into two homogeneous groups with regard to age, sex, and disease severity. The first group of 23 patients, 14 women and 9 men, was treated with 250 mg of clarithromycin for 4 weeks twice daily, and then with 250 mg once daily for the following 4 weeks. The second group of 17 patients, 11 women and 6 men was treated with 100 mg of doxycycline for 4 weeks twice daily, and then with 100 mg once a day for the following 4 weeks. Both objective and subjective evaluations of the dermatosis were performed prior to therapy and after 4, 6, and 8 weeks of treatment.

## Objective evaluations

### Erythema

The erythema status was assessed by a colorimetric technique performed on color prints of the patients.<sup>1</sup> This system (Minolta Chromameter model CR 300, Osaka, Japan) enables the measurement of the skin color. Variations of erythema are represented by a single numerical value.<sup>1</sup>

### Telangiectases, papules, and pustules

The numbers and dimensions of telangiectases (TAE) were evaluated from the color prints and a score was assigned on the basis of the following scale: 0, no TAE; 1, less than five TAE located in the nasolabial sulcus and in the regio zygomatica; 2, 5–10 TAE located in the nasolabial sulcus and in the regio zygomatica; 3, between 10 and 20 confluent TAE; 4, 20–30 TAE, also diffused to the chin and forehead; 5, more than 30 TAE.

The numbers of papules and pustules were evaluated from the color prints and a score was assigned on the basis of the following scale: 0, no lesions; 1, less than 5 lesions; 2, 5–10 lesions; 3, 10–20 lesions; 4, 20–30 lesions; 5, more than 30 lesions.

## Subjective evaluations

Each patient was requested to express a subjective evaluation about the efficacy and tolerability of the treatment by assigning a score based on a scale ranging from 0 to 5. *Efficacy*: 0, no efficacy; 1, low efficacy; 2, traceable efficacy; 3, mild efficacy; 4, good efficacy; 5, high efficacy. *Tolerability*: 0, no side-effects; 1, occasional symptoms; 2, many symptoms; 3, mild side-effects; 4, severe side-effects; 5, very serious side-effects (inducing patients to discontinue the therapy).

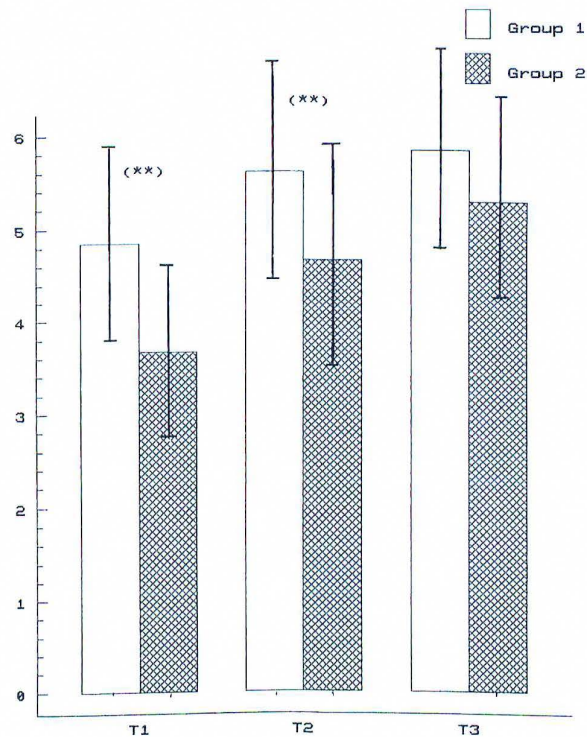
## Statistical methods

Statistical evaluation of the data collected from clarithromycin- and doxycycline-treated patients was performed by univariate and multivariate statistical analyses.

The mean values of the erythema index in the two groups of patients were compared by a Student's *t*-test, after 4 weeks (T<sub>1</sub>), 6 weeks (T<sub>2</sub>), and 8 weeks (T<sub>3</sub>) of therapy.

Nonparametric testing of the differences between the mean values of the other variables under examination (TAE, papules, pustules, efficacy, and tolerability) was carried out by a Mann-Whitney *U*-test.

The homogeneity of the two groups of patients was assessed by comparison, prior to treatment, of the mean



**Figure 1** Erythema. Mean values of  $\Delta E$  in clarithromycin- and doxycycline-treated groups of patients after 4, 6, and 8 weeks. At time T<sub>3</sub>, after 8 weeks of treatment, no significant difference was observed. Asterisks denote the level of statistical significance: \* $P < 0.05$ ; \*\* $P < 0.005$ ; \*\*\* $P < 0.0005$ .

TAE values and papule and pustule variables (no significant difference was expected at T<sub>0</sub>).

In addition, a multivariate statistical analysis was performed. According to the discriminant function method, a new variable was calculated for each patient, as a linear combination of the values obtained for erythema, TAE, papules, and pustules. The mean values of this new variable in the two groups of patients were statistically compared at T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub> by analysis of variance.

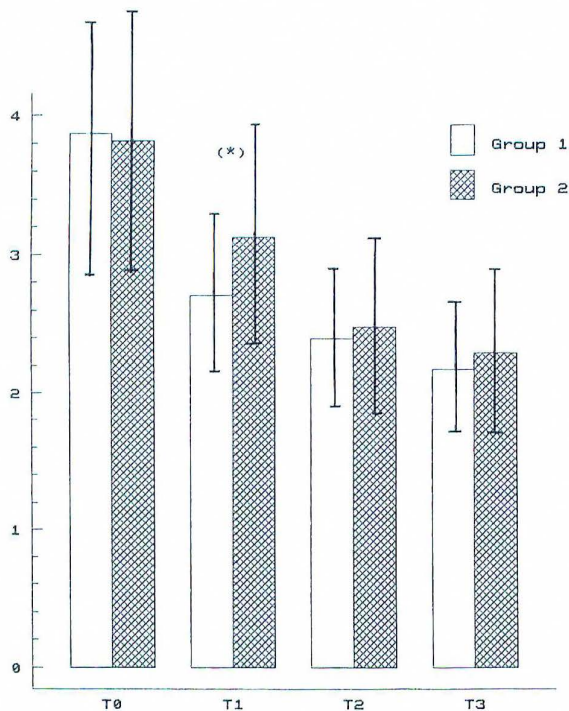
## Results

At the end of the treatment, the overall results provided evidence for a higher clarithromycin efficacy profile in comparison with doxycycline. The outcome assessment, based on the different parameters considered, revealed the following data.

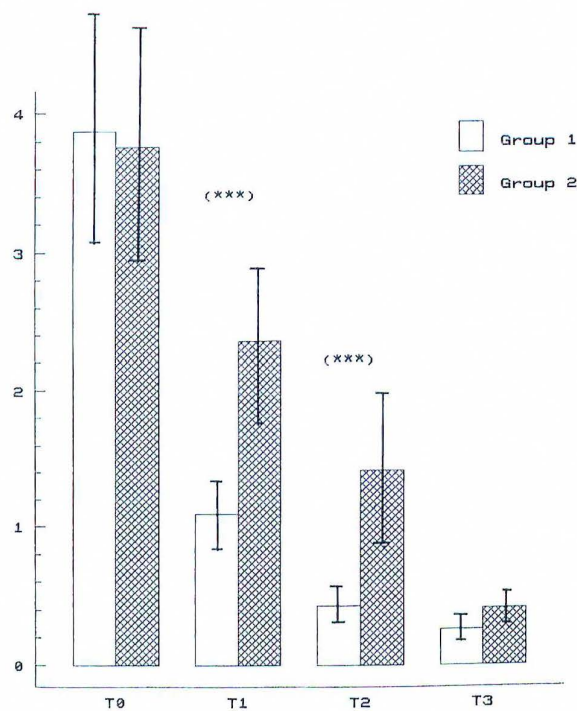
### Objective evaluations

#### Erythema (Fig. 1)

Figure 1 shows the significant difference ( $P < 0.005$ ) between the mean values of the erythema index in the two



**Figure 2** Telangiectases (TAE). Mean values of TAE score in the two groups of patients at T<sub>0</sub> (before starting treatment), T<sub>1</sub> (4 weeks of treatment), T<sub>2</sub> (6 weeks of treatment), and T<sub>3</sub> (8 weeks of treatment). Asterisks represent the level of statistical significance: \* $P < 0.05$ ; \*\* $P < 0.005$ ; \*\*\* $P < 0.0005$ . The homogeneity of the two groups is indicated by the lack of statistical significance at time T<sub>0</sub>



**Figure 3** Papules. Mean values of papule score in the two patient groups before starting treatment (T<sub>0</sub>) and after 4 weeks (T<sub>1</sub>), 6 weeks (T<sub>2</sub>), and 8 weeks (T<sub>3</sub>) of treatment. The homogeneity of the groups is indicated by the lack of statistical significance at time T<sub>0</sub>. Asterisks represent the level of statistical significance: \* $P < 0.05$ ; \*\* $P < 0.005$ ; \*\*\* $P < 0.0005$

groups of patients observed after both 4 and 6 weeks of treatment (mean  $\pm$  standard error). At time T<sub>3</sub>, after 8 weeks of treatment, no significant difference was demonstrated.

#### Telangiectases (Fig. 2)

A significant difference ( $P < 0.05$ ) between the mean values of the specific score evaluating the numbers and dimensions of TAE in the two groups of patients was observed after 4 weeks of treatment. No significant differences were demonstrated at T<sub>2</sub> and T<sub>3</sub>.

#### Papules (Fig. 3)

A significantly faster decrease ( $P < 0.0005$ ) of the mean score evaluating the number of papules was assessed in the clarithromycin-treated patients, when compared with the doxycycline-treated patients, after 4 and 6 weeks of therapy. No significant differences were found at T<sub>3</sub>.

#### Pustules (Fig. 4)

The results obtained from a statistical comparison between the mean values of the score evaluating the number of

pustules were found to be strictly similar to those reported for the number of papules. A significant difference ( $P < 0.0005$ ) between the effects of the two regimens was assessed at times T<sub>1</sub> and T<sub>2</sub>. A comparison of the mean values observed at the end of therapy did not reveal a level of statistical significance.

#### Subjective evaluations

##### Efficacy (Fig. 5)

No statistically significant differences were observed in the two groups of patients at T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>.

##### Tolerability (Fig. 6)

The total mean tolerability measured in Group 1 patients at the clarithromycin treatment rate used was equal to 0.32 (occasional side-effects). The total mean tolerability score measured in Group 2 patients at the doxycycline treatment rate used was equal to 1.06 (mild side-effects). A comparison of the mean values of the efficacy and tolerability

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