Gaias research

# Clinical evaluation of the safety and efficacy of the Milesman 445 nm blue laser on acne inflammatory lesions.

**RESEARCH PROTOCOL**

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# Clinical evaluation of the safety and efficacy of the Milesman 445 nm blue laser on acne inflammatory lesions.

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- **Principal investigator and co-investigators**

Principal investigator

José Luis Torregrosa

Co-investigators:

Sandra Rodríguez

Juan Amarelo

Laura Segura

- **Contact data**

Sponsor: Milesman

Project Manager: Gaias Research

## Abbreviations

| ABBREVIATION | DEFINITION |
|---|---|
| AC | Acne Vulgaris |
| AR | High Energy Light |
| HEL | High Energy Light |
| PDL | Pulsed Laser |
| SASS | Spanish Acne Severity Scale |

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# 1. CLINICAL REVIEW

## 1.1 Executive summary

This report summarizes the efficacy, safety and satisfaction obtained with application of the Milesman Blauman laser in patients with mild and moderate acne and inflammatory lesions (papules and pustules) on the face. This is a clinical trial with 25 subjects and representative population characteristics of facial acne followed for 14 days. After application of treatment with Milesman Blauman laser, a statistically significant reduction ($P<0.001$) was observed in the number of facial lesions of 69% at 72 hours (before/after 18.6 versus 5.5) and 83% (before/after 18.6 versus 3.0) at 7 days.

The procedure was safe, no relevant adverse effects appeared, and the degree of patient satisfaction with the procedure was widespread. To conclude, the Milesman Blauman laser is a therapeutically useful option to treat acne inflammatory lesions after a single laser session.

## 1.2 Rationale

### 1.2.1 The disease

Acne vulgaris (AV) is a polygenic multifactorial disease of the pilosebaceous glands, which leads to formation both of non-inflammatory (blackheads) and inflammatory lesions (papules, pustules, nodules and cysts) (1, 2), which affect approximately 85% of the population (3).

Its pathogeny involves follicular keratinization, production of denser keratin obstructs the pilosebaceous follicle, sebaceous hypersecretion, bacterial proliferation and inflammation.

Acne lesions can be classed as inflammatory (papule, pustule and nodule) and non-inflammatory (closed blackhead, open blackhead and post-inflammatory hyperpigmentation):

- Papule: raised erythematous lesion of < 1 cm (in general 1-5 mm)
- Pustule: raised lesion of < 1 cm with pus in its centre (in general 1-5 mm)
- Nodule: solid lesion of > 1 cm the colour of normal skin or erythematous and raised and/or induration on touch
- Closed blackhead: papule the colour of normal skin or white (in general 1 mm), without a follicular opening or associated erythema

- Open blackhead: papule with dilated follicular opening full of black keratin.
- Post-inflammatory erythema: erythematous macula
- Post-inflammatory hyperpigmentation: brown or light black macula

Although the morphological classification of acne lesions is simple to evaluate, grading the severity is extremely difficult. The Spanish Acne Severity Scale enables differentiating severity levels in accordance with number of lesions and correct sensitivity in the event of changes. The SASS is based on analysis of four photos for the facial scale. It is comfortable to use and dependable in routine clinical practice (4). It includes 4 degrees of severity; Grade 1 (mild) with blackheads and an isolated papule or pustule; Grade 2 (moderate) with blackheads, numerous papules and pustules, but involving less than 50% of the face; Grade 3 (severe) with blackheads, papules and pustules involving more than 50% of the face; some nodules may appear. Finally, Grade 4 (very severe) with inflammatory nodules that affect the entire face.

### 1.2.2 Current treatments

AV treatment includes topical or systemic use of medicines and physical treatment (1, 2).

The choice of pharmacological treatment (5) is based on the different aetiopathogenesis.

| THERAPEUTIC TARGET | PHARMACOLOGICAL TREATMENT |
|---|---|
| Abnormality in the follicular keratinization | Systemic retinoids and topical azelaic acid and alfa/beta hydroxy acids lead to keratolysis. |
| Sebaceous hypersecretion | Hormonal treatment with anti-androgens and isotretinoin act by reducing sebum production and the size of the sebaceous gland. |
| Bacterial proliferation | Topical and systemic antibiotics and benzoyl peroxide are of major use in these cases. |
| Inflammation | Isotretinoin and some antibiotics are used as anti-inflammatories. |

Physical treatment has been used as a complement to other treatments and includes physical methods such as extraction of blackheads, intralesional injection of corticosteroids, chemical

peeling and cryotherapy, treatments with light, laser, radiofrequency, heat sources and photodynamic treatment (6).

### 1.2.3 Uncovered needs

The slowness of the response and adverse effects of routine treatments has led to the need to research other treatments for acne.

## 2. RATIONALE FOR USE OF THE MILESMAN BLAUMAN LASER

The use of laser has different applications in medicine and the wavelength 445 nm has been positively evaluated in different studies, both because of its efficacy and safety (7-11).

Some systems used are based on the ability of porphyrins produced by P. acnes to absorb energy at spectra close to UV and blue light. This leads to photo-excitation, production of oxygen radicals and bacterial destruction (12).

Blue light optimized with broad spectrum 400 to 420 nm and with UV filters has a good photo-excitation coefficient for not so deep porphyrins. Red light (660 nm), which is also used (using oxyhaemoglobin as chromatophore), has a lower excitation coefficient but higher anti-inflammatory properties. A comparative work using blue light alone, blue/red light, white light and PB reveals at 3 months a 76% reduction in inflammatory lesions with the combination of lights, compared to 25% with white light. This treatment does not serve for managing blackheads (13). Another study (14) used phototherapy with a 585 nm laser and acne improved clinically in the 30 patients treated. Moreover, physical tolerance was good and few side effects were recorded.

There are other treatments used to manage inflammatory acne. They are diode laser (1450 nm), pulsed diode laser (PDL 585 nm), high energy light (HEL); in addition to radiofrequency associated with cryotherapy with liquid nitrogen (15, 16). The use of light sources and laser in acne therapy is based on different mechanisms of action:

- Photoactivation of endogenous porphyrins that P. acnes produce under normal conditions.
- Photothermolysis of the sebaceous gland when acting on water as a target.

- Reduction of inflammation by the selective photothermolysis phenomenon on melanin and haemoglobin. In addition, promotion of anti-inflammatory immune responses.

Therefore, according to the light therapy wavelength, absorption is determined; that is, the light reaction with the tissue and the mechanism of action on the acne.

Acne treatment with laser or other light devices is a currently accepted procedure (17). It enables faster resolution of lesions with less collateral effects and greater patient satisfaction (18). Currently commercialized light devices use incoherent light sources or laser light sources (coherent). Their use has been observed not only in active lesions but also in scars (19, 20). The past few decades has meant major progress in the development of new therapeutic methods in the field of light sources, laser and photodynamic therapy to treatment acne (21).

## 3. THE EVALUATION OF THE MILESMAN BLAUMAN LASER'S EFFICACY TO TREAT ACNE

This was performed according to the protocol approved by the AEMPS and Galicia CREC

### 3.1 Methodology

#### 3.1.1 Design of the trial

This is a single-arm, interventionist, prospective, open-label, before and after, quasi-experimental, analytical study. This design is based on measurement and comparison of the response variable before and after the subject's exposure to the experimental intervention. It enables the investigator being able to manipulate exposure with just one group but does not include a comparison group. Each subject acts as their own control. We avoid injuring the patient by only treating part of the face.

This is a national, single centre trial that includes outpatient adult patients previously diagnosed with mild to moderate acne and not receiving any pharmacological treatment for this.

##### 3.1.1.2 Patient recruitment

###### 3.1.1.2.1 Inclusion criteria

- Adults aged 18 to 50
- Diagnosis of mild to moderate acne on the face

- Have 10-50 inflammatory lesions (papules and pustules) on the face
- Be in good health

##### 3.1.1.3.1.1 Exclusion criteria

- Allergies or sensitivity to light
- Severe acne or pre-existing dermatological facial involvement
- Existence of cysts on the face
- More than one nodule on the face
- Have uncontrolled disease or immunodeficiency
- Pregnant or breastfeeding
- Oral and/or topical antibiotic treatment in the last two weeks.
- Current treatment with hormonal contraceptives.
- Impossibility of avoiding excessive exposure to the sun and any treatment with light or any similar professional or aesthetic procedure during the two weeks prior and two weeks after the treatment.
- Previous history of wounds not fully cured, keloid formation or haemorrhagic disorders
- Process of active infection or history of herpes simplex.
- Extreme sensitivity to hydroquinone or other whitening agents.
- Personal or family history of melanoma.
- Dysplastic naevus.

Given the design of this study, no criteria for premature termination of the trial was foreseen, given that all patients received a single laser session. Those patients unable to attend revision and unable to undergo controls for the set visits except the safety visit (phone) will be withdrawn from the study. In the end no patient was withdrawn from the study. All patients were able to complete all visits and their variables were correctly collated.

#### 3.1.1.3 Capture and recruitment

The doctor decided on the suitability of including the patient. When the patient came to the dermatology consultation the doctor notified them of the aim, design, risks and benefits of the study. The patient signed the informed consent form freely and according to Rules of Good Clinical Practice.

#### 3.1.1.4 Size of the sample

The sample was calculated to reveal a statistically significant difference between values before and after treatment using a student *t* test for paired values (number of lesions). We expected

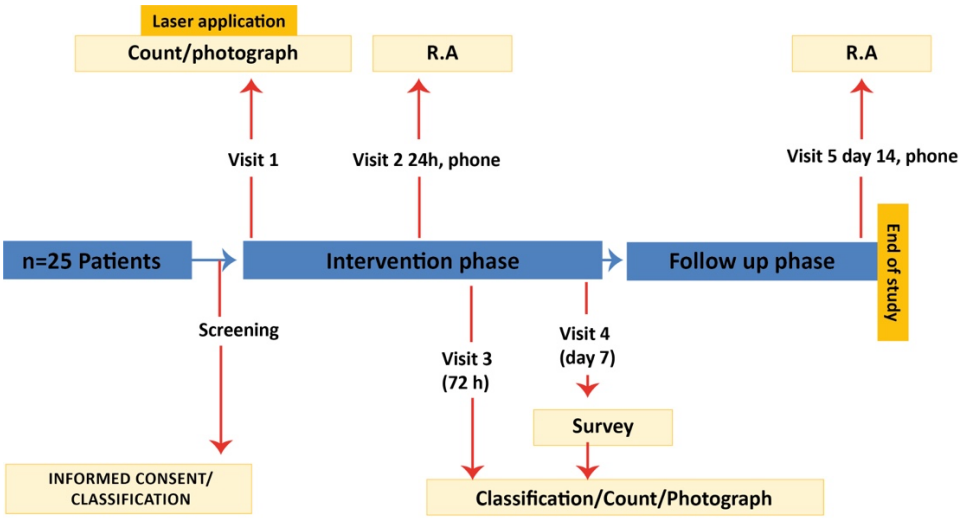
to see an effect of 60% reduction in lesions, whereby we needed n=25 (number of pairs) to attain a power of 80% and a significance level of 5% (two sides), to detect an effect size of 0.6 between pairs.

According to the inclusion and exclusion criteria for each case we should obtain 10 to 50 inflammatory lesions when treating with the laser, whereby at the end of the study at least 250 lesions would have been treated. In the end 467 lesions obtained from 25 samples (n) were treated.

### 3.1.2 Study duration

A study duration of three months from recruiting the first patient was calculated. As set out the COVID-19 pandemic affected the study onset and duration. In the end the study lasted four months and the start was delayed until October. The corresponding insurance policy was extended at the time.

*MILESMAN-ACNE Clinical Trial*




**MILESMAN-ACNE Clinical Trial**

### 3.1.1 Description of the procedure

All investigators who handled this device underwent prior training given by the sponsor. Before each session the following parameters were set out in the team:

- Watts: 2-3 w
- Pulse duration: 50-70 milliseconds
- Inter-pulse time: 100 milliseconds between shots

The Milesman laser has a hand piece, which enables pointing at each lesion by means of an indicator light and the person handling it activates the shot with a pedal. A maximum of 10 shots, according to size and type of lesion, was applied to each acne lesion.

Finally, 2-3 shots were applied to photocoagulate the follicle walls and thereby avoid the lesion relapsing or reinfecting (bactericide action) with the parameters indicated to the research team (7-8 w; long distance head; pulse: 50-70 milliseconds). At the researcher's discretion and to facilitate application of the laser in samples with numerous lesions, laser application was permitted as a sweep of the area; as long as each lesion received 2-3 shots.

The laser was applied to all facial inflammatory lesions in just one session. The session's duration was estimated at approximately 20 minutes according to the number of lesions.

Everyone exposed to the laser used laser goggles with nominal optical density, appropriate for the Milesman Blauman wavelength, provided by the sponsor according to the investigator's brochure.

At visit 1, at most 10 pulses were fired (plus 2-3 bactericidal action) on each patient's acne inflammatory lesion. The area to treat was the patient's entire face.

### 3.1.4 Outcome variables

#### 3.1.4.1 Primary endpoint

The most important variable in this study is the number of acne lesions in the selected patient area.

#### 3.1.4.2 Secondary endpoints

The following exploratory-descriptive variables were also collated.

- Modification on the SASS scale classification
- Degree of patient satisfaction (survey).
- Adverse events during the study period

### 3.1.5 Study aim

#### 3.1.5.1 Primary aim

The primary aim was to reveal a significant reduction in the number of lesions at 72 hours comparing the values before and after the treatment

#### 3.1.5.2 Exploratory aims

To reveal a significant reduction in the number of lesions at 7 days comparing the values before and after the treatment

Report the change in class on the SASS scale comparing values before and after treatment at 72 hours and 7 days

### 3.1.6 Statistical analysis

The significance of the difference between the number of lesions before and after the treatment was analyzed using the *t*-test for paired values if the difference has a normal distribution. The effect size (Cohen's d effect size) will also be calculated. To analyze the normality of the distribution the Shapiro-Wilk (a=0.05) test will be used: If distribution of the difference were not normal the non-parametric Wilcoxon contrast test would be used for paired values (before/after). A descriptive analysis of the remaining values collated was performed.

### 3.1.7 Subjects to include in the analysis

All subjects for whom there is a valid result for the study's primary endpoint, in this case all the patients, were included in the analysis. (n=25)

### 3.1.8 Lost data

Lost data will be processed as such and no method to attribute lost values was used. Only in the case when lost data did not enable evaluating the primary endpoint will the subject be eliminated from the analysis. This did not occur and no patient had to be removed from the study.

## 3.2 Procedures

### 3.2.1 Obtaining informed consent

According to rules of Good Clinical Practice.

### 3.2.2 Patient screening: Review of all inclusion and exclusion criteria

Patient clinical history: History, age, sex, relevant history.

### 3.2.3 Classification of the acne on the SASS scale by a specialist.

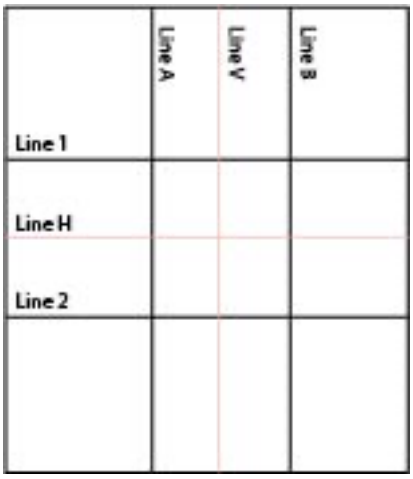
The sponsor provided the scale with the corresponding photos to classify acne according to the SASS scale. If eligible, a patient code will be assigned according to that specified in the patient inclusion list to ensure anonymity of the data collated.

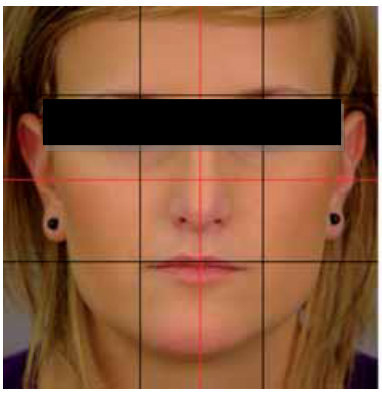
### 3.3. Taking of photos:

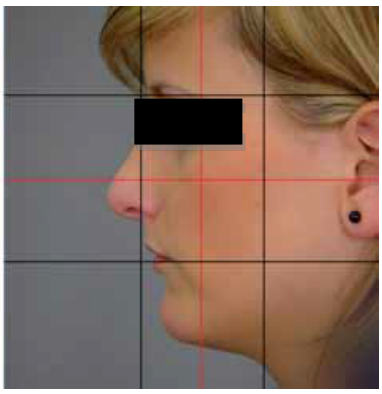
Photos were taken according to the technique reported by F Solesio in (Cir.plást. iberolatinoam. - Vol. 35 - No. 2/Page. 79-9). Photos were used as support material for the researcher both for counting lesions and classifying acne. For correct interpretation of these it was important to adhere to the following methodology:

- The same camera was always used (provided by the sponsor),
- All photos were taken in the same closed room and with the same light blue or medium grey background (provided by the sponsor)
- The background should be lit to remove the patient's shadow
- A flash attached to the camera will be used
- A frontal photo and two lateral photos at 90° (left and right)
- Guidelines that help to better frame the photo's motif and reveal asymmetry will be used. We will call the horizontal middle and vertical lines, H and V respectively, A and B the vertical separating lines and 1 and 2 the horizontal lines for separation of thirds (Fig. 2)
- Orientation of the camera: Vertical
- Camera height: On the patient's Frankfort horizontal line
- Distance: 1 metre from the patient
- Speed: At least 1/125. If lower, use the tripod
- Opening: Sufficient to attain speeds of 1/125 or slightly above
- Patient positions: Standing, in anatomical position looking at the horizon with front views
- Zoom: That necessary so that lines 1 and 2 coincide with the eyebrows and mouth, respectively (approximately X3)
- Frame limits: From the neck to the scalp
- Focal point: Eyelashes
- Reference points:
- Line 1 on the eyebrows and line 2 on the mouth.
- Front photo: Sagittal midline on line V

- Lateral photo (90a): V line passing through the external lateral of the eye and H through the external auditory conduct





Once the photo is taken the photo's biometric data were made anonymous by means of a computer programme. This positions an opaque element over the eyes that should be large enough to cover the area (see above photo). Any copy of the original photo was eliminated. The anonymous photo was stored in a protected format so that it cannot be manipulated subsequently.

The investigator team received training on how to take photos, make them anonymous and store them in the investigator file. Once the study was completed, they will be stored for a period set by prevailing legislation. They will be subsequently destroyed.

## 4. ETHICS AND LEGAL ASPECTS OF THE STUDY

This study focused at all times on the biomedical research law (Spanish Law 14/2007) and the Basic Regulator Law of Patient Autonomy and Rights and Obligations on Clinical Information and Documentation (Spanish Law 41/2002) and the Helsinki Declaration and Oviedo Agreement. This study will also focus on Spanish Law 3/2001, of 28 May, which regulates informed consent and patients' clinical histories.

All data collated in this project were recorded pseudo-anonymously and will be processed in accordance with prevailing laws and regulations on data protection (EU Regulation 2016/679 of the European Parliament and Council, of 27 April 2016, in regard to protection of physical persons as to processing of personal data and free circulation of these data and by which Directive 95/46/EC and Spanish Organic Law 3/2018, of 5 December on Protection of Personal Data and guarantee of digital rights) are repealed. With the purpose of protecting the identity of patients and maintaining the confidentiality of this personal information it is guaranteed that: a) all personal data collated in the framework of this study, including tests that enable identifying patients will be kept and stored separately in technical and functional terms from pseudo-anonymous data; b) each study patient will be randomly assigned an identification code that will be the one that appears on the databases. The relationship between the patient code and his clinical history will remain solely in the records of the site that recruited this patient, such that only the study's principal investigator can establish a relationship between the patient code and his identity. Therefore, no personal data that enables identifying the patient will be accessible to anybody other than the principal investigator, nor will they be aggregate and never individual form; d) all investigators involved in the study hereby undertake to comply with the necessary rules to keep personal data and any other information provided confidential; and (e) all study databases will be protected by means of specific technical and organisational safety information aimed at avoiding repeat identification and unauthorized third party access, which limits access solely to project investigators.

The sponsor hereby undertakes to store all the source information and documents from this study in a safe place and for the period set by prevailing legislation. The sponsor will make this information available to the competent authorities in case of the corresponding audit and inspections.

## 5. RESULTS

### 5.1 Characteristics of the population

Age and sex characteristics of cases, number of inflammatory lesions on the face and the SASS scale of lesions are shown in Table 1. The mean age was 24.8 (SD, 6.5), distribution by sex (M/F) was 10/15. All of them had mild or moderate involvement in accordance with the SASS. No patient included was receiving oral or topical medication for his acne.

*Table 1: Characteristics of the population*

| SAMPLE | AGE | SEX (M/F) | Nº LESIONS PRE-TREATMENT | SASS PRE- TREATMENT |
|---|---|---|---|---|
| MILESMAN-01 | 19 | H | 37 | 2 |
| MILESMAN-02 | 40 | M | 12 | 1 |
| MILESMAN-03 | 18 | M | 28 | 2 |
| MILESMAN-04 | 18 | H | 21 | 2 |
| MILESMAN-05 | 21 | M | 10 | 1 |
| MILESMAN-06 | 19 | H | 23 | 2 |
| MILESMAN-07 | 22 | M | 12 | 1 |
| MILESMAN-08 | 22 | M | 14 | 1 |
| MILESMAN-09 | 28 | M | 15 | 1 |
| MILESMAN-10 | 23 | H | 17 | 2 |
| MILESMAN-11 | 19 | H | 27 | 2 |
| MILESMAN-12 | 18 | M | 30 | 2 |
| MILESMAN-13 | 30 | H | 10 | 1 |
| MILESMAN-14 | 23 | H | 27 | 2 |
| MILESMAN-15 | 19 | H | 29 | 2 |
| MILESMAN-16 | 39 | M | 11 | 1 |
| MILESMAN-17 | 30 | M | 10 | 1 |
| MILESMAN-18 | 24 | M | 12 | 1 |
| MILESMAN-19 | 23 | H | 22 | 2 |
| MILESMAN-20 | 31 | M | 12 | 1 |
| MILESMAN-21 | 23 | M | 12 | 1 |
| MILESMAN-22 | 24 | M | 17 | 1 |
| MILESMAN-23 | 37 | M | 10 | 1 |
| MILESMAN-24 | 23 | M | 29 | 2 |
| MILESMAN-25 | 23 | H | 20 | 2 |

## 5.2 Primary aim

The number of lesions before and after treatment at 72 hours and their differences are shown in Table 2.

The mean (SD) number of lesions pre-treatment and at 72 hours was 18.7 (8.0) and 5.9 (5.7), respectively. The before/after difference was 12.8 (7.4), represents a reduction in the number of lesions of 69% and has a normal distribution with a *P* value 0.0879 in accordance with the Shapiro-Wilk test (a=0.05). In accordance with the test for comparison of paired *t* values this attains the level of statistical significance (*P*<0.001), with a large effect size (1.7, Cohen's d effect size). Therefore, the study's primary aim was attained.

*Table 2. Differences in the number of lesions 72 hours from treatment*

| SAMPLE | Nº. LESIONS AT PRE-TREATMENT | Nº. LESIONS AT 72H | DIFFERENCE N IN LESIONS |
|---|---|---|---|
| MILESMAN-01 | 37 | 12 | 25 |
| MILESMAN-02 | 12 | 11 | 1 |
| MILESMAN-03 | 28 | 6 | 22 |
| MILESMAN-04 | 21 | 8 | 13 |
| MILESMAN-05 | 10 | 5 | 5 |
| MILESMAN-06 | 23 | 16 | 7 |
| MILESMAN-07 | 12 | 0 | 12 |
| MILESMAN-08 | 14 | 4 | 12 |
| MILESMAN-09 | 15 | 2 | 13 |
| MILESMAN-10 | 17 | 2 | 15 |
| MILESMAN-11 | 27 | 4 | 23 |
| MILESMAN-12 | 30 | 26 | 4 |
| MILESMAN-13 | 10 | 1 | 9 |
| MILESMAN-14 | 27 | 3 | 24 |
| MILESMAN-15 | 29 | 5 | 24 |
| MILESMAN-16 | 11 | 6 | 5 |
| MILESMAN-17 | 10 | 7 | 3 |
| MILESMAN-18 | 12 | 6 | 6 |
| MILESMAN-19 | 22 | 4 | 18 |
| MILESMAN-20 | 12 | 4 | 8 |
| MILESMAN-21 | 12 | 3 | 9 |
| MILESMAN-22 | 17 | 1 | 16 |
| MILESMAN-23 | 10 | 3 | 7 |
| MILESMAN-24 | 29 | 7 | 22 |
| MILESMAN-25 | 20 | 2 | 18 |

### 5.3 Exploratory aims

The number of lesions before and after treatment at 7 days and their differences is shown in Table 3.

The mean (SD) number of lesions pre-treatment and at 7 days was 18.7 (8.0) and 3.08 (3,13), respectively. The before/after difference was 15.5 (7.6) and represents a reduction in the number of lesions of 83% and has a normal distribution with a *P* value 0.0879 in accordance with the Shapiro-Wilk test (a=0.05). In accordance with the test to compare paired *t* values this attains statistical significance (*P*<0.001), with a large size effect (2.06, Cohen's d effect size).

*Table 3. Differences in the number of lesions at 7 days from treatment*

| SAMPLE | Nº. LESIONS AT PRE-TREATMENT | Nº. LESIONS AT 7 DAYS | DIFFERENCE N IN LESIONS |
|---|---|---|---|
| MILESMAN-01 | 37 | 3 | 34 |
| MILESMAN-02 | 12 | 9 | 3 |
| MILESMAN-03 | 28 | 6 | 22 |
| MILESMAN-04 | 21 | 2 | 19 |
| MILESMAN-05 | 10 | 3 | 5 |
| MILESMAN-06 | 23 | 2 | 21 |
| MILESMAN-07 | 12 | 0 | 12 |
| MILESMAN-08 | 14 | 2 | 12 |
| MILESMAN-09 | 15 | 1 | 14 |
| MILESMAN-10 | 17 | 0 | 17 |
| MILESMAN-11 | 27 | 4 | 23 |
| MILESMAN-12 | 30 | 14 | 16 |
| MILESMAN-13 | 10 | 1 | 9 |
| MILESMAN-14 | 27 | 1 | 26 |
| MILESMAN-15 | 29 | 7 | 22 |
| MILESMAN-16 | 11 | 4 | 7 |
| MILESMAN-17 | 10 | 3 | 7 |
| MILESMAN-18 | 12 | 3 | 9 |
| MILESMAN-19 | 22 | 1 | 21 |
| MILESMAN-20 | 12 | 3 | 9 |
| MILESMAN-21 | 12 | 2 | 10 |
| MILESMAN-22 | 17 | 2 | 15 |
| MILESMAN-23 | 10 | 0 | 10 |
| MILESMAN-24 | 29 | 3 | 26 |
| MILESMAN-25 | 20 | 1 | 19 |

The variation in the SASS at 72 hours and 7 days after the treatment is shown in Table 4.

There was a tendency to improvement or stabilization of lesions. There was no worsening in either case. At the end of the study 17 patients were at level 1 of the scale.

*Table 4. The variation in SASS at 72 hours and 7 days after treatment*

| SAMPLE | SASS PRE-TREATMENT | Nº. LESIONS AT 72 HOURS | SASS AT 7 DAYS |
|---|---|---|---|
| MILESMAN-01 | 2 | 2 | 2 |
| MILESMAN-02 | 1 | 1 | 1 |
| MILESMAN-03 | 2 | 2 | 2 |
| MILESMAN-04 | 2 | 2 | 1 |
| MILESMAN-05 | 1 | 1 | 1 |
| MILESMAN-06 | 2 | 2 | 2 |
| MILESMAN-07 | 1 | 1 | 1 |
| MILESMAN-08 | 1 | 1 | 1 |
| MILESMAN-09 | 1 | 1 | 1 |
| MILESMAN-10 | 2 | 2 | 2 |
| MILESMAN-11 | 2 | 2 | 2 |
| MILESMAN-12 | 2 | 2 | 2 |
| MILESMAN-13 | 1 | 1 | 1 |
| MILESMAN-14 | 2 | 1 | 2 |
| MILESMAN-15 | 2 | 2 | 2 |
| MILESMAN-16 | 1 | 1 | 1 |
| MILESMAN-17 | 1 | 1 | 1 |
| MILESMAN-18 | 1 | 1 | 1 |
| MILESMAN-19 | 2 | 1 | 1 |
| MILESMAN-20 | 1 | 1 | 1 |
| MILESMAN-21 | 1 | 1 | 1 |
| MILESMAN-22 | 1 | 1 | 1 |
| MILESMAN-23 | 1 | 1 | 1 |
| MILESMAN-24 | 2 | 1 | 1 |
| MILESMAN-25 | 2 | 1 | 1 |

## 6. SAFETY OF THE MILESMAN BLAUMAN LASER

The penetration capacity of the 445 nm laser in the skin is very superficial and only reaches the epidermis. The laser's own action mechanisms leads to a controlled microabrasion of the epidermis.

Nonetheless, the laser can cause damage to healthy skin. The risk may be greater according to the laser's increased yield. In general, in the next few days it can be observed as a response to swelling or redness of the area that in the next few days may turn into a scab just like a wound.

Therefore, expected intrinsic adverse effects are:

- Swelling
- Redness of the area

This study collated all adverse effects related to application of the laser exception swelling and redness of the area, which are intrinsic to the treatment. All those severe and unexpected adverse effects were also collated.

Adverse effects were collated either at in-person or phone visits.

Patients included did not have any adverse effect except for local reactions in the treatment area.

The areas treated were with a maximum sun protection cream.

## 7. SATISFACTION

Patient satisfaction with the treatment was evaluated by means of the survey, which was filled in and sent at visit 4. The survey (23) is a specific survey for patients with acne and it was adapted to use in this study (as an appendix). The result and answers are shown in Table 5.

Overall results reflected that there was improvement or significant improvement (Table 5). A total of 92% reported that they had improved in terms of number of lesions and 59% had improved pain.

Only once was there a negative answer to questions: How satisfied are you with your current acne in regard to your social life? Are you satisfied with the treatment's efficacy? and Are you satisfied with how often the current treatment has to be administered for acne?

The assignation of a score from 5 to 1 respectively to the response scales Significantly improved, Improved, Neither improved nor worsened, Worsened, Significantly worsened, enabled calculating an overall score for the answers (Table 6). The mean result was 4.39 on a total average score of 5. It can be concluded that the degree of satisfaction of patients recruited to the study was high.

*Table 5. Degree of satisfaction of the population of treated patients*

| 1. In regard to symptoms you had before starting the current treatment | *A:* Significantly improved. *n (%)* | *B* Improved *n (%)* | C Neither improved nor worsened *n (%)* | D: Worsened *n (%)* | *E:* Significantly worsened. *n (%)* | *F:* No procede. No |
|---|---|---|---|---|---|---|
| 1.1 Spots (no blackheads) | 5 (20) | 18 (72) | 2 (8) | 0 | 0 | 0 |
| 1.1. Pain: | 4 (21) | 7 (36,8) | 8 (42,1) | 0 | 0 | 6 |
| | **a) Very satisfied n (%)** | **b) Satisfied. n (%)** | **c) Neither satisfied nor dissatisfied n (%)** | **d) Dissatisfied n n (%)** | **e) Very dissatisfied (%)** | |
| 2. How satisfied are you with the information provided by your doctor on your current acne treatment? | 22 (88) | 3 (12) | 0 | 0 | 0 | 0 |
| 3. How satisfied are you with your current acne treatment in regard to your mood? | 12 (48) | 7 (28) | 5 (20) | 1 (4) | 0 | 0 |
| 4. How satisfied are you with your current acne treatment in regard to your social life (going out with friends, going to the theatre, going for a | 6 (24) | 13 (52) | 5 (20) | 0 | 1 (4) | 0 |
| 5. Are you satisfied with the treatment's efficacy (reduction of number of spots, pain, itching, burning, etc.)? | 9 (36) | 13 (52) | 1 (4) | 1 (4) | 1 (4) | 0 |
| 6. Are you satisfied with the safety (adverse effects) of your acne treatment? | 17 (68) | 7 (28) | 1 (4) | 0 | 0 | 0 |
| 7. Are you satisfied with the mode of administration of your current acne treatment? | 18 (72) | 6 (24) | 1 (4) | 0 | 0 | 0 |
| 8. Are you satisfied with how often your current acne treatment has to be administered? | 18 (72) | 5 (20) | 1 (4) | 1 (4) | 0 | 0 |
| 9. In general are you satisfied with your current acne treatment? | 11 (44) | 12(48) | 2 (8) | 0 | 0 | 0 |
| | a) Completely agree. n (%) | b) Agree. n (%) | c) Neither agree nor disagree. n (%) | d) Disagree. n (%) | e) Completely disagree. n (%) | |
| 10. Would you be willing to undergo this acne treatment again if necessary? | 18 (72) | 5 (20) | 2 (8) | 0 | 0 | 0 |
| 11. Would you recommend the treatment to other acne sufferers? | 18 (72) | 5 (20) | 2 (8) | 0 | 0 | 0 |

*Table 6. Score assigned to each answer from Table 5. Include the study's final evaluation.*

| 1. In regard to symptoms you had before starting the current treatment | *A:* Significantly improved. *n (%)* | *B* Improved *n (%)* | C Neither improved nor worsened *n (%)* | D: Worsened *n (%)* | *E:* Significantly worsened. *n (%)* |
|---|---|---|---|---|---|
| 1.1 Spots (no blackheads) | 5 | 4 | 3 | 2 | 1 |
| 1.2. Pain: | 5 | 4 | 3 | 2 | 1 |
| | **a) Very satisfied n (%)** | **b) Satisfied. n (%)** | **c) Neither satisfied nor dissatisfied n (%)** | **d) Dissatisfied n n (%)** | **e) Very dissatisfied (%)** |
| 2. How satisfied are you with the information provided by your doctor on your current acne treatment? | 5 | 4 | 3 | 2 | 1 |
| 3. How satisfied are you with your current acne treatment in regard to your mood? | 5 | 4 | 3 | 2 | 1 |
| 4. How satisfied are you with your current acne treatment in regard to your social life (going out with friends, going to the theatre, going for a | 5 | 4 | 3 | 2 | 1 |
| 5. Are you satisfied with the treatment's efficacy (reduction of number of spots, pain, itching, burning, etc.)? | 5 | 4 | 3 | 2 | 1 |
| 6. Are you satisfied with the safety (adverse effects) of your acne treatment? | 5 | 4 | 3 | 2 | 1 |
| 7. Are you satisfied with the mode of administration of your current acne treatment? | 5 | 4 | 3 | 2 | 1 |
| 8. Are you satisfied with how often your current acne treatment has to be administered? | 5 | 4 | 3 | 2 | 1 |
| 9. In general are you satisfied with your current acne treatment? | 5 | 4 | 3 | 2 | 1 |
| | a) Completely agree. n (%) | b) Agree. n (%) | c) Neither agree nor disagree. n (%) | d) Disagree. n (%) | e) Completely disagree. n (%) |
| 10. Would you be willing to undergo this acne treatment again if necessary? | 5 | 4 | 3 | 2 | 1 |
| 11. Would you recommend the treatment to other acne sufferers? | 5 | 4 | 3 | 2 | 1 |

**Calculation overall score: sum of points/no. of completed answers**

**Average mark for the study's satisfaction out of 5: 4.39**

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## 9. APPENDICES

Questionnaire of patient satisfaction with the treatment

We are interested in knowing a few things about you and your health. Please answer all questions personally marking with an X the answer best applicable to your case. There are no "right" or "wrong" answers. The information you give us will be treated as strictly confidential.

Please initial:
Your date of birth (day, month, year):
Today's date (day, month, year):

**You have to mark the best applicable answer with an "X"**

**Question 1.**
*In regard to symptoms you had before starting the current treatment*

1.1. Spots (no blackheads)

| A) Significantly improved, | B) Improved | C) Neither improved nor worsened | D) Worsened | E) Significantly worsened |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

1.1 Pain:

| A) Significantly improved, | B) Improved | C) Neither improved nor worsened | D) Worsened | E) Significantly worsened |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 2.**
*How satisfied are you with the information provided by your doctor on your current acne treatment?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 3.**
*How satisfied are you with your current acne treatment in regard to your mood?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 4.**

*How satisfied are you with your current acne treatment in regard to your social life (going out with friends, going to the theatre, going for a walk, etc)?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 5.**

*Are you satisfied with the treatment's efficacy (reduction of number of spots, pain, itching, burning, etc.)?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 6.**

*Are you satisfied with the safety (adverse effects) of your acne treatment?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 7.**

*Are you satisfied with the mode of administration of your current acne treatment?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 8.**

*Are you satisfied with how often your current acne treatment has to be administered?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 9.**
*In general are you satisfied with your current acne treatment?*

| A) Very satisfied | B) Satisfied. | C) Neither satisfied nor dissatisfied | D) Dissatisfied | E) Very dissatisfied |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 10.**
*Would you be willing to undergo this acne treatment again if necessary?*

| A) Completely agree | B) Agree | C) Neither agree nor disagree | D) Disagree | E) Completely disagree |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**Question 11.**
*Would you recommend the treatment to other acne sufferers?*

| A) Completely agree | B) Agree | C) Neither agree nor disagree | D) Disagree | E) Completely disagree |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |


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