A LED BLUE LIGHT DEVICE WITH SPECIFIC PHOTOCONVERTER CROMOPHORES COMBINED WITH SYSTEMIC DRUGS: EFFICACY AND SAFETY IN THE TREATMENT OF MODERATE TO SEVERE ACNE.

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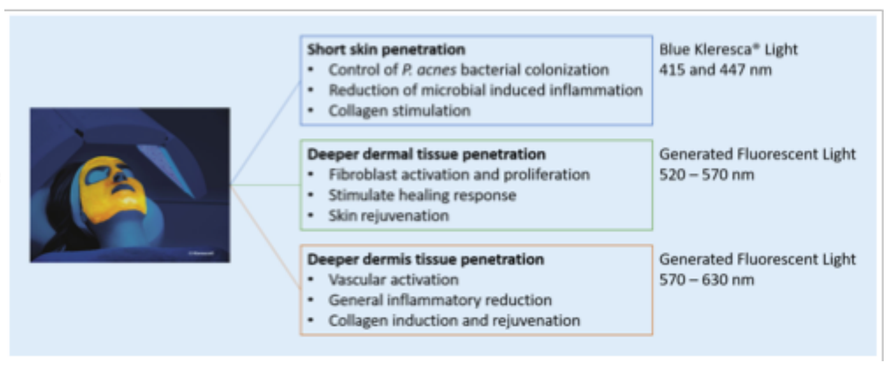
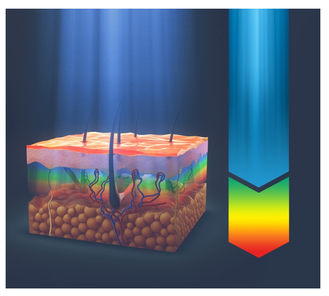
Acne is one of the most frequent skin diseases. The estimated prevalence of acne in adolescents living in Western industrialized countries ranges between 50% and 95% and the only moderate or severe manifestations represent the 20–35% of the total.
At present, systemic isotretinoin is considered the first-choice treatment for severe acne for clinical effectiveness, prevention of scarring and quick improvement of a patient's QOL. Systemic antibiotics are recommended for the treatment of severe papulo-pustular acne.
Visible light as monotherapy is not recommended for the treatment of conglobate acne even if blue light monotherapy could be considered for the treatment of mild to moderate papulo-pustular acne, but with a low strength of recommendation.
However, the efficacy of a novel treatment with LED blue light device (415/446 nm), using specific photo-converter chromophores contained in a gel (LED/gel), has been described in the treatment of acne, but never combined with systemic drugs.
Our objective is to describe the efficacy and safety of the combination of LED/gel with systemic drugs such as low-dose isotretinoin or tetracycline in moderate to severe acne in patients not eligible to standard dose of retinoids or in whom a tetracycline combined with topical drugs could not be sufficient.

WAY OF ACTION

The chromophore gel-assisted light therapy is based on photophysical reactions between a photoconverter gel and a blue light.
A thin layer of a topical Photo Converter Gel containing specific chromophores (light-absorbing molecules mainly composed of eosin), which are not absorbed by the skin, is topically applied to the targeted skin area.
The gel is subsequently illuminated by a Multi-LED lamp delivering non-coherent blue light with an optimized peak wavelength and fluency at a distance of 5 cm from the skin surface (power density of 150 mW/cm2) for a duration of 9 min per facial subunit to ensure complete facial coverage.
The blue light alone exerts a selective cytotoxic effect on P. acnes acting on the Porphyrins (coproporphyrin) synthetized by the bacteria by the production of singlet oxygen and reactive radicals leading to a membrane damage and cell death.
But the blue light creates moreover a biophotonic action; namely the gel excited releases photons generating a unique dynamic hyperpulsed multi-wavelengths of fluorescent energy shifting the light (Stoke's shift phenomenon) from shorter blue wavelengths to longer wavelengths within the blue, green, yellow, orange, and red spectrum (400 to 650nm). Compared to blue light, which has limited skin penetration these wavelengths have the capacity to penetrate to various depths of the skin and to stimulate the skin tissues and cells (red light for example can reach deeper sebaceous glands and may have an anti-inflammatory effect through cytokine release).
No UV light or infrared light is emitted or generated.
Afterwards, the exhausted photoconverter gel is fully removed by cleansing just after the illumination period.



Investigator's Global Assessment (IGA) of acne severity		
0	'Clear'	Residual hyperpigmentation and erythema may be present
1	'Mild'	A few scattered comedones and a few small papules
2	'Moderate'	Easily recognisable; less than half the face is involved. Some comedones and some papules and pustules
3	'Severe'	Easily recognisable; less than half the face is involved. Some comedones and some papules and pustules



PATIENTS AND METHODS

CASE STUDY:

10 patients affected by severe papulo-pustular or conglobate acne (6 males and 4 females) were treated

INCLUSION CRITERIA:

- **IGA 3-4 (severe papulo-pustular or conglobate acne)**
- **absent or partial response to previous acne treatments**
- **patients not eligible to standard dose of retinoids or refusing a standard dosage therapy with isotretinoin for collateral effects or not reaching clearance with tetracyclines added to topical therapy**
- **no isotretinoin or tetracyclines systemic treatments in last 12 months**
- **no topical retinoid treatments in last 6 months**
- **no use of drugs known to increase photosensitivity**
- **no use of corticosteroids within last 6 months**
- **no pregnancy or breast-feeding**

MATERIALS AND METHODS

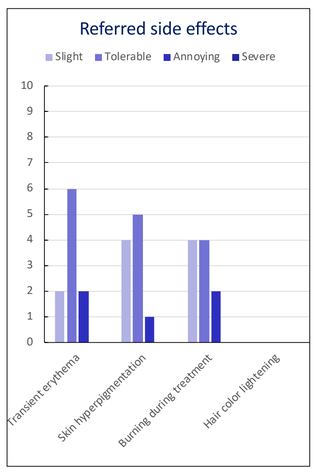
Baseline grading of acne was performed according to the Investigator's Global Assessment (IGA) scale.
Each patient received 6 weeks of treatment, once weekly with two treatments in the same day with a time interval of 2 hours and using one box of gel a week splitting material need for one-session treatment in two.
On the first day of light therapy the patients started systemic treatment too that was regularly continued after the end of biophotonic cycle.
Efficacy evaluations at week 6 and 12 were performed.

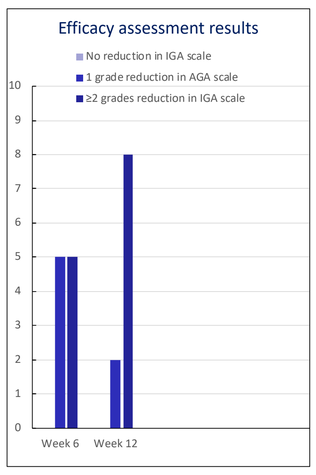
EFFICACY E SAFETY

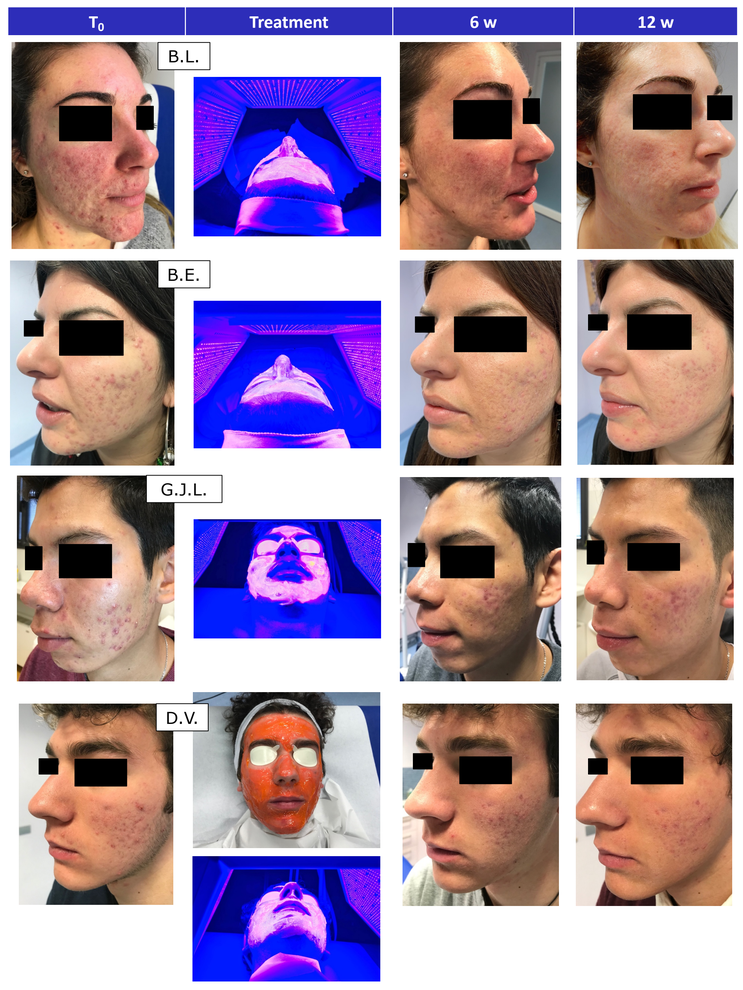
Some patients reported treatment-related adverse events of varying degrees, but never severe or impairing the therapy, as transient erythema rarely lasting more than 36 hrs, skin hyperpigmentation of a few days after treatment and a slight sensation of burning during the treatment; no one reported hair colour lightening.
No patients discontinued the study.
Efficacy evaluations at week 6 and 12 were performed using IGA scale.

RESULTS

Pz.	Age	Controndication or refuse to other treatments	Previous therapy	Systemic Treatment associated with LED blu light and photoconverter	IGA T_0	IGA 6 w	IGA 12 w
B.M.	18 y.o. M	Elevation of CPK during previous attempts with retinoids	Topical treatments, Tetracycline, Isotretinoin (discontinued)	Isotretinoin 5 mg die	4	3	3
B.L.	27 y.o. F	Pseudotumor cerebri	Topical treatments, Tetracycline	Isotretinoin 5 mg die Levonogestrel IUD	4	2	2
B.E.	28 y.o. F	Extreme skin dryness during previous attempts with retinoids because of atopyc dermatitis	Topical treatments, Tetracycline, Isotretinoin (discontinued)	Isotretinoin 5 mg die OCP (Drospirenone/ethinyl estradiol)	4	3	1
B.R.	41 y.o. M	Refuse because front office worker, needing fast resolution, unable to frequent blood analysis	Topical treatments, Tetracycline	Isotretinoin 5 mg die	3	2	1
D.V.	19 y.o. M	Refuse of retinoids for collateral effects	Topical treatments, Tetracycline, Isotretinoin (discontinued)	Tetracycline 300 mg die	3	2	1
G.M,	18 y.o. M	Weakness during previous attempts wiith retinoids, with CPK elevation	Topical treatments, Tetracycline, Isotretinoin (discontinued)	Isotretinoin 5 mg die	3	1	1
S.G.	20 y.o. F	Non-tolerated, initial worsening during previous attempts wiith retinoids	Topical treatments, Tetracycline, Isotretinoin (discontinued)	Isotretinoin 5 mg die OCP (Dienogest/ethinyl estradiol)	4	2	1
G.J.L.	20 y.o. M	Craving for a fast improvemente while approaching summertime	Topical treatments, Tetracycline	Isotretinoin 5 mg die	4	2	1
M.I.	24 y.o. F	Previous treatment failure	Topical treatments, Tetracycline, Evra	Tetracycline 300 mg die BCP (Norelgestromin/ethinyl estradiol)	3	1	1
P.M.	18 y.o. M	CPK and transaminase increase during previous attempts with retinoids	Topical treatments, Tetracycline, Isotretinoin (discontinued)	Isotretinoin 5 mg die	3	2	2







CONCLUSIONS

80% of patients treated achieved at week 12 the primary endpoint of a reduction of at least 2 grades in the IGA scale. In 50% this reduction was evident from week 6. This fast clinical improvement, most of all when using low doses of isotretinoin, seems to be related to the concomitant use of biophotonic therapy. No severe adverse event was reported during the treatment, with special reference to photosensitivity manifestations, and a good tolerance to the treatment was referred by patients.

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