

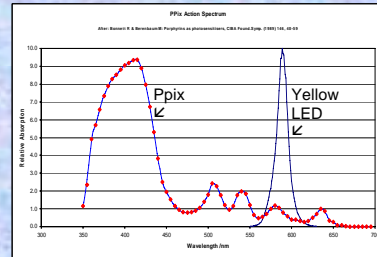
A Safe and Effective Yellow LED Treatment for Mild to Moderate Acne: A Within-Patient Half-Face Dose Ranging Study.

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Introduction:

Previous studies have shown that visible light phototherapy has a beneficial effect on mild to moderate acne. Lipophilic Propionibacterium acnes (P. acnes), a Gram positive, microaerophilic organism, plays a major role in the pathogenesis of acne; it produces large amounts of porphyrins, which can absorb light energy in the visible light spectrum. Irradiation leads to photoexcitation of bacterial porphyrins, singlet oxygen production and eventually bacterial destruction. The porphyrin absorption spectrum is maximal in the blue, but has other peaks throughout the visible spectrum. A marked improvement in acne, reduction in P. acnes counts and seborrhoea has been observed with blue light. One absorption peak lies within the yellow area of the spectrum, and light at this wavelength, should photoactivate bacterial porphyrins. Because of its greater penetration yellow light may be more effective than blue wavelengths. This modality may provide a useful alternative to oral antibiotics for moderate acne.

In this study the efficacy and safety of a yellow high intensity LED source, employing a narrowband yellow LED at wavelength between 570 – 600nm was assessed for mild to moderate acne..



Methods:

This was a prospective single-blind within patient study to assess the safety and efficacy of an intense visible light treatment for acne. 30 patients with mild to moderate facial acne were recruited. Each patient had the left and right side of their face exposed to different intensities of yellow light. One of three treatments was randomly allocated to each site: a sham treatment, a moderate dose treatment of 1.5 Joules/cm², and a high dose treatment of 3.0 Joules/cm². The design of allocation followed an incomplete blocks design. The high dose was achieved illuminating the treatment area for twice as long as the moderate dose. There was no change in the peak power between moderate and high doses. For the sham treatment a time period the same as the moderate dose was provided but the LED light output was reduced to negligible proportions. This procedure was repeated twice a week for four weeks. Assessments were carried out before, immediately after and at 2, 4 and 6 weeks post treatment.

Main outcome measures were standardised clinical grading (Leeds Acne Score), lesion counting, and Dermatology Life Quality Index (DLQI) score. Secondary outcome measures were visual assessment of standardised normal digital photography.

Ethical approval was obtained from Gwent Local Research Ethics Committee. The study complied with the current revision of the Declaration of Helsinki.

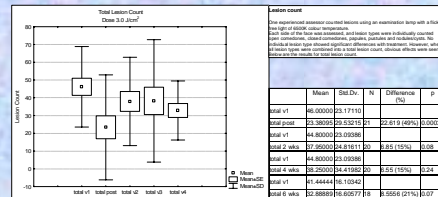
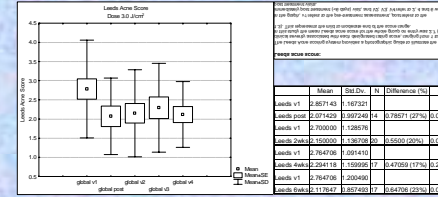
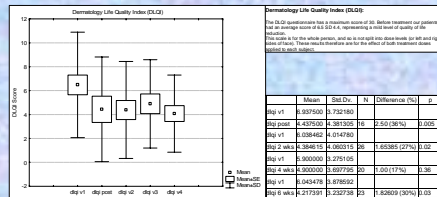
Safety:

Approximately 150 treatments have been administered amongst 20 patients at the highest dose. Patients were assessed for adverse events during the 4 weeks treatment and for a further 6 weeks after the last treatment.

No treatment-related adverse events occurred. No patient dropped out due to treatment related events.

Conclusion:

The treatment is completely safe, and is well tolerated by the patients. There seems no indications to prevent the treatment being applied more frequently than twice a week, or for more than 8 treatments.



Photographic assessment.

Three independent dermatologists assessed pairs of photographs of a single site on each subject where one of the pair was the pre-treatment photograph, and the other was from a post-treatment assessment. On 20 subjects who had one side of the face treated with 3.0J/cm² dose, and three assessors, a total of 60 assessments are possible.

The following shows the results of 3.0J/cm².

Pre Vs immediately post treatment: Overall score of 40/52 (77%) assessments judged treatment had improved acne.

Pre Vs 2 weeks post treatment: Overall score of 39/50 (65%) judged treatment had improved acne.

Conclusion:

The assessment of visible change of the high-dose site is straightforward, and confirms the lesion count reductions. The treatment induced visible improvement on the high dose site.

Comparative assessments:

The same three independent dermatologists assessed photographs on a different occasion. The comparisons assessed were between high dose and sham dose within each patient. These assessments were made for each visit: pre-treatment, immediately post-treatment, 2, 4 and 6 weeks post treatment. For each time point, the assessors judged which side of the face had 'less acne' or 'looked better', a global assessment.

The result of the pre-treatment evaluation was then compared to the subsequent post-treatment time points. On patients where the sham site was 'better' on the pre-treatment photographs a score of one was assigned if the subsequent photographs showed that the high-dose site was better (ie an improvement). On patients where the high-dose site was 'better' on the pre-treatment photographs, a score of one was assigned if the subsequent photographs showed that the high-dose site remained better (ie a maintenance of the difference).

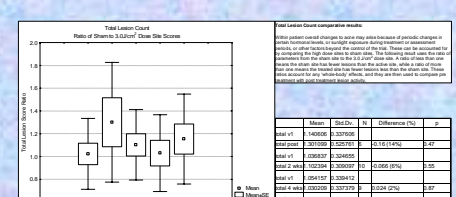
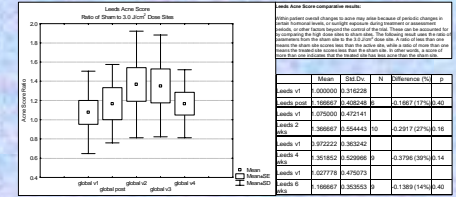
With 30 patients, two sites (left and right face), and three doses (sham, 1.5 J/cm² and 3.0 J/cm²), then a maximum of 10 within-patient comparisons are possible for any two doses. With three independent assessors, this results in a maximum of 30 assessments. Some drop-outs were replaced, so the initial number of patients assessed was 33. Subsequently, some assessment appointments were missed. The results given below are, therefore, on the 'intention to treat' group.

Total scores. Numbers refer to sites receiving the 3.0J/cm² dose which were judged 'better' than the sham dose site (ie least acne). Test of difference of proportions between pre treatment and subsequent time points was used to generate the p value. ns = not significant.

Time point	Number	Proportion	p value
Pre-treatment	17/33	0.515	-
Immediately post	10/20	0.5	0.89 ns
2 weeks post	11/29	0.38	0.27 ns
4 weeks post	11/26	0.42	0.45 ns
6 weeks post	12/27	0.44	0.54 ns

Conclusion:

The comparison of two sides of the face is more difficult than assessing difference from one side of the face, and the changes due to treatment are not enough to overcome the variability in judgement inherent in such an assessment. Pre-treatment assessments indicate that the subjects started with very similar levels of acne on each side of the face. The assessors were not able to see a significant change in the difference in visible acne between high dose and sham sites at any time point.



Global assessment of treatment efficacy:

This was a subject and assessor judgment of overall improvement or deterioration at 6 weeks post treatment. This was done for each dose site (ie each side of the face).

t-test for single means, compared to zero (no treatment effect).

Dose	Mean patient score (95% CI)	Mean assessor score (95% CI)
3.0J/cm ²	0.68 (0.2-1.14), p = 0.005	0.82 (0.33-1.31), p = 0.002
1.5J/cm ²	0.22 (0.25-0.69), ns	0.19 (0.26-0.63), ns
Sham	0.43 (0.06-0.82), p=0.03	0.19 (0.21-0.59), ns

Neither patients nor the assessor thought that acne had become worse on the high dose site. On the high dose site, 42% of patients reported an improvement and the assessor reported 65% of patients had improved.

Improvement assessed by a global score of 1 or above:

Dose	Patient reported improvement	Assessor reported improvement
3.0J/cm ²	8/19, 42%	11/17, 65%
1.5J/cm ²	5/17, 29%	5/15, 33%
Sham	7/15, 47%	4/15, 27%

CONCLUSION:

The treatment of facial acne with intense yellow incoherent light at doses up to 3.0J/cm² twice a week for eight treatments is safe and well tolerated by our subjects. There is no indication that higher doses, or more and more frequent treatments would elicit any adverse events, although such regimens have not been tested in this study. As with any treatment applying significant doses of light to the skin, patients with visible light photosensitivity should avoid this treatment. There is good evidence of treatment efficacy. The efficacy effects were highest in the assessments of a single site on the highest dose. Where two sites were compared, as in the high versus sham within-patient assessments, efficacy was demonstrated in all but the photographic tests. This could be due to the difficulty in judging the severity of two different sites: where one side of the face is being assessed from different time point photographs, each small area or group of lesions can be identified and compared. This is not possible when comparing different sides of the face. We can conclude that the treatment tested is safe and effective in mild to moderate acne.

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