FBDermatology
FLETECH INNOVATION

Light wavelengths and bioactivities.

Synopsis:

Light is a term for the visible and near-visible portions of electromagnetic radiation. It is composed of magnetic and electric oscillating sinusoidal waves perpendicular to each other and propagates in the same direction. Probably the single most defining characteristic of electromagnetic radiation is its wavelength. Electromagnetic radiation exists over a vast range of wavelengths, ranging in scale from picometers (one trillionth of a meter) to kilometres. This range of wavelengths is collectively referred to as the electromagnetic spectrum. Since the energy of a photon is inversely proportional to its wavelength. Among the broad spectrum of electromagnetic radiation, 'light' comprises the visible spectrum from violet/blue to near-infrared (NIR) and offers a distinct safety advantage with photon energy in the range of 0.5–3 eV.

Poly-chromatic light: The term polychromatic means having several colours. It is used to describe the light that exhibits more than one colour, which also means that it contains radiation of more than one wavelength.

Monochromatic light: The term monochromatic comes from the Greek word mono, meaning single, and chroma, meaning colour. So monochromatic light means light of one colour. In scientific terms, it means light of a single wavelength.

Conclusions:

Whilst being safe, this photonic energy can interact with organic molecules. It is emerging that various types of extra-ocular photoreceptors can absorb light of multiple wavelengths and trigger a variety of molecular cascades, culminating in altered cellular energy production and gene expression, a significant benefit for the energy demand of cells.

Indeed, polychromatic light might have multiple beneficial effects at the same time concerning a monochromatic light source.

FLE platform differs from other LED modalities since the photoconverter gel emits polychromatic fluorescent light covering the continuum of the visible spectrum (~415–610 nm).

The wavelength of light determines the depth of tissue penetration.

Table 1: Light bioactivities (nm).

Blue light	(415–500) nm has the shortest tissue penetration, reaching the stratum corneum and epidermis. It is used to treat acne vulgaris, it is also thought to have an anti-inflammatory effect regulating cytokines.
Green light	(500–570 nm) targets the epidermis and upper dermis to access fibroblasts and endothelial cells mediating proliferation and healing, the key elements in skin rejuvenation.
Yellow light	(570–590 nm) is indicated in wound healing by reaching the papillary dermal layer. It is used in post-laser recovery and is implicated in photoaging modulating ATP and fibroblast activity.
Orange and Red light	(590–760 nm) with the deepest skin penetration are noted for vascular activation, reducing inflammation, improving wound healing, and increasing collagen production.

Reference:

Edge, D. et al. 2020. Biophotonic Therapy Induced Photobiomodulation. In: Technology in Practical Dermatology. Springer, Cham.

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Benefits of pulsed light and evaluation of pulsed light versus continuous light.

Synopsis:

The concept of super-pulsing was originally developed for the carbon dioxide laser used in high-power tissue ablative procedures. The idea was that by generating relatively short pulses (?second) the laser media could be excited to higher levels than those normally allowed where heat dissipation constraints limit the maximum amounts of energy that can be used to excite the lasing media.

Pulsed light offers numerous potential benefits. Because there are "quench periods" (pulse OFF times) following the pulse ON times, pulsed light can generate less tissue heating. In instances where it is desirable to deliver light to deeper tissues increased powers are needed to provide adequate energy to the target tissue. This increased power can cause tissue heating at the surface layers and in this instance, pulsed light could be very useful.

Whereas continuous waves (CW) cause an increase in temperature of the intervening and target tissues or organ, pulsed light has been shown to cause no measurable change in the temperature of the irradiated area for the same delivered energy density.

Secondly, potassium and calcium ion channels in the mitochondria and the sarcolemma may be involved in the cellular response to LLLT.

Thirdly, by dissociating NO from CCO, an increased ATP production appears. If the light is pulsed multiple photodissociation events could occur, while in CW mode the number of dissociations may be much smaller.

Conclusion:

Overall pulsed light may be superior to continuous light due to the key points below:

- As pulsed light has 'quench periods', it can deliver energy to deep into the tissues while generating less heat at the surface layers;
- The logic in favour of pulsed light is that cells may need periods of rest, without which they can no longer be stimulated further;
- An increased ATP production may be stimulated by pulsed light.

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Chung H, Dai T, Sharma SK, Huang YY, Carroll JD, Hamblin MR. The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng. 2012 Feb;40(2):516-33. doi: 10.1007/s10439-011-0454-7.

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FBDermatology
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Cellular and tissutal mechanisms of LLLT.

LLLT has a wide range of effects at the molecular, cellular, and tissular levels. Within the cell, there is strong evidence to suggest that LLLT acts on the mitochondria to increase adenosine triphosphate (ATP) production, modulation of reactive oxygen species (ROS), and the induction of transcription factors.

Several transcription factors are regulated by changes in cellular redox state. These transcription factors then cause protein synthesis that triggers further effects down-stream, such as increased cell proliferation and migration, modulation in the levels of cytokines, growth factors and inflammatory mediators, and increased tissue oxygenation.

Immune cells appear to be strongly affected by LLLT. Mast cells, which play a crucial role in the movement of leukocytes, are of considerable importance in inflammation. Specific wavelengths of light can trigger mast cell degranulation which results in the release of the pro-inflammatory cytokine TNF-a from the cells. This leads to increased infiltration of the tissues by leukocytes.

LLLT also enhances the proliferation, maturation, and motility of fibroblasts, and increases the production of basic fibroblast growth factor.

Lymphocytes become activated and proliferate more rapidly, and epithelial cells become more motile, allowing wound sites to close more quickly. The ability of macrophages to act as phagocytes is also enhanced under the application of LLLT.

At the most basic level, LLLT acts by inducing a photochemical reaction in the cell, a process referred to as biostimulation or photobiomodulation. When a photon of light is absorbed by a chromophore in the treated cells, an electron in the chromophore can become excited and jump from a low-energy orbit to a higher-energy orbit. This stored energy can then be used by the system to perform various cellular tasks. There are several pieces of evidence that point to a chromophore within mitochondria being the initial target of LLLT.

Radiation of tissue with light causes an increase in mitochondrial products such as ATP, NADH, protein, and RNA, as well as a reciprocal augmentation in oxygen consumption, and various in vitro experiments have confirmed that cellular respiration is upregulated when mitochondria are exposed to a form of illumination.

Cytochrome c oxidase (CCO) is the crucial chromophore in the cellular response to LLLT. CCO is a large transmembrane protein complex, which is a component of the respiratory electron transport chain. The electron transport chain passes high-energy electrons from electron carriers through a series of transmembrane complexes (including CCO) to the final electron acceptor, generating a proton gradient that is used to produce ATP.

Thus, the application of light directly influences ATP production by affecting one of the transmembrane complexes in the chain: in particular, LLLT results in increased ATP production and electron transport.

The observation that NO is released from cells during LLLT has led to speculation that CCO and NO release are linked by two possible pathways. It is possible that LLLT may cause photodissociation of NO from CCO.

References:

Chung H, Dai T, Sharma SK, Huang YY, Carroll JD, Hamblin MR. The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng. 2012 Feb;40(2):516-33. doi: 10.1007/s10439-011-0454-7.

FBDermatology
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Light and skin receptors: the role of Opsins.

Synopsis:

Life on earth depends on sunlight; it is a sine qua non condition for human survival. Skin, the largest organ of our body, is also constantly exposed to sunlight. Solar UV radiation is comprised of ~95% long wavelength UVA and ~5% short wavelength UVB, each activating distinct signaling pathways in the skin. UVB induces DNA damage, triggering the increase in pigmentation within many hours to days, while physiological doses of UVA trigger a retinal-dependent G-protein coupled signaling pathway causing immediate pigment darkening via activation of an unknown receptor (Olinki et al 2020).

Human skin is structured in layers: the uppermost layer, the epidermis, is comprised of keratinocytes surrounding a single basal layer of melanin-producing melanocytes; the dermis comprises a middle fibrous layer; and the subcutis is a cushioning layer upon which the epidermis and dermis rest. High energy UVA penetrates through both the epidermis and dermis, whereas UVB is primarily confined to the epidermis (Olinki et al 2020).

In the early 2000s, different wavelengths of light have different effects on human epidermal permeability were determined, indicating a potential array of spectrally distinct light receptors within the skin. Shortly thereafter, OPN1s and OPN2 were identified in human epidermal skin. (Olinki et al 2020).

Opsins are a large group of light-sensitive G protein–coupled receptors (GPCRs) that use retina as a ligand and trigger signaling cascades upon distinct wavelength of light. Opsins, primarily found in light-detecting cells such as the retinal photoreceptors, are widely known for their key role in visual transduction (Sadowska et al., 2021). Indeed, depending on location of the expression, there are different categories of opsins. OPN2, OPN3, and OPN4 are expressed in the epidermis (Olinki et al 2020).

The role of opsin is also investigated as they are activated by blue light (415 nm). Blue light can increase pigmentation in normal human melanocytes (NHMs) via OPN3 photoactivation. The opsin receptor is possibly excited by blue light, stimulating the transient receptor potential channels and then causing a flood of calcium, which triggers calcium/calmodulin-dependent protein kinase-II (CAMKII) and in the end causes gene transcription changes. OPN2 (Rhodopsin) and OPN3 (Panopsin, Encephalopsin) were found to be expressed not only in the skin, but also in the anagen hair follicle. Opsin's role has also been investigated in the modulation of pigmentation and melanogenesis, but only in the Fitzpatrick skin type III and higher (Sadowska et al., 2021). Downregulation of OPN3 reduces the expression of OPN1 and OPN5, suggesting a potential interaction between OPN3, OPN1 and OPN5 which could explain UVA-dependent responses. (Olinki et al., 2020).

Conclusions:

Several studies demonstrated that opsins modulate various physiological processes of the skin, including wound healing, melanogenesis, photoaging, and hair growth. Since each opsin has distinct absorption spectra and signaling transduction, the optimization of light therapy tailored to the features of each opsin will maximize the benefit that PBM can offer in the clinic. There has been a growing interest in the application of light therapy to clinical cases owing to the advantages of a cost-effective and non-invasive approach (Suh et al., 2020).

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Suh S, Choi EH, Atanaskova Mesinkovska N. The expression of opsins in the human skin and its implications for photobiomodulation: A Systematic Review. Photodermatol Photoimmunol Photomed. 2020 Sep;36(5):329-338. doi: 10.1111/phpp.12578.

Safety and efficacy of Energy Based Devices in combination with injectables.

Synopsis:

Combining aesthetic interventions to target ageing processes often leads to better results than a single treatment. Nevertheless, few guidelines using multiple interventions have been published to date. This review aims to summarize and critically appraise recent developments and clinical investigations on the safety and efficacy of combining Injectables and Energy Based Devices (EBD). A thorough analysis of the literature using PubMed and Scopus using the keywords; dermal filler, hyaluronic acid, Botox, BoNT (Botulinum neurotoxin), combination, LLLT (low level light therapy), light, energy based and LED was performed. A total of 9 clinical research articles were selected from the aforementioned databases. In these studies, the use of EBDs in combination with Fillers and/or BoNT included over 125 patients and 400 treatments in total.

Results and Discussion:

According to the Carruthers consensus study, BoNT often provides a synergistic effect, leading to superior results of greater duration when combined with fillers, lasers, light- or energy-based devices or surgical procedures. The consensus was defined as approval from 75% to 94% of all participants, whereas agreement of 95% denoted a strong consensus. For same-day treatments, BoNT and fillers may be performed together in either sequence, whereas micro-focused ultrasound with visualization (MFU-V) is recommended before injectable agents (Carruthers et al., 2016).

The concomitant use (same day) of laser and HA fillers for facial rejuvenation represents an effective and safe strategy which improves clinical results and patient satisfaction (Urdiales-Gàlvez et al., 2019) The panel recommendations are: If we want to perform a combined procedure on the same day (HA and light treatments), start always with the light treatments, avoiding skin manipulations after having injected.

Six studies by Cuerda-Galindo and co-workers (2015) documented no histological changes in fillers injected after applying radiofrequency, IPL or laser treatments and one study documented improvement in collagen after IPL treatment and toxin injection.

Akerman et al. (2022) successfully combined the non-ablative 1,540nm erbium with glass laser treatment followed by administering a highly purified hyaluronic acid injectable into the post-acne facial scars. The novel combination treatment overall demonstrated an average mild to moderate improvement in post-acne facial scars appearance, with high patient satisfaction three months after treatment and a good safety profile.

According to Wang et al. (2021) in 41 single-session treatments with fillers and EBDs, there were no documented adverse events related to the spreading of fillers or energy treatment of filled areas, including product migration, unexpected loss of filler volume, vascular occlusion, acute pain, cutaneous necrosis, blindness and cutaneous burn.

No histological changes in PMMA (polymethylmethacrylate) microspheres were observed in any treatment area. An expected lymphohistiocytic response was identified in all areas where PMMA microspheres were present. Laser, light, and ultrasound treatments can safely be administered following a PMMA-collagen injection (Wu et al., 2016).

Studies examining the efficacy and safety of intense pulsed light, ablative fractional lasers, nonablative fractional lasers, micro-focused ultrasound with visualization, thermistor-controlled subsurface monopolar radiofrequency, cryolipolysis, liposuction, laser lipolysis, neuromodulators, and hyaluronic acid dermal fillers in the neck were assessed. The authors' experience in clinical practice is that many neck rejuvenation techniques can be combined safely (Vanaman et al., 2016).

Using the review of the literature and clinical experience, Langelier and colleagues (2016) discuss our strategy for combining botulinum toxin, facial filler, ablative laser, intense pulsed light (IPL), micro-focused ultrasound, and microneedle fractional radiofrequency to treat aesthetic problems of the upper face. With attention to safety recommendations, injectable, light, laser, and energy-based treatments can be safely combined with experienced hands to provide enhanced outcomes.

Providing multiple treatments in 1 session improves patient satisfaction by producing greater improvements in a shorter amount of time and with less overall downtime than would be necessary with multiple office visits (Lengelier et al., 2016).

Most studies found no evidence of filler degradation, adverse events, or histologic changes after treatment with non-ablative lasers, IPL, or radiofrequency, even when administered immediately after filler implantation. It would be reasonable to suggest administering deeper lasers, if required, before soft-tissue augmentation.

Fillers may be combined with lasers, IPL, or radiofrequency devices in any order on the same day without an increase in adverse effects or decrease in efficacy. Without the guiding evidence for the order or sequence of combination treatments, there is great variation in the pattern of practice (Humphrey et al., 2016).

FLE + Injectables | Protocol Recommendations:

Based on the scientific evidence, the following protocols can be recommended;

- Fluorescent Light Energy (FLE) can be used before a Filler injection
- Fluorescent Light Energy (FLE) can be used immediately prior (same session) to a Filler injection
- Fluorescent Light Energy (FLE) can be used two weeks post a Filler injection
- Fluorescent Light Energy (FLE) can be used before a BoNT injection
- Fluorescent Light Energy (FLE) can be used immediately prior (same session) to a BoNT injection
- Fluorescent Light Energy (FLE) can be used two weeks post a BoNT injection.

Conclusions:
The use of Energy Based Devices (including Fluorescent Light Energy, FLE) combined with an injectable dermal filler such as Botox and Hyaluronic Acid could be considered safe according to the literature data.
A review of the literature demonstrates the safety of same day combined treatments for rejuvenation (Cuerda-Galindo et al. 2015).
BoNT often provides a synergistic effect, leading to superior results of greater duration when combined with fillers, lasers, light- or energy-based devices or surgical procedures (Carruthers et al., 2016)
Providing multiple treatments in 1 session improves patient satisfaction by producing greater improvements in a shorter amount of time and with less overall downtime than would be necessary with multiple office visits (Lengelier et al., 2016).
A combination approach often produces the most optimal outcome for a patient seeking skin rejuvenation.
Procedures may vary across the clinics. Some physicians use energy-based therapies before the injection, others after the injection.
The physician's clinical evaluation should consider the patient's case by case needs. All the parameters involved in these procedures should be assessed along with the temperatures and the depth of both the energy based device and the fillers' chemical-physical properties.

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Dermatologic Therapy

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RESEARCH ARTICLE OPEN ACCESS

Light-Emitting Diode–Activated Gel Fluorescent Light Energy Therapy as Maintenance Treatment Following Aminolevulinic Acid Photodynamic Therapy for Severe Acne: A Case Report

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ABSTRACT

Severe acne frequently relapses after aminolevulinic acid photodynamic therapy (ALA-PDT), and adverse reactions such as erythema and dryness may limit tolerability. We report a 24-year-old woman with Grade IV acne treated with two ALA-PDT sessions followed by light-emitting diode–activated gel fluorescent light energy (FLE) therapy as posttreatment maintenance. FLE was applied twice weekly for six weeks. Compared with the discomfort of ALA-PDT (VAS: 7), FLE was painless (VAS: 0) and well tolerated during the maintenance phase. At 1 month after completion of the combined regimen, lesions continued to resolve with decreased erythema and porphyrin fluorescence on VISIA imaging, without relapse or adverse events. At 3- and 12-month follow-ups, clinical improvement was maintained, with progressive improvements in lesion counts and skin quality. This case illustrates the feasibility of incorporating FLE as a maintenance approach following ALA-PDT and highlights its potential clinical value in the management of severe acne.

1 | Introduction

Acne vulgaris, a chronic inflammatory disorder of the pilosebaceous unit, affects approximately 9% of the global population, and patients with severe acne often experience considerable psychosocial burdens [1]. Systemic therapies such as isotretinoin and antibiotics remain first-line options, but their use is constrained by teratogenicity, antibiotic resistance, and frequent relapse, underscoring the need for effective noninvasive alternatives [2]. Aminolevulinic acid photodynamic therapy (ALA-PDT) is a safe and effective physical modality that targets multiple pathogenic mechanisms, including reduction of *Cutibacterium acnes*, suppression of sebaceous gland activity, and modulation of inflammation [3]. Nevertheless, patients commonly experience posttreatment erythema, dryness, and discomfort, and recurrence remains a challenge.

Photobiomodulation (PBM), which employs red (620–700 nm) or near-infrared (700–1440 nm) light to activate mitochondrial chromophores such as cytochrome c oxidase, has been reported to modulate inflammation and promote tissue repair [4]. Within PBM approaches, fluorescent light energy (FLE) therapy—based on light-emitting diode (LED) activation of a chromophore-containing gel—has emerged as a novel modality with demonstrated effects on epidermal recovery, erythema reduction, and collagen remodeling [5]. Clinical reports also suggest reductions in inflammation and improvements in skin texture across several dermatological concerns [6, 7]. Although the role of FLE as a dedicated post-ALA-PDT maintenance therapy has not been

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systematically evaluated, preliminary reports support its potential to mitigate postprocedural erythema and dryness and to sustain clinical improvement, providing a rationale for exploration in this setting. In this report, we describe a case of severe acne in which LED-activated gel FLE was applied as a post-ALA-PDT maintenance therapy to mitigate treatment-related adverse effects and prolong clinical improvement.

2 | Case Report

A 24-year-old woman with a five-year history of widespread papules, severe nodules, and cystic lesions affecting the cheeks and chin was diagnosed with Grade IV acne according to the Chinese Guidelines for the Treatment of Acne [8], defined as nodular or cystic acne with more than 100 lesions and at least three nodules or cysts. She had previously received topical anti-inflammatory agents without satisfactory results and declined oral retinoids due to pregnancy planning. On examination, five cysts or nodules and approximately 110 inflammatory and noninflammatory lesions were noted on the face.

Baseline and follow-up assessments were performed using the VISIA Skin Analysis System (Canfield Scientific, Parsippany, NJ, USA), a standardized facial imaging platform with fixed camera positioning and controlled lighting to ensure reproducible image acquisition. Red-area and protoporphyrin IX (PpIX) fluorescence imaging were obtained to document erythema and porphyrin distribution. Lesion counts included comedones, papules, pustules, and cystic nodules, and a clearance rate was calculated. Treatment response was classified as marked improvement (60%–89% clearance), moderate improvement (30%–59%), or no improvement (< 30%). Pain was assessed using the visual analog scale (VAS), with scores categorized as mild (1–3), moderate (4–6), or severe (7–10).

3 | First Stage: ALA-PDT Treatment

The first stage comprised two ALA-PDT sessions conducted at one-week intervals. Each session began with facial disinfection using 75% ethanol, followed by sterile needle puncture of cysts and nodules to facilitate ALA penetration. The skin was then rinsed with sterile saline. After a 15-min interval, 5% 5-ALA gel (Shanghai Fudan Zhangjiang Biomedical, Shanghai, China) was applied to the lesional areas, occluded, and kept in the dark for 30 min. Irradiation was then delivered with a 635-nm LED device (Wuhan Aiguo Optoelectronics Technology Co, Ltd., Wuhan, China) at an irradiance of 60 mW/cm^2 for 20 min. Afterward, the treated area was cooled with saline-soaked gauze for 20 min. Patients were instructed to strictly avoid direct sun exposure for 72 h after each session.

4 | Second Stage: FLE Maintenance Therapy

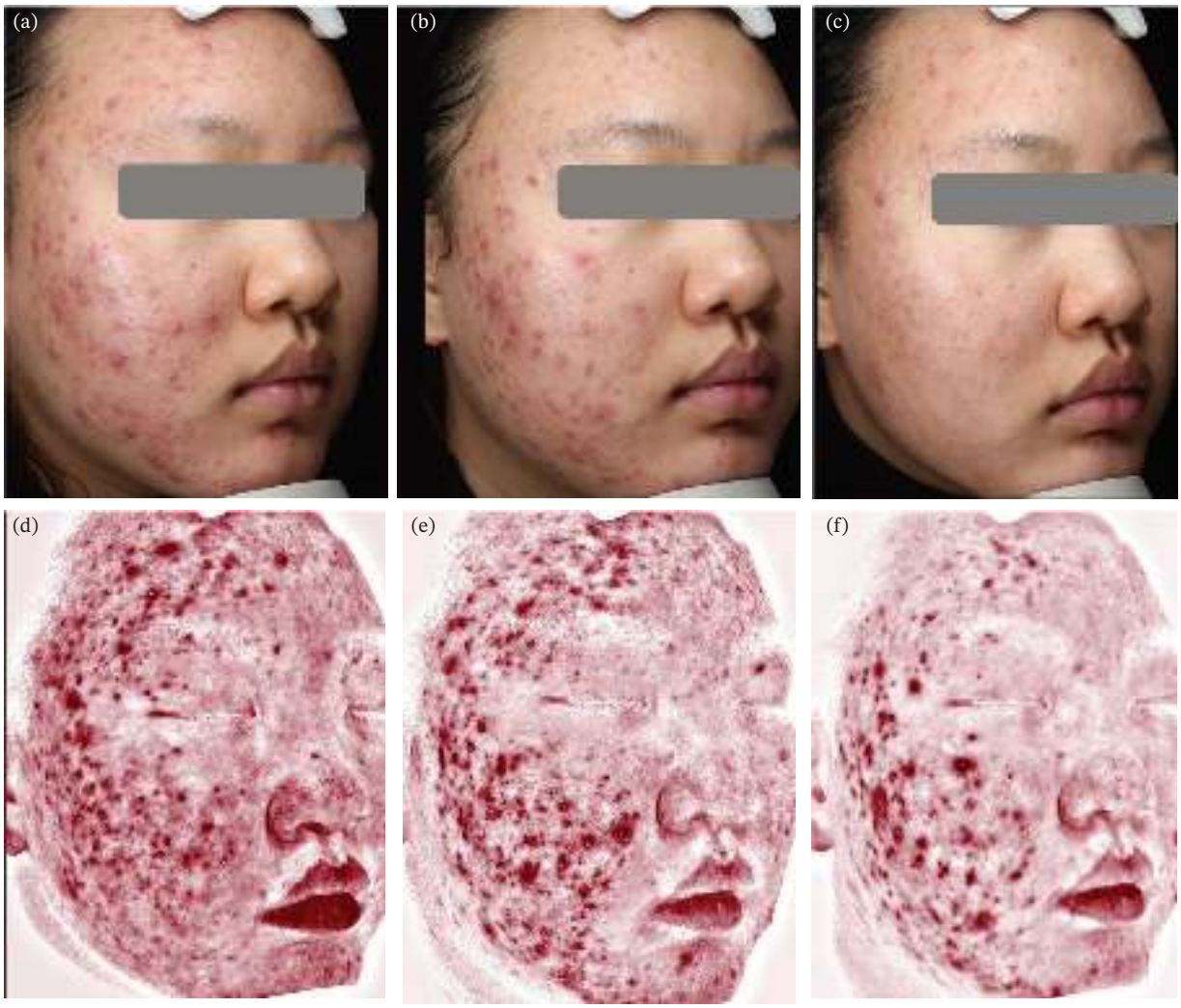
After two ALA-PDT sessions, the patient showed marked improvement in nodules and cysts, although inflammatory papules persisted. A maintenance phase with FLE therapy was then initiated, administered twice weekly (with an interval of approximately 3-4 days between sessions) for six weeks (12 sessions in total). For each session, the face was cleansed, and a ~2-mm layer of chromophore-containing gel was applied evenly to entire face. The gel was illuminated using a multi-LED lamp (Kleresca A90, FB Dermatology, San Benedetto del Tronto, Italy), delivering blue LED light (peak wavelength approximately 440–460 nm) to activate the photoconverter gel and generate FLE (emission range approximately 500–650 nm). The lamp was positioned at a fixed distance of approximately 5 cm from the skin surface and operated using the manufacturer-preset cycle of 9 min per session, corresponding to a reported delivered light dose of approximately 30–40 J/cm^2 [6, 9, 10]. After illumination, the gel was removed using a sterile gauze and the skin was rinsed with sterile saline, followed by gentle cleansing and moisturizing. Serial clinical photographs and VISIA imaging demonstrated progressive improvement, with an approximately 65%–70% reduction in erythema and lesion counts compared with the initial presentation, observed after completion of two ALA-PDT sessions followed by twelve sessions of FLE therapy (Figure 1), porphyrin fluorescence was reduced on PpIX imaging (Figure 2), and at 3- and 12-month follow-ups, remission was sustained with further clinical improvement (Figure 3). Overall, the treatment was considered highly effective.

5 | Discussion

This case highlights the potential complementary roles of ALA-PDT and FLE therapy in the management of severe acne. ALA-PDT targets the pathogenesis of acne by reducing *Cutibacterium acnes* colonization, suppressing sebaceous activity, and improving inflammatory nodules and cysts [3]. However, adverse reactions such as erythema and dryness often persist after treatment, underscoring the need for adjunctive strategies.

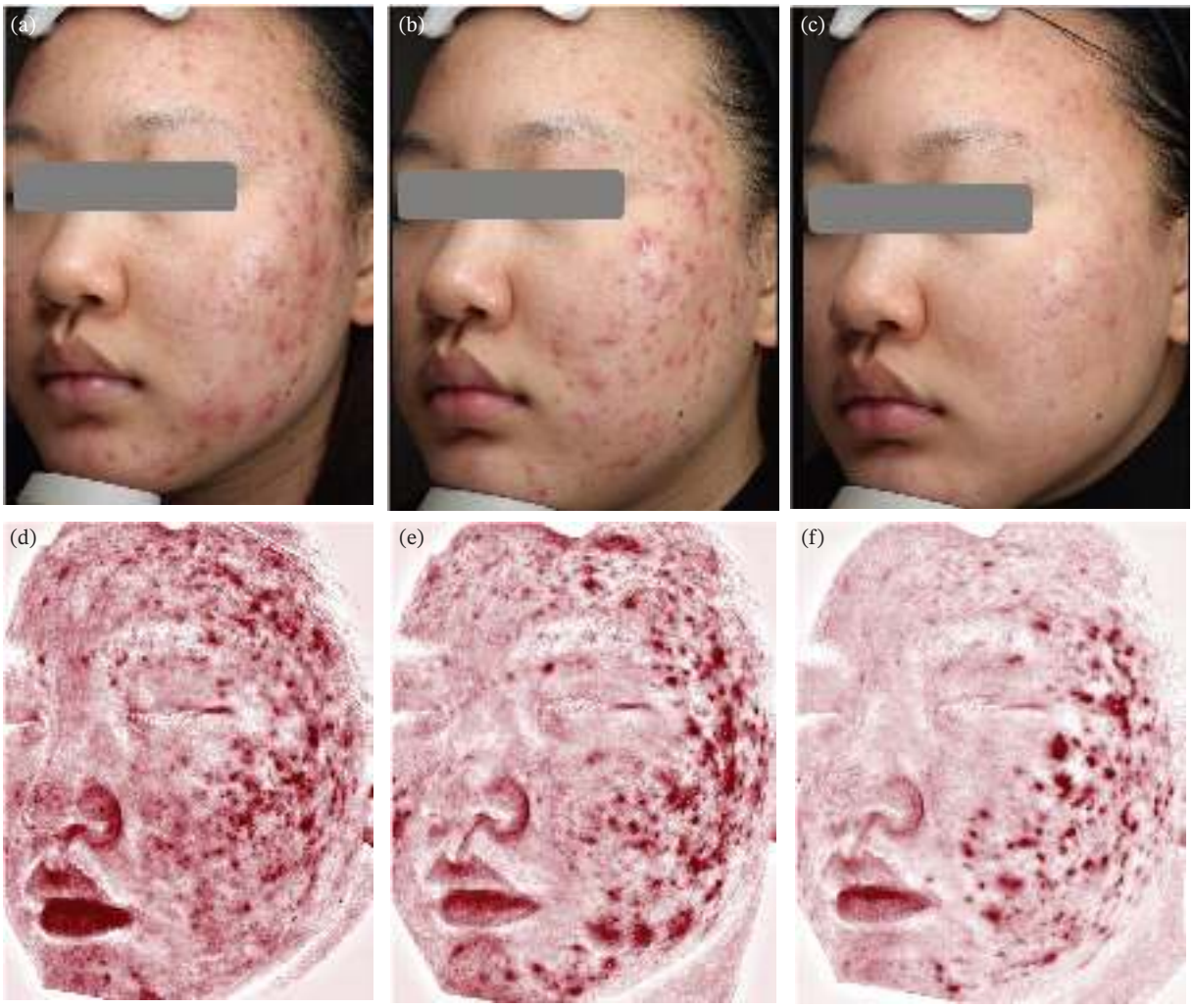
FLE, generated through activation of a photoconverter gel by blue LED light, provides noncytotoxic photobiomodulatory effects that may promote epidermal repair, alleviate residual inflammation, and improve skin texture [9, 11]. Beyond acne, FLE has been investigated in wound healing [12], acne [13], skin rejuvenation [6, 11], and in combination with picosecond lasers for solar lentigines [7]. The Kleresca system has also demonstrated efficacy in inflammatory dermatoses such as rosacea and acne [9, 14], likely through modulation of immune response and reduction of erythema.

In this case, two sessions of ALA-PDT followed by twelve sessions of FLE maintenance therapy resulted in marked clinical improvement and high patient satisfaction. Lesion counts declined substantially, with only 10 inflammatory and 15 non-inflammatory lesions remaining at the end of treatment, meeting the criteria for marked improvement (60%–89% clearance). FLE also offered important practical advantages: it was painless (VAS score = 0), in contrast to the moderate-to-severe discomfort during ALA-PDT (VAS score = 7). VISIA imaging documented reductions in facial erythema (red-area) and PpIX fluorescence, supporting the clinical findings [15]. Although the precise mechanisms of FLE remain under investigation, available evidence suggests that it may stimulate fibroblast-driven collagen synthesis, attenuate proinflammatory cytokine release, and enhance angiogenesis [5, 6]. In vitro data indicate that FLE modulates inflammatory pathways in keratinocytes and dermal fibroblasts, which could underlie its anti-inflammatory and reparative effects [6].



(A)

FIGURE 1 | (Continued)



(B)

FIGURE 1 | (A) Right-side and (B) left-side facial images. (a, d) Lesion at initial presentation and corresponding VISIA red area image. (b, e) Lesion after two ALA-PDT sessions post-treatment and corresponding VISIA image. (c, f) Lesion at 4-week follow-up after completion of the combined regimen (two ALA-PDT sessions plus twelve FLE sessions) and corresponding VISIA red area images.



(a) (b) (c)

FIGURE 2 | (Continued)



(d) (e) (f)

FIGURE 2 | VISIA PpIX fluorescence images of the right (a–c) and left (d–f) facial regions at baseline, post-two ALA-PDT sessions, and 4-week follow-up after completion of the combined regimen (two ALA-PDT sessions plus twelve FLE sessions).



(a) (b) (c)

(d) (e) (f)

FIGURE 3 | Clinical photographs at 3-month (a–c: frontal, left, and right views) and 12-month (d–f: frontal, left, and right views) follow-up after two ALA-PDT sessions combined with twelve sessions of FLE maintenance therapy.

Despite these encouraging results, this report has limitations. The evidence is derived from a single case, and although the follow-up extended to 12 months, long-term outcomes remain unknown. Importantly, given the single-patient design and absence of a within-patient control (e.g., split-face comparison), it is not possible to isolate the specific contribution of FLE after ALA-PDT, and a similar improvement might have been achieved with ALA-PDT alone. In addition, no cost-effectiveness assessment was performed. Future multicenter studies should aim to standardize treatment protocols, define optimal session intervals and light parameters, and evaluate relapse rates beyond 12 months. Controlled study designs will be needed to better delineate the role of FLE as a maintenance or complementary therapy following ALA-PDT. Comparative trials with systemic retinoids would further clarify whether ALA-PDT combined with FLE maintenance could represent a viable alternative for patients in whom oral therapies are contraindicated.

6 | Conclusions

Combining ALA-PDT with FLE maintenance therapy may be a feasible and well-tolerated approach for the management of severe acne. Larger controlled studies are warranted to standardize treatment protocols and to clarify the long-term role of FLE in sustaining clinical remission.

Author Contributions

All authors made a significant contribution to the work reported. Rongxin Ren—conceptualization, data curation, and writing–original draft; Wenjiang Qian—methodology; and Hongyi Zhao—resources, supervision, and writing–review and editing.

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Ethics Statement

This study was approved by the Ethics Committee of Beijing Hospital (2025BJYYEC-KY056-02) and complied with the tenets of the Declaration of Helsinki. Informed consent was obtained from the patient included in this study.

Consent

The patient's written informed consent has been obtained to have the case details and any accompanying images published.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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Consensus-based alternative regimes for treating inflammatory acne and rosacea using fluorescent light energy with or without low-dose isotretinoin therapy



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ABSTRACT

Fluorescent light energy (FLE) namely Kleresca® treatment is a non-invasive novel photobiomodulation (PBM) therapy with anti-inflammatory effects and an efficacy profile for treating acne and rosacea. The inflammatory skin conditions acne and rosacea are chronic, complex different diseases with few targeted, non-invasive and efficient therapies available. Isotretinoin is often used for moderate to severe acne with a high efficacy profile, but is associated with significant and undesirable side-effects, while rosacea treatments target arising symptoms with different approaches.

The objective of this article is to provide updated consensus-based regimes that combine the use of FLE and low-dose isotretinoin for the treatment of acne and rosacea based on the consensus review of in-market applied alternatives from a group of highly experienced dermatologists, whom have worked extensively with FLE.

Observations suggest that based on the multifactorial pathogenesis and heterogeneity in clinical appearance of acne and rosacea, there is limited data available on how to optimally integrate therapies for these chronic inflammatory skin conditions. We here present consensus for a novel treatment regime using the combination of FLE alone or in combination with low-dose isotretinoin to be utilized to optimize and accelerate clinical resolution.

In conclusion, this consensus-based regimes of FLE and low-dose isotretinoin could support the use of this non-invasive and efficient innovative energy-based biophotonic platform as a promising treatment option, nevertheless further robust clinical evidence and metanalysis are recommended to comprehensively understand these innovative therapeutic options.

Keywords: **Photobiomodulation, Fluorescent Light Energy, Isotretinoin, Consensus Treatment, Acne, Rosacea**

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INTRODUCTION

Acne and rosacea are two different and complex multifactorial inflammatory skin diseases that greatly affect patients´ quality of life[1,2].

Rosacea is estimated to affect up to 10% of the population, typically diagnosed in people with fair skin (Fitzpatrick I-II) between the ages of 45-60[3,4].

Most people are affected by some degree of acne throughout their life, and for many especially during puberty[5]. Acne is a chronic disease caused by excess sebum production, Cutibacterium acnes (C. acnes formerly named Propionibacterium acnes, P. acnes) colonization of hair follicles, hyperkeratinisation, and inflammation[6].

The underlying reasons for acne development is debated but alterations in, or abnormal (androgen), hormone levels as well as genetics are seemingly often involved.

The impact of factors such as stress and diet are, however less clear[5,6]. Symptoms caused by acne often impact patients psychological well-being and self-esteem, whereas scarring of the skin is a common permanent consequence that underlines the need for early and swift interventions[7].

The pathophysiology of rosacea is unclear; however, it involves vascular changes, dysregulated immune responses, and excessive inflammation[8].

Diagnosis is based on a defined set of criteria, which means that if one diagnostic criteria (persistent erythema or phymatous changes) or two major phenotypic criteria (flushing, papules/pustules, telangiectasias, or ocular symptoms) are present, the patient is diagnosed with rosacea[3].

There are four subtypes of rosacea based on manifestation of symptoms; 1) erythematotelangiectatic (ETR), 2) papulopustular (PPP), 3) phymatous (PhR), and 4) ocular (OR)[8]. Furthermore, many patients experience secondary symptoms to rosacea, such as plaque formation, oedema, phymatous alterations as well as a burning or stinging sensation in the skin[4]. Symptoms of rosacea can be induced or aggravated by several environmental factors, such as high or low temperatures, alcohol, spicy food, UV-exposure, and exercise[8].

Treatment of acne is often characterized by topical and systemic administration of antibiotics or retinoids with varying effects, risk of bacterial resistance, and potential severe side-effects. Therapies target different aspects of acne pathology and is often sucessfully used in combination; however, improvements in the skin are usually slow to visualize[9].

Oral isotretinoin treatment is one of the most efficient therapies for acne as well as other inflammatory skin conditions like rosacea, but has numerous documented adverse effects including cheilitis, xerosis, hyperlipidemia, and renal dysfunction[10].

When used at the recommended doses, these adverse effects challenge the use of isotretinoin especially in a central and growing patient group such as children in early onset of puberty as well as in women developing hormonal acne in relation to pregnancy[5].

Treatment for rosacea is as complex as the diagnosis and is often based on targeting specific symptoms. Erythema is treated with topical intervention to either α1- or α2-adrenergic agonists or with invasive light/laser therapies, such as pulsed dye (PDL) or potassium-titanyl –phosphate.

For papules and pustules a larger range of both topical and oral interventions are used.

Tetracycline antibiotics (e.g. doxycycline) are highly efficient, although the risk of resistance is high, since rosacea is a chronic disease.

Advanced phymata with pronounced hypertrophy and nodular growth can only be treated using surgical interventions, while in earlier stages the use of anti-inflammatory agents also used for PPP treatment and is found advantageous[3].

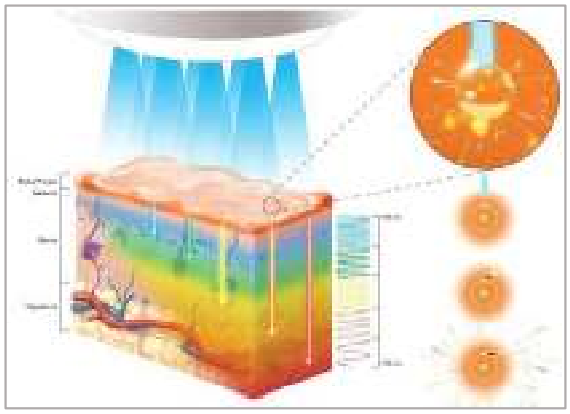
With limited valid non-invasive treatment options, novel, applicable and efficient therapies are needed for acne and rosacea treatments.

Fluorescent light energy

Fluorescent light energy is generated by a topical chromophore-containing amorphous hydrogel that upon activation by a blue multi-LED lamp emits a broad spectrum fluorescent light that is targeted to different layers of the skin tissue.

The energy transfer from the blue LED light from the lamp source (446 nm) to FLE multiple wavelenghts ranging from 500-700 nm via the suspended chromophores within the amorphous hydrogel[11]. The chromophores absorb the photons from the blue multi-LED light and enter an excited state. The chromophore is unable to remain in an excited state for more than pico seconds, and re-emits a photon constituted of longer wavelength with lower energy characteristics[12]. This shift in energy by photon absorption and emission is called Stokes shift [11,13](Figure 1).

Figure 1. Fluorescence light energy (FLE) photobiomodulation technology. The chromophore-containing gel (orange) is activated by a blue LED lamp (upper part). Through the physical mechanism of the Stokes shift, green, yellow, and orange/red wavelengths are emitted and delivered to the different layers of the skin.



The safety profile of FLE has previously been demonstarted in mulitple clinical studies and case reports to be safe and well tolerated[14–19]. Clinical studies have shown long-term efficacy of FLE treatment for moderate to severe acne[14,16]

Furthermore, several case reports have been published on FLE for rosacea[17,20], as well as other inflammatory skin conditions, such as acneiforme eruption[21], acne fulminans[22], acne conglobate[18], hidradenditis suppurativa[18], senile lentigines[23], and solar lentigines[24]. Finally, the anti-inflammatory properties of the FLE biophotonic platform is documentated in the treatment of acute and chronic wounds, including second-degree burns[25], venous leg ulcers, diabetic foot ulcers, and pressure ulcers[19].

The mode of action for FLE therapy is multifactorial, and still not fully understood.

Studies have shown reduced levels of central pro-inflammatory cytokines (tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6)) from in vitro cultures of primary human fibroblasts[11,26] while fibroblast cultures increased their collagen production after direct FLE stimulation[11] in line with a clinical study showing efficacy of FLE in skin rejuvenation[15,27].

Finally, mitochondria are the main energy-producing organelles of human cells and recent findings showed a direct effect of FLE on mitochondrial number, size and morphology, indicating enhanced mitochondrial activity after FLE stimulation[28].

Isotretinoin in treatment of acne and rosacea

The efficacy of isotretinoin (13-cis retinoic acid) for treatment of acne was published in the late 70´s and introduced to the US market in 1982[29,30]. Isotretinoin is a synthetic vitamin A derivative that targets and reduces sebum production through induced apoptosis of sebocytes[31]. Moreover, studies have suggested that isotretinoin has direct effects on the endogenous anti-microbial response. Dispenza and coworkers showed an exaggerated innate immunity via toll-like receptor 2 (TLR2) response to C. acnes bacteria, which could be dampened by isotretinoin therapy[32]. In line with the aforementioned, another study found that acne patients express reduced levels of antimicrobial peptides in the skin, and this could partly be rescued by lower dose of isotretinoin treatment[33].

Isotretinoin treatment is associated with adverse effects of varying severity, including headache, altered appetite, cheilitis, xerosis of the skin and mucous membranes, hyperlipidemia, inflammatory bowel disease, and renal dysfunction; reported psychiatric adverse events requiring monitoring have also been reported in case reports and regulatory safety warnings, but causality remains debated, and recent population-level meta-analytic evidence has not demonstrated an increased relative risk of suicide or psychiatric disorders among isotretinoin users[10,34,35].

Moreover, isotretinoin is teratogenic to the developing fetus, affecting development of the central nervous system, craniofacial and cardiac systems[30,36].

It has been speculated whether these adverse effects are all caused by or related to the pro-apoptotic effect of isotretinoin therapy.

Studies have suggested that isotretinoin induces apoptosis through increased p53, fork-head box class O transcription factor 3a (FoxO3a), and tumor necrosis factor-related apoptosis inducing ligand (TRAIL) signaling, which are known to promote apoptosis in a number of human cells and involved in progression of fibrosis and several cancers[37].

Severity of isotretinoin mediated adverse effects are seemingly related to the administred dose[31,38]. However, studies have suggested that low-dose (2.5-20 mg/day) isotretinoin administration reduces sebum production, acne lesions, C. acnes colonization, and significantly reduced PPR and PhR rosacea, although with some adverse effects still appearing including cheilitis, skin xerosis, edema, and erythema[39,40].

Determining isotretinoin dosage based on body weight (mg/kg/day) is fundamental for therapeutic precision. Standard therapy typically involves 0.5 to 1.0 mg/kg/day to reach a cumulative dose of 120 to 140 mg/kg. However, these doses can be excessive for mild to moderate acne, and low dose protocols have emerged as cost effective alternatives that reduce dose dependent side effects. These variations include intermittent cycles (e.g., one week of 0.5 mg/kg every month for six months) or low-dose fixed daily administration (20 mg/day), both aimed at improving tolerability and reducing treatment costs.

Nevertheless, the lack of uniformity across protocols necessitates that they should be based on specific daily weight-based dosage.

According to Sadeghzadeh-Bazargan and coworkers[41], daily doses between 0.1 and 0.3 mg/kg are recommended due to their superior safety profile. Despite concerns about relapse, studies show no significant difference in recurrence rates between s‘ˆndard and low dose

treatments (34.6% versus 21.5%).
Newer formulations also offer higher bioavailability to optimize the outcomes and dietary factors might affect the success of long term treatment are also a relevant consideration in these regimens.
In the light of the above, a daily range of 0.1 to 0.3 mg/kg/day could be considered as a clinical definition of a low dose regimen[41]. Use of isotretinoin for other dermatological conditions such as hidradenitis suppurativa, scarring alopecia, and rosacea was recently reviewed [39]. Interestingly, several studies and reviews have reported the use of isotretinoin especially for PPP and PhR rosacea with succesful outcomes, although with the limitations associated with the known adverse effects of the treatment[2,40,42,43].

Combining FLE and low-dose isotretinoin for treatment of acne and rosacea

Combination therapies are often efficient when treating complex multifactorial diseases like acne and rosacea[5,44,45]. FLE is extensively used for treatment of different severities of acne and rosacea in clinics throughout Europe and Australia.
With the direct anti-inflammatory effects of FLE and the reduced sebocyte activity from low-dose isotretinoin, we hypothesize a treatment for acne and rosacea that targets several pathophysiological pathways underlying these inflammatory conditions.
The proposed regimens will ensure an efficacious regulation of essential processes to control inflammation, normalize the skin, and ultimately lower the risk of scarring as well as other undesired factors associated with acne and rosacea.

Materials and methods

Expert Panel Composition and Selection

A formal consensus process was conducted.
The Nominal Group Technique (NGT) expert panel consisted of 7 international specialists in the field of dermatology.
Participants were selected based on pre-defined eligibility criteria, including: (a) a minimum of 5 years of clinical experience with FLE therapy, (b) a proven record of peer-reviewed or conference publications in the subject area, and (c) active involvement in national or international scientific societies[46].

Procedure and Rounds

The consensus development was structured into three distinct phases to ensure methodological transparency and minimize bias:

Phase I (Preparatory):
A research committee performed a comprehensive literature review to identify key results and potential clinical uncertainty and drafted an initial set of preliminary items and recommendations.
Phase II (Face-to-Face Meeting):
The expert panel convened during the 22nd IMCAS World Congress to facilitate discussion (Paris, France). Each item was presented, followed by a structured discussion to refine the wording and address ambiguities. A round of voting was conducted during this session to assess the clinical relevance and feasibility of the selected item.
Phase III (Validation):
Following the meeting, the consolidated document was circulated via electronic platforms to all panel members for revision rounds and for a final confirmation round ensuring that the written recommendations accurately reflected the verbal consensus reached.
The panel members further confirmed that the treatment approaches reflected in these recommendations have continued to be used in their routine clinical practice since the consensus meeting and remain updated and in use at the time of manuscript preparation.

Consensus Thresholds and Levels of Evidence

A pre-defined consensus threshold of 90% agreement was required for the inclusion of any recommendation in the final manuscript.
Items failing to reach this threshold were either revised for further evaluation until it reached the 90 % or excluded if failed the thresold.
In instances where high-level clinical trial data were unavailable, recommendations were classified Expert Opinion, representing the collective agreement reached by a panel of seven clinical experts during a dedicated consensus meeting held at the 22nd IMCAS international conference.

Patients included

Mild to severe acne and rosacea patients were included based on diagnosis by the treating doctors.

Ethics Statement

Written consent was provided by patients for the use of their photos in Figures 2-4.
Since these consensus guidelines are based on protocol use of an existing approved therapy for acne and rosacea, no approval from ethics committees was needed.

Figure 2. Kleresca® FLE treatment for acne.
Mild-moderate acne patient (not wishing to take isotretinoin) was treated with Consensus Acne Protocol 1: 2 Kleresca® FLE treatments per session (10 min pause between treatments), twice a week for 3 weeks. Appearance of the skin as presented at:
A) baseline, B) 7 days after last treatment, and C) 6 month follow-up.



Figure 4. Kleresca® FLE and very low-dose isotretionin treatment for papulopustular rosacea. Patient was treated with Consensus rosacea protocol 4: double Kleresca® FLE treatments every other week for 6 weeks (6 Kleresca® FLE treatments) combined with 5 mg/day isotretinoin. For maintenance, patient was treated with double Kleresca® FLE treatments every other month. Appearance of the skin as presented at: A-B) baseline, C-D) at first maintenance treatment, 2 months after last treatment and E-F) maintenance treatment 6 months after last treatment.



Treatment protocol

Pretreatment

As ordinary pretreatment program, facial cleansers and rinse with warm water were used to clean facial skin to remove grease, dirt, make-up etc.

Light source

The traditional excitation light sources to generate FLE treatments mainly include blue light-emitting diode (LED) lightsources

The LED light sources with a large irradiation spot as the Tri-panel LED Facial Lamp is recommended for facial treatment, while a portable LED lamp or single panel LED Lamp is ideal for treatment accross the whole body.

Fluorescent Light Energy (FLE) System: Kleresca

The FLE procedure was standardized according to the manufacturer's recommended parameters to ensure consistent energy delivery.

The gel used in the system is a topical photoconverter gel containing specific chromophores which are illuminated by a LED activator, which is a device delivering photons with wavelengths between 440 nm and 460 nm, and a fluency between 30- 39 joule/cm2, at 5 cm from the light source.

Upon illumination by the LED activator, the chromophores produce fluorescence in the visible range with a broad spectrum of wavelengths.

The topical chromophore is presented in two jars, which must be mixed before application.

Each session involved the application of a freshly prepared 2 mm layer of photoconverter gel over the treatment area. The skin was then exposed to a LED lamp for exactly 9 minutes, positioned at a fixed distance of 5 cm. The LED light source emitted blue light at 440 to 460 nm to activate the chromophores. Following the 9-minute exposure, the exhausted gel was gently removed using a spatula, and the skin area was rinsed with water.

For patients undergoing a single session, habitual topical creams were applied before discharge. In cases of a double session, a 5-minute resting period was observed before applying a second layer of freshly prepared gel for a subsequent 9-minute exposure, following the same cleaning procedure afterward.

These parameters remained constant throughout the treatment cycle to ensure the reproducibility of clinical outcomes in strict adherence to the manufacturer's safety and efficacy guidelines.

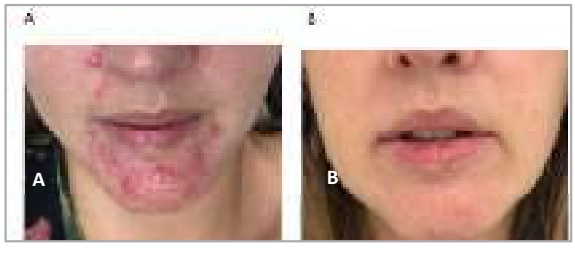
Kleresca® FLE and low dose isotretinion

The standard treatment protocol for FLE targeting moderate-severe acne or PhR rosacea is a single treatment twice a week for 6 consecutive weeks[14,16], which represents a total of 12 effective treatments.

FLE for mild-moderate acne and PPP rosacea is a single treatments once or twice weekly for 4-6 consecutive weeks[17,20], which represents a total of 4-12 effective treatments.

However, the strong safety profile of FLE has reassured experienced dermatologists to adapt and combine therapies from standard protocols.
This in turn allowing the flexibility to meet the demands of different patients.
All tested and reported protocols within this consensus guidelines revealed clereance of inflammation, improved skin quality, and patient satisfaction.
There are several options for scheduling treatment for acne (summarized in Table I) that can be planned to account for several personal conditions essential for the patient, such as distance from place of residence to the clinic, work plan and flexibility, as well as individual wishes related to treatment, adverse effects, and speed of response.
For patients not wishing to take even low-dose isotretinoin previously described as a daily range of 0.1 to 0.3 mg/kg/day, a double FLE treatments (two single treatments with 10 minutes break in between) twice weekly for 3 weeks was reported (Figure 2, Table I, Consensus acne protocol 1).
The short duration of this protocol makes it applicable for patients wanting a shorter therapy schedule and faster response.
The shorter protocol might be too compact for some patients and can be prolonged to comprise less frequent visits to the clinic by suggesting double FLE treatments every other week for 12 weeks combined with isotretinoin at 5 mg/day (Table I, Consensus acne protocol 2).
Finally, when weekly treatments are possible single FLE treatments one-two times weekly for 4-12 weeks combined with isotretinoin at 5-10mg/day (Table I, Consensus acne protocol 3), single FLE treatments two times weekly for 6 weeks combined with isotretinoin at 10mg/day (Table I, Consensus acne protocol 4), or single FLE treatment once weekly for 4-8 weeks combined with 10-20mg/day isotretinoin have been reported (Table I, Consensus acne protocol 5).
Similar flexibility is applicable for the rosacea protocols (summarized in Table II). For patients not suitable or not wishing to take low-dose isotretinoin, single FLE treatment once weekly for 4-6 weeks (Table II, Consensus rosacea protocol 1).
However, for more severe or complex cases, single FLE treatment twice weekly for 12 weeks combined with 5mg/day isotretinoin (Table II, Consensus rosacea protocol 2) or single FLE treatment once weekly for 4-8 weeks combined with 5mg/day isotretinoin have have shown promising results (Figure 3, Table II, Consensus rosacea protocol 3).
Finally, for patients where weekly sessions are challenging, double FLE treatment every other week for 6 weeks combined with isotretinoin at 5mg/day is also an option (Figure 4, Table II, Consensus rosacea protocol 4).
Isotretinion dosing is generally used in the range of 5-100 mg/day, considering a daily range of 0.1 to 0.3 mg/kg/day for low dose regimen, where 5-40 mg/day is considered low-dose[38,41].
When combined with FLE, low-dose isotretinion has shown extraordinary results for treatment of acne and rosacea. Authors reported variations in onset of use of low-dose isotretinoin and FLE, which reflects a flexible combination treatment regimes. Most often the combination therapy was initiated simultaneously.
However, in some cases a FLE treatment schedule was started in advance before isotretinoin was introduced, since European legislation causes a delay in use of isotretinoin in women of childbearing age due to adverse effects previously reported on fetus development.
Finally, FLE was documented to be used in combination with erythomycin or metronidazole as a replacement to low-dose isotretinion with similar results.
In summary, treatment protocols can be significantly shortened or extended to fit patients individuals' requests and preferences, without compromising efficacy or safety.
In general, the response and efficacy of the FLE for acne have been observed faster when applying more compact protocols.

Figure 3. Klerescа®
FLE and very low-dose isotretionin treatment for rosacea. Moderate acne patient treated with Consensus acne protocol 4: 1 Klerescа® FLE treatment per session, once a week for 4 weeks in combination with 5mg/day isotretinoin. Appearance of the skin as presented at:
A) baseline, and B) 8 weeks after last treatment.



When using FLE in combination with low-dose isotretinoin faster responses were observed for shorter protocols (e.g. single FLE treatments twice a week for 6 weeks combined with isotretinion) compared with the longer protocol (e.g. double FLE treatments every other week for 12 weeks combined with isotretinion).
A similar response and flexibility was observed when using FLE stand-alone therapy (e.g. double FLE treatments twice a week for 3 weeks) compared with more delayed responses when protocols are elongated (e.g. single FLE treatments twice a week for 6 weeks).
Moreover, low-dose isotretinoin can be modulated in concentration (0.1 to 0.3 mg/kg/day) while varying the duration of treatment, which further underlines the flexibility in tailoring of the combination therapy.

Additional topical treatment
Topicals, including cleansers, and moisturizers that contain antioxidants, hydrate, provide sebum control, or provide UV-protection can be used adjunctly to any FLE treatment regimen.

Follow-up treatment
A follow-up program can be tailored specifically to the individual patient´s needs, wishes, and skin condition.
Many patients schedule a follow-up treatment when a flushing event (rosacea) or a flair up (acne) occur. For acne and rosacea treatments, a topical protocol is usually also continued.
For acne patients follow-up treatment supporting the primary protocol may be performed through single FLE treatments either as a stand alone therapy or combined with continued low-dose isotretinoin.
For rosacea patients the primary protocols are often followed by more long-term treatment regimes, which could consist of either single or double treatment sessions following the occurrence of flushing events post termination of the primary treatment schedule.
Similar to acne low-dose isotretinoin treatment can also be continued for rosacea patients.

Safety profile
The combination of FLE and low-dose isotretinoin for treatment of acne and rosacea is based on the consensus panel recommendation and is considered safe and efficacious.
The expert panel reached a consensus that the therapy demonstrates a highly favorable safety profile, characterized by optimal tolerability and with the benefit-risk ratio supporting its use in clinical practice.
No severe adverse effects from FLE alone has been observed. Moreover, the well-documented isotretinoin adverse effects, even when used in low-doses, were noticed by the physicians to be reduced when combined with FLE.
It has previously been reported that some patients experience transient hyperpigmentation after FLE therapy[14,16].
Finally, the combined used of FLE with erythomycin or metronidazole was reported to demonstrate similar results with a satisfying safety profile without any adverse effects such as photosensitivity, as previously suggested[47].
A clear advantage acknowleged by the consensus panel is that the combination of these two therapies provides results in an accelerated efficacy profile without compromising safety. Clinically, this is translated into rapid reduction and clearance of inflammation, erythema, and lesions throughout the various protocols. Additionally, all cases showed that when patients were treated with FLE and low-dose isotretinoin simultaneously, the initial flares of acne which are usually caused by isotretinoin were absent, indicating that FLE could abrogates this isotretinoin-mediated effect. Finally, accelerated healing and general improved skin quality, as reported, are essential factors for lowering the risk of scarring and ultimately increase patients´ satisfaction and quality of life.
Studies show that onset of puberty is in general receding[48]. Conventional use of isotretinoin is not advised in young children; however, in this consensus panel the combined use of FLE and low-dose isotretinoin was acknowledged as suitable for children as young as 12 years of age. Although the consensus panel did not report any challenges, some patients may experience transient hyperpigmentation, following a FLE treatment, as is also observed with other PBM based treatments[49].
This, according to the consensus panel, can be mitigated with proper knowledge of the patient history, patient selection and expectation management, patient information and disclosure as well as adjustments to the treatment schedule as is found appropriate.

Study Limitations

Despite the clinical significance some limitations should be acknowledged. First, the retrospective nature of some data may introduce inherent selection bias across both acne and rosacea groups.

To improve clinical stratification, the reported rosacea protocol in future studies and regimens should aligns with a phenotype-based approach. By moving beyond a general severity assessment, it is possible utilize specific objective endpoints for each manifestation.

For the papulopustular phenotype, efficacy measured through inflammatory lesion counts and IGA scores. Conversely, for the erythematotelangiectatic phenotype, the Clinician Erythema Assessment (CEA) could provide a standardized metric for evaluating redness and vascular response.

This approach ensures that clinical outcomes are both measurable and reproducible.

Second, while the low-dose isotretinoin regimen (0.1 to 0.3 mg/kg/day) demonstrated high efficacy and safety, the influence of individual dietary factors on drug bioavailability was not strictly controlled, which remains a variable in long-term treatment success for both conditions.

Furthermore, the adjunctive skincare routines followed by patients were not standardized, introducing potential variability in skin barrier maintenance and overall treatment tolerance.

Additionally, while the FLE protocol followed standardized manufacturer guidelines, the comparison between single and double sessions could benefit from further prospective evaluation to better define the optimal frequency for specific acne severities and rosacea phenotypes.

Finally, although objective endpoints were utilized, the wide variability in clinical presentation between inflammatory acne and vascular rosacea poses a challenge for universal standardization.

These limitations, however, do not diminish the clinical relevance of the consensus findings, which provide a first practical framework for the integration of low-dose isotretinoin and FLE in dermatological clinical practice.

Conclusion

Acne and rosacea are different complex chronic inflammatory diseases characterized by varying degrees of disease severity, which is highly reflected in the various treatment protocols.

The use of FLE combined with low-dose isotretinoin treatment for acne and rosacea has shown preliminary satisfying observations.

The protocol developed obtained a satisfactory evaluation and agreement between the evaluators.

These consensus-based guidelines may provide new protocols for using FLE as a stand alone therapy or in combination with low-dose isotretinoin to provide healthcare practitioners the flexibility required to meet the needs and schedules of patients while improving efficacy without compromising safety.

This consensus aims to support clinicians in the evidence-informed and consistent use of FLE and isotretinoin-based combination approaches, while providing a framework for further refinement of treatment protocols.

The technique and potential applications of FLE therapy continue to evolve, and ongoing clinical experience may help optimize patient selection, treatment parameters, and combination strategies to enhance efficacy while maintaining a favorable safety profile.

As with any clinical protocol, these recommendations should be periodically reviewed and adapted as new evidence becomes available.

Table I. Protocols for acne treatment.

Kleresca® FLE Acne Treatment Stand Alone			
Standard Acne Protocol	***Consensus Acne Protocol 1***		
Duration: 6 weeks Frequency: 1 Kleresca® FLE treatments per session, twice a week	Duration: 3 weeks Frequency: 2 Kleresca® FLE treatments per session (10 min pause between treatments), twice a week		
Consensus Combination Protocols for Acne: Kleresca® FLE with very low-dose isotretinoin			
Consensus Acne Protocol 2	***Consensus Acne Protocol 3***	***Consensus Acne Protocol 4***	***Consensus Acne Protocol 5***
Duration: 12 weeks Frequency: 1 Kleresca® FLE treatments per session, every other week + 5 mg/day isotretinoin	Duration: 4 – 12 weeks Frequency: 1 Kleresca® FLE treatments per session, once/twice a week or every other week + 5-10 mg/day isotretinoin	Duration: 6 weeks Frequency: 1 Kleresca® FLE treatments per session, twice a week + 10 mg/day isotretinoin	Duration: 4 – 8 weeks Frequency: 1 Kleresca® FLE treatments per session, once a week + 10-20 mg/day isotretinoin

Table II. Protocols for rosacea treatment.

Kleresca® FLE Rosacea Treatment Stand Alone		
Standard Rosacea Protocol	***Consensus Rosacea Protocol 1***	
Duration: 4-6 weeks Frequency: 1 Kleresca® treatment once or twice a week	Duration: 4-6 weeks Frequency: 1 Kleresca® treatment once a week	
Consensus Combination Protocols for Rosacea: Kleresca® FLE with very low-dose isotretinoin		
Consensus Rosacea Protocol 2	***Consensus Rosacea Protocol 3***	***Consensus Rosacea Protocol 4***
Duration: 12 weeks Frequency: 1 Kleresca® FLE treatments per session, twice a week + 5 mg/day isotretinoin	Duration: 4-8 weeks Frequency: 1 Kleresca® FLE treatments per session, once a week + 5 mg/day isotretinoin	Duration: 6 weeks Frequency: 2 Kleresca® FLE treatments per session (10 min pause between treatments), every other week + 5 mg/day isotretinoin

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