EXCILITE-µ: 308nm MONOCHROMATIC EXCIMER LIGHT. A CRITICAL REVIEW.

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INTRODUCTION

Exposure to the sun has always been exploited for the treatment of many diseases. For this reason it has obviously been imitated in many different ways with artificial sources, so that it could be used in every moment. The different kinds of electromagnetic radiation that reach the surface of the earth can be subdivided as follows:

- 50 % INFRARED RADIATION (800 - 2,500 nm.)
- 40 % VISIBLE SPECTRUM (400 - 800 nm.)
- 10 % ULTRAVIOLET RADIATION (100 - 400 nm.)

Phototherapy is based on the application of ultraviolet radiation (UV). Like with visible light, which can be subdivided into the colours of the spectrum from violet to red, similarly ultraviolet rays are subdivided into single bands of different wavelengths. This division is made based on the biological effect it provokes, so that the three following bands are obtained:

- UV-C (100 - 280 nm). UVC light has a germicidal effectiveness due to its absorption by the DNA. These wavelengths causes adjacent thymine molecules on DNA to dimerize, if enough of these defects accumulate on a microorganism's DNA its replication is inhibited, thereby rendering it harmless (even though the organism may not be killed outright).

The ultraviolet frequencies responsible for tanning are often divided into the UVA and UVB ranges. UVB waves have higher energy than UVA waves and are therefore more damaging and more carcinogenic.

- UV-B (280 - 315 nm). UVB light triggers creation and secretion of new melanin into the skin. It is thought to cause the formation of moles and some types of skin cancer (but not melanoma). It causes skin aging (but at a far slower rate than UVA.). It produces Vitamin D in human skin. It is more likely to cause a sunburn than UVA as a result of overexposure. It is reduced by virtually all sunscreens in accordance with their SPF.
- UV-A (315 - 380 nm). UVA light causes release of preexisting melanin from the melanocytes. It causes the melanin to combine with oxygen (oxidize), which creates the actual tan color in the skin. It seems to cause cancer less than UVB, but causes melanoma, a far more dangerous type of skin cancer than other types. It is blocked less than UVB by many sunscreens but is blocked to some degree by clothing. It is present more uniformly throughout the day, and throughout the seasons than UVB.

In the course of the years several types of UVB radiation have been used for clinical application:

- traditional or broad band UVB lamps which delivers radiation over 280-320 nm;
- selective UVB phototherapy (SUP) that has peaks at 305 and 325 nm;
- narrow band UVB lamps deliver 311 ± 2 nm radiation.

In human experiments, carried out in 1981, Parrish showed that monochromatic radiation have advantages over broadband sources. This was the starting point for developing and using new monochromatic devices.

In 2000 Asawanonda P et al. presented their preliminary study to determine the dose-response relationship of the 308nm excimer laser radiation for treating psoriasis. The favourable final remark was that “in contrast to traditional phototherapy techniques, this handheld excimer laser UV-B therapy is selectively directed toward lesional skin, thus sparing the surrounding normal skin from unnecessary radiation exposure. Treatment of other inflammatory diseases and limited psoriasis seems reasonable to pursue with this modality”. Since then, the number of scientific publications about the efficacy of 308nm radiation has been multiplied.

In 2002 Campolmi P et al. demonstrated that the light generated by a new sophisticated devices with a peak of 308 nm (Excilite™, Deka - Italy) induces clearance of psoriatic spots, although through not completely defined mechanisms and in the absence of adverse side effects. Repetitive treatments with 308 nm Monochromatic Excimer Light (MEL@308nm) cause the stabilization of the results with prolonged time of relapses. Besides the positive clinical results, MEL@308nm offers several advantages compared with the excimer laser, especially in the treatments of medium-large areas.

Since 2002, groups of investigators working in Belgium, Czech Republic, Italy, Spain and USA, have verified results on a large population and identified the principal immunologic modifications produced
by the effect of MEL@308nm for psoriasis and other inflammatory diseases.

**MEL@308nm**

Excimers are molecules that are able to bind with other atoms only when electronically excited, such as in an unstable electron configuration. The excimer, therefore, has an extremely short lifetime (10 thousand millionths of a second).

The term “excimer” derives from the expression “excited dimer”. A dimer is a molecule formed by the combination of two atoms, a polymer composed only by two components. Noble gases are gases whose atoms do not combine with atoms of the same or of different kinds since the number of electrons in the outer shell makes them stable. For this reason these atoms do not combine with other atoms to generate an energetically stable configuration. Even though we manage to modify the electronic structure of a noble gas, it loses its stability and combines with other atoms to achieve a more stable energetic condition. It is worth observing that the noble gas with a modified electronic structure represents an unstable atom which strives to come back to its original form.

When the excitation energy decreases, the excimers emit an ultraviolet photon of extremely precise energy.

<table>
<thead>
<tr>
<th>Excimer</th>
<th>Wavelength (nm)</th>
<th>Excimer</th>
<th>Wavelength (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ArF</td>
<td>193</td>
<td>F₂</td>
<td>157</td>
</tr>
<tr>
<td>KrF</td>
<td>248</td>
<td>Kr₂</td>
<td>146</td>
</tr>
<tr>
<td>XeF</td>
<td>351</td>
<td>Xe₂</td>
<td>72</td>
</tr>
<tr>
<td>XeCl</td>
<td>308</td>
<td>KrCl</td>
<td>222</td>
</tr>
<tr>
<td>ArO</td>
<td>558</td>
<td>KrO</td>
<td>556</td>
</tr>
<tr>
<td>XeO</td>
<td>558</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tab. 1: Examples of excimers and their output wavelength.

In 2002 a new device was introduced in the market. This source was a Monochromatic Excimer Light with a special sealed XeCl gas lamp that emits within a very narrow band, centred around 308 nm, with only a minimum ±1 nm amplitude (MEL@308nm). Till then only lasers have been used for excimer phototherapy. Compared to them, MEL@308nm offers several advantages. The laser has always a much smaller spot compared to the MEL@308nm, so that treatment times are considerably longer, especially for treating wide areas. In addition to the initial cost of the laser, one should also consider the very high maintenance costs and the need to handle and frequently replace the fluid cylinders, while MEL@308nm is a sealed-off device.

Excilite-µ is a MEL@308nm tabletop system at first studied in the treatment of psoriasis and then also for vitiligo, atopic dermatitis, mycosis fungoides and alopecia areata.

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**Fig. 1: XeCl excimer molecule.**

Excilite-µ is approved by the FDA and safe for Fitzpatrick skin phototypes 1 through 6. It consists of a power density of 50 mW/cm², with irradiation fields of 30, 6, and 1 cm².

**PSORIASIS**

Psoriasis is a genetically-determined disease, characterized by immunomediated pathogenesis and unpredictable, often chronic course. The disease varies in severity depending on inheritance and environmental factors. Some patients have mild disease with isolated scaling erythematous plaques on the elbows, knees, or scalp, whereas others can have up to 100% of their cutaneous surface affected. Waiting for future genetic interventions, treatment is based on symptomatic therapy that induces temporary remission of lesions and makes the disease more acceptable to the patients. To date, there is a multitude of more or less effective drugs and treatments to which each patient reacts differently. Some therapies are very effective on some patients, while they do slightly improve the condition in others. For these reasons, it is very important to adjust the therapy according to the different features of the disease (type, extension, localization, infiltration, relapse, remission, etc.) and the characteristics of the patient (age, sex, state of health, life style, previous results obtained with other therapies, any side effects observed, etc.).

It is important to remind that the therapy should never be more annoying or dangerous than the disease itself. As long as a definitive cure is not available, the best treatment is the treatment that allows for the highest effectiveness/side effect ratio. However, the balance between side effects and therapeutic effects must always be in the favour of the latter.

Data in literature indicate that MEL@308nm is an effective alternative to traditional phototherapy for psoriasis.

In their first work, Campolmi et al. studied the effect of MEL@308nm radiation on eleven patients with clinically defined palmoplantar psoriasis (PPP). PPP presents with typical scaly patches sometimes studded with sterile pustules. It often causes itching, burning, painful ragades and can lead to severe disabilities. Patients with palm and sole involvement show an increased negative social and
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psychosocial impact with decrements in quality of life. This condition is chronic and often recalcitrant to therapy. Topical and systemic treatments are often disappointing and have proven to be highly effective in the treatment of psoriasis.

At the end of the 6th week of treatment only with MEL@308nm, all patients showed an improvement ranging from 75% to 100% (as evidenced by flattening of plaques, decreased scaling and erythema, and decreased vesicle and pustule formation) and further improvement was noted at 10th week. No relapse was detected at the 16-week follow-up. Only one patient showed few scaly elements on plants at the 12-week post-treatment observation. Unwanted side-effects such as erythema, pain, blistering or hyperpigmentation were not observed. Therapy was well-tolerated by all patients.

In their final conclusion the authors highlight that the MEL@308nm, in contrast to traditional ultraviolet phototherapy, can achieve quick clearance and it can be used without any drugs. Compared to excimer laser, the MEL@308nm offers several advantages. In facts, this new therapy is able to perform a more uniform and fast treatment of the skin lesion, not mentioning that this device has sealed-off source instead of having toxic gas bottles. The possibility to clear quickly and selectively psoriatic areas (saving uninvolved skin from long-term UVB effects) with a well-tolerated and safe modality may represent a new strategy in the treatment of psoriasis and other immunomediated skin diseases too.

Cappugi et al.5 reported an improvement in PPP lesions (flattening of plaques, decreased scaling and erythema) from 50% to 100% after 1-15 sessions of MEL@308nm in 81 patients. This study suggested that 308-nm of MEL@308nm plays an essential role in drastically decreasing cytokine expression in psoriatic skin which is accompanied by clinical remission through a modulation of the local immune response and T-cell depletion and alterations in apoptosis-related molecules. After remission, the levels of cutaneous cytokines evaluated in the study showed equivalent levels to those of non affected skin as compared to levels before treatment.

Similar results are achieved by Bianchi et al.6. MEL@308nm treatment was found to cause a significant decrease in the rate of proliferation of keratinocytes and a relevant depletion of T cells in all psoriatic lesions, 48 h after the first irradiation: 308 nm light eliminated T cells from the psoriatic epidermis and also from the dermis, highlighting the ability of this UVB source to penetrate the skin compared with normal UVB and establish direct cytotoxic action on T cells infiltrating skin lesions. In summary, most of the cellular and histopathological changes that typify the psoriatic epidermis reverted to normal in all patients treated.

Aubin et al.7, after a preliminary evaluation of MEL@308nm in different chronic localized dermatoses, concluded that this source was the most effective for PPP with a mean improvement of 79% on 17 patients, while in case of plaque-type psoriasis (7 patients) the mean improvement was of 47%.

Mavilia et al.8 studied two different groups of patients with localized psoriasis and diffuse psoriasis. In the first group of 44 patients they achieved the complete remission in 68% of cases, partial remission in 23%, a minimal response in 7% and only 2% (one patient) showed no response. In the second group of 25 patients they achieved the complete remission in 32% of cases, partial remission in 48%, a minimal response in 12% and 8% (two patients) showed no response.

Nisticò et al.9, after 4 months from the treatment in 54 patients with PPP, observed a complete remission in 57% of cases, a partial remission in 24% and a moderate improvement in 19%.

In conclusion, all these studies consider the use of the MEL@308nm as a valid choice in the treatment of selected forms of psoriasis with an overall efficacy even in absence of topical/systemic drugs. MEL@308nm represents a novel and useful alternative to existing therapy (e.g. PUVA treatment or oral retinoids) and these results suggest that it is an effective and well-tolerated treatment for psoriasis.
The choice of the dose and the selection of patients represent the most important features in the variability of clinical responses. Table 2 shows a comparison among different studies.

<table>
<thead>
<tr>
<th>Scientific paper</th>
<th>Psoriasis &amp; no. patients</th>
<th>Protocol</th>
<th>Improvement score</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campolmi et al. (2002)</td>
<td>Palmoplantar psoriasis. 11 patients</td>
<td>Starting dose of 750mJ/cm². Increase of 250mJ/cm² during the following treatments (3 times for the first 4 weeks of the treatment and twice a week for 5th and 6th week)</td>
<td>75-100% (in all treated patients)</td>
<td>No side effects</td>
</tr>
<tr>
<td>Cappugi et al. (2002)</td>
<td>Plaque-type psoriasis vulgaris 70 patients</td>
<td>Starting to MED dose and increase of 150-500mJ/cm² during the following sessions. 2-3 sessions per week. No. of treatment session variable from 1 to 15.</td>
<td>50-100% (in all treated patients)</td>
<td>Unwanted side effects such as pain or blistering were not observed. Minimal erythema and itching and a transitory modest hyperpigmentation were noted in all patients.</td>
</tr>
<tr>
<td>Bianchi et al. (2003)</td>
<td>Plaque-type psoriasis vulgaris 10 patients</td>
<td>Starting to MED dose and increase of 150-500mJ/cm² during the following sessions. 3 sessions per week.</td>
<td>Not available (immunohistochemical study)</td>
<td></td>
</tr>
<tr>
<td>Aubin et al. (2005)</td>
<td>Palomplantar pustular psoriasis 17 patients</td>
<td>Mean dose per treatment : 11.8 MED. Mean no. of treatments : 5.3</td>
<td>79% (mean value)</td>
<td>Erythema and, more rarely, blisters but well tolerated. No scarring or pigmentation was observed. One patient with plaque-type psoriasis developed a Kobner phenomenon after a single treatment with MEL.</td>
</tr>
<tr>
<td></td>
<td>Plaque-type psoriasis vulgaris 7 patients</td>
<td>Mean dose per treatment : 13 MED. Mean no. of treatments : 5.3</td>
<td>47% (mean value)</td>
<td></td>
</tr>
<tr>
<td>Mavilia et al. (2005)</td>
<td>Localized psoriasis vulgaris. 44 patients.</td>
<td>Starting to 2-4 MED dose increase of 150-500mJ/cm² during the following sessions. 1 session every 1-2 weeks. Mean no. of treatments : 5.2 (localized p); 5.8 (diffuse p)</td>
<td>76-100% in 30 patients 51-75% in 10 patients 26-50% in 3 patients 0-25% in 1 patient</td>
<td>The most common side-effects were minimal erythema and itching, with mild and transient hyperpigmentation. These were recorded in all patients, but were well tolerated (no drop-outs). Only three lesions showed blisters after the first or second session.</td>
</tr>
<tr>
<td></td>
<td>Diffuse psoriasis vulgaris. 25 patients.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nisticò et al. (2006)</td>
<td>Palmoplantar psoriasis 54 patients</td>
<td>Starting to 2-3 MED dose increase of 250-500mJ/cm² during the following sessions. 1 session every 7-10 days. Mean no. of treatments : 10</td>
<td>76-100% in 31 patients 51-75% in 13 patients 26-50% in 0 patients</td>
<td>A prolonged erythema (24-48 h) was evidenced in 20 of the 54 patients after the first and second sessions with a mild pruritic sensation. Formation of vesicles and oedema were observed after three sessions in one patient.</td>
</tr>
</tbody>
</table>

Tab. 2: “MEL@308nm & Psoriasis” literature comparison.

**VITILIGO**

Vitiligo is a common idiopathic acquired depigmentation disorder, affecting 1-2% of the world population with no predilection for age, sex or racial background, caused by selective destruction of melanocytes. The disease is characterized by circumscribed white spots on the skin tending to enlarge centrifugally over time or,
less frequently, to recover spontaneously at least in part. The exact pathogenesis is unknown and several hypotheses have been proposed. They include the autoimmune hypothesis, the autocytotoxic or self-destruction theory, where reactive oxygen species (ROS) and free radicals exert melanocytotoxic activity, and the neuronal theory, which advocates the release of a chemical, toxic to the melanocytes, from the dermal nerve endings. A genetic basis is supported by the familial cases of vitiligo: a family history is found in 6-38% of cases. There is now convincing evidence for the presence of oxidative stress in the skin of patients with vitiligo; high concentrations of hydrogen peroxide together with low catalase levels have been demonstrated in the epidermis. A possible autoimmune mechanism has been considered as an increased incidence of auto antibodies and specific T cytotoxic lymphocytes have been found in patients with active disease. Furthermore, vitiligo is often associated with autoimmune disorders such as thyroid disease and diabetes mellitus.

Various treatments have been proposed. The non-surgical modalities, considered first-line therapy, include corticosteroids (oral, topical and intralesional), oral or topical psoralens plus ultraviolet A (PUVA), and recently, narrow-band ultraviolet B (UVB) therapy. The surgical modalities consist of autologous transplantation and include split-thickness epidermal grafting, epidermal blister grafting, and grafting of cultured melanocytes. Among the non-surgical modalities phototherapy is the treatment of choice for vitiligo with > 10% body surface involved. The goal of phototherapy is to stimulate melanocytes present in the adjacent area to migrate and repopulate the vitiliginous areas. Until a few years ago, PUVA therapy was the most popular treatment for vitiligo worldwide. The limitations of PUVA include acute side effects such as nausea and phototoxic reactions, as well as long term carcinogenic risk. Moreover a recent retrospective study on systemic PUVA has pointed out that this treatment is only moderately effective in widespread vitiligo.

Narrow-band UVB (NB UVB), with a peak emission at 311-313 nm, is more recent and was initially used for psoriasis. This light source has also been found useful in the treatment of vitiligo. Westerhof and Nieuweboer-Krobotova compared NB UVB with topical PUVA and found that NB UVB was more effective in the treatment of vitiligo, with fewer side-effects. More recently, Scherschun et al. have confirmed favourable results with NB UVB used as monotherapy.

Interesting results in the treatment of vitiligo have been described by Lotti et al. A recent report on a trial using the 308 nm excimer laser in vitiligo has been published by Spencer et al. The authors conclude that the degree of repigmentation in a period of 2-4 weeks is much higher than that achieved with any other current vitiligo therapy and that the xenon-chloride excimer laser may represent a new treatment modality far the management of stable vitiligo.

Fig.4: Vitiligo on the forehead. Before and after 8 treatments with MEL@308nm. (Courtesy of G Leone, P Iacovelli, A Paro Vidolin, M Picardo - San Gallicano Dermatological Institute of Rome, Italy)

The effectiveness of MEL@308nm was investigated because this source may present some advantages over the laser: larger irradiation field with the possibility to treat larger areas at a time, with shorter treatment duration; reduced risk of accidents due to over-exposure. Leone et al. have conducted a pilot open trial with MEL@308nm on 37 vitiligo patients. All patients were treated with MEL as mono-therapy from March 2002 to September 2002. Therapy was administered twice a week, on non-consecutive days. The initial fluence for each patient was 70% of the MED. Dose increments at every other treatment were: 40% from treatment 1 to 4; 30% from treatment 4 to 8; 20% constantly from treatment 8 onwards. The dose was held constant when minimal asymptomatic erythema occurred in the lesions. If symptomatic erythema (burning, pain) or blistering developed, treatment was omitted (once or twice), and when treatment was resumed the last dose was decreased by 20%.

Fig.5: Vitiligo. Before and after 33 treatment with MEL@308nm. (Courtesy of A Alomar, E Roe, CL Pimentel - Hospital de la Santa Creu i Sant Pau of Barcelona, Spain)
The response to treatment was expressed as 'no repigmentation' (score 0), 'poor repigmentation' (between 1% and 25%, score 1), 'moderate repigmentation' (between 26% and 50%, score 2), 'good repigmentation' (between 51% and 75%, score 3), and 'excellent repigmentation' (more than 75%, score 4).

Fig. 6: Vitiligo. Appearance of repigmentation by week 2 in a patient with localized lesions to the hands treated with MEL@308nm. (Courtesy of SM Chimento, M Newland, C Ricotti - University of Miami Miller School of Medicine, Florida; S Nisticò, P Romanelli - Tor Vergata University of Rome, Italy)

Thirty-three patients (89%) obtained an acceptable degree of repigmentation after 3 months; 21 (57%) of these patients achieved 'good repigmentation' and 12 (32%) achieved 'excellent repigmentation'. At the end of the evaluation period the number of patients with grade 4 repigmentation increased to 18 (49%). In the 'excellent repigmentation' group, two patients have achieved complete repigmentation after 3 months and consequently the treatment was stopped. Distribution of patients on the basis of the degree of repigmentation obtained can be seen in Table 3. In 35 patients (95%) repigmentation began within the first eight sessions.

<table>
<thead>
<tr>
<th>Repigmentation score</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (0%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 (1-25%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2 (26-50%)</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3 (51-75%)</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>4 (&gt;75%)</td>
<td>12</td>
<td>18</td>
</tr>
</tbody>
</table>

Tab. 3: Repigmentation at 6 months.

The contraindications and risks (short-term and long-term) are the same as with conventional NB UVB, but the possibility of obtaining satisfactory results in terms of repigmentation with significantly lower cumulative doses is an important advantage. The use of this new source with high fluences for NB UVB phototherapy can shorten the duration of UV exposure, leading to a decrease in the dose-dependent side-effects typically associated with phototherapy. Results with MEL@308nm show that the cumulative dose at the end of the treatment cycle is significantly lower than that reported in other studies with conventional NB UVB.\textsuperscript{15,16} The rapid onset of repigmentation may also play an important role in ameliorating patient motivation and compliance. In conventional NB UVB phototherapy, one reason for early interruption is difficulty in complying with the frequency of treatments. The possibility of having biweekly and weekly treatments with the MEL@308nm was greatly appreciated by the patients. Finally, three patients who did not respond to previous treatments with NB UVB showed excellent repigmentation after MEL@308nm therapy. This finding may be useful in the interpretation of the mechanism of action of MEL@308nm compared to conventional NB UVB. The difference in the mode of action of these two sources, which have substantially the same spectra of emission, may be due to the ability of the MEL@308nm device to deliver higher fluences to the target tissue in less time. In other words, the induction of pigmentation by NB UVB may not obey the 'reciprocity law'.

The findings concerning the response of different body sites to treatment are in agreement with previous studies in vitiligo using narrow-band UVB, broad-band UVB, or oral PUVA therapy. Nevertheless, a satisfactory response on the hands was noted: two patients achieved grade 3 repigmentation. Even if this finding is not significant because of the limited number of patients that received treatment on the hands (n = 3), it may suggest the efficacy of higher NB UVB fluences on these locations that usually respond poorly to conventional treatment. Also Chimento SM et al.\textsuperscript{17} got remarkable repigmentation in one patient with localized lesions on both hands.

\textbf{ATOPIC DERMATITIS}\textsuperscript{18}

Atopic dermatitis (AD) is a pruritic disease of unknown origin that usually starts in early infancy and is typified by pruritus, eczematous lesions, xerosis (dry skin), and lichenification on the skin (thickening of the skin and increase in skin markings). AD is associated with other atopic diseases (asthma, allergic rhinitis, urticaria, acute allergic reactions to foods, increased immunoglobulin E [IgE] production) in many patients. It is a disease of great morbidity, and the incidence appears to be increasing. The pathophysiology of AD is poorly understood. Several cell types seem to be involved, including T lymphocytes, eosinophils, Langerhans cells, and keratinocytes. Other factors, including cytokines and IgE, are also implicated. Laboratory findings suggest a number of different pathogenetic mechanisms. One invokes an immune defect involving an abnormality of T_{H2} cells that interacts with Langerhans cells and results in increased production of some interleukins. Another theory involves defective barrier function in the stratum corneum leading to the entry of antigens, which results in the production of various inflammatory cytokines. A third mechanism involves...
environmental antigens from food (the gut), dust mites (the lungs), and other factors and portals of entry that react with antibodies to produce increased levels of IgE and, possibly, increased histamine reactions from mast cells. Superimposed with these mechanisms is a genetic predisposition to react to various environmental allergens.

AD affects 2%-5% of the general population. The prevalence is estimated between 10% and 20% in infants and children and 1%-3% in adults. Dry skin and intense itching often lead to cutaneous excoriations as well as sleeplessness and restrictions on daily activities. Management currently focuses on skin hydration, topical corticosteroids, avoidance of triggers, and nonsteroidal immunomodulators. The latter, in conjunction with emollients to treat dry skin, provide satisfactory management in most patients. Other approved therapies include phototherapy.

Aubin et al. reported encouraging results using MEL@308nm for treating AD lesions of the hands. Recently, Nisticò et al. carried out an open pilot study to evaluate the efficacy and safety of MEL@308nm in the treatment of AD lesions in both adult and paediatric patients. 6 children and 12 adults completed the study. At the end of the treatment, complete remission was observed in 12 patients (66.7%), partial remission in 3 (16.7%) and no remission in 3 (16.7%). A significant improvement was achieved after 4 week. The significance of the results was maintained at the end of treatment and after 16-week follow-up in a large number of patients.

**MYCOSIS FUNGOIDES**

Mycosis fungoides (MF) is the most common form of cutaneous T-cell lymphoma. It generally affects the skin, but may progress internally over time. The cause of MF is unknown, but it is not believed to be hereditary or genetic. It is not contagious. Typical visible symptoms include rash like patches, tumors, or lesions. Itching is common, perhaps in 20% of patients, and is not universal. Diagnosis is sometimes difficult because the early phases of the disease often resemble eczema or even psoriasis. The diagnosis is made through a combination of the clinical picture and examination, and is confirmed by biopsy.

MF progresses in stages, which are defined by the skin symptoms:

- **Patch phase** - The skin has flat, red patches often very itchy. Some areas may be raised and hard (plaques). The patches and plaques often appear on the buttocks, groin, hips, under the arms, and on the breasts/chest.
- **Skin tumors phase** - Red-violet raised lumps (nodules) appear and may be dome-shaped (like a mushroom) or be ulcerated.
- **Skin redness (erythroderma) stage** - In addition to the patches and tumors, the individual's skin developed large red areas that are very itchy and scaly. Skin folds in the face may thicken, and skin of the palms and soles may thicken and crack.
- **Lymph node stage** - In this stage, mycosis fungoides begins to move to other parts of the body. The first parts affected are the lymph nodes, which become inflamed, and often cancerous. Cancer may spread to the liver, lungs, or bone marrow.

Stage IA disease (as defined by the tumor, node, metastases, blood [TNM] system) is defined as patchy or plaque like skin disease involving less than 10% of the skin surface area (T1 skin disease).

Treatment of patch-stage IA of MF consists of various options such as topical steroids, ultraviolet (UV) B phototherapy, psoralen plus UVA (PUVA) photochemotherapy and topical chemotherapy. Good results with broadband UVB phototherapy (280–320 nm wavelength) have been reported previously. More recently, several studies have demonstrated the efficacy of narrowband UVB phototherapy (311 nm) in the treatment of early stage MF. This specific condition, characterized by limited extension of the disease and thickness of the lesions, was considered ideal to check safely the possible benefits of MEL@308nm treatment.
Mori et al.21 in their pilot study, treated 7 lesions in 4 patients with patch stage IA MF, with clinicopathologic complete remission in all cases. Compared with traditional phototherapy, MEL can selectively treat single lesions, sparing clinically non-affected skin and achieving clinical remission very quickly. Compared with UVB 311-nm therapy, usually administered 2 to 3 times a week on non-consecutive days, MEL treatment sessions were performed weekly, with very good patient compliance. Nisticò et al.22 treated 10 lesions. All achieved complete clinical remission with a marked reduction in size and infiltration of the patches and a normalization of skin colour from bright red to a slightly brownish post-treatment hyperpigmentation. All histological specimens of irradiated lesions showed a reduction of the lymphocytic infiltrate in the papillary dermis. No signs of epidermotropism and atypical lymphocytes along the dermo-epidermal junction were found in the control biopsies. All lesions were in complete stable remission, with a follow-up of 12 months. A slight erythema was evidenced in two patients after the first and second treatments, with a mild pruritic sensation. Transient hyperpigmentation in the treated areas was noticed in all patients, with spontaneous resolution after 2 weeks following the end of treatment.

PRURIGO NODULARIS
Prurigo nodularis (PN) is a chronic condition characterized by papulonodular pruriginous eruptions chiefly on the extremities, especially on the anterior surfaces of the legs. The course of the disease is chronic, the cause is unknown and several systemic disorders are associated. Itching is severe, paroxysmal, but usually confined to the lesions themselves. Treatment is challenging and choices are limited. Topical or intralesional glucocorticoids are frequently used although they are not uniformly effective. Several other therapies have been tried such as topical tacrolimus, vitamin D analogues and the substance P depletor, capsaicin, generally without good results. Ultraviolet B radiation has also been used in the treatment of PN. In particular, sequential combined treatment of UVB irradiation and topical PUVA has been reported with satisfactory results and a good response has been reported to the combination of thalidomide and UVB, although with a high number (average 32) of UVB treatments. Saraceno et al.23 reported for the first time that MEL@308nm produces a therapeutic response in PN, representing a potential advance in the treatment of this condition. Clinical remissions observed might be explained by the immunosuppressive effect of MEL on T cells and pro-inflammatory cytokine responses as seen in the treatment of psoriasis6. A partial or complete remission was achieved in 9 patients after a mean of eight applications and was documented histologically. A partial remission was observed on 3 patients (33%) while a complete clinical remission in 6 (66%) patients. After 4 months, 8 (88%) patients maintained the results achieved. Mild hyperpigmentation occurred at the lesional sites in 7 (77%) patients, especially on the pre-tibial nodules. Common side effect included a mild erythema after the first and second application; formation of vesicles and oedema was observed in 1 patient.

Fig.9: Prurigo nodularis.Before and after 15 treatments (for right elbow) and 2 treatments (for left elbow) with MEL@308nm. (Courtesy of of L Mavilia, P Campolmi, M Mori, R Rossi, P Cappugi - University of Florence, Italy)

Although the relatively small patient group and the uncontrolled nature of the study are limitations of this work, the excellent results in this usually resistant condition are encouraging. Controlled trials are now indicated to confirm these preliminary results.

ALOPECIA AREATA
Alopecia areata (AA) is the most common form of hair loss after androgenic alopecia. The loss of hair usually occurs without subjective complains. However, more severe forms of the disease can lead to marked psycho-social problems. The pathogenesis of AA is unknown to date. Numerous studies of its etiology have been concluded from different perspectives of specialized branches of medicine. Hypotheses have been made about influences that ranges from psychosomatics, environmental effects such as toxins and immunology. In general, the use of effective medicines is complicated by the fact that not all of the options have a tolerable scope of adverse effects. The results of new research, however, make it possible to recognize aspects of the pathogenesis of this disorder and indicate that it can likely be classified among autoimmune diseases24.

To date, topical immunotherapy in clinically controlled studies has been shown to be the most effective method of available treatment. As the 308nm XeCl excimer light is an efficient and promising therapeutic option in current treatment of psoriasis and vitiligo, it is possible to assume that the same light can create an immune response in a focus affected by alopecia areata. Gundogan et al.25 reported two successful cases using 308nm excimer laser. Aubin et al.7 reported about four complete
regrowths among eight patients with alopecia areata treated with MEL@308nm. The treatment is a marked improvement for patients because of the simplified ease of administration and the rapid evidence of improvement. Furthermore, the ability to aim the MEL@308nm precisely and locally is practical in terms of reducing any undesired side effect.

Fig.10: Alopecia areata. Before and after 4 treatments with MEL@308nm. (Courtesy of F Aubin, C Robert, I Cardon, P Humbert; R Laurent - University Hospital of Besançon, France)

As with psoriasis treatment, an increased induction of T-cell apoptosis plays a central role in the effect of MEL@308nm. Based on this, it can be postulated that in the case of alopecia areata, the immunosuppressive mechanism is likely to result from an interruption of the autoimmune immune cascade that results from MEL@308nm induced T-cell apoptosis. The change of interleukin production cascade that results from MEL@308nm induced T-cell apoptosis is likely to result that in the case of alopecia areata, the apoptosis of T-cell plays a central role in the effect of MEL@308nm. Based on this, it can be postulated that in the case of alopecia areata, the immunosuppressive mechanism is likely to result from an interruption of the autoimmune immune cascade that results from MEL@308nm induced T-cell apoptosis. The change of interleukin production cascade that results from MEL@308nm induced T-cell apoptosis is likely to result that in the case of alopecia areata, the apoptosis of T-cell plays a central role in the effect of MEL@308nm.

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REFERENCES