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# Micro - Focused Phototherapy Associated To Janus Kinase Inhibitor: A Promising Valid Therapeutic Option for Patients with Localized Vitiligo

Serena Gianfaldoni[1*], Georgi Tchernev[2], Uwe Wollina[3], Maria Grazia Roccia[4], Massimo Fioranelli[5], Jacopo Lotti[5], Miriam Rovesti[6], Francesca Satolli[6], Yan Valle[7], Andy Goren[8], Michael Tirant[9], Mirna Situm[10], Maja Kovacevic[8,10], Katlein França[11], Torello Lotti[8]

*[1]University G. Marconi of Rome - Dermatology and Venereology, University G. Marconi of Rome, Rome, Italy; [2]Medical Institute of Ministry of Interior (MVR), Department of Dermatology, Venereology and Dermatologic Surgery, Sofia, Bulgaria; [3]Städtisches Klinikum Dresden, Department of Dermatology and Venereology, Dresden, Sachsen, Germany; [4]University B.I.S. Group of Institutions, Punjab Technical University, Punjab, India; [5]G. Marconi University - Department of Nuclear Physics, Subnuclear and Radiation, Rome, Italy; [6]Department of Dermatology, University of Parma, Parma, Italy; [7]Vitiligo Research Foundation, New York, United States; [8]University G. Marconi of Rome, Dermatology and Venereology, Rome, Italy; [9]Psoriasis & Skin Clinic, 374 Nepean Highway Frankston Victoria, Melbourne 3199, Australia; [10]Department of Dermato-Venereology, Zagreb University Hospital Center Sisters of Charity, University of Zagreb, Zagreb, Croatia; [11]University of Miami School of Medicine Ringgold standard institution, Miami, Florida, United States*

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***Correspondence:** Serena Gianfaldoni. University G. Marconi of Rome - Dermatology and Venereology, University G. Marconi of Rome, Rome, Italy. E-mail: serena.gianfaldoni@gmail.com

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**Abstract**

**BACKGROUND:** Vitiligo is an acquired pigmentary cutaneous disease, characterised by the progressive loss of melanocytes, resulting in hypopigmented skin areas which progressively become amelanotic. Classically, vitiligo treatments are unsatisfactory and challenging. Despite the continuous introduction of new therapies, phototherapy is still the mainstay for vitiligo repigmentation.

**AIM:** The aim of this multicenter observational retrospective study was to evaluate the efficacy and safety of the nb - UVB micro - phototherapy (BIOSKIN EVOLUTION®), used alone or in associations with an oral Janus kinase inhibitor (Tofacitinib citrate), in the treatment of stable or active forms of localised vitiligo.

**MATERIAL AND METHODS:** Fifty eight patients had been treated with n-UVB micro-photootherapy (Group A); 9 patients had been treated with phototherapy plus Tofacitinb citrate (Group B).

**RESULTS:** Among Group A, 42 patients (72%) obtained a re-pigmentation rate higher than 75%, with a medium value of 77%. 11 patients (19%) achieved a marked improvement of the clinical findings with a repigmentation rate between 50-75%; 4 patients (8%) showed a moderate response with a lesional repigmentation of 25-50%. Only one patient (1%) had a poor response to the phototherapeutic treatment

**CONCLUSION:** Nb - UVB micro-focused phototherapy is one of the most effective therapeutic options for vitiligo treatment. The association of micro-focused phototherapy to Tofacitinib citrate seems to provide better clinical results in term of repigmentation rate.

## Introduction

Vitiligo is an acquired, chronic, cutaneous hypopigmentary disorder, which results in the progressive loss of melanocytes from the epidermis and its appendages.

Even if the precise aetiology and pathobiology of the disease are still unclear [1], recent data support that vitiligo is a T - cell-mediated autoimmune disease, maybe triggered by oxidative stress [2]. Many data support the autoimmune nature of the disease, such as the evidence of autoimmune T cells epidermotropic T cells exerting anti melanocytic cytotoxicity activity [3], the presence of circulating antibodies versus melanocyte antigens [4][5], the association with another kind of autoimmune syndromes [6], and the clinical response to immunosuppressive therapies [7]. Since the deep psychological impact of vitiligo on patients and their quality of life [8], to treat the disease is very important.

The aim of this multicenter observational retrospective study was to evaluate the efficacy and safety of the nb - UVB micro - phototherapy (BIOSKIN EVOLUTION®), used alone or in associations with an oral Janus kinase inhibitor (Tofacitinib citrate), in the treatment of stable or active forms of localized vitiligo.

## Patients and Methods

This observational retrospective study has been conducted in Italy, Germany, Croatia, Bulgaria, America and Australia.

We evaluated 67 subjects (44 women, 23 men), aged from 25 to 61 years, who suffered from stable or active vitiligo Vulgaris by more than 2 years and less than 10. In the recent past (more than 5 months), none of them had been treated for the cutaneous disease. Nine of those patients (7 women, 2 men) were also affected by rheumatoid arthritis since more than 3 years (mean duration: 5 years). Those patients were in treatment with Tofacitinib citrate (10 mg/die), an oral Janus kinase inhibitor. We decided to treat all the patients with BIOSKIN EVOLUTION®; a special cold light generator micro-focused phototherapy. BIOSKIN EVOLUTION® can provide a spectrum of intensity up to 400 mW/cm$^2$ with a peak of emission at 311 nm.

Patients had been irradiated once every three weeks for a total of 12 sessions, with an average dose of 50 mW/cm$^2$. The starting dose of irradiation was 20% less than the minimal erythema dose (MED), which had been evaluated on a vitiliginous area of each patient, during a test, performed 3 days before the treatment.

Time of emission and spot diameters were regulated by the operator, on the base of the clinical characteristic of the patients. In the following sessions of treatment, we progressively increased the irradiation dose by 20% until the development of erythema was noted. When was noted, the dose of the following treatment was diminished by 20% in the erythematous area.

For all patients, digital images of the cutaneous lesions, both with normal ambient light and with Wood's lamp, have been obtained before the treatment beginning and at each session, for all the treatment period. Response to the treatment was determined by assigning to each lesion a 0% score before therapy and a second percentage value at the end of the same, to represent the level of repigmentation.

## Results

At the end of the treatment, we evaluated the repigmentation rate achieved by every single patient treated with BIOSKIN EVOLUTION® alone (Group A) or in association with oral Tofacitinib citrate (Group B). Among Group A, 42 patients (72%) obtained a re-pigmentation rate higher than 75%, with a medium value of 77%. Eleven patients (19%) achieved a marked improvement of the clinical findings with a repigmentation rate between 50 - 75%; four patients (8%) showed a moderate response with a lesional repigmentation of 25 - 50%. Only one patient (1%) had a poor response to the phototherapeutic treatment. In any case, we did not observe side effects.

Surprising, the Group B patients showed better results in term of repigmentation rate in comparison to the patients of Group A. All the 9 subjects achieved a nearly complete re-pigmentation of the vitiliginous areas, with a re -pigmentation rate of 92%. Also in Group B, we did not observe side effects.

## Discussion

In this retrospective study, we evaluated the treatment of 67 patient affected by a stable or active form of localised vitiligo with BIOSKIN EVOLUTION®, a micro-focused phototherapy device (peak of emission of 311 nm), used alone or in association to oral Tofacitinib citrate, an oral Janus kinase inhibitor.

As we had supposed, the study confirms the effectiveness and safe-profile of nb - UVB micro-focused phototherapy in the treatment of localised forms of vitiligo. As well known, nb - UVB micro-focused phototherapy is now considered as one of the best treatment for localised vitiligo. As the classical phototherapeutic devices, the micro-focused one act stimulating silent melanocytes and modulating the immune skin system. Differently by classical devices, the micro-focused one has the major advantages that, treating only skin lesions, the operator may use more appropriate doses achieving better results in less time and in a safer way, reducing the side effects due to radiations [9][10][11]. Moreover, another important data has emerged from our retrospective study: the combination of BIOSKIN EVOLUTION® to systemic Tofacitinib citrate, allows to achieve better clinical results in term of repigmentation rate.

Tofacitinib citrate is an oral Janus kinase inhibitor. Janus kinases (JAKs) are intracellular protein kinases, crucial for the transmission of extracellular cytokines and cells communication. Even if they act in different ways (e.g. cells growth and maturation), JAKs have a fundamental role for innate

and adaptive immunity. Recent data have shown that their up-regulation is implicated in autoimmune disorders (e.g. rheumatoid arthritis), which may be successfully treated with JAKs inhibitors, such as Tofacitinib citrate, for their immunosuppressive and anti-inflammatory actions [13][14][15].

In our case, patients treated with micro-focused phototherapy plus Tofacitinib citrate achieved better results in term of repigmentation (repigmentation rate of 92%) than phototherapy alone. This can be explained by the imbalance of proinflammatory cytokines, mainly derived from The/Thl7 lymphocytes, in vitiligo [16].

In conclusion, nb - UVB micro-focused phototherapy is one of the most effective therapeutic options for vitiligo treatment. The association of micro-focused phototherapy to Tofacitinib citrate seems to provide better clinical results in term of repigmentation rate. New studies have now to be conducted to elucidate the exact mechanism of actions and the possibility to use this therapeutic protocol for the treatment of vitiligo.

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