



















POSITION STATEMENT

Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the international Vitiligo Task Force—Part 2: Specific treatment recommendations

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Abstract

Background: The treatment of vitiligo can be challenging. Up-to-date agreed consensus recommendations on the use of topical and systemic therapies to facilitate the clinical management of vitiligo are currently lacking.

Objectives: To develop internationally agreed-upon expert-based recommendations for the treatment of vitiligo.

Methods: In this consensus statement, a consortium of 42 international vitiligo experts and four patient representatives participated in different online and live meetings to develop a consensus management strategy for vitiligo. At least two vitiligo experts summarized the evidence for different topics included in the algorithms. A survey was then given to a core group of eight experts to resolve the remaining issues. Subsequently, the recommendations were finalized and validated based on further input from the entire group during two live meetings.

Results: The recommendations provided summarize the latest evidence regarding the use of topical therapies (steroids, calcineurin inhibitors and Jak-inhibitors) and systemic therapies, including steroids and other systemic immunomodulating or antioxidant agents. The different modalities of phototherapies (NB-UVB, photochemotherapy, excimer devices and home phototherapy), which are often combined with other therapies, are also summarized. Interventional approaches as well as depigmentation strategies are presented

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for specific indications. Finally, the status of innovative and targeted therapies under development is discussed.

Conclusions: This international consensus statement culminated in expert-based clinical practice recommendations for the treatment of vitiligo. The development of new therapies is ongoing in vitiligo, and this will likely improve the future management of vitiligo, a disease that still has many unmet needs.

INTRODUCTION

The treatment of vitiligo can be particularly challenging. Clear guidelines for choosing among the therapeutic options available are important given the variable response rates. Long-term treatment is usually necessary due to the high relapse rate and chronic disease course.¹ In recent years, systemic treatments (including the emerging use of JAK inhibitors) have gained increased attention.² However, while disease stabilization is a likely outcome for most patients, repigmentation rates remain variable. In part 2 of this international consensus statement, recommendations for the use of topical and systemic treatments are outlined in more detail. It should be noted that many vitiligo therapies are not licensed and can only be prescribed 'off-label.'

MATERIALS AND METHODS

In order to reach a broad international consensus, a consortium of 42 international experts and four patient representatives participated in this consensus effort. To summarize the up-to-date evidence on vitiligo, each topic was assigned to a writing group (ranging from 3 to 8 members) represented by at least two vitiligo experts who searched the literature and provided the essential data (narrative review) on which recommendations could be made for this consensus statement. The results and remaining issues were discussed during three online VTF meetings (30 September, 28 October and 9 December 2021). To get preliminary approval on the remaining issues, a digital survey was sent out to a core review group of eight vitiligo experts. Additionally, two meetings were carried out with this core review group to reach a final consensus based on the answers to the survey. Each statement received unanimous agreement, unless specified otherwise. These results were further discussed in detail with patient representatives and vitiligo experts at the Vitiligo International Patient Organizations Committee (VIPOC) meeting (Amsterdam April 2022) and the Vitiligo Task Force meeting (Milan, September 2022) until full agreement was reached. In total, 18 patient representatives (15 present live and 3 participating online) participated in this VIPOC meeting.

RESULTS

Topical steroids/topical immunomodulators (TIMS: topical calcineurin inhibitors/topical Jak-inhibitors)

Topical corticosteroids

Topical corticosteroids (TCS) are recommended for vitiligo, particularly for extrafacial locations and more limited treatment areas; however, they can also serve as an alternative to TIMS for treatment of the face. TCS are often considered to be more effective for stabilization of vitiligo than for repigmentation, although clear evidence is lacking.³ The best results of TCS in terms of repigmentation can be expected in the face and neck. In adults and children, once-daily application of potent TCS is recommended for patients with limited involvement. Like all other treatments, acral lesions and lesions with poliosis usually respond poorly. Most studies used potent to very potent corticosteroids once daily, applied topically for 3–6 months. Based on expert opinion, the risk of local side effects (skin atrophy, telangiectasia, hypertrichosis, acneiform eruptions and striae) can be reduced by using an intermittent/alternating treatment scheme (e.g. 2 weeks on 2 weeks off) and will enable longer treatment periods. These considerations apply particularly to prolonged treatment and facial lesions, where topical calcineurin inhibitor (TCI) have a better safety profile. Based on expert consensus, TCS should be used with caution on the eyelids (risk of cataract and glaucoma) or other sensitive areas (e.g. axillar and inguinal regions). For children, TCS are considered safe if they are continuously used for no more than 2–4 months. For prolonged use, the same intermittent scheme and precautions are strongly preferred. Systemic absorption is a concern when large areas of skin or regions with thin skin are treated with ultra-potent TCS for a prolonged period of time without intervals. Long-term maintenance treatment may be necessary to maintain repigmentation (see part 1).

Topical immunomodulators

Topical calcineurin inhibitors

TCIs are first-line treatment in adults and children with limited involvement, especially for lesions in the face, neck

and body folds with thin skin (e.g. inguinal, axillary regions). No differences in efficacy were found between TCI and TCS although TCI might be less effective for extra-facial lesions.^{4,5} The topical safety profile of TCI is better when compared to potent TCS, especially the risk of skin atrophy. TCI are particularly useful in areas where prolonged use of potent TCS is contraindicated. A twice-daily application of TCI can be recommended (Radakovic-Fijan et al., 2009).⁶ The treatment should be prescribed initially for 6 months. When effective, prolonged treatment (e.g. up to 12 months or more) can be proposed. TCI are also useful for younger patients. The efficacy of TCI may be comparable to that of highly potent steroids in both facial and non-facial paediatric vitiligo.⁷ As with all treatments, physicians will need to consider the pros and cons of the use of TCS, tacrolimus ointment and pimecrolimus cream in paediatric patients.

For optimal repigmentation, the combination of TCI with UV light can be considered, taking safety aspects into account. TCI monotherapy can induce $\geq 25\%$ repigmentation in 55.0% of patients and $\geq 75\%$ repigmentation in 18.1% after 3 months.⁸ More favourable results were observed in the head and neck region of children ($\geq 75\%$ repigmentation in 35.4%). The most commonly reported early side-effects of TCI are local reactions (burning sensation, pruritus and erythema). To date, the use of TCI has not been associated with significant systemic immunosuppression, skin infections or increased risk for skin cancer and other malignancies (including lymphoma) in clinical vitiligo trials.⁹ A higher risk of non-Hodgkin lymphoma has been observed with the use of TCI in dermatology. However, most of the data came from patients with atopic dermatitis treated with TCI.¹⁰ The severity of atopic dermatitis was associated with a greater risk of lymphoma.¹¹ In addition, studies have also suggested the possibility that some early cases of lymphoma, including cutaneous T-cell lymphoma, may be misdiagnosed as atopic dermatitis and treated with TCI, leading to overestimation of the effect of this treatment. It should be noted that TCI still constitute an off-label prescription for vitiligo in all countries, and costs are often not reimbursed. Patients should be informed about all these aspects as part of the shared decision-making process.

Topical JAK-inhibitors

The topical JAK-inhibitor ruxolitinib is now the first treatment approved for the repigmentation of vitiligo. Two randomized, double-blind, phase III studies were conducted in 674 patients. Response rates were much better than placebo, with 50.3% and 74.6% of patients achieving a Facial-VASI (F-VASI) 75 and 50, respectively, at week 52. Moreover, 51.1% of patients achieved a total VASI (T-VASI) of 50 at week 52. Treatment-related adverse events (AEs) occurred in 13.7% of patients who applied ruxolitinib cream over the course of the study, with the most common AEs being application site acne (4.4%) or pruritus (3.5%).¹²

Phototherapies

Phototherapy remains an essential tool in the treatment of vitiligo (Table 1). Treatment results can be optimized with careful patient selection, focusing on patient awareness and compliance. Decisions between localized and total body phototherapy are based on extent, feasibility and lesion distribution.¹³ Moderate natural UV exposure has also been proposed, taking into account the UV index, skin phototype and safety aspects.

NB-UVB

NB-UVB is the preferred first-line therapy for widespread or rapidly progressive disease. NB-UVB is the modality of choice to administer total body UV treatment, while excimer lamp or laser 308 nm UV sources are preferred for limited vitiligo. Early initiation of NB-UVB is encouraged, because of its ability to halt disease activity and induce repigmentation.¹⁴ This is especially important in segmental and acral vitiligo, where repigmentation is notoriously difficult in later stages. Limitations include resistant anatomical sites (e.g. fingers, toes, bony prominences) and areas lacking a melanocyte reservoir (e.g. lesions with leukotrichia).¹⁵

Rather than performing minimal erythema dose testing, experts propose to start at a fixed dose and use a recommended dosing schedule (Table 1).¹⁶ Starting dose and dose increments need to be adjusted according to the patient's phototype and response. For children, the use of phototherapy has been reported for patient as young as 3 years of age, when assisted by a parent or nurse.¹⁷ Specific eligibility considerations for NB-UVB use in children include the child's ability to comprehend basic instructions, ability to remain still for focal and whole body phototherapy and absence of known phobias for enclosed spaces. Precautions should be taken to limit risk of phototoxicity. To limit cumulative exposure risks, in children and adults, experts recommend that phototherapy should be stopped if there is no improvement after 3 months or unsatisfactory results after to 6 months.¹⁸

The most common acute adverse effects of NB-UVB therapy are erythema and xerosis. There has been no significant association between NB-UVB therapy and basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and/or melanoma in vitiligo trials to date, while there is a small increased risk of in BCCs among those also treated with PUVA therapy.¹⁹ A recent study from Korea reported that among 60,321 cases, more than 200 sessions of NB-UVB increased the risk of actinic keratosis, while up to 500 sessions did not increase the risks of melanoma or non-melanoma skin cancer.²⁰ Lichenoid papules in vitiligo lesions develop in about 4% of patients, especially in individuals undergoing more than 300 treatment sessions.²¹

TABLE 1 Phototherapy pearls in vitiligo (Modified table from Mohammad et al. 2017¹⁶).

Types	<p>NB-UVB (peak 311 nm) Total body</p> <hr/> <p>Targeted</p> <ul style="list-style-type: none"> NB-UVB Excimer lamps or laser: Deliver targeted UVB (peak 308 nm) <hr/> <p>Photochemotherapy</p> <p>PUVA exposes patients to UVA (320–400 nm) after treatment with psoralen</p> <p>Oral PUVA is no longer recommended for vitiligo and contraindicated in children and pregnancy, has ocular and systemic toxicity, and increases the risk of both melanoma and non-melanoma skin cancer; commonly causes nausea and headache</p> <p>TOPICAL PUVA</p> <p>Fewer treatments, smaller cumulative dose of UVA is safe for children; causes blistering and perilesional hyperpigmentation, is less effective at arresting disease activity</p> <p>KUVA uses khellin as the photosensitizer</p> <p>PUVASOL: Uses sun light as a source of UVA: Cost effective when machines are not available</p>	<ul style="list-style-type: none"> Early localized or with signs of rapid progression Active or stable vitiligo (non-segmental) <hr/> <ul style="list-style-type: none"> Segmental vitiligo Stable localized non-segmental Vitiligo (non-segmental) in light skin (time consuming if extensive vitiligo)
Pretreatment monitoring	Routine antinuclear antibody screening is not mandatory but may be recommended for non-photoadaptors ⁶¹	
NBUVB starting dose	<ul style="list-style-type: none"> For light skin populations: 200 mJ/cm² for all skin types to avoid phototoxic reactions For darker skin populations: higher starting doses 400–500 mJ/cm² are considered 	
Dose escalation	Each dose is increased by 10%–20% or held depending on the severity of erythema, up to a maximum dose of 1500 mJ/cm ² for the face and 3000 mJ/cm ² for the body	
Response predictors	<p>Before starting treatment: Favourable response predictors include paediatric age, location on face and neck, recent disease onset. In contrast, areas with white hair and large, longstanding-lesions and acral areas are not expected to repigment readily</p> <p>During treatment: The presence of perifollicular pigmentation on dermoscopy is predictive of a positive response to NB-UVB⁶²</p>	
Number of sessions	<ul style="list-style-type: none"> Consider non-responders after 30–48 sessions, some late responders may require 72 sessions⁶³ No consensus about the maximum allowed number of sessions Ideal frequency is three sessions per week, but twice weekly treatment is also reasonable for convenience 	
Excimer light	<p>Dosing may start at 100 mJ/cm² and is gradually increased weekly by 10%–25%¹⁹</p> <p>Three session/week causes faster repigmentation than two sessions/week, but the final response depends on the total number of treatments and not frequency²⁵</p>	
Related medications	<ul style="list-style-type: none"> No topicals are allowed before the session except for mineral oil to help UV penetration of xerotic skin. NSAIDs helps achieving therapeutic doses for non-photoadaptors by minimizing burns and session interruption⁷⁰ Sun protection is recommended between the sessions to prevent phototoxicity from additional exposure to the sun 	
Dose adjustment	Mandatory if the patient misses more than a week of sessions	
Stopping treatment	UVB can be stopped abruptly but a maintenance scheme is recommended with topical treatments after stop of UVB. Tapering has also been suggested after complete repigmentation by the phototherapy Vitiligo Working Group: twice a week for a month, then once a week for 1 month, then once every other week for 2 months, then stop ¹²	

Photochemotherapy

Oral PUVA is no longer recommended.²² Topical PUVA or topical PUVA SOL therapy is useful for localized lesions without systemic complications associated with oral psoralen (e.g. gastralgia and/or nausea, risk of severe generalized phototoxicity that could be increased in case of kidney and/or liver insufficiency).^{13,22} The most common side effect of topical PUVA or topical PUVA SOL therapy is erythema and the risk of skin phototoxicity. However, the possible association of topical PUVA and/or topical PUV-Asol with an increased risk of skin cancer still needs more investigation.

Excimer devices

Excimer laser and lamp treatment are equally effective or even superior compared to NB-UVB.^{23–26} The required treatment duration is shorter, which improves patient compliance.^{27,28} Excimer devices can be considered for localized disease.²⁹ The targeted nature of these devices may prevent the darkening of non-lesional skin at a distance. Excimer treatment is also excessively time-consuming for both the patient and the health care professional when treating large areas.¹³

Reports are variable regarding the superiority of excimer laser for segmental vitiligo.^{13,30} The presence of melanocyte reservoir in the form of pigmented hairs improves

the likelihood of success. Safety and tolerability of excimer laser therapy are comparable to NB-UVB,²⁵ but the cost of therapy is often higher and will need to be considered during the shared decision-making process. Acute adverse effects include erythema and blistering, while long-term adverse effects are not well established.²⁶ The risk of acute adverse effects is most likely operator-dependent and may be reduced by proper training. One study using excimer treatment for children with vitiligo found it to be effective, although transient side effects were observed in 9 of 30 included patients.³¹

Home phototherapy

Home phototherapy saves patients the enormous burden of multiple visits to phototherapy centres. The shortage of home phototherapy units, high initial cost, low energy output of the device over time, lack of mechanical servicing and unfamiliarity of patients with the modality are important limitations to the use of these units. Available units include handheld devices for the treatment of focal lesions, medium-sized panels for small areas of the body and multi-panelled full-body devices for extensive BSA involvement. An initial period of in-office phototherapy may be helpful to evaluate treatment responsiveness prior to prescribing a home unit.^{15,16}

Compared to in-office treatment, home phototherapy demonstrated better compliance, similar repigmentation outcomes, similar frequency of adverse effects and lower time investment, but significantly less patient satisfaction.^{32–35} Newer devices are designed to be user-friendly with higher safety standards and easier dose adjustment, which may improve patient satisfaction. Thorough patient education regarding shielding of sensitive sites, recognizing adverse effects and regular follow-up are essential to treatment success.³⁶

Systemic treatments for vitiligo

Oral steroids and immunosuppressants (including biologics)

Oral steroid minipulse (OMP) therapy

The experts recommend oral mini-pulses of moderate doses of betamethasone (5 mg) or dexamethasone (2.5–5 mg depending on body weight) twice weekly on 2 consecutive days per week for the treatment of rapidly progressive vitiligo to stop disease progression, after careful consideration of the risks and benefits. The recommended duration is up to 3 months, with a maximum of 6 months due to the risk of adverse effects. While treatment can usually be stopped abruptly, tapering of the dose can also be performed 1–3 months after initiation. Instead of dexamethasone, methylprednisolone (equivalent to dexamethasone at fivefold higher dose), prednisone and

prednisolone (both equivalent to dexamethasone at 6.25-fold higher dose) were suggested by some experts. OMP therapy in patients with extensive and rapidly spreading disease was reported to arrest the activity of the disease in more than 80% of patients.^{6,37,38} Repigmentation seems difficult to achieve with OMP monotherapy. Combined with UV exposure, OMP therapy may achieve a higher degree of repigmentation, but safety aspects of long-term treatment with steroids need to be considered and discussed.³⁹ As relapse of vitiligo is common after discontinuation of treatment, topical maintenance therapy can be considered (see Part 1). Adverse effects associated with short- and long-term use of OMP therapy have to be taken into consideration and should be discussed with the patient. The possible development of weight gain, insomnia, agitation, acne, menstrual disturbances, hypertrichosis, growth retardation in children and immunosuppression are potential side effects, although they can be minimized with intermittent, low-dose use.

The use of systemic steroids (prednisolone 20 mg/day or 0.3 mg per kg body weight/day in children) for 3 weeks in combination with excimer laser and TCI has also been reported to be beneficial in early SV.³⁰

Other immunomodulating agents

Methotrexate, cyclosporine, azathioprine and minocycline can be used in patients with progressive vitiligo, although strong evidence for efficiency and safety is lacking.^{40–42} Immunosuppressants such as methotrexate, cyclosporine and azathioprine have not been studied in combination with phototherapy. No biologics can currently be recommended for vitiligo (e.g. anti-TNF- α and anti-IL-17).^{43,44} Systemic JAK inhibitors are promising, and their use can be considered when available and approved by regulatory agencies.

Other systemic interventions

Vitamin E, vitamin C, resveratrol, ubiquinone, alpha lipoic acid, pantothenic acid, catalase/superoxide dismutase combination and Ginkgo biloba are antioxidants that have been used alone or in combination with phototherapy with the aim of achieving stabilization and repigmentation of vitiligo lesions.^{45–48} Due to differences in patient selection, protocols, mixture of compounds used in trials, poor methodology in some studies using these different combinations of antioxidants and a lack of corroborating reports, there is little or no consensus on their use for vitiligo. There is, however, some evidence for improvement with the combination of phototherapy with oral antioxidants like Polypodium leucotomos and gliadin-protected superoxide dismutase (SOD).^{46,48,49} RCTs with good methodology and reproducible results are needed to fully consider the use of antioxidants and vitamins in vitiligo.

Surgical interventions

Surgery should be reserved for patients with SV and other localized and stabilized forms of vitiligo (non-segmental) after the documented failure of medical interventions. For vitiligo (non-segmental), patients with a stable form of the disease and a negative history of Koebner phenomenon are eligible, but the risk of relapse must be explained thoroughly to the patient.⁵⁰ Disease activity can be assessed using objective clinical follow-up based on photographs comparing two time points (e.g. using Vitiligo Disease Activity Score (VDAS)). The Vitiligo Disease Activity Index (VIDA) score, mini-punch test grafting, dermoscopy and *in vivo* reflectance confocal microscopy have also been used within this context, but their exact value remains uncertain.^{51–53} Several techniques exist, including punch grafting, suction blister grafting, non-cultured epidermal cellular grafting and cultured epidermal cellular grafting. Each method has its pros and cons. Surgical interventions are often performed differently depending on the location and size of the treated lesions (Table 2).²⁶

Depigmentation

The potential sociocultural issues linked to depigmentation therapies, especially in patients with darker skin types, should be thoroughly explored before initiating therapy.⁵⁴ In case of depigmentation failure, it was recommended to postpone the treatment until the disease flares.⁵⁵ Topical depigmenting agents include monobenzyl ether of hydroquinone (MBEH), 4-methoxyphenol (4MP, mequinol or p-hydroxyanisole) and phenol. MBEH (p-benzyloxy-phenol, monobenzene) is the only topical depigmenting agent that is currently approved for vitiligo by the Food and Drug Administration. The drug may induce depigmentation at sites

distal to the drug application. The expected results (61%–92% depigmentation) with 20% MBEH are usually achieved at treated sites after 10 months.⁵⁶ However, in successfully depigmented areas, 78% of patients can experience repigmentation after the end of MBEH therapy, which should be explained to the patient. Nearly half of the subjects can experience dose-dependent skin irritation, which may be resolved with a reduction in MBEH concentration. MBEH is better suited for treating larger remaining areas of pigmentation compared to laser and cryotherapy; however, MBEH is not currently available in all countries.

Cryotherapy and pigment lasers are the two options for physical depigmentation therapies.⁵⁷ Cryotherapy can achieve rapid depigmentation via irreversible tissue damage, in particular in patients sensitive to Koebner's phenomenon. The advantages of cryotherapy remain its low cost and excellent safety profile, but it requires an experienced physician for optimal results and to minimize the risk of scarring.

Several types of lasers involving wavelengths between 532 and 755 nm targeting pigmentation are also used for depigmentation. The Q-switched ruby laser (QSR) exhibits high absorption by melanin and is therefore more suited for lighter skin types. Meanwhile, the Q-switched alexandrite laser (QSA) has a faster pulse frequency than the QSR that permits more rapid therapy and emits light of a greater wavelength (755 vs. 694 nm), which may provide better tissue penetration. The Nd:YAG laser has been used at a wavelength of 532 nm to target only epidermal pigment and to induce koebnerization of vitiliginous lesions.⁵⁸

Innovative and emergent therapies

Vitiligo patients can be strongly encouraged to participate in the latest clinical trials to promote the development of

TABLE 2 Different options for surgery.

1. Mini Punch grafting	<ul style="list-style-type: none"> • A method of directly transferring 1–2 mm punch grafts from donor to recipient sites • The simplest and least expensive method^{64,65} • Often limited for large area due to time restrictions • Can lead to a cobblestone appearance • Micropunch grafting using a motorized 0.8-mm punch can be used to reduce the time to perform the procedure^{66,67}
2. Suction blister grafting	<ul style="list-style-type: none"> • Excellent cosmetic results • Practically no scarring of the donor site • Raising suction blisters can be painful and time-consuming (ameliorated by local anaesthesia and heat induction, respectively) • Cumbersome when treating large lesions • Associated with adverse events, such as colour mismatch and perilesional halo⁶⁸
3. Split thickness grafting	Ultrathin epidermal sheet grafting can treat larger areas (up to 200 cm ²), but requires skill and experience to harvest an extremely thin split-skin graft from the donor site to avoid scarring
4. Cellular grafting using non-cultured suspensions of epidermal cells	<ul style="list-style-type: none"> • Large recipient sites with small amounts of donor tissue are possible⁶⁹ • Can be completed in 3–4 h in an outpatient setting, and given areas can be treated with donor to recipient ratio of between 1:5 and 1:10
5. Cellular grafting using pure cultured melanocytes	<ul style="list-style-type: none"> • Best for large lesions • Expensive, time-consuming and requires a GMP-certified laboratory, making it impractical for routine clinical use⁶⁸

Abbreviation: GMP, good manufacturing practice.

new and more efficient therapies. Topical JAK inhibitor (e.g. ruxolitinib cream) has shown clinical efficacy and is now FDA and EMA approved for vitiligo. Oral JAK inhibitors upadacitinib and povorcitinib (JAK1 inh), Baracitinib (JAK1/2 inh) are currently being tested in phase II ongoing trials. Ritlecitinib (JAK3/TEC inh) has been evaluated with different doses in a phase II trial including 364 patients. After 24 weeks, the proportion of change from baseline was significantly different compared to placebo in F-VASI for the ritlecitinib 50 mg groups with (−21.2 vs. 2.1, $p < 0.001$).⁵⁹ Strategies to target IL-15 or its receptor CD122 to inhibit the generation and the maintenance of skin resident memory T cells demonstrated durable treatment responses in a pre-clinical mouse model of vitiligo, and clinical trials using this strategy are under way.⁶⁰

Blocking the initiation of the disease could also be an important step for future therapies for vitiligo. Older and more recent data shed light on the role of innate immunity in vitiligo that connects cellular stress pathways [through PAMPs and DAMPs (pathogen- and danger-associated molecular patterns: ROS or heat shock protein 70i)] to adaptative autoimmunity against melanocytes.⁶¹ HP70i seems to be a critical DAMP in the initiation of the disease. Blocking HSP70i activity might offer a good strategy, as shown in preclinical animal models. Preventing melanocyte detachment, by using anti-matrix metalloproteinase-9 antibodies could also be effective.⁶² Recent data suggest dysbiosis in the skin and gut of vitiligo patients.^{63,64} Modulating the vitiligo microbiome offers appealing strategies, but no therapeutic intervention using this strategy has yet been reported.

In contrast to other chronic skin inflammatory diseases, targeting the immune response in vitiligo will likely not be sufficient to obtain maximal repigmentation in all patients.² Promoting the differentiation and proliferation of melanocyte stem cells in vitiligo lesions located on acral areas or in areas with poliosis is more challenging due to the limited availability of melanocyte stem cells. WNT signalling, which is repressed in the depigmented skin of vitiligo patients, may be an important pathway to target to induce melanocyte differentiation.⁶⁵

DISCUSSION/CONCLUSION

Current therapeutic options for vitiligo are backed by substantial evidence. Although strategies that provide complete clearance will warrant further research, this should not discourage dermatologists and patients from treating vitiligo, as disease stabilization is within reach in most cases. To date, the odds of repigmentation remain primarily dependent on the involved body areas and grade of disease activity; therefore, early treatment is recommended. Options such as JAK inhibitors and research into other drugs that affect adaptive and innate immunity are exciting developments that continue to pave a promising way forwards.

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CONFLICT OF INTEREST STATEMENT

Nanja van Geel MD, PhD received grants, is consultant and/or investigator for AbbVie, Incyte, Merck/MSD, Pfizer and Sun Pharma; and is chair of the Vitiligo Task Force for the European Academy of Dermatology and Venereology (EADV). She was involved in the development of several measurement instruments for vitiligo. Khaled Ezzedine MD, PhD has served as a consultant for AbbVie, Incyte Corporation, Pfizer, Pierre Fabre Pharmaceuticals, Merck/MSD and Almirall. Amit G. Pandya MD, has served as an investigator for Incyte. He is a consultant for AbbVie, Avita Medical, Immune Tolerance Network, Incyte, Pfizer, Thalocan, Trifecta, TWi, Viela Bio, Vyne and Villarlis and holds stock options for Tara Medical and Zerigo Health. Thierry Passeron MD, PhD received consultancy fees from Abbvie, Incyte, Pfizer, Vyne therapeutics and Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Abbvie, Incyte, Pfizer, Vyne therapeutics. Albert Wolkerstorfer MD, PhD, is consultant for InCyte, Novartis, AvitaMedical, Candela and Lumenis. Jung Min Bae MD, PhD has served as a consultant for Pfizer, AbbVie, LaserOptek, Ilooda and Cotech Korea. Viktoria Eleftheriadou MD, PhD VE is a consultant for Incyte, Abbvie, Pfizer and Almirall. Samia Esmat MD, is consultant for Pfizer. Pearl Grimes MD, conducts clinical trials, for which the Vitiligo & Pigmentation Institute of Southern California receives financial support for purposes of conducting these trials, from Procter & Gamble, Clinuvel, L'Oreal, Johnson & Johnson, LaserOptek, Mother Science, Incyte, Pfizer, AbbVie/Allergan and SkinBetterScience. Dr. Grimes receives no direct compensation for this work. Somesh Gupta MD, is conducting a clinical trial sponsored by Pfizer on Abrocitinib and Ritlecitinib. Iltefat H. Hamzavi MD is Consultant to Abbvie, Pfizer, Incyte, UCB, Boehringer Ingelheim, Sonoma, Union therapeutics, Novartis, Jansen, Avita, Galderma and is Investigator for Lenicura, Pfizer, Incyte, Avita, L'oreal/La Roche Posay. He is also Board member and Past-president of the HS foundation and Global Vitiligo foundation. John E. Harris MD, PhD, 3rd Rock Venture—Consultant (Fees); AbbVie, Inc—Consultant (Fees); Aclaris Therapeutics, Inc—Consultant (Fees), Investigator (Grants/Research Funding); Admirx—Consultant (Fees); Aldena—Consultant (Fees), Founder (Stock); Almirall—Consultant (Fees); AnaptysBio—Consultant (Fees); Avita—Consultant (Fees); BiologicsMD—Consultant (Fees); Boston Pharma—Consultant (Fees); BridgeBio—Consultant (Fees); Celgene—Investigator (Grants/

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

None declared.

DISCLAIMER

This recommendation was proposed based on expert opinions, feedback from patient representatives and published evidence. Future updates of these recommendations are inevitable as new treatments may override current management recommendations as well as in response to potential adverse responses. The Vitiligo Task Force does not represent or warrant a legislative or all-encompassing consensus based on the contents of this documentation. Medical professionals may treat vitiligo following procedures and treatment plans which substantially differ from those mentioned or described in this recommendation. The Vitiligo Task Force expressly disclaims any responsibility or liability for any damages, loss, injury, or liability whatsoever experienced as a result of reliance on the information contained in this publication. The contents of this manuscript can in no way be regarded as advice in legal matters (including use for claims). Inquiring about allergies and intolerance reactions, as well as detecting probable contraindications and risks, should be considered to be part of a physician's general responsibilities when prescribing medications. It is assumed that all patients should be informed of the specific risks associated with a given treatment.

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