







## Phototherapy in the management of vitiligo – an updated narrative review

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### ABSTRACT

**Introduction and aim.** Vitiligo is a chronic skin disease characterized by progressive loss of melanocytes. Various treatment options have been developed to manage vitiligo, however, phototherapy has emerged as one of the most effective treatment options. Therefore, this review has been written to examine the mechanisms of this particular treatment approach and its optimal implementation.

**Material and methods.** A review of the literature regarding combination of word vitiligo with the following: psoralen ultraviolet A (PUVA), narrowband ultraviolet B (NB-UVB) and excimer laser (EL) was performed using the PubMed database.

**Analysis of the literature.** NB-UVB has demonstrated safety and efficacy in stimulating melanocyte proliferation and melanin synthesis, making it an attractive treatment option for both localized and generalized vitiligo. PUVA therapy, combining psoralen photosensitization with UVA irradiation, has shown remarkable efficacy in repigmentation, particularly in refractory or extensive vitiligo. However, because of possible side effects, it is not recommended as a first line phototherapy. With its targeted and precise approach, EL offers a localized treatment and has produced impressive results in localized and segmented vitiligo.

**Conclusion.** Despite limitations, phototherapy continues to evolve, offering hope for individuals with vitiligo. Further research and advancements in treatment protocols are needed.

**Keywords.** NB-UVB, phototherapy, vitiligo

### Introduction

Vitiligo is a common depigmentation disorder affecting about 1–2% of the world's population. It is characterized by the formation of hypopigmented patches on the skin corresponding to the dysfunction and loss of epidermal melanocytes.<sup>1</sup> Vitiligo is more prevalent in female patients. As for geographic region and ethnicity, evidence suggests that people on the African continent are more affected by this condition.<sup>2</sup> The lesions may be localized or generalized, although they most commonly affect vis-

ible parts of the body, namely skin of palms, soles and head. Pathophysiology of the disease is complex and includes a genetic predisposition, an autoimmune response or oxidative stress, and autoinflammatory mechanisms.<sup>1</sup> To date, options for vitiligo treatment remain limited, with therapeutic strategies targeting inflammation and immune responses, such as topical or systemic steroids, topical calcineurin inhibitors alongside topical and systemic Janus kinase inhibitors or surgical procedures. One of the options gaining ground in recent years

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is phototherapy, which promotes reduction of inflammation and melanocyte regrowth. In general, efficacy of phototherapy can be assessed after at least six months, and its effect depend on the type of phototherapy, duration of treatment, and body site. However, phototherapy should be considered as ineffective if no repigmentation (mainly perifollicular) is seen during the first 3 months of treatment or the degree of repigmentation is less than 25% after 6 months of therapy.<sup>3,4</sup> The main phototherapy methods include psoralen-UV-A (PUVA) and narrow band UV-B (NB-UVB) therapies, which are used for large lesions. In contrast, relatively new excimer laser is used mainly for small lesions. Currently, NB-UVB is considered as first-line treatment for body surface area (BSA) > 10–20%, while PUVA is used as a second-choice treatment, mainly in adults.<sup>4,5</sup> While achieving good clinical results with a lower total cumulative UV dose than the other methods, the excimer laser is limited by high acquisition and maintenance costs, limited availability, and time-consuming procedure.<sup>5</sup>

### Aim

The purpose of this paper is to assess the treatment response of vitiligo to phototherapy.

### Material and methods

A comprehensive research was carried out on the PubMed databases, covering period between 2000 and 2024. Search terms included phototherapy, vitiligo, psoralen ultraviolet A, narrowband ultraviolet B, and excimer laser. A thorough analysis of literature was conducted, focusing on the most recent articles published within the last five years. However, older papers were also considered if they presented noteworthy findings. Findings from a total of 68 selected papers were compiled and organized in this review.

### Analysis of the literature

#### *Psoralen ultra-violet A*

PUVA photochemotherapy (Fig. 1), which is the use of psoralens as a photosensitizer in combination with ultraviolet (UVA) radiation (320–400 nm), have been used to treat vitiligo since the 1950s and was the main type of phototherapy until the development of NB-UVB.<sup>6,7</sup> Psoralens are natural phototoxic furanocoumarins found in plants.<sup>8</sup> They are administered systemically or topically, followed by exposure to UVA radiation.<sup>9</sup> This combination triggers a strong phototoxic reaction that allows the skin to repigment. The most commonly used photosensitizer is 8-methoxy psoralen (8-MOP), usually taken at 0.6–0.8 mg/kg.<sup>5</sup> Photosensitivity develops after 1 hour, peaks after approximately 2 hours and disappears after roughly 8 hours.<sup>10</sup> Psoralens rapidly enter the cell and intercalate between DNA base pairs and, upon absorption of photons, undergo chemical activation to

crosslink DNA. This causes a range of antiproliferative, antiangiogenic, apoptotic and immunosuppressive effects. Through some unknown mechanism, melanogenesis is also stimulated and the expression of vitiligo-associated antigens on melanocyte cell membranes is reduced.<sup>6,11</sup> Nevertheless, the exact mechanism of action of pigmentation induction by PUVA in acquired vitiligo is still unknown. Anbar et al. showed that PUVA therapy increases the number and activity of epidermal melanocytes in all areas and reduces degenerative changes in both melanocytes and keratinocytes. The reversal of degeneration in depigmented and seemingly normal skin after PUVA indicates the role of this modality in both repigmentation and protection against further depigmentation.<sup>12</sup> Indications for using PUVA in vitiligo treatment include BSA of more than 10% of the body surface area of vitiligo, for which other treatments, including NB-UVB, have not guaranteed satisfactory results.<sup>10</sup> It is crucial to evaluate the patient's condition carefully for long-term treatment. When evaluating a patient before treatment, key elements are age, skin type (according to Fitzpatrick types) and past medical history (including the history of skin cancer, immunosuppression, and current medications).<sup>7</sup> The best effects of PUVA therapy are achieved on the face, trunk and proximal limbs<sup>13</sup> with acral areas most resistant to treatment<sup>14</sup> and requires 1 year to achieve a maximal treatment.<sup>3</sup> More than 25% repigmentation occurred in 51.4% of patients at 6 months, 61.6% at 12 months after receiving PUVA therapy, and ≥75% repigmentation occurred in 8.5% of patients at 6 months and 13.6% at 12 months.<sup>14</sup> There was no effect of disease elapsed duration on the response rate to PUVA.<sup>10</sup> Although PUVA therapy is effective, it has many limitations. It is associated with, higher risk of skin cancer compared to other forms of phototherapy. In addition, non-specific side effects such as erythema, dryness, pruritus, blistering, and hyperpigmentation or photoaging may occur.<sup>10,15</sup> Due to the systemic use of psoralen, exclusion criteria for PUVA treatments include pregnancy and lactation, premenstrual photosensitivity disorders and age (children below 12 shall be excluded). After UVA irradiation, psoralens generate photosensitizing reactions and reactive oxygen species (ROS). Certain transient receptor potential (TRP) channels, such as TRP Ankyrin type 1 (TRPA1) and TRP Vanilloid type 1 (TRPV1) in peripheral nerve endings, which are involved in pain and itch signaling, as well as neurogenic inflammation, are assumed to be sensitive detectors of ROS.<sup>16</sup> The mechanisms above underlie some of the adverse effects of PUVA therapy, including the most serious one known as PUVA pricks. This sensation has been reported as a persistent severe burning pain deep under the skin, of a degree more severe than renal colic.<sup>17</sup> There is a variant of PUVA therapy called PUVA sol therapy, in which the radiation

source is sunlight. However, in a study comparing the efficacy of these two therapies in the treatment of vitiligo, it was found that oral PUVA was more effective than PUVA sol in terms of early onset of repigmentation, speed of repigmentation, total repigmentation achieved after nine months of therapy, and improvement in quality of life (QOL). Nonetheless, phototoxicity was higher with oral PUVA therapy.<sup>18</sup> In patients who experienced gastrointestinal side effects after taking a photosensitizer, topical PUVA therapy can be considered by applying psoralen in cold cream, solution, or emulsion only to the lesions.<sup>19</sup> The effects of vitamin D analogs such as calcipotriol or tacalcitol on the effects of phototherapy have also been analyzed. However, none of the vitamin D analogs enhanced the efficacy of PUVA.<sup>20</sup>



**Fig. 1.** Equipment used to perform PUVA therapy, A: whole body cabinet, B: body part machine

### **Narrow-band ultraviolet B**

Narrow-band ultraviolet B (NB-UVB) therapy was first used in vitiligo treatment in 1997 by Westerhof and Nieuweboer-Krobotova.<sup>21</sup> NB-UVB uses light beam of 311 nm wavelength and is significantly more broadly used due to its weaker radioactive effect. In recent years, NB-UVB has established itself as the standard treatment for vitiligo (Fig. 2). Before initiating therapy, patients with history of taking medications with photosensitizing potential should be ruled out, considering that regardless of radiation dosage, this is associated with a higher risk of erythema as a complication of therapy.<sup>22</sup> The dose is selected by establishing the so-called MED, which is the lowest dose that causes marked erythema. Usually, therapy is started with a dose equal to 70% of MED, and with subsequent sessions, dosage would be increased by 10–20%. Caution should be maintained as 1/3 of patients are photo resistant, and in these patients, doses should not be increased. Alternatively, the dose can be determined by skin phototype according to Fitzpatrick scale, although a safe and practical option is to start therapy with a dose of 200 mJ/cm<sup>2</sup> regardless of skin type.<sup>23</sup> Maximum

permissible dose for the face per m<sup>2</sup> of a given treatment is 1500 mJ/cm<sup>2</sup>, while the maximum dose for the body is 3000 mJ/cm<sup>2</sup>.<sup>23</sup> The most significant effect is noticeable after about 12–24 h. The appropriate skin reaction to this therapy is a pink, symptom-free erythema that lasts for 24 hours. Once this reaction is observed, the current dosage should be maintained until the erythema subsides. Following this, the subsequent dosage can be raised by 10% to 20%. Treatments are applied 2–3 times a week until remission or stabilization of the clinical condition is achieved.<sup>23</sup> Once stabilization is achieved, treatments are performed twice a month for the first month, once a week for the next month, once every two weeks for the third month, and then therapy can be discontinued in the fourth month.<sup>23</sup> Approximately 15% of patients experience a relapse within one year after discontinuation.<sup>24</sup> The effectiveness of vitiligo treatment with NB-UVB can be estimated after 18–36 irradiations and its ineffectiveness after 48.<sup>23</sup> In case of some patients being slow responders 72 sessions may be considered before stopping phototherapy. NB-UVB therapy can be combined with topical treatment achieving better clinical results; however, 4 hours before skin irradiation, no topical products should be applied to the skin other than mineral oil.<sup>23</sup> It is common for patients to miss a dose in case of patients receiving hospital phototherapy. If the treatment intervals are between 4 to 7 days, the dosage should stay the same. However, if the intervals are longer, the management strategy will differ.<sup>23</sup> It is important for patient to take photos of the lesions throughout the treatment to provide the doctor with a reference point for comparison. To guarantee the therapy's efficacy, follow-up appointments every 3 months are recommended to evaluate the treatment's progress. Early initiation of NB-UVB is crucial due to its ability to halt disease progression and promote repigmentation. The longer vitiligo persists, the less effective treatment tends to be.<sup>25</sup> This is especially significant in cases of segmental and acral vitiligo, where achieving repigmentation becomes increasingly challenging as the condition progresses.<sup>26</sup> It is important to assess specific factors that can impact the success of therapy. Factors such as difficult-to-treat anatomical sites (e.g., fingers, toes, bony areas) and areas lacking melanocyte reservoirs (e.g., patches with leukotrichia) can pose limitations to treatment effectiveness.<sup>26</sup> The mechanisms of UVB phototherapy involve immunosuppression induction of keratinocyte T-lymphocyte apoptosis and stimulation of peri-follicular cells to migrate and differentiate into melanocytes.<sup>11,27</sup> In addition, there has been noticed an increase in acetylcholinesterase levels.<sup>28</sup> NB-UVB increases the activity of proteins responsible for the production of tyrosine, whose metabolism is impaired in the melanocytes of vitiligo patients. NB-UVB therapy not only leads to the stimulation of melanocytes but also leads to a decrease in

CD4+ and CD8+ lymphocytes and level decrease of chemokines CXCL9 and CXCL10 in the peripheral blood.<sup>29</sup> A positive therapeutic response to NB-UVB phototherapy in patients with vitiligo is often observed when lesions are localized to the face, and perifollicular pigmentation is present on dermatoscopic examination.<sup>30</sup> This phenomenon is explained by the reservoir of stem cells in hair follicles which, stimulated by radiation, differentiate into melanocytes. Among the most stable repigmentation patterns are the marginal and perifollicular mechanisms, hence NB-UVB therapy is more effective on the scalp in favor of less effective on the skin of the hands and feet.<sup>31</sup> NB-UVB phototherapy in patients with vitiligo is not associated with an increased risk of melanoma, basal cell carcinoma (BCC), or squamous cell carcinoma (SCC); regardless, patients who have had 200 or more treatment sessions have an increased risk of solar keratosis.<sup>32</sup> In the treatment of vitiligo, combination therapies have been found to be more beneficial than monotherapies. For instance, the combination of narrowband ultraviolet B with topical medications like tacrolimus 0.1%, calcipotriol/betamethasone dipropionate, Er: YAG laser, and micro-needling has shown to be more effective compared to using only one treatment method.<sup>25,33</sup> Studies have also explored the use of off label medications, such as methotrexate gel, which has demonstrated positive effects when combined with NB UVB but not when used alone.<sup>34</sup> Another combination currently being investigated is the intradermal injections of prostaglandins the PGE2 or PGF2 $\alpha$ .<sup>35</sup> However, focus of researchers in dermatology lies on Jak Inhibitors, which are being considered as a valuable treatment option for vitiligo. Hongbin Song et al. conducted a research study to evaluate the efficacy of combining tofacitinib with NB UVB in comparison to a control group treated with betamethasone cream, tacrolimus 0.1% ointment, or pimecrolimus cream, in combination with NB-UVB therapy.<sup>36</sup> The results of the study demonstrated a significant increase in repigmentation starting from eighth week in the tofacitinib group when compared to NB-UVB therapy alone. Moreover, the level of repigmentation was notably higher in the tofacitinib group when compared to control group. These findings suggest that combination of tofacitinib and NB-UVB therapy is a safe and effective treatment for refractory vitiligo, including lesions on acral areas.<sup>36</sup> On the other hand, Xiu-kun Sun highlighted in a case report that while tofacitinib is a valid treatment option, it is important to note that it primarily acts as an inhibitor of the inflammatory pathway, suppressing the autoimmune response of vitiligo by targeting IFN- $\gamma$  signaling and reducing T cell numbers in the skin. Therefore, tofacitinib alone may not be able to restore melanocytes and should be used in conjunction with NB UVB phototherapy.<sup>37</sup> Additionally, ruxolitinib, another JAK inhibitor, is also

considered a viable treatment option when combined with NB UVB for patients with extensive and progressive vitiligo lesions.<sup>38</sup> We compared effectiveness of therapies used in mentioned studies (Table 1). The advantages of NB-UVB compared to PUVA are the higher levels of repigmentation, shorter treatment, no use of psoralens, and possibility of use during pregnancy and for children. Combining psolarin with NB UVB, so-called P-NBUVB allows for faster repigmentation on the Vitiligo Area Scoring Index (VASI) scale, especially when lesions involve the lower extremities, but at the cost of increased risk of side effects.<sup>39</sup> El Mofty et al. first stated that use of psoralen plus broadband UVB (P-NBUVB) can be as effective as PUVA in the treatment of vitiligo.<sup>40</sup> P-NBUVB has been shown to be effective especially for facial lesions. In a randomized clinical trial (RCT), 45 Indian patients with vitiligo involving more than 5% of the body. The extent of repigmentation in the P-NBUVB group was statistically significantly more pronounced in the face, neck, and hands than in the NBUVB group. Also, erythema and perifollicular pigmentation appeared earlier at a lower cumulative dose in the P-NBUVB group compared to the NB-UVB group.<sup>41</sup> Similarly, in RCT from Iran the P-NBUVB group showed more remarkable VASI improvement in the lower extremities.<sup>42</sup> Given the cost and maintenance involved, phototherapy equipment is currently mostly accessible in dermatology clinics located in larger cities. This limited availability poses a challenge for patients seeking treatment. As a result, the concept of home phototherapy has gained significant attention over the years despite that according to studies few doctors including dermatologists know about home phototherapy and even fewer prescribe it.<sup>43</sup> For patients who frequently commute before work for phototherapy sessions, purchasing home phototherapy equipment can be a viable option to reduce travel expenses and enhance convenience. One study found that 7 weeks of therapy made it more financially viable to have a home device than to go to the hospital.<sup>44</sup> Nevertheless, not everyone who can afford the equipment will qualify for NB-UVB home phototherapy. Certain exclusion factors, such as history of photosensitivity disorders (xeroderma pigmentosum, lupus erythematosus, dermatomyositis, porphyria) and use of photosensitizing medications like thiazide diuretics, amiodarone, and antibiotics (tetracyclines, sulfonamides, fluoroquinolones), need to be taken into account.<sup>43</sup> Additionally, patient's BSA is another factor that needs to be considered. Patients requiring whole-body in-office phototherapy may prefer in-hospital treatment, as the multi-panel three-dimensional devices used at home require changes in body position during treatment, resulting in uneven illumination of the skin surface. Patients receiving home phototherapy should schedule a follow-up appointment every 3 months to assess potential side effects such as erythema,

burning sensation, pruritus, nausea, blistering, ocular damage, theoretical risk of skin cancer, and accidental overexposure.<sup>43</sup> Additionally, the device used for home phototherapy needs to be recalibrated every 3 months due to a decrease in irradiance.<sup>45</sup> The biggest advantage of home phototherapy is its convenience, as patients can receive treatment every other day. This allows for a faster cumulative dose and quicker results compared to hospital treatment.<sup>45</sup> The requirement for a prescription for such a device varies by country.<sup>43</sup> Patients undergoing home phototherapy should attend a follow-up visit once every 3 months for evaluation of potential erythema, burning sensation, pruritus, nausea, blistering, ocular damage, theoretical risk of skin cancer, and death from accidental overexposure. During those appointments the device requires periodic recalibration, that is, due to decay in irradiance.<sup>45</sup> The matter of a prescription for such a device depends on the country – in Canada it is not needed, but insurance companies ask for it for reimbursement purposes.<sup>43</sup> The question arises whether home phototherapy is as effective as hospital procedure. Singh et al. conducted a study which found that the percentage of repigmentation was similar between the two methods at each follow-up visit and after 4 months of therapy.<sup>45</sup> It is worth noting that patients using home NB UVB devices had fewer missed treatment sessions. This finding was consistent with other studies as well.<sup>31,44</sup>

### Excimer laser

Excimer lasers (ELs) combine a noble inert gas and a halogen, forming excited dimers when activated. These

dimers are created using a high-energy electrical current and have a short lifespan. Upon dissociation, they emit ultraviolet photons, releasing the stored energy post.<sup>46,47</sup> There has been growing interest in the 308 nm xenon chloride laser as an exceptionally effective treatment option for various dermatological conditions.



**Fig. 2.** Equipment used to perform NB UVB therapy, A and B: body part machines

Excimer 308-nm light is a type of targeted phototherapy that utilizes a specific wavelength of UVB radiation through the use of an excimer laser.<sup>48</sup> Baltás et al. first introduced an excimer laser in 2001 to treat vitiligo patients' loss of pigmentation.<sup>49</sup> Excimer therapy offers several advantages compared to other phototherapy approaches. These advantages include a lower overall

**Table 1.** Comparison of repigmentation rates and therapeutic responses of NB-UVB treatment combined with other vitiligo medications (0 – no response, I – poor, II – moderate, III – good, IV – excellent)

Authors and year	Intervention	Mean percentage (%) of repigmentation after treatment	Therapeutic response visual analog system score (VAS) grade					Conclusion
			0	I	II	III	IV	
Alshiyab et al., 2023	Tacrolimus 0.1% ointment + NB-UVB	45.6	0%	28%	43%	10%	19%	There were no significant differences between interventions in efficacy at three and six-month follow-up points.
	Calcipotriol/betamethasone + NB-UVB	54.7	0%	10%	30%	45%	15%	
Gharib et al., 2023	Methotrexate gel	19.3	37.5%	37.5%	18.8%	6.3%	0%	Methotrexate gel could increase the therapeutic effect of NB-UVB and excimer laser.
	Methotrexate gel + NB-UVB	49.7	18.8%	12.5%	12.5%	31.3%	25%	
	Methotrexate gel + excimer light	39.9	25%	18.8%	18.8%	25.0%	12.5%	
Neinaa et al., 2023	PGE2 + NB-UVB	54.4	0%	23.3%	20%	26.7%	30%	The intradermal injection of either PGE2 or PGF2α in association with NB-UVB is considered therapeutically successful for vitiligo with non-significant difference between them.
	PGF2α + NB-UVB	48.67	0%	33.3%	16.7%	23.3%	26.7%	
	Saline (as placebo) + NB-UVB	39.9	0%	76.7%	13.3%	10.0%	0%	
Song et al., 2022	Tofacitinib + halometasone + tacrolimus + NB-UVB	No data	0%	0%	6.6%	6.6%	86.6%	Tofacitinib in combination with NB-UVB phototherapy may be an effective and safe alternative modality for refractory vitiligo.
	Halometasone + tacrolimus + NB-UVB	No data	5.2%	57.9%	26.3%	10.5%	0%	

UV exposure, a shorter treatment time, and the capacity to target specific lesions while limiting side effects on healthy skin nearby.<sup>50</sup> The 308-nanometer excimer laser has proven to be a highly effective treatment option in restoring pigmentation in individuals with vitiligo. However, it has some limitations. It is recommended for depigmented BSA that are lower than 10%.<sup>51</sup> There is a lack of clear clinical guidelines regarding the frequency, dosage, and duration of excimer laser therapy. Two studies compared the effectiveness of therapy with this laser administered 2 and 3 times a week. However, there wasn't enough evidence to conclusively determine the extent of repigmentation between these two dosage frequencies. The degree of repigmentation was found to correlate with the overall number of treatment sessions, showing an earlier onset of pigmentation with a dosage administered three times a week.<sup>52,53</sup> Bae et al. proposed excimer laser treatment protocols based on their published experiences. The initial therapeutic dose ranges from 100 to 300 mJ/cm<sup>2</sup> and varies depending on the skin phototype. Subsequently, the dose is increased by 50 mJ/cm<sup>2</sup> during each therapeutic session until erythema appears post-treatment. The suggested optimal dose by the team is one that induces asymptomatic erythema, which persists for 24–48 hours. Radiation sessions can be conducted from 1 to 3 times a week. However, researchers emphasize that the ultimate effect of achieved repigmentation seems to depend on the total number of treatment sessions rather than their frequency.<sup>54</sup> The therapeutic mechanism of EL involves inducing apoptosis in T cells and stimulating the proliferation of melanocytes.<sup>55</sup> The efficacy of the 308-nm excimer laser in treating non-segmental vitiligo is confirmed by significant research. The 308-nm excimer laser displayed equal efficacy to the NB-UVB control group in attaining 75% repigmentation of vitiligo patches, according to a systematic review of seven randomized controlled trials (RCTs).<sup>49</sup> Bae et al., evaluating the long-term use of a 308-nanometer EL for localized vitiligo, found no significant increase in the risks of actinic keratosis, non-melanoma skin cancers, or melanoma. This suggests that EL treatment is a safe option for patients with vitiligo and does not pose an elevated risk of skin cancer.<sup>56</sup> Recently, EL treatment's safety has been confirmed in a substantial group of 25,694 patients diagnosed with vitiligo.<sup>57</sup> A notable association exists between the disease's location and duration and repigmentation's effectiveness. UV-sensitive areas such as face and neck tend to respond more rapidly to treatment, leading to an earlier reduction of lesions than UV-resistant areas like joints and extremities.<sup>58</sup> The application of EL is considered permissible for pediatric patients, indicating that this treatment modality can also be safely extended to children. Among the anticipated long-term skin photodamage associated with this treatment, the most frequent side effects include burns, perilesional hyper-

pigmentation, and folliculitis.<sup>59</sup> The EL can also be used with topical therapy, which translates into improved treatment outcomes. Based on the analysis of 8 randomized controlled trials involving 425 patches/patients, the combination of EL treatment with topical calcineurin inhibitors demonstrated superior efficacy compared to EL monotherapy for treating vitiligo. However, based on the existing evidence, there is inadequate support for the efficacy of combining topical vitamin D<sub>3</sub> analogs and corticosteroids with EL treatment.<sup>60</sup> On the other hand, Deng et al. demonstrated the application of a combination of intradermal platelet-rich plasma (PRP) injections with a 308 nm EL, resulting in positive therapy outcomes and a shortened duration of treatment.<sup>61</sup> The meta-analysis conducted by Chen et al., which included 6 studies involving 302 patients, provided further evidence supporting the superiority of combining PRP with EL therapy compared to laser monotherapy.<sup>62</sup> Moreover, Chang et al. performed a meta-analysis to evaluate the outcomes of combining topical therapy with an EL.<sup>63</sup> The meta-analysis included three RCTs involving 40 patients with vitiligo. The findings demonstrated significantly greater efficacy in achieving ≥75% repigmentation when utilizing the combination of topical therapy with tacrolimus and EL.<sup>64-66</sup> Recently, Liu et al conducted a meta-analysis on various therapeutic combinations with excimer laser. The combination of excimer laser with antioxidants achieved the best therapeutic effects, while the weakest therapeutic effects were observed when the laser was used alone. Thus, it appears that combined therapeutic methods with various points of intervention will be of interest to researchers in the future in order to obtain the most effective form of treatment for vitiligo.<sup>67</sup> This treatment option appeals to individuals who want to prevent the darkening of their skin resulting from NB-UVB therapy. While NB-UVB is successful in repigmenting stable patches, it often doesn't stabilize vitiligo because it doesn't treat clinically unaffected skin. For segmental vitiligo, early use of excimer laser appears to offer the most advantageous treatment.<sup>68</sup>

## Conclusion

Despite new therapeutic options for vitiligo emerging, phototherapy (especially NB-UVB) remains as preferred treatment option due to its effectiveness and safety. Acknowledging that phototherapy alone may not be sufficient for complete repigmentation in all cases is essential. Combining phototherapy with other treatments can accelerate repigmentation process and reduce number of required phototherapy sessions. This approach is beneficial as it minimizes the risk of potential side effects while boosting the overall efficacy of the treatment. The advantage of phototherapy as a primary or maintenance therapy is also that it can be performed at home. Despite its proven benefits, usage

of phototherapy has limitations. Treatment requires adherence to the prescribed regimen and multiple sessions over an extended time period. Additionally, certain patient groups may not be suitable for phototherapy, such as those suffering from photosensitivity disorders or having a history of skin cancer. In summary, phototherapy is a valuable tool in treating vitiligo, as it provides significant repigmentation results and improves patient quality of life. With ongoing research and treatment protocol advances, phototherapy may evolve and bring hope to those with this chronic skin condition.

## Declarations

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### Author contributions

Conceptualization, A.W.; Validation, R.C.; Resources, A.W., A.B. and B.K.; Data Curation, A.W., A.B. and B.K.; Writing – Original Draft Preparation, A.W., A.B. and B.K.; Writing – Review & Editing, A.W., A.B. and B.K.; Supervision, R.C.; Project Administration, A.W., A.B. and B.K.

### Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

### Data availability

Not applicable.

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