

# Efficacy and Safety of 308-nm Monochromatic Excimer Lamp Versus Other Phototherapy Devices for Vitiligo: A Systematic Review with Meta-Analysis

Celso Lopes<sup>1</sup> · Virginia Fernandes Moça Trevisani<sup>2,3,6</sup> · Tamara Melnik<sup>4,5</sup>

Published online: 31 October 2015  
© Springer International Publishing Switzerland 2015

## Abstract

**Background** Various phototherapy methods are used to treat vitiligo; however, the recent emergence of new devices has heightened debate concerning the best treatment method.

**Objective** We aimed to systematically review and meta-analyze published data comparing the efficacy and adverse effects of monochromatic excimer lamps versus excimer

laser and narrowband ultraviolet B (NB-UVB) in treating vitiligo.

**Methods** A systematic search of PubMed, EMBASE, LILACS, Cochrane Central Register of Controlled Trials (CENTRAL), and clinical trials registries identified randomized controlled trials that included vitiligo patients, regardless of age, sex, or study language. We evaluated studies comparing excimer lamps with excimer laser or NB-UVB phototherapy.

**Results** The review included six studies (411 patients, 764 lesions). No study found significantly different efficacy between excimer lamps and excimer laser using the outcomes of  $\geq 50$  % repigmentation [risk ratio (RR) = 0.97, 95 % confidence interval (CI) 0.84–1.11] and  $\geq 75$  % repigmentation (RR = 0.96, 95 % CI 0.71–1.30). Likewise, no study found significant differences between excimer lamps and NB-UVB (RR = 1.14, 95 % CI 0.88–1.48 for  $\geq 50$  % repigmentation; RR = 1.81, 95 % CI 0.11–29.52 for  $\geq 75$  % repigmentation). Adverse effects were mild, including pruritus, burning sensation, and dryness, none of which interrupted treatment.

**Conclusions** To our knowledge, this is the first systematic review of the efficacy and safety of excimer lamp treatment for vitiligo. Excimer lamps, excimer laser, and NB-UVB are all safe and effective in repigmentation of vitiligo lesions. Safety, effectiveness, and cost are considerations when choosing treatment.

**PROSPERO Registration Number** CRD42014015237.

---

**Electronic supplementary material** The online version of this article (doi:10.1007/s40257-015-0164-2) contains supplementary material, which is available to authorized users.

---

✉ Virginia Fernandes Moça Trevisani  
viticlinsp@yahoo.com.br

<sup>1</sup> Dermatology Department, Federal University of São Paulo (UNIFESP), São Paulo, Brazil

<sup>2</sup> Division of Emergency Medicine and Evidence-Based Medicine, Federal University of São Paulo (UNIFESP), São Paulo, Brazil

<sup>3</sup> Discipline of Rheumatology, Santo Amaro University (UNISA), São Paulo, Brazil

<sup>4</sup> Internal Medicine and Evidence-Based Medicine, Federal University of São Paulo (UNIFESP), São Paulo, Brazil

<sup>5</sup> Brazilian Cochrane Center, São Paulo, Brazil

<sup>6</sup> Disciplina de Medicina Baseada em Evidência, Universidade Federal de São Paulo, Rua Botucatu, 740-3° andar-Vila Clementino, São Paulo, SP 04023-900, Brazil

## Key Points

Monochromatic excimer lamps, excimer lasers, and conventional narrowband ultraviolet B phototherapy are all safe and effective in the treatment of vitiligo lesions, and show no significant differences in repigmentation efficacy.

Large-scale, randomized controlled trials with clearly defined criteria for patient recruitment and an objective means of assessing repigmentation are needed to confirm the long-term safety and efficacy of phototherapy in the treatment of vitiligo.

## 1 Introduction

Vitiligo is an acquired pigment disorder of the skin [1] that is characterized by areas of depigmentation resulting from loss of epidermal melanocytes [2] and clinically evidenced by circumscribed white maculae [3]. The disease affects approximately 1 % of the population [4], including all age groups, without sex or racial differences [5]. Half of vitiligo patients develop the disease before 20 years of age [6]. Vitiligo is a chronic disease that is difficult to treat and has negative psychosocial impacts [7, 8] that affect the quality of life of patients [9–11] and family members [12].

Many theories exist to explain the pathogenesis of vitiligo, but the cause remains poorly understood [13]. The autoimmune hypothesis involves multiple susceptibility genes [14, 15] and unknown environmental factors that lead to autoimmune destruction of melanocytes [16, 18]. Other theories include oxidative stress and autotoxicity [19–21], increased expression of tumor necrosis factor (TNF)- $\alpha$  [22], melanocyte detachment, and melanocytorrhagy [23, 24]. The treatment of vitiligo is challenging and includes the use of systemic or topical immunosuppressants [25, 26], immunomodulators [27, 28], vitamin D analogs [29, 30], calcineurin inhibitors [5, 31], afamelanotide [32, 33], melanocyte transplantation [34–36], and (predominantly) combinations of different therapies [17]. Different methods and devices of phototherapy have been used for many years, including psoralen plus ultraviolet (UV) A [37], broadband UVB [38], narrowband UVB (NB-UVB) [39–41], and targeted phototherapy using excimer lasers [42] or monochromatic excimer lamps [43].

Phototherapy enhances the migration and proliferation of melanocytes, resulting in repigmentation [44] and influencing the immune response [45, 46]. Since the first

reports of their use two decades ago, NB-UVB phototherapy, excimer laser, and excimer lamps have shown efficacy in treating vitiligo [47]. Although the three devices emit a similar wavelength, they have different radiation properties. The excimer laser and excimer lamp are considered targeted phototherapy, treating a small area and avoiding unnecessary exposure of normal skin to radiation [48–51]. Targeted phototherapy is usually recommended for localized forms of vitiligo affecting less than 10 % of the body surface area [52–54]. Excimer lasers are considerably more expensive than excimer lamps and have higher operational and maintenance costs [43]. In addition, because the lamp is smaller than the laser, it requires less space and has the advantage of portability. Both excimer laser and excimer lamps are more expensive than conventional NB-UVB phototherapy.

The terms monochromatic excimer lamp and monochromatic excimer light are used to describe the same type of device. Excimer lamps use a noble gas (xenon chloride) that decomposes in the presence of another reactive gas, emitting UV radiation at a wavelength of 308 nm [43]. In contrast to excimer lasers, excimer lamps emit incoherent light. Both laser and lamp deliver UVB to lesional skin only, resulting in a lower cumulative dose and lower risk of carcinogenicity and minimizing the color contrast between normal and affected skin [55]. The lamp usually requires a longer time than the laser to deliver the same fluence. The mechanism of action of 308-nm monochromatic excimer lamps in vitiligo treatment is unclear, but there is evidence that they act through immunosuppression and immunomodulation in response to apoptosis and T cell depletion [43, 56]. UVB radiation can lead to upregulation of endothelin-1 in keratinocytes, which is an important factor in melanocyte function [57, 58]. Repigmentation can occur with migration of melanocytes from normal skin to depigmented areas [59, 60].

Various methods of phototherapy have been used for many years; however, the emergence of new devices in the last two decades has created doubts and speculation about the best treatment options. Controversies exist concerning the best type of equipment for repigmentation of lesions. We performed a systematic review of the literature to compare the efficacy and safety of monochromatic excimer lamps with excimer laser and conventional NB-UVB in the treatment of vitiligo.

## 2 Methods

This study was submitted to the local ethical committee of Federal University of São Paulo, São Paulo, Brazil (number 41065514.8.0000.5505) and registered at PROSPERO

(international prospective register of systematic reviews; registration number CRD42014015237). We selected randomized controlled trials that included patients with any type of vitiligo, regardless of age or sex. Studies in all languages were included. We assessed studies that compared monochromatic excimer lamps with 308-nm excimer laser or conventional NB-UVB phototherapy.

## 2.1 Outcome Measures

The primary outcomes assessed in this study were 50 and 75 % repigmentation of lesions and adverse effects (blistering, burning sensation, pruritus) with the different devices. The secondary outcome was quality of life measured with a validated tool (e.g., the Dermatology Quality of Life Index or the World Health Organization Quality of Life instrument).

## 2.2 Search Methods for Identification of Studies

In March 2015 we performed a search of PubMed, EMBASE, LILACS, Cochrane Central Register of Controlled Trials (CENTRAL), clinical trials registries, and a manual search of the Internet. The search strategy designed for PubMed is shown in Electronic Supplementary Material 1.

## 2.3 Data Collection and Analysis

Two review authors (CL and TM) independently assessed all potential studies identified with the search strategy. Any disagreement about inclusion was resolved through discussion or, if required, consultation with a third review author (VFMT). We designed a form for data extraction. At least two reviewers extracted data from eligible studies using the form. We resolved discrepancies through discussion or, if required, consultation with a third review author. We entered data into RevMan 5.3 (Cochrane Collaboration, Oxford, UK), according to Cochrane Handbook for Systematic Reviews of Interventions [61] and checked the data for accuracy. We attempted to contact authors of the original reports to provide further details when information was unclear.

## 2.4 Assessment of Risk of Bias in Included Studies

Two reviewers (CL and TA) independently assessed the risk of bias in each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* [61]. We resolved any disagreement by discussion or by involving a third review author (VFMT).

## 2.5 Measures of Treatment Effect

For dichotomous outcomes, the risk ratio (RR) was calculated with 95 % confidence intervals (CIs). For

continuous outcome data, we used the mean difference with 95 % CIs for trials that used the same assessment scale. When trials used different assessment scales, we used the standardized mean difference with 95 % CIs.

## 2.6 Dealing with Missing Data

For included studies, we noted levels of attrition. We used sensitivity analysis to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect. For all outcomes, we carried out analyses on an intention-to-treat basis. We planned to perform a sensitivity analysis if ten or more studies were included.

## 2.7 Assessment of Heterogeneity

The decision to undertake a meta-analysis was made after data extraction. We examined forest plots to assess heterogeneity, which we quantified with the  $I^2$  statistic, together with the  $p$  value from the Chi-squared test for statistical heterogeneity. We considered results heterogeneous if we obtained an  $I^2$  statistic value greater than 50 % [61]. We decided not to perform subgroup analysis because of the small number of patients in the studies.

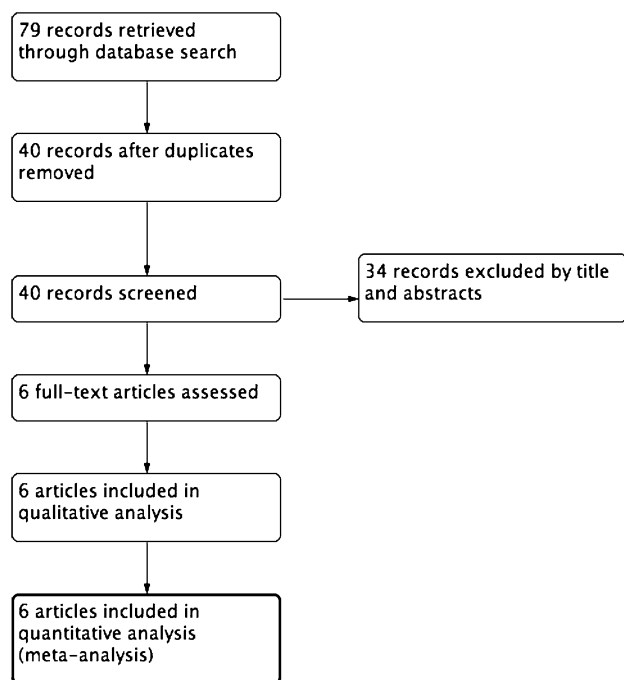
# 3 Results

## 3.1 Search Results

A total of 40 potentially eligible studies were identified; 34 of these were excluded after review of abstracts. The full texts of the remaining six studies were analyzed for eligibility and all of these were included in qualitative and quantitative synthesis (meta-analysis) (Fig. 1). The six studies included 411 patients and 764 lesions. Five studies conducted intra-patient comparison (self-control) and one analyzed two groups with distinct treatments (one group treated with monochromatic excimer lamp and the other with NB-UVB). The time since diagnosis, affected regions, and extent of disease varied among the studies. All studies included participants regardless of age or sex. Three studies were performed in China, one in Belgium, one in France, and one in both France and Italy. The studies in China included the largest number of patients. Characteristics of the included studies are described in Table 1. No ongoing studies were found in the ClinicalTrials.gov registry.

## 3.2 Risk of Bias in Included Studies

We present our assessment of the risk of bias in Fig. 2, which provides a cross-tabulation of each trial for all risk



**Fig. 1** Flow chart of study selection process

of bias items. When evaluating random sequence generation (selection bias), four studies were classified as having a low risk of bias [62–64, 66] and two studies had unclear risk [65, 67]. For allocation concealment (selection bias), we judged all studies to have an unclear risk of bias. Five studies had an unclear risk of performance bias (blinding of participants and personnel) [63–67] and one study had low risk of bias [62]. Evaluation of blinding of outcome assessment (detection bias) showed that four studies had low risk of bias [62–65] and two had unclear risk of bias [66, 67]. For incomplete outcome data (attrition bias), four studies were considered to have low risk of bias [62, 64, 66, 67] and two had high risk of bias [63, 65]. In relation to selective reporting (reporting bias), we considered three studies to be at low risk of bias [62–64] and three at unclear risk of bias [65–67]. When evaluating other types of bias, we classified all of the studies as being at unclear risk of bias.

### 3.3 Comparison of Excimer Lamp and Excimer Laser

Three studies compared the efficacy and safety of the excimer lamp with excimer laser [64, 65, 67]. All three studies were eligible for meta-analysis for the outcome of  $\geq 50\%$  repigmentation. Meta-analysis revealed no difference between the devices (RR = 0.97, 95% CI 0.84–1.11)

(Fig. 3). Two of the studies [64, 67] were eligible for meta-analysis for the outcome of  $\geq 75\%$  repigmentation; again, meta-analysis revealed no difference between the two devices (RR = 0.96, 95% CI 0.71–1.30) (Fig. 4). None of the studies assessed the secondary outcome (quality of life).

#### 3.3.1 Repigmentation $\geq 50\%$

Le Duff et al. [65] reported equivalence between the excimer lamp and excimer laser in  $\geq 50\%$  repigmentation of vitiligo ( $p = 0.006$ ). Lesions on the extremities and bony prominences showed the poorest response to treatment. The authors discuss that their treatment success rate was lower than that reported in other studies, results they attributed to the limited number of treatment sessions and the presence of lesions in difficult-to-treat areas. The authors observed that the excimer lamp is less expensive than the laser, allowing a more favorable cost/effectiveness ratio, although treatment takes a bit longer. The meta-analysis showed no significant difference between the excimer lamp and excimer laser in  $\geq 50\%$  repigmentation outcomes (RR = 1.00; 95% CI 0.41–2.46) (Fig. 3).

Liu et al. [67] concluded that both the excimer lamp and excimer laser successfully treat depigmentation and found no difference between the treatments ( $p > 0.05$ ). Lesions on the face and neck responded better to treatment than those on the trunk and limbs. Lesions on the trunk responded better than those on the extremities. The meta-analysis showed no significant difference between the two devices (RR = 0.94; 95% CI 0.80–1.10) (Fig. 3).

Shi et al. [64] reported that improvement was observed with both the excimer lamp and excimer laser, and found no significant difference between the devices in repigmentation  $\geq 50\%$  ( $p > 0.05$ ). The meta-analysis showed no significant difference between the devices (RR = 1.11; 95% CI 0.86–1.43) (Fig. 3).

#### 3.3.2 Repigmentation $\geq 75\%$

Le Duff et al. [65] did not measure repigmentation  $\geq 75\%$ . Liu et al. [67] concluded that both the excimer lamp and excimer laser are efficient and equivalent for repigmentation  $\geq 75\%$ . The meta-analysis showed no significant difference between the devices (RR = 0.88; 95% CI 0.61–1.26) (Fig. 4). Shi et al. [64] reported no significant difference in the mean repigmentation time between the devices ( $p > 0.05$ ). The meta-analysis showed no significant difference between the devices (RR = 1.27; 95% CI 0.73–2.21) (Fig. 4).

**Table 1** Characteristics of included studies

Study (year), location	Treatments compared	Number of patients	Number of lesions (MEL/C)	Number of sessions	Mean patient age [years (range)]	Median duration of disease [years (range)]	Skin phototype	Location (number) of lesions	Percentage of lesions with repigmentation >50% [MEL (C)]	Repigmentation >50% (meta-analysis risk ratio)	Percentage of lesions with repigmentation >75% [MEL (C)]	Repigmentation >75% (meta-analysis risk ratio)	Lost patients	Adverse effects
Le Duff et al. [65] (2010), France	MEL vs. laser	20	52/52 (C)	24 (2×/week)	38 (21–54)	17 (3–35)	II/III/IV/V	Face (32) Extremities (28)	15.3 (15.3)	M-H 1.0 [fixed 95% CI 0.41–2.46]	3	MEL: blister (n = 3) C: blister (n = 1)		
Shi et al. [64] (2013), China	MEL vs. laser	14	24/24 (C)	20 (3×/week)	22.2 (2–39)	3.46 (0.48–20)	III	Other (44) Face/neck (20) Trunk (24) Limbs (4)	87.5 (79)	M-H 1.11 [fixed 95% CI 0.86–1.43]	58.3 (45.8)	M-H 1.27 [fixed 95% CI 0.73–2.21]	0	MEL: persistent erythema (n = 12) C: persistent erythema (n = 13)
Liu et al. [67] (2013), China	MEL vs. laser	62	132/128 (C)	30 (2×/week)	22.2 (18–45)	3.2 (18–45)	II/III/IV	Face/neck (82) Trunk (78) Limbs (58) Hands/feet (42)	68.9 (73.41)	M-H 0.94 [fixed 95% CI 0.8–1.10]	28.7 (32.8)	M-H 0.88 [fixed 95% CI 0.61–1.26]	0	Burning sensation (n = 1) Blistering (n = 1)
Casacci et al. [63] (2007), France/Italy	MEL vs. NB-UVB	16	21/21 (C)	48 (2×/week)	38 (16–58)	9.5 (0.5–24)	II/III/IV	Neck (1) Trunk (4) Limbs (11)	47.6 (28.5)	M-H 1.67 [fixed 95% CI 0.74–3.75]	28.5 (4.7)	M-H 6.00 [random 95% CI 0.79–45.63]	5	Adverse effects were similar Symptomatic erythema in 56.2% No blistering or bullous reaction Erythema (all patients) Mild burning or pain (n = 3) Burning sensation (lamp group) E: bullous reaction (n = 16) C: burning, pruritus, dryness (n = 9)
Verhaeghe et al. [62] (2011), Belgium	MEL vs. NB-UVB	11	11/11 (C)	24 (2×/week)	41.18 (22–57)	13.11 (1–40)	II/III/IV	Neck (1) Trunk (15) Limbs (6)	0 (18.1)	M-H 0.20 [fixed 95% CI 0.01–3.74]	0 (0.9)	M-H 0.33 [random 95% CI 0.02–7.39]	0	
Yan et al. [66] (2013), China	MEL vs. NB-UVB	288	145/143 (C)	30 (2×/week)	32.1 (4–63)	5.50 (0.16–27)	III/IV	Face/neck (107) Trunk (95) Limbs (52) Skin folds (21) Hands/feet (13)	44.13 (39.16)	M-H 1.67 [fixed 95% CI 0.75–3.75]	0	0		

C control (excimer laser or NB-UVB), CI confidence interval, MEL monochromatic excimer lamp, M-H statistical method of analysis (Mantel-Haenszel), NB-UVB narrowband ultraviolet B



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Casacci (2007)	+	?	?	+	-	+	?
Le Duff (2010)	?	?	?	+	-	?	?
Liu (2013)	?	?	?	?	+	?	?
Shi (2013)	+	?	?	+	+	+	?
Verhaeghe (2011)	+	?	+	+	+	+	?
Yan (2013)	+	?	?	?	+	?	?

**Fig. 2** Risk of bias summary [62–67]. *Plus* Low risk of bias, *minus* high risk of bias, *question mark* unclear risk of bias

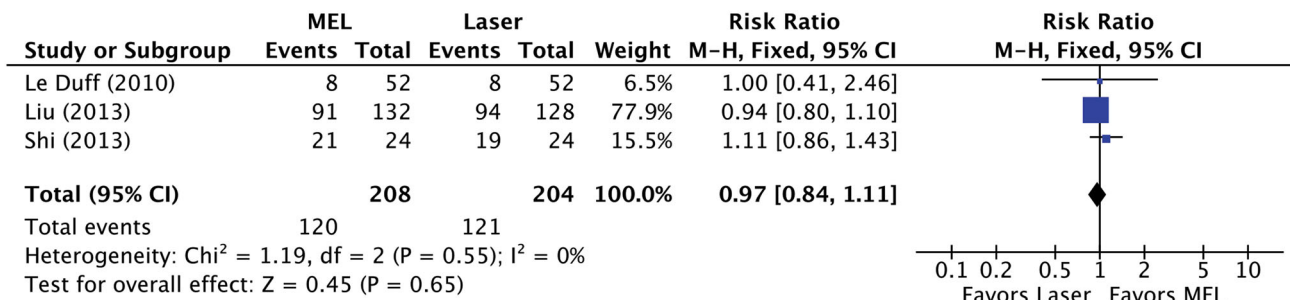
### 3.4 Comparison of Excimer Lamp and Narrowband Ultraviolet B

Three studies compared the excimer lamp with NB-UVB [62, 63, 66]. All three studies were eligible for meta-analysis for the outcome of  $\geq 50\%$  repigmentation; none of the three found any difference between the two devices (RR = 1.14, 95% CI 0.88–1.48) (Fig. 5). Two of the studies [62, 63] were eligible for meta-analysis for the outcome of  $\geq 75\%$  repigmentation and also found no difference between the devices (RR = 1.81, 95% CI 0.11–29.52) (Fig. 6). None of the studies assessed the secondary outcome (quality of life).

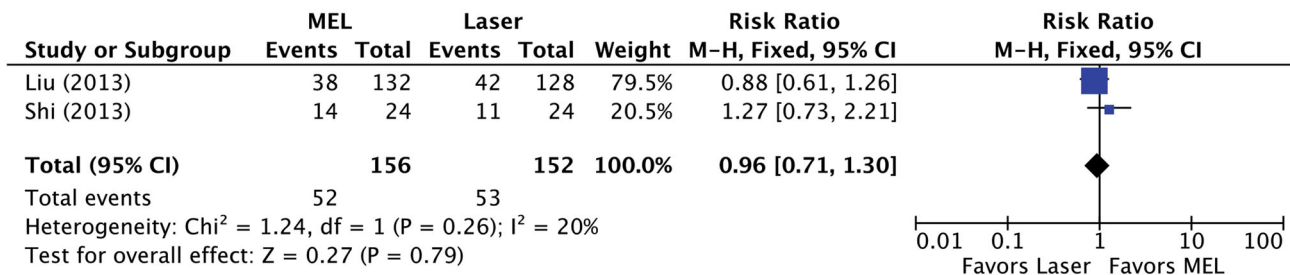
#### 3.4.1 Repigmentation $\geq 50\%$

Casacci et al. [63] concluded that improvement was seen with both the excimer lamp and NB-UVB. Although the mean repigmentation score was higher for the excimer lamp ( $p = 0.04$ ), the meta-analysis showed no significant difference between the devices (RR = 1.67; 95% CI 0.74–3.75) (Fig. 5).

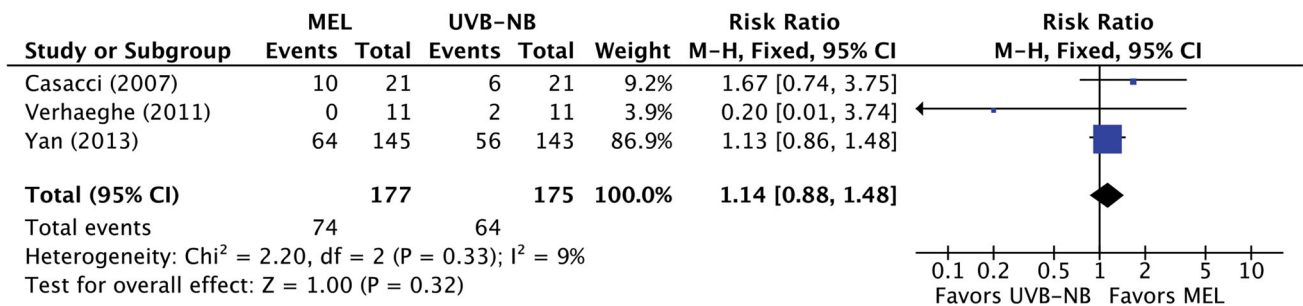
Verhaeghe et al. [62] observed that they had poorer results than previous studies and formed several hypotheses to explain their outcomes. In contrast to other reports, their study used an objective measuring instrument to evaluate repigmentation. Their study also had a limited number of



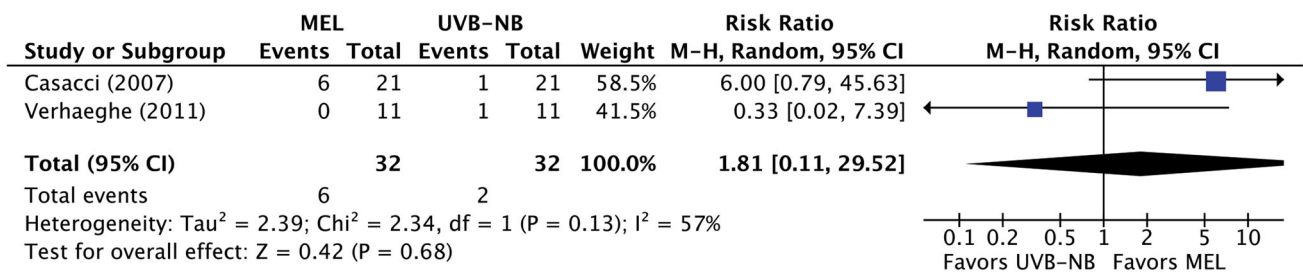
**Fig. 3** Monochromatic excimer lamp vs. laser ( $\geq 50\%$  repigmentation) [64, 65, 67]. *CI* confidence interval, *df* degrees of freedom, *events* number of lesions that achieved the given repigmentation percentage, *MEL* monochromatic excimer lamp, *M-H* statistical method of analysis (Mantel-Haenszel), *total* number of lesions treated



**Fig. 4** Monochromatic excimer lamp vs. laser ( $\geq 75\%$  repigmentation) [64, 67]. *CI* confidence interval, *df* degrees of freedom, *events* number of lesions that achieved the given repigmentation percentage, *MEL* monochromatic excimer lamp, *M-H* statistical method of analysis (Mantel-Haenszel), *total* number of lesions treated



**Fig. 5** Monochromatic excimer lamp vs. narrowband Ultraviolet B ( $\geq 50\%$  repigmentation) [62, 63, 66]. *CI* confidence interval, *df* degrees of freedom, *events* number of lesions that achieved the given repigmentation percentage, *MEL* monochromatic excimer lamp, *M-H* statistical method of analysis (Mantel-Haenszel), *NB-UVB* narrowband ultraviolet B, *total* number of lesions treated



**Fig. 6** Monochromatic excimer lamp vs. narrowband Ultraviolet B ( $\geq 75\%$  repigmentation) [62, 63]. *CI* confidence interval, *df* degrees of freedom, *events* number of lesions that achieved the given repigmentation percentage, *MEL* monochromatic excimer lamp, *M-H* statistical method of analysis (Mantel-Haenszel), *NB-UVB* narrowband ultraviolet B, *total* number of lesions treated

treatment sessions and lesions. Finally, the small number of patients in their study could have played a role in their results. The meta-analysis showed no significant difference between excimer lamp and NB-UVB devices for the outcome of repigmentation  $\geq 50\%$  ( $\text{RR} = 0.20$ ;  $95\%$   $\text{CI}$   $0.01\text{--}3.74$ ) (Fig. 5).

Yan et al. [66] concluded that patients under 12 years of age showed better repigmentation with both the excimer lamp and NB-UVB treatment ( $p < 0.05$ ). Lesions located on the face and neck had better repigmentation scores with excimer lamp treatment ( $p < 0.05$ ) and lesions on the limbs had better repigmentation with NB-UVB ( $p < 0.05$ ). The meta-analysis showed that there was no significant difference between the devices for the outcome measure of repigmentation  $\geq 50\%$  ( $\text{RR} = 1.13$ ;  $95\%$   $\text{CI}$   $0.86\text{--}1.48$ ) (Fig. 5).

### 3.4.2 Repigmentation $\geq 75\%$

Casacci et al. [63] concluded that the cumulative UV light dose for lesions treated with an excimer lamp was lower than that necessary with NB-UVB ( $p < 0.0001$ ). The meta-analysis showed no significant difference between the devices for the outcome measure of repigmentation  $\geq 75\%$  ( $\text{RR} = 6.0$ ;  $95\%$   $\text{CI}$   $0.79\text{--}45.63$ ) (Fig. 6). Verhaeghe et al.

[62] confirmed the efficacy of both the excimer lamp and NB-UVB. The meta-analysis showed no significant difference between the devices for the outcome measure of repigmentation  $\geq 75\%$  ( $\text{RR} = 0.33$ ;  $95\%$   $\text{CI}$   $0.02\text{--}7.39$ ) (Fig. 6). Yan et al. [66] did not measure repigmentation  $\geq 75\%$ .

### 3.5 Adverse Effects

Le Duff et al. [65] reported that both the excimer lamp and excimer laser were well-tolerated, although one blister occurred with the lamp and three blisters with the laser. They observed that the lamp induced more erythema than the laser, suggesting that the devices have different photobiological effects at the cellular level. Liu et al. [67] reported that one patient had a burning sensation and one developed a blister and dryness; however, the study did not specify which treatment (excimer lamp or laser) caused the reactions. Shi et al. [64] concluded that the adverse effects of both the excimer lamp and laser were mild. The majority of patients (85.7% with the lamp and 92.9% with laser) had persistent erythema, which was well-tolerated. Casacci et al. [63] reported similar adverse effects with both the excimer lamp and NB-UVB, restricted to symptomatic erythema with no blistering or bullous reactions.

Verhaeghe et al. [62] reported that adverse effects included erythema in all patients after about half of the treatment sessions. Three patients reported mild burning or pain, on two or three occasions each. Yan et al. [66] observed that patients in the lamp group experienced redness and a burning sensation, but that symptoms disappeared with silicone gel application; 16 patients had bullous reactions, necessitating a 2-week treatment interruption. In the NB-UVB group, nine patients experienced burning, pruritus, and dryness. None of these effects interfered with treatment in either group.

## 4 Discussion

In recent years, numerous reports have highlighted the importance of phototherapy in the treatment of vitiligo. The present systematic review found that NB-UVB, excimer lasers, and excimer lamps are all effective in the treatment of vitiligo; meta-analysis revealed no significant differences in efficacy among the three devices when evaluating repigmentation  $\geq 50$  and  $\geq 75$  %. The treatments were most effective in lesions located on the face, whereas lesions on the extremities had the worst response, a finding that is in agreement with the literature.

This review and meta-analysis has limitations. First, therapies in these studies varied in duration and frequency of treatment, complicating comparisons between studies. Three studies [62, 64, 66] included stable and active vitiligo, while three studies [63, 65, 67] did not mention stability or activity of the disease, which could influence the results. Second, none of the studies defined disease activity. Third, the mean patient age and mean duration of disease varied considerably among studies. Fourth, the NB-UVB devices used in the studies varied in dimension and in numbers of UVB tubes, with possible differences in irradiance. A recent study demonstrated the influence of irradiance differences on pigment cell development [68]. Finally, none of the studies evaluated quality of life.

In a systematic review evaluating 308-nm excimer laser treatment for vitiligo, Sun et al. [69] concluded that there was no difference between excimer laser and excimer lamp treatment. In a systematic review evaluating the treatment of vitiligo with NB-UVB, Xiao et al. [70] found no difference between excimer lamp and NB-UVB treatment. These findings are in agreement with those of the present review. Our study differed from the above because we focused on excimer lamp treatment and included studies published in any language, which provided a considerably larger number of patients. To our knowledge, this systematic review is the first to focus on the safety and efficacy of excimer lamp treatment in vitiligo.

## 5 Conclusion

We aimed to systematically review and meta-analyze published data comparing the efficacy and adverse effects of monochromatic excimer lamps versus excimer lasers and NB-UVB in treating vitiligo. Based on this review, excimer lamps, excimer lasers, and NB-UVB are all safe and effective in repigmentation of vitiligo lesions. The adverse effects of treatment are mild and acceptable, including pruritus, burning sensation, and dryness. None of these effects interfered with treatment in the included studies. From a practical standpoint, safety, effectiveness, and cost should be considered when choosing equipment. Randomized controlled trials with greater numbers of patients and better methodological quality, including more clearly defined criteria for patient recruitment and a standardized method of measuring repigmentation, are needed to assess the efficacy and safety of phototherapy in patients with vitiligo. Because vitiligo can have a great negative social impact [9–12], we consider it relevant to evaluate the quality of life of treated individuals. Future trials should be conducted over a longer time period to determine the safety and long-term effects of phototherapy.

### Compliance with Ethical Standards

**Conflicts of interest** The authors, Celso Lopes, Virginia Fernandes Moça Trevisani, and Tamara Melnik, declare no conflicts of interest.

**Funding sources** No funding was received.

## References

- Lotti T, D'Erme AM. Vitiligo as a systemic disease. *Clin Dermatol.* 2014;32:430–4.
- Ding GZ, Zhao WE, Li X, Gong QL, Lu Y. A comparative study of mitochondrial ultrastructure in melanocytes from perilesional vitiligo skin and perilesional halo nevi skin. *Arch Dermatol Res.* 2015;307:281–9.
- Yaghoobi R, Omidian M, Bagherani N. Vitiligo: a review of the published work. *J Dermatol.* 2011;38:419–31.
- Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. *Lancet.* 2015;386:74–84.
- Taieb A, Alomar A, Böhm M, Dell'anna ML, De Pase A, Eleftheriadou V, et al. Guidelines for the management of vitiligo: the European Dermatology Forum consensus. *Br J Dermatol.* 2013;168:5–19.
- Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: a comprehensive overview. Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. *J Am Acad Dermatol.* 2011;65:473–91.
- Teovska Mitrevska N, Eleftheriadou V, Guarneri F. Quality of life in vitiligo patients. *Dermatol Ther.* 2012;25:S28–31.
- Sampogna F. Life course impairment and quality of life over time. *Curr Probl Dermatol.* 2013;44:47–51.
- Mishra N, Rastogi MK, Gahalaut P, Agrawal S. Dermatology specific quality of life in vitiligo patients and its relation with



- various variables: a hospital based cross-sectional study. *J Clin Diagn Res.* 2014;8:YC01–3.
10. Krüger C, Schallreuter KU. Stigmatisation, avoidance behaviour and difficulties in coping are common among adult patients with vitiligo. *Acta Derm Venereol.* 2015;95:553–8.
  11. Ezzedine K, Grimes PE, Meurant JM, Seneschal J, Léauté-Labrèze C, Ballanger F, et al. Living with vitiligo: results from a national survey indicate differences between skin phototypes. *Br J Dermatol.* 2015;173:607–9.
  12. Bin Saif GA, Al-Balbeesi AO, Binshabaib R, Alsaad D, Kwatra SG, Alzolibani AA, et al. Quality of life in family members of vitiligo patients: a questionnaire study in Saudi Arabia. *Am J Clin Dermatol.* 2013;14:489–95.
  13. Malhotra N, Dytoc M. The pathogenesis of vitiligo. *J Cutan Med Surg.* 2013;17:153–72.
  14. Czajkowski R, Męcińska-Jundził K. Current aspects of vitiligo genetics. *Postepy Dermatol Alergol.* 2014;31:247–55.
  15. Spritz RA. Modern vitiligo genetics sheds new light on an ancient disease. *J Dermatol.* 2013;40:310–8.
  16. Ghafourian A, Ghafourian S, Sadeghifard N, Mohebi R, Shokohini Y, Nezamoleslami S, et al. Vitiligo: symptoms, pathogenesis and treatment. *Int J Immunopathol Pharmacol.* 2014;27:485–9.
  17. Speeckaert R, Speeckaert MM, van Geel N. Why treatments do(n't) work in vitiligo: an autoinflammatory perspective. *Autoimmun Rev.* 2015;14:332–40.
  18. Lin X, Tang LY, Fu WW, Kang KF. Childhood vitiligo in China: clinical profiles and immunological findings in 620 cases. *Am J Clin Dermatol.* 2011;12:277–81.
  19. Laddha NC, Dwivedi M, Mansuri MS, Singh M, Gani AR, Yeola AP, et al. Role of oxidative stress and autoimmunity in onset and progression of vitiligo. *Exp Dermatol.* 2014;23:352–3.
  20. Zedan H, Abdel-Motaleb AA, Kassem NM, Hafeez HA, Hussein MR. Low glutathione peroxidase activity levels in patients with vitiligo. *J Cutan Med Surg.* 2015;19:144–8.
  21. Güntaş G, Engin B, Ekmekçi ÖB, Kutlubay Z, Ekmekçi H, Songür A, et al. Evaluation of advanced oxidation protein products, prooxidant-antioxidant balance, and total antioxidant capacity in untreated vitiligo patients. *Ann Dermatol.* 2015;27:178–83.
  22. Camara-Lemarrooy CR, Salas-Alanis JC. The role of tumor necrosis factor- $\alpha$  in the pathogenesis of vitiligo. *Am J Clin Dermatol.* 2013;14:343–50.
  23. Kumar R, Parsad D, Kanwar AJ. Role of apoptosis and melanocytorrhagy: a comparative study of melanocyte adhesion in stable and unstable vitiligo. *Br J Dermatol.* 2011;164:187–91.
  24. Kumar R, Parsad D. Melanocytorrhagy and apoptosis in vitiligo: connecting jigsaw pieces. *Indian J Dermatol Venereol Leprol.* 2012;78:19–23.
  25. Kanwar AJ, Mahajan R, Parsad D. Low-dose oral mini-pulse dexamethasone therapy in progressive unstable vitiligo. *J Cutan Med Surg.* 2013;17:259–68.
  26. Whitton ME, Pinart M, Batchelor J, Leonardi-Bee J, González U, Jiyad Z, et al. Interventions for vitiligo. *Cochrane Database Syst Rev.* 2015;2:CD003263. doi:10.1002/14651858.CD003263.pub5.
  27. Du J, Wang XY, Ding XL, Xu QX, Chen Z, Chang JM, et al. Long-term efficacy and safety of tacrolimus ointment in the treatment of vitiligo. *J Dermatol.* 2013;40:935–6.
  28. Cavalié M, Ezzedine K, Fontas E, Montaudié H, Castela E, Bahadoran P, et al. Maintenance therapy of adult vitiligo with 0.1 % tacrolimus ointment: a randomized, double blind, placebo-controlled study. *J Invest Dermatol.* 2015;135:970–4.
  29. Newman MD, Silverberg NB. Once-daily application of calcipotriene 0.005%-betamethasone dipropionate 0.064% ointment for repigmentation of facial vitiligo. *Cutis.* 2011;88:256–9.
  30. Hossani-Madani A, Halder R. Treatment of vitiligo: advantages and disadvantages, indications for use and outcomes. *G Ital Dermatol Venereol.* 2011;146:373–95.
  31. Wong R, Lin AN. Efficacy of topical calcineurin inhibitors in vitiligo. *Int J Dermatol.* 2013;52:491–6.
  32. Lim HW, Grimes PE, Lebwohl M. Indications and limitations of afamelanotide for treating vitiligo-reply. *JAMA Dermatol.* 2015;151:350.
  33. Lim HW, Grimes PE, Agbai O, Hamzavi I, Henderson M, Hadican M, et al. Afamelanotide and narrowband UV-B phototherapy for the treatment of vitiligo: a randomized multicenter trial. *JAMA Dermatol.* 2015;151:42–50.
  34. Singh C, Parsad D, Kanwar AJ, Dogra S, Kumar R. Comparison between autologous noncultured extracted hair follicle outer root sheath cell suspension and autologous noncultured epidermal cell suspension in the treatment of stable vitiligo: a randomized study. *Br J Dermatol.* 2013;169:287–93.
  35. Bacigalupi RM, Postolova A, Davis RS. Evidence-based, non-surgical treatments for vitiligo: a review. *Am J Clin Dermatol.* 2012;13:217–37.
  36. Machado Filho CD, Timoner FR. Epidermal curettage technique (ECT) for tissue harvest from the donor area for melanocyte autologous grafting in cases of vitiligo. *An Bras Dermatol.* 2014;89:681–3.
  37. Sapam R, Agrawal S, Dhali TK. Systemic PUVA vs. narrowband UVB in the treatment of vitiligo: a randomized controlled study. *Int J Dermatol.* 2012;51:1107–15.
  38. Akar A, Tunca M, Koc E, Kurumlu Z. Broadband targeted UVB phototherapy for localized vitiligo: a retrospective study. *Photodermatol Photoimmunol Photomed.* 2009;25:161–3.
  39. Yazdani Abyaneh M, Griffith RD, Falto-Aizpurua L, Nouri K. Narrowband ultraviolet B phototherapy in combination with other therapies for vitiligo: mechanisms and efficacies. *J Eur Acad Dermatol Venereol.* 2014;28:1610–22.
  40. Hallaji Z, Ghiasi M, Eisazadeh A, Damavandi MR. Evaluation of the effect of disease duration in generalized vitiligo on its clinical response to narrowband ultraviolet B phototherapy. *Photodermatol Photoimmunol Photomed.* 2012;28:115–9.
  41. Akdeniz N, Yavuz IH, Gunes Bilgili S, Ozaydn Yavuz G, Calka O. Comparison of efficacy of narrow band UVB therapies with UVB alone, in combination with calcipotriol, and with betamethasone and calcipotriol in vitiligo. *J Dermatolog Treat.* 2014;25:196–9.
  42. Alhawaish AK, Dietrich N, Onder M, Fritz K. Effectiveness of a 308-nm excimer laser in treatment of vitiligo: a review. *Lasers Med Sci.* 2013;28:1035–41.
  43. Park KK, Liao W, Murase JE. A review of monochromatic excimer light in vitiligo. *Br J Dermatol.* 2012;167:468–78.
  44. Lee BW, Schwartz RA, Hercogová J, Valle Y, Lotti TM. Vitiligo road map. *Dermatol Ther.* 2012;25(Suppl 1):S44–56.
  45. Bulat V, Situm M, Dediol I, Ljubicić I, Bradić L. The mechanisms of action of phototherapy in the treatment of the most common dermatoses. *Coll Antropol.* 2011;35(Suppl 2):147–51.
  46. Lee CH, Wu SB, Hong CH, Yu HS, Wei YH. Molecular mechanisms of UV-induced apoptosis and its effects on skin residential cells: the implication in UV-based phototherapy. *Int J Mol Sci.* 2013;14:6414–35.
  47. Korobko IV. Review of current clinical studies of vitiligo treatments. *Dermatol Ther.* 2012;25(Suppl 1):S17–27.
  48. Itoi S, Tanemura A, Nishioka M, Sakimoto K, Iimuro E, Katayama I. Evaluation of the clinical safety and efficacy of a newly developed 308-nm excimer lamp for vitiligo vulgaris. *J Dermatol.* 2012;39:559–61.
  49. Mehraban S, Feily A. 308 nm excimer laser in dermatology. *J Lasers Med Sci.* 2014;5:8–12.

50. Al-Shobaili HA. Treatment of vitiligo patients by excimer laser improves patients' quality of life. *J Cutan Med Surg.* 2015;19:50–6.
51. Mouzakis JA, Liu S, Cohen G. Rapid response of facial vitiligo to 308nm excimer laser and topical calcipotriene. *J Clin Aesthet Dermatol.* 2011;4:41–4.
52. Welsh O, Herz-Ruelas ME, Gómez M, Ocampo-Candiani J. Therapeutic evaluation of UVB-targeted phototherapy in vitiligo that affects less than 10 % of the body surface area. *Int J Dermatol.* 2009;48:529–34. doi:10.1111/j.1365-4632.2009.03928.x.
53. Majid I. Efficacy of targeted narrowband ultraviolet B therapy in vitiligo. *Indian J Dermatol.* 2014;59:485–9.
54. Kaliyadan F, Ashique KT. Optimizing the efficacy of targeted phototherapy by marking early vitiligo lesions after visualizing under a Wood's lamp. *J Am Acad Dermatol.* 2014;71:e69.
55. Lotti TM, Hercogová J, Schwartz RA, Tsampau D, Korobko I, Pietrzak A, et al. Treatments of vitiligo: what's new at the horizon. *Dermatol Ther.* 2012;25(Suppl 1):S32–40.
56. Hamzavi IH, Lim HW, Syed ZU. Ultraviolet-based therapy for vitiligo: what's new? *Indian J Dermatol Venereol Leprol.* 2012;78:42–8.
57. Lee KY, Jeon SY, Hong JW, Choi KW, Lee CY, Choi SJ, et al. Endothelin-1 enhances the proliferation of normal human melanocytes in a paradoxical manner from the TNF- $\alpha$ -inhibited condition, but tacrolimus promotes exclusively the cellular migration without proliferation: a proposed action mechanism for combination therapy of phototherapy and topical tacrolimus in vitiligo treatment. *J Eur Acad Dermatol Venereol.* 2013;27:609–16.
58. Noborio R, Morita A. Preferential induction of endothelin-1 in a human epidermal equivalent model by narrow-band ultraviolet B light sources. *Photodermatol Photoimmunol Photomed.* 2010;26:159–61.
59. Goldstein NB, Koster MI, Hoaglin LG, Spoelstra NS, Kechris KJ, Robinson SE, et al. Narrow band ultraviolet B treatment for human vitiligo is associated with proliferation, migration, and differentiation of melanocyte precursors. *J Invest Dermatol.* 2015;135:2068–76.
60. Eby JM, Kang HK, Tully ST, Bindeman WE, Peiffer DS, Chatterjee S, et al. CCL22 to activate treg migration and suppress depigmentation in vitiligo. *J Invest Dermatol.* 2015;135:1574–80.
61. Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions.* Version 5.1.0 [Updated March 2011]. The Cochrane Collaboration, 2011. <http://handbook.cochrane.org>. Accessed Oct 26 2015.
62. Verhaeghe E, Lodewick E, van Geel N, Lambert J. Inpatient comparison of 308-nm monochromatic excimer light and localized narrow-band UVB phototherapy in the treatment of vitiligo: a randomized controlled trial. *Dermatology.* 2011;223:343–8.
63. Casacci M, Thomas P, Pacifico A, Bonneville A, Paro Vidolin A, Leone G. Comparison between 308-nm monochromatic excimer light and narrowband UVB phototherapy (311–313 nm) in the treatment of vitiligo—a multicentre controlled study. *J Eur Acad Dermatol Venereol.* 2007;21:956–63.
64. Shi Q, Li K, Fu J, Wang Y, Ma C, Li Q, et al. Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo—a randomized bilateral comparison study. *Photodermatol Photoimmunol Photomed.* 2013;29:27–33.
65. Le Duff F, Fontas E, Giacchero D, Sillard L, Lacour JP, Ortonne JP, et al. 308-nm excimer lamp vs. 308-nm excimer laser for treating vitiligo: a randomized study. *Br J Dermatol.* 2010;163:188–92.
66. Yan Y, Li J, Wang R, Zhong RP, Guo LH, Zhu MH. A randomized comparative clinical trial of 308 monochromatic excimer light and 311 nm narrow-band ultraviolet in treating vitiligo [in Chinese]. *J Clin Dermatol.* 2013;2:120–3.
67. Liu YB, Yang YF, Song LX, Shan YH, Wang Y, Ma TQ, et al. Comparison of 308 nm excimer laser and 308 nm excimer lamp in treatment of vitiligo [in Chinese]. *Clin Misdiagnosis Mis-therapy.* 2013;6:58–61.
68. Lan CC, Yu HS, Lu JH, Wu CS, Lai HC. Irradiance, but not fluence, plays a crucial role in UVB-induced immature pigment cell development: new insights for efficient UVB phototherapy. *Pigment Cell Melanoma Res.* 2013;26:367–76.
69. Sun Y, Wu Y, Xiao B, Li L, Chen HD, Gao XH. Treatment of 308-nm excimer laser on vitiligo: a systemic review of randomized controlled trials. *J Dermatolog Treat.* 2015;26:347–53.
70. Xiao BH, Wu Y, Sun Y, Chen HD, Gao XH. Treatment of vitiligo with NB-UVB: a systematic review. *J Dermatolog Treat.* 2015;26:340–6.