Original Article

Efficacy of NB-UVB in Progressive Versus Non-Progressive Non-Segmental Vitiligo: A Prospective Comparative Study

Saurabh Bhatia, Binod K. Khaitan, Vishal Gupta, Sujay Khandpur, Kanika Sahni, Vishnubhatla Sreenivas[1]

Departments of Dermatology and Venereology and [1]Biostatistics, All India Institute of Medical Sciences, New Delhi, India

Abstract

Introduction: Narrow-band (NB) ultraviolet B (UVB) phototherapy has been shown to halt disease progression in vitiligo, but whether there is any difference in the response to NB-UVB seen in patients with progressive vitiligo versus non-progressive vitiligo has not been evaluated. **Objectives:** To evaluate the effect of NB-UVB on progressive versus non-progressive non-segmental vitiligo. **Study Design:** Prospective observational comparative study. **Duration:** April 2016-November 2017. **Methods:** Adult patients having non-segmental vitiligo involving 2-50% body surface area were divided into two subsets; patients developing >5 lesions in the last 1 month or >15 lesions in the last 3 months (progressive vitiligo, Group I) and patients with static disease for the last 6 months (non-progressive vitiligo, Group II). Both groups were treated with NB-UVB for 6 months (26 weeks) cumulatively and its efficacy in halting disease progression, re-pigmentation, side effects and psychosocial impact were evaluated. **Results:** Nineteen out of 24 patients with progressive vitiligo had arrest of disease progression. Rest five patients developed lesions at a slower pace. Group II had earlier onset of re-pigmentation, while Group I had more NB-UVB fluence (34.73 J/cm^2 vs 25.2 J/cm^2, *P* value = 0.034), more time for the fluence to be fixed (*P* value = 0.001) and more pruritus (*P* value = 0.001). **Conclusions:** NB-UVB has the potential to halt disease progression in some patients with progressive vitiligo; but is associated with more total NB-UVB fluence and time taken for fixing it. Progressive vitiligo patients have more pruritus as compared to patients with non-progressive vitiligo.

Keywords: *Narrow band, NB-UVB, non-segmental vitiligo, phototherapy, progressive vitiligo, vitiligo*

Introduction and Objectives

Vitiligo is an acquired, multifactorial, autoimmune disorder characterized by well-defined, hypopigmented or depigmented macules, leading to significant psychosocial impact on the patients. In India, the prevalence varies in available literature from 0.46 to 8.8%.[1] Vitiligo has also been classified on the basis of natural course of disease; as active and stable disease. However, the notion of stability is too rigid and sometimes difficult to ascertain alone clinically. Hence, the term progressive and non-progressive vitiligo should be preferred over active and stable vitiligo, respectively. In many instances, re-pigmentation in vitiligo patches is considered the cornerstone of the management. But without arresting the progression of the disease, benefit of re-pigmentation can quickly become futile. Pasricha and Khaitan[2,3] have previously enunciated that as a first step the primary focus of the treatment should be arrest of the progression of the disease, followed by modalities to augment re-pigmentation.

In progressive vitiligo, available therapeutic modalities to achieve arrest of progression are limited. Systemic corticosteroids in the form of oral mini-pulse therapy (OMP) has remained the main modality to achieve this.[3] Recently, azathioprine has also been found to have some effect.[4] Narrow band ultraviolet (NB-UVB) therapy with effective wavelength of 311 ± 3 nm, is a widely used modality for the treatment of vitiligo. NB-UVB acts through immunosuppression by increasing regulatory T-lymphocytes and inhibiting the number of CD8 + T-lymphocytes.[5] So far, NB-UVB has been considered a promising therapy for generalized vitiligo which is

How to cite this article: Bhatia S, Khaitan BK, Gupta V, Khandpur S, Sahni K, Sreenivas V. Efficacy of NB-UVB in progressive versus non-progressive non-segmental vitiligo: A prospective comparative study. Indian Dermatol Online J 2021;12:701-5.

Received: 03-Feb-2021. **Revised:** 10-Mar-2021. **Accepted:** 15-Apr-2021. **Published:** 02-Aug-2021.

Address for correspondence:
Prof. Binod K. Khaitan, Room No: 4067, Department of Dermatology and Venereology, 4th Floor, All India Institute of Medical Sciences, New Delhi - 110 029, India. E-mail: binodkhaitan@hotmail.com

Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.IDOJ_40_21

Quick Response Code:

either non-progressive or slowly progressive, mainly as an adjunctive therapy with prime focus on re-pigmentation. However, its efficacy in inducing stability in progressive vitiligo and whether there is any difference in the onset and extent of re-pigmentation between progressive and non-progressive vitiligo is not yet studied.

The primary objective of our study was to evaluate the effect of NB-UVB therapy in patients with progressive or non-progressive non-segmental vitiligo with respect to the arrest of progression in progressive vitiligo and the difference in re-pigmentation among the two groups. We also assessed the improvement in the quality of life as measured by Vitiligo Impact Scale-22 (VIS-22).

Methods

We conducted a prospective comparative study at the Department of Dermatology and Venereology from April 2016 to November 2017 after approval from institutional ethics committee (Ref. No. IECPG/80/30.12.2015) and registering the protocol with the Clinical Trial Registry of India (Ref. No.: 2016/04/006809). Patients aged between 15 and 60 years, having non-segmental vitiligo involving body surface area more than 2%, were included in the study. If the patients were developing more than 5 lesions in the last 1 month or more than 15 lesions in the last 3 months, they were considered to be progressive (Group I) and if the disease was static for the last 6 months, they were labelled as non-progressive patients (Group II).[4] Patients with segmental vitiligo; focal vitiligo; pure mucosal vitiligo; having surface area involvement >50%; pregnant/lactating females; having history of photodermatoses were excluded. Patients were off all systemic or topical treatment for a minimum of 1 month. All patients were administered whole-body NB-UVB in the body chamber [Waldmann chamber; UV Therapy System UV 7002], starting at 0.28 J/cm^2, thrice a week with a minimum of one-day gap between two doses with increments of 10% of previous dose till minimal erythema dose (MED) was reached. Then the dose was fixed on MED and NB-UVB was continued for a cumulative period of 6 months (26 weeks). The outcome was noted by weekly clinical evaluation by at least two observers along with clinical photographs and marking on a body diagram looking for number of new lesions, change in size of existing lesions and extent of re-pigmentation, color match and side effects as compared to the previous visit. Re-pigmentation was noted on an ordinal scale: some (0-10%), mild (10-25%), moderate (25-50%), good (50-75%), excellent (75-90%) and near complete (90-100%). If there was no decrease in area of depigmentation; or appearance of new depigmented lesions, even after 3 months (13 weeks) of continuous treatment with NB-UVB therapy (with at least two sessions every week); patients were excluded from the study and shifted to other modalities for treatment. Re-pigmentation was assessed semi-quantitatively by marking the lesional areas on a body diagram, and photographic documentation. Vitiligo Impact Scale-22 was used at the baseline and 26 weeks to evaluate the psychosocial impact of the disease on each participant. Intra-group analysis was done using paired t-test and inter-group analysis was done using independent t-test and Chi-square test; while VIS-22 was assessed by Wilcoxon-sign-rank test. *P* value of <0.05 was taken as statistically significant.

Results

Forty-eight patients with non-segmental vitiligo were recruited (details of patients: Table 1); 31 with progressive vitiligo (Group I) and 17 with non-progressive vitiligo (Group II). Out of them, 24 completed the study period of 26 weeks in Group I, and 9 in Group II [Figure 1]. Patients' age ranged from 15 to 56 years with a mean of 29.2 ± 4.27 years. Type and duration of vitiligo and extent of body surface area were evenly distributed among the two groups. Seventeen patients out of 48 had koebnerization (15 patients in Group I and 2 patients in Group II). The difference in vitiligo patients having koebnerization among the two groups was found to be statistically significant (*P* value = 0.006, odds ratio = 8). Similar distribution, *P* value and odds ratio were found to be associated with leucotrichia as well, however, this was independent of koebnerization.

Four out of initial 31 patients in Group I were lost to follow-up. Additionally, two patients were excluded due to persistent phototoxicity (not controlled with 2 weeks of

Table 1: Details of patients in the two groups

Baseline characteristics	Progressive vitiligo (*n*=31)	Non-progressive vitiligo (*n*=17)	*P*
Sex distribution (male:female)	14:17	11:6	0.195
Age at presentation (mean±SD) years	26.4±9.9 years	28.3±10.3 years	0.456
Duration of disease (mean±SD)	8.1±7.0 years	9.7±7.0 years	0.659
Age at onset of disease (mean±SD)	19.2±13.8 years	19.9±11.1 years	0.470
Skin type			
IV	14 (45.2%)	10 (58.8%)	0.211
V	17 (54.8%)	7 (41.2%)	
Koebnerization	15 (88%)	2 (12%)	0.006
Leucotrichia	15 (88%)	2 (12%)	0.006

daily topical fluocinolone acetonide, 0.1% w/w, cream). One patient opted out due to pregnancy. At the end of 26 weeks, 19 patients out of the remaining 24 in Group I had an apparent arrest of disease progression while the rest 5 patients were still developing lesions, but at a slower pace [Figure 2].

Among the progressive vitiligo group, 13 out of 24 patients (54.2%) had the onset of re-pigmentation after 2 weeks of NB-UVB phototherapy, as compared to 6 out of 9 patients (55.6%) of the non-progressive Group II who had their onset after 1 week (P = 0.007). Nineteen out of twenty-four progressive vitiligo patients (79.2%) had re-pigmentation of 25-50% of the depigmented area [Figure 3a and b]. Six out of nine non-progressive vitiligo patient (66.7%) had re-pigmentation of 25-50% [Figure 3c and d]. The maximum effect, with regard to re-pigmentation, was noted over the lesions on the trunk, followed by face and neck, while it was minimal on the lesions at the acral sites. All patients had good color match, except one patient who had peri-lesional hyperpigmentation.

Total cumulative NB-UVB fluence was 34.73 ± 10.04 J/cm^2 in Group I and 25.2 ± 13.85 J/cm^2 in Group II, with the difference as statistically significant (P value = 0.034). The time taken to fix the fluence was more in Group I than in Group II, and was found to be statistically significant (Group I: 8.46 ± 1.74 weeks, Group II: 6.22 ± 1.72 weeks, P value = 0.001).

The most common side effect of NB-UVB phototherapy was found to be tanning, which was seen in all the progressive vitiligo patients and five out of nine non-progressive vitiligo patients. The mean onset of tanning was found to be at 5.9 ± 3.9 weeks in Group I, while it was 5.2 ± 1.9 weeks in Group II. The second most common side effect was pruritus, seen in 18 out of 24 patients in Group I and 2 out of 9 patients in Group II. Non-lesional pruritus preceded lesional pruritus by 1-2 weeks. This difference was found to be statistically significant (P value = 0.001). Out of 48 vitiligo patients, all of them had perceptible erythema in the lesions at the time when NB-UVB fluence (J/cm^2) was stabilized. As per protocol, the therapy was interrupted by a week and re-started at 10% lower fluence which was well tolerated. On continuing the fluence at the fixed value, there was no further development of phototoxicity. Six patients out of 24 progressive vitiligo patients had acute phototoxicity manifesting as blistering over vitiligo lesions [Figure 4a] which resolved with once daily application of fluocinolone acetonide (0.1% w/w) cream for 1 week, and further NB-UVB therapy was continued as per protocol. One patient had persistent asymptomatic erythema beyond 48 hours which could be easily appreciated as the patient did not wish to expose the genitalia and the erythema was present only in the exposed area just above the undergarments [Figure 4b]. Two patients with progressive vitiligo whose side effects did not improve were excluded from the study. Some of the known side effects like herpes virus reactivation, lentigines, freckles, acquired melanocytic nevi, telangiectasias and elastosis were not seen in any of our patients. No patients were excluded due to no significant response after 3 months (13 weeks) of cumulative NB-UVB phototherapy.

VIS-22 was used to assess the impact of vitiligo on quality of life of the patients at the time of recruitment and at the end of 26 weeks. Mean values of VIS-22 were found to be

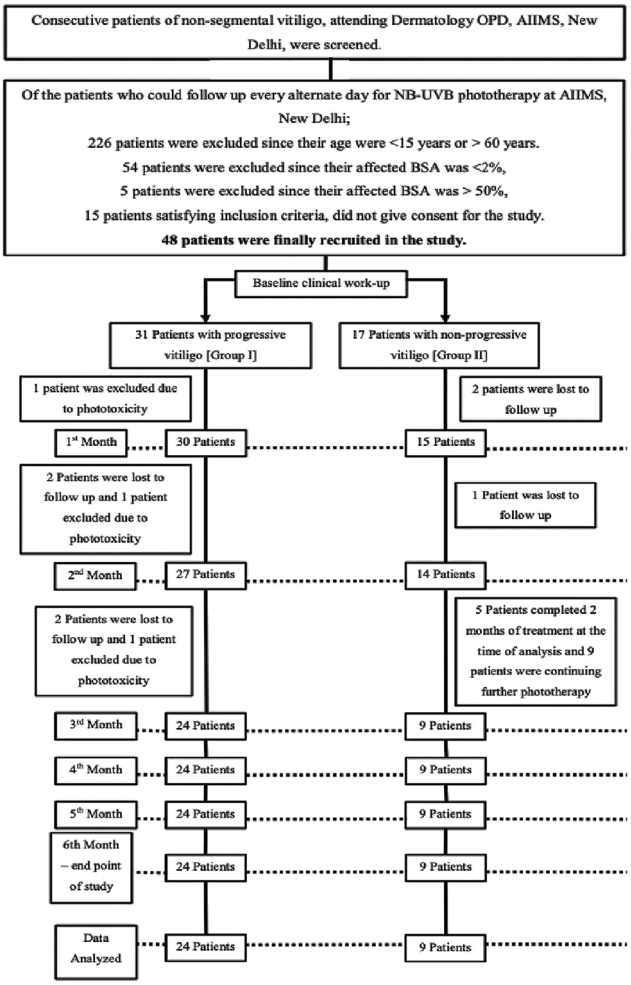

Figure 1: Flowchart of the study

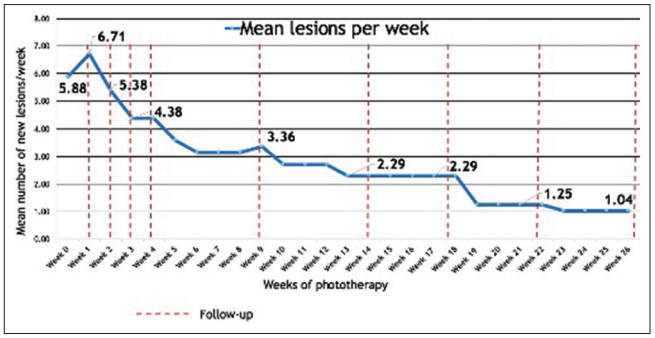

Figure 2: New vitiligo lesions (mean) per week in progressive vitiligo patients

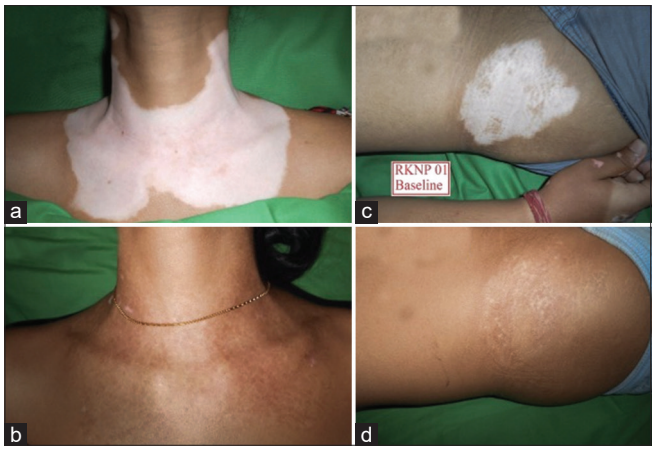

Figure 3: Re-pigmentation of vitiligo lesions with NB-UVB phototherapy; in Group I (a and b) and Group II (c and d)

22.9 ± 10.3 in Group I and 19.2 + 10.9 in Group II. At the end of 26 weeks, all vitiligo patients showed a decrease in VIS-22 (mean decrease of 5.6 in Group I; *P* value = 0.002, vs 6.3 in Group II; *P* value = 0.027). However, the baseline and post-treatment inter-group difference was not statistically significant.

Discussion

In vitiligo, NB-UVB is known to induce re-pigmentation. Whether it also has some systemic immunosuppressive effect or not; whether it can arrest the progression of the disease, simultaneously achieving re-pigmentation, is not well established. Therefore, we tried to evaluate the effect of whole-body NB-UVB on the disease progression.

Among 31 patients with progressive vitiligo, 24 completed the study period of 26 weeks. Multiple studies have only analyzed re-pigmentation of vitiligo lesions rather than stabilization of the disease. In our study, 19 out of 24 progressive vitiligo patients (79.2%) had an eventual halting of disease activity after 26 weeks of NB-UVB. The other five patients (20.8%) were still developing new vitiligo lesions, though at a slower pace. In a previous study done by Bhatnagar *et al.,*[6] NB-UVB phototherapy was compared with PUVA, to study the stabilization achieved by these modalities. In their study, 84.6% of patients developing new lesions in the past 6 months showed stabilization[6]; which is comparable to our study (79.2%). Re-pigmentation was found to be variable in both the groups. In Group I, comprising of patients with progressive vitiligo, at the end of 26 weeks, out of 24 patients, 19 (79.2%) achieved good re-pigmentation (25-50%), while 1 (4.2%) achieved excellent re-pigmentation (75-90%). In the Group II consisting of patients with non-progressive vitiligo, at the end of 26 weeks, majority of patients (66.6%, 6 out of 9) had re-pigmentation of 25-50%, while one patient each had 50-75% and 75-90% re-pigmentation; the progressive vitiligo group achieving more than the non-progressive group (79.2% vs 66.6%). Onset of re-pigmentation was earlier in Group II compared to Group I (first week vs second week, respectively, *P* = 0.007). Because of ongoing melanocyte depletory activity in Group I, which may be quiescent in Group II, the onset of re-pigmentation could be delayed as the immunosuppression or immunomodulation provided by NB-UVB may need to counteract the melanocyte depletion in Group I. This is exemplified by higher NB-UVB cumulative dose and higher fixed fluence in Group I as compared to Group II. The final extent of re-pigmentation was comparable among the two groups, similar to the study by Bhatnagar *et al*.[6]

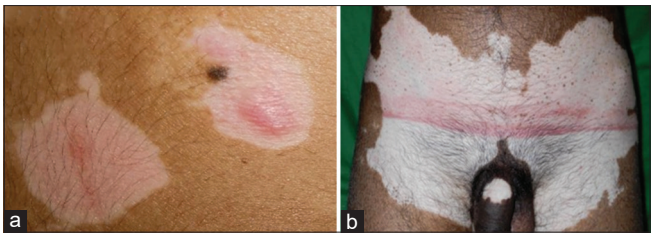

Figure 4: Side effects of NB-UVB phototherapy: (a) Blistering over vitiligo lesion, (b) Well-defined erythema on areas exposed to NB-UVB phototherapy (note the sparing of area covered by undergarments)

The major side effect was generalized tanning (87.9%), observed in all patients in Group 1 as compared to 5 out of 9 (55.5%) in Group 2. This could be due to a higher total cumulative fluence in Group 1 compared to Group 2 (34.73 ± 10.04 J/cm^2 vs 25.2 ± 13.85 J/cm^2, respectively). Seven patients out of 33 (21.2%) developed blistering due to NB-UVB; six patients in Group I (25%) and a single patient in Group II (11%). In a systematic review conducted by Almutawa F *et al*,[7] blistering was reported in 7.8% of psoriasis patients receiving NB-UVB. Our study had more patients with lesional blistering because vitiliginous area is more prone to phototoxicity[8] as compared to thick papulosquamous lesions of psoriasis. Therefore, in the absence of personalized MED for each patient, it is advised to start therapy at 0.28 J/cm^2, with increments of 10% every session so that phototoxicity is minimized. In our study, erythema was observed in 39.4% of patients (41.7% in Group I and 33.3% in Group II). This was not statistically significant. However, development of mild perceptible erythema is a known effect of NB-UVB, and not an adverse effect, which is easily avoided with diligent monitoring.[9] In this study, the minimum fluence was chosen as 0.28 J/cm^2 as this was the least available fluence in the NB-UVB chamber.

Another common side effect was generalized pruritus occurring in 75% in Group I, and 22.2% in Group II. Generalized xerosis is a known side effect of the NB-UVB,[7] but difference depending upon the stability of vitiligo, has not been highlighted previously. It could be hypothesized that the increased number of inflammatory cells in progressive vitiligo, under stimulation by NB-UVB, can release more pruritogenic mediators than patients of non-progressive vitiligo, where the inflammatory

infiltrate/damage is comparatively less. However, further controlled studies with adequate sample size, including histopathological and cytokine analysis, are needed to accurately study this conjecture.

Quality of life in patients were assessed using VIS-22, a vitiligo specific scale.[10] In Group I, mean VIS-22 significantly improved from 22.2 at baseline to 16.6 at the end of 26 weeks (P = 0.002). In Group II, it significantly improved from 19.8 at baseline to 13.5 at 26 weeks (P = 0.027). The improvement in VIS-22 can be due to the apparent arrest of progression of disease, re-pigmentation of older lesions, mindfulness towards the disease, and continuous counselling from the physicians.

Limitations of the study

The limitation of our study is the small sample size. Also, since the progression of the disease activity in vitiligo patients varies, some having rapidly progressive disease while others having slowly progressing disease, the results may vary in different sub-groups of progression. There are some patients with slow progression with occasional periods of rapid exacerbation. Another limitation was the high dropout rates as the study progressed. This could be due to the requirement of frequent follow-up hospital visits making it cumbersome and difficult to adhere. This study also limited the observation up to 26 weeks of active treatment. Therefore, the sustained effect on progression could not be ascertained.

Conclusions

This is the first comparative observational study to evaluate the effect of NB-UVB therapy in patients with two groups of vitiligo: progressive versus non-progressive non-segmental vitiligo. NB-UVB phototherapy in appropriate fluence individualized for the patient can substantially decrease the rate of new vitiligo lesions in a majority of progressive non-segmental vitiligo patients, with earlier onset of re-pigmentation in non-progressive vitiligo, and comparable final extent of re-pigmentation after 26 weeks. Progressive patients required more NB-UVB fluence than non-progressive patients. Pruritus was the most common side effect (more in Group I than Group II), followed by tanning, blistering, pain and burning sensation in the lesions. NB-UVB significantly improved the quality of life.

Ethics registration

Institutional ethics committee (Ref. No. IECPG/80/30.12.2015).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Handa S, Kaur I. Vitiligo: Clinical findings in 1436 patients. J Dermatol 1999;26:653-7.
2. Pasricha J, Khaitan BK. Drugs for Vitiligo. 1st ed. New Delhi: New Age International Publications (P) Limited; 1996. p. 37-43.
3. Pasricha JS, Khaitan BK. Oral mini-pulse therapy with betamethasone in vitiligo patients having extensive or fast-spreading disease. Int J Dermatol 1993;32:753-7.
4. Patra S, Khaitan BK, Sharma VK, Khanna N. A randomized comparative study of the effect of betamethasone oral mini-pulse therapy versus oral azathioprine in progressive non-segmental vitiligo. J Am Acad Dermatol 2019;S0190-9622(19)30439-6. doi: 10.1016/j.jaad.2019.03.025.
5. Rana S, Rogers LJ, Halliday GM. Systemic low-dose UVB inhibits CD8 T cells and skin inflammation by alternative and novel mechanisms. Am J Pathol 2011;178:2783-91.
6. Bhatnagar A, Kanwar AJ, Parsad D, De D. Psoralen and ultraviolet A and narrow-band ultraviolet B in inducing stability in vitiligo, assessed by vitiligo disease activity score: An open prospective comparative study. J Eur Acad Dermatol Venereol 2007;21:1381-5.
7. Almutawa F, Alnomair N, Wang Y, Hamzavi I, Lim HW. Systematic review of UV-based therapy for psoriasis. Am J Clin Dermatol 2013;14:87-109.
8. Gawkrodger DJ, Ormerod AD, Shaw L, Mauri-Sole I, Whitton ME, Watts MJ, *et al*. Guideline for the diagnosis and management of vitiligo. Br J Dermatol 2008;159:1051-76.
9. Suh KS, Roh HJ, Choi SY, Jeon YS, Doh KS, Bae JH, *et al*. Long-term evaluation of erythema and pigmentation induced by ultraviolet radiations of different wavelengths. Skin Res Technol. 2007;13:154-61
10. Gupta V, Sreenivas V, Mehta M, Khaitan BK, Ramam M. Measurement properties of the Vitiligo Impact Scale-22 (VIS-22), a vitiligo-specific quality-of-life instrument. Br J Dermatol 2014;171:1084-90.