Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck

F. Sassi,* S. Cazzaniga,*† G. Tessari,‡ L. Chatenoud,§ A. Reseghetti,¶ L. Marchesi,¶ G. Girolomoni‡ and L. Naldi*¶

*Centro Studi GISED and ¶Department of Dermatology, Ospedali Riuniti, 24100 Bergamo, Italy
†Department of Mathematics, University of Milan, Italy
‡Department of Dermatology, University of Verona, Italy
§Unit of Analytic Epidemiology, Mario Negri Institute for Pharmacological Research, Milan, Italy

Summary

Correspondence
Luigi Naldi.
E-mail: luigi.naldi@gised.it

Accepted for publication
19 April 2008

Key words
excimer laser, phototherapy, randomized controlled trial, topical corticosteroids, vitiligo

Conflicts of interest
None declared.

This trial has been registered under Cochrane Skin Group, Ongoing Skin Trial Register in March 2007, registration number CSG47.

DOI 10.1111/j.1365-2133.2008.08793.x

Background Vitiligo is a pigmentary disorder which may have disfiguring consequences. Its treatment remains a challenge.

Objectives We designed a parallel-group randomized controlled trial to compare the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in patients with vitiligo unresponsive to previous treatment with topical steroids or narrow-band ultraviolet (UV) B phototherapy.

Methods Consecutive patients aged 18–75 years with nonsegmental vitiligo localized on the face and/or neck lacking response to previous conventional treatment were eligible. In total, 84 patients (44 women and 40 men, mean age 44 years) were randomized to 308-nm excimer laser phototherapy twice weekly alone or in combination with topical hydrocortisone 17-butyrate cream twice daily for three periods of 3 weeks followed by a 1-week steroid-free interval. The primary outcome was a reduction of at least 75% of the overall lesional areas as judged by automatic image analysis on reflected UV photographs, conducted blind to treatment assignment, at 12 weeks compared with baseline. Secondary outcomes were clearance, and improvements on Physician's Global Assessment (PGA) and Skindex-29 scores.

Results A total of 76 (90%) patients completed the study. In an intention-to-treat analysis, seven [16·6%; 95% confidence interval (CI) 5·3–27·8%] patients in the excimer monotherapy arm and 18 (42·8%; 95% CI 27·8–57·8%) in the combination arm showed ≥ 75% reduction of vitiligo lesions at 12 weeks (χ^2 test 6·89, $P = 0·0087$). Clearance was observed in two (4·7%; 95% CI 1·6–11·2%) and nine (21·4%; 95% CI 9·0–33·8%) patients, respectively (Fisher's exact test $P = 0·04$). A significant difference also emerged for PGA scores, while no difference was documented for Skindex-29.

Conclusions Recalcitrant vitiligo of the face and neck may benefit from the combination of excimer laser phototherapy with topical hydrocortisone 17-butyrate cream.

Vitiligo is an acquired cutaneous disorder characterized by well-circumscribed depigmented macules due to the disappearance of functional melanocytes in the lesional areas, affecting 0·1–1% of the general population.[1–4] In the vast majority of patients, depigmentation is accompanied by influx to the skin of T lymphocytes reactive with melanocyte-specific antigens and secreting type 1 proinflammatory cytokines.[5] All body surface areas can be affected, the most common ones

being the face, the dorsum of the hands, the axillae, the umbilicus, the sacrum and the inguinal region. According to the distribution of depigmented lesions, focal, generalized (usually symmetrical) or universal varieties are distinguished. Segmental vitiligo is characterized by unilateral lesions with dermatomal distribution and is considered as a separate entity. The natural course of vitiligo is highly variable but is usually slowly progressive in a stepwise manner. Spontaneous repigmentation is not uncommon but is rarely complete.

Vitiligo patches are asymptomatic but may be disfiguring especially in dark-skinned populations.[6] A systematic review published in 2006 pointed out that the methods currently available to treat vitiligo are largely unsatisfactory and vary widely between cultures and within health systems.[7] An earlier meta-analysis which included large case series besides randomized trials concluded that class III topical steroids and ultraviolet (UV) B phototherapy were the most effective and safest therapies for localized and generalized vitiligo, respectively.[8] No data are available about the combination of UVB phototherapy and topical steroids.

The introduction of xenon chloride excimer laser generating monochromatic light at 308 nm allows for targeted phototherapy and selective treatment of localized lesions.[9,10] We hypothesized that 308-nm excimer laser phototherapy and topical steroids could have a synergistic effect in treating recalcitrant vitiligo lesions. We designed a parallel-group randomized controlled trial (RCT) to compare the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in patients with vitiligo unresponsive to previous treatment with topical steroids or narrow-band UVB (NB-UVB) phototherapy.

Materials and methods

Patients

Patients were recruited between November 2005 and June 2007 from the Department of Dermatology of the General Hospital of Bergamo and from the Department of Dermatology of the University of Verona, in Italy. Eligible patients aged 18–75 years had focal or generalized vitiligo, were looking for treatment of vitiligo lesions of the face and/or neck, had a history of insufficient response to previous NB-UVB phototherapy or topical steroids (a minimum 16-week NB-UVB treatment course at a recognized phototherapy centre, or a 12-week intermittent or continuous treatment with potent topical steroids under medical supervision), and had not been previously treated by 308-nm excimer laser. Patients with purely segmental vitiligo, characterized by unilateral lesions with dermatomal or quasidermatomal distribution, were excluded.

Patients were excluded if they were pregnant or breast-feeding, and if they had a history of diseases associated with excessive reaction to visible or UV radiation (e.g. porphyria cutanea tarda, polymorphic light eruption) or reported photosensitivity. The study was approved by the medical ethics committee at each centre.

Design

Eligible patients who had given written informed consent were randomly assigned on a 1 : 1 basis to receive 12 weeks of treatment with either 308-nm excimer laser or excimer laser plus topical hydrocortisone 17-butyrate cream. Stratified, blocked randomization was used to balance age and gender. Centralized telephone randomization procedures were adopted and investigators were blinded to the randomization rule. The screening period, during which no active treatment for vitiligo was permitted, lasted 4 weeks in subjects on topical steroids and 8 weeks in subjects on phototherapy or photochemotherapy. After 12 weeks of treatment, the patients were monitored for another 4 weeks.

Treatment regimens

The laser used was a xenon chloride excimer laser generating monochromatic light at 308 nm, with pulse frequency of 200 Hz, pulse duration of about 30 ns, energy density (fluence) of 3 mJ cm^{-2} and spot size of 4·0 cm^2 (XTRAC excimer laser; PhotoMedex, Montgomeryville, PA, U.S.A.). All the lesions in the affected areas were treated at each treatment session. Lesions were treated twice weekly for 12 weeks. Initial fluences in the vitiligo areas were half the minimal erythema dose (MED) determined on normal nonsun-exposed skin. Fluences were increased by half the MED at every other session. If intense local reactions with vesicles or bullae developed, the treatment was withheld and then resumed after resolution, at the last dose without reaction. If an intense reaction followed the first laser application then the initial dose was further reduced by one half after the resolution of the reaction. Patients randomized to the combination treatment arm received 308-nm excimer laser treatment as indicated above plus topical hydrocortisone 17-butyrate 0·1 g/100 g hydrophilic cream twice daily during three periods of 3 weeks, followed by a 1-week steroid-free interval. Patients were instructed to apply one thin layer of the cream over all the vitiligo patches of the face and neck. Topical steroids were applied twice daily, in the morning and in the evening. The phototherapy sessions were conducted at midday or during early afternoon. During the study period no treatment or only camouflage was allowed on body areas other than face and neck.

Outcomes

Effectiveness

Standardized photographs under visible and UV (Wood's lamp) illumination were taken at baseline and after 4, 8, 12 and 16 weeks of starting treatment. A Wood's lamp delivers UV radiation at a wavelength of approximately 365 nm and through the technique of reflected UV photography it allows vitiligo lesions to be traced unambiguously. The primary outcome measure was a reduction of at least 75% of the overall lesional areas as judged by image analysis on reflected UV

photographs at 12 weeks compared with baseline. Image analysis was based on software specifically developed using MATLAB® (MathWorks, Natick, MA, U.S.A.) and was conducted by an investigator who was unaware of treatment assignments. Clearance, i.e. disappearance of all the vitiligo lesions in the treated areas, as judged by image analysis on reflected UV photographs, at 12 weeks after starting treatment, represented a secondary outcome measure. Physician's Global Assessment (PGA) was evaluated on an anchored horizontal 10-cm visual analogue scale at baseline and at 8, 12 and 16 weeks after starting treatment. Improvement at 12 weeks was assessed as percentage over values at baseline as a secondary outcome measure.

Quality of life

As a patient-reported outcome we used the Italian version of Skindex-29, a validated, self-administered questionnaire, including 30 items all of which are weighted equally to produce an overall composite score.[11] Patients completed Skindex-29 at baseline and at weeks 8, 12 and 16 thereafter. Normalized Skindex scores ranged from 0 to 100, with higher values indicating a higher impact on the quality of life. Changes were expressed as differences between final and initial scores.

Side-effects

We evaluated side-effects known to be associated with phototherapy and topical steroid use, and any other unexpected adverse event. In particular, we considered erythemal reactions needing temporary or permanent treatment discontinuation and steroid atrophic changes and hypertrichosis. These were evaluated at each treatment session.

Statistical analysis

The proportion of treatment successes, i.e. improvement ≥ 75% on image analysis of reflected UV photographs, was compared between groups by using the χ^2 test. An intention-to-treat approach was adopted in the primary analyses. This considered patients withdrawn prematurely from the study as a treatment failure for the corresponding treatment arm. Intention-to-treat analysis was further complemented by per-protocol analyses, which considered only those patients who completed the study period. Similar analyses but using Fisher's exact test were conducted when considering clearance as a secondary outcome measure. Nonparametric analytical tests (i.e. Mann–Whitney U-test) were used to compare mean differences in vitiligo areas, PGA scores, and Skindex-29 scores.

When designing this trial, we calculated that 42 patients would be needed in each group for the study to have a 95% power to rule out a difference of 20% or more in the proportion of responders between randomized groups at 12 weeks. No interim analyses were performed. Two-sided P-values of $< 0{\cdot}05$ were considered to indicate statistical significance.

Results

Patients

Between November 2005 and June 2007, 102 patients were screened, 84 of whom (44 women and 40 men, mean age 44 years) underwent randomization (Fig. 1). Reasons for not including screened patients were vitiligo in areas other than face and neck (n = 6), nonvitiligo lesions (n = 4), no previous treatment with topical steroids or NB-UVB (n = 3), inability to comply with treatment schedule (n = 3), previous treatment with excimer laser (n = 1) and pregnancy (n = 1).

The baseline characteristics of randomized patients are shown in Table 1. Eight patients, six in the excimer laser monotherapy group and two in the combined excimer laser plus topical hydrocortisone 17-butyrate cream group, withdrew after inclusion in the study.

Cumulative UV doses ranged from 3·0 to 18·1 J cm^{-2} (mean 8·8) in the monotherapy group and from 3·5 to 20·1 J cm^{-2} (mean 9·2) in the combination group (Mann–Whitney U-test P = 0·573).

Effectiveness

The distribution of patients according to the degree of repigmentation at 12 weeks is reported in Fig. 2. The mean repigmentation percentage was 20·5% in the excimer laser monotherapy group and 40·0% in the excimer laser plus topical steroid combination group (Mann–Whitney U-test

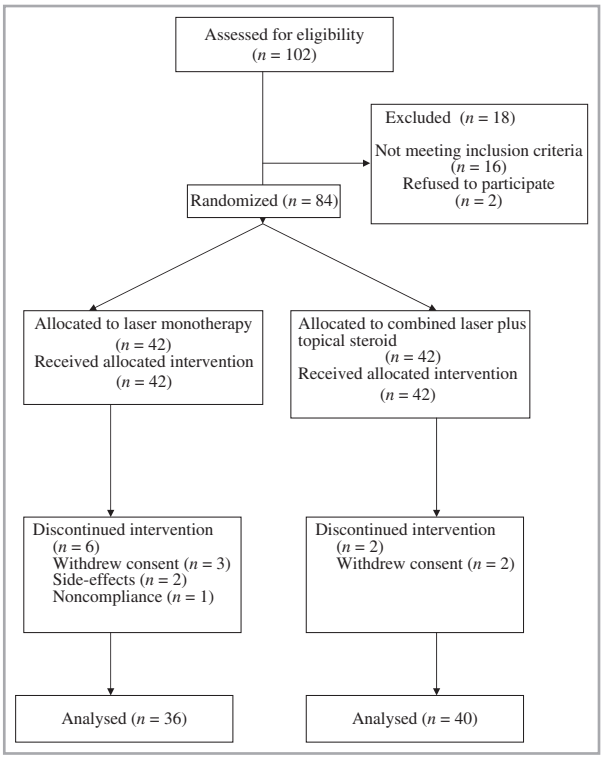

Fig 1. Consort diagram of patient disposition.

Table 1 Baseline characteristics of randomized patients

	Excimer laser monotherapy (n = 42)	Combination therapy (n = 42)	P-value
Gender			
Male	20	20	
Female	22	22	1
Age (years), mean ± SEM	44·1 ± 2·1	42·4 ± 1·8	0·632
Weight (kg), mean ± SEM	68·32 ± 1·93	69·21 ± 1·89	0·615
Height (cm), mean ± SEM	170·44 ± 1·08	171·14 ± 1·19	0·746
Smoking habits			
Smokers	15	11	
Nonsmokers/previous smokers	27	31	0·345
Alcohol consumption			
Regular drinkers	8	6	
Occasional/nondrinkers	34	36	0·558
Skin phototype (Fitzpatrick classification)			
I–II	24	26	
III–IV	18	16	0·656
Eye colour			
Blue-green	11	14	
Brown	31	28	0·474
Hair colour			
Blond/red/light brown	12	11	
Dark brown/black	30	31	0·806
Family history of vitiligo (first-degree relatives)			
Yes	19	16	
No	23	26	0·506
Personal history of autoimmune diseases[a]			
Yes	9	7	
No	33	35	0·578
Vitiligo variety			
Focal	10	9	
Generalized	32	33	0·80
Percentage of area involved at starting treatment (face and neck)			
< 3%	17	15	
3–15%	20	19	0·656
> 15%	5	8	
Disease duration (years), mean ± SEM	21·6 ± 1·7	18·6 ± 1·7	0·1679
No. previous different treatments for vitiligo			
1	32	28	
2+	10	14	0·334

[a]These included eight cases of autoimmune thyroid disease and one case of chronic inflammatory bowel disease in the excimer laser monotherapy arm, and seven cases of autoimmune thyroid disease in the combination therapy arm. For continuous variables, values are expressed as means ± SEM, otherwise, as the number of patients in the specified category. P-values are calculated from Mann–Whitney U-test for continuous variables and χ^2 test for categorical or discrete variables.

P = 0·02). A total of 25 patients reached the threshold for a satisfactory response as indicated by our primary endpoint, i.e. a reduction of ≥ 75% in the treated vitiligo areas compared with baseline, at 12 weeks (Table 2). There were seven patients [16·6%; 95% confidence interval (CI) 5·3–27·8%] in the monotherapy group and 18 (42·8%; 95% CI 27·8–57·8%) in the combined treatment group (χ^2 test 6·89, P = 0·0087 on intention-to-treat analysis). Clearance was observed in two (4·7%; 95% CI 1·6–11·2%) and nine (21·4%; 95% CI 9·0–33·8%) patients, respectively (Fisher's exact test P = 0·04). A significant difference between treatment groups was also documented for variations in PGA at 12 weeks. The mean PGA improvement was 29·7% (SEM 4·4) in the laser monotherapy group and 51·2% (SEM 5·1) in the combination group (Mann–Whitney U-test P = 0·004). No documentation of an impact of associated autoimmune disease or clinical variety of vitiligo (i.e. focal vs. generalized lesions) was obtained in subgroup analyses. However, this result should be taken with caution due to limited sample size and *post-hoc* analyses (data not presented).

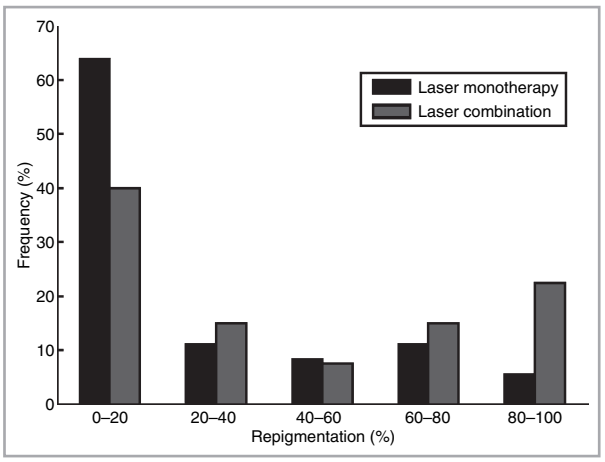

Fig 2. Distribution of patients according to percentage of repigmentation at 12 weeks.

Table 2 Number of patients achieving ≥ 75% repigmentation of vitiligo lesions at 12 weeks (primary outcome of treatment)

Percentage of repigmentation	Laser monotherapy	Laser plus topical steroid combined treatment	Total
Intention-to-treat[a]			
< 75%	35	24	59
≥ 75%	7	18	25
Per-protocol[b]			
< 75%	29	22	51
≥ 75%	7	18	25

[a]χ^2 test (d.f. = 1) 6·8908, P = 0·0087; [b]χ^2 test (d.f. = 1) 5·6058, P = 0·0179.

Quality of life

Quality of life indices improved to a similar extent in the two treatment groups. The values of the composite score at entry were 19·4 (SEM 2·53) in the laser monotherapy group and 23·71 (SEM 2·18) in the combination group. At the end of the treatment course, values decreased to 14·22 (SEM 2·25) and 18·97 (SEM 2·3), respectively (Mann–Whitney U-test for between-group comparison, P = 0·727).

No significant differences were found between groups for any of the Skindex-29 subscales. Overall, variations were −0·50 (SEM 1·72) for symptoms, −7·5 (SEM 1·21) for emotion, and −2·08 (SEM 0·97) for social functioning subscales.

Side-effects

A total of 71 (84·5%) patients developed some degree of erythema at some stage during their treatment. Moderate-to-severe erythemal reactions requiring temporary withdrawal of treatment occurred in a total of 50 (59·5%) patients, 28 (66·6%) in the monotherapy and 22 (52·3%) in the combination group. There was one patient with some degree of hyperpigmentation in the monotherapy group and five in the combination group. No clinically appreciable occurrence of skin atrophy or hypertrichosis was reported. No other serious or irreversible side-effects were observed.

Follow-up

All the 76 patients who completed a 12-week treatment period were followed up for an additional 4 weeks. At week 16 there were no substantial differences compared with observations at week 12.

Discussion

This RCT provides evidence that twice weekly phototherapy delivered by a xenon chloride excimer laser generating monochromatic light at 308 nm combined with cycles of topical hydrocortisone 17-butyrate cream twice daily for 3 weeks followed by a 1-week steroid-free interval provides better repigmentation results than excimer laser phototherapy alone, in patients with vitiligo of the face and neck and a history of unsatisfactory response to NB-UVB or topical steroids.

Even though both UVB phototherapy and topical steroids are established treatment for vitiligo, little is known about their combined effect and no RCTs are available. Interestingly, encouraging results were obtained a few years ago, in a within-patient control study combining UVA with topical steroids for the treatment of vitiligo lesions on the arms, legs and trunk.[12] We aimed to assess whether the use of topical corticosteroids added to the efficacy of excimer laser and was worth the risk of atrophogenic effects or hypertrichosis. Actually, by adopting our intermittent regimen no clinically evaluable steroid-related adverse effect was documented while it is conceivable that steroid use, besides adding to efficacy, influenced a reduced rate of UV-related erythematous reactions in the combination arm compared with excimer laser monotherapy.

To date, NB-UVB therapy is one of the most established treatments for extensive vitiligo lesions.[7] The mechanism of action of UVB-based treatment is not fully understood. Proliferation and migration of melanocytes present in the hair follicles certainly play a role. In addition, UV may exert an immunosuppressive action with depletion of Langerhans cells and apoptosis of activated T lymphocytes.[13] In principle, excimer laser presents several advantages compared with NB-UVB therapy especially for treating vitiligo of limited extent. Photobiological effects are deemed to be stronger due to a greater induction of lymphocyte apoptosis.[14] Moreover, the laser articulated arm can reach virtually any kind of localization and selectively target vitiliginous lesions while sparing the healthy skin.[15–18] Differences in treatment response according to body areas have been repeatedly documented in vitiligo, and UV-sensitive and UV-resistant areas are identified.[19] We restricted our study to UV-sensitive areas, i.e. face and neck. This aspect of the study obviously limits the generalization of our results to other more challenging skin regions, e.g. dorsum of hands.

Besides topical steroids, to increase response rates of phototherapy, several combination modalities have been proposed, including topical vitamin D derivatives and topical calcineurin inhibitors. While for the combination of UVB with topical steroids no RCTs were identified before we performed our study, for the other combinations a few RCTs are available.[18,20–22] Unfortunately, these studies adopted a within-patient study design where individual patches rather than whole patients were evaluated. As a consequence, the studies provide only hints about the overall therapeutic effect of the strategies being assessed. Based on our results, parallel-group RCTs of different phototherapy combination treatments, including a steroid combination arm, are necessary to identify the best management strategy. Our study was not designed to document long-term effects and longer studies are needed to confirm the efficacy and safety of the treatment we have evaluated. As for other vitiligo therapies, an increased duration of treatment may increase the percentage of responders.[19]

Our clinical results were not paralleled by a difference in quality of life scores as assessed by Skindex-29, because similar improvements in quality of life indices were observed at the end of the study in the two treatment groups. Skindex-29 is a dermatology-specific quality of life questionnaire but it may not be best suited to assess vitiligo and its sensitivity to change may be limited.[23] On the other hand, that objective clinical improvements may not be paralleled by similar changes in quality of life indices is not surprising and has been documented for other skin disorders as well.[24] Physicians treating skin disorders should be aware that even in the presence of substantial clinical improvement patients may still substantially suffer psychologically.[24]

In conclusion, vitiligo of the face and neck unresponsive to previous treatment with conventional phototherapy and/or topical steroids may benefit from the combination of 308-nm excimer laser phototherapy with topical hydrocortisone 17-butyrate cream. The treatment is well tolerated. Clinical effects do not necessarily translate into improvements in quality of life scores.

Acknowledgments

The study was conducted under the patronage of the Italian Psoriasis and Vitiligo Patient Association (ASNPV) and the Spanish Vitiligo Patient Association (ASPAVIT). The study was supported financially by Centro Studi GISED. Laser equipment for this study was kindly provided by Sternlaser, hydrocortisone cream by Astellas. We are indebted to Dr Alida Depase for her helpful suggestions and support.

References

1 Howitz J, Brodthagen H, Schwartz M, Thomsen K. Prevalence of vitiligo: epidemiological survey on the isle of Bornholm, Denmark. *Arch Dermatol* 1977; **113**:47–52.
2 Johnson M-LT, Roberts J. *Skin Conditions and Related Need for Medical Care among Persons 1–74 Years*. Publication No. (PHS) 79-1660. Hyattsville, MD: U.S. Department of Health, Education and Welfare, 1978.
3 Das S, Majumder P, Chakraborty R *et al.* Studies on vitiligo. I. Epidemiological profile in Calcutta, India. *Genet Epidemiol* 1985; **2**:71–8.
4 Naldi L, Colombo P, Placchesi EB *et al.* Study design and preliminary results from the pilot phase of the PraKtis study: self-reported diagnoses of selected skin diseases in a representative sample of the Italian population. *Dermatology* 2004; **208**:38–42.
5 Le Poole IC, Wankowicz-Kalinska A, van den Wijngaard RM *et al.* Autoimmune aspects of depigmentation in vitiligo. *J Investig Dermatol Symp Proc* 2004; **9**:68–72.
6 Kent G, Al'Abadie M. Psychologic effects of vitiligo: a critical incident analysis. *J Am Acad Dermatol* 1996; **35**:895–8.
7 Whitton ME, Ashcroft DM, Barrett CW, Gonzalez U. Interventions for vitiligo. *Cochrane Database Syst Rev* 2006; **1**:CD003263.
8 Njoo MD, Westerhof W, Bos JD, Bossuyt PM. The development of guidelines for the treatment of vitiligo. *Arch Dermatol* 1999; **135**:1514–21.
9 Bónis B, Kemény L, Dobozy A *et al.* 308 nm UVB excimer laser for psoriasis. *Lancet* 1997; **350**:1522.
10 Baltas E, Nagy P, Bonis B *et al.* Repigmentation of localised vitiligo with the xenon chloride laser. *Br J Dermatol* 2001; **144**:1266–7.
11 Nijsten T, Meads DM, de Korte J *et al.* Cross-cultural inequivalence of dermatology-specific health-related quality of life instruments in psoriasis patients. *J Invest Dermatol* 2007; **127**:2315–22.
12 Westerhof W, Nieuweboer-Krobotova L, Mulder PG, Glazenburg EJ. Left-right comparison study of the combination of fluticasone propionate and UV-A vs. either fluticasone propionate or UV-A alone for the long-term treatment of vitiligo. *Arch Dermatol* 1999; **135**:1061–6.
13 Chow J, Tron VA. Molecular aspects of ultraviolet radiation-induced apoptosis in the skin. *J Cutan Med Surg* 2005; **9**:289–95.
14 Novák Z, Bónis B, Baltás E *et al.* Xenon chloride ultraviolet B laser is more effective in treating psoriasis and in inducing T cell apoptosis than narrow-band ultraviolet. *J Photochem Photobiol B* 2002; **67**:32–8.
15 Baltas E, Csoma Z, Ignacz F *et al.* Treatment of vitiligo with the 308-nm xenon chloride excimer laser. *Arch Dermatol* 2002; **138**:1619–20.
16 Spencer JM, Nossa R, Ajmeri J. Treatment of vitiligo with the 308-nm excimer laser: a pilot study. *J Am Acad Dermatol* 2002; **46**:727–31.
17 Taneja A, Trehan M, Taylor CR. 308-nm excimer laser for the treatment of localized vitiligo. *Int J Dermatol* 2003; **42**:658–62.
18 Passeron T, Ostovari N, Zakaria W *et al.* Topical tacrolimus and the 308-nm excimer laser. *Arch Dermatol* 2004; **140**:1065–9.
19 Lim HW, Hexsel CL. Vitiligo. To treat or not to treat. *Arch Dermatol* 2007; **143**: 643–6.
20 Arca E, Tastan HB, Erbil AH *et al.* Narrow-band ultraviolet B as monotherapy and in combination with topical calcipotriol in the treatment of vitiligo. *J Dermatol* 2006; **33**:338–43.
21 Ermis O, Alpsoy E, Cetin L, Yilmaz E. Is the efficacy of psoralen plus ultraviolet A therapy for vitiligo enhanced by concurrent topical calcipotriol? A placebo controlled double-blind study. *Br J Dermatol* 2001; **145**:472–5.
22 Goldinger SM, Dummer R, Schmid P *et al.* Combination of 308-nm xenon chloride excimer laser and topical calcipotriol in vitiligo. *J Eur Acad Dermatol Venereol* 2007; **21**:504–8.
23 Lewis VJ, Finlay AW. A critical review of quality-of-life scales for psoriasis. *Dermatol Clin* 2005; **23**:707–16.
24 Sampogna F, Tabolli S, Abeni D, IDI Multipurpose Psoriasis Research on Vital Experiences (IMPROVE) investigators. The impact of changes in clinical severity on psychiatric morbidity in patients with psoriasis: a follow-up study. *Br J Dermatol* 2007; **157**:508–13.

