ORIGINAL REPORT

Narrowband-ultraviolet B vs Broadband-ultraviolet B in Treatment of Chronic Pruritus: A Randomized, Single-blinded, Non-inferiority Study

Romana KUPSA[1], Alexandra GRUBER-WACKERNAGEL[1], Angelika HOFER[1], Franz QUEHENBERGER[2], Peter WOLF[1] and Franz J. LEGAT[1]

[1]Department of Dermatology and [2]Institute for Medical Informatics, Statistics and Documentation, Medical University of Graz, Graz, Austria

Narrowband-ultraviolet B has shown increased efficacy over broadband-ultraviolet B in pruritic skin diseases, such as psoriasis and atopic dermatitis. In patients with chronic pruritus, e.g. in end-stage renal disease, broadband-ultraviolet B is recommended, but narrowband-ultraviolet B has also shown efficacy in reducing pruritus. This randomized, single blinded, non-inferiority study investigated the effects of narrowband-ultraviolet B compared with broadband-ultraviolet B. Patients with chronic pruritus were treated with either broadband- or narrowband-UVB 3 times a week for 6 weeks and clinical response was monitored. Pruritus, sleep disturbance, and the patients' subjective overall response to treatment were evaluated by the patients on a visual analogue scale (0–10). Skin excoriations were evaluated by investigators on a 4-point scale (0–3). Both phototherapeutic modalities showed significant antipruritic activity (itch reduction 48% and 66.4%, respectively) by broadband-ultraviolet B and narrowband-ultraviolet B. Narrowband-ultraviolet B proved to be not inferior to broadband-ultraviolet B in treating pruritus in patients with chronic pruritus, assuming a 20% non-inferiority margin.

Key words: chronic pruritus; itch; prurigo; phototherapy.

Accepted Mar 28, 2023; Published Jun 26, 2023

Acta Derm Venereol 2023; 103: adv9403.

DOI: 10.2340/actadv.v103.9403

Corr: Franz J. Legat, Department of Dermatology and Venerology, Medical University of Graz, Auenbruggerplatz 8, AT-8036 Graz, Austria. E-mail: franz.legat@medunigraz.at

SIGNIFICANCE

Phototherapy is an important treatment modality in inflammatory skin diseases such as psoriasis, atopic dermatitis and cutaneous T-cell lymphoma (e.g. mycosis fungoides/ Sézary syndrome). In patients with chronic pruritus, with or without pruriginous skin lesions, ultraviolet light therapy is capable of reducing pruritus. However, it remains unclear whether narrowband-ultraviolet B or broadband-ultraviolet B treatment is more effective to combat chronic pruritus. This study investigated the effects of narrowband-ultraviolet B and broadband-ultraviolet B on chronic pruritus, patients' sleep quality and subjective treatment effects, as well as on skin excoriations. Narrowband-ultraviolet B was found to be not inferior to broadband-ultraviolet B in the treatment of patients with chronic pruritus.

Chronic pruritus (CP), i.e. pruritus for ≥6 weeks, has a lifetime prevalence of 22% in the general population and occurs in more than 50% of patients with skin diseases (1, 2). The International Forum for the Study of Itch (IFSI) defined 3 groups of patients with CP: group I – pruritus on primarily diseased/ inflamed skin, group II – pruritus on normal skin, and group III – pruritus with chronic secondary scratch lesions (3). The third group includes the skin disease of chronic prurigo (CPG), which is characterized by CP of the skin, signs or history of chronic scratching, and pruriginous skin lesions ranging from small papules to nodules, plaques, umbilicated lesions, or even linear and scarring scratch lesions (LSSL) (4).

Common to all 3 groups is the fact that patients with CP experience a strong desire to scratch (5, 6). Peripheral and central sensitization to chronic itch may eventually lead to the development of a vicious circle of itching and scratching, the so-called "itch-scratch-cycle" (7). The pathophysiological mechanisms of CP and the development of the itch-scratch-cycle resulting in CPG are still incompletely understood (8).

However, treatment with ultraviolet (UV) light, i.e. UV phototherapy, is long known to be effective in the treatment of pruritic skin diseases such as psoriasis, atopic dermatitis (AD) and mycosis fungoides (9–11).

In phototherapy units, as well as in private dermatological offices, broadband ultraviolet B (BB-UVB) has been almost completely replaced by narrow-band ultraviolet B (NB-UVB) in the treatment of various skin diseases. However, although studies on the antipruritic potential of NB-UVB in skin diseases have been published and have shown its efficacy, to the best of our knowledge, the effects of NB-UVB in reducing pruritus in patients with CP have not been compared with BB-UVB. Thus, the aim of the current study was to investigate the effects of NB-UVB and BB-UVB in reducing pruritus in patients with CP and, in a non-inferiority study, to evaluate whether NB-UVB is not less effective than BB-UVB.

METHODS

Subjects

This was a randomized, single-blinded, non-inferiority study. A total of 49 patients were recruited from the Department of *Dermatology and Venereology,* Medical University of Graz, *Austria, between* October 2002 and June 2013. The study was approved by the ethics committee at the Medical University of Graz. After signing informed consent, patients were randomly assigned to BB-UVB or NB-UVB. Inclusion/exclusion criteria are detailed in **Table I**. The demographic profile associated with comorbid internal conditions/skin disorders, baseline and diagnostic details are shown in **Table II.**

Patients presented with one or more clinical manifestation of CP.

Set-up

After testing for the individual minimal erythema dose (MED) with the respective light source, patients were treated with whole-body UV 3× per week for 6 weeks. Light sources for MED testing (UV800 lamps) and Conformité Européenne (CE)-certified UV cabins looked identical, but were equipped with either NB-UVB or BB-UVB fluorescent lamps. For NB-UVB treatment a UV 7001 K cabinet containing TL01 fluorescent lamps with a maximum emission of 311–313 nm was used. For BB-UVB treatment a UV 7001 cabinet containing TL12 fluorescent lamps was used. The starting doses of UVB treatments were 50% of the respective MEDs. UV dose increments were 20% per week.

Primary and secondary endpoints

Data were collected before and after each week during and at the end of the 6-week treatment course. The primary endpoint of the study was to evaluate patients mean pruritus during the last week using a visual analogue scale (VAS) ranging from 0 (no itch) to 10 (worst imaginable itch). As secondary endpoints patients evaluated their sleep disturbance during the last week using a VAS ranging from 0 (no sleep disturbance) up to 10 (worst sleep disturbance imaginable). In addition, as another secondary endpoint, patients assessed their personal impression of the therapeutic benefit on pruritus from their UV treatment using a VAS from 0 to +10 for improvement of pruritus, or a VAS from –10 to 0 for worsening of pruritus (VAS of 0=no change). Skin excoriations, also a secondary endpoint, were assessed by the investigators on a scale ranging from 0 to 3 (0=no excoriations, 1=mild excoriations, 2=moderate excoriations, 3=severe excoriations) on the skin regions (head, arms, trunk, legs).

Statistical analysis

All statistical analyses were performed using R (www.r-project.org) version 3.6.2.

All *p*-values except test for non-inferiority were from 2-sided tests and results were deemed statistically significant at $p<0.05$. Two-sided 95% confidence intervals (95% CI) were calculated, if applicable. Group differences were tested by the Wilcoxon-Mann-Whitney test. Box-and-whiskers plots were used for descriptive analysis.

Non-inferiority testing

The treatment effect was defined as the relative change after 6 weeks as a percentage compared with the state before treatment. The null hypothesis stated that the efficacy of NB-UVB was lower compared with BB-UVB. The range of non-inferiority was up to 20 percentage points less than the efficacy of BB-UVB. A 2-sided *p*-value of the Wilcoxon-Mann-Whitney test of 0.05 indicated the significance of non-inferiority of NB-UVB. The test was performed by subtracting 20 percentage points from each of the relative treatment effects in the BB-UVB group before performing the statistical test.

Table I. Inclusion and exclusion criteria

Inclusion criteria
- Male/female, age 19 years or older
- Pruritus that lasted longer than 6 weeks with or without skin lesions

Exclusion criteria
- Skin cancer or history of skin cancer (especially malignant melanoma)
- Dysplastic naevus syndrome
- Skin diseases associated with photosensitivity (e.g. porphyria, chronic actinic dermatitis, xeroderma pigmentosum, naevoid basal cell carcinoma syndrome, autoimmune disorders, e.g. lupus erythematosus, dermatomyositis)
- Systemic corticosteroid therapy and/or immunosuppressive agents
- Abnormal elevated titres of antinuclear antibodies (ANA) with autoantibodies directed against Ro/SSA and La/SSB autoantigens

Sample size calculations

The study assumed a Student's *t*-test with mean difference 20% and standard deviation (SD) 20% at 90% power. The sample size was divided by 0.95 because of the efficiency of the Wilcoxon-

Table II. Patient characteristics

Patient characteristics	
All patients being evaluated, *n*	39
Age, years, mean (range)	62.6 (20–87)
Sex, *n* (%)	
Male	15 (38.5)
Female	24 (61.5)
UV-treatment modality, *n* (%)	
Narrowband ultraviolet phototherapy	20 (51.3)
Broadband ultraviolet phototherapy	19 (48.7)
Skin lesions, *n* (%)	
Patients with skin lesions	36* (92.3)
Patients without skin lesions	3 (7.7)
Chronic prurigo type, *n* (%)	34**
Nodular type	10 (29.4)
Plaque type	13 (38.2)
Papular type	11 (32.4)
Umbilicated type	–
Linear type	–
Comorbidity, *n* (%)	
Arterial hypertension	16 (42.1)
Chronic renal insufficiency	16 (42.1)
Dialyses	5 (13.2)
No dialyses	11 (29)
Hypothyreosis	11 (29)
No internal disease	8 (20.5)
Chronic cardiac insufficiency	7 (18.4)
Diabetes mellitus	6 (15.8)
Non-insulin dependent	5 (13.2)
Insulin-dependent	1 (2.6)
Chronic liver insufficiency	5 (13.2)
COPD	5 (13.2)
Anaemia	7 (18.5)
Iron deficiency anaemia	5 (13.2)
Renal anaemia	2 (5.3)
Hyperlipidaemia	4 (10.5)
Hyperuricaemia	3 (7.9)
Chronic atrial fibrillation	3 (7.9)
Depression	2 (5.3)
Hepatitis C	1 (2.6)
Additional skin disorder, *n* (%)	
Atopic predisposition	4 (10.5)
Notalgia paraesthetica	2 (5.3)
Acne excoriée (AE)	1 (2.6)
Vitiligo	1 (2.6)

*Subtype classification defined by the Task force pruritus of the European Academy of Dermatology and Venereology in 2018; **2 patients had only superficial scratch lesions.

Mann-Whitney test relative to the *t*-test. Using the package SampleSize4ClinicalTrials 0.2.3 (CRAN (https://cran.r-project.org/)) 24 patients per treatment group were required.

RESULTS

A total of 49 patients (30 females, 19 males) signed informed consent and were randomized. Ten patients were excluded from analysis: 3 patients did not start the treatment, because they decided to receive another treatment for CP. Two patients did not start the treatment because they had to be hospitalized for the treatment of end-stage renal insufficiency. Two patients were excluded because they described pruritus intensity as too low at the beginning of the study (pruritus VAS < 1). A further 2 patients were excluded because data on pruritus VAS was missing. One patient was excluded because of a screening failure. High levels of blood antinuclear antibody (ANA) and autoantibodies directed against Ro/SSA and La/SSB autoantigens were measured at the screening visit.

Finally, data from 39 patients with CP and receiving at least 1 UV therapy were analysed. Twenty patients (13 females, 7 males; mean age 60.5 ± 16.6; median 63.5; range 26–84 years, at the time of enrolment into the study) were treated with NB-UVB and 19 patients were treated with BB-UVB (11 females, 8 males; mean age 64.9 ± 16.1; median 67; range 20–87 years). Of these 39 patients, 36 had either CPG or secondary scratch lesions, and 3 had no skin lesions. The mean (± SD) number of treatment sessions for the participating 39 patients was 17.5 ± 0.7 treatments (median 18; range 15–18). The mean (± SD) duration of treatment was 5.8 ± 0.2 weeks (median 6 weeks; range 5–6 weeks). Data were analysed from the first 6 weeks of treatment. After this time-point subjects were able to continue treatment until complete remission was achieved or they decided to stop treatment.

By the end of the 6-week treatment, the mean (± SD) cumulative UV dose was 10.5 ± 2.9 J/cm^2 (median 10.0; range 6.8–17.2) in the NB-UVB treatment group (mean starting dose: 0.3; SD ± 0.1; median 0.4; range 0.2–0.5 J/cm^2 and mean maximum dose: 0.9; SD ± 0.2; median 1.0; range 0.5–1.2 J/cm^2). The BB-UVB treatment group received a mean (± SD) cumulative UV dose of 1.1 ± 0.2 J/cm^2 (median 1.2; range 0.8–1.7; mean starting dose: 0.04 SD ± 0.01; range 0.02–0.05 J/cm^2, mean maximum dose 0.1; SD ± 0.03; range 0.07–0.19 J/cm^2).

The side-effects during the treatment period were mild regional erythema in 1 (2.6%) patient in the BB-UVB treatment group. This patient showed regression of symptoms after symptomatic treatment without discontinuation of phototherapy. One patient had to pause treatment for 1 week because he was hospitalized for an umbilical hernia repair. No serious adverse event was recorded in this case because the surgical procedure had already been planned before start of treatment. No other treatment-related adverse events were observed.

According to the subtype classification defined by the Task Force Pruritus of the European Academy of Dermatology and Venereology in 2018 (12) the following subtypes of CPG could be identified in the current 36 subjects: 11 "papular types", 10 "nodular types" and 13 "plaque types". The other 2 patients had only a few superficial scratch lesions. The most common comorbidities in this study were arterial hypertension and chronic kidney disease (42.1% each), followed by hypothyroidism (29%); only 8 out of 39 (20.5%) patients had no internal disease.

Pruritus

BB-UVB reduced pruritus mean (± SD) 6.13 ± 2.35 (median 5.6; range 2.2–10) to mean (± SD) 2.75 ± 2.28 (median 2.1; range 0–7.5; mean reduction 48.0%; relative treatment effect 66.7%). NB-UVB reduced pruritus from mean (± SD) 6.09 ± 2.81 (median 6.8; range 1.1–10) to mean (± SD) 2.42 ± 2.93 (median 1.2; range 0–8.7; mean reduction 66.4%, relative treatment effect 80.7%) on the VAS. The combined treatment effect of both NB-UVB and BB-UVB resulted in a significant reduction ($p < 0.0001$) in pruritic activity (mean itch relative reduction 57.4%). The differences between treatment groups were not statistically significant ($p = 11$). Testing for non-inferiority indicated that NB-UVB was not inferior to BB-UVB in the ability to reduce pruritus ($p = 0.0043$). **Fig. 1** provides an overview of the results.

Sleep disturbance

BB-UVB reduced sleep disturbance VAS from mean (± SD) 3.28 ± 3.31 (median 3; range 0–9) to mean (± SD) 1.16 ± 2.45 (median 0; range 0–9; mean reduction 62.6%; relative treatment effect 100%). NB-UVB reduced mean sleep disturbance VAS from mean (± SD) 4.1 ± 3.06 (median 4; range 0–10) to 1.73 ± 2.85 (median 0; range 0–9.5; mean reduction 69.1%; relative treatment effect 85.3%). The relative reduction in sleep disturbance was 66.4%. There was no statistically significant difference ($p = 0.69$) between BB-UVB and NB-UVB in sleep disturbance VAS reduction. Testing for non-inferiority could not establish that NB-UVB was non-inferior to BB-UVB in the ability to improve patients' sleep disturbance ($p = 0.18$).

Evaluation of response to treatment

Both groups evaluated their therapeutic response to treatment positively by using a VAS scale from –10 to + 10. In the BB-UVB group patients showed a mean improvement of 4.75 ± 3.95 (median 4.7; range –4.5 to 10; relative treatment effect 40%) after BB-UVB treatment.

Patients in the NB-UVB treatment group indicated a mean (± SD) improvement of 6.54 ± 0.38 (median 7.8; range –0.5–10; relative treatment effect 78%). There was a statistically significant difference ($p = 0.036$) between the 2 treatment groups. However, testing for non-inferio-

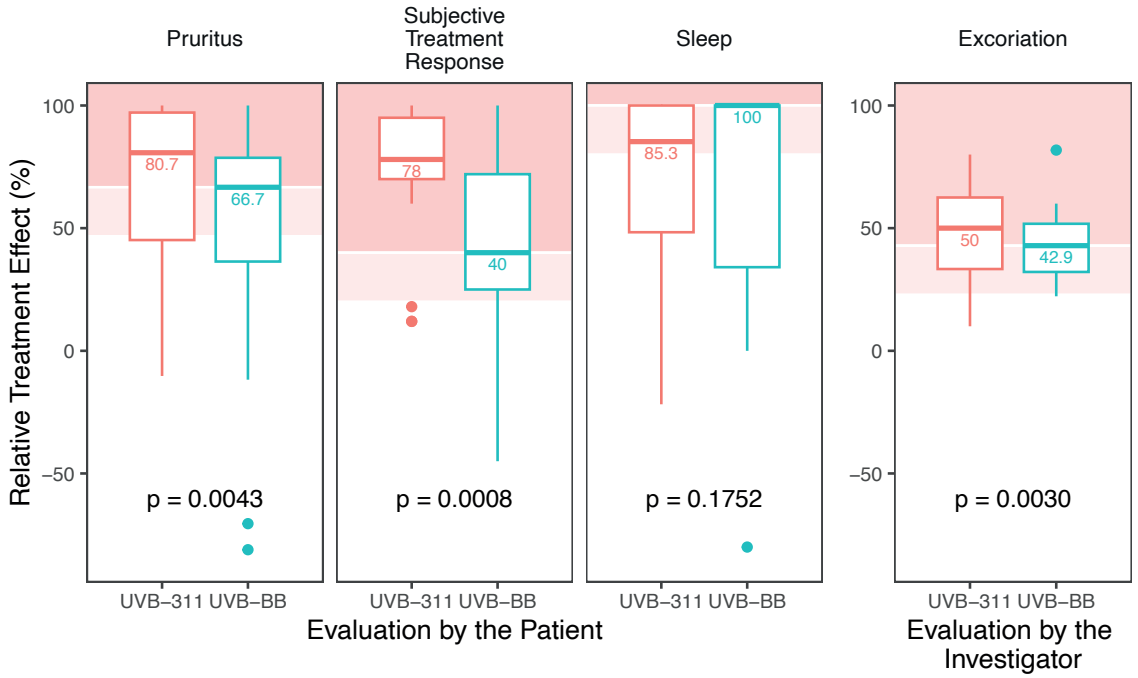

Fig. 1. Comparison of narrow-band ultraviolet B (UVB)311 and broadband ultraviolet B (BB-UVB) before and at 6 weeks' treatment. Non-inferiority testing of the UVB-311 treatment effect. Non-inferiority *p*-values are shown in the figure. The relative treatment effect is the difference between initial state and the state after 6 weeks divided by the initial state. The lower limit is the median of the relative treatment effect of the BB-UVB group minus 20%.

rity indicated that NB-UVB was not inferior to BB-UVB to enhance patients' treatment response ($p<0.0001$).

Excoriations

BB-UVB reduced excoriations from mean (±SD) 1.25±0.85 (median 1.5; range 0–2.8) to mean (±SD) 0.78±0.47 (median 0.75; range 0–1.8; mean reduction: 43.5%, relative treatment effect 42.9%). NB-UVB decreased the severity of excoriations from mean (±SD) 1.59±0.62 (median 1.6; range 0.25–2.2) to mean (±SD) 0.90±0.43 (median 0.88, range 0.25–1.8, mean reduction: 48.5%, relative treatment effect 50%). There were no significant differences ($p=0.56$) between BB-UVB and NB-UVB. Testing for non-inferiority indicated that NB-UVB was not inferior to BB-UVB in the ability to reduce skin excoriations ($p=0.003$).

DISCUSSION

UV phototherapy is an effective treatment that has long been used for the various pruritic skin diseases and is basically acknowledged to provide an essential contribution in reducing CP (13). Currently NB-UVB is the preferred treatment modality of phototherapy (14) and it has been shown to be superior to BB-UVB in the treatment of psoriasis and AD as well as for other pruritic skin disorders (15).

The ongoing debate, regarding which phototherapeutic modality is more effective in the treatment of CP and if there is still a role for UV therapy in treatment of pruritus (16), prompted us to evaluate the effectiveness of NB-UVB phototherapy and to compare it with that of BB-UVB.

The results of this study clearly show that both NB-UVB and BB-UVB significantly reduced CP in the study participants, and that the antipruritic effect of NB-UVB is not inferior to that of BB-UVB. The extent of the reduction in pruritus after 6 weeks was 48% for BB-UVB and 66.4% for NB-UVB.

In a study to assess the safety and efficacy of the neurokinin 1 receptor antagonist serlopitant in treating CP, patients treated with serlopitant had a mean difference in change from baseline pruritus of –1.6 on the VAS (0–10) within 8 weeks (17). In the current study, during a period of 6 weeks a mean difference in change from baseline pruritus of –3.4 and –3.7 on the VAS could be achieved in the BB-UVB and NB-UVB treatment groups, respectively. In a clinical study in end-stage renal disease (ESRD) patients undergoing haemodialysis, the peripheral k-opioid receptor agonist difelikefalin significantly reduced itch intensity ≥3 on the 24h-worst-itch NRS in 51.9% of patients (compared with 30.9% in the placebo group) and improved itch-related quality of life (18). Likewise, in a randomized, double-blind, phase 2 trial to assess the safety and efficacy of the interleukin 31 receptor alpha antagonist nemolizumab in patients with chronic nodular prurigo, Ständer et al. (19) showed a significant reduction in pruritus by 53% (i.e. 4.5 points) of 24-h peak pruritus NRS within 4 weeks (compared with 20.2% in the placebo group) in these difficult-to-treat CP patients.

The results of these double-blinded, randomized, placebo-controlled trials including a higher number of participants with nemolizumab, difelikefalin, and serlopitant, cannot directly be compared with the current study and the antipruritic effects of UVB.

However, the fact that BB-UVB and NB-UVB, respectively, reduced pruritus in the patients by –3.4 to –3.7 points on the VAS, or in percentage of baseline pruritus by –48% to –66.4%, clearly shows the antipruritic potential of both UVB regimens in patients with or without chronic pruriginous skin lesions. The significant subjective impression of improvement by approximately 4.8–6.5 on the VAS (0–10) during the 6 weeks' treatment with BB-UVB and NB-UVB, respectively, also supports the current findings and the positive effects of UVB for CP in the patients.

BB-UVB and NB-UVB, UVA-1, targeted treatments with an excimer laser or with psoralen plus ultraviolet A (PUVA) have previously shown considerable improvements in pruritus and pruriginous skin lesions (20, 21). In a double-blind randomized clinical trial Maul et al. (22) compared the effect of NB-UVB with or without UVA in the treatment of CP patients with inflammatory skin diseases, such as AD, other eczema subtypes, psoriasis, prurigo simplex subacuta and others. After UV treatment, pruritus VAS scores decreased in both groups (NB-UVB, 2.0, $p<0.0001$; NB-UVB/UVA, 2.5, $p=0.0001$) to comparable levels of 27.96% (±standard error of the mean (SEM) of 6.859%) and 35.21% (±SEM of 10.60%) by NB-UVB and combined NB-UVB/UVA, respectively. They concluded that UV therapy with NB-UVB alone and NB-UVB combined with UVA are equally effective in the treatment of inflammatory skin disease-associated pruritus.

In addition, Legat et al. (23) investigated the effect of NB-UVB irradiation and medium-dose UVA-1 in the treatment of 9 patients with chronic AD during a median of 7 weeks of half-side phototherapy. After a median of 23 treatments, reduction in pruritus VAS was superior with NB-UVB compared with UVA-1 (67% vs 34%) (23).

Together, these studies have also shown the antipruritic effects of various phototherapeutic regimens in patients with CP, while there was still a lack of studies comparing NB-UVB with BB-UVB in the treatment of CP. The current study at least partially addresses this knowledge gap by showing no inferiority of NB-UVB compared with BB-UVB in significantly reducing CP.

Study limitations

Limitations of this study include that it was a single-centre, single-blinded study with no placebo control group. However, the intention of the study was primarily to show the non-inferiority of NB-UVB compared with BB-UVB in patients with CP.

Conclusion

To date, NB-UVB therapy has largely replaced BB-UVB therapy. With its low level of acute side-effects and low number of contraindications, together with the possibility of easily combining it with other treatment modalities, NB-UVB-phototherapy is a valuable option for treatment of CP of various origins.

The authors have no conflicts of interest to declare.

REFERENCES

1. Metz M. Treatments for chronic pruritus outside of the box. Exp Dermatol 2019; 28: 1476–1481.
2. Matterne U, Apfelbacher CJ, Loerbroks A, Schwarzer T, Büttner M, Ofenloch R, et al. Prevalence, correlates and characteristics of chronic pruritus: a population-based cross-sectional study. Acta Derm Venereol 2011; 91: 674–679.
3. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the international forum for the study of itch. Acta Derm Venereol 2007; 87: 291–294.
4. Pereira MP, Zeidler C, Nau T, Bobko S, Evers AWM, Garcovich S, et al. Position statement: linear prurigo is a subtype of chronic prurigo. J Eur Acad Dermatol Venereol 2019; 33: 263–266.
5. Andrade A, Kuah CY, Martin-Lopez JE, Chua S, Shpadaruk V, Sanclemente G, et al. Interventions for chronic pruritus of unknown origin. Cochrane Database Syst Rev 2020; 2020 (1) CD013128.
6. Grundmann S, Ständer S. Chronic pruritus: clinics and treatment. Ann Dermatol 2011; 23: 1–11.
7. Ishiuji Y. Addiction and the itch-scratch cycle. What do they have in common? Exp Dermatol 2019; 28: 1448–1454.
8. Mack MR, Kim BS. The itch–scratch cycle: a neuroimmune perspective. Trends Immunol 2018; 39: 980–991.
9. Park J Bin, Jang JY, Kwon DI, Seong SH, Suh KS, Jang MS. The effectiveness of high-dose ultraviolet A-1 phototherapy for acute exacerbation of atopic dermatitis in Asians. Photodermatol Photoimmunol Photomed 2020; 36: 263–270.
10. Yanovsky RL, Huang KP, Buzney EA. Optimizing narrowband UVB phototherapy regimens for psoriasis. Dermatol Clin 2010; 38: 1–10.
11. Atci T, Baykal C. Efficacy of narrow-band ultraviolet-B therapy in patch-stage mycosis fungoides: a clinical study and review of the literature. Photodermatol Photoimmunol Photomed 2020; 36: 271–277.
12. Pereira MP, Steinke S, Zeidler C, Forner C, Riepe C, Augustin M, et al. European Academy of Dermatology and Venereology European prurigo project: expert consensus on the definition, classification and terminology of chronic prurigo. J Eur Acad Dermatol Venereol 2018; 32: 1059–1065.
13. Weisshaar E, Kucenic MJ, Fleischer AB. Pruritus: a review. Acta Derm Venereol 2003; 213: 5–32.
14. Ibbotson SH. A perspective on the use of NB-UVB phototherapy vs. PUVA photochemotherapy. Front Med (Lausanne) 2018; 5: 184.
15. Singer S, Berneburg M. Phototherapy. J Dtsch Dermatol Ges 2018; 16: 1120.
16. Legat FJ. Is there still a role for UV therapy in itch treatment? Exp Dermatol 2019; 28: 1432–1438.
17. Ständer S, Kwon P, Hirman J, Perlman AJ, Weisshaar E, Metz M, et al. Serlopitant reduced pruritus in patients with prurigo nodularis in a phase 2, randomized, placebo-controlled trial. J Am Acad Dermatol 2019; 80: 1395.
18. Fishbane S, Jamal A, Munera C, Wen W, Menzaghi F. A phase 3 trial of difelikefalin in hemodialysis patients with pruritus. N Engl J Med 2020; 382: 222–232.
19. Ständer S, Yosipovitch G, Legat FJ, Lacour JP, Paul C, Narbutt J, et al. Trial of nemolizumab in moderate-to-severe prurigo

nodularis. N Engl J Med 2020; 382: 706–716.
20. Qureshi AA, Abate LE, Yosipovitch G, Friedman AJ. A systematic review of evidence-based treatments for prurigo nodularis. J Am Acad Dermatol 2019; 80: 756–764.
21. Nakamura M, Koo JYM. Phototherapy for the treatment of prurigo nodularis: a review. Dermatol Online J 2016; 22: 13030.
22. Maul JT, Kretschmer L, Anzengruber F, Pink A, Murer C, French LE, et al. Impact of UVA on pruritus during UVA/B phototherapy of inflammatory skin diseases: a randomized double-blind study. J Eur Acad Dermatol Venereol 2017; 31: 1208–1213.
23. Legat FJ, Hofer A, Brabek E, Quehenberger F, Kerl H, Wolf P. Narrowband UV-B vs medium-dose UV-A1 phototherapy in chronic atopic dermatitis. Arch Dermatol 2003; 139: 223–224.