Phototherapy as a treatment of early-stage mycosis fungoides and predictive factors for disease recurrence: A 17-year retrospective study

Corresponding author:
Dr. Ploysyne Rattanakaemakorn, Division of Dermatology, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, 270 Rama IV Road, Ratchatewi Bangkok 10400, Thailand.
ploysyne@gmail.com

Received: July, 2019
Accepted: November, 2020
Published:

DOI:
10.25259/IJDVL_555_19

PMID:
***

Ploysyne Rattanakaemakorn, Monthanat Ploydaeng, Siriorn Udompanich, Kunlawat Thadanipon, Suthinee Rutnin, Natta Rajatanavin

Division of Dermatology, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Abstract

Background: Mycosis fungoides is the most common form of cutaneous T-cell lymphoma. Narrowband ultraviolet B and psoralen and ultraviolet A are effective treatment options, but studies of their treatment efficacy and disease relapse remain limited.

Objectives: This study aimed (1) to determine the efficacy of narrowband ultraviolet B and psoralen and ultraviolet A as a treatment for early-stage mycosis fungoides and explore the predictive factors for complete remission and (2) to determine the relapse rate and analyze their predictive factors, including the utility of maintenance therapy.

Methods: This was a retrospective cohort study consisting of 61 patients with early-stage mycosis fungoides (IA - IB) treated with narrowband ultraviolet B or psoralen and ultraviolet A as the first-line therapy from January 2002 to December 2018 at the Division of Dermatology, Ramathibodi Hospital, Bangkok, Thailand. Cox regression analysis and Kaplan–Meier survival curve were performed for the main outcomes.

Results: A complete remission was achieved by 57 (93.5%) patients. The median time to remission was 7.80 ± 0.27 months. Types of phototherapy (narrowband ultraviolet B or psoralen and ultraviolet A), age and gender did not associate with time to remission, while the presence of poikiloderma and higher disease stage led to a longer time to remission. The cumulative incidence of relapse was 50.8%. The median time to relapse was 24.78 ± 5.48 months. In patients receiving phototherapy during the maintenance period, a treatment duration longer than six months was associated with a significantly longer relapse-free interval.

Conclusion: Narrow-band-ultraviolet B and psoralen and ultraviolet A are effective treatment options for early-stage mycosis fungoides. Maintenance treatment by phototherapy for at least six months seems to prolong remission.

Key words: Maintenance, mycosis fungoides, narrow-band-ultraviolet B, phototherapy, psoralen and ultraviolet A, recurrence

Plain Language Summary

Mycosis fungoides is the most common form of cutaneous T-cell lymphoma. Phototherapy (narrowband ultraviolet B and psoralen and ultraviolet A) is one of the most common methods

How to cite this article: Rattanakaemakorn P, Ploydaeng M, Udompanich S, Thadanipon K, Rutnin S, Rajatanavin N. Phototherapy as a treatment of early-stage mycosis fungoides and predictive factors for disease recurrence: A 17-year retrospective study. Indian J Dermatol Venereol Leprol 2021;XX:1-7.

for treatment of early-stage mycosis fungoides because of its high efficacy. However, disease relapse after treatment discontinuation is common. Therefore, this 17-year retrospective study was conducted to determine the efficacy of phototherapy as the treatment of early-stage mycosis fungoides, including exploration of the predictive factors for complete remission and disease recurrence, including the utility of maintenance therapy. The results found that 93.5% of patients achieved complete remission. The presence of altered skin color together with thinning of skin and visible blood vessels on the skin and higher disease stage led to a longer time to subside. Maintenance treatment with phototherapy for at least six months was beneficial prolonging remission. In conclusion, phototherapy is an effective treatment option for early-stage mycosis fungoides.

Introduction

Mycosis fungoides can be described as the most common form of cutaneous T-cell lymphoma.[1] A majority of cases are diagnosed at an early stage (95% stage IA – IIA),[2] with an incidence rate of 0.36 per 100,000 person-years.[1] Mycosis fungoides is diagnosed from the clinicopathological features according to the consensus criteria by the World Health Organization and the European Organization for Research and Treatment of Cancer.[3] The treatment aims to clear all lesions to prolong the relapse-free interval and overall survival with least toxicity.[1,4]

The first-line treatment of early-stage mycosis fungoides is skin-directed therapy which includes the following: topical corticosteroids, topical nitrogen mustard (HN2), topical BCNU (carmustine), psoralen and ultraviolet A, narrowband ultraviolet B, total skin electron beam therapy and superficial X-irradiation.[1,5]

Phototherapy has been established as one of the most suitable treatments for mycosis fungoides, especially narrowband ultraviolet B and psoralen and ultraviolet A, because of its effectiveness in lesion clearance and minimal side effects. Complete remission rates of narrowband ultraviolet B and psoralen and ultraviolet A were 62.2% and 73.8%, respectively.[6]

Although phototherapy is an effective treatment option, rapid disease relapse after treatment discontinuation appears to interfere with its efficacy.[7] Currently, the information on disease relapse and its predictive factors, including the usefulness of maintenance therapy, is still lacking.

This study aimed (1) to determine the efficacy of narrowband ultraviolet B and psoralen and ultraviolet A as the treatment of early-stage mycosis fungoides and explore the predictive factors for complete remission and (2) to explore the disease recurrence and analyze the predictive factors for disease recurrence, including the utility of maintenance therapy.

Methods

This is a 17-year retrospective study of patients with early-stage mycosis fungoides (IA - IB) treated with narrowband ultraviolet B or psoralen and ultraviolet A as the first-line treatment from the division of dermatology at the Ramathibodi Hospital, Bangkok, Thailand between January 2002 and December 2018. Approval from the research ethics committee was obtained with an ID number 12-61-96.

The inclusion criteria included patients diagnosed with early-stage mycosis fungoides by skin biopsy who had started their first narrowband ultraviolet B or psoralen and ultraviolet A course as the first-line treatment and achieved a complete remission by the end of 2018. We excluded all patients who had previous treatments with systemic agents (interferon and retinoids) or other skin-directed agents (topical chemotherapy and electron beam therapy), who had stopped phototherapy before a response was defined (complete, partial or nonresponse), who were lost to follow-up or who had incomplete data on the electronic medical record.

The stage of the disease was classified according to the tumor-node-metastasis-blood (TNMB) classification by the International Society for Cutaneous Lymphoma and Cutaneous Lymphoma Task Force of the European Organization for the Research and Treatment of Cancer.[8] For the analysis, the patients were divided into groups with stage IA and stage IB. Complete remission or complete response was defined as having ≥95% clearance of skin lesions, partial response as 50% to 95% clearance, and nonresponse as less than 50% clearance.[2,7] Relapse was defined as a clinically significant disease requiring further therapy. Relapse-free interval or time to relapse was defined as the period between a complete response and relapse.[9] Maintenance treatment was any treatment after complete remission.

Data collection from medical records was divided into three parts. Part one was demographic data and history of the disease, including age at diagnosis, gender, underlying diseases and the disease stage. Part two was the treatment protocols from the initial diagnosis to complete remission, including the type of phototherapy (narrowband ultraviolet B or psoralen and ultraviolet A), cumulative dose, number of cumulative sessions, side effects and concomitant therapy. The last part was the maintenance protocols, from the time of complete remission to disease relapse. Treatment regimens were based on patient skin type and disease stage.

The analysis was completed by Cox regression and presented as hazard ratios. The Kaplan–Meier survival curve was

performed to plot the relationship between the relapse-free interval and duration of phototherapy during the maintenance period. The cumulative dose and cumulative sessions were also divided into two groups, based on their median values and analyzed as categorical data. Univariate analysis for disease remission and relapse was done for the following variables: age at diagnosis, gender, stage of the disease, cumulative dose and cumulative sessions. Multivariate analysis was done for statistical and clinical reasons. $P \leq 0.05$ was considered significant and missing values were not replaced.

Results

Eighty-five patients were diagnosed with an early-stage mycosis fungoides and received phototherapy as the first-line treatment. Twenty-three of them had an incomplete medical record and one of them stopped phototherapy because of side effects before the response was defined. Therefore, 61 patients met the eligibility criteria. Fifty-three patients received narrowband ultraviolet B and eight patients received psoralen and ultraviolet A as an initial treatment.

From this cohort, 57 (93.4%) patients achieved complete remission. Three patients reached partial remission in 6.14 months, 6.34 months and 17.38 months, respectively. One case had no response after receiving the treatment for 8.16 months. The mean age at diagnosis was 44.0 ± 18.8 years, 38 (62.3%) of whom were women. Among these patients, 50 (87.7%) patients were treated with narrowband ultraviolet B and 7 (12.3%) patients with psoralen and ultraviolet A. The disease stage was recorded to be stage IA in 36 patients (67.9%) and IB in 17 patients (32.1%). Median cumulative dose with interquartile range and median cumulative sessions during treatment were 42.9 (22.6–67.7) KJ/cm^2 and 38 (30–67) sessions, respectively. The demographic data and disease characteristics are displayed in Table 1.

The total follow-up time to remission was 734.62 person-months. Overall, the median time to complete a response with a 95% confidence interval (95% CI) was 7.8 months (95% CI 6.68–9.54). There was no significant difference between the narrowband ultraviolet B group (7.57 months [95% CI 5.8–8.3]) and the psoralen and ultraviolet A group (9.18 months [95% CI 3.1–28.13]). The overall incidence rate of complete remission was 0.077 (95% CI 0.059–0.100), and the rate was higher in the group treated with narrowband ultraviolet B than in the group treated with psoralen and ultraviolet A (narrowband ultraviolet B 0.08 [95% CI 0.06–1.00]) versus (psoralen and ultraviolet A 0.058 [95% CI 0.023–0.12]). The incidences rate of complete remission at 3 months and 6 months were 0.06 (95% CI 0.03–0.16) and 0.34 (95% CI 0.24–0.47), respectively. The univariate analysis for predictors of complete remission revealed that the presence of poikiloderma was a predictive factor for a poor response (hazard ratio 0.33, 95% CI 0.12–0.87, P = 0.026), while age, gender and type of phototherapy did not affect the rate of complete remission [Table 2].

As psoralen and ultraviolet A was mainly administered to patients with more infiltrative disease, such as in cases of plaques or a higher disease stage, adjustments for the following factors were made to eliminate the confounding factors: types of phototherapy, disease stage and initial clinical presentation.[10] After the adjustments, poikiloderma and high stage of disease (IB) were found to be associated with a longer time of treatment to remission (20.9 ± 4.35 months in cases with poikiloderma vs 7.57 ± 0.43 months in cases without poikiloderma, $P = 0.02$ and 7.44 ± 0.46 months for stage IA vs 9.54 ± 2.99 months for stage IB, $P = 0.035$).

Total follow-up time to relapse was 999.51 person-months. Twenty-nine (50.8%) patients had recurrent mycosis fungoides. Among them, 26 were treated with narrowband ultraviolet B, while three were treated with psoralen and ultraviolet A. Median time of relapse-free interval was 24.78 months (95% CI 15.2–39.6) overall, (24.78 ± 4.67 for narrowband ultraviolet B and 19.9 months for psoralen and ultraviolet A). The overall incidence of relapse was 0.029 (0.034 for narrowband ultraviolet B and 0.012 for psoralen and ultraviolet A).

The univariate analysis had demonstrated that there were no statistically significant differences in age, sex, disease stage, type of phototherapy, cumulative dose and cumulative

Table 1: Demographic data and clinical presentations

Number of patients	61
Age of diagnosis (years; mean±SD)	44.0±18.8
Sex, *n* (%)	
Male	23 (37.7)
Female	38 (62.3)
Disease stage (by clinical), *n* (%)	
IA	36 (67.9)
IB	17 (32.1)
Disease stage (by pathological), *n* (%)	
Patch stage	23 (74.2)
Plaque stage	8 (25.8)
Skin lesion	
Patch, *n* (%)	
Yes	54 (93.1)
No	4 (6.9)
Plaque, *n* (%)	
Yes	15 (28.9)
No	43 (74.1)
Hypopigmented, *n* (%)	
Yes	42 (75)
No	14 (25)
Poikiloderma, *n* (%)	
Yes	7 (16.3)
No	36 (83.7)
Type of phototherapy, *n* (%)	
Narrowband ultraviolet B	53 (86.9)
psoralen and ultraviolet A	8 (13.1)

Table 2: Predictive factors for complete remission

Patient characteristics	Univariate analysis			Multivariate analysis†		
	Hazard ratio	95% CI	*P*-value	Hazard ratio	95% CI	*P*-value
Age at diagnosis (years)	0.99	0.97–1.00	0.29			
Sex						
Male	1					
Female	1.29	0.75–2.32	0.37			
Type of phototherapy						
Narrowband ultraviolet B	1			1		
Psoralen and ultraviolet A	0.66	0.29–1.45	0.31	0.40	0.13–1.29	0.13
Clinical presentation						
Patch	1.01	0.36–2.89	0.98	2.4	0.51–12.8	0.29
Plaque	1.2	0.64–2.23	0.56	1.77	0.70–4.99	0.27
Hypopigmented	1.26	0.7–2.26	0.459	0.61	0.19–1.72	0.40
Poikiloderma	0.33	0.12–0.87	0.026*	0.23	0.06–0.78	0.02*
Disease stage						
IA	1			1		
IB	0.75	0.41–1.37	0.36	0.40	0.16–0.93	0.035*

*Statistically significant

†Multivariate analysis adjusted for type of phototherapy, disease stage and clinical presentation

sessions during the treatment phase between patients with and without relapse.

We further evaluated the effect of maintenance therapy on disease recurrence. Of all our patients, 42 received phototherapy during their maintenance period, while 14 did not (one patient was lost to follow-up after achieving complete response). In the group with phototherapy during the maintenance period ($n = 42$), more than half still experienced recurrence (27/42 cases). Further details are displayed in Table 3. The analysis found that the longer duration of phototherapy, higher cumulative dose (≥10 KJ/cm^2) and higher cumulative sessions (≥25 sessions) throughout the maintenance period could diminish disease recurrence. However, after adjustment for the variable stated above, only maintenance duration showed a significant correlation with a duration of six months or longer significantly increased relapse-free interval period (hazard ratio 0.13, 95% CI 0.04–0.41, $P = 0.001$) [Figure 1].

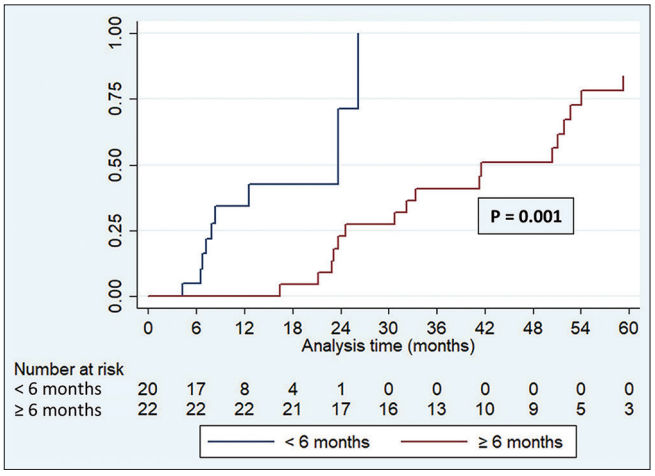

Figure 1: Relapse-free interval analysis according to the duration of phototherapy during the maintenance period

Of note, topical corticosteroids were widely prescribed during the maintenance phase, 33 cases used topical steroids during maintenance therapy, but there was no significant correlation between their use and disease recurrence rate ($P = 0.15$). Nevertheless, in the steroid group, a longer median time to recurrence was observed (29.24 ± 3.22 months vs 20.06 ± 0.19 months in nonsteroid group).

Discussion

Our study has demonstrated a high rate of complete remission (93.4%) in patients receiving either narrowband ultraviolet B or psoralen and ultraviolet A. The results from Table 2 showed different hazard ratios in the multivariable analysis than the univariate analysis in several factors, especially hypopigmented type and patch type. We believe that these hazard ratios from the univariate analysis were confounded by other factors. Therefore, the results from the multivariate model should be more reliable because they were already controlled for the confounding factors.

As found in previous studies, age and gender did not correlate with treatment response.[11,12] Several studies in the past have compared the efficacy of treatment between narrowband ultraviolet B and psoralen and ultraviolet A.Diederen *et al*.,[13] Ponte *et al*.[14] and El-Mofty *et al*.[15] reported a higher complete remission rate for patients who received narrowband ultraviolet B compared with that for those who received psoralen and ultraviolet A (81% vs 71%, 68.4% vs 62.1% and 90% vs 80%, respectively), but these were not statistically significant. In contrast, Ahmad *et al*.[9] and Almohideb *et al*.[11]

Table 3: Role of phototherapy during maintenance period and relapse-free interval

Maintenance treatment (*n*=42)	Univariate analysis			Multivariate analysis†		
	Hazard ratio	95% CI	*P*-value	Hazard ratio	95% CI	*P*-value
Longer duration of phototherapy during maintenance period	0.87	0.82–0.93	<0.001*	0.87	0.82–0.93	<0.001*
Cumulative dose (KJ/cm^2)						
<10	1			1		
≥10	0.41	0.18–0.92	0.03*	0.63	0.25–1.60	0.37
Cumulative sessions						
<25	1			1		
≥25	0.31	0.12–0.85	0.02*	0.56	0.16–1.97	0.34

*Statistically significant

†Multivariate analysis adjusted for the duration, cumulative doses and cumulative sessions

reported that psoralen and ultraviolet A had a higher complete remission rate than narrowband ultraviolet B. However, their results did not show any statistical significance either. Recently, a study of 227 cases with early mycosis fungoides[10] concluded that psoralen and ultraviolet A led to a significantly higher complete response rate (77.1% in psoralen and ultraviolet A vs 53.8% in narrowband ultraviolet B, P = 0.001). The superiority of psoralen and ultraviolet A was later emphasized in a meta-analysis of seven studies, comparing the efficacy and adverse effects of psoralen and ultraviolet A and narrowband ultraviolet B.[6] Altogether, 778 cases with early-stage mycosis fungoides (stage IA - IIB) were studied with at least 10 patients in each comparator group. The analysis found a significantly higher complete response in psoralen and ultraviolet A (73.8% vs 62.2%, P = 0.04) across all disease stages. Our study suggests otherwise with no significant difference in the rates of complete remission between the two groups, even after adjustments for disease stage and clinical presentation. This could be explained by the small number of subjects in the psoralen and ultraviolet A group (n = 7).

In terms of adverse reactions, mild erythema following phototherapy was reported in only three cases, one from psoralen and ultraviolet A and two from narrowband ultraviolet B. In the meta-analysis, no significant difference in adverse events were found between psoralen and ultraviolet A and narrowband ultraviolet B, but the percentages of erythema, nausea, phototoxic effects and dyspepsia were frequently higher in psoralen and ultraviolet A.[6,16,17] In addition, nonmelanoma skin cancers were reported in some psoriatic patients with psoralen and ultraviolet A therapy in a dose-dependent manner, occurring when the cumulative dose exceeded 2000 J/cm^2 or 200 sessions.[18,19] With narrowband ultraviolet B, patients do not have to take psoralen or use sun-protective methods.[6] There have not been any reports on the association with skin cancers.

Patients' initial clinical presentation may also affect the treatment response. Our study reveals that poikiloderma is a predictive factor for poor response. In our study, poikiloderma was found in seven patients, of which five (71%) achieved complete remission. Although the rate of complete response was high, the median time to remission in patients who had poikiloderma was significantly longer (20.9 ± 4.35 months vs 7.57 ± 0.43 months in those without poikiloderma). The results might guide physicians to choose a more aggressive treatment for patients with poikiloderma, such as psoralen and ultraviolet A or combination therapy. Abbott *et al*.[20] conducted a retrospective study to improve the data availability of poikiloderma in mycosis fungoides and concluded that 24/27 (89%) patients with poikiloderma responded to phototherapy, but they did not mention the time to remission. Another clinical feature known to affect treatment response is rash morphology. Gökdemir *et al*. found that the patch presentation has a significantly higher rate of complete remission when compared with the plaque type (P = 0.04).[21] However, the difference was not highlighted in our study.

Disease recurrence in early-stage mycosis fungoides after narrowband ultraviolet B or psoralen and ultraviolet A treatment still poses a challenge. The percentage of relapse in our study was up to 50.8%, but the number of studies on the predictive factors for relapse is small. Felix *et al*. conducted a study to evaluate the long-term disease-free survival after narrowband ultraviolet B treatment in stage I mycosis fungoides and its predictive factors.[22] The study found that younger age (<50 years) and earlier stage (stage IA) had a significant effect on longer disease-free survival time. In contrast with other studies,[11,23] we failed to establish the correlation between disease stage and recurrence. Age, sex and cumulative sessions during treatment also did not associate with disease recurrence in our study which agreed with another study.[11] When compared with narrowband ultraviolet B, psoralen and ultraviolet A had a lower incidence of relapse but a shorter time to relapse, also inconsistent with the previous data.[6]

Currently, a guideline for the dose and duration of maintenance phototherapy is still based on expert opinion. Previous studies have compared the relapse-free interval

directly between patients who received and did not receive maintenance therapy.[10,24-26] All of them reported no significant difference in relapse-free interval between the two groups. For the patients who did not receive maintenance phototherapy, the relapse ranged from 29% to 100% with a mean relapse-free interval between 5.9 and 14.5 months.[2] Nikolaou *et al*. reported that maintenance therapy does not associate with a reduction in relapse rate ($P = 0.51$) but do prolong the time to relapse (32.3 months in maintenance vs 19.5 months in nonmaintenance, $P < 0.002$).[10] Similarly, the maintenance treatment in our study had no role in reduction of relapse rate, even after adjustment for the disease stage, but a duration of six months or longer could increase the relapse-free interval period. It must be noted that most (73.7%) of the patients in our center received phototherapy during their maintenance period.

Limitations

The limitation of our study is that it is a retrospective study with a small number of subjects. In the future, stronger evidence-based research, such as randomized control trial or meta-analysis, may help clarify the subject.

Conclusion

Narrowband ultraviolet B and psoralen and ultraviolet A are suitable options for the treatment of early-stage mycosis fungoides. The presence of poikiloderma may indicate a predictive factor for poor prognosis and a longer time to complete remission. The relapse rate in our study was high, occurring around two years after complete remission. Maintenance phototherapy after disease remission for at least six months can significantly prolong the relapse-free interval period. In addition, topical steroid usage during this period might help prolong the time to relapse.

Acknowledgments

This study was supported by the Division of Dermatology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Trautinger F, Knobler R, Willemze R, Peris K, Stadler R, Laroche L, *et al*. EORTC consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome. Eur J Cancer 2006;42:1014-30.
2. Olsen EA, Hodak E, Anderson T, Carter JB, Henderson M, Cooper K, *et al*. Guidelines for phototherapy of mycosis fungoides and Sézary syndrome: A consensus statement of the United States Cutaneous Lymphoma Consortium. J Am Acad Dermatol 2016;74:27-58.
3. Lim HL, Tan ES, Tee SI, Ho ZY, Boey JJ, Tan WP, *et al*. Epidemiology and prognostic factors for mycosis fungoides and Sézary syndrome in a multi-ethnic Asian cohort: A 12-year review. J Eur Acad Dermatol Venereol 2019;33:1513-21.
4. Grandi V, Fava P, Rupoli S, Alberti Violetti S, Canafoglia L, Quaglino P, *et al*. Standardization of regimens in Narrowband UVB and PUVA in early stage mycosis fungoides: Position paper from the Italian Task Force for Cutaneous Lymphomas. J Eur Acad Dermatol Venereol 2018;32:683-91.
5. Whittaker SJ, Marsden JR, Spittle M, Russell Jones R; British Association of Dermatologists, U.K. Cutaneous Lymphoma Group. Joint british association of dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the MANAGEMENT of primary cutaneous T-cell lymphomas. Br J Dermatol 2003;149:1095-107.
6. Phan K, Ramachandran V, Fassihi H, Sebaratnam DF. Comparison of narrowband UV-B with psoralen-UV-a phototherapy for patients with early-stage mycosis fungoides: A systematic review and meta-analysis. JAMA Dermatol 2019;155:335-41.
7. Boztepe G, Sahin S, Ayhan M, Erkin G, Kilemen F. Narrowband ultraviolet B phototherapy to clear and maintain clearance in patients with mycosis fungoides. J Am Acad Dermatol 2005;53:242-6.
8. Olsen EA, Whittaker S, Kim YH, Duvic M, Prince HM, Lessin SR, *et al*. Clinical end points and response criteria in mycosis fungoides and Sézary syndrome: A consensus statement of the international society for cutaneous lymphomas, the United States cutaneous lymphoma consortium, and the cutaneous lymphoma task force of the european organisation for research and treatment of cancer. J Clin Oncol 2011;29:2598-607.
9. Ahmad K, Rogers S, McNicholas PD, Collins P. Narrowband UVB and PUVA in the treatment of mycosis fungoides: A retrospective study. Acta Derm Venereol 2007;87:413-7.
10. Nikolaou V, Sachlas A, Papadavid E, Economidi A, Karambidou K, Marinos L, *et al*. Phototherapy as a first-line treatment for early-stage mycosis fungoides: The results of a large retrospective analysis. Photodermatol Photoimmunol Photomed 2018;34:307-13.
11. Almohideb M, Walsh S, Walsh S, Shear N, Alhusayen R. Bath psoralen-ultraviolet a and narrowband ultraviolet B phototherapy as initial therapy for early-stage mycosis fungoides: A retrospective cohort of 267 cases at the university of toronto. Clin Lymphoma Myeloma Leuk 2017;17:604-12.
12. Pavlotsky F, Barzilai A, Kasem R, Shpiro D, Trau H. UVB in the management of early stage mycosis fungoides. J Eur Acad Dermatol Venereol 2006;20:565-72.
13. Diederen PV, van Weelden H, Sanders CJ, Toonstra J, van Vloten WA. Narrowband UVB and psoralen-UVA in the treatment of early-stage mycosis fungoides: A retrospective study. J Am Acad Dermatol 2003;48:215-9.
14. Ponte P, Serrão V, Apetato M. Efficacy of narrowband UVB vs. PUVA in patients with early-stage mycosis fungoides. J Eur Acad Dermatol Venereol 2010;24:716-21.
15. El-Mofty M, El-Darouty M, Salonas M, Bosseila M, Sobeih S, Leheta T, *et al*. Narrow band UVB (311 nm), psoralen UVB (311 nm) and PUVA therapy in the treatment of early-stage mycosis fungoides: A right-left comparative study. Photodermatol Photoimmunol Photomed 2005;21:281-6.
16. Coronel-Pérez IM, Carrizosa-Esquivel AM, Camacho-Martínez F. Narrow band UVB therapy in early stage mycosis fungoides. A study of 23 patients. Actas Dermosifiliogr 2007;98:259-64.
17. Stern RS, Nichols KT, Väkevä LH. Malignant melanoma in patients treated for psoriasis with methoxsalen (psoralen) and ultraviolet A radiation (PUVA). The PUVA Follow-Up Study. N Engl J Med 1997;336:1041-5.
18. Archier E, Devaux S, Castela E, Gallini A, Aubin F, Le Maître M, *et al*. Carcinogenic risks of psoralen UV-A therapy and narrowband UV-B therapy in chronic plaque psoriasis: A systematic literature review. J Eur Acad Dermatol Venereol 2012;26 Suppl 3:22-31.
19. Stern RS, Lunder EJ. Risk of squamous cell carcinoma and methoxsalen (psoralen) and UV-A radiation (PUVA). A meta-analysis. Arch Dermatol 1998;134:1582-5.
20. Abbott RA, Sahni D, Robson A, Agar N, Whittaker S, Scarisbrick JJ.

Poikilodermatous mycosis fungoides: A study of its clinicopathological, immunophenotypic, and prognostic features. J Am Acad Dermatol 2011;65:313-9.
21. Gökdemir G, Barutcuoglu B, Sakiz D, Köşlü A. Narrowband UVB phototherapy for early-stage mycosis fungoides: Evaluation of clinical and histopathological changes. J Eur Acad Dermatol Venereol 2006;20:804-9.
22. Felix P, Marwan D, Aviv B. Potential of narrow band UVB to induce sustained durable complete remission off-therapy in stage I mycosis fungoides. J Am Acad Dermatol 2019;80:1550-5.
23. Kural Y, Onsun N, Aygin S, Demirkesen C, Büyükbabani N. Efficacy of narrowband UVB phototherapy in early stage of mycosis fungoides. J Eur Acad Dermatol Venereol 2006;20:104-5.
24. Hernández Z, Peñate Y, Hernández-Machín B, Pérez-Méndez L, Suárez-Hernández J, Hernández J, *et al*. Treatment of stage Ia and Ib mycosis fungoides with psoralen UVA monotherapy: An observational study in tertiary hospitals in the Canary Islands. Int J Dermatol 2014;53:1417-22.
25. Sánchez MA, González T, Gaitán MF, Zuluaga A, Jiménez SB, de Galvis YT. Is PUVA maintenance therapy necessary in patients with early-stage mycosis fungoides? Evaluation of a treatment guideline over a 28-month follow-up. Int J Dermatol 2011;50:1086-93.
26. Wackernagel A, Hofer A, Legat F, Kerl H, Wolf P. Efficacy of 8-methoxypsoralen vs. 5-methoxypsoralen plus ultraviolet A therapy in patients with mycosis fungoides. Br J Dermatol 2006;154:519-23.