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ORIGINAL ARTICLE

Evaluation of mycosis fungoides management by total skin electron beam therapy with "translational technique"

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Summary

Purpose: *The aim of this study was to evaluate the outcomes of total skin electron beam therapy (TSEBT) with "translational technique" in the management of mycosis fungoides (MF).*

Methods: *Between January 1995 and October 2014, 51 patients with MF were treated using TSEBT with translational technique. The total dose was 2800-3600 cGy, delivered in 7 to 20 fractions. Out of the total 51 patients, 22 (43.1%) had T2 (generalized patch/plaque) disease, 20 (39.3%) had T3 disease (tumor stage), and 9 (17.6%) had T4 (erythrodermic) disease. Radiation-related late skin injury parameters including atrophy, pigmentation changes, hair loss, telangiectasia and ulceration were assessed according to RTOG/EORTC Late Radiation Morbidity Scoring Schema after at least 3 months from TSEBT.*

Results: *Treatment response was categorized as complete remission (CR), partial remission (PR), or non-responding (NR) lesions. After TSEBT with translational technique, CR rate was 68.6% and PR rate 23.5%, while the NR rate was 7.9%. Overall, the rates of grade 1, grade 2, grade 3, and grade 4 toxicity were 17.6% (9 patients), 39.3% (20 patient), 35.3% (18 patients), and 7.8% (4 patients), respectively. At a median follow-up of 79 months (range 14-142), overall survival (OS) and disease-free survival (DFS) rates were 83% and 46%, respectively.*

Conclusion: *For patients with MF refractory to topical chemotherapy and phototherapy, TSEBT with translational technique offers excellent local control (LC: CR+PR) and favorable OS rates along with substantial relief of symptoms.*

Key words: *mycosis fungoides, radiotherapy, total skin electron beam therapy, translational technique*

Introduction

Non-Hodgkin lymphomas may involve the skin, either primarily or secondarily. Primary cutaneous lymphomas occur in the skin with no evidence of extracutaneous involvement at the time of diagnosis. The diversity of clinical and pathological features in subgroups of primary cutaneous lymphomas has led to controversies in diagnosis and classification. A joint effort of the World Health Organization and European Organization for Research and Treatment of Cancer (WHO-EORTC) published a consensus guideline in 2005 to address these controversies [1]. The WHO-EORTC classification defines 3 groups of cutaneous lymphomas: the cutaneous T-cell and natural killer (NK) cell lymphomas, and cutaneous B-cell lymphomas, and precursor hematologic neoplasms with widely varying clinical presentations, histopathology, immunophenotyping, gene rearrangement, and prognosis [1]. The Dutch and Austrian Cutaneous Lymphoma Registries report that more than 70% of all cutaneous lymphomas are of T-cell origin, and 85% of diagnoses in the Central Cutaneous Lymphoma Registry of the German Society of Dermatology are cutaneous T-cell lymphomas (CTCL) [1,2].

MF is the most common type of CTCL and low-

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grade lymphoproliferative disorder of skin-homing CD4+ T cells that form cutaneous patches, plaques, and tumors [3]. MF incidence increases with age with most patients being diagnosed at the 4th to 6th decades of life, showing also a male preponderance [1]. Selection of optimal treatment strategy for a patient with MF is based on the clinical stage of disease. Prevention of disease progression and amelioration of patient symptoms are primary aims of management. There is a high chance of cure or long-term disease control for early stage MF localized to skin (patch or plaque disease) using treatment modalities of topical chemotherapy, phototherapy, TSEBT and local superficial radiotherapy (RT) [4-10]. Systemic treatment with oral bexarotene, denileukin diftitox, extracorporeal photochemotherapy, histone deacetylase inhibitors, monoclonal antibodies and cytotoxic chemotherapy is a typical management strategy for advanced or refractory disease [11-20]. Stem cell transplantation may be considered for patients who are deemed to have MF refractory to other therapies. Allogeneic stem cell transplantation has been reported to have a greater success than autologous stem cell transplantation for disease management [21-23].

RT is a viable treatment option for both limited and advanced stage MF. Owing to the rarity of the disease, there are no randomized trials assessing the comparative safety and efficacy of different treatment strategies, and most relevant literature regarding MF management include retrospective single-center series. RT may be used with palliative or curative intent for MF management. RT may also be used as part of multidisciplinary management, typically delivered sequentially with other treatment options. Since lymphocytes are highly radiosensitive, RT is well suited to MF management. RT in the form of local superficial irradiation or TSEBT with optimal selection of photon or electron energies may provide excellent treatment of lesions limited to the dermis and/or epidermis.

The first description of TSEBT is credited to Trump et al. in 1953 [24]. Since then, various centers throughout the world have reported their treatment outcomes using several treatment techniques. The International Atomic Energy Agency's (IAEA) classification of TSEBT techniques includes 3 different modalities [25]. With translational techniques, the patient is translated on a stretcher through an electron beam of sufficient width to cover the patient's transverse dimensions; with large electron field techniques, a standing stationary patient is treated at a large source-skin distance (SSD) with a single large electron beam or a combination of large electron beams; finally, with rotational techniques the patient stands on a rotating platform in a large electron field. Dosimetric, geometric and patient positioning details are reported in AAPM Report No. 23 [26].

In this study, we retrospectively evaluated the outcomes of TSEBT in patients with MF and report our single center experience.

Methods

Between January 1995 and October 2014, 51 patients with MF received RT at the Department of Radiation Oncology, Gulhane Military Medical Academy. Out of the total 51 patients, 22 (43.1%) had T2 (generalized patch/plaque) disease, 20 (39.3%) had T3 disease (tumor stage), and 9 (17.6%) had T4 (erythrodermic) disease according to T-stage classification.

Clinical and histopathologic diagnosis was established using the criteria of the World Health Organization-European Organization for Research and Treatment of Cancer classification, confirmed in consensus meetings of the Dutch Cutaneous Lymphoma Working Group [1]. Staging work-up included physical examination, routine blood analysis with lactate dehydrogenase (LDH), chest X-ray, thoracoabdominal and pelvic computed tomography (CT), ultrasonographic examination of liver and spleen and bone marrow biopsies. All patients in this study were previously treated with other treatments including topical treatment (51 patients), Psoralen plus ultraviolet A (PUVA) therapy (46 patients), and systemic therapy (8 patients), all of which failed to achieve cure.

CR was defined as the disappearance of all clinical, blood, bioptical or radiographic features of MF; PR was defined as a reduction of ≥50% of the largest dimension of each measurable anatomical disease site for at least 1 month. NR lesions were defined as <50% post-therapy lesion downsizing or progressing disease during and after treatment. Relapse for CR patients was defined as the reappearance of disease at least 4 weeks after RT. All patients with CR or PR were followed up usually for 3 to 4-month intervals. High dose rate electron energy (4 MeV) from Philips SL-25 linear accelerator was used to deliver a median total dose of 3060 cGy (range 2800-3600) using weekly fraction sizes of 1.8 Gy to 4 Gy with the dose prescription being done along the central axis of the beam according to ICRU-62 guidelines [27].

TSEBT with translational technique is delivered using translational technique at our department to treat CTCL [28,29]. In this technique, patients are laid on a moving couch at 10 cm height from the floor and operated manually after completion of each radiotherapy field with supine and prone positions in 8 different fields (4 anterior and 4 posterior). Treatment fields are matched appropriately to obtain dose homogeneity

Table 1. Patient, tumor and previous treatment characteristics

Characteristics	*N (%)*
Gender	
Male	35 (68.6)
Female	16 (31.4)
Age, years	
Range	19-78
Median	51
T stage	
T2	22 (43.1)
T3	20 (39.3)
T4	9 (17.6)
Previous treatment	
Topical therapies	51 (100)
Psoralen plus ultraviolet A (PUVA)	46 (90.1)
Systemic therapies	8 (15.6)
RT fractionation, Gy	
7 x4	18 (35.2)
17 x1.8	17 (33.4)
20 x1.8	16 (31.4)

RT: Radiation therapy

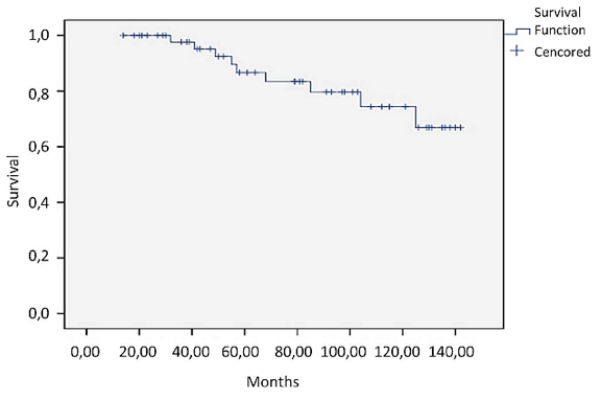

Figure 1. Overall survival.

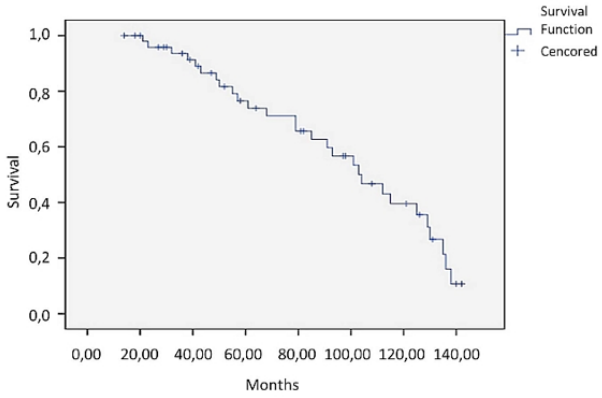

Figure 2. Disease-free survival.

by moving to predetermined position in every fraction allowing 15% dose homogeneity for all patients. Positioning of the lying patients is done in an individualized manner to allow electron beam coverage of the entire transverse dimensions of the patients. Arms and legs are supported with foams to obtain comparable SSD of the patients' trunk with SSD ranging between 192.5 and 205.5 cm according to patient thickness. Hence, radiation fields drawn on patients skin range between field sizes of 50.6x50.6 cm and 53.5x53.5 cm, changing for each radiotherapy session. TLD-100 dosimeters placed on organ at risk sites of the patient such as skin folds, periorbital sites and susceptible hotpoint sites are used to read absorbed dose in patients both on anterior and posterior superficial skin surfaces.

Statistics

The Statistical Package for Social Sciences, version 15.0 (SPSS Inc., Chicago, ILL) was used for data analysis in this study. Descriptive statistics (numbers, percents, medians, range) were used in the description of data. OS and DFS were generated using the Kaplan-Meier method. OS was calculated from diagnosis to death and DFS from diagnosis to the date of disease progression/relapse.

Results

The median patient age was 51 years (range 19-78). Thirty-five patients (68.6%) were male and

Table 2. Treatment and toxicity outcomes

Outcomes	*N (%)*	*N (%)*	*N (%)*
Follow-up (months)			
Range	14-142		
Median	79		
Treatment response	T2	T3	T4
CR	19 (86.3)	9 (45)	6 (66.7)
PR	3 (13.7)	8 (40)	2 (22.2)
NR	-	3 (15)	1 (11.1)
Total dose (cGy)	T2	T3	T4
2800	10 (45.4)	8 (40)	-
3060	9 (40.9)	7 (35)	1 (11.1)
3600	3 (13.7)	5 (25)	8 (88.9)
Toxicity *			
Grade 1	9 (17.6)		
Grade 2	20 (39.3)		
Grade 3	18 (35.3)		
Grade 4	4 (7.8)		

CR: complete remission, PR: partial remission, NR: no response, *according to RTOG/EORTC Late Radiation Morbidity Scoring Schema

16 (31.4%) female. Patient and treatment characteristics are summarized in Table 1. T-stage classification of the whole group consisted of 22 patients (43.1%) with T2 (generalized patch/plaque) disease, 20 patients (39.3%) with T3 (tumor stage) disease, and 9 patients (17.6%) with T4 (erythrodermic) disease. Of these 51 patients, 18 (35.3%) received 28 Gy in 7 fractions, 16 (31.4%) received 36 Gy in 20 fractions, and 17 (33.3%) received 30.6 Gy in 17 fractions, with fraction sizes ranging between 1.8 to 4 Gy.

Treatment response was categorized as CR, PR or NR. After TSEBT with translational technique, the CR rate was 68.6% and the PR rate was 23.5%, while the NR rate was 7.9%. At a median follow-up of 79 months (range 14-142) OS and DFS rates were 83% and 46%, respectively (Figures 1 and 2). Treatment response by T stage was as follows: For patients with T2 disease stage, the rates of CR and PR were 86.3% and 13.7%, respectively. For patients with T3 disease stage, the rates of CR, PR, and NR were 45%, 40%, and 15%, respectively. For patients with T4 stage disease, the rates of CR, PR, and NR were 66.7%, 22.2%, and 11.1%, respectively (Table 2).

Common radiation-related morbidities included skin erythema, skin blisters, joint swelling and various degrees of dry and wet desquamations, which were transient and fully reversible within 4 weeks. Radiation-related late skin injury parameters including atrophy, pigmentation changes, hair loss, telangiectasia and ulceration were assessed according to RTOG/EORTC Late Radiation Morbidity Scoring Schema after at least 3 months from TSEBT. Overall, the rates of grade 1, grade 2, grade 3, and grade 4 toxicity were 17.6% (9 patients), 39.3% (20 patients), 35.3% (18 patients), and 7.8% (4 patients), respectively. Outcomes of treatment are summarized in Table 2. All 4 patients with grade 4 late toxicity were treated using a fraction size of 4 Gy. Patients with grade 4 toxicity were hospitalized for treatment of ulcerations, and 3 of these patients also received hyperbaric oxygen treatment. One patient with T4 stage disease developed pancytopenia due to bone marrow involvement and died 8 months after completion of TSEBT albeit with regression of his skin lesion.

Discussion

Because cutaneous lymphocytes give rise to MF and the disease typically follows an indolent course, management of MF differs from nodal lymphomas. Talpur et al. recently assessed long-term outcomes of 1,263 patients treated between 1982 and 2009 for MF and Sezary syndrome [30]. Median OS was 24.4 years and PFS 16 years with most patients (76.6%) being diagnosed at early stages (IA-IIA) of MF [30]. Another study by Agar

Table 3. Published series of standard (high dose) TSEBT for mycosis fungoides

First author [Ref]	*Number of patients*	*TNM stage (Patients, N)*	*TSEBT dose (Gy)*	*Median follow-up (months)*	*Outcomes: complete response (CR) and survival*	*Toxicity*
Navi D et al. [35] (2011)	180	T2 (103) T3 (77)	30–40	77	Overall CR: 60% T2 CR: 75% T3 CR: 47% 5 year overall survival: 59% 10 year overall survival: 40%	All patients experienced mild to moderate radiation-induced dermatitis, partial or complete alopecia, nail dystrophy, and generalized xerosis.
Lindahl LM et al. [36] (2011)	35	T1 (2) T2 (14) T3 (17) T4 (2)	30 (25 patients) 4 (10 patients)	7.6	Overall CR for 30 Gy: 60% Overall CR for 4 Gy: 10% T2 CR: 66.7% T3 CR: 78.6%	Acute side effects including erythema and ulceration were observed in 80.0%. The most common long-term, although not permanent side effects were alopecia (44.0%), dry skin (36.0%), hyperpigmentation (28.0%), ocular irritation (24.0%) and temporary loss of fingernails (16.0%).
Maingon P et al. [37] (2003)	45	T1 (2) T2 (4) T3 (21) T4 (18)	24-30	85	Overall CR: 51% T3 CR: 67% T4 CR: 28% 5 year overall survival for T3: 37 % 5 year overall survival for T4: 44 %	Grade3 erythema with phlyctenes and bullous reactions were recorded in 3 (T3) and 7 (T4) patients. 1 patient died because of a large skin necrosis by septic collapse. Myelosuppression was noted in 17 patients.
Funk A et al. [38] (2008)	18	IIB (1) IVA (10) IVB (7)	<25 (6 patients) >25 (12 patients)	11	Overall CR: 50% 1 year overall survival: 48 %	Grade1-2 acute side effects were observed in all patients. Grade1-2 late skin effects were observed in 89% and hypohidrosis was seen 33%.
Harrison C et al. [39] (2011)	102	T2 (51) T3 (29) T4 (22)	5-<10 10-<20 20-<30	–	Overall CR: 31% CR: 16% [<10 Gy] CR: 35% [<20 Gy] CR: 34% [<30 Gy]	–
Jones GW et al. [42] (1999)	45	III (28) IVA (13) IVB (4)	Median 32	2.3 (years)	Overall CR: 60% 5 year progression free survival: 26 % Median overall survival: 3.4 years	All patients experienced temporary alopecia and suppressed growth of nails.
Ysebaert L et al. [40] (2004)	141	T1 (24) T2 (33)	Mean 30	114	T1 CR: 87.5% T2 CR: 84.8% 5 year survival: 90% 10 year survival: 65% 15 year survival: 42%	grade 1-2 skin toxicity 75.5% grade 3 skin toxicity 24.5%.
Chinn DM et al. [41] (1999)	148	T2 (55) T3 (27)	36 Gy in most of the patients	6.9 (years)	T2 CR: 76% T3 CR: 44% Median survival for T2 11.7 years and 5.1 years for T3	Erythema and dry skin were most frequent acute toxicities. 21 patients (14%) developed skin cancer.

et al. reported long-term outcomes of 1502 patients with MF treated between 1980 and 2009 [31]. The proportion of patients with early stage disease was 71% in their study [31]. The majority of patients with MF are diagnosed in early stages of disease as reported in the aforementioned studies [30,31]. NCCN guidelines suggest the use of skin-directed therapies as first-line treatment for

patients with early stage disease (T1, T2, and for selected T3 tumors) [32].

CR rates of 63% and 25% have been reported with the use of topical corticosteroids as skin-directed treatment for patients with T1 and T2 stage disease, respectively [6]. With topical nitrogen mustard treatment, CR rates have been reported to be 76-80% and 35-68% for patients with limited patch/plaque (stage IA) disease, and generalized patch/plaque (stage IB) disease, respectively [4]. Phototherapy with PUVA has a reported complete clinical and histologic clearing rate of 65% for all stages [5]. Phototherapy with narrow band ultraviolet B (NB-UVB) achieves a CR rate of 54.2% for stage IA and IB disease [7].

RT is a very effective skin-directed treatment for MF management given the extreme sensitivity of lymphocytes to ionizing radiation. Both local superficial irradiation and TSEBT are viable treatment options for patients with MF [8-10]. Wilson et al. reported a CR rate of 97% with local superficial irradiation of stage IA MF using a total dose of 20 to 40 Gy [9]. Piccinno et al. reported a CR rate of 94.45% at 1 month after RT using a median total dose of 22 Gy for patients with stage IA MF [10]. Given the favorable results of the aforementioned studies, local superficial irradiation at a dose of 20 to 40 Gy may be used to achieve excellent CR rates with negligible toxicity for patients with minimal stage I A MF [8-10]. However, only a very small proportion of patients (approximately 5%) with MF have minimal stage I disease. NCCN guidelines suggest the use of TSEBT to achieve local control of generalized locally advanced disease [32].

Complex skin surface of MF patients poses a formidable challenge to the treatment team while delivering TSEBT with any technique. Increasing the number of treatment fields and optimal positioning of the patients may be considered to achieve a homogeneous dose distribution. Nevertheless, there are still technical and practical challenges in delivering TSEBT, which makes it a less appealing treatment option and limits its use in several centers worldwide. Set-up procedures for performing TSEBT warrant the availability of proper infrastructure. Close collaboration between radiation oncologists, medical physicists and dermatologists is of utmost importance for optimal management of patients.

The translational technique was developed at the Christie Hospital in England [33]. Northern Israel Oncology Center has modified this initial technique [34]. A stationary reclined patient at the same SSD is treated using large electron fields including 4 to 5 pairs of transversally angled beams.

We have been using TSEBT with translational technique for MF management since 1984. Our 3 decades of experience reveals that TSEBT with translational technique offers a viable treatment option in the management of both early and advance disease [28,29]. We typically use an electron energy of 4 MeV to treat epidermal and dermal lesions homogeneously. Concurrent or adjuvant boost with electron fields is used for shadowed irregular regions including the scalp, perineum, sole and other skin folds.

In the study by Ysebaert et al., TSEBT without adjuvant treatment has proved to be effective for the management of early stage MF [40]. At 3 months after TSEBT, they reported a CR rate of 87.5% for the 24 patients with T1 disease stage and a CR rate of 84.8% for the 33 patients with T2 disease stage using a median total dose of 30 Gy [40].

In their retrospective series with 148 patients, Chinn et al. reported that TSEBT with or without adjuvant topical nitrogen mustard was highly effective in the initial management of patients with T2 and T3 stage MF [41].

TSEBT may be used to ameliorate severe cutaneous symptoms of patients with T4 (erythrodermic) MF. In the study by Jones et al. with 54 erythrodermic MF patients, TSEBT was used as monotherapy [42]. They reported a CR rate of 60% using a median RT dose of 32 Gy [42]. In our study, CR rates were 86.3, 45, and 66.7% for patients with T2, T3, and T4 MF stage, which appears to be consistent with the literature. A summary of published series using TSEBT for MF management is shown in Table 3.

Making a direct comparison between different treatment options for MF is complicated by several factors. MF is a rare and typically chronic disease. There may be significant diversity in patient and treatment characteristics, and available treatments are used interchangeably, sequentially, or simultaneously to achieve optimal outcomes.

TSEBT is generally a well-tolerated treatment for MF, and toxicity may be minimized by decreasing the fraction size. Acute side effects of TSEBT include pruritus, dryness, erythema, alopecia and formation of bullae in hands and feet. Late toxicities include loss of nails, alopecia, telangiectasias, and local sensory loss. Systemic adverse effects are infrequent given the limited penetration range of electrons. In our study, most patients receiving daily fractions of 1.8 Gy had excellent treatment

tolerance while 4 patients receiving daily fractions of 4 Gy to expedite treatment experienced grade 4 late skin toxicity.

We acknowledge the limitations of our study including its retrospective design and limited number of patients. Nevertheless, clinical data on the management of MF is mostly based on retrospective series due to its rarity.

In conclusion, TSBET with translational technique offers excellent local control and favorable OS rates along with substantial relief of symptoms for patients with MF refractory to topical chemotherapy and phototherapy. However, the clinical management of MF is complex and an interdisciplinary team approach is warranted to achieve optimal treatment outcomes.

References

1. Willemze R, Jaffe ES, Burg G et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005;105:3768-3785.
2. Assaf C, Gellrich S, Steinhoff M et al. Cutaneous lymphomas in Germany: an analysis of the Central Cutaneous Lymphoma Registry of the German Society of Dermatology (DDG). J Dtsch Dermatol Ges 2007;5:662-668.
3. Girardi M, Heald PW, Wilson LD The pathogenesis of mycosis fungoides. N Engl J Med 2004;350:1978-1988.
4. Kim YH. Management with topical nitrogen mustard in mycosis fungoides. Dermatol Ther 2003;16:288-298.
5. Herrmann JJ, Roenigk HH Jr, Hurria A et al. Treatment of mycosis fungoides with photochemotherapy (PUVA): long-term follow-up. J Am Acad Dermatol 1995;33(2 Pt 1):234-242.
6. Zackheim HS, Kashani-Sabet M, Amin S. Topical corticosteroids for mycosis fungoides. Experience in 79 patients. Arch Dermatol 1998;134:949-954.
7. Gathers RC, Scherschun L, Malick F, Fivenson DP, Lim HW. Narrow band UVB phototherapy for early-stage mycosis fungoides. J Am Acad Dermatol 2002;47:191-197.
8. Jones GW, Kacinski BM, Wilson LD et al. Total skin electron radiation in the management of mycosis fungoides: consensus of the European Organization for Research and Treatment of Cancer (EORTC) Cutaneous Lymphoma Project Group. J Am Acad Dermatol 2002;47:364-370.
9. Wilson LD, Kacinski BM, Jones GW. Local superficial radiotherapy in the management of minimal stage IA cutaneous T-cell lymphoma (mycosis fungoides). Int J Radiat Oncol Biol Phys 1998;40:109-115.
10. Piccinno R, Caccialanza M, Percivalle S. Minimal stage IA mycosis fungoides. Results of radiotherapy in 15 patients. J Dermatolog Treat 2009;20:165-168.
11. Duvic M, Martin AG, Kim Y et al. Phase 2 and 3 clinical trial of oral bexarotene (Targretin capsules) for the treatment of refractory or persistent early-stage cutaneous T-cell lymphoma. Arch Dermatol 2001;137:581-593.
12. Olsen E, Duvic M, Frankel A et al. Pivotal phase III trial of two dose levels of denileukin diftitox for the treatment of cutaneous T-cell lymphoma. J Clin Oncol 2001;19:376-388.
13. Olsen EA, Kim YH, Kuzel TM et al. Phase IIb multicenter trial of vorinostat in patients with persistent, progressive, or treatment refractory cutaneous T-cell lymphoma. J Clin Oncol 2007;25:3109-3115.
14. Whittaker SJ, Demierre MF, Kim EJ et al. Final results from a multicenter, international, pivotal study of romidepsin in refractory cutaneous T-cell lymphoma. J Clin Oncol 2010;28:4485-4491.
15. Kennedy GA, Seymour JF, Wolf M et al. Treatment of patients with advanced mycosis fungoides and Sézary syndrome with alemtuzumab. Eur J Haematol 2003;71:250-256.
16. Chiarion-Sileni V, Bononi A, Fornasa CV et al. Phase II trial of interferon-alpha-2a plus psolaren with ultraviolet light A in patients with cutaneous T-cell lymphoma. Cancer 2002;95:569-575.
17. Wollina U, Looks A, Meyer J et al. Treatment of stage II cutaneous T-cell lymphoma with interferon alfa-2a and extracorporeal photochemotherapy: a prospective controlled trial. J Am Acad Dermatol 2001;44:253-260.
18. Duvic M, Talpur R, Wen S et al. Phase II evaluation of gemcitabine monotherapy for cutaneous T-cell lymphoma. Clin Lymphoma Myeloma 2006;7:51-58.
19. Foss FM. Evaluation of the pharmacokinetics, preclinical and clinical efficacy of pralatrexate for the treatment of T-cell lymphoma. Expert Opin Drug Metab Toxicol 2011;7:1141-1152.
20. Girardi M, Berger CL, Wilson LD et al. Transimmunization for cutaneous T cell lymphoma: a phase I study. Leuk Lymphoma 2006;47:1495-1503.
21. Molina A, Zain J, Arber DA et al. Durable clinical, cytogenetic, and molecular remissions after allogeneic hematopoietic cell transplantation for refractory Sezary syndrome and mycosis fungoides. J Clin Oncol 2005;23:6163-6171.

22. Wu PA, Kim YH, Lavori PW, Hoppe RT, Stockerl-Goldstein KE. A meta-analysis of patients receiving allogeneic or autologous hematopoietic stem cell transplant in mycosis fungoides and Sézary syndrome. Biol Blood Marrow Transplant 2009;15:982-990.
23. Jacobsen ED, Kim HT, Ho VT et al. A large single-center experience with allogeneic stem cell transplantation for peripheral T-cell non-Hodgkin lymphoma and advanced mycosis fungoides/Sezary syndrome. Ann Oncol 2011;22:1608-1613.
24. Trump JG, Wright KA, Evans WW, Anson JH, Hare HF. High energy electrons for the treatment of extensive superficial malignant lesions. Am J Roentgenol 1953;69:623-629.
25. Podgorsak EB (Ed): Radiation oncology physics: A handbook for teachers and students. Vienna, Austria: I.A.E. Agency; 2005.
26. AAPM report no:23. Total skin electron therapy: technique and dosimetry. New York: American Institute of Physics; 1987.
27. Prescribing, Recording and Reporting Photon Beam Therapy. J ICRU, Report 62; 1999.
28. Oysul K, Dirican B, Beyzadeoglu M, Surenkok S. Evaluation of total skin electron beam therapy and treatment morbidity in mycosis fungoides. THOD Turk J Hematol Oncol 2004;3:153-160.
29. Ulutin Hc, Beyan C, Pak Y. Total skin electron beam therapy for cutaneous T-cell lymphoma: Turkish experience with translational technique. Hematologia (Budap) 2002;32:397-403.
30. Talpur R, Singh L, Daulat S et al. Long-term outcomes of 1,263 patients with mycosis fungoides and Sézary syndrome from 1982 to 2009. Clin Cancer Res 2012;18:5051-5060.
31. Agar NS, Wedgeworth E, Crichton S et al. Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. J Clin Oncol 2010;28:4730-4739.
32. Zelenetz AD, Abramson JS, Advani RH et al. NCCN clinical practice guidelines in oncology for non-Hodgkin's lymphomas. J Natl Compr Canc Netw 2010;8:288-334.
33. Williams PC, Hunter RD, Jackson SM. Whole body electron therapy in mycosis fungoides – a successful translational technique achieved by modification of an established linear accelerator. Br J Radiol 1979;52:302-307.
34. Kuten A, Stein M, Mandelzweig Y et al. Total-skin electron irradiation for cutaneous T-cell lymphoma: the Northern Israel Oncology Center experience. Strahlenther Onkol 1991;167:392-396.
35. Navi D, Riaz N, Levin YS, Sullivan NC, Kim YH, Hoppe RT. The Stanford University Experience With Conventional-Dose, Total Skin Electron-Beam Therapy in the Treatment of Generalized Patch or Plaque (T2) and Tumor (T3) Mycosis Fungoides. Arch Dermatol 2011;147:561-567.
36. Lindahl LM, Kamstrup MR, Petersen PM et al. Total skin electron beam therapy for cutaneous T-cell lymphoma: a nationwide cohort study from Denmark. Acta Oncol 2011;50:1199-1205.
37. Maingon P, Truc G, Dalac S et al. Radiotherapy of advanced mycosis fungoides: indications and results of total skin electron beam and photon beam irradiation. Radiother Oncol 2000;54:73-78.
38. Funk A, Hensley F, Krempien R et al. Palliative total skin electron beam therapy (TSEBT) for advanced cutaneous T-celllymphoma. Eur J Dermatol 2008;18:308-312.
39. Harrison C, Young J, Navi D et al. Revisiting low dose total skin electron beam therapy in mycosis fungoides. Int J Radiat Oncol Biol Phys 2011;81:e651-e657.
40. Ysebaert L, Truc G, Dalac S et al. Ultimate results of radiation therapy for T1-T2 mycosis fungoides (including reirradiation). Int J Radiat Oncol Biol Phys 2004;58:1128-1134.
41. Chinn DM, Chow S, Kim YH, Hoppe RT. Total skin electron beam therapy with or without adjuvant topical nitrogen mustard or nitrogen mustard alone as initial treatment of T2 and T3 mycosis fungoides. Int J Radiat Oncol Biol Phys 1999;43:951-958.
42. Jones GW, Rosenthal D, Wilson LD. Total skin electron radiation for patients with erythrodermic cutaneous T-cell lymphoma (mycosis fungoides and the Sézary syndrome). Cancer 1999;85:1985-1995.