



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Basic Original Report

# Low-Dose Hypofractionated Total Skin Electron Beam Therapy for Adult Cutaneous T-Cell Lymphoma



Elizabeth B. Jeans, MEd, MD,<sup>a</sup> Yue-Houng Hu, PhD,<sup>a</sup>  
Bradley J. Stish, MD,<sup>a</sup> Brian King, MD,<sup>b</sup> Mark Davis, MD,<sup>b</sup>  
William S. Harmsen, MS,<sup>c</sup> Kristin M. Fruth, BS,<sup>c</sup> Sarah E. Locher, PhD,<sup>a</sup>  
Christopher L. Deufel, PhD,<sup>a</sup> Jaden D. Evans, MD,<sup>a,d</sup>  
James A. Martenson, MD,<sup>a</sup> and Scott C. Lester, MD<sup>a,\*</sup>

<sup>a</sup>Department of Radiation Oncology, Mayo Clinic, Rochester, Minnesota; <sup>b</sup>Department of Dermatology, Mayo Clinic, Rochester, Minnesota; <sup>c</sup>Department of Biomedical Statics and Informatics, Mayo Clinic, Rochester, Minnesota; and <sup>d</sup>Department of Radiation Oncology, Intermountain Healthcare, Ogden, Utah

Received 9 April 2020; revised 8 July 2020; accepted 4 August 2020

## Abstract

**Purpose:** Historically, the standard of care for total skin electron beam therapy (TSEBT) delivered 30 to 36 Gy over 5 to 10 weeks. Given the high risk of relapse, a majority of patients require additional treatments. Therefore, attempts to use a shortened course of TSEBT have been investigated.

**Methods and Materials:** We conducted a single-institution retrospective review to evaluate disease response, control, and toxicity using a low-dose, hypofractionated course of TSEBT (HTSEBT) in patients with mycosis fungoides.

**Results:** Forty patients received 57 courses of HTSEBT. Median dose (Gy)/fractionation was 12/3, spanning a median time of 2.4 weeks. Overall response rate of patients assessed (n = 54) was 100%. Thirty-one courses (57.4%) resulted in a complete response and 23 courses (42.6%) resulted in a partial response. Cumulative incidence of progressive skin disease at 3 months was 37.2%, at 6 months, 56.9%, and at 1 year, 81.5%. Of the 40 patients treated with a first course of HTSEBT, 31 received subsequent courses of radiotherapy. Cumulative incidence of subsequent treatment was 28.0% at 3 months, 46.8% at 6 months, and 70.0% at 1 year. Patients who underwent repeat courses of HTSEBT continued to have similar treatment responses to repeat courses without increased toxicities. Toxicities from all courses were acceptable with the exception of 1 patient, who experienced grade 4 skin toxicity (moist desquamation requiring hospitalization).

**Conclusions:** Low-dose HTSEBT provides good palliation in patients with cutaneous T-cell lymphoma with a satisfactory response and toxicity profile. HTSEBT allows therapy to be completed in far fewer treatments. Low-dose HTSEBT is an appropriate treatment option for patients unable to come for daily treatment. HTSEBT provides a way to decrease exposure to other patients and staff during public health emergencies such as the coronavirus disease 2019 (COVID-19) pandemic.

© 2020 The Author(s). Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Sources of support: This work had no specific funding.

Disclosures: The initial findings of this study were presented in abstract format at American Society for Radiation Oncology 2019.

\* Corresponding author: Scott C. Lester, MD; E-mail: [lester.scott@mayo.edu](mailto:lester.scott@mayo.edu).

<https://doi.org/10.1016/j.prro.2020.08.001>

1879-8500/© 2020 The Author(s). Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Total skin electron beam therapy (TSEBT) is a highly effective palliative treatment for patients with mycosis fungoides and other forms of cutaneous T-cell lymphoma (CTCL). Dose guidelines published by the National Comprehensive Cancer Network recommend a total dose of 12 to 36 Gy in TSEBT patients, and the International Lymphoma Radiation Oncology Group has recommended total doses ranging from 8 to 36 Gy.<sup>1,2</sup> Despite a lack of guidelines regarding fraction size, most reports have described a daily dose of 1 Gy administered 4 to 5 times per week.<sup>3</sup>

Following TSEBT, most patients will experience progressive disease within 6 to 12 months. Low-dose TSEBT using 12 Gy in 8 to 12 fractions has the potential to decrease the burden of treatment for patients. Favorable results, including response rates of 87% to 88%, have been reported by Stanford<sup>4</sup> and the UK Cutaneous Lymphoma Group.<sup>5</sup>

Hypofractionated regimens are more convenient for patients.<sup>6,7</sup> We have combined the concept of low-dose palliative TSEBT with hypofractionation, resulting in a regimen that can generally be completed with 4 or fewer treatments. Previous results have been published from a database of patients with cutaneous lymphoma who were treated with radiation therapy using a variety of techniques, including focal radiation therapy, regional radiation therapy, and TSEBT between January 2000 through September 2017.<sup>8</sup> This study was undertaken to provide a detailed assessment of outcomes in the subset of patients treated with hypofractionated total skin electron beam therapy (HTSEBT), further defined below. The database in this subset of patients was updated to include all patients treated with HTSEBT from 2000 to 2020.

## Methods and Materials

This study was performed with institutional review board approval utilizing the aforementioned institutional database. Patients included in this study had a diagnosis of CTCL and were treated with HTSEBT, defined as  $\geq 2.5$  Gy per fraction typically given once every 1 to 2 weeks, delivered at the Mayo Clinic in Rochester, MN, from January 2000 to January 2020. This report includes a description of an illustrative case, including photographs. Written permission was obtained from the patient to disclose this case-specific information.

Patients were included for analysis if age 18 or older, Eastern Cooperative Oncology Group performance status 0 to 3, and had biopsy-confirmed stage IB to III CTCL. Patient characteristics, treatment details, toxicities, and oncologic outcomes were recorded and updated for each patient. Additionally, given the rarity of centers delivering TSEBT, the 2-way travel distance by road between our

center and each patient's home was collected (<https://www.google.com/maps>).

The primary objectives of this study were to examine the effectiveness and toxicity of HTSEBT. Endpoints included clinical response of cutaneous lesions, date of progressive skin disease, and date of subsequent radiation therapy treatments. Toxicities were recorded using Common Terminology Criteria for Adverse Events version 4.03.

Electrons with an extended source to surface distance were used to deliver total skin electron therapy.<sup>9</sup> For 55 of 57 courses, the Stanford technique was used.<sup>10</sup> The Stanford technique has the patient assume 6 standing poses at 60° increments: anterior, posterior, right anterior oblique, right posterior oblique, left anterior oblique, and left posterior oblique. At each angle, 2 fields are treated, one for the upper body and a second for the lower body, resulting in a total of 12 fields. A thin polycarbonate scattering panel was used at approximately 212 cm from the isocenter. A 6-MeV energy linear accelerator in high-dose total skin electron treatment mode was used to deliver dual electron fields at each of the 6 positions with central rays  $\pm 20^\circ$  from the horizontal. In all treatments where the patient could stand, 12 fields were treated daily. Two courses were delivered using a lying-on-the floor position due to poor performance status and inability to remain standing throughout the length of treatment.<sup>9,11</sup> Most patients had significant debility and were unable to tolerate eye shields because of an unacceptable risk of falling. Accordingly, eye shields were not routinely used.

Initial follow-up and assessment of response was largely completed by radiation oncology teams with experience in the treatment and assessment of cutaneous lymphoma. At follow-up visits, response assessment was recorded in the medical record. Pretreatment and post-treatment photography of either the entire body or large areas of the body (eg, the entire trunk) was extensively used at follow-up to aid in assessing and documenting response. Patients were not routinely seen by a hematologist or dermatologist at the time of initial follow-up and response assessment. Full details regarding personnel involved in response assessment are described in the Results. Follow-up subsequent to assessment of response was generally performed at the time of patient-reported progression of disease, which initiated prompt scheduling of the patient for a visit with the patient's physician.

Response to treatment was assessed according to International Society for Cutaneous Lymphoma criteria<sup>12</sup> with the exception of a subdivision of patients with partial response, as described below. Complete response was defined as 100% clearance of skin lesions. Initial analysis of the data subdivided partial response (PR) into PR $_{\geq 50-95}$ , which were cases with  $\geq 50\%$  to 95% clearance of skin lesions and near complete response, (NCR) $_{>95-99}$ , defined as  $>95\%$  to 99% clearance. In a post hoc analysis, we sought to provide preliminary evidence regarding the

validity of this subdivision of partial response by determining whether time to progressive skin disease in patients with  $NCR_{>95-99}$  was more prolonged than in patients with  $PR_{\geq 50-95}$ .

Progressive skin disease was defined as  $\geq 25\%$  increase in skin disease from baseline or any disease recurrence in those with a complete response. Date of skin progression was recorded as the date assessed by the physician. Subsequent radiation therapy treatments were collected as repeat total skin therapy, repeat focal treatment, or both. Date of subsequent radiation therapy treatment, defined as time from completion of total skin radiation therapy to subsequent start of radiation therapy treatment was collected for applicable patients. Toxicities were retrospectively assessed according to Common Terminology Criteria for Adverse Events version 4.03 using medical photographs and information in the medical record, obtained through clinic follow-up appointments, telephone communication, or outside hospital records.

All outcomes were assessed starting on the date that the radiation therapy was completed. The cumulative incidence of skin progression and subsequent radiation therapy delivery was estimated, treating death as a competing risk. A univariate cox model was calculated to discern a difference in skin progression based on course number for patients who underwent repeat courses of HTSEBT. In a post hoc analysis, the cumulative incidence of skin progression and subsequent radiation therapy was estimated (using death as a competing risk factor) by grouping patients into cohorts based on response to first course of HTSEBT. In the first analysis, patients were grouped into CR,  $PR_{\geq 50-95}$ , and  $NCR_{>95-99}$ , and in the second analysis, patients were grouped into CR and PR alone, eliminating the  $NCR_{>95-99}$  cohort. Univariate cox models were calculated to discern a difference in time to progressive skin disease or subsequent radiotherapeutic interventions among these various groupings. Data was analyzed using SAS version 9.4. A 2-sided  $P$  value of  $\leq .05$  was considered significant in all analyses.

## Results

Forty-seven patients were identified as having one or more courses of HTSEBT. Seven patients were excluded from the analysis: 5 patients with atypical histology and 2 patients declined use of their medical record for research purposes. Therefore, 40 patients who received 57 courses of hypofractionated TSEBT were included; including 14 patients who received a second course of HTSEBT and 3 who received a third course of HTSEBT. With the exception of a single patient, no patients were treated with antineoplastic pharmaceutical agents or other therapies for cutaneous lymphoma during their HTSEBT course or before assessment of response. One patient was inadvertently left on oral bexarotene during radiotherapy, despite

having experienced progression on this agent. Bexarotene was promptly discontinued after the first fraction.

Of the 40 patients evaluated (Table 1), median age at diagnosis was 67 years old (range, 33-93). Patients were predominantly male (70%). Eighty-one percent of patients had Eastern Cooperative Oncology Group performance status 0 or 1 before course of radiation therapy. Most patients had stage IB or IIB disease before initiation of radiotherapy. The median round-trip distance between patients' homes and our treatment center was 284 miles (range, 4-1150).

Median dose and fractionation was 12 Gy in 3 fractions, spanning a median time of 2.4 weeks. The most common regimen was 12 Gy in 3 fractions (17 courses of treatment, 29.8%). The second most common regimen was 8 Gy in 2 fractions (14 courses of treatment, 24.6%). Additional dose and fractionation schemes are shown in Table 2.

Three patient courses had no reported follow-up but still contributed to the database with regard to presenting features, toxicity, and distance traveled from home. Of the

**Table 1** Patient demographics and characteristics of each patient before course of hypofractionated total skin electron beam therapy

Patients	N = 40
Age, y	
Median	67.0
Range	(33.0-93.0)
Sex, n (%)	
F	12 (30.0)
M	28 (70.0)
HTSEBT course, n (%)	
Single	26 (65.0)
Multiple	14 (35.0)
Courses	N = 57
ECOG at treatment, n (%)	
0	13 (22.8)
1	33 (57.9)
2	6 (10.5)
3	5 (8.8)
Stage (%)	
Unknown	4 (7.0)
IA	1 (1.8)
IB	4 (7.0)
IIB	6 (10.5)
III	2 (3.5)
IVA	38 (66.7)
IVB	2 (3.5)
T-stage, n (%)	
T1b	1 (1.8)
T2	36 (63.2)
T3	15 (26.3)
T4	5 (8.7)

Abbreviation: ECOG = Eastern Cooperative Oncology Group; HTSEBT = hypofractionated total skin electron beam therapy.

**Table 2** Dose and fractionation regimens

Total dose, Gy	Number of fractions				
	1	2	3	4	5
	<i>Number of cases (total n = 57)</i>				
2.5	1				
3.5	1				
4	4	1			
4.5	4				
8		14		1	
9			2		
12			17	1	
12.5			1		
14				1	
15			1		1
16				4	
20					2
26.4				1	

**Table 3** Response rate after HTSEBT

Response	No. of courses (N = 57)	% of assessed (N = 54)
Complete	31	57.4
Partial	23	42.6
Not evaluable	3	-

*Abbreviation:* HTSEBT = hypofractionated total skin electron beam therapy.

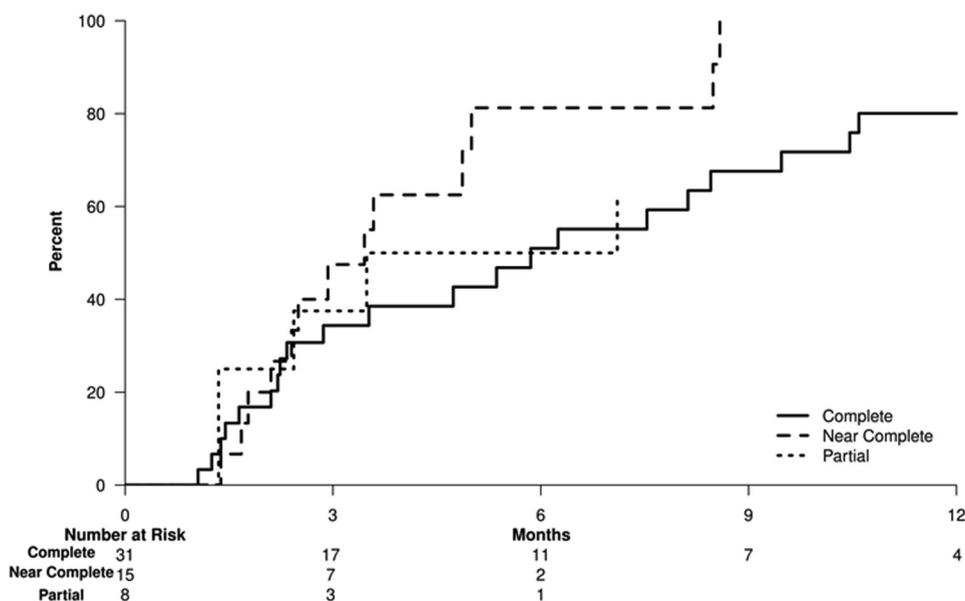
remaining 54 courses, patients were assessed for response at a median follow up of 29 days (range, 7-216 days; interquartile range, 19.0-65.5 days). Forty-nine of 54 responses (91%) were assessed at the time of follow-up by a radiation oncology team with experience in the treatment and assessment of cutaneous lymphoma. Of the 49 responses assessed in office, all cases were evaluated by the initial treating provider with the exception of one case that was transitioned between 2 radiation oncology providers at the time of retirement of the initial treating radiation oncologist. Two cases were assessed in follow-up by the patient’s hematologist. The other 3 responses were recorded after a thorough conversation with the patient on the phone regarding disease burden. All patients with

complete responses were evaluated in office by the treating radiation oncologist.

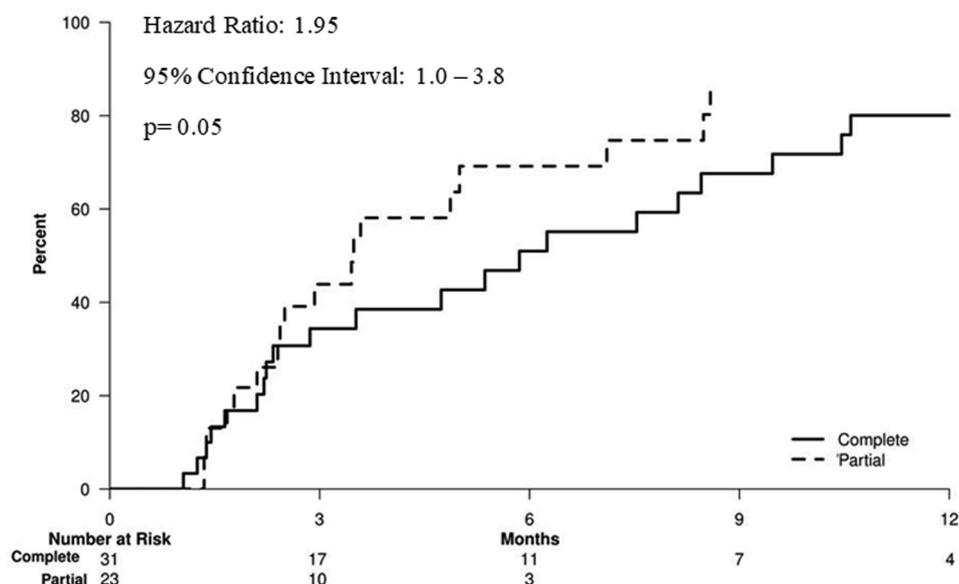
The overall response rate for patients was 100%. Thirty-one courses (57.4%) resulted in a complete response, and 23 courses (42.6%) resulted in a partial response (Table 3).

An exploratory analysis did not provide evidence for the validity of subdivision of patients with PR. Specifically, patients with  $NCR_{>95-99}$  did not have a more prolonged time to skin progression than those with  $PR_{\geq 50-95}$  (Fig 1). Accordingly, we eliminated the subdivision of near complete response from our summary of response rates (Table 3). Additional post hoc analyses did demonstrate that patients who experienced a CR had a more prolonged time to skin progression than patients who experienced a PR (Fig 2).

The median time to skin progression was 89 days. As previously stated, we used the principle that a >25% increase in disease constituted progression in patients who previously had a partial response. It was not possible to calculate the percentage increase in disease in the context of a retrospective study. However, it was our uniform experience that progression was sufficiently dramatic as to clearly



**Figure 1** Cumulative incidence of progressive skin disease based upon response to initial course of hypofractionated total skin electron beam therapy (complete response vs near complete response<sub>>95-99</sub> vs partial response<sub>≥50-95</sub>).



**Figure 2** Cumulative incidence of progressive skin disease based upon response to initial course of hypofractionated total skin electron beam therapy (complete response vs partial response).

be above the 25% threshold. Cumulative incidence of progressive skin disease at 3 months was 37.2%, at 6 months, 56.9%, and at 1 year, 81.5% (Table 4, Fig 3).

Thirty-nine courses of subsequent radiation therapy were delivered. This comprised 17 repeat HTSEBT courses and 23 repeat focal skin treatments. Cumulative incidence of subsequent treatment (either HTSEBT or focal skin treatment) was 28.0% at 3 months, 46.8% at 6 months, and 70.0% at 1 year. (Table 4, Fig 4a). Cumulative incidence of repeat HTSEBT was 9.6% at 3 months, 14.4% at 6 months, and 30.8% at 1 year (Table 4, Fig 4b). The cumulative incidence of repeat HTSEBT or focal treatment was longer for patients with a complete response to their prior treatment compared with a partial response, 32.5% (95% confidence interval [CI], 18.9-56.0) at 6 months versus 64.8% (95% CI, 47.2-89.0), respectively (hazard ratio 3.28,  $P < .01$ ).

Patients who underwent repeat courses of HTSEBT did not experience more rapid skin progression than seen after a first course of radiation therapy (Fig 5). With the first courses of treatment as reference, the hazard ratio for skin progression for a second course of treatment was 0.52 (95% CI, 0.12-2.19) and 0.87 (95% CI, 0.38-2.00) for a third course of treatment.

The most common acute radiation-induced side effects were grade 1 or 2 and included pruritus (n = 9, 16%),

diffuse erythema (n = 12, 21%), skin pain or discomfort (n = 8, 14%), lower extremity swelling (n = 5, 9%), swelling localized around the original lesions (n = 1, 2%), finger swelling (n = 1, 2%), upper-lip swelling (n = 1, 2%), and desquamation or blister formation (n = 9, 16%). Four patients reported acute fatigue (7%) and 2 patients experienced eye irritation and dryness (5%). Treatment-related alopecia was reported in 41% (n = 22) of cases, whereas nail ridging was present in 17% of cases (n = 9). No acute grade 3 toxicity was observed. One patient experienced acute grade 4 diffuse moist desquamation requiring hospitalization. Two patients reported late hyperpigmentation.

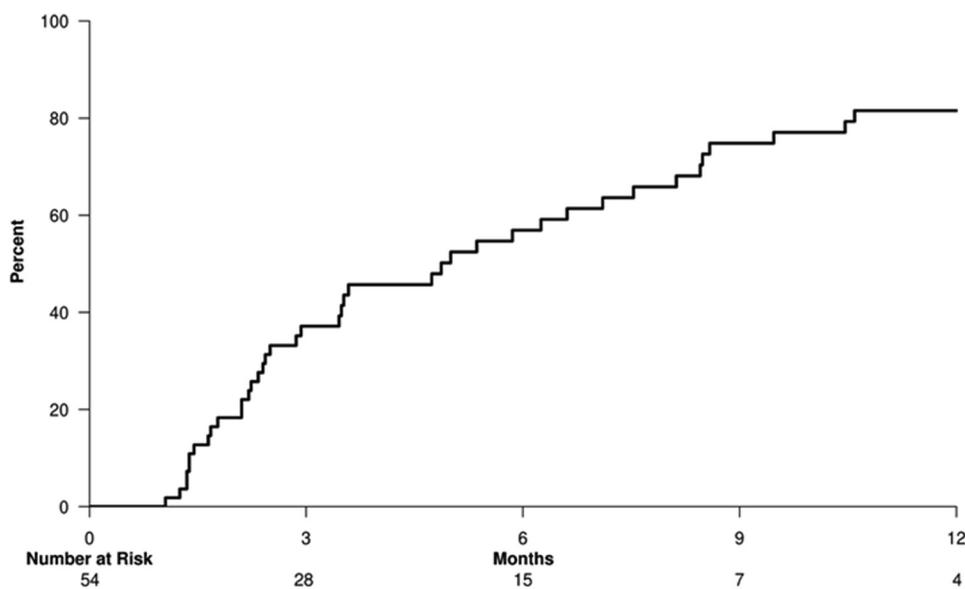
## Discussion

Multiple previous studies have analyzed response rates of TSEBT delivered with a total dose of 30 to 36 Gy delivered over 5 to 10 weeks. These studies typically describe an excellent overall response rate of greater than 90% with complete response rates ranging between 60% and 95%.<sup>10,13</sup> Although these noted a median time until disease progression varying from 6 to 12 months,<sup>10,13</sup> patients on average spend approximately 2

**Table 4** Progressive skin disease and subsequent treatment outcomes (with 95% confidence intervals)

Outcome	3 mo	6 mo	1 y
Cumulative incidence of progressive skin disease, %	37.2 (26.2-52.7)	56.9 (71.3-93.2)	81.5 (71.3-93.2)
Cumulative incidence of subsequent treatment (focal or HTSEBT), %	28.0 (18.2-43.1)	46.8 (34.8-62.8)	70.0 (58.1-84.5)
Cumulative Incidence of Subsequent HTSEBT, %	9.62 (4.18-22.2)	14.4 (7.2-28.8)	30.8 (18.8-50.5)

Abbreviation: HTSEBT = hypofractionated total skin electron beam therapy.



**Figure 3** Cumulative incidence of progressive skin disease after completion of all courses of hypofractionated total skin electron beam therapy.

to 3 months undergoing treatment. Results from a pooled analysis of phase 2 clinical trials published by Hoppe et al in 2015<sup>4</sup> analyzed 33 patients treated with low-dose total skin electron beam radiation therapy, 12 Gy delivered as 1 Gy per fraction over 3 weeks. In this series, the response rate was 88%, and the complete response rate was 27%.<sup>4</sup>

Hypofractionated low-dose total skin electron beam therapy resulted in a 100% response rate in evaluable patients in the present study, with 57.4% experiencing a complete response and 42.6% experiencing a partial response. The durability of response was very heterogeneous, with 62.8% free of skin progression at 3 months and 43.1% free of skin progression at 6 months.

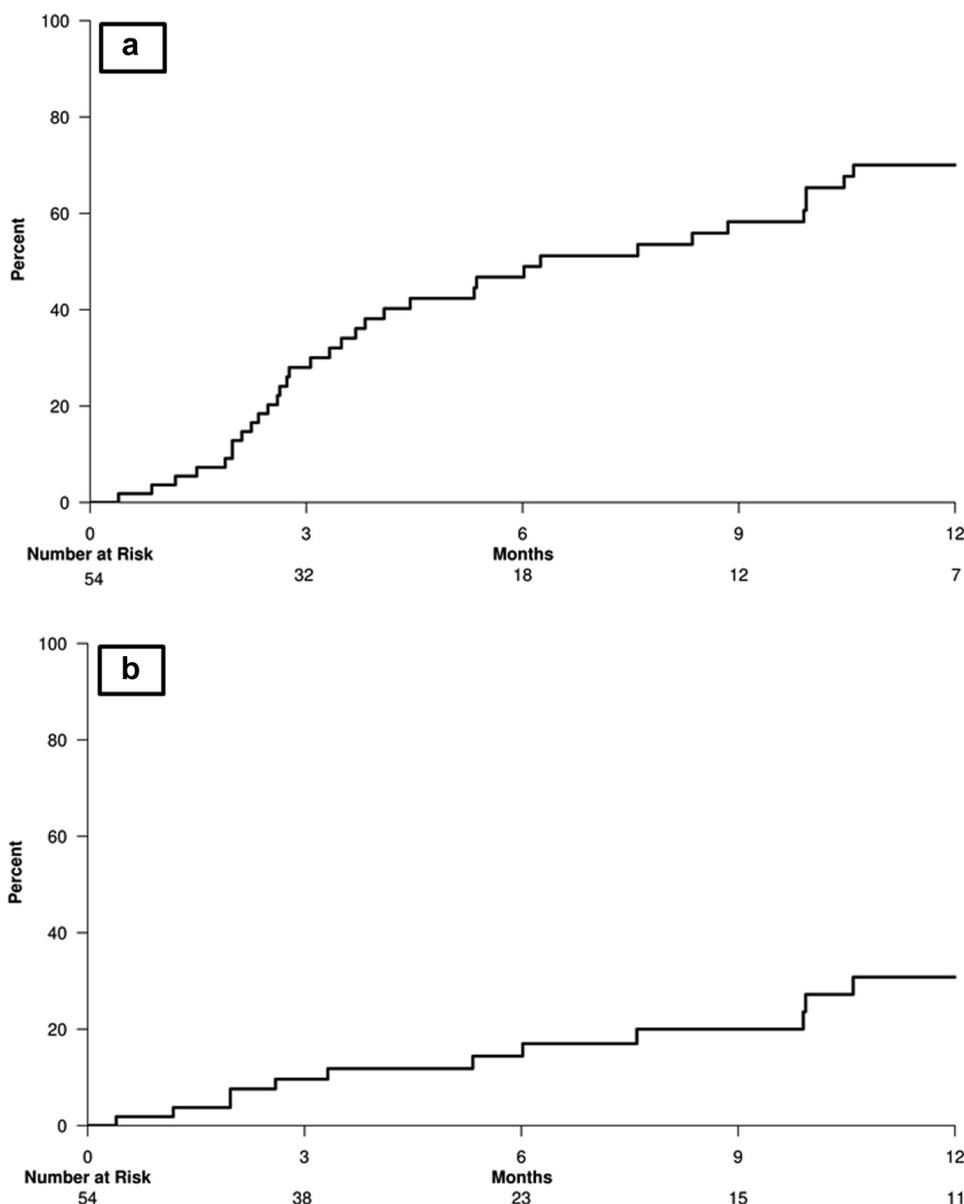
Our results do not provide evidence that a subdivision of partial response into patients with >95% clearance of disease and those with 50% to 95% clearance of disease is clinically useful (Fig 1). Validation of any subdivision of partial response is needed before use in routine clinical practice or use as a measure of patient benefit. Validation studies would preferably use prospectively acquired data and could include evaluation of symptoms at the time of response assessment and determination of the prognostic significance of different levels of response.

A decreased likelihood of response has been reported after retreatment with TSEBT.<sup>10</sup> In contrast, the response rate was 100% among evaluable patients after a second or third course of HTSEBT in the present study. Patients treated with a second or third course of HTSEBT did not experience a more rapid rate of skin progression than was observed after a first course of HTSEBT (Fig 5).

Treatment was generally well-tolerated, and our regimen compares favorably with other published toxicity data.<sup>14,15</sup> An exception occurred in one patient, who experienced grade 4 toxicity. The patient presented with

severely painful erythroderma and was not a candidate for other treatment options. Because of the potential for severe cutaneous toxicity, erythroderma has been described as a relative contraindication to TSEBT.<sup>16,17</sup> Before proceeding with palliative TSEBT, the patient was provided with thorough informed consent, including the option of supportive measures only. The patient expressed a preference to proceed with HTSEBT and received a total dose of 8 Gy delivered in 2 fractions over 2 weeks. Two days after the second fraction, the patient developed grade 4 skin toxicity requiring hospitalization. After recovery from toxicity, the patient had a complete response to treatment and was pain-free (21 days after radiation therapy delivery). The patient was again in severe pain after recurrence 3 months later and a second course of palliative treatment was discussed, again with thorough informed consent. Based on the palliation obtained from the first course, the patient requested retreatment. A second course of 4.5 Gy delivered in a single fraction of HTSEBT had a similar outcome with regard to toxicity. No follow-up in disease response is available after the patient's second course of HTSEBT.

This retrospective study has several limitations. The patients represent a heterogeneous population, in particular with respect to stage, and the stage could not be determined in 7% of the cases. Scheduling of follow-up was not standardized. Direct comparison to other studies is difficult as the Modified Severity Weighted Assessment Tool was not recorded, similar to other retrospective studies<sup>18,19</sup> and 1 prospective study.<sup>20</sup> Reliable information regarding other nonradiotherapeutic treatments subsequent to last assessment of response was not available and is not reported. Another limitation of this study is that some toxicities were almost certainly underreported, particularly alopecia and nail ridging.

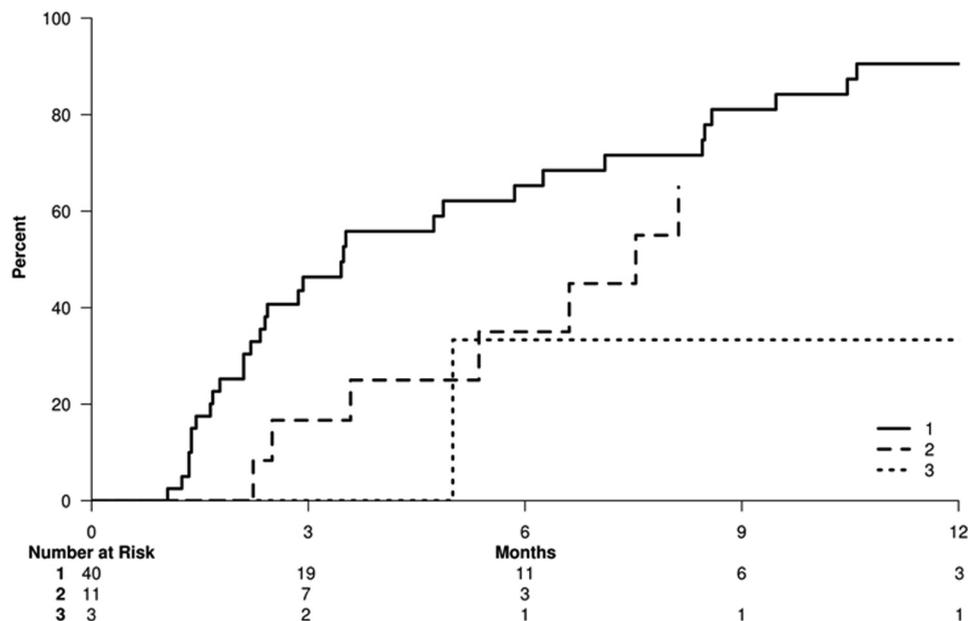


**Figure 4** Cumulative incidence of repeat treatment, including (a) focal or repeat HTSEBT or (b) repeat HTSEBT alone, after completion of HTSEBT. *Abbreviation:* HTSEBT = hypofractionated total skin electron beam therapy.

Our overall response rate was 100%, similar to that of other comparable studies<sup>6,7,20-22</sup> using hypofractionated or low-dose TSEBT. The rate of 57.4% for complete response is lower than other complete response rates reported in hypofractionated series, including a complete response rate of 83% reported by Le Bourgeois et al using 30 Gy in 12 fractions over 40 days<sup>6</sup> and a complete response rate of 90% reported by Nisce and colleagues<sup>7</sup> in patients treated with 4 Gy weekly for 4 to 6 fractions. Notably, these series include hypofractionation, but to a higher total dose. In comparable low-dose series<sup>20-22</sup> not using hypofractionation, our response rate appears similar or improved. Kamstrup et al<sup>20</sup> reported a 57% complete response rate after delivering 10 Gy in 10 fractions over 2.5 weeks, and Georgakopoulos et al<sup>22</sup> and Rivers et al<sup>21</sup>

reported a 25% complete response rate after delivery of 12 Gy in 6 fractions over 3 weeks or  $\leq 12$  Gy in standard fractionation over an uncertain time interval. Our results provide the first response of combined low dose and hypofractionated TSEBT.

Total skin electron beam therapy is a highly specialized form of radiation therapy that is only available in a limited number of centers. As such, this places a significant burden on many patients who need this treatment. The median round-trip distance between our treatment center and patients' homes was 284 miles. We instituted HTSEBT in response to patients who were unable to come for daily treatment owing to one or more of the following factors: limitations in patient resources, inability or unwillingness to travel over long distances



**Figure 5** Cumulative incidence of progressive skin disease after completion of hypofractionated total skin electron beam therapy based on hypofractionated total skin electron beam therapy course number. (1 = first course, 2 = second course, 3 = third course.)

and remain at our center for several weeks, inability to tolerate daily treatment or unwillingness to consent to daily treatment.

These findings are also relevant to health system emergencies, such as the coronavirus disease 2019 (COVID-19) pandemic. Multiple centers have recommended hypofractionation, whenever possible, during this health system emergency.<sup>23-26</sup> Decreasing the number of radiation fractions from 12, as in the Stanford report,<sup>4</sup> to 3 or 4 may be particularly desirable during an infectious disease outbreak, both for the protection of patients with CTCL and the protection of other patients and health care workers. HTSEBT may also be a consideration when health care resources are limited.

The case of one of our patients is particularly illustrative with regard to the utility of HTSEBT. She had a 12-year history of mycosis fungoides and prior systemic treatment and focal radiation therapy elsewhere. At the time of her presentation, she had extensive, severely painful ulcerative disease (Fig 6a). She was on intravenous antibiotics because of infection related to loss of skin integrity. Standing for TSEBT was extraordinarily painful, and the patient expressed both an inability and unwillingness to come for daily treatment. She was treated with HTSEBT, 12 Gy in 3 fractions over 18 days. By the time she completed treatment, her pain had dramatically improved, and she had much less difficulty tolerating her last session of HTSEBT. She experienced a dramatic response as documented at follow-up (Fig 6b). She experienced multiple areas of limited recurrence over the ensuing 7 months, treated on each occasion with



**Figure 6** (A) Extensive ulcerative lesions before hypofractionated total skin electron beam therapy. (B) Complete response of lesions on the trunk 45 days after completion of hypofractionated total skin electron beam therapy, 12 Gy in 3 fractions, given over 18 days.

palliative, single-fraction radiation therapy, always resulting in complete in-field response, and then experienced spontaneous resolution of all remaining lesions, including lesions deep to the skin, as documented by positron emission tomography scan 15 months after initiation of TSEBT. She remains free of disease and is working full-time as of last follow-up, 3 years after starting palliative TSEBT. This favorable outcome would not have been possible without the use of HTSEBT.

## Conclusions

Low-dose hypofractionated total skin electron beam therapy provides good palliation in patients with CTCL with a satisfactory response rate and an acceptable toxicity profile. HTSEBT provides an opportunity for treatment with a high response rate for patients who otherwise might not otherwise be candidates for TSEBT. It is an option that should be considered during health system emergencies, when prolonged courses of radiation therapy need to be avoided owing to limitations in resources or for protection of patients and their health care providers.

## References

1. National Comprehensive Cancer Network. Primary cutaneous lymphoma (version 1.2020). Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/primary\\_cutaneous.pdf](https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf). Accessed March 23, 2020.
2. Specht L, Dabaja B, Illidge T, Wilson LD, Hoppe RT. International Lymphoma Radiation Oncology Group. Modern radiation therapy for primary cutaneous lymphomas: Field and dose guidelines from the International Lymphoma Radiation Oncology Group. *Int J Radiat Oncol Biol Phys*. 2015;92:32-39.
3. Moraes FY, Carvalho Hde A, Hanna SA, Silva JL, Marta GN. Literature review of clinical results of total skin electron irradiation (TSEBT) of mycosis fungoides in adults. *Rep Pract Oncol Radiother*. 2013;19:92-98.
4. Hoppe RT, Harrison C, Tavallae M, et al. Low-dose total skin electron beam therapy as an effective modality to reduce disease burden in patients with mycosis fungoides: Results of a pooled analysis from 3 phase-II clinical trials. *J Am Acad Dermatol*. 2015; 72:286-292.
5. Morris S, Scarisbrick J, Frew J, et al. The results of low-dose total skin electron beam radiation therapy (TSEB) in patients with mycosis fungoides from the UK Cutaneous Lymphoma Group. *Int J Radiat Oncol Biol Phys*. 2017;99:627-633.
6. Le Bourgeois JP, Haddad E, Marinello G, Marin L, Mazon JJ, Ganem G. The indications for total cutaneous electron beam radiation therapy of mycosis fungoides. *Int J Radiat Oncol Biol Phys*. 1987;13:189-193.
7. Nisce LZ, Chu FC, Lee HS, Filippa D, Kempin S, Coleman M. Total skin electron beam therapy for cutaneous lymphomas and leukemias. *Int J Radiat Oncol Biol Phys*. 1982;8:1587-1592.
8. King BJ, Lester SC, Tolkachjov SN, Davis MDP, Gibson LE, Martenson JA. Skin-directed radiation therapy for cutaneous lymphoma: The Mayo Clinic experience. *J Am Acad Dermatol*. 2020; 82:634-641.
9. Deufel CL, Antolak JA. Total skin electron therapy in the lying-on-the-floor position using a customized flattening filter to eliminate field junctions. *J Appl Clin Med Phys*. 2013;14:115-126.
10. 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.
11. Evans JD, Haley LL, Locher SE, et al. Clinical application of lying-on-the-floor total skin electron irradiation for frail patients with cutaneous lymphoma: An emphasis on the importance of in vivo dosimetry. *Adv Radiat Oncol*. 2016;1:101-105.
12. Olsen EA, Whittaker S, Kim YH, 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; 29:2598-2607.
13. Morris SL, McGovern M, Bayne S, Wain M, Child F, Whittaker S. Results of a 5-week schedule of modern total skin electron beam radiation therapy. *Int J Radiat Oncol Biol Phys*. 2013;86:936-941.
14. Micaily B, Vonderheid EC, Brady LW. Combined moderate dose electron beam radiotherapy and topical chemotherapy for cutaneous T-Cell lymphoma. *Int J Radiat Oncol Biol Phys*. 1983;9: 475-479.
15. Kroeger K, Elsayad K, Moustakis C, Haverkamp U, Eich HT. Low-dose total skin electron beam therapy for cutaneous lymphoma: Minimal risk of acute toxicities. Niedrigdosis-Ganzhautelektronenbestrahlung bei Patienten mit kutanen Lymphomen: Minimales Risiko für akute Toxizitäten. *Strahlenther Onkol*. 2017;193:1024-1030.
16. Hoppe RT, Wood GS, Abel EA. Mycosis fungoides and the Sézary syndrome: Pathology, staging, and treatment. *Curr Probl Cancer*. 1990;14:293-371.
17. Hoppe RT. Total skin electron beam therapy in the management of mycosis fungoides. *Front Radiat Ther Oncol*. 1991;25:80-133.
18. 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.
19. Elsayad K, Kriz J, Moustakis C, et al. Total skin electron beam for primary cutaneous T-cell lymphoma. *Int J Radiat Oncol Biol Phys*. 2015;93:1077-1086.
20. Kamstrup MR, Gniadecki R, Iversen L, et al. Low-dose (10-Gy) total skin electron beam therapy for cutaneous T-cell lymphoma: An open clinical study and pooled data analysis. *Int J Radiat Oncol Biol Phys*. 2015;92:138-143.
21. Rivers CI, Singh AK. Total skin electron beam therapy for mycosis fungoides revisited with adjuvant systemic therapy. *Clin Lymphoma Myeloma Leuk*. 2019;19:83-88.
22. Georgakopoulos I, Papadavid E, Platoni K, et al. Clinical application of Total Skin Electron Beam (TSEB) therapy for the management of T cell cutaneous lymphomas. The evolving role of low dose (12 Gy) treatment schedule. *Clin Transl Radiat Oncol*. 2018;15:26-30.
23. Achard V, Tsoutsou P, Zilli T. Radiotherapy in the time of the Coronavirus pandemic: When less is better. *Int J Radiat Oncol Biol Phys*, in press.
24. Zaorsky NG, Yu JB, McBride SM, et al. Prostate cancer radiotherapy recommendations in response to COVID-19. *Adv Radiat Oncol*, in press.
25. Filippi AR, Russi EG, Magrini S, Corvò R. COVID-19 outbreak in Northern Italy: First practical indications for radiotherapy departments. *Int J Radiat Oncol Biol Phys*, in press.
26. Wang H, Zhang L. Risk of COVID-19 for patients with cancer. *Lancet Oncol*. 2020;21:e181.