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Dermatofibrosarcoma Protuberans (DFSP): Predictors of Recurrence and the Use of Systemic Therapy

Ryan C. Fields, M.D.^{*}, Meera Hameed, M.D.[#], Li-Xuan Qin, Ph.D.[†], Nicole Moraco, M.A.^{*}, Xiaoyu Jia, M.S.[†], Robert G. Maki, M.D., Ph.D.[‡], Samuel Singer, M.D.^{*}, and Murray F. Brennan, M.D.^{*}

^{*}Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY 10065

[#]Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY 10065

[†]Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY 10065

[‡]Department of Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY 10065

Abstract

BACKGROUND—DFSP is an uncommon soft tissue malignancy that typically presents with local invasion but rarely metastasizes. We examine clinicopathologic factors associated with disease-free survival (DFS) in patients with primary and recurrent DFSP and evaluate responses to multimodality therapy.

METHODS—Patients treated for DFSP were identified in a prospectively maintained database. Clinicopathologic factors associated with DFS were analyzed using uni- and multi-variate analysis.

RESULTS—244 patients with DFSP were identified. Median follow-up was 50 months. 14 patients had LR and two patients had distant recurrence (DR), with a median time to recurrence of 35 months. At time of last follow-up, 70% and 47% of patients were NED in the primary (n=197) and recurrent groups (n=47), respectively. On univariate analysis, tumor location and depth were associated with DFS in the primary group, while margin status (R1 v. R0) was associated with DFS in the LR group. On multivariate analysis, only depth (primary group) and margin status (LR group), remained significant. 22 patients had therapy other than surgical resection: 14 radiotherapy, 4 tyrosine kinase inhibitor (TKI) only, 2 conventional chemotherapy only, and 2 chemotherapy plus TKI. Responses to other therapies were variable.

CONCLUSIONS—DFS after treatment for DFSP is strongly predicted by tumor depth in the primary setting and margin status in recurrent tumors. The treatment for DFSP in the primary or recurrent setting is excision with negative margins, resulting in low recurrence rates and

Address correspondence to: Murray F. Brennan, M.D., Benno C. Schmidt Chair in Clinical Oncology, Vice President for International Programs, Attending, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, (212) 639-8691 – voice, (212) 794-3184 – fax, brennanm@mskcc.org.

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infrequent metastatic spread. Multimodality treatment, especially TKI use, can be effective, but is not curative.

Keywords

Dermatofibrosarcoma protuberans; DFSP; Surgery; Chemotherapy; Radiation; Targeted Agents; Tyrosine kinase inhibitors; Treatment; Outcomes

INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is a rare, superficial sarcoma characterized by its infiltrative growth pattern. [1–2] It is predisposed to local recurrence (LR) after primary resection, has low metastatic potential, and patients rarely die from DFSP. [3] The classically described histologic pattern of DFSP can transform into a more aggressive fibrosarcomatous variant (FS-DFSP). [4–5] This subtype is more aggressive and displays higher metastatic potential. On a molecular level, 90% of DFSPs possess a unique translocation that fuses the highly expressed collagen type-1 alpha-1 (*COL1A1*) gene with the platelet-derived growth factor-beta (*PDGFβ*) chain, [6–7] providing the rationale for the use of imatinib mesylate (IM) and other tyrosine kinase inhibitors (TKIs) in the treatment DFSP. [8–10]

The standard treatment for DFSP is surgical excision with wide margins, [11–13] which has resulted in low (<15%) rates of LR. The use of other therapies, including radiation therapy (RT) [14–16] and TKIs [8, 17–18], has been described, both in the neoadjuvant and adjuvant settings, as well as for definitive treatment in patients unfit for surgery. The use of multimodality therapy is not standard and its effectiveness in cases of microscopically positive margins after excision is not known.

Several single institution reports, [13, 16, 19–21] including our own, [12] have identified clinicopathologic factors associated with disease-free survival (DFS). In 2000, we reported that margin status and fibrosarcomatous transformation (FS-DFSP) predicted recurrence in 159 patients with DFSP. [12] The rare nature of the tumor, coupled with the low rates of recurrence, has limited such analyses from making definitive, consistent conclusions. The advent of targeted medical therapy in the form of TKIs may further alter such findings. In the current analysis, we investigated our institutional experience with DFSP in a modern series to clarify factors associated with DFS and the effectiveness of multimodality therapy.

METHODS

Two hundred forty-four patients treated at Memorial Sloan-Kettering Cancer Center (MSKCC; New York, NY) for primary or recurrent DFSP from July, 1982 to July, 2009 were identified from our prospectively maintained clinical sarcoma database (approximately 3% of all sarcoma cases) of patients presenting to MSKCC with a diagnosis of DFSP and receiving treatment (all modalities) at our institution.. Clinical and pathologic variables obtained from the database included: patient age, sex, presentation date, presentation status (primary v. recurrent), tumor variables (location, size, depth, grade, histology, invasion),

treatment information (surgery, chemotherapy, RT), date of last follow-up, recurrence, and vital status. This project was approved by the MSKCC Institutional Review Board (IRB).

Patients with recurrent DFSP were initially treated at an outside institution (OSH) and referred to MSKCC for subsequent care. Recurrent disease was defined as histologically-proven tumor arising within or adjacent to the previous tumor bed 6 months after previous treatment.

Patients were followed at 3–6 month intervals for the first year, then every 6–12 months thereafter. Follow-up consisted of a clinical exam, with laboratory and radiology studies performed to evaluate suspicious clinical findings at the discretion of the attending physician. Response to chemotherapy was graded using World Health Organization (WHO) criteria. Follow-up information was updated to July, 2009.

Patients who presented with primary (1°-DFSP) versus locally recurrent (LR-DFSP) disease were analyzed separately. Patient characteristics were described for the two groups and Fisher's exact test or the Wilcoxon rank sum test were used to compare the distributions.

DFS, which counts all LR, distant recurrence (DR), and death as events, was defined as the length of time from the date of surgery at our institution to the time the event was captured in our database or last follow-up. Due to the very small number of DR, LR-free survival (counting LR/Death as events) would be essentially the same as DFS. DFS curves were generated using the Kaplan-Meier method. Univariate analysis on DFS was performed using the log-rank test. Variables significant at the 0.05 level in the univariate setting were entered to a multivariate model, using the Cox proportional hazard analysis.

We also ran a separate analysis treating LR as events of primary interest and death as competing risk events. Univariate analysis on LR was performed using Gray's test to compare cumulative incidence curves for LR. No multivariate analysis was performed due to the low incidence of LR.

The competing risk analysis was performed using the R package (www.r-project.org); the other analyses were performed using SAS Software, Version 9.1 (Cary, NC).

RESULTS

Clinicopathologic and Treatment-Related Data

Two hundred forty-four patients with primary and recurrent DFSP were treated at MSKCC from 1982 – 2009. The median age was 42 years (range 16 – 79). Median follow-up was 4.1 years. One hundred ninety-seven patients (81%) presented with 1°-DFSP, 44 patients (18%) presented with LR-DFSP, and 3 patients (1.2%) presented with metastatic DFSP (2 patients with distant metastatic disease only and 1 patient with metastatic disease in combination with LR). One patient presented with 1°-DFSP and underwent a palliative R2 resection. These 4 patients were excluded from subsequent analysis.

Table 1 summarizes the remaining 240 patients included in the analysis, subdivided by presentation status (80% 1°-DFSP, 20% LR-DFSP). There was equal distribution between

males and females. The majority (74%) of lesions were asymptomatic. Extremity location was the most common site of presentation with 71 (29%) and 55 tumors (23%) occurring in the upper and lower extremities, respectively. There were 76 tumors (31%) on the trunk, 33 tumors (14%) on the head/neck, and 5 tumors (2%) in other locations. Histologic review of all cases by a dedicated sarcoma pathologist (M.H.) found the presence of FS-DFSP in 35 cases (15%). One hundred eighty-five patients (77%) had superficial tumors, while 54 (23%) had deep tumors invading the fascia directly beneath the primary lesion.

Patients with LR-DFSP were older (46 years) than those with 1°-DFSP (39 years). There were no differences between 1°- and LR-DFSP with respect to gender, tumor location, depth, histology, and margin.

Complete surgical excision was achieved in all cases. Post-operatively, microscopically negative margins (R0 resection) were achieved in 169 patients (86%) in the primary group and 35 patients (80%) in the LR group. All patients were treated with wide surgical excision. There were no patients in this series treated with Mohs micrographic surgery.

Disease-Free Survival

During the follow-up, there were 17 events (9 LR, 1 DR [in a patient that also had LR], and 8 deaths) in the primary group and 9 events (5 LR, 1 DR, and 3 deaths) in the LR group (Table 1), corresponding to 70% and 47% DFS for primary and LR patients, respectively, at the time of last follow-up.

In the primary group, of the 9 patients with a LR, 1 patient had a subsequent LR that was managed with re-excision and is currently NED. Pathologic review demonstrated an R0 resection after all 3 excisions, but his tumor demonstrated the FS-DFSP variant. In the LR group, 3 patients had subsequent LRs, one of whom developed DR and died of disease.

Patients presenting with 1°-DFSP had significantly improved median DFS ($P = 0.043$; Figure 1a) and longer times to local recurrence ($P = 0.04$; Figure 1b) when compared to those presenting with LR-DFSP (15.2 months for LR-DFSP versus median DFS not reached for 1°-DFSP, 95% CI 9.4 – not reached). Overall, 2 patients had distant metastases, both with lung as the first site of metastases. No patient presenting to our institution with 1°-DFSP has died of disease, while 1 patient presenting with LR-DFSP, who subsequently developed metastatic DFSP, died of disease. The DFS for 1°-DFSP at 5 and 10 years after treatment was 92% (95% CI 85 – 96%) and 87% (95% CI 77 – 92%), respectively, compared to 87% (95% CI 68 – 95%) and 67% (95% CI 40 – 84%) for LR tumors.

Uni- and Multi-Variate Analysis

For patients presenting with 1°-DFSP, tumor depth and location significantly predicted recurrence ($P = 0.024$ and 0.049 , respectively by log-rank test). For patients presenting with LR-DFSP, a negative margin (R0) resection significantly predicted DFS (HR = 22.43, 95% CI = 2.61 – 192.94, $P < 0.001$). On multivariate analysis, depth remained a significant predictor of recurrence (HR = 3.14, 95% CI = 1.18 – 8.32, $P = 0.022$) and location (extremity vs. others) was marginally significant (HR = 2.94, 95% CI = 0.96–9.09, $P = 0.059$) for patients with 1°-DFSP. Table 2 summarizes the results of the uni- and multi-

variate analysis. Figures 2 and 3 illustrate Kaplan-Meier curves of DFS for primary and LR patients, respectively, stratified by the aforementioned significant variables (tumor location and depth for primary patients, and margin status for LR patients).

When univariate analysis is performed using the competing risk method, depth ($P = 0.08$) is marginally significant for 1°-DFSP. For LR patients, margin status ($P < 0.001$) remains significantly associated with recurrence.

Other Therapy

Twenty-two of the 244 patients who presented with or developed locally advanced or metastatic disease were treated with non-surgical therapy: 14 RT, 4 TKIs, 2 conventional chemotherapy, and 2 TKIs and conventional chemotherapy. Table 3 summarizes the results of our institutional experience with systemic treatment.

All patients who received RT for DFSP had their treatment initiated at OSH's. Ten patients were treated with adjuvant external beam radiation at an OSH after a positive margin excision. Nine of these 10 patients were evaluated at our institution and underwent re-excision with negative margins and are all NED with an average of 34 ± 9 months of followup. Of note, 7 of these 9 patients had viable, residual disease in their re-excision specimens. One patient was recommended re-excision and elected observation and is NED after 28 months of follow-up. One patient received adjuvant RT for a <1 mm margin and is NED after 37 months of follow-up. One patient had multifocal recurrence of a groin DFSP and underwent RT, followed by re-excision at our institution, and died of other causes 17 months later with no evidence of recurrence. Two patients received intraoperative brachytherapy at an OSH during an incomplete excision. Both underwent re-excision to negative margins at our institution and are NED after 14 and 20 months of follow-up.

Two patients were treated with conventional chemotherapy alone. One was treated with cisplatin and paclitaxel at an outside institution after a close margin. The patient underwent re-excision at our institution and is currently NED after 49 months of follow-up. Another patient was one of the three who presented with metastatic disease and was treated with systemic chemotherapy (cisplatin, mitomycin, and vinblastine). This tumor was not responsive to any treatment modality and the patient died of disease.

Two other patients with metastatic disease were treated conventional chemotherapy and TKIs. One of these patients demonstrated a partial (50%) response to IM, but progressed after 6 months and died of disease 3 months later. The other patient is alive with disease (AWD) after a partial (50%) response to IM for a duration of 12 months prior to progression and addition of etoposide and cyclophosphamide.

Four patients were treated with TKIs alone. One who developed metastatic disease was treated with IM and demonstrated a partial (75%) response and is currently AWD after 9 months of follow-up. One patient had an unresectable, multiply recurrent lesion that partially responded to IM (50% for 36 months) and sorafenib (stable disease during current 12 months of treatment). One patient with LR and metastatic DFSP was unresponsive to both IM and sorafenib and died of disease. A fourth patient was treated with pre-operative

IM after presenting with a large LR. This patient had a partial response (33%), followed by excision with negative margins and is currently NED after 31 months of follow-up. To summarize our experience with TKIs, we have had 5 partial responses in 6 patients treated with IM with a duration of response from 6 – 36 months. In the two patients treated with sorafenib after failure of IM, one had a partial response and one progressed.

DISCUSSION

DFSP is a rare soft tissue malignancy that often shows extensive local invasion but rarely metastasizes. [22] It can lead to significant morbidity from repeated surgical excisions, but infrequently leads to death. [3, 5, 12–13, 20] The combination of the rarity of DFSP and the low number of recurrence events, has precluded any large, randomized trials to address the optimal management of DFSP. To our knowledge, this series of 244 patients with DFSP is one of the largest in the literature and represents an update of our institutional experience from 2000. [12]

Our reported rates of R0 resection (86% and 80% for primary LR tumors, respectively) and DFS (92% and 87% at 5 years for primary and recurrent tumors, respectively) are consistent with other large series, including a report of 218 patients from Fiore, et. al in 2005 [13] (crude cumulative incidence [CCI] of sarcoma-specific mortality of 1.5% and 2.8% at 5- and 10-years, respectively and CCI of local relapse of 3.0% and 4.2% at 5- and 10-years, respectively). In contrast to our current findings, Fiore, et. al report a CCI of sarcoma-specific mortality of 6.2% in patients presenting with a LR tumor. This observation is likely due to differences in patient selection, demographics, and referral patterns between our two institutions.

Our rates of microscopically positive margins after resection for 1°- (14%) and LR-DFSP (20%) are also consistent with other series. [13, 20] The slight variation between series may also reflect differences in tumor pathology, as our current series contains a high percentage (17%) of patients with the more aggressive FS-DFSP variant. Interestingly, however, and in contrast to our previously published series, the presence of FS-DFSP histology did not predict DFS. This may be explained by the more modern cohort of patients analyzed in the present series (1982 – 2009 v. 1950 – 1998). Patients prior to 1982 were not included in the present series, partly due to both the inability to independently verify their histologic and treatment profiles and the desire to analyze a modern cohort of prospectively studied patients that represents current treatment standards for DFSP.

Our institutional practice is to achieve gross negative margins of 2–3cm whenever possible. This leads to the high rates of R0 resections achieved in our series, which is our goal of any operation for DFSP. We do not routinely use frozen section analysis to assess margin status, as our sarcoma pathologists we have found it unreliable in differentiating scattered spindle cells in normal dermis from minimal-residual DFSP-cells. [23–24] Our series is not able to comment on the use of Mohs surgery in the treatment of DFSP, as there were no patients in our database either treated with Mohs at an outside institution and referred to MSKCC for follow-up or patients offered Mohs surgery as a treatment modality at MSKCC for 1°-DFSP.

We feel the aforementioned limitation of frozen section analysis for DFSP also limits the application of Mohs surgery in the treatment of DFSP.

Our finding that tumor location significantly predicts DFS on univariate, but not multivariate, analysis for 1°-DFSP may reflect the small number of events in these 196 patients (Table 2). Conceptually, with larger numbers of patients, tumor location may predict DFS, as wider margins, and thus lower rates of LR, may be more easily obtainable on the trunk/thorax versus the extremities and head/neck.

The finding that tumor depth significantly predicts DFS on both uni- and multi-variate analysis is in line with the histopathologic observation that DFSP, especially when invasive beneath fascial plains, is likely biologically more aggressive than those infiltrating through subcutaneous fat. [25–26] Thus, wide margins in both the radial and deep planes are critical to achieve tumor clearance and the deep fascia should always be excised. We found no correlation between deep tumors and the FS-DFSP histology.

We found that margin status (R0 v. R1) significantly predicted DFS in patients treated for LR-DFSP, with a HR of 22.43 (Table 2). This is also consistent with other published series. Of the 9 patients who had microscopically positive margins after resection of LR-DFSP, 3 (33%) had a subsequent recurrence on follow-up, all of which were managed by re-excision. At the time of last follow-up (32, 61, and 48 months after re-excision), all 3 were NED. Because of this low rate of observed LR after positive margins and the ability to treat such recurrences with repeat excision, it has been our practice to closely follow these patients. This is in contrast to other institutions that will routinely use immediate re-excision of microscopically positive margins and/or adjuvant RT in such cases, with similar rates of both local and distant recurrence. [14, 16, 21] However, in our series, only 33% of patients with microscopically positive margins will develop a clinically significant recurrence, and re-excision and RT carries significant morbidity. The use of adjuvant radiation treatment for all patients with microscopically positive margins will result in overtreatment of at least 2 patients for every 1 that will possibly benefit in our 33% of patients with microscopically positive margins that require any such intervention. So, the potential benefit versus the morbidity of re-resection and RT versus observation and directed treatment of clinical recurrences must be considered. It is possible, however, that longer follow-up will reveal increased rates of LR in this patient group. As figure 1 demonstrates, there are a large number of recurrences after 5 years, owing to the indolent nature of DFSP. Thus, close follow-up is certainly warranted in such patients, with treatment directed at clinical recurrences.

The response of metastatic DFSP to conventional chemotherapy has classically been poor, [1, 3, 27] as is supported by our small experience. Reports from Rubin, et. al [28] and Maki, et. al [8] in 2002 were the first to demonstrate that TKIs are effective in the treatment of DFSP. Our experience with TKIs mirrors the literature: we had 5 of 6 patients with PR's to IM with durations of response from 6 – 36 months. One patient progressed. In two patients treated with sorafenib, one had a PR and one progressed.

In total, there are approximately 60 described cases of TKI treatment for DFSP in 14 publications. [1] The largest series, presented at the 2007 American Society of Clinical Oncology (ASCO) Annual Meeting, contains 25 patients, with responses in 36% of patients with a median tumor decrease of 20%. [17] The Phase II IM Target Exploration Consortium B2225 Study evaluated the activity of IM treating advanced IM-sensitive tumors, which included 12 patients with DFSP. [29] Four patients (33%) had complete responses, 6 patients had PR's (50%), 1 patient (8%) had progression of disease (PD), and 1 patient (8%) was lost to follow-up. The median time to progression was 23.9 months. In a recent pooled analysis of 24 patients from two phase II clinical trials of IM in the treatment of DFSP (16 patients from the European Organization for Research and Treatment of Cancer [EORTC] and 8 patients from the Southwest Oncology Group [SWOG]), 9 patients (38%) had PR's, 8 patients (33%) had stable disease, 4 patients (17%) had PD, and 3 patients (13%) were lost to follow-up. [30] The median time to progression was 20.4 months. Thus, similar to their use in gastrointestinal stromal tumors (GISTs), TKIs are not considered curative in DFSP. [31] Our practice is to utilize TKIs in cases of locally advanced/unresectable cases, metastatic disease, or in patients unfit for surgery. Currently, several clinical trials, including multicentric phase II studies, are recruiting patients with DFSP, along with other solid malignancies, to further define the indications for TKI use. [32]

In summary, DFSP is a locally aggressive tumor that can usually be cured with wide excision. LR tumors can lead to significant morbidity, but rarely lead to death. Tumor depth significantly predicts recurrence in cases of 1°-DFSP, while margin status predicts recurrence in cases of LR-DFSP. The majority of cases of recurrent DFSP are cured with re-excision. The treatment of 1°- and recurrent-DFSP should be an R0 resection whenever possible. TKIs are effective in treating DFSP and should be used for the infrequent cases of unresectable or metastatic disease.

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Figure 1. Kaplan-Meier curves of disease-free survival (a) and cumulative incidence of local recurrence (b) in patients with DFSP, stratified by presentation status (LR = locally recurrent).

Figure 2.
Kaplan-Meier curves of disease-free survival in patients presenting with primary DFSP stratified by tumor location (a) and tumor depth (b).

Figure 3.
Kaplan-Meier curve of disease-free survival in patients presenting with locally recurrent DFSP stratified by margin status.

Patient and Tumor Characteristics of 240 Patients Treated for Primary and Recurrent DFSP at MSKCC from 1982–2009

Table 1

Characteristic	Primary (n=196)		LR (n=44)		P Value*
	Number	%	Number	%	
Median Age (years)	39		46		0.03
Gender					
Male	95	48	21	47	1.00
Female	101	52	23	53	
Primary Site					
Extremity	101	52	25	57	
Trunk/Thorax	63	32	13	29	0.66
Head & Neck	29	15	4	10	
Other	3	1	2	4	
Tumor Size					
< 5cm	152	78	36	81	
5 – 10 cm	36	19	5	11	0.27
> 10 cm	6	2	3	7	
Unknown	2	1	0	0	
Tumor Depth					
Deep	42	21	12	27	
Superficial	154	79	31	70	0.42
Unknown	0	0	1	3	
Tumor Histology					
“Classic” DFSP	166	68	39	88	0.64
FS-DFSP	30	32	5	12	
Surgical Margin					
R0 (Negative)	169	86	35	80	
R1 (Microscopically Positive)	26	14	9	20	0.24
Unknown	1	<1	0	0	
Recurrence Events					
Local Recurrence	9	4	5	11	NE†

Characteristic	Primary (n=196)		LR (n=44)		P Value*
	Number	%	Number	%	
Distant Recurrence	1 [#]	<1	1	<1	
Vital Status ^{\$}					
No Evidence of Disease	185	94	37	84	
Alive with Disease	3	2	3	7	NE [†]
Died of Other Causes	8	4	3	7	
Died of Disease	0	0	1	2	

* Fisher's exact test for all variables (except age, which was analyzed using Wilcoxon rank sum test)

[#] Synchronous distant and local recurrence

^{\$} as of July, 2009

[†] Not evaluable. See text for explanation and Kaplan-Meier analysis for comparison of disease-free survival.

Abbreviations: DFSP = dermatofibrosarcoma protuberans, FS-DFSP = fibrosarcomatous DFSP, LR = locally recurrent, MSKCC = Memorial Sloan-Kettering Cancer Center, NE = not evaluable.

Table 2

Results of Univariate and Multivariate Analysis of Factors Associated with Disease-Free Survival in 240 patients treated for Primary and LR-DFSP at MSKCC from 1982–2009*

	Primary (n=196)	LR (n=44)
Characteristic	P Value	
Univariate Analysis [†]		
Age (< 40 years v. > 40 years)	0.078	0.33
Sex (male v. female)	0.72	0.70
Site (extremity v. trunk v. H&N)	0.049	0.32
FS-DFSP (yes v. no)	0.83	0.80
Tumor Size (< 5cm v. > 5cm)	0.081	0.32
Tumor Depth (superficial v. deep)	0.024	0.80
Margin Status (R1 v. R0)	0.87	<0.001
Invasion [§]	0.85	N/A [#]
	HR (95% CI, P Value)	
Multivariate Analysis [‡]		
Site (extremity v. all others)	2.94 (0.96 – 9.09, 0.059)	–
Tumor Depth (superficial v. deep)	3.14 (1.18 – 8.32, 0.022)	–
Margin Status (R1 v. R0)	–	22.43 (2.61 – 192.94, < 0.0001)

Significant *P* values are shown in **bold** (*P* < 0.05)

* as of July, 2009

[†] Univariate analysis performed using log-rank test.

[‡] Multivariate analysis performed using Cox proportional hazard models.

[§] Involving underlying fascia, muscle, bone, or neurovascular structures

[#] Invasion information not available on pathology reports for 25 of the 44 patients with LR

Abbreviations: CI = confidence interval, DFSP = dermatofibrosarcoma protuberans, H&N = head and neck, LR = locally recurrent

Table 3

Results of Multimodality Treatment in 22 of 244 patients treated for DFSP at MSKCC from 1982–2009

	Indication for Treatment	MSKCC Treatment	Status
RT	9 patients treated with RT at OSH after (+) margin excision	R0 re-excision	NED, 34 ± 9 months of follow-up
	1 patient treated with RT at OSH after (+) margin excision	Observation (patient preference)	NED, 28 months of follow-up
	1 patient treated with adjuvant RT at OSH after a close (<1 mm) excision	Observation	NED, 37 months of follow-up
	1 patient treated with adjuvant RT at OSH after a multifocal groin recurrence	R0 re-excision	DOC 17 months post-surgery
	2 patients treated with intra-op brachytherapy at OSH after an R2 excision	R0 re-excision	NED, 14 and 20 months of follow-up
Conventional Chemotherapy	1 patient treated with cisplatin and taxol at OSH after a close (<1 mm) excision	R0 re-excision	NED, 49 months of follow-up
	Metastatic disease	Cisplatin, mitomycin, and vinblastine	DOD, no response to treatment
Conventional Chemotherapy + TKI	Metastatic disease	AI × 3 cycles Imatinib	Progression on AI PR (50%) to imatinib for 6 months DOD
	Metastatic disease	AI, etoposide, cyclophosphamide, Imatinib	PR (50%) to imatinib for 12 months AWD
	Metastatic disease	Imatinib	PR (75%) stable after 9 months AWD
TKI Alone	Unresectable LR	Imatinib Sorafenib	PR to imatinib (50%) for 36 months SD on sorafenib for 12 months AWD
	Metastatic disease	Imatinib Sorafenib	Progression on imatinib and sorafenib DOD
	LR of ankle lesion	Imatinib × 3 months, then wide excision	PR (33%) on imatinib NED, 31 months of follow-up

Abbreviations: AI = Adriamycin/ifosfamide, DFSP = dermatofibrosarcoma protuberans, DOC = died of other causes, DOD = died of disease, MSKCC = Memorial Sloan-Kettering Cancer Center, NED = no evidence of disease, OSH = outside hospital, PR = partial response, RT = radiation therapy