Clinical staging and prognostic factors in folliculotropic mycosis fungoides

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RECOMMENDATIONS FOR TREATMENT IN FOLLICULOTROPIC MYCOSIS FUNGOIDES: EXPERIENCE OF THE DUTCH CUTANEOUS LYMPHOMA GROUP

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British Journal of Dermatology. 2017;177(1):223-228 (extended version)

ABSTRACT

Background: Folliculotropic mycosis fungoides (FMF) is an aggressive variant of mycosis fungoides (MF) and generally less responsive to standard skin-directed therapies (SDTs). Recent studies distinguished an indolent (early-stage FMF) and a more aggressive (advanced-stage FMF) subgroup. The optimal treatment for both subgroups needs still to be defined.

Objectives: Evaluation of initial treatment results in patients with early- and advanced-stage FMF.

Methods: 203 Patients (84 early-stage, 102 advanced-stage, 17 extracutaneous FMF), included in the Dutch Cutaneous Lymphoma Registry between 1985 and 2014 were studied. Type and results of initial treatment were retrieved from the Dutch Registry. Main outcomes were complete remission (CR), sustained complete remission (SCR), partial remission (>50% improvement; PR) and overall response (OR; CR+PR).

Results: Patients with early-stage FMF were treated with non-aggressive SDTs in 67 of 84 cases, resulting in CR and OR of 28% and 83% for monotherapy topical steroids, 0% and 83% for UVB and 30% and 88% for PUVA, respectively. In patients with advanced-stage FMF these SDTs were less effective (combined CR and OR: 10% and 52%, respectively). In patients with advanced-stage FMF local radiotherapy (CR 63%; OR: 100%), total skin electron beam irradiation (CR: 59%; OR: 100%) and PUVA combined with local radiotherapy (CR: 5%; OR: 75%) were most effective.

Conclusions: The results of the present study demonstrate that not all patients with FMF should be treated aggressively. Patients with early-stage FMF may benefit very well from standard SDTs also used in early-stage classic MF and have an excellent prognosis.

INTRODUCTION

Folliculotropic mycosis fungoides (FMF) is a variant of mycosis fungoides (MF) with distinctive clinicopathologic features.[1-7] Previous studies emphasized that FMF is generally less responsive to several first-line skin-directed therapies (SDTs) and runs a more aggressive disease course, which is similar to tumor-stage classic MF and should therefore be treated accordingly.[2,3] However, more recent studies defined a subgroup of FMF patients whose FMF showed an indolent clinical behavior and an excellent prognosis. These studies indicate that not every case of FMF behaves as tumor-stage disease and that early- and advanced-stage FMF may require a different therapeutic approach. Treatment results in FMF have thus far received very little attention in the medical literature and the prevailing instructions have not been based on the most recent insights into the disease. In the present study we evaluated the results of initial treatment in the Dutch cohort of 203 FMF patients used in our previous study.[8] The main purpose of this study was to propose recommendations for optimal initial treatment in patients with early- and advanced-stage FMF.

PATIENTS AND METHODS

We studied 203 FMF patients included in the Dutch Cutaneous Lymphoma Registry between 1985 and 2014. In all cases the diagnosis of FMF and selection of initial treatment had been made by an expert panel of dermatologists and pathologists at one of the regular meetings of the Dutch Cutaneous Lymphoma Group, and all cases met the diagnostic criteria of FMF.[1] Based on the results of our previous study distinction was made between patients with early-stage skin-limited FMF (group A, n=84), advanced-stage skin-limited FMF (group B, n=102) and FMF with extracutaneous disease at first presentation (group C, n=17) (**Table 1**).[8] For each patient follow-up data, including results of initial treatment had been entered yearly in the registry. Since 1985, results of initial treatment assessed at the time of discontinuation of treatment because of (near) complete response or lack or loss of response, had been scored by means of clinical evaluation of skin lesions as: complete remission (CR; complete clearance of all skin lesions), near CR (>75% clearance of skin lesions), partial response (PR; >50% clearance of skin lesions), stable disease (SD; <25% increase to <50% clearance of skin lesions) or progressive disease (PD; ≥ 25% increase in skin lesions or progression to higher stage during treatment). Overall response (OR) rate

indicates the percentage of patients that obtained (near) CR or PR.[9] The term sustained complete remission (SCR) is used in case of no relapse during follow-up after initial CR.

Table 1 – Types of skin lesions and survival rates of three subgroups of FMF

Subgroup	Skin lesions	N	5-year OS (%)	10-year OS (%)	5-year DSS (%)	10-year DSS (%)
A	Early-stage skin-limited FMF presenting with follicular papules, follicle-based, acneiform or keratosis pilaris-like lesions and/or 'early-stage' plaques*	84	92	72	96	93
B	Advanced-stage skin-limited FMF presenting with 'advanced-stage' plaques**, tumors, nodules or erythroderma	102	55	28	65	40
C	FMF with extracutaneous localisations at first presentation (stage IVA-IVB).***	17	23	2	23	2
Total		203	67	45	75	60

N: number, OS: overall survival, DSS: disease-specific survival
** Early-stage plaques were defined as more or less elevated or infiltrated skin lesions, histologically characterized by sparse intra- or perifollicular neoplastic infiltrates containing relatively few and mainly small neoplastic T-cells.[8]*
*** Advanced-stage plaques were defined as more or less elevated or infiltrated skin lesions, histologically characterized by by extensive confluent or diffuse infiltrates containing many often medium-sized to large tumor cells. Clinically, 'early-stage plaques' and 'advanced-stage plaques' can be indistinguishable.[8]*
**** Extracutaneous FMF includes patients presenting with nodal, visceral and/or peripheral blood involvement.*

RESULTS

Type of initial treatment

The different types and results of initial treatment in the total group of FMF patients (n=203) and subgroups A (n=84), B (n=102) and C (n=17) are presented in **Table 2**.

In group A, 67 of 84 patients (80%) had primarily been treated with non-aggressive SDTs, including topical steroids, topical nitrogen mustard, UVB therapy, PUVA therapy or had received no therapy, compared with only 31 of 102 patients (30%) in group B. Combined treatment results for non-aggressive SDTs in group A showed a CR and OR of 27% and 87%, compared to 10% and 52%, respectively, in group B (p-value < 0.01). The latter group had been treated most frequently with radiotherapy-based treatment modalities, including local radiotherapy, total skin electron beam irradiation (TSEBI) and PUVA therapy combined with local radiotherapy (53 of 102; 52%), or with PUVA therapy combined with acitretin, interferon alpha or methotrexate (13 of 102; 13%). In group C, nine of 17 patients (53%) had been treated with chemotherapy.
The results of the different initial treatment modalities are described in more detail below.

Table 2 – Type and results of initial treatment in subgroups and total group of FMF patients

Group A (n=84)								
			CR	PR	OR	SD	PD	SCR
Type of therapy	n	%	%	%	%	%	%	%
Topical steroids	**18**	**21**	28	56	83	17	0	22
UVB	**6**	**7**	0	83	83	17	0	0
PUVA	**40**	**48**	30	58	88	13	0	18
PUVA+ retinoids or IFNa	**5**	**6**	0	60	60	40	0	0
PUVA+ local RT	**5**	**6**	60	40	100	0	0	40
Local RT alone	**4**	**5**	75	25	100	0	0	75
TSEB	**1**	**1**	0	100	100	0	0	0
Systemic chemotherapy	**1**	**1**	0	100	100	0	0	0
Miscellaneous*	**4**	**5**	25	50	75	25	0	25
Total group A	**84**	**100**	**29**	**57**	**86**	**14**	**0**	**20**
Group B (n=102)								
			CR	**PR**	**OR**	**SD**	**PD**	**SCR**
Type of therapy	n	%	%	%	%	%	%	%
Topical steroids	**4**	**4**	0	25	25	75	0	0
UVB	**5**	**5**	0	20	20	80	0	0
PUVA	**20**	**20**	10	50	60	25	15	5
PUVA+ retinoids or IFNa **	**13**	**13**	0	67	67	17	17	0
PUVA+ local RT	**20**	**20**	5	70	75	5	20	0
Local RT alone	**16**	**16**	63	37	100	0	0	19
TSEB	**17**	**17**	59	41	100	0	0	18
Systemic chemotherapy	**5**	**5**	20	40	60	20	20	0
Miscellaneous*	**2**	**2**	50	50	100	0	0	0
Total group B	**102**	**100**	**25**	**50**	**74**	**16**	**10**	**7**
Group C (n=17)								
			CR	**PR**	**OR**	**SD**	**PD**	**SCR**
Type of therapy	n	%	%	%	%	%	%	%
Topical steroids	**-**	**-**	-	-	-	-	-	-
UVB	**-**	**-**	-	-	-	-	-	-
PUVA	**2**	**12**	0	0	0	50	50	0
PUVA+ retinoids or IFNa	**-**	**-**	-	-	-	-	-	-
PUVA+ local RT	**2**	**12**	0	50	50	0	50	0
Local RT alone	**1**	**6**	0	100	100	0	0	0
TSEB***	**2**	**12**	0	100	100	0	0	0
Systemic chemotherapy	**9**	**53**	11	22	33	22	44	11
Miscellaneous*	**1**	**6**	0	0	0	0	100	0
Total group C	**17**	**100**	**6**	**31**	**38**	**19**	**44**	**6**
Total group (n=203)								
			CR	**PR**	**OR**	**SD**	**PD**	**SCR**
Type of therapy	n	%	%	%	%	%	%	%
Topical steroids	**22**	**11**	23	50	73	27	0	18
UVB	**11**	**5**	0	55	55	45	0	0
PUVA	**62**	**31**	23	53	76	18	6	13
PUVA+ retinoids or IFNa **	**18**	**9**	0	65	65	24	12	0
PUVA+ local RT	**27**	**13**	15	52	78	4	19	7
Local RT alone	**21**	**10**	62	38	100	0	0	29
TSEB***	**20**	**10**	53	47	100	0	0	15
Systemic chemotherapy	**15**	**7**	13	33	47	20	27	7
Miscellaneous*	**7**	**3**	29	43	71	14	14	14
Total group	**203**	**100**	**25**	**51**	**76**	**15**	**8**	**12**

*Group A: Early-stage skin-limited FMF, Group B: Advanced-stage skin-limited FMF, Group C: Extracutaneous FMF, n: number, UVB: ultraviolet B therapy, PUVA: psoralen + ultraviolet A therapy, RT: radiotherapy, TSEB: total skin electron beam therapy, CR: complete remission, PR: partial remission (>50% improvement), OR: overall response (CR+PR), SD: stable disease, PD on tx: progressive disease during initial therapy. * Miscellaneous therapies included topical nitrogen mustard (two cases in group A), methotrexate (one case in group A) or no therapy (other four cases). ** 1 missing value for therapy response *** 1 missing value for therapy response*

TREATMENT RESULTS PER TREATMENT MODALITY

Topical steroids (n=22)

Monotherapy with highly potent topical steroids had been used in 22 patients, mainly patients with early-stage FMF (18 of 22 patients). It was most effective in group A patients with limited follicle-based patches (T1-score; **Figure 1**) resulting in CR in 5 of 6 patients, in four of them without relapse during a median FU period of 26 months (range 17-63). Patients presenting with plaques, including 12 in group A and 4 in group B, showed PR in 9 of 12 (75%) and 1 of 4 (25%) cases respectively, but did not achieve CR.

UVB therapy (n=11)

Narrow-band UVB (nbUVB) therapy had been used as initial treatment in 11 patients (group A: 6 cases, group B: 5 cases), in particular in patients with widespread skin lesions localized outside the head and neck area (T2-score). None of the patients achieved CR, but PR was found in 5 of 6 cases of group A and in 1 of 5 of group B. PR occurred particularly in patients with widespread follicle-based patches, while patients with plaques, both in group A and group B, did generally not respond to this treatment.

PUVA therapy (n=62)

PUVA monotherapy was the most frequently used initial treatment modality in our cohort of FMF patients. In patients in group A CR was achieved in 12 of 40 cases (30%); seven of them did not show a relapse during a median FU of 116 months (range 12-144). Another 23 of 40 patients (57%) attained PR, including 14 patients with near CR. In contrast to treatment with potent topical steroids or nbUVB, no significant differences in results were observed between patients with follicle-based patches (n=25) and patients with plaques (n=15) (**Figure 2**), neither between patients with T1 and T2 scores. PUVA treatment appeared less effective in patients in group B, which included 20 patients with generalized plaques, in five of them with concurrent small tumorous lesions. In this group CR was observed in 2 of 20 patients (10%) and PR in another ten patients, including six patients with a near CR, resulting in an OR rate of 60%.

PUVA therapy combined with oral retinoids (n=13), interferon alpha (n=4) or methotrexate (n=1) (n=18)

This combined treatment modality had been used in 13 patients in group B presenting with plaques, or tumors or erythroderma (2 of 13 patients). In addition, a combination of PUVA and acitretin (RePUVA) was given to five patients in group A, all presenting with widespread follicular papules. None of the patients achieved CR. PR was attained in 11 of 18 cases (61%), including seven patients with near CR and one patient of which response to therapy was unknown. No significant differences in treatment results were observed between patients in group A and group B, neither between patients treated with PUVA and acitretin or PUVA combined with IFN alpha.

PUVA therapy combined with local RT (n=27)

In patients with widespread patches and plaques, PUVA therapy had often been combined with low-dose local radiotherapy for isolated tumorous plaques or tumors (**Figure 3A and 3B**). Initially, skin lesions had been treated with a dose of 20 Gy, but since 2002 low-dose RT (2x4 Gy) was preferrerd.[10] In 7 of 27 patients with more extensive plaques and tumors either acitretin (three cases) or interferon alpha (four cases) had been added as well. In general, the combination of PUVA and local RT was the most frequent treatment modality for FMF patients in group B, and resulted in CR in 1 of 20 patients (5%), near CR in 6 of 20 patients (30%) and PR in 8 of 20 (40%) cases. In group A, local RT following PUVA treatment for persistent plaques resulted in (sustained) CR in 3 of 5 cases and near CR in the other 2 patients.

Local radiation therapy (local RT) (n=21)

Local RT had been used in patients that had either presented with solitary or few localized plaques (**Figure 4**), tumors or nodules either without further skin lesions (n=11) or with concurrent follicle-based patches that were treated with topical steroids (n=10). In the first category CR was seen in all eleven cases, in four of them without relapse during a median FU period of 92 months (range 54-163). In the second category, two patients achieved sustained CR and the other eight patients a PR.

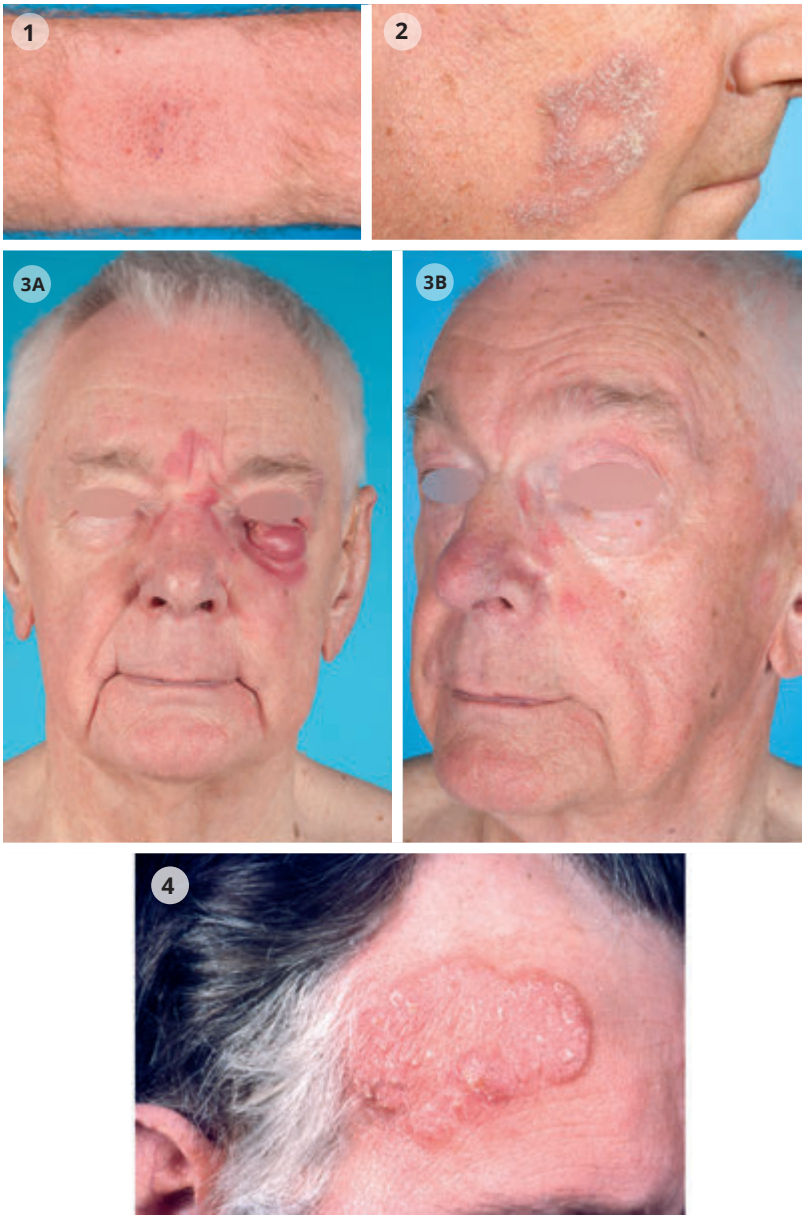

Figure 1. Detail of follicle-based patch on lower right arm with marked local alopecia.
Figure 2. Detail of a plaque (histological sparse peri-follicular neoplastic infiltrate) on the right cheek in a patient with early-stage FMF.
Figure 3. Patient with advanced-stage FMF with a subocular tumor treated with local radiotherapy (A) and result of treatment at 6 months follow-up (B).
Figure 4. Patient with advanced-stage FMF with a solitary plaque (histological diffuse neoplastic infiltrate) on the right fronto-temporal area.

Total skin electron beam irradiation (TSEBI) (n=20)

TSEBI with a standard dose of 35 Gy had mainly been used in patients presenting with widespread plaques, tumors or nodules . Results for TSEBI were excellent, resulting in CR in 10 of 20 (50%), near CR in 7 of 20 (35%) and PR in 2 of 20 (10%) and in one patient the result was unknown. Three patients had a sustained CR for 38, 57 and 169 months, but in most patients response to treatment was short lived.

Chemotherapy (n=15)

Eleven patients received CHOP(-like) courses as initial treatment: seven patients with stage IVA-IVB (group C), three patients with extensive plaques and tumors (group B) and one patient with early-stage FMF (group A), because of a concurrent clonally unrelated systemic anaplastic large cell lymphoma. Results showed sustained CR in one patient, PR in four patients, while six patients did not respond or had progressive disease. Seven of eleven patients died of lymphoma after a median follow-up of 21 months (range 7-68). The other four patients had been treated with prednisone, in two of them combined with chlorambucil. One patient with erythroderma (stage III) achieved sustained CR for more than eight years. The other three patients, who received this treatment as palliation continued to have progressive disease and died 12 to 15 months after diagnosis.

DISCUSSION

The present study showed that patients with early-stage FMF can benefit very well from non-aggressive SDTs and that not all patients with FMF should be treated similarly to patients with tumor-stage classic MF, as suggested previously.[2,3] Based on the results of this study and few available reports in literature, recommendations for effective initial treatment for different stages and clinical manifestations of FMF were formulated and consensus was reached after discussions at the regular quarterly meeting of the Dutch Cutaneous Lymphoma Group in 2015 and 2016 (see **Figure 5**). Treatment recommendations for FMF patients with extracutaneous disease (group C) have never been different from those for classic MF patients with extracutaneous disease[11] and will therefore not be further discussed.

Treatment of early-stage skin-limited FMF (group A)

Clinically, these patients present with localized or more extensive follicular papules or follicle-based patches often associated with hair loss, keratosis pilaris-like and acneiform lesions or plaques with histologically sparse peri- and intrafollicular infiltrates. This group has an excellent prognosis with a 5-year OS of 92-94%.[8,12] We have noted that patients with only limited follicle-based patches (T1) respond very well to monotherapy with potent topical steroids with CR and OR rates of 83% and 100%, respectively. Some of these patients even achieved durable SCR and may be considered cured. However, it has not been found effective in patients with plaques. In case of more widespread skin lesions nbUVB may produce PR in patients with only follicle-based patches, in particular localized outside the head/neck area, but it has again been found ineffective in patients with plaques. PUVA treatment proves much more effective, both in patients with patches and patients with plaques with CR and OR rates of 30% and 88%, respectively and sustained CR in 18% of cases. PUVA proved effective irrespective of localization and degree of extension (T1 or T2) of skin lesions. Because of the preferential localization of FMF in the head and neck area and the presumed superior efficacy we normally advise oral rather than bath PUVA. However, one study reported high efficacy of bath PUVA in 14 early-stage FMF cases with superficial or keratosis pilaris-like skin lesions that were mainly localized outside the face, resulting in CR and OR rates of 71% and 100%, respectively.[13] Taken together, non-aggressive SDTs had been used as initial treatment in 80% of early-stage FMF patients and were sufficient in most cases with a CR and OR rates of 27% and 87%, respectively. In case of residual lesions after SDTs low-dose radiotherapy (2 x 4 Gy) proves highly effective.[10] In rare cases presenting with a solitary skin lesion local radiotherapy (20 Gy) had resulted in CR in all cases.

Treatment of advanced-stage skin-limited FMF (group B)

These patients present with infiltrated plaques, histologically characterized by extensive confluent or diffuse infiltrates containing many often medium-sized to large T-cells, tumors, nodules or in rare cases erythroderma and have a less favorable prognosis with a 5-year OS of 55%, respectively.[8] Treatment with potent topical steroids or nbUVB had been ineffective in this group. PUVA monotherapy was found to be less effective than in group A, but the OR rate was still 60%. In patients with plaques this treatment can therefore be attempted first. When treatment fails or when patients present with very thick plaques or tumors, several options may be considered: (i) PUVA therapy combined

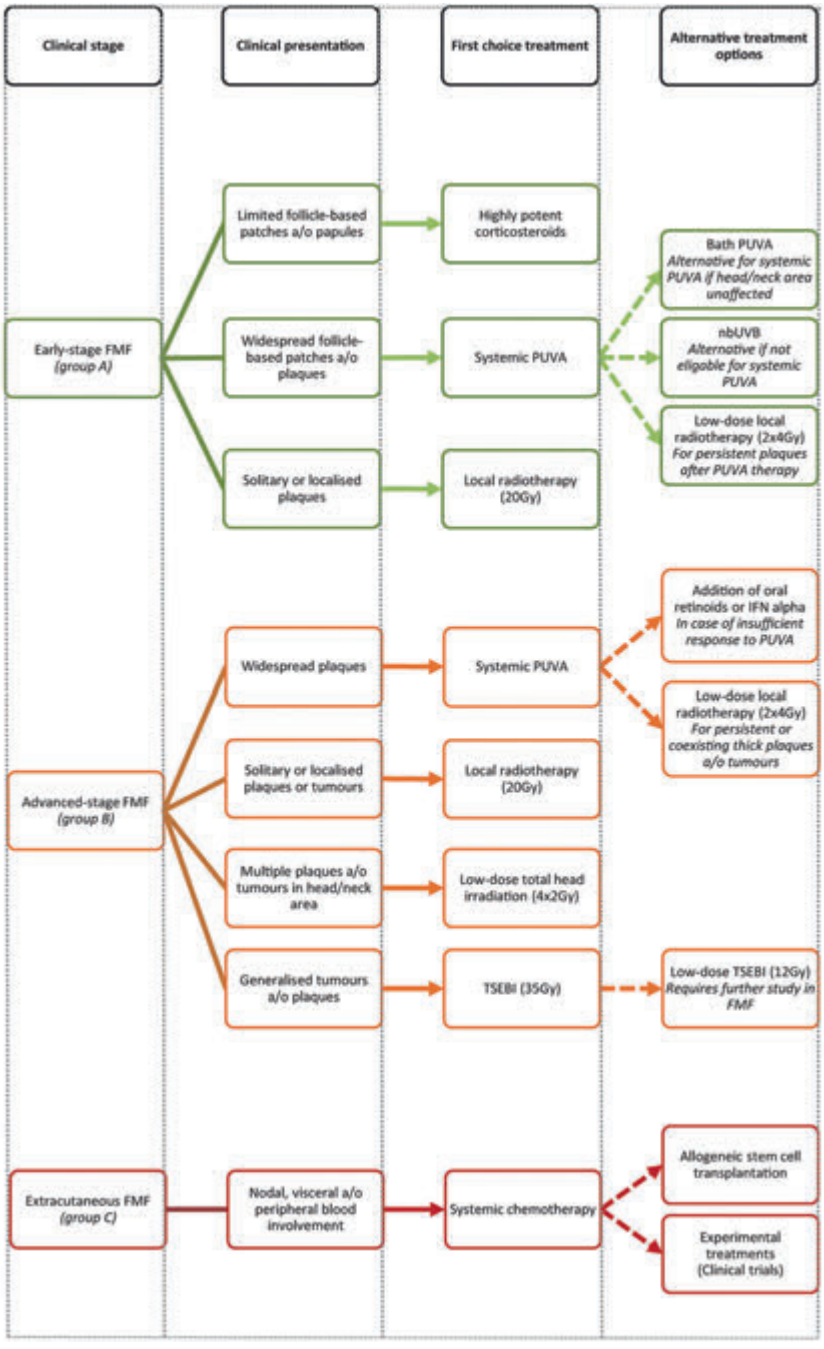

Figure 5. Algorithm with recommendations for initial treatment in patients with FMF**.**
FMF: Folliculotropic Mycosis Fungoides; a/o: and/or; PUVA: psoralen plus ultraviolet A; nbUVB: narrow-band UVB; Gy: Gray; IFN alpha: Interferon alpha; TSEBI: Total skin electron beam irradiation.

with local RT for most infiltrated lesions; (ii) TSEBI; (iii) PUVA therapy combined with IFNa or retinoids. In patients with widespread skin lesions we often prefer PUVA with additional low-dose radiotherapy for (persistent) thick plaques or tumors. This approach is very patient- and department-friendly (only two irradiations), has no side effects other than temporary hair loss in some patients, and is highly effective.[10] As patients with FMF may typically present with skin lesions on the head, total head irradiation with the same technique as used for TSEBI, but with a dose of 4 x 2 Gy and shielding of non-facial skin when appropriate, was found a very useful approach for extensive and infiltrated lesions. Concurrent less infiltrated skin lesions on trunk and extremities can be treated with PUVA. For patients presenting with a solitary or few localized plaques or tumors local radiotherapy is highly effective, may give durable CR and is the preferred mode of treatment.[2,14,15]

In patients presenting with widespread thick plaques and/or tumors TSEBI with a standard dose of 35 Gy proved an effective initial treatment with high CR and OR rates. In three of 19 cases durable complete remissions were observed, but in most patients response to treatment was short lived. Repeated use of TSEBI with a dose of 35 Gy is limited due to cumulative toxicity. Recent studies reported favorable responses of low-dose TSEBI (10-12 Gy) in classic MF, although the CR rates are lower than with conventional TSEBI (>30 Gy). An advantage of low-dose TSEBI, which is intended as palliative treatment, is that it can be used multiple times.[16,17] However, efficacy of low-dose TSEBI in FMF needs further study.

PUVA combined with retinoids or IFNa has been suggested as first-line therapy in patients with early-stage FMF with OR rates of 61% and 50%, respectively.[3] The results of the present study, in which these combinations were particularly used in patients with advanced-stage skin-limited FMF (group B) showed an OR rate of 65%, but CR was not achieved. After a good initial response disease can often be controlled effectively by continued treatment with retinoids or IFNa, without further PUVA therapy. While several studies describe efficacy of bexarotene monotherapy in patients with FMF, results on bexarotene as initial treatment have not been reported.[5,18]

Our cohort contained six patients presenting with erythrodermic FMF (stage III). They had been treated variously with PUVA combined with IFNa (two patients) or acitretin

(one patient), TSEBI, a combination of prednisone and chlorambucil and nbUVB. The OR rate was 67% and only one patient treated with prednisone and chlorambucil achieved a CR for more than eight years. Other options that can be considered are methotrexate and extracorporeal photopheresis with or without IFNa.[11] However, our small series and the lack of published reports precludes any conclusion on the optimal treatment of patients with stage III FMF.

In conclusion, the present study demonstrates that not all patients with FMF require aggressive initial treatment. Patients with early-stage FMF have an indolent disease course and may benefit very well from non-aggressive SDTs.

REFERENCES

1. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood.* 2005;105(10):3768-3785.
2. van Doorn R, Scheffer E, Willemze R. Follicular mycosis fungoides, a distinct disease entity with or without associated follicular mucinosis: a clinicopathologic and follow-up study of 51 patients. *Arch Dermatol.* 2002;138(2):191-198.
3. Gerami P, Rosen S, Kuzel T, Boone SL, Guitart J. Folliculotropic mycosis fungoides: an aggressive variant of cutaneous T-cell lymphoma. *Arch Dermatol.* 2008;144(6):738-746.
4. Lehman JS, Cook-Norris RH, Weed BR, et al. Folliculotropic mycosis fungoides: single-center study and systematic review. *Arch Dermatol.* 2010;146(6):607-613.
5. Muniesa C, Estrach T, Pujol RM, et al. Folliculotropic mycosis fungoides: clinicopathological features and outcome in a series of 20 cases. *J Am Acad Dermatol.* 2010;62(3):418-426.
6. Demirkesen C, Esirgen G, Engin B, Songur A, Oguz O. The clinical features and histopathologic patterns of folliculotropic mycosis fungoides in a series of 38 cases. *J Cutan Pathol.* 2015;42(1):22-31.
7. Marschalko M, Eros N, Kontar O, et al. Folliculotropic mycosis fungoides: clinicopathological analysis of 17 patients. *J Eur Acad Dermatol Venereol.* 2015;29(5):964-972.
8. van Santen S, Roach RE, van Doorn R, et al. Clinical Staging and Prognostic Factors in Folliculotropic Mycosis Fungoides. *JAMA Dermatol.* 2016.
9. Olsen EA, Whittaker S, Kim YH, et al. Clinical end points and response criteria in mycosis fungoides and Sezary 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(18):2598-2607.
10. Neelis KJ, Schimmel EC, Vermeer MH, Senff NJ, Willemze R, Noordijk EM. Low-dose palliative radiotherapy for cutaneous B- and T-cell lymphomas. *Int J Radiat Oncol Biol Phys.* 2009;74(1):154-158.
11. Trautinger F, Knobler R, Willemze R, et al. EORTC consensus recommendations for the treatment of mycosis fungoides/Sezary syndrome. *Eur J Cancer.* 2006;42(8):1014-1030.
12. Hodak E, Amitay-Laish I, Atzmony L, et al. New insights into folliculotropic mycosis fungoides (FMF): A single-center experience. *J Am Acad Dermatol.* 2016.
13. Pavlotsky F, Hodak E, Ben Amitay D, Barzilai A. Role of bath psoralen plus ultraviolet A in early-stage mycosis fungoides. *J Am Acad Dermatol.* 2014;71(3):536-541.
14. Kempf W, Kazakov DV, Schermesser M, et al. Unilesional follicular mycosis fungoides: report of two cases with progression to tumor stage and review of the literature. *J Cutan Pathol.* 2012;39(9):853-860.
15. Amitay-Laish I, Feinmesser M, Ben-Amitai D, Fenig E, Sorin D, Hodak E. Unilesional folliculotropic mycosis fungoides: a unique variant of cutaneous lymphoma. *J Eur Acad Dermatol Venereol.* 2016;30(1):25-29.
16. Hoppe RT, Harrison C, Tavallaee 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(2):286-292.
17. 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(1):138-143.
18. Drugeon C, Charlat I, Boulinguez S, Viraben R. [Bexarotene therapy in folliculotropic cutaneous T-cell lymphoma]. *Ann Dermatol Venereol.* 2007;134(8-9):639-643.