Introduction

Primary cutaneous T-cell lymphoma (CTCL) encompasses a heterogenous group of non-Hodgkin’s lymphoma (NHL), which are responsible for two-thirds of cutaneous lymphoma cases. Mycosis fungoides (MF) is the most common variant of CTCL, accounting for over half of all cases, and tends to be indolent in nature in the early stages, although it may progress to advanced stage disease. The incidence of MF is estimated at 5.6 per million persons, according to the Surveillance, Epidemiology and End Results (SEER) program of the United States National Cancer Institute and has remained steady since 1995 (1).

The CTCLs are currently classified according to the 2016 revision of the World Health Organization (WHO) classification of lymphoid neoplasms (2), which mostly integrates the WHO-EORTC cutaneous lymphoma classification from 2005 (3,4). The CTCL staging systems are based on the Bunn and Lamberg's tumour, lymph node, metastasis (TNM) system established in 1979 (5), which was revised to include a blood stage, TNMB in 2007 (Figure 1) (6). There are MF variants, namely folliculotropic MF, pagetoid reticulosis, and granulomatous slack skin, which have distinct clinical presentations and prognoses (3).

MF presents with localised cutaneous patches and plaques, which has a favourable survival outcome, but nearly a quarter progress to late stage with tumours, erythroderma, and systemic involvement. The majority of patients present with early stage MF (IA–IIA) with survival often of 10+ years (7) but because of the lack of any curative therapies patients suffer poor quality of life from painful, itchy and disfiguring lesions (8). A quarter of early stage patients will progress to advanced stage disease with a poor prognosis and median survival of 3 years (9). Sézary syndrome (SS) accounts for 5% of cases, and is characterised by erythroderma, lymphadenopathy and
leukemic involvement at diagnosis, with a median survival of 32 weeks (7).

Management is based on stage directed treatment with early stage MF (I1-IIA) using skin directed therapies (SDTs), including topical corticosteroids (TCS), phototherapy, topical chemotherapy or retinoids, and radiotherapy (4). There is no specific algorithm for management of early stage disease and treatments should be tailored according to individual patients needs and their side-effect profile (Table 1). Advanced stage (IIB–IV) or refractory MF often requires systemic treatments in combination with SDT for symptomatic relief. The impact of SDT in preventing MF progression is not fully known (4), and is primarily used as a palliative approach, aiming to improve the patient’s quality of life (10). SDTs may improve, pruritus, pain or clinical appearance. There is no evidence that more aggressive therapies prolong survival. The rationale is in part based on a key randomised controlled trial (RCT) comparing parenteral chemotherapy combined with electron beam radiation, against topical treatment. There were higher complete response (CR) rates in the systemic group at 38%, compared with 18% in the topical group. However, there was no significant difference in the disease-free or overall survival between the two groups after a median of 75 months follow-up. The combination group had considerable adverse effects and morbidity (11).

To provide standardised MF/SS trial assessments specific endpoints and response criteria were defined in a consensus statement in 2011 (12). The National Comprehensive Cancer Network Clinical Practice Guideline in Oncology on T-cell lymphomas has recently published updated guidance on the step-wise approach to MF/SS management (13). However there are only a very limited number of RCTs of SDTs in MF and most are single cohort reports. This review will focus on SDTs and their role in the management of classic MF/SS.

**Topical therapies**

There is limited evidence for topical therapies in MF due to the lack of RCTs or well-controlled studies. The therapies discussed have some clinical efficacy for patch and thin-plaque stage MF, however, information about specific response outcomes, such as duration of response and freedom from relapse is limited. The majority of topical therapies are not licensed for the MF usage.

**Emollients**

Emollients are frequently prescribed for patients with inflammatory skin conditions, including MF, and may reduce the itch sensation and scaling. Emollients reduce the transepidermal water loss, which may be further reduced with the use of humectants, that can reduce the corneocyte...
loss and alter the lipid barrier (10,14). A randomised, double-blind, placebo-controlled study assessed the efficacy of topical peldesine compared with emollient cream as placebo in patients with patch and plaque stage CTCL; the response rate was 28% and 24%, respectively, which was not statistically significant (15). The high emollient placebo response rate suggests the potential therapeutic value in moisturisers, which may be an important adjunctive alongside other topical therapies, and should be considered when assessing other treatments for early stage MF.

**TCS**

TCS are frequently prescribed for patients with early stage MF with patches or thin plaques as palliation. Despite their frequent usage, evidence for TCS is sparse. Zackheim et al. published the largest prospective study of 79 patients with stage T1 or T2 MF with the majority using class 1 TCS (very potent) mostly twice daily. Complete remission was achieved in 63% and partial remission in 31%, with a total response rate of 94% in the T1 group. The figures for the T2 patients were 25%, 57% and 82%, respectively. The response durations are rarely prolonged, and on stopping TCS therapy, only 37% of T1 and 18% of T2 patients remained in complete remission over the median follow-up period of 9 months (16). Lower strength topical steroids, fluocinolone acetonide 0.01% to 0.025%, in a small case series provided a response, which was less dramatic than stronger concentrations (17). Based on the limited data, the recommendation is to use high potency TCS over weaker concentration, which are typically well-tolerated with minimal risk of side-effects, if used in accordance with other inflammatory disease regimes (4).

**Topical mechlorethamine (nitrogen mustard)**

Since 1949, topical mechlorethamine (MCH, nitrogen mustard), a chemotherapeutic alkylating agent, has been approved as SDT for MF in the United States of America (USA) (4). The efficacy of MCH is around 51–84% CR for patients with stage T1 MF and 31–62.2% for T2 MF disease (18).

A key randomized, controlled, multi-centre trial with 260 patients evaluated the efficacy and safety of a novel MCH 0.02% gel compared with MCH 0.02% compounded ointment in stage IA–IIA MF. The primary endpoint was the Composite Assessment of Index Lesion Severity (CAILS), which demonstrated the MCH 0.02% gel was non-inferior to 0.02% MCH ointment with an overall RR of 58% versus 48%, respectively (19). The study was extended and 98 of the patients, who had not achieved CR applied a MCH 0.04% gel, where 26.5% achieved at least a

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical corticosteroids: potent/very potent (smaller surface areas treated)</td>
<td>Ease of use, Cheap, Available</td>
<td>Effective against inflammation/itch +/- anti-CTCL, Timely applications if large areas, Repeat prescriptions, large volumes, Skin thinning, striae, Systemic absorption, cortisol suppression</td>
</tr>
<tr>
<td>Phototherapy; (UV-B &amp; PUVA)</td>
<td>Highly effective, Durable response</td>
<td>Travel specialised centres, Longer term increase skin cancers</td>
</tr>
<tr>
<td>Radiotherapy: localised superficial radiotherapy; 8 Gy in 2 fractions, total skin electron beam (TSE); 2 weeks low dose course (12 Gy in 8 fractions)</td>
<td>Treatment over 2–3 days, Few systemic side effects</td>
<td>Travel to hospital, Increased cancer risk especially repeated treatments in younger patients</td>
</tr>
<tr>
<td>Alkylation agents: topical chlorimethine (nitrogen mustard)—new gel formulation EMA approved 2017 (LEDAGA®), topical Carmustine (BCNU)</td>
<td>Ease of use, Convenient application</td>
<td>Availability, Dermatitis</td>
</tr>
</tbody>
</table>

Table 1 Select the SDT therapy tailored to individual patients needs
50% reduction of their CAILS score, 6.1% CR and 20.4% partial response, suggesting a potential benefit with the higher strength MCH, if patients fail on 0.02% (20).

These studies highlight that topical MCH is effective for early stage MF. In 2017, the European Medicines Agency (EMA) approved MCH 0.02% gel (Ledaga®) for treatment in MF. The US Food and Drug Administration approved MCH 0.016% gel (Valchlor) for stage IA and IB MF in 2013 for patients, who had received other SDTs first. This eases the treatment access as it was historically on site prepared ointment and aqueous solutions.

A French study demonstrated that twice-weekly applications with MCH 0.02% aqueous solution followed by a potent TCS for 6 months in early stage MF achieved a 58% CR rate (21). The limitation of the published MCH studies, is that they are predominantly retrospective often complicated by using other therapies alongside topical MCH. There are variable response durations to topical MCH, but stage 1A MF patients may rarely be cured. The optimal treatment regime looking at frequency, spot or whole-body applications and use of combination or maintenance therapy is yet to be established.

Local adverse effects are common, particularly irritant contact dermatitis in 10–40% of cases, but also allergic contact dermatitis and hyperpigmentation. The risk of developing secondary malignancies as a direct result of topical MCH has been controversial with conflicting results, and patients were often managed with other treatment modalities known to increase the risk, including phototherapy and total skin electron beam therapy. In 2014, a 30-year population-based cohort study comparing MF patients, who had used topical MCH with patients not having received topical MCH. They concluded there was no increased risk of non-melanoma or melanoma skin cancers or pulmonary disease or cancer. Topical MCH did not affect the mortality and cause-specific mortality, indicating it as a safe therapy (22).

**Topical carmustine (BCNU)**

Carmustine, also known as bis-chloroethyl nitrosourea (BCNU) is an alkylating chemotherapy agent that has been used in patch and early-plaque stage MF. It needs to be compounded in an aqueous or ointment formulation. The efficacy appears similar to topical MCH with CR rates of 86%, 48% and 21% in stage T1, T2 and T4, respectively, with a median time of 11.5 weeks (23).

There are limited studies assessing the efficacy of BCNU. Compared with MCH, BCNU causes less hypersensitivity reactions, affecting around 5–10% of cases (7). The main concern with BCNU is the systemic absorption in up to 28% of patients, predisposing to myelosuppression (10). Consequently, full blood count monitoring is required and treatment given for short periods, 2–4 weeks for widespread disease. It is contraindicated to use maintenance BCNU (7).

**Other topical therapies**

The retinoid X-receptor bexarotene (1%) gel has been effectively used in patients where other topical therapies have failed. In a phase 1 and 2, open-label, dose-escalation trial of topical bexarotene gel the overall response rate was 63%, and CR rate of 21% in stage IA and IB disease. The response rate was higher (75%) if patients had not tried other topical therapies (67%) previously; 23 months was the estimated median response duration (24). A phase III trial assessing efficacy of topical bexarotene 1% gel in 50 patients with refractory or persistent early-stage MF patients, showed a CAILS response rate of 46% (25).

The Food and Drug Administration (FDA) has approved topical bexarotene 1% gel (Targetretin®) in CTCL stage IA and IB, who have refractory or persistent disease after other treatments (26). It is currently unlicensed in Europe.

Predominantly case reports and series have suggested other topical retinoid preparations, such as tazarotene 0.1% (27,28) and alitretinoin 0.1% (29) may be helpful in early MF stages. Imiquimod 5% (30-32), 5-fluorouracil cream (33), topical methotrexate-laurocapram (34) and tacrolimus 0.1% ointment (35) may also be beneficial. It is difficult to translate the data from uncontrolled topical studies, given the high response rate with emollients alone. Future randomised controlled trials are required to validate these topical modalities efficacy in MF.

**Phototherapy**

Phototherapy is a frequent key therapy in managing patients with MF and tends to produce high complete remission rates with variable response duration. Broadband, narrowband UVB light and psoralen plus ultraviolet A light photochemotherapy (PUVA) are traditional treatments, but more recently UVA1 and excimer laser are other emerging modalities. UVB therapy is recommended for patch or thin plaque MF and PUVA for thicker plaques (13). In 2016, the United States Cutaneous Lymphoma Consortium published a comprehensive review of the available data and
guidelines on phototherapy in MF/SS (36). Disadvantages include travel time to hospital and increase risk of other skin cancers.

**Ultraviolet B (UVB) phototherapy**

Broadband ultraviolet B (290–320 nm, bbUVB) is rarely in clinical use today, as it has been replaced by narrowband UVB (TL-01: 311–312 nm, nbUVB) lamps, given these are less erythemogenic and more effective in managing psoriasis (4). There are high and comparable response rates with early stage MF patients treated with nbUVB and bbUVB. A retrospective study reviewed 111 early stage MF patients treated with nbUVB and bbUVB. CR with nbUVB and bbUVB was achieved in 84% and 89% of IA patients and 78% and 44% of IB patients, respectively, after a mean time of 12.6 weeks (37).

In a review of patch and plaque stage MF patients treated nbUVB without systemic therapy, the CR rates were on average 84% (range =54% to 90%). Most received 3 treatments weekly (12/16 studies). nbUVB was more effective for patch stage MF and patients with fairer skin types (Fitzpatrick I–III). The relapse-free period ranged from 5.9 to 14.5 months in patients without maintenance nbUVB, and the relapse rate affected 29% to 100% (36).

In the literature there is a consensus that nbUVB is less effective with lower remission durations compared with PUVA, particularly for thicker plaques, but there are few comparative studies (9). A retrospective study with 95 early stage MF (IA, IB and IIA) patients treated with PUVA and 19 with nbUVB, suggested nbUVB was as effective as PUVA with compatible CR rates at 62.1% and 68.4%. There was no significant difference in the relapse times at 11.5 and 14.0 months for PUVA and nbUVB, respectively (38).

In a recent case series of 34 paediatric patients with MF, 17/21 (81%) of patients treated primarily with phototherapy responded. CRs were seen in 3/18 (17%) hypopigmented MF cases, all of whom were treated with nbUVB (39).

The value of maintenance UVB therapy in MF is to be defined, but there may be a reduction in the relapse rate and prolonged relapse-free intervals in some cases (36). In stage 1A MF, which has a normal or near normal long-term survival rate, it is likely that prolonged remission has little impact on prognosis (40,41). The nbUVB data is limited by a lack of prospective RCTs.

The risk of skin cancer development with nbUVB is overall reassuring (36). A literature review of around 3,400 patients, who predominantly had psoriasis, demonstrated no overall increase in skin cancer risk if treated with UVB, but there was an increased risk with patients treated with both UVB and PUVA in one study (42). Similarly, a Scottish study reviewing nearly 3,900 patients, mostly with psoriasis, who had been treated with nbUVB, did not have a significant risk of skin cancer compared with age- and sex-matched controls. However, caution has to be applied, as the median number of nbUVB treatments was 29 with only 352 receiving ≥100 treatments (43).

**PUVA photochemotherapy**

UVA penetrates the dermis deeper than UVB, is more effective at treating thicker plaques or MF refractory to UVB. The British Association of Dermatologists recommends PUVA as the first-line treatment of choice for plaque stage MF (44). The NCCN recommends PUVA for early stage or advanced MF if the plaques are thicker (13).

When used for MF, PUVA is often prescribed with 8-methoxypsoralen (MOP) given 2–3 times weekly. Oral 5-MOP is an alternative that is available in Europe and other parts of the world, but not in the USA, which causes less nausea (36). Bath PUVA has been shown to be effective in small case series, but is rarely used as the head is untreated, which may lead to early relapse at this site (4,45,46).

There are multiple non-randomised retrospective case series documenting the efficacy of PUVA in MF, but these are often difficult to compare, due to wide study heterogeneity. The United States Cutaneous Lymphoma Consortium summarised 6 PUVA studies and the CR rates were reported as 85%, 65%, and 85% for stage IA (13/152 patients), stage IB (114/175 patients), and stage IIA (30/35 patients), respectively (36). MF patches and thin plaques achieved CR quicker and more effectively than thicker plaques (47). A RCT showed that 25% of stage IB and IIA MF patients, who achieved CR with PUVA had a sustained duration of response (48).

There is limited data on the use of 5-MOP for MF. A retrospective study with small numbers found 5-MOP and 8-MOP PUVA to have similar efficacy in early stage MF (49).

Maintenance PUVA is an area of controversy, but is reported in the majority of studies, yet it remains uncertain if it prolongs remission (36). A small recent survey of International Society of Cutaneous Lymphoma members revealed that maintenance PUVA would be used by
88% of respondents, ranging from once weekly to once monthly (50). A single centre retrospective analysis of early stage MF evaluated long-term outcomes of patients having achieved complete remission with PUVA monotherapy. They concluded that 30–50% had prolonged remission (nearly 10 years disease-free survival rates), but the majority received maintenance PUVA. There was no difference in the overall survival rate between the relapsing and non-relapsing groups, but nearly a third of patients developed photodamage and cutaneous cancers (51). Another study by Höningsmann et al. reported just over half (55%) of stage IA and 39% of stage IB patients treated with PUVA were disease free at the end of a mean 44 months follow-up period, but maintenance was implemented (52). Maintenance PUVA did not prevent relapses in stage IA and IB MF disease in a recent prospective study (53).

Patients with stage IIB MF, often have tumours associated with patches and plaques. Phototherapy may be helpful in achieving response in the patches and plaques, whilst the tumours are managed with for example localised radiotherapy. Erythrodermic MF/SS patients (stage III/IVA) tolerate phototherapy poorly and it may exacerbate pruritus. A review of published cases of erythrodermic MF, including some with SS, receiving PUVA monotherapy had a CR rate of 43% (16/37) (36). For advanced MF/SS, salvage PUVA therapy can be employed for persistent patches and plaques or quickly relapsing disease after systemic therapies.

High cumulative dosages of PUVA are associated with an increased risk of non-melanoma skin cancers, particularly squamous cell carcinoma (SCC) (54). A meta-analysis demonstrated that patients with psoriasis, who had been exposed to high-dose PUVA (>200 treatments or 2,000 J/cm²) had a 14 times higher incidence than low dose patients (<100 treatments or <1,000 J/cm²) of developing SCCs (55). There may also an increased incidence of melanoma, although this is controversial (36). A study found the incidence of invasive melanoma to be 10 times greater than the general population for patients having received PUVA (56). Given this increased risk of skin cancers, the British Association of Dermatologists (BAD) and British Photodermatology Group guidelines for the safe and effective use of PUVA therapy 2015 recommend limiting the lifetime cumulative exposure to 1,200 J/cm² and/or 250 sessions (44). According to the BAD guidelines on CTCL, maintenance PUVA should ideally be avoided as it is rarely effective in preventing relapse (7). Maintenance PUVA may be considered in preventing MF that promptly relapses (44) and in rare cases of refractory MF for symptomatic benefit. This has to be carefully considered as patients with MF may require systemic chemotherapy in the future, which further increases their chances of secondary malignancy.

**UVA1**

UVA1 phototherapy (340–400 nm) penetrates more deeply into the dermis, compared with UVB and UVA, and small case series have shown benefit in MF (57-59). A recent case series with 19 early stage MF patients (IA–IIA) received UVA 5 times weekly for 5 weeks, and CR was 63% and partial response 37%. However, there was a high relapse rate within 3 months of stopping UVA1, affecting over half (58%) of patients who had achieved a CR (60).

UVA1 has been shown to be effective in advanced stage MF with widespread plaques, nodules and erythrodermic MF in a case series with 13 patients. CR was achieved in 85% and the remaining 15% achieved partial response, whilst the patients’ own unirradiated control lesions did not improve (57). These studies suggest UVA1 may be a useful addition to the MF treatment options but availability is limited.

**Combination PUVA regimes**

PUVA has been combined with systemic therapies, to try and improve efficacy and prolong remission. A systematic review of PUVA combination therapies concluded that for MF the addition of interferon-alpha or bexarotene was not superior to PUVA monotherapy in achieving an overall response (61). However, the combination may prolong the response and reduce the cumulative dosages of UVA, thereby reducing long-term side-effects (36). For advanced stage MF/SS, combination PUVA are not typically used as the first management step, but are employed as adjunctive or salvage therapy for residual MF lesions following other treatments for the tumours or nodal/visceral disease, although the data is lacking.

**PUVA and interferon-alpha**

Multiple studies have demonstrated that CR rates are often similar for PUVA combined with interferon-alpha compared to PUVA monotherapy (62–66). Retrospective trials have shown that PUVA combined with interferon-alpha reduced the cumulative dose of UVA and improved the duration of response compared with PUVA monotherapy.
A prospective randomised multicentre clinic trial assessed patients with stage I and II MF, and found there was a significantly higher complete remission rate (70%) and reduced time to response in the interferon alpha 2a and PUVA group compared with interferon alpha 2a and acitretin (38% complete remission) (68).

**PUVA and retinoids**

Oral retinoids may reduce the chances of developing non-melanoma skin cancers (69). Hence combining retinoids with phototherapy, particularly PUVA, may be pragmatic. The Scandinavian Mycosis Fungoides Group reviewed the CR rate of retinoids plus PUVA (re-PUVA) and PUVA, which was achieved in 73% and 72% respectively, with no significant difference. However, re-PUVA led to reduced phototherapy sessions and UVA dosages. The relapse rates were similar but a few patients experienced increased remissions if maintenance retinoids were given (70). A recent study showed that low-dose bexarotene combined with PUVA in patients with relapsed or treatment-refractory MF, achieved an overall response rate of 67%, which is similar to PUVA monotherapy, and was well-tolerated (69).

Similarly, the EORTC Cutaneous Lymphoma Task Force phase III RCT comparing oral bexarotene and PUVA with PUVA alone in stage IB and IIA MF. They did not demonstrate a significant response rate or duration difference between the two groups; 71% in the PUVA group and 77% in the combination group achieved CR at a median duration of 9.7 and 5.8 months respectively. There was a non-significant trend towards fewer PUVA sessions and lower UVA dose in the combination group. Interestingly 25% of patients achieving CR with either PUVA or the combination treatment had a sustained long-term response (48). For the PUVA and retinoid studies there is often limited data regarding outcomes, such as disease-free and overall survival.

**Photodynamic therapy**

Photodynamic therapy (PDT) is a new treatment option in MF patients with isolated skin lesions, not responding to other SDTs, which is well-tolerated and safe. A small case series has shown PDT to be efficacy in achieving complete or partial response in 70% (7/10), and 86% (6/7) remained in remission during the 8–31 months follow-up period (71). A comparable response rate (75%) was observed in another prospective study with early stage MF (72). The role of PDT in MF management has yet to fully established.

**Excimer laser**

Recent evidence suggests the excimer 308 nm laser is safe and potentially effective in early stage MF. Small case series have demonstrated its efficacy on isolated patches or difficult to reach anatomical sites (73-75). Its role within MF management has not been formalized yet and availability is limited.

**Radiotherapy**

**Localised radiotherapy**

Radiotherapy is used for all stages of MF, as it is an extremely radiosensitive condition (76-78). Superficial, localised radiotherapy is often employed as a palliative measure for localised plaques and tumours, which may be performed in combination with other therapeutic modalities, including phototherapy, other SDTs or systemic therapy (4). Consensus radiotherapy guidelines have been published by the International Lymphoma Radiation Oncology Groups in 2015 (79).

Low-grade localised radiotherapy may be used successfully in stage IA–IIB MF. Neelis et al. showed a high CR rate of 92% (60 out of 65 lesions) in patients with MF treated with 8 Gy in 2 fractions, whilst the lower dose of 4 Gy in 2 fractions only achieved a response rate of 30% (80). The lowest effective radiation dose is typically used given the palliative nature. Dosages of 8–12 Gy allow repeat treatment (79) of the same or adjacent area, despite field overlap, which is particularly helpful for difficult to treat areas, such as the lower legs.

Unilesional MF is rare, but localised higher dose radiotherapy (20 to 30 Gy in 2 fractions) may have a curative role (81-84). Tumours may require higher doses (79), and the depth of the lesions can be assessed by ultrasound, CT or MRI scan as necessary. Local radiotherapy also has a role in stage III–IVA erythrodermic MF/SS if it is associated are isolated tumours or severe hand and foot involvement. For advanced MF/SS limited peripheral nodes or visceral metastases can be managed with local external beam radiotherapy (85). Protocols are based on NHL management with low radiation doses used (86).

The dose and fractionation should consider the site, lesion type, potential acute and late complications to
surrounding skin and organs, and whether total skin electron beam therapy is required. If large affected areas, such as the trunk, limbs or scalp require radiotherapy, smaller dose per fractions should ideally be given. Increasingly, new radiotherapy techniques including complex matched electrons, intensity-modulated radiotherapy (IMRT) (87), helical Hi-ART therapy (88) and high-dose rate brachytherapy (89), are used to treat these areas. Curved skin surfaces, including the scalp and face can be effectively treated with these methods, providing prolonged control of MF.

Total skin electron beam radiotherapy (TSEBT)
TSEBT can be used for MF patients with extensive patches and plaques at any stage. Multiple retrospective studies have demonstrated that TSEBT has one of the highest overall response rates (90). The European Organization for Research and Treatment of Cancer (EORTC) Cutaneous Lymphoma Project Group has published guidance on clinical indications and technical delivery of TSEBT in MF management (91).

A retrospective cohort study demonstrated that stage 1A patients treated with TSEBT achieved a complete higher response rate at 97%, while it was 68% for topical MCH. The TSEBT group had a higher freedom from relapse at 59 % compared with 45% for topical MCH (P<0.05), but the long-term survival was similar (41). TSEBT has also been effective in generalised patch or plaque (T2) and tumour (T3) MF, as demonstrated by a CR in stage T2 at 75% and T3 at 47%. The group also compared TSEBT monotherapy with TSEBT using topical MCH, and both treatments achieved similar freedom from relapse, progression-free survival and overall survival (92). Hence TSEBT should be considered after patients have not responded to other first or second line treatments (7,93). For more advanced MF (T4) or SS, TSEBT can be used and combined with systemic therapies (90). Jones et al. showed that 60% of erythrodermic patients (T4) receiving TSEBT had a CR and at 5 years, 26% were disease free (94).

Standard TSEBT courses induce high remission rates, and typically 30–36 Gy are given over 8–10 weeks (4). TSEBT tends be to be given once only, but repeated treatments often at lower dosages without severe toxicities are an option (85). A pooled analysis of three phase-II clinical trials using low-dose TSEBT, included 33 patients with stage IB to IIA, had an overall response rate of 88% with a median response duration of 70.7 weeks, and repeated courses caused only mild toxicities (95). A recent prospective study assessed the efficacy of low-dose TSEBT, using 12 Gy in 8 fractions over 2 weeks in 103 patients with MF stage IB to IV. CR was observed in 18%, and 69% had a partial response with 11.8 months median response duration (96). There is a recent trend towards lower dose TSEBT (12 Gy in 8 fractions). This dose appears efficacious and may be given safely with less side-effects and repeated if needed. TSEBT using combination therapies and maintenance regimes, may improve the length of disease remission, but requires further long-term data (90).

The TSEBT beams are limited to a particular skin depth, thus reducing systemic toxicity. Acute adverse effects are dose-dependent and include local skin reactions, pain, loss of nails, and anhidrosis. Long-term effects include telangiectasias, alopecia, and secondary cutaneous cancers have been reported in patients having received multiple TSEBTs (85,97).

Conclusions
MF is a rare condition, leading to a paucity of RCTs comparing the different skin directed treatments. Treatments should be selected on an individual patient basis according to the common side-effects and preference of patients. Early stage MF patients may be controlled for many years with SDTs and periods of expectant (i.e., no therapy) are common. There are no curative therapies for early stage MF and as such patients suffer pain, itching and disfigurement for many years impacting on their quality of life (8). In addition to early stage skin lesions, skin tumours of MF are highly radiosensitive, and localised tumours may be treated with radiotherapy. The recent EMA approval of chloromethine gel will increase the availability of topical chemotherapy treatment and will be a useful addition to early stage treatments. Further studies are required to assess the efficacy of SDT combinations and maintenance therapies.

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None.

Footnote
Conflicts of Interest: JJ Scarisbrick has undertaken consultancy work in the past 5 years from Takeda, Helsinn, Actelion, Malinckrodt, Kyowa Kirin, 4SC. ML Lovgren has no conflicts of interest to declare.
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