Mogamulizumab & concomitant ultra-hypofractionated low-dose total skin electron beam therapy (2 x 4 Gy) in Cutaneous T-cell lymphoma: Proof of principle, report of two cases

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Rationale

Primary cutaneous lymphomas are a group of non-Hodgkin lymphomas with a global incidence of about 1 case per 100,000 annually, and around 800 new cases per year in Germany [1,2]. The most common subtype, mycosis fungoides (MF), constitutes 60% and typically presents with patches and plaques in its early stages, but up to 34% of patients progress to advanced stages with tumors and erythroderma. Sézary syndrome (SS) is more aggressive but rare (2–5%) and marked by erythroderma, lymphadenopathy, and the presence of Sézary cells in the skin, lymph nodes, and blood [3]. Advanced stages of MF and SS have poor prognoses, with survival ranging from 1.4 to 4.7 years [4]. Mogamulizumab and low-dose total skin electron beam therapy (TSEBT) are established treatments, though the combined effect of both therapies remains unclear.

Methods

Mogamulizumab

Mogamulizumab is a humanized antibody targeting C–C chemokine receptor type 4, approved for adults with MF and SS after prior systemic therapy. The phase III MAVORIC trial showed superior progression-free survival (PFS) with mogamulizumab (7.7 months) compared to vorinostat (3.1 months) [5]. Mogamulizumab is especially effective in patients with high blood tumor burden. In real-world studies, the overall response rate was 58.7%. Common side effects include rash, lymphopenia, infusion reactions, and fatigue. Mogamulizumab-associated rash (MAR) may correlate with better clinical outcomes [6]. Blood responses occur faster (median 1.1 months) than skin responses (median 3 months).

Total skin electron beam therapy

Local radiotherapy is effective for patients with localized skin lesions, but widespread involvement in MF and SS often requires total skin electron beam therapy (TSEBT). Though controversial in SS due to limited long-term remission, TSEBT reduces circulating Sézary cells [7]. Combining TSEBT with immunotherapies and stem cell transplantation may improve outcomes [8]. TSEBT can rapidly improve skin symptoms and quality of life, reduce tumor burden, and alter the tumor microenvironment [9]. Low-dose TSEBT (8–12 Gy) is increasingly used for symptom relief, with ultra-hypofractionated low dose TSEBT (2 x 4 Gy) emerging for rapid remission in advanced-stage disease [10].

With this background, mogamulizumab and low-dose TSEBT in concurrent combination could have the potential to benefit patients from the outset of treatment by addressing the blood and skin compartments in particular [11, 12]. This report details two case studies of patients with SS for whom multiple treatments have previously failed due to poor tolerability and lack of response. The patients were both treated with mogamulizumab in combination with concurrent ultra-hypofractionated low-dose TSEBT [13].

Patients

Patient 1: A 66-year-old woman with SS was treated with concomitant mogamulizumab and TSEBT (Fig. 1 & 2) in July 2020 due to disease progression. This resulted in near-complete remission (CR) of skin involvement and pruritus within 2 weeks. By August 2020, blood analysis confirmed CR with reduced lymphocyte counts. The treatment was well tolerated with no adverse events. As of June 2024, the patient continues on mogamulizumab monotherapy every two weeks, maintaining near CR in the skin and CR in the blood.

Patient 2: In October 2021 a 83-year-old man with SS underwent combined mogamulizumab and TSEBT (Fig.1 & 3). Within 2 weeks, early remission was achieved in the skin, with complete remission (CR) in the blood. CR was maintained through 11 mogamulizumab administrations, which were well tolerated. After the last dose in March 2022, the patient relapsed with skin involvement and is currently being treated with brentuximab vedotin, achieving partial remission and maintaining a good quality of life.

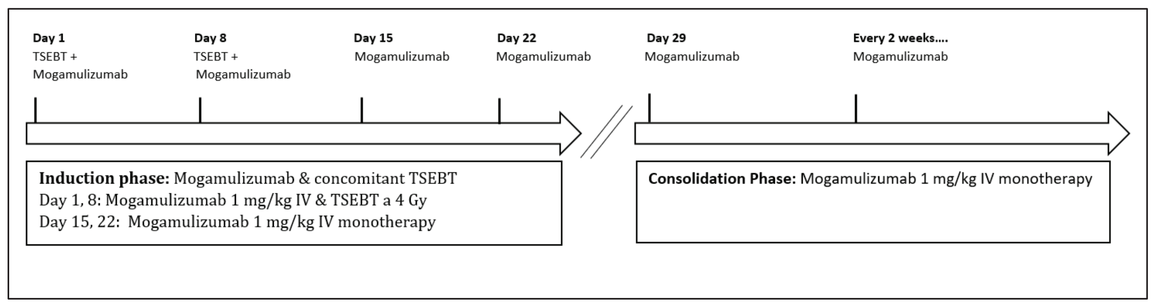

Fig.1: Concurrent ultra-hypofractionated low-dose TSEBT & Mogamulizumab

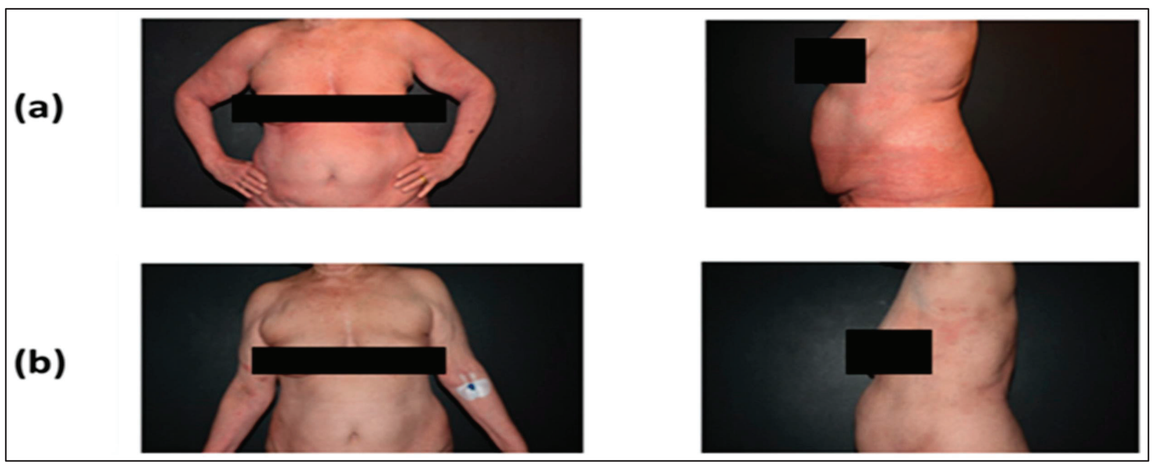

Fig.2: Patient 1 (a) before and (b) after concurrent mogamulizumab and TSEBT

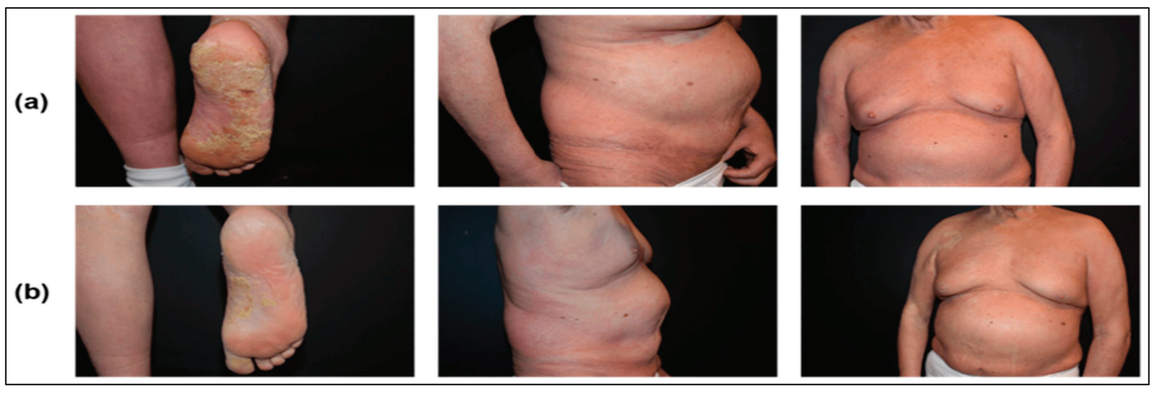

Fig.3: Patient 2 (a) before and (b) after concurrent mogamulizumab and TSEBT

Conclusion

Concurrent therapy with mogamulizumab and ultra hypofractionated low-dose TSEBT was associated with excellent tolerability and promising and fast clinical responses in the blood and skin compartments in two patients with Sézary syndrome. This concurrent combination regimen may be a possible treatment option for patients with SS, including those who are heavily pretreated. However, these limited observations should be investigated in further research, including clinical trials, to confirm the efficacy and safety and to determine if there is an additive effect of the combination on the response rates when compared with the monotherapy.

Contact

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