USE OF MOGAMULIZUMAB FOR REFRACTORY SÉZARY SYNDROME IN REAL CLINICAL PRACTICE: REPORT OF THREE CASES.

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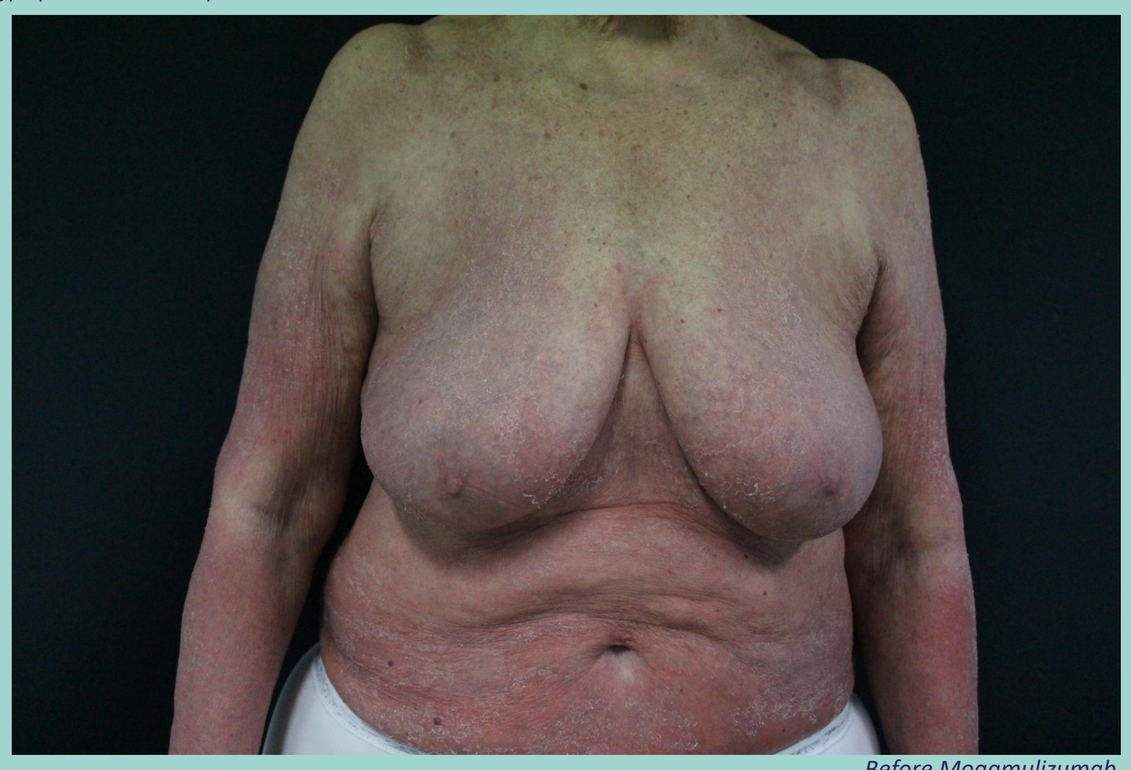
INTRODUCTION

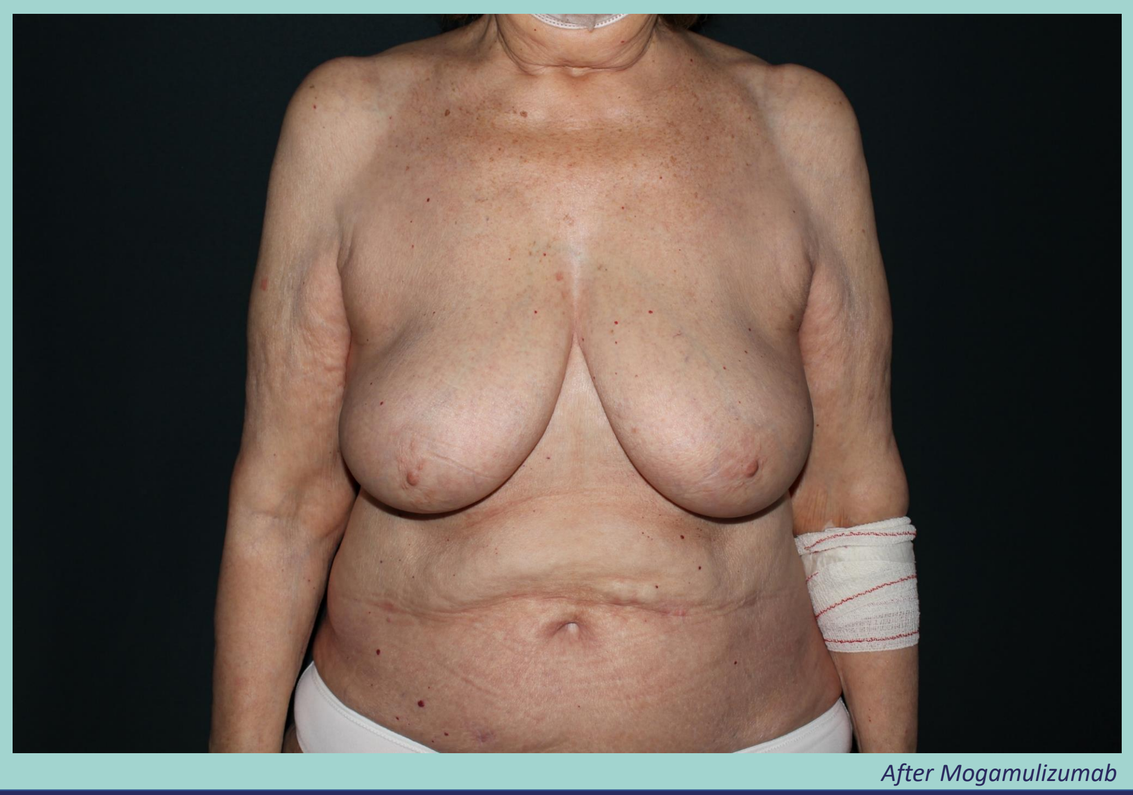
Sézary syndrome (SS) is a cutaneous T cell lymphoma (CTLC) with poor prognosis which can present *de novo* or secondary to mycosis fungoides (MF). We report our experience treating patients with SS with mogamulizumab (n=3).

CASE 1

A 76-year-old woman presented with an 8-year history of refractory erythroderma. Skin biopsy showed dermal lymphocytic infiltrate with aberrant phenotype. Flow cytometry blood analysis detected 77% pathologic T-lymphocytes (TL) with SS phenotype and positive T-cell receptor (TCR) ϒ gene rearrangement. Lymph node biopsy showed SS infiltration. She was diagnosed with stage IVA1 SS (T4N1M0B2). Due to disease progression after treatment with bexarotene, mogamulizumab was started following the usual protocol. Patient achieved complete clinical response (CR) since the 2nd infusion in skin, blood and lymph nodes. She presented grade IV neutropenia after the 6th infusion which resolved with filgastrim, and a grade II lymphopenia after the 5th infusion which resolved with posology spaced to every 6 weeks. Patient continues disease-free after 15 months of treatment.



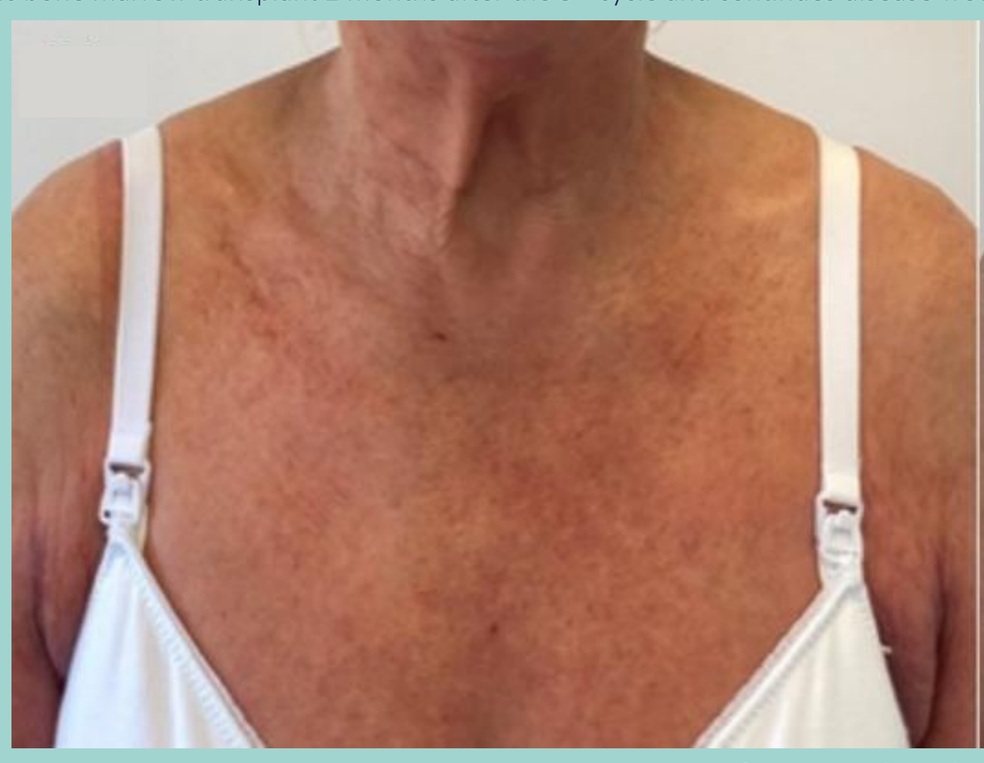
Before Mogamulizumab



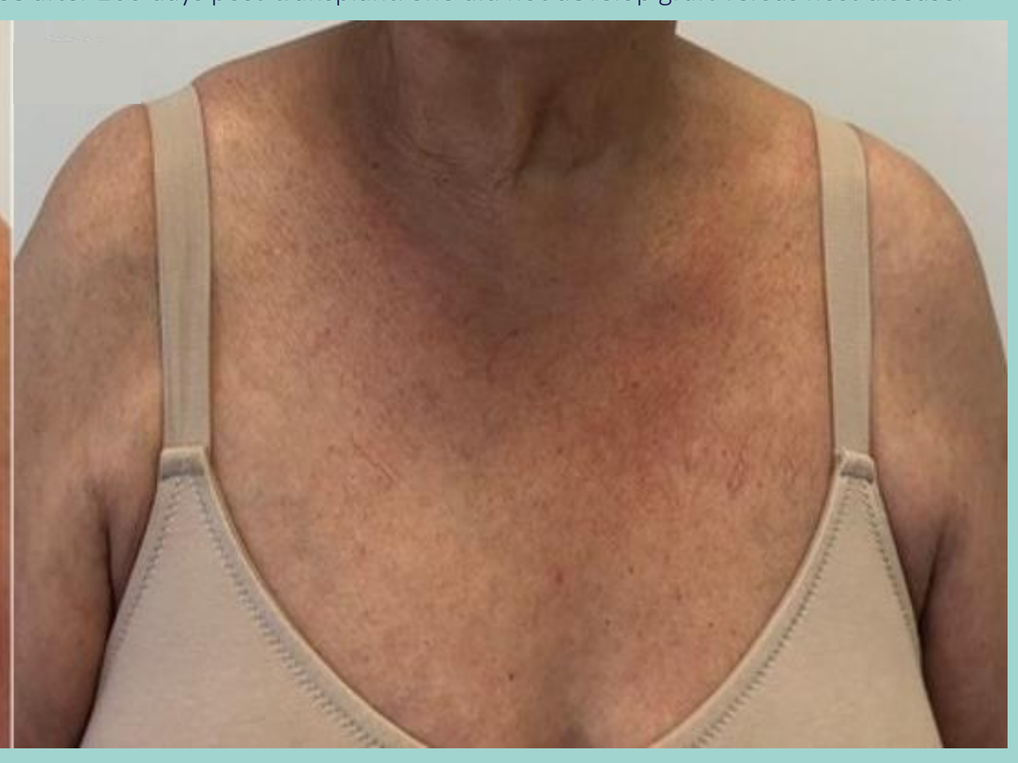
After Mogamulizumab

CASE 2

A 66-year-old woman presented with a 1-year history of erythroderma. Skin biopsies were consistent with MF. Flow cytometry blood analysis detected 59.2% of pathological TL with SS phenotype and positive TCR ϒ gene rearrangement. Lymph node biopsy showed SS infiltration. Diagnosis of stage IVA2 SS (T4N3M0B2) was established. She was treated with extracorporeal photopheresis, interferon α-2B, bexarotene and gemcitabine with partial response. Treatment with mogamulizumab was started with complete CR after the 4th infusion in skin, lymph nodes, and blood with good tolerability. She received an allogeneic bone marrow transplant 2 months after the 5th cycle and continues disease-free after 200 days post-transplant. She did not develop graft versus host disease.



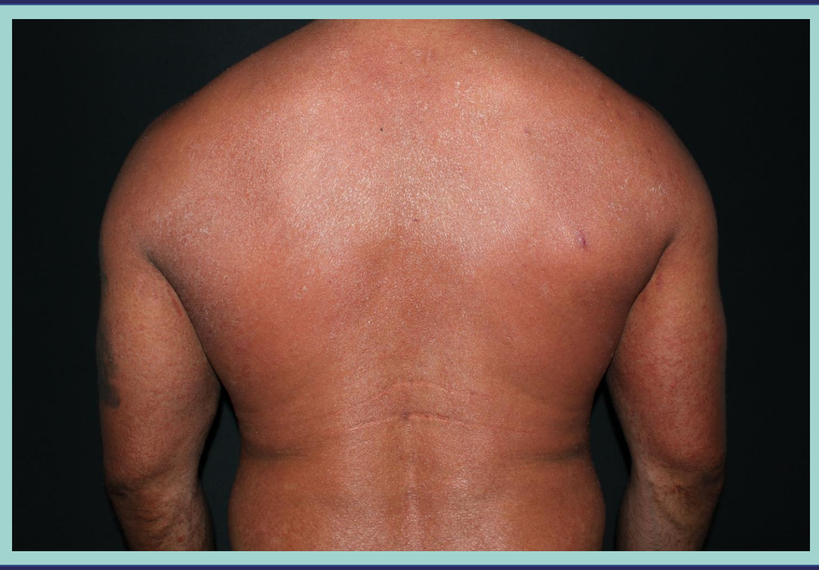
Before Mogamulizumab

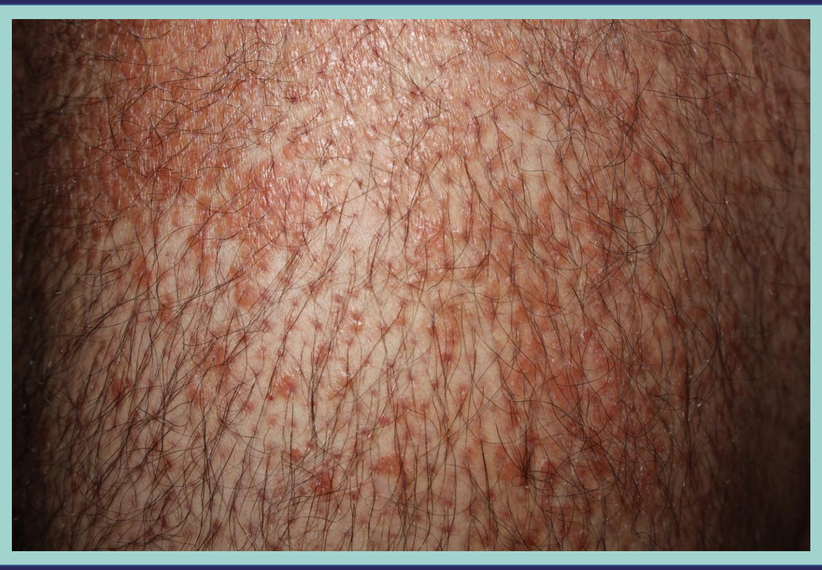


After Mogamulizumab

CASE 3

A 36-year-old man presented with follicular infiltrated papules and alopecia affecting most of the body surface. Flow cytometry blood analysis showed 93% of pathological TL and positive TCR ϒ gene rearrangement. Skin biopsy was consistent with MF. Lymph nodes showed SS infiltration. Patient was diagnosed with Stage IVA2 SS (T2N3M0B2). He was treated with bexarotene and brentuximab with initial CR, but disease progressed after 10 cycles. Treatment with mogamulizumab was started with initial improvement. However, it did not persist after 6 months.





DISCUSSION

Mogamulizumab is a monoclonal antibody that selectively binds to CCR4 present on atypical TL. To date, only a series of 13 patients with CTCL treated with mogamulizumab in routine clinical practice has been reported, with good tolerability and CR in blood (76.9%) and skin (66.7%) compartments, whereas lymph node compartment remained stable in most patients or presented partial response. In our series 2 out of 3 patients presented an impressive CR in all aspects of the disease (blood, skin and lymph node compartments). The patients who responded to mogamulizumab presented an early remission since the firsts infusions of the drug. One patient developed neutropenia and lymphopenia in relation to mogamulizumab, which resolved after specific treatment.

This series supports the use of mogamulizumab in patients with refractory SS. The use of biomarkers which predict the response to mogamulizumab in SS patients should be further investigated in order to estimate which patients will achieve CR. Larger series are needed to evaluate the use mogamulizumab for CTCL in routine clinical practice.

REFERENCES

1. Agar NS, Wedgeworth E, Crichton S, et al. Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. J Clin Oncol. 2010;28:4730-4739.
2. Ishii T, Ishida T, Utsunomiya A, et al. Defucosylated humanized anti-CCR4 monoclonal antibody KW-0761 as a novel immunotherapeutic agent for adult T-cell leukemia/lymphoma. Clin Cancer Res. 2010;16:1520-1531.
3. Kim YH, Bagot M, Pinter-Brown L, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial [published correction appears in Lancet Oncol. 2018 Nov;19(11):e581]. Lancet Oncol. 2018;19:1192-1204.
4. Molloy K, Vico C, Ortiz-Romero PL, Scarisbrick JJ. Real-world experience of using mogamulizumab in relapsed/refractory mycosis fungoides/Sézary syndrome Br J Dermatol. 2020;10.1111/bjd.19720.

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