

Change in Lymphocyte Count as a Predictor of Response to Mogamulizumab in Patients with Mycosis Fungoides or Sézary Syndrome

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Plain Language Main Finding

- Patients on mogamulizumab showed an early decrease in lymphocyte counts, which could be an early marker for response

Introduction

- Malignant lymphocytes in cutaneous T-cell lymphomas (CTCLs), the two most common forms of which are mycosis fungoides (MF) and Sézary syndrome (SS), consistently express the chemokine receptor CCR4, which is involved in T-cell homing to the skin¹
- Mogamulizumab is a humanized, defucosylated, anti-CCR4 antibody approved for use in patients with relapsed/refractory MF or SS^{2,3}
- Reduced lymphocyte count can occur in patients treated with mogamulizumab⁴

Objectives

- This *post hoc* analysis evaluated the shift in lymphocyte populations during mogamulizumab treatment and correlated changes from baseline to highest grade of lymphopenia with clinical outcomes in MAVORIC

Methods

- Patients with histologically confirmed MF or SS received mogamulizumab (1.0 mg/kg IV weekly for 4 wks then biweekly, n=186) or vorinostat (400 mg/d PO, n=186)
- Cell populations were assessed by flow cytometry; lymphocyte data were available for 174 and 169 mogamulizumab- and vorinostat-treated patients, respectively
- In this *post hoc* analysis, highest grade shift in total absolute lymphocyte count from baseline was assessed along with global response
 - Relatively few patients had Grade ≥1 lymphopenia at baseline; therefore, this analysis primarily focused on patients with Grade 0 lymphopenia
 - Lymphocyte shifts were defined using CTCAE v5.0 definitions of lymphopenia (**Table 1**)⁵

Table 1. Lymphocyte Grade Definitions⁵

Lymphocyte Grade	Absolute Lymphocyte Count, mm ³
Grade 0	≥1000
Grade 1	800-1000
Grade 2	<800-500
Grade 3	<500-200
Grade 4	<200

- Patients were stratified by baseline blood involvement (B0, detectable Sézary cells <250/μl; B1, ≥250 to <1000 cells/μl; B2, ≥1000/μl)
- Global composite response was based on response in skin, blood, lymph nodes, and viscera

Results

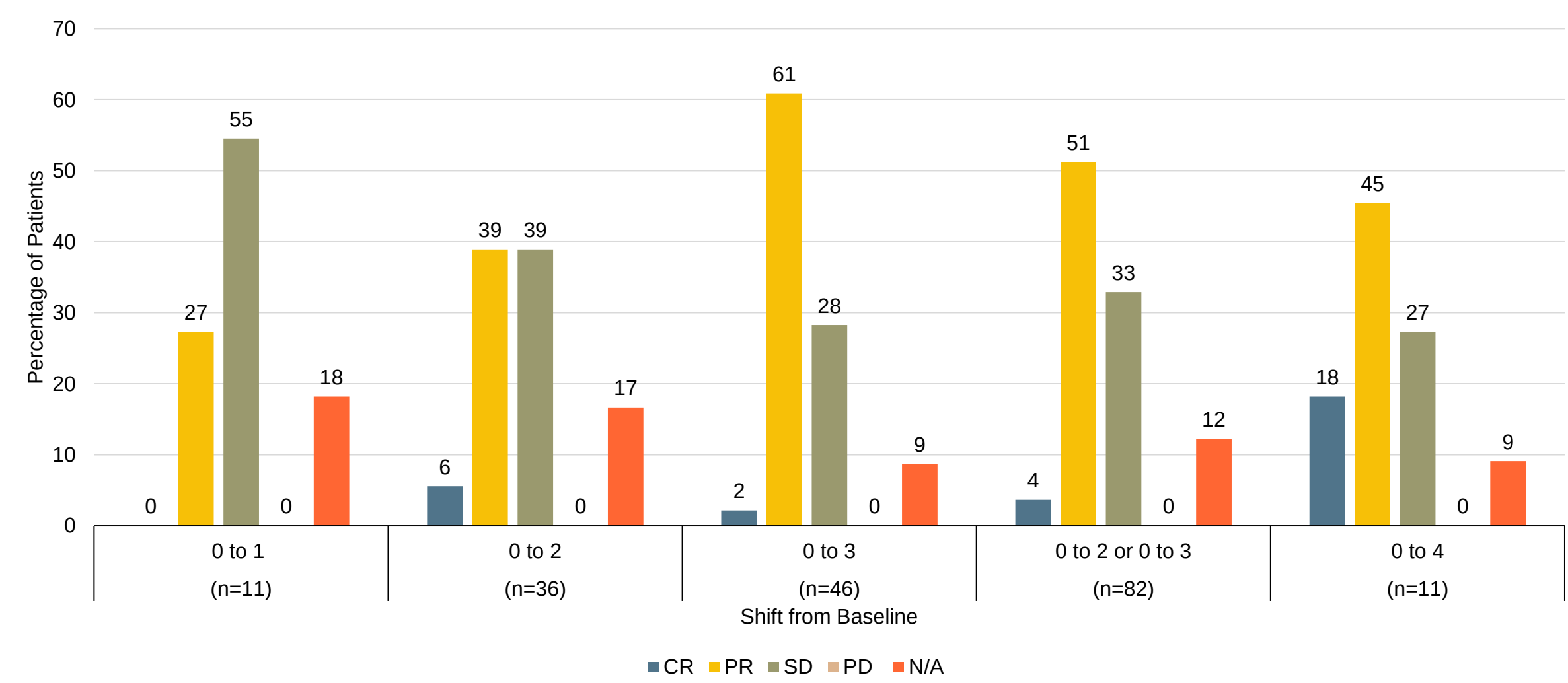
- In the mogamulizumab arm, Grade 1-4 lymphopenia occurred in approximately 80% (138/174) of patients and was most often observed following one cycle of mogamulizumab treatment
- In the vorinostat arm, 38% of patients (65/169) developed Grade 1-4 lymphopenia
- Most mogamulizumab patients had a shift from Grade 0 to Grade 1-3 lymphopenia (93/174, 53.4%)
- The number of patients with shifts from Grade 0 at baseline to Grades 1-4 is reported in **Table 2**

Table 2. Highest Grade Shifts for Patients Receiving Mogamulizumab or Vorinostat

Grade Shift	Mogamulizumab, n (%) n=174	Vorinostat, n (%) n=169
0 to 1	11 (6.3)	16 (9.5)
0 to 2	36 (20.7)	15 (8.9)
0 to 3	46 (26.4)	5 (3.0)
0 to 2 or 3	82 (47.1)	20 (11.8)
0 to 4	11 (6.3)	0 (0.0)

- Infections and infestations after a reduction in absolute lymphocyte count were reported in 18 (11.3%), 53 (33.3%), 22 (13.8%), and 5 (3.2%) of mogamulizumab-treated patients with grade 1, 2, 3, or ≥4 lymphopenia, respectively
- Mogamulizumab-treated patients with a shift from Grade 0 to Grade 1-4 lymphopenia were more likely to exhibit disease control (complete response [CR], partial response [PR], or stable disease [SD]) (**Figure 1**)
 - No significant difference was observed (p=0.085) in objective response rate (ORR; CR, PR) between patients with shifts from Grade 0 to 1 (27.3% ORR [3/11]) and from Grade 0 to 2 or 3 (54.9% ORR [45/82]) (**Figure 1**)

Figure 1. Best Response and Highest Grade Shifts in Absolute Lymphocytes for Mogamulizumab Patients (N=174)



CR, complete response; N/A, not applicable; PD, progressive disease; PR, partial response; SD, stable disease.

- A higher percentage of patients with MF B2 or SS (69% and 58%, respectively) had a lymphocyte shift from Grade 0 to either Grade 2 or 3 than patients with less blood involvement (B1, 39%; B0, 32%)
- The ORRs for patients receiving mogamulizumab with shifts from Grade 0 to 1 and 0 to 2 or 3 were 27.3% (3/11) and 54.9% (45/82), respectively (**Table 3**)
 - Mogamulizumab-treated patients who had no lymphopenia at baseline and did not develop lymphopenia during treatment had an ORR of 11.1% (4/36) and a DCR of 77.8% (28/36)

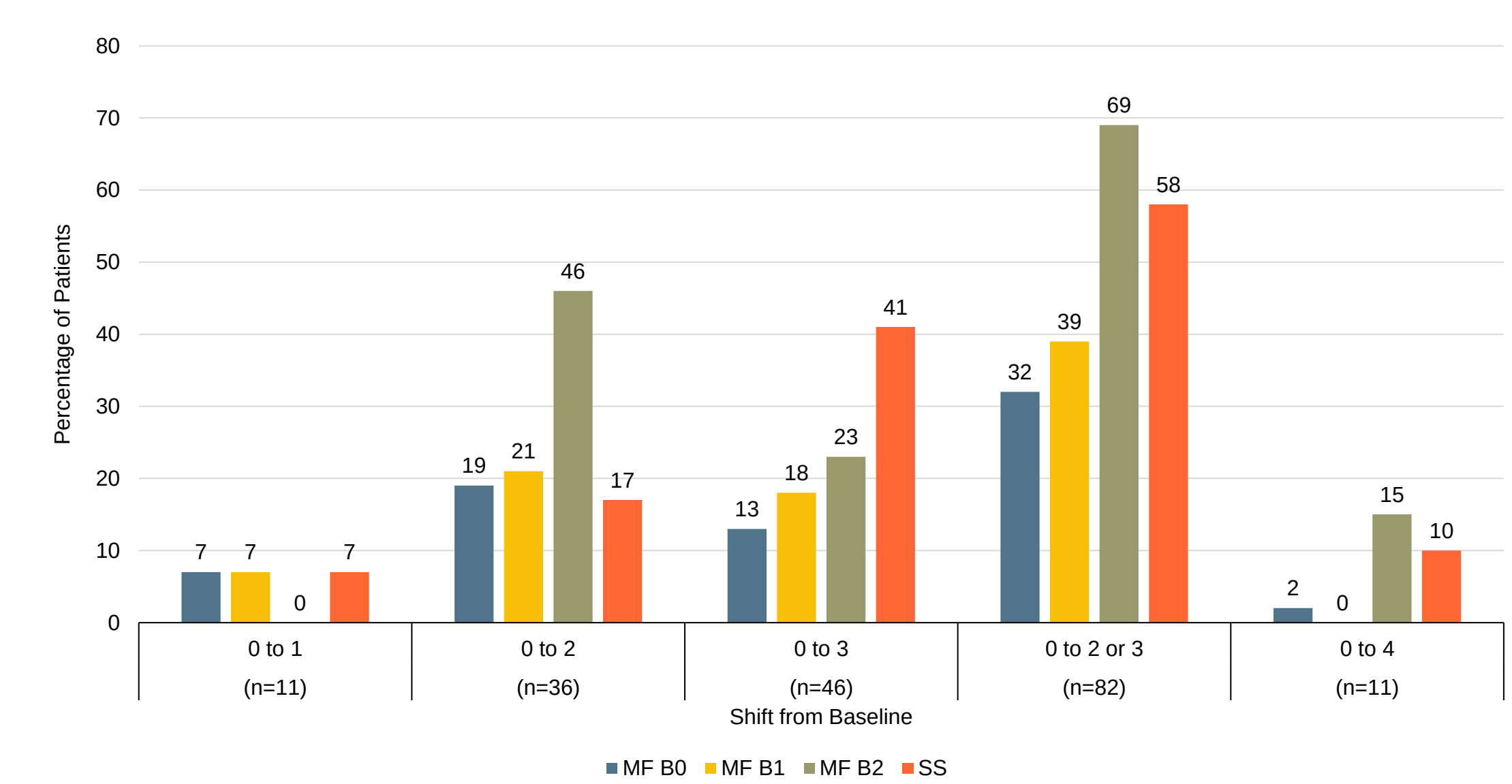
Table 3. ORR and DCR in Mogamulizumab-Treated Patients (N=174)

Grade Shift	ORR, n/N (%)	DCR, n/N (%)
0 to 1	3/11 (27.3)	9/11 (81.8)
0 to 2	16/36 (44.4)	30/36 (83.3)
0 to 3	29/46 (63.0)	42/46 (91.3)
0 to 2 or 3	45/82 (54.9)	72/82 (87.8)
0 to 4	7/11 (63.6)	10/11 (90.1)

DCR, disease control rate; ORR, objective response rate.

- When assessed by blood classification, patients with SS or MF B2 had generally higher rates of shift from Grade 0 to 1-4 than other blood classes (**Figure 2**)

Figure 2. Blood Classification and Highest Grade Shifts in Absolute Lymphocytes for Mogamulizumab Patients (N=174)



- Lymphopenia in mogamulizumab-treated patients did not show a consistent pattern with regard to skin response, but early change CD4+/CD8+ corresponded to skin improvements in B2 patients (data not shown)

Conclusions

- Patients receiving mogamulizumab experienced an early decrease in lymphocyte counts, which could be an early marker for response**
- Patients with blood classification MF B2 and SS had higher grade lymphopenia, which may be the result of mogamulizumab's effect on clearing CCR4-expressing malignant cells from blood**
- Depth of lymphopenia in mogamulizumab-treated patients did not correlate with clinical response**
- No evident increase in the incidence of infections with severity of lymphopenia was observed**

References

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Disclosures

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