The Correlation Between Skin Response and Blood Involvement with Mogamulizumab

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Introduction

- The prognosis for patients with advanced-stage mycosis fungoides (MF) or Sézary syndrome (SS) is poor, with a median survival of between 4.7 and 1.4 years depending on a patient's exact stage.[1] Advanced-stage MF and SS patients therefore have an unmet clinical need for effective treatments
- Disease staging in MF and SS was based on the tumour-node-metastasis (TNM) classification and involved disease specific findings
- In 2007, blood classification (blood tumour burden B0, B1, or B2) was added to disease staging in MF and SS based on the recognition of blood involvement as a prognostic factor[2]
  - Increasing blood tumour burden portends worse overall and disease-specific survival and an increased risk of disease progression[1]
  - The median survival time for patients with blood tumour burden B1 and B2 is 3.2 years and 3.1 years, respectively, independent of disease stage[1]
- Mogamulizumab was compared with vorinostat in the international, open-label, randomized, controlled phase 3 MAVORIC trial in patients with relapsed or refractory MF or SS (disease stages IB–IVB) who had failed at least 1 prior systemic therapy[3]
  - Mogamulizumab significantly improved progression-free survival and overall response rates versus vorinostat
  - 68% of patients treated with mogamulizumab achieved a blood response (median time 1.1 months)
  - The median duration of the blood response in patients treated with mogamulizumab was 25.5 months

Objective

- The objective of this post hoc analysis was to examine the correlation between levels of blood involvement and skin response in patients treated with either mogamulizumab or vorinostat in the MAVORIC trial

Methods

- Patients were randomized 1:1 to receive either intravenous mogamulizumab 1.0 mg/kg once weekly for the first 28-day cycle, then on Days 1 and 15 of subsequent cycles, or oral vorinostat 400 mg once daily
- Skin response was assessed every 4 weeks using the modified Severity Weighted Assessment Tool (mSWAT)
- The median percentage change in mSWAT score per treatment cycle and best overall response by percentage change in mSWAT score per patient were examined in patients in each treatment group in patients in each treatment arm stratified by blood classification (B0, B1, or B2)

Results

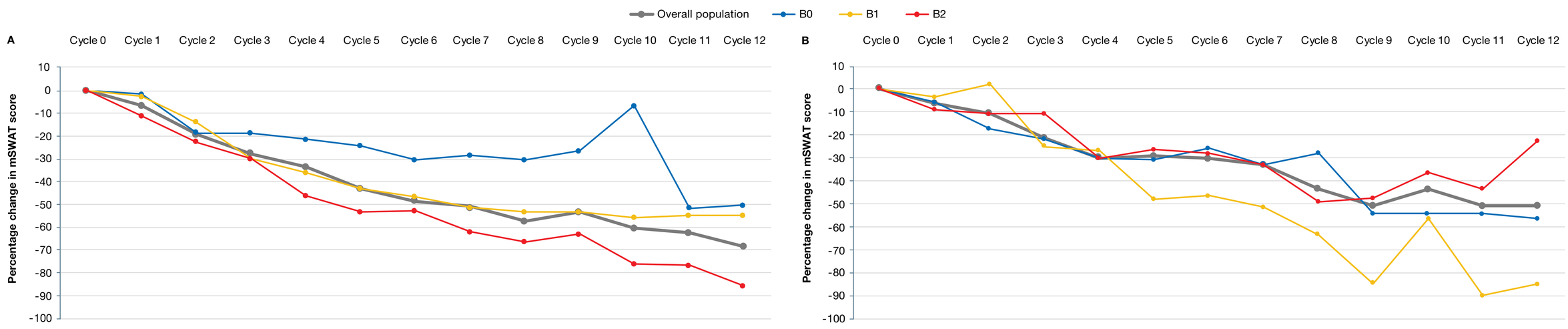
Response in mSWAT per treatment cycle

- Over 12 treatment cycles, mogamulizumab-treated patients with blood tumour burden B1 or B2 experienced a significantly greater ($p \leq 0.001$; $\chi^2=13.66$) improvement in mSWAT score compared with mogamulizumab-treated patients with no blood involvement (blood tumour burden B0), with at least a 50% median percentage change in mSWAT score occurring by Cycle 7 of mogamulizumab in the overall population and in the blood tumour burden B1 and B2 groups (**Figure 1A**)
  - Patients with blood tumour burden B2 experienced the greatest improvement in median percentage change in mSWAT score by Cycle 12 of mogamulizumab (–86.0%)
- The response by median percentage change in mSWAT score per patient shows that the overall population of vorinostat-treated patients experienced less improvement in skin response compared with the overall population of mogamulizumab-treated patients, with little-to-no correlation with blood classification (**Figure 1B**)

Best overall response in mSWAT per patient

- In the mogamulizumab treatment arm, 81 patients (43.5%; B0, n=16; B1, n=14; and B2, n=51) had a best overall response of at least a 50% change in mSWAT score compared with 41 vorinostat-treated patients (22.0%; B0, n=14; B1, n=5; and B2, n=22), and these responses to mogamulizumab occurred most often in patients with blood tumour burden B1 and B2 (**Figure 2A**)
  - 16 mogamulizumab-treated patients with blood tumour burden B2 experienced a 100% change in mSWAT score compared with 3 vorinostat-treated patients with blood tumour burden B2
- In the vorinostat treatment arm, 4 patients experienced a 100% change in mSWAT score (**Figure 2B**)

Figure 1. Skin Response Based on Median Percentage Change in mSWAT Score per Treatment Cycle Stratified by Blood Classification in the Mogamulizumab (A) and Vorinostat (B) Treatment Arms.

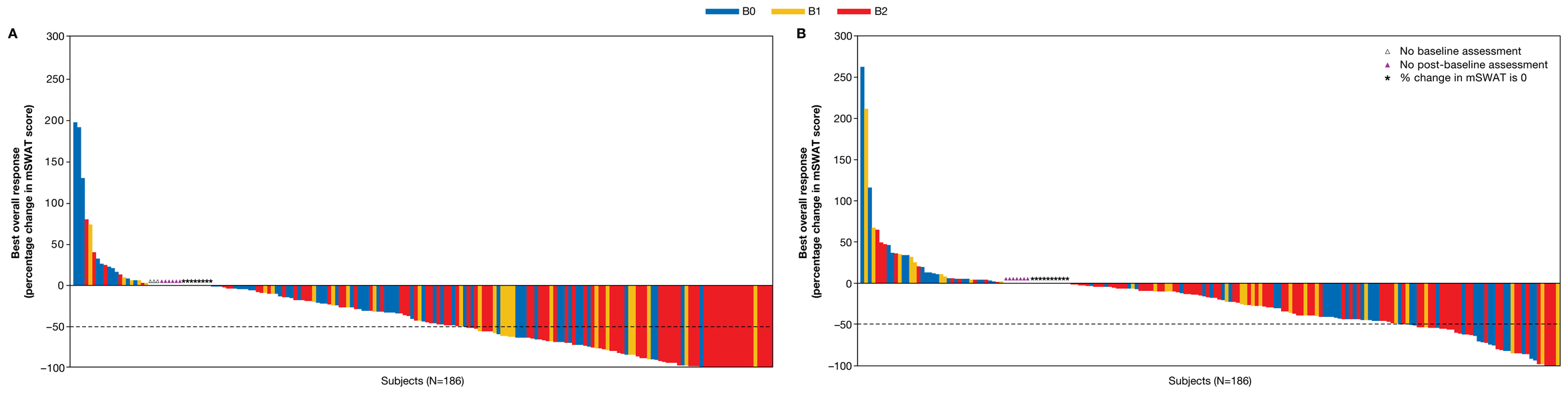


Cycle	0	1	2	3	4	5	6	7	8	9	10	11	12
Overall population	186	174	155	129	112	103	96	88	81	75	62	55	45
B0	64	61	51	39	32	27	21	19	14	12	9	7	7
B1	31	30	25	21	19	17	19	18	16	15	13	11	9
B2	91	83	79	69	61	59	56	51	51	48	40	37	29
MF, n (%)	105 (56.5)												20 (44.4)
SS, n (%)	81 (43.5)												25 (55.6)
T4, n (%)	92 (49.5)												31 (68.9)

Cycle	0	1	2	3	4	5	6	7	8	9	10	11	12
Overall population	186	174	136	96	66	58	48	39	34	27	25	22	19
B0	62	54	44	35	26	23	20	15	14	10	9	9	8
B1	31	29	19	13	8	6	6	4	4	3	4	2	3
B2	93	91	73	48	32	29	22	20	16	14	12	11	8
MF, n (%)	99 (53.2)												14 (73.3)
SS, n (%)	87 (46.8)												5 (26.3)
T4, n (%)	84 (45.2)												5 (26.3)

B0 = <15% CD4+CD26– cells or CD4+CD7– cells by flow cytometry. B1 = ≥15% CD4+CD26– cells or CD4+CD7– cells by flow cytometry. B2 = ≥1,000 mcg/L Sézary cells with positive clone, CD4/CD8 ratio ≥10, ≥40% CD4+CD7– cells, or ≥30% CD4+CD26– cells. T4, erythroderma (erythema covering ≥80% of the body surface area).

Figure 2. Waterfall Plot of Skin Response Based on Percentage Change in mSWAT Score per Patient in the Mogamulizumab (A) and Vorinostat (B) Treatment Arms Stratified by Blood Classification.



B0 = <15% CD4+CD26– cells or CD4+CD7– cells by flow cytometry. B1 = ≥15% CD4+CD26– cells or CD4+CD7– cells by flow cytometry. B2 = ≥1,000 mcg/L Sézary cells with positive clone, CD4/CD8 ratio ≥10, ≥40% CD4+CD7– cells, or ≥30% CD4+CD26– cells.T4, erythroderma (erythema covering ≥80% of the body surface area).

Conclusions

- **Mogamulizumab-treated patients with blood tumour burden B1 and B2 experienced a greater skin response, as measured by mSWAT, compared with mogamulizumab-treated patients with no blood involvement**
- **Vorinostat-treated patients experienced less improvement in skin response overall compared with mogamulizumab-treated patients, and the correlation between blood classification and skin improvement was not shown with vorinostat**
- **Disease control in the skin is important for improving patients' quality of life and the level of blood tumour burden may be a predictor of skin response to mogamulizumab**

References

1. Agar NS, et al. *J Clin Oncol*. 2010;28:4730-9.
2. Olsen E, et al. *Blood*. 2007;110:1713-22.
3. Kim YH, et al. *Lancet Oncol*. 2018;19:1192-204.

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Disclosures

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