Impact of Concomitant Steroids on Mogamulizumab Efficacy in MAVORIC

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Background

- Cutaneous T-cell lymphoma (CTCL) is a rare group of non-Hodgkin lymphomas that can result in substantial negative impact on patient quality of life as well as increased mortality risk in advanced-stage disease
  - Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common forms of CTCL[1,2]
  - Topical corticosteroids, a mainstay for patients with MF and SS, are generally considered first-line treatment in patients who present with early-stage disease and are used as adjunctive therapy in later stages[3,4]
- Mogamulizumab is a first-in-class, defucosylated monoclonal antibody directed against C-C chemokine receptor 4 (CCR4), which is highly expressed on malignant T-cells in CTCL[5,6]
- Primary results from MAVORIC (NCT01728805), a phase 3, open-label, randomized, international trial comparing mogamulizumab with US Food and Drug Administration-approved vorinostat in adults with relapsed/refractory MF/SS, showed that mogamulizumab significantly prolonged median progression-free survival (PFS, 7.7 months) compared with vorinostat (3.1 months, $P<0.0001$)[7]
  - Patients on mogamulizumab had a confirmed overall global response rate (across all disease compartments) of 28%[7]
  - Mogamulizumab treatment was generally manageable, with the most common AEs being infusion-related reactions (33%) and drug eruption (skin rash attributed to mogamulizumab, 24%)[7]
- Because patients undergoing treatment with mogamulizumab are likely to also receive steroid therapy, an understanding of the safety and efficacy of concomitant steroid use would be beneficial for physician decision-making

Objective

- This *post hoc* analysis aims to identify the number of patients treated with steroids and assess the impact of steroids on the safety and efficacy of mogamulizumab in MAVORIC

Materials & Methods

- Patients with MF/SS who were treated with ≥1 prior systemic therapy were randomized 1:1 to receive mogamulizumab (1.0 mg/kg, administered once weekly for the first 28-day cycle, then on Days 1 and 15 of subsequent cycles) or oral vorinostat (400 mg/day)
- Patients on a stable, low dose of corticosteroids for ≥4 weeks prior to the initial study visit could continue at the same dose; investigators were instructed to attempt to taper steroids to the lowest tolerable dosage
  - Intra-articular corticosteroid injections, intraocular corticosteroid drops, inhalation or nasal corticosteroids, and replacement systemic corticosteroids were allowed
  - Because of the nature of topical steroid administration, it was not possible to capture data on tapering of steroid use
- In this *post hoc* analysis, PFS, overall response rate (ORR, confirmed complete response + partial response), and response within individual disease compartments are reported for patients randomized to mogamulizumab or vorinostat with concomitant steroids at any time during the study period
  - An overall global composite score, based on response assessed for each compartment (skin, blood, lymph nodes, and viscera), was used to determine overall response
  - Safety assessments occurred throughout the study and included adverse events, physical examinations, vital signs, weight, laboratory tests, and electrocardiograms

Results

- Steroid use occurred in the majority of patients, and the frequency of use was similar between treatment groups (**Table 1**)
  - Similar numbers of patients were treated with low-/intermediate-potency and high-potency steroids in each arm (**Table 1**)

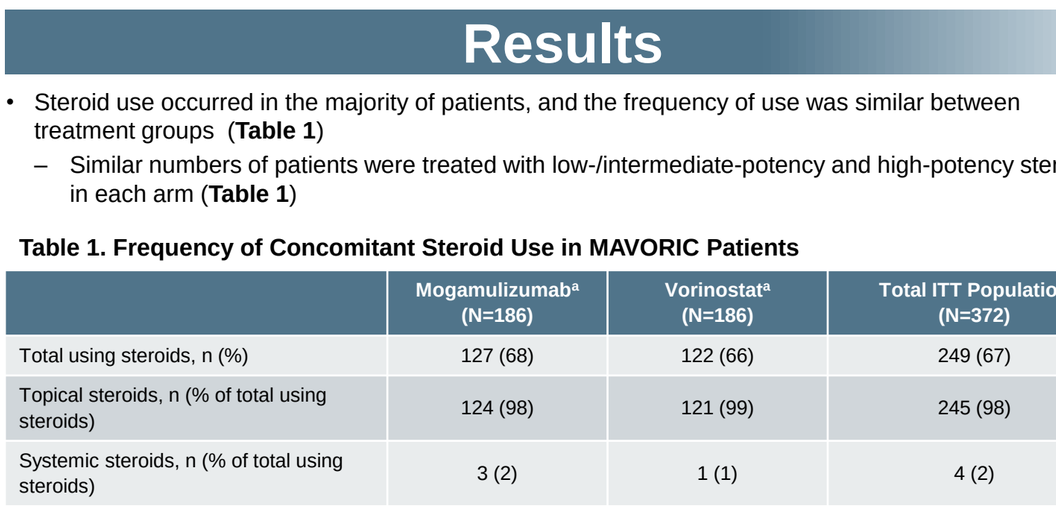
Table 1. Frequency of Concomitant Steroid Use in MAVORIC Patients

	Mogamulizumab[a] (N=186)	Vorinostat[a] (N=186)	Total ITT Population (N=372)
Total using steroids, n (%)	127 (68)	122 (66)	249 (67)
Topical steroids, n (% of total using steroids)	124 (98)	121 (99)	245 (98)
Systemic steroids, n (% of total using steroids)	3 (2)	1 (1)	4 (2)
Steroid potency, n (%)			
Low/Intermediate	45 (24)	42 (23)	87 (23)
High potency	82 (44)	80 (43)	162 (44)

ITT, intent-to-treat.

- Similar numbers of patients at each disease stage were treated with mogamulizumab and steroids
- Patients receiving mogamulizumab with concomitant steroids had a longer median PFS vs mogamulizumab-treated patients in the ITT population (**Figure 1**)
  - Among vorinostat-treated patients, PFS did not change with concomitant steroids (**Figure 1**)

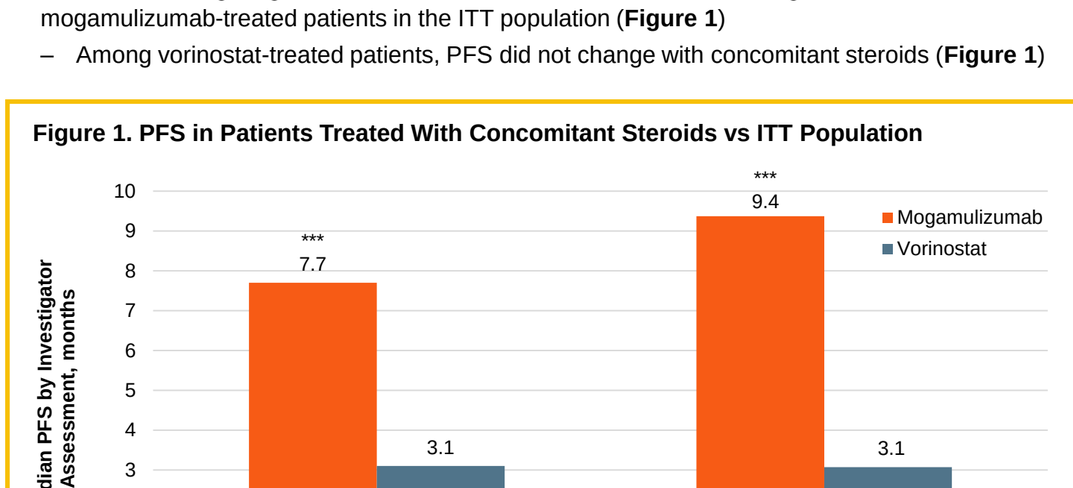
Figure 1. PFS in Patients Treated With Concomitant Steroids vs ITT Population



***P<0.0001 vs vorinostat.
ITT, intent-to-treat; PFS, progression-free survival.

- Mogamulizumab also resulted in a higher ORR (confirmed complete response + partial response) in patients receiving concomitant steroids relative to those in the ITT population (**Figure 2**)
  - ORR was not significantly different between vorinostat-treated patients who received concomitant steroids and vorinostat-treated patients in the ITT population (**Figure 2**)

Figure 2. ORR in Patients Treated With Concomitant Steroids vs ITT Population



***P<0.0001 vs vorinostat.
CR, complete response; ITT, intent-to-treat; ORR, overall response rate; PR, partial response.

- For most disease stages, ORR was higher in mogamulizumab-treated patients receiving concomitant steroids relative to those in the ITT population (**Table 2**)

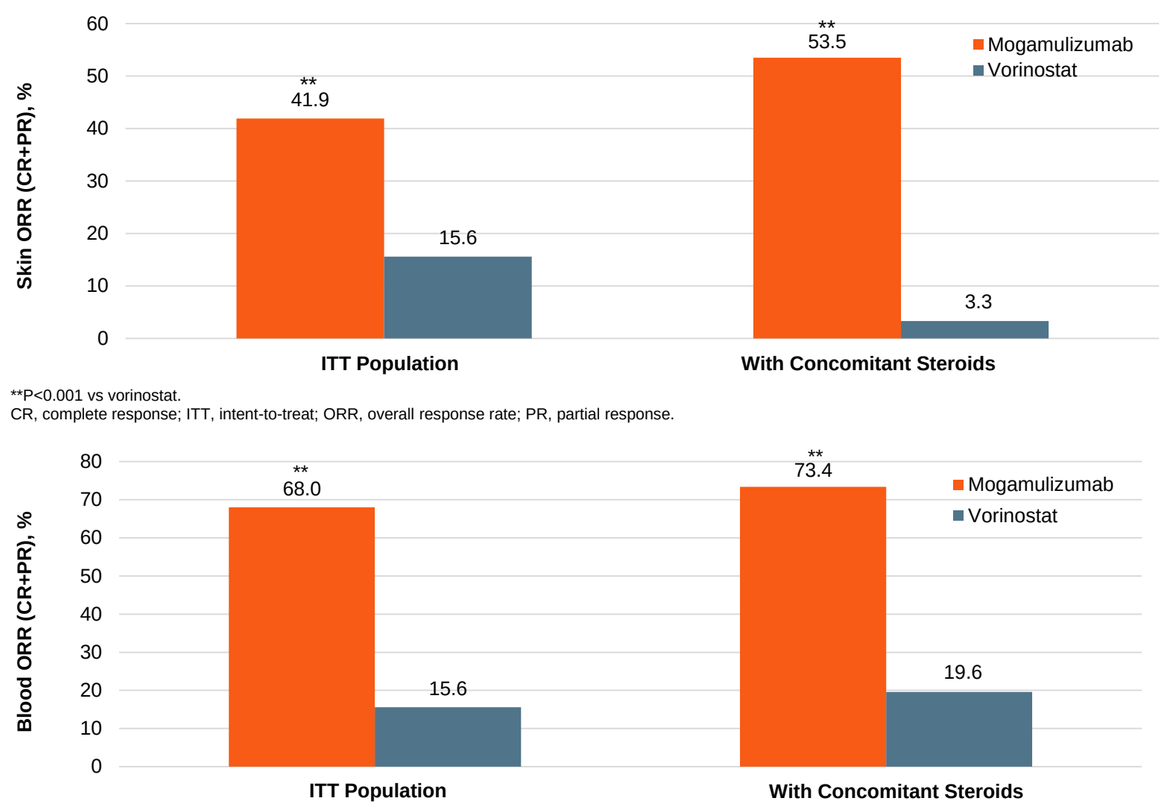
Table 2. ORR by Disease Stage in Patients Treated With Concomitant Steroids vs ITT Population

	Mogamulizumab (N=186)					
	ITT Population			With Concomitant Steroids		
	N	ORR		N (% of ITT population)	ORR	
Stage		n (%)	95% CI		n (%)	95% CI
IB	15	3 (20.0)	0.0-40.2	9 (60.0)	3 (33.3)	7.5-70.1
IIA	21	4 (19.0)	2.3-35.8	14 (66.7)	4 (28.6)	8.4-58.1
IIB	32	5 (15.6)	3.0-28.2	14 (43.8)	4 (28.6)	8.4-58.1
IIIA	9	1 (11.1)	0.0-31.6	6 (66.7)	1 (16.7)	0.4-64.1
IIIB	13	4 (30.8)	5.7-55.9	10 (76.9)	3 (30.0)	6.7-65.2
IVA	92	35 (38.0)	28.1-48.0	72 (78.3)	32 (44.4)	32.7-56.6
IVB	4	0	0.0-60.2	2 (50.0)	0	0.0-84.2

ORR=CR+PR.
CI, confidence interval; CR, complete response; ITT, intent-to-treat; ORR, overall response rate; PR, partial response.

- Differences were noted between mogamulizumab-treated patients receiving concomitant steroids and mogamulizumab-treated patients in the ITT population within the skin and blood compartments (**Figure 3A**,**B**)
  - For both the skin and blood compartment, the ORR of mogamulizumab-treated patients was significantly higher than that of vorinostat-treated patients receiving steroids and in the ITT population
  - In the skin compartment, ORR was higher in vorinostat-treated patients in the ITT population than in those receiving concomitant steroids (**Figure 3A**)

Figure 3. ORR in Patients Treated With Concomitant Steroids vs ITT Population in A) Skin and B) Blood Compartments



**P<0.001 vs vorinostat.
CR, complete response; ITT, intent-to-treat; ORR, overall response rate; PR, partial response.

- There were no unexpected differences in treatment-emergent adverse event (TEAE) profiles between mogamulizumab-treated patients in the safety analysis set and those receiving concomitant steroids (**Table 3**)

Table 3. TEAEs Reported by ≥10% of Patients in the Safety Population During Randomized Treatment

	Safety Analysis Set	
	Mogamulizumab (N=184) n (%)	With Concomitant Steroids (N=127) n (%)
Infusion-related reaction	61 (33.2)	44 (34.6)
Drug eruption[a]	44 (23.9)	35 (27.6)
Diarrhea	43 (23.4)	32 (25.2)
Fatigue	43 (23.4)	33 (26.0)
Pyrexia	31 (16.8)	19 (15.0)
Nausea	28 (15.2)	23 (18.1)
Peripheral edema	27 (14.7)	18 (14.2)
Headache	23 (12.5)	19 (15.0)
Constipation	21 (11.4)	18 (14.2)
Thrombocytopenia	21 (11.4)	16 (12.6)
Upper respiratory tract infection	19 (10.3)	16 (12.6)
Anemia	19 (10.3)	14 (11.0)
Cough	18 (9.8)	15 (11.8)
Back pain	18 (9.8)	15 (11.8)
Hypertension	17 (9.2)	15 (11.8)
Skin infection	17 (9.2)	13 (10.2)

[a]Skin rashes that were assessed by investigator or sponsor as possibly, probably, or definitely related to study drug.

Conclusions

- **The majority of patients in MAVORIC received concomitant topical steroids, which likely mirrors clinical practice for patients with MF/SS**
  - **For patients receiving steroids during mogamulizumab treatment, PFS was improved relative to the ITT population**
  - **A potential ORR improvement was observed in patients receiving mogamulizumab and steroids concomitantly across most disease stages**
  - **ORR was also improved in the skin and blood compartments in mogamulizumab-treated patients receiving concomitant steroids compared with those in the ITT population**
- **Although concomitant steroid therapy was associated with increased patient benefit for mogamulizumab-treated patients, there was no apparent increased benefit of steroids for vorinostat-treated patients**
- **These results suggest that the combination of topical steroids with mogamulizumab may produce a response that is superior to treatment with mogamulizumab alone**
- **Corticosteroid treatment is a backbone of CTCL therapy, and the increased efficacy observed with the combination of mogamulizumab and steroids is likely reflective of what would be observed with real-world use**

References

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