Patient Characteristics Of Long-Term Responders To Mogamulizumab: Results From The Mavoric Study

Poster Tre-P-07

Youn H. Kim, MD[1]; Michael Khodadoust, MD, PhD[2]; Adèle de Masson, MD, PhD[3]; Hélène Moins-Teisserenc, MD, PhD[4]; Takahiro Ito, MSc[5]; Karen Dwyer, BA[5]; Fiona Herr, PhD[6]; Martine Bagot, MD, PhD[4]

[1]Stanford Cancer Center, Stanford, CA, USA; [2]Stanford University School of Medicine, Stanford, CA, USA; [3]Hôpital Saint Louis, APHP, INSERM U976, Université de Paris, Paris, France; [4]INSERM UMR-1160, Institut Universitaire d'Hématologie, Paris, France; University of Paris Diderot, Sorbonne Paris Cité, Paris, France; Laboratoire d'Immunologie-Histocompatibilité, Hôpital Saint Louis, AP-HP, Paris, France; [5]Kyowa Kirin, Inc., Princeton, NJ, USA; [6]Kyowa Kirin, Inc., Bedminster, NJ, USA

Plain Language Main Finding

- This analysis of the MAVORIC trial demonstrated that mogamulizumab treatment can produce long-term and deep responses (≥12 months) in patients with mycosis fungoides or Sézary syndrome

Background

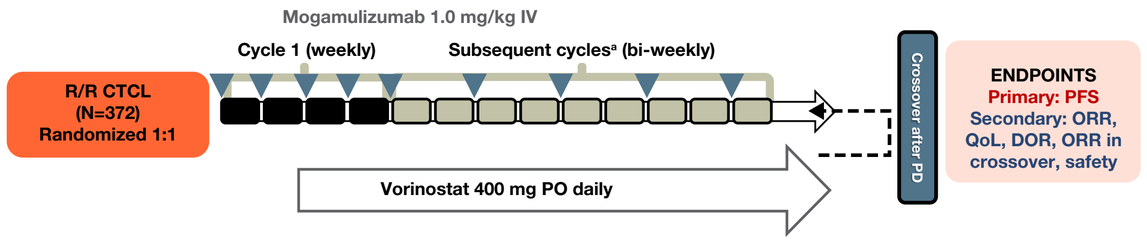
- MAVORIC was a phase 3, international, open-label, randomized controlled study (NCT01728805) comparing the safety and efficacy of mogamulizumab to vorinostat in patients with relapsed or refractory (R/R) mycosis fungoides (MF) or Sézary syndrome (SS) who had failed at least 1 prior systemic therapy[1]
- Results from the MAVORIC trial led to FDA and EMA approval of mogamulizumab[1]
  - The primary endpoint of the trial was progression-free survival (PFS), with a median of 7.7 months reported for mogamulizumab compared to 3.1 months for vorinostat
  - One of the secondary endpoints, overall response rate (ORR), was measured by global composite score (based on confirmed responses in skin, blood, lymph nodes, and viscera)
  - Patients remained on treatment until progression or intolerable toxicity
  - Global confirmed ORR for MAVORIC patients randomized to mogamulizumab (n=186) was 28%, and median duration of response (DOR) was 14.1 months
- In the pivotal trial for brentuximab in CTCL, a primary endpoint combining ORR and DOR data was used, specifically, ORR4, the proportion of patients who had a response duration of at least 4 months[2]
  - Additional benefits of mogamulizumab can be evaluated using such an endpoint that combines ORR and DOR information
- For example, ORR12 would describe the rate at which patients achieved a global response lasting ≥12 months, which would be considered a long-term response

Objective

- The objective of this post hoc analysis of MAVORIC was to compare the clinical and demographic characteristics of mogamulizumab-treated patients in a study-defined long-term responder cohort (ORR12) to subgroups with a global response of <12 months

Methods

Figure 1. MAVORIC Study Design



[a]1 cycle = 28 days.
CTCL, cutaneous T-cell lymphoma; DOR, duration of response; IV, intravenously; MF, mycosis fungoides; ORR, overall response rate; PD, disease progression; PFS, progression-free survival; PO, orally; QoL, quality of life; R/R, relapsed/refractory; SS, Sézary syndrome.

- In this post hoc analysis of MAVORIC (**Figure 1**), ORRn was evaluated, with "long-term response" defined as % of patients achieving ORR lasting ≥12 months (ORR12)
- Patients were divided into 4 response cohorts by minimum duration of overall response: ORR4, ORR6, ORR8, ORR12
- Baseline characteristics of patients in the ORR12 cohort (long-term responders) were compared with the characteristics of all other patients (non-responders + response duration <12 months)
  - Linear regression analyses and stepwise multivariate analysis were performed for sex, Eastern Cooperative Oncology Group Performance Status (ECOG PS), disease type (MF vs SS), clinical stage (IB-IV), blood involvement, CCR4 expression, age, time from diagnosis, mSWAT (skin disease burden), and lactate dehydrogenase (LDH)
- Blood samples were collected from 2 patients with SS at Stanford in the ORR12 cohort (global CR)
  - Frequency of the malignant T-cell (clonal) complementarity-determining region 3 (CDR3) of T-cell receptor beta (TCRβ) was monitored using the clonoSEQ next-generation sequencing (NGS) platform (Adaptive Biotech)[3]
  - Samples were assessed using standard flow cytometry at baseline and every 3-6 months to monitor minimal residual disease (MRD)[3]

Results

- Among patients randomized to mogamulizumab, confirmed global response durations of at least 4, 6, 8, and 12 months (designated as ORR4, 6, 8, 12) were seen in 25.3%, 21.0%, 16.1%, and 10.8% of patients, respectively (**Table 1**)

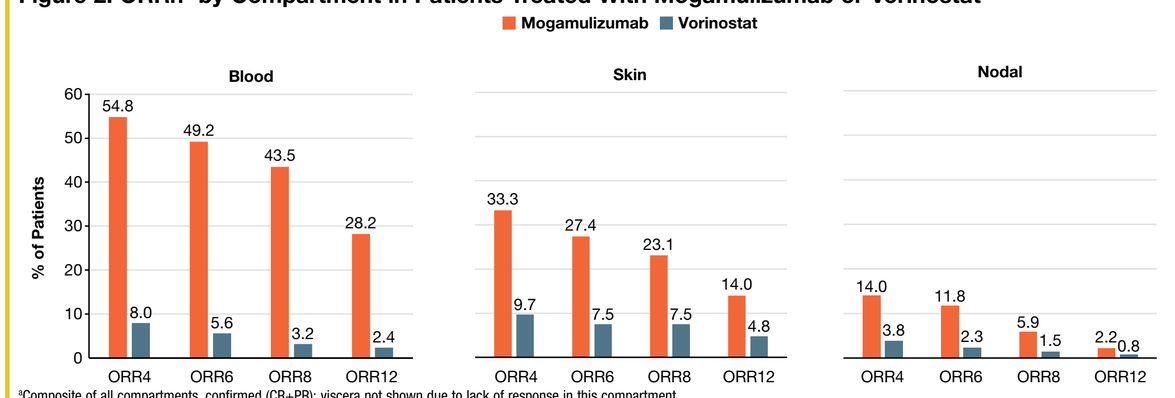
Table 1. ORRn in Patients Treated With Mogamulizumab or Vorinostat

	ORR4		ORR6		ORR8		ORR12	
	Moga	Vori	Moga	Vori	Moga	Vori	Moga	Vori
	n=186	n=186	n=186	n=186	n=186	n=186	n=186	n=186
Global ORR[a], n (%)	47 (25.3)	8 (4.3)	39 (21.0)	6 (3.2)	30 (16.1)	4 (2.2)	20 (10.8)	0
95% CI	(19.2, 32.1)	(1.9, 8.3)	(15.4, 27.5)	(1.2, 6.9)	(11.2, 22.2)	(0.6, 5.4)	(6.7, 16.1)	-

CI, confidence interval; ORR, overall response rate.

- ORRn data were also evaluated by disease compartment (**Figure 2**):
  - In blood, responses lasting at least 4 months occurred in >50% versus 8% of patients for mogamulizumab and vorinostat, respectively, and those lasting at least 12 months occurred in 28% versus 2% of patients for mogamulizumab and vorinostat
  - In skin, responses lasting at least 4 months occurred in 33% versus 10% of patients for mogamulizumab and vorinostat, respectively, and those lasting at least 12 months occurred in 14% versus 5% of patients for mogamulizumab and vorinostat
- When baseline characteristics of patients in the ORR12 cohort were compared via linear regression analysis to those of all other patients treated with mogamulizumab with shorter response durations, those in ORR12 were more likely to have SS, stage IVA1 disease, and blood involvement (**Table 2**)

Figure 2. ORRn[a] by Compartment in Patients Treated With Mogamulizumab or Vorinostat



[a]Composite of all compartments, confirmed (CR+PR); viscera not shown due to lack of response in this compartment.
CR, complete response; ORR, overall response rate; PR, partial response.

Table 2. Long-Term Response (ORR12) in Patients Treated With Mogamulizumab

	Not Achieved[a] n=166	Achieved n=20	OR	p-value
Disease Type, n (%)				
MF	99 (59.64)	6 (30)	0.29	0.016
SS	67 (40.36)	14 (70)		
Stage, n (%)[b]				
IVA1	56 (33.73)	17 (85)	11.13	0.0002
Blood Involvement (B1-2), n (%)				
No	61 (36.75)	2 (10)	0.19	0.03
Yes	105 (63.25)	18 (90)		
mSWAT				
Mean (SD)	86.25 (48.7)	100.18 (50.7)	-	-
Median (min, max)	85 (4, 231)	86.5 (19, 190)		

[a]Includes non-responders and short-term responders; [b]OR was calculated for only stage IVA1 because n≤5 in other stages.
MF, mycosis fungoides; mSWAT, modified Severity Weighted Assessment Tool; OR, odds ratio; SS, Sézary syndrome.

- No statistically significant relationship between long-term response and age, sex, ECOG PS, time from initial diagnosis, or skin CCR4 at baseline
- Stepwise regression analysis found that disease stage IVA1 was the primary predictor of ORR12 versus non-responders

Case report: 2 patients in the ORR12 cohort from a single center

- Two patients, both of whom had SS, sustained deep, durable global CR with mogamulizumab treatment in the MAVORIC trial (best response global CR): a 71-year-old man (Case 1) and a 77-year-old woman (Case 2)
  - Both demonstrated CR in blood after 1 moga cycle and in skin at cycle 3

Case 1: 71-year-old man with SS	Case 2: 77-year-old woman with SS (Table 3)
• Achieved blood CR (moga cycle 1), skin CR (cycle 3) • Maintained blood remission for ≥47 months • Malignant TCR sequence barely detectable (<1 copy/million nucleated cells)	• Achieved blood CR (cycle 1), skin CR (cycle 3) • Discontinued for hip replacement (cycle 16) • Maintained global CR and blood CR for ≥63 months—50+ months after discontinuing treatment • Maintained nearly undetectable MRD in blood for 30+ months

CR, complete response; moga, mogamulizumab; MRD, minimal residual disease; SS, Sézary syndrome; TCR, T-cell receptor.

Table 3. Clonal Cells Detected by Malignant Sequence Tracking in 77-Year-Old Patient With SS (Case 2)

Malignant Sequence Tracking: 77-year-old SS patient		
Collection Date	**Specimen Type**	**Detected Clonal Cells**
02/20/2020	Blood	6
07/25/2019	FFPE Scrolls	not detected
07/25/2019	FFPE Scrolls	not detected
07/25/2019	Blood	not detected
07/25/2019	Blood	not detected
02/21/2019	Blood	1
08/23/2018	Blood	not detected
03/29/2018	FFPE Scrolls	not detected
03/29/2018	FFPE Scrolls	not detected
03/28/2018	Blood	not detected
10/16/2017	Blood	not detected
04/20/2017	Blood	not detected
01/19/2017	Blood	not detected
08/12/14	Pre-moga	2,08,492

CR, complete response; FFPE, formalin-fixed paraffin-embedded; moga, mogamulizumab; MRD, minimal residual disease.

Conclusions

- **Patients in the MAVORIC trial who achieved long-term (≥12 months) responses were more likely to have SS (stage IVA1) or blood involvement, although lasting responses were also seen in patients with MF**
- **MRD analyses using TCR NGS in patients achieving ORR12 demonstrated that mogamulizumab was able to produce lasting and deep responses in some patients**

References

1. Kim YH, et al. *Lancet Oncol.* 2018;19(9):1192-204.
2. Prince HM, et al. *Lancet.* 2017;390(10094):555-66.
3. Weng WK, et al. *Sci Transl Med.* 2013;55(214):1-9.

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