Characterization and Outcomes of Mogamulizumab-Associated Skin Reactions in Patients With MF/SS From the Phase 3 MAVORIC Trial

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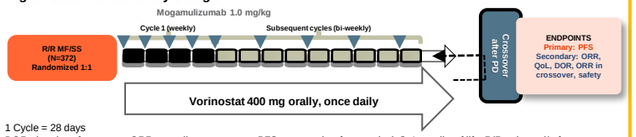
Background of Study

- Mogamulizumab is an anti-CCR4 antibody approved by the FDA and EMA for the treatment of patients with relapsed or refractory (R/R) mycosis fungoides (MF) or Sézary syndrome (SS) based on MAVORIC, a phase 3, open-label, randomized, international trial that evaluated the safety and efficacy of mogamulizumab versus vorinostat in patients with R/R MF or SS after ≥1 systemic therapy (NCT01728805)[1]
- Among mogamulizumab-treated patients in MAVORIC, 24% (44/184) reported treatment-emergent rash[1]
  - Grade 1-2 and Grade 3 drug rashes occurred in 20% (36/184) and 4% (8/184) of mogamulizumab-treated patients, respectively[1]
- Mogamulizumab-associated rash was the most common treatment-emergent adverse event leading to treatment discontinuation in MAVORIC (7% [13/184])[1]
- **Purpose of Study**: to report drug rash characteristics and associated outcomes in patients who received mogamulizumab in MAVORIC to allow optimal management

Methodology/Methods

- In MAVORIC, 372 patients were randomized 1:1 to receive either intravenous mogamulizumab at 1.0 mg/kg once weekly for Cycle 1 (28 days) and then on days 1 and 15 of subsequent cycles or oral vorinostat at 400 mg daily (**Figure 1**)

Figure 1. MAVORIC Study Design



1 Cycle = 28 days
DOR, duration of response; ORR, overall response rate; PFS, progression-free survival; QoL, quality of life; R/R, relapsed/refractory.

- Confirmed overall response rate (ORR; complete + partial response) was based on a global composite response involving all four disease compartments (skin, blood, lymph nodes, and viscera) and verified at two consecutive visits
- Patients on stable (≥4 weeks) low-potency or intermediate-potency topical steroids or low-dose (≤20 mg) systemic steroids at study entry could continue steroid use; however, initiation of systemic steroids was prohibited during the study, and initiation of high-potency topical steroids was prohibited except to treat rash
- Guidance for evaluation and management of new drug rash during mogamulizumab treatment was provided to investigators (**Table 1**)
- Skin biopsies, conducted before any topical steroids were applied, were evaluated by an on-site pathologist, and a central blinded review was conducted

Table 1. Management of Drug Rash in MAVORIC

Grade	CTCAE v5.0 Description[2]	Management and Dosing Recommendations[3]
4 (life-threatening)	Life-threatening consequences; urgent intervention indicated	Permanently discontinue mogamulizumab for life-threatening rash or for any SJS or TEN • If SJS or TEN is suspected, stop mogamulizumab. Do not resume unless SJS or TEN has been excluded and the cutaneous reaction has been resolved to Grade ≤1
3 (severe)	Prolonged (eg, not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Temporarily interrupt treatment and administer at least 2 weeks of topical corticosteroids • If, after administration of topical corticosteroids, the rash improves to Grade ≤1, mogamulizumab may be resumed
2 (moderate)	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (eg, antihistamines, NSAIDs, narcotics, IV fluids); prophylactic medications indicated ≤24 hours	
1 (mild)	Mild transient reaction	Consider using topical corticosteroids

CTCAE, Common Terminology Criteria for Adverse Events; NSAID, nonsteroidal anti-inflammatory drug; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.

Results

- Among the 44 patients who experienced mogamulizumab-associated rash during MAVORIC, 59.1% (26/44) were ≥65 years of age, and more patients with SS (56.8 [25/44]) than MF (43.2% [19/44]) experienced drug rash (**Table 2**)

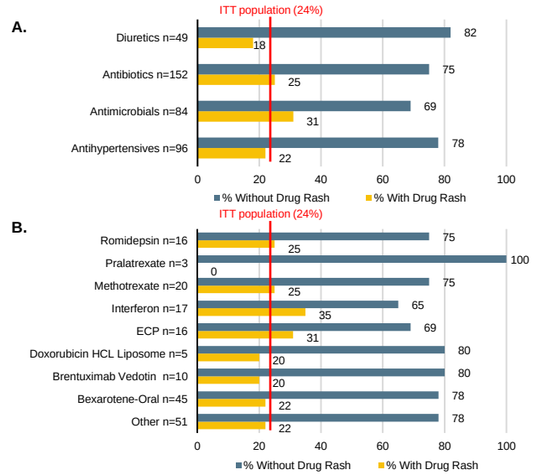
Table 2. Summary of Baseline Patient Demographics and Disease Characteristics

	With Drug Rash (n=44)	Without Drug Rash (n=140)	Total (N=184)
Age, years			
Mean (SD)	65.4 (12.3)	61.9 (13.7)	62.8 (13.4)
Age group, n (%)			
<65 years	18 (40.9)	81 (57.9)	99 (53.8)
≥65 years	26 (59.1)	59 (42.1)	85 (46.2)
Male sex, n (%)	26 (59.1)	81 (57.9)	107 (58.2)
ECOG PS, n (%)			
0	26 (59.1)	79 (56.4)	105 (57.1)
1	18 (40.9)	59 (42.1)	77 (41.8)
2	0	2 (1.4)	2 (1.1)
Disease Type, n (%)			
MF	19 (43.2)	86 (61.4)	105 (57.1)
SS	25 (56.8)	54 (38.6)	79 (42.9)

ECOG PS, Eastern Cooperative Oncology Group performance status; MF, mycosis fungoides; SS, Sézary syndrome.

- Median (Q1, Q3) exposure among patients with drug rash was 344 days (162, 652) in patients with SS and 185 days (85, 463) in patients with MF
- Central review assessed rashes as granulomatous, histiocytic spongiotic, lichenoid, eosinophilic, or psoriasiform with no clear predominant histological pattern
  - Immunohistochemistry on TCR gene rearrangement was often required to differentiate disease from rash[4]
- No trend toward increased incidence of drug rash was observed among the concomitant medications (**Figure 2A**) or immediate prior therapy used by patients in MAVORIC (**Figure 2B**).

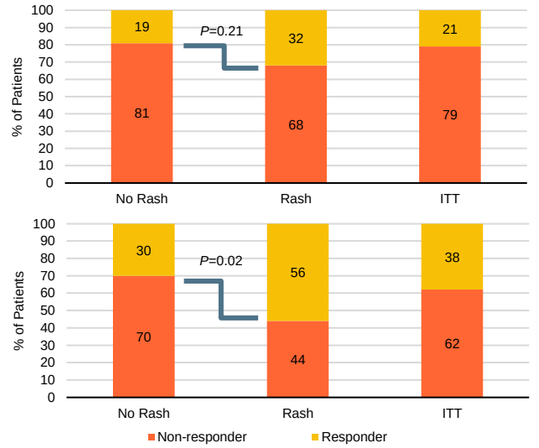
Figure 2. (A) Concurrent Medications and (B) Immediate Prior CTCL Therapies from MAVORIC Patients A.



CTCL, cutaneous T-cell lymphoma; ECP, extracorporeal photopheresis; ITT, intent-to-treat.

- Among patients with MF, the proportion of responders with drug rash did not differ significantly from responders without rash (P=0.21); the proportion of SS responders with drug rash was significantly higher than responders without rash (P=0.02) (**Figure 3A** and **B**)

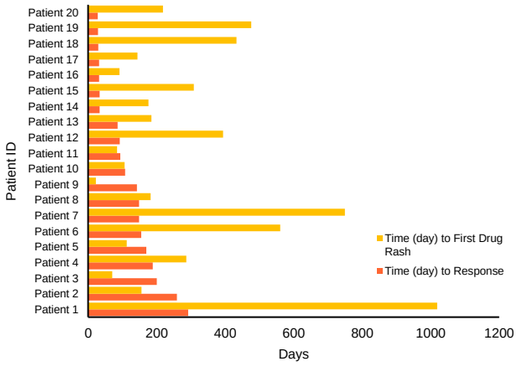
Figure 3. Response Rate in (A) Patients With MF and (B) Patients With SS



ITT, intent-to-treat; MF, mycosis fungoides; SS, Sézary Syndrome.

- Initial drug rash occurred after response to mogamulizumab in 70% (14/20) of patients who experienced both
- Overall, the median (Q1, Q3) time to onset of drug rash was 106 days (36, 254) (**Figure 4**)

Figure 4. Time to Onset of First Drug Rash and Mogamulizumab Response in Patients Experiencing Both



- Thirty-five patients (80%) in the drug rash cohort resumed mogamulizumab treatment after resolution of initial drug rash per protocol
- After these patients resumed treatment, the median (Q1, Q3) duration of exposure to mogamulizumab was 183 days (58, 332)

Conclusions

- Mogamulizumab-associated rashes displayed heterogeneous histopathology without predominant features
- Correlation of rash with clinical features via biopsy is advised to differentiate drug rash from disease progression
- Patients with SS were associated with a higher rate of drug rash than patients with MF
- After resolution of initial drug rash, 80% of patients were able to continue mogamulizumab for >6 months
- Nurse involvement in evaluation, identification, and management of mogamulizumab-associated rash may prevent premature treatment discontinuation

References

1. Kim YH, et al. *Lancet Oncol.* 2018;19(9):1192-204.
2. National Cancer Institute. 2018. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50.
3. Poteligeo® (mogamulizumab-kpkc) injection, for intravenous use [prescribing information]. Bedminster, NJ: Kyowa Kirin, Inc.; August 2018.
4. Chen L, et al. *JAMA Dermatol.* 2019;155(8):968-71.

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