

Characterization and Outcomes in Patients with Mogamulizumab-Associated Skin Reactions in the MAVORIC Trial

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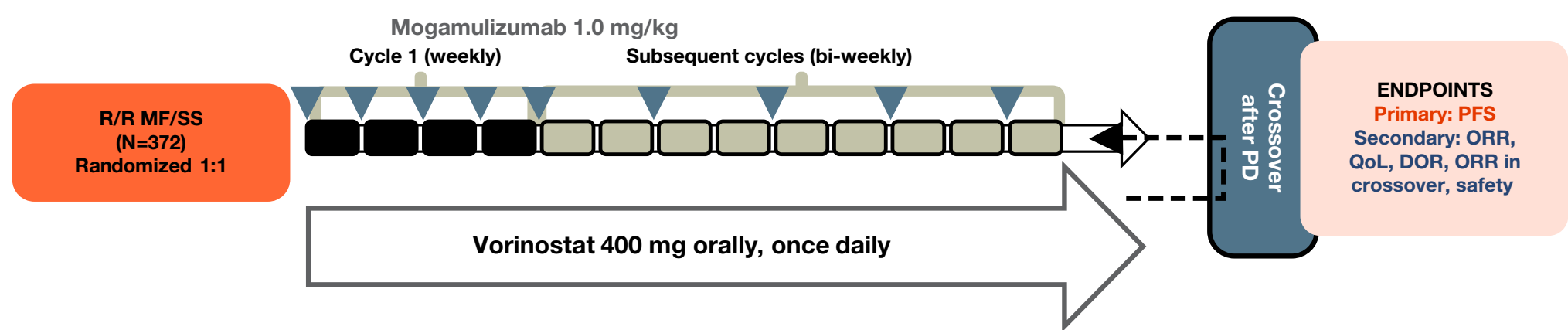
Background of Study

- 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 rash¹
 - Grade 1-2 and Grade 3 drug rashes occurred in 20% (36/184) and 4% (8/184) of mogamulizumab-treated patients, respectively¹
- 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



- 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 rash⁴
- 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**).
- 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**)
- 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**)
- 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)

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

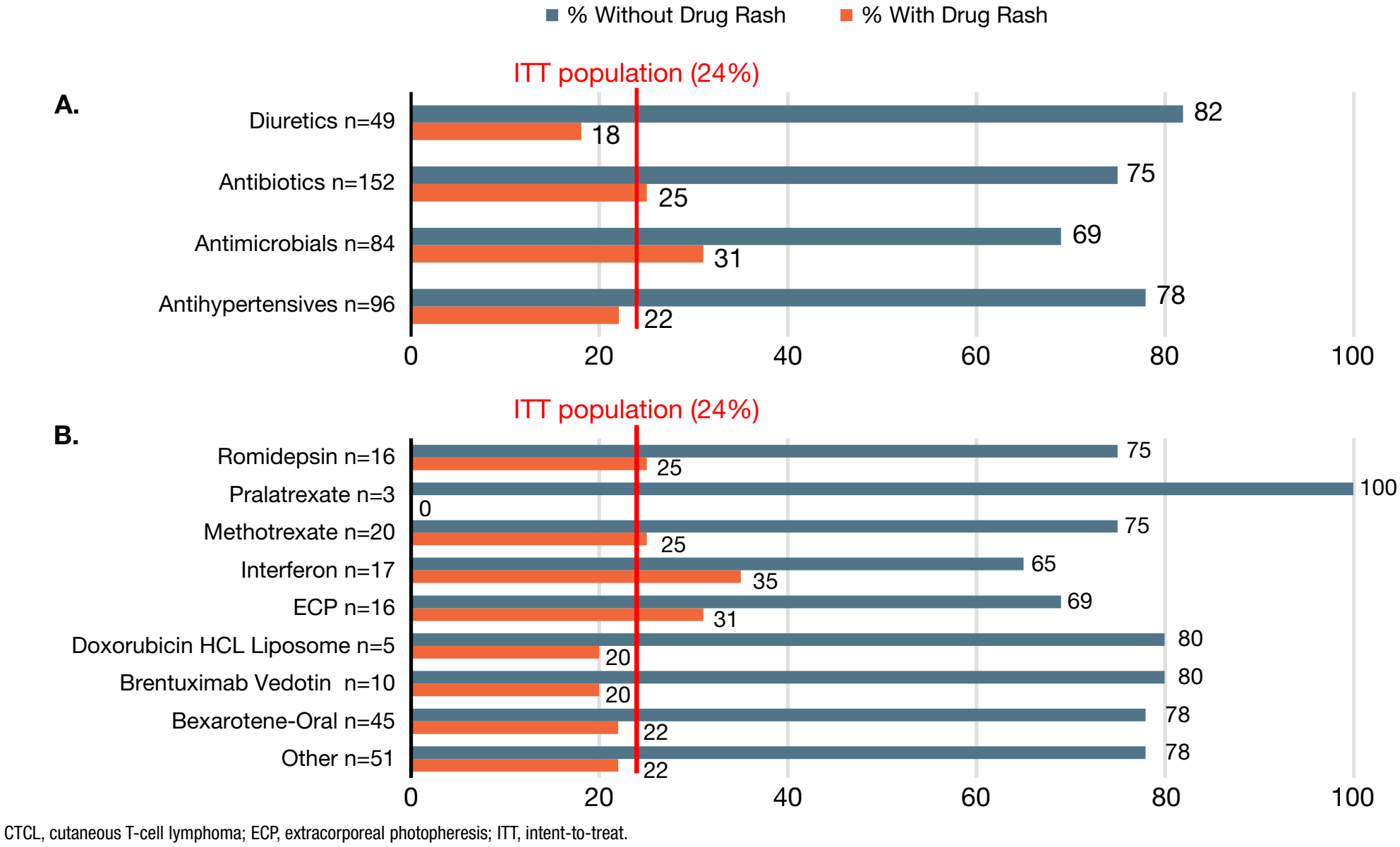


Figure 3. Response Rate in (A) Patients With MF and (B) Patients With SS

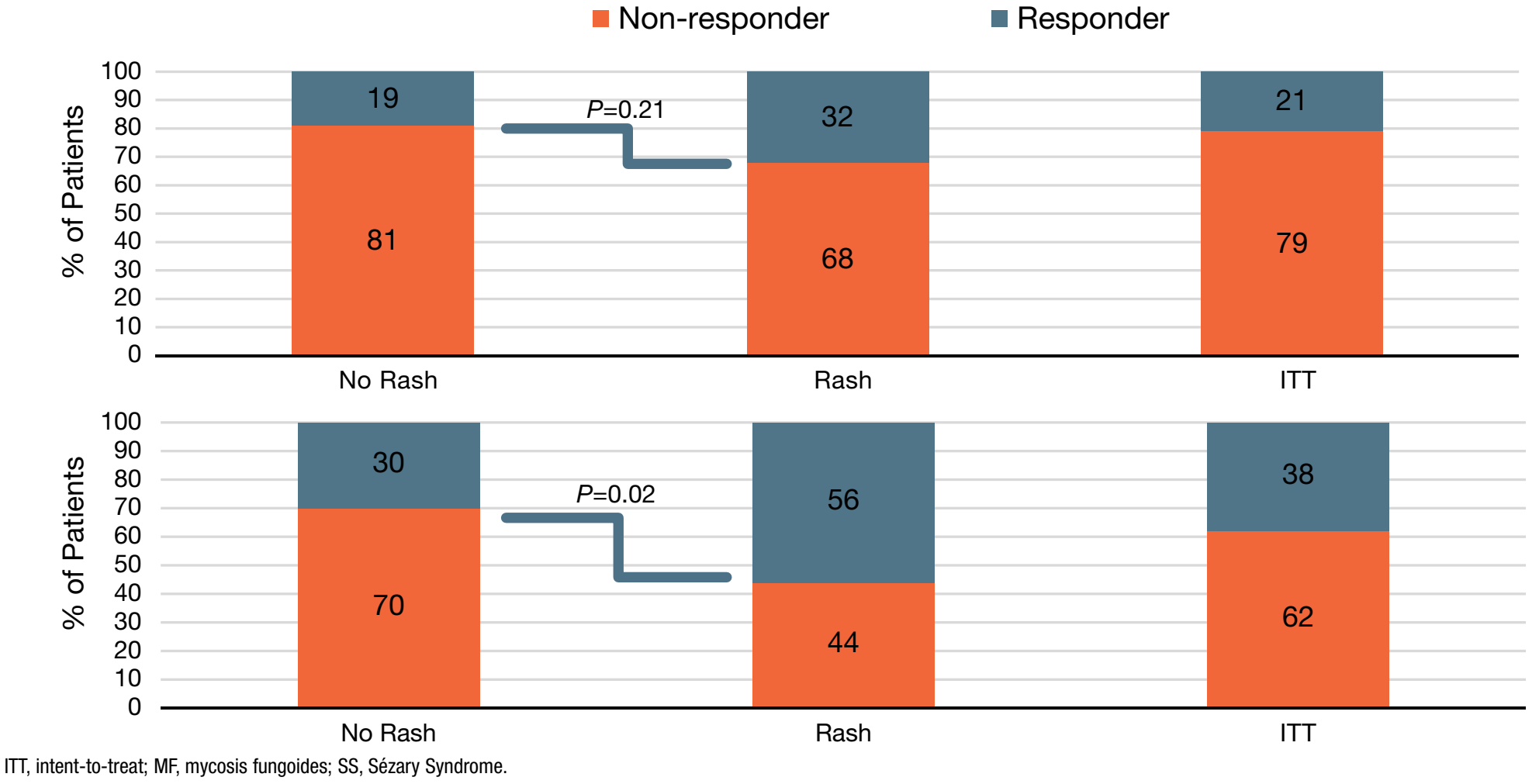
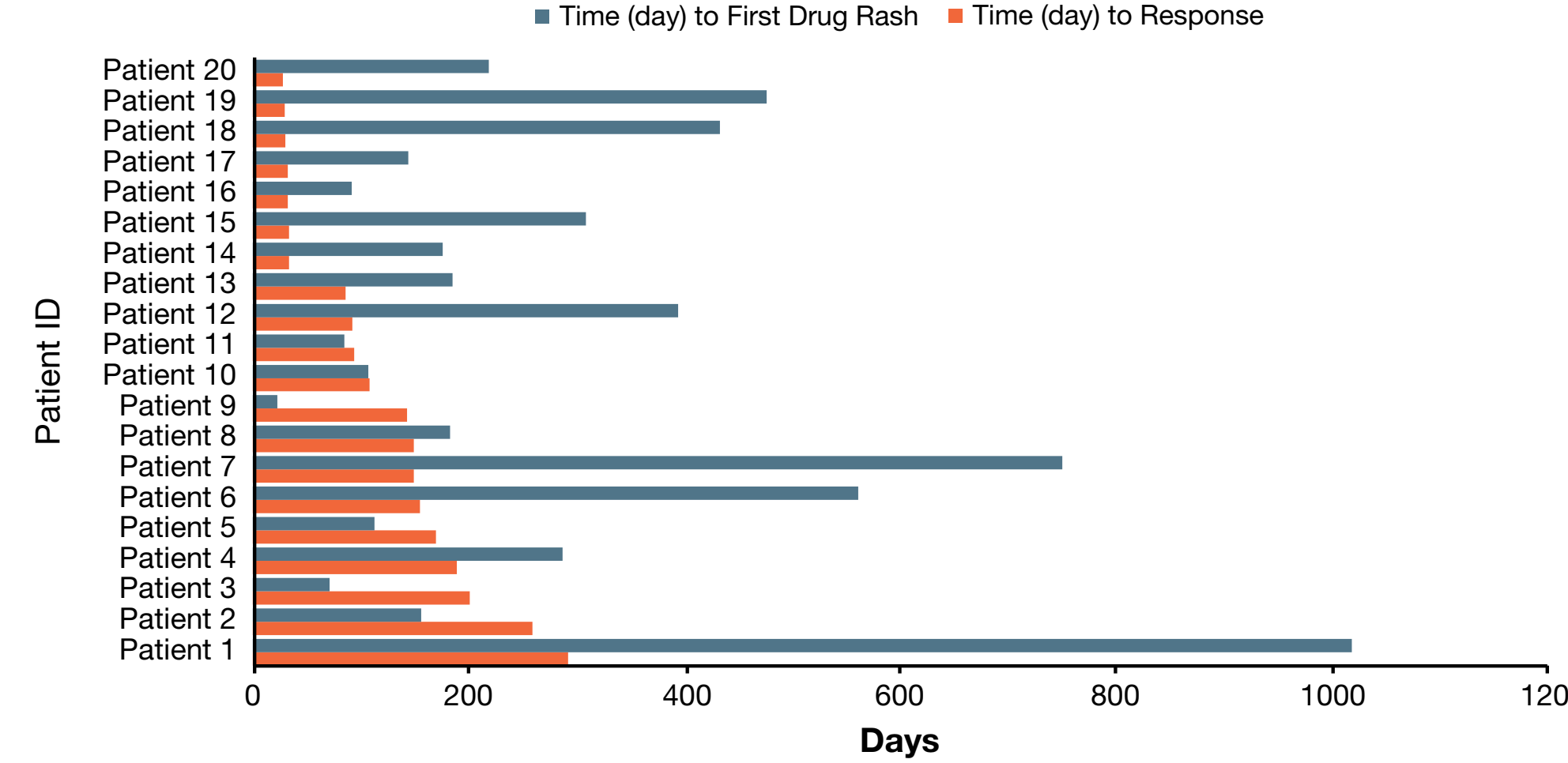


Figure 4. Time to Onset of First Drug Rash and Mogamulizumab Response in Patients Experiencing Both



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

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Acknowledgements

The study was sponsored by Kyowa Kirin. Medical writing assistance was provided by Jonathan Mitchell, PharmD, of MedVal Scientific Information Services (Princeton, NJ, USA) and was funded by Kyowa Kirin, Inc. (Princeton, NJ, USA).

Disclosures

ACMM: Kyowa Kirin: Honoraria; Helsinn: Honoraria; mRagen: Other: Investigator; Elorac: Other: Investigator; Soligenix: Other: Investigator. **SW:** No relevant conflicts of interest to declare. **SMH:** ASTEX: Consultancy; Affirmed: Consultancy; Vividion Therapeutics: Consultancy; Verastem: Consultancy; Research Funding; Kyowa Hakka Kirin: Consultancy; Research Funding; Millenium/Takeda: Consultancy; Research Funding; Seattle Genetics: Consultancy; Research Funding; Trillium: Consultancy; Research Funding; Corvus: Consultancy; Innate Pharma: Consultancy; Mundipharma: Consultancy; Portola: Consultancy; Research Funding; Beigene: Consultancy; C4 Therapeutics: Consultancy; Daiichi Sankyo: Research Funding; GlaxoSmithKline: Consultancy; Janssen: Consultancy; ADCT Therapeutics: Consultancy; Research Funding; Forty Seven: Consultancy; Research Funding; Kura Oncology: Consultancy; Miragen: Consultancy; Myeloid Therapeutics: Consultancy; Aileron: Consultancy; Research Funding; Celgene: Consultancy; Research Funding; **MB:** Helsinn/Recordati: Membership on an entity's Board of Directors or advisory committees; Takeda: Membership on an entity's Board of Directors or advisory committees; Kyowa Kirin: Membership on an entity's Board of Directors or advisory committees; Innate Pharma: Consultancy; Membership on an entity's Board of Directors or advisory committees, Research Funding. **AOH:** Kyowa Kirin: Membership on an entity's Board of Directors or advisory committees, Research Funding; Medivir: Membership on an entity's Board of Directors or advisory committees, Research Funding; GlaxoSmithKline: Research Funding; Seattle Genetics: Membership on an entity's Board of Directors or advisory committees, Research Funding; Galderma: Other: Travel expense reimbursement, Research Funding; mRagen: Membership on an entity's Board of Directors or advisory committees, Research Funding; Helsinn: Membership on an entity's Board of Directors or advisory committees; Innate Pharma: Research Funding; Rhizon: Consultancy, Research Funding. **DOF:** Dana-Farber Cancer Institute: Current Employment; Kyowa Kirin: Membership on an entity's Board of Directors or advisory committees. **PH:** Kyowa Kirin: Membership on an entity's Board of Directors or advisory committees; Karger, Inc.: Patents & Royalties: Textbook royalties. **MV:** Kyowa Kirin: Consultancy; Research Funding; Takeda: Research Funding; PIQUR: Research Funding; Innate Pharma: Consultancy. **Tt:** Kyowa Kirin Pharmaceutical Development, Inc.: Current Employment. **FH:** Kyowa Kirin, Inc.: Current Employment. **YHK:** Elorac: Research Funding; Eisai: Membership on an entity's Board of Directors or advisory committees, Research Funding; Corvus: Research Funding; Medivir: Membership on an entity's Board of Directors or advisory committees; Kyowa-Kirin Pharma: Research Funding; Innate Pharma: Consultancy, Membership on an entity's Board of Directors or advisory committees, Research Funding; Forty Seven Inc: Research Funding; Galderma: Membership on an entity's Board of Directors or advisory committees, Research Funding; Horizon Pharma: Consultancy, Research Funding; mRagen: Research Funding; Merck: Research Funding; Soligenix: Research Funding; Trillium: Research Funding; Takeda: Membership on an entity's Board of Directors or advisory committees, Research Funding; Neumedicine: Consultancy; Research Funding; Portola: Research Funding; Seattle Genetics: Membership on an entity's Board of Directors or advisory committees.