Efficacy of Mogamulizumab in combination therapy for relapsed or refractory Sezary syndrome

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Abstract #3

BACKGROUND

- **Sezary syndrome (SS) is an aggressive variant of cutaneous T-cell lymphoma (CTCL) characterized by tetrad of erythroderma lymphadenopathy, pruritus and abnormal cells in the blood.**
- **Treatments for Sezary syndrome remain limited with no standard approach for relapsed or refractory disease.**
- **Mogamulizumab is a novel humanized afucosylated monoclonal antibody that targets CCR4**
- **Mogamulizumab as monotherapy has been shown to be superior to traditional therapies in an international, open-label, randomized, controlled phase 3 trial known as the MAVORIC trial [1].**
- **The US FDA approved Mogamulizumab for treatment of refractory mycosis fungoides or Sezary syndrome after at least one previous systemic therapy.**
- **In this study, we present the experience of 10 patients with relapsing or refractory Sezary syndrome treated with Mogamulizumab in combination with other therapies.**

Table 1. Characteristics

Treated with Mogamulizumab	
Total	*n* = 10
Age - average [range]	69.1 [43–83]
Sex	
Male	6
Female	4
Race	
White	8
Black	2
Stage	
IIB	1
IVA	1
IVB	8

METHODS

- **A retrospective review of Sezary syndrome patients in the Cutaneous Lymphoma Clinic at the University of Arkansas for Medical Sciences (UAMS) between 2013-2023 was conducted.**
- **Inclusion into the Mogamulizumab treatment analysis included those patients who had failed at least 3 systemic treatments. Eligible patients received Mogamulizumab with the scheduled doses of: 1.0mg/kg weekly for the first 28-day cycle, then on days 1 and 15 of subsequent cycles.**
- **The primary objective was to assess the objective response rate (ORR) when combined with other therapies, with duration of response and toxicity assessment as secondary objectives.**
- **Response was determined through use of a global score which was calculated by combining clinical exam findings of adenopathy, erythema, and pruritus with hematologic response.**
- **Responses were determined as complete response (CR), partial response (PR), stable disease (SD), and relapse (R).**
- **ORR was calculated as the proportion of patients with global response of CR and PR [2].**

RESULTS

- **Ten patients met the inclusion criteria Table 1.**
- **Patients' prior treatment and clinical characteristic shown in Table 2. Combination of treatments with Mogamulizumab shown.**
- **3 patients achieved complete clinical remission, 4 with partial response, 2 with stable disease, and 1 with disease progression as determined by the global score shown in Table 2.**
- **An ORR of 70% was observed.**
- **Median response duration of 21.5 months.**
- **Treatment was halted for 4 patients after 1, 4, or 8 cycles due to adverse reactions including an exfoliative, pruritic rash, diarrhea, and fatigue.**
- **One death occurred in this cohort of patients; case 9 had a progressive disease requiring bone marrow transplant and died of pneumonia soon after.**

Table 2. Treatment Outcomes and Regimens of Patients Receiving Mogamulizumab

Clinical Characteristics					*Previous/Concurrent Treatments*								*Mogamulizumab Regimen and Outcomes*						
Case #	Age	Stage	Sex	Race	Bexarotene	Romidepsin	Interferon	Photopheresis	NB-UVB	Acitretin	Other	Topicals	# of cycles	Toxicities	Skin	Lymph nodes	Blood	Viscera	Global Score	DOR (Months)
1	75	IVb	M	W	+	‡		+	+	+	Brentuximab+ Dupilumab* Cyclosporine*	Triamcinolone*	7		CR	CR	CR	NI	CR	24
2	72	IVb	F	W	+		+	*			Mycophenolate* Dupilumab*	Triamcinolone* Fluocinonide*	22		CR	CR	CR	NI	CR	19
3	65	IVb	M	AA	*	*	*	*		+	CHOP+ Vorinostat*	Triamcinolone+ Tacrolimus+	6		CR	PR	CR	NI	PR	27
4	77	IVb	M	W	*		*	*	*			Triamcinolone+	14	diarrhea	CR	CR	CR	NI	CR	27
5	83	IVa	F	W	*		+		+	+		Triamcinolone+ Tacrolimus+	10		PR	CR	CR	NI	PR	12
6	43	IIb	M	AA	+		+	+	+	+	PUVA+ ILK+ Local radiation+	Triamcinolone+ Tacrolimus+ Imiquimod+ Halobetasol+	42		PR	PR	CR	NI	PR	32
7	79	IVb	M	W	+		+	*		*		Triamcinolone+ Clobetasol+	8	rash, AKI hypotension	SD	CR	CR	NI	SD	12
8	77	IVb	M	W	+		*	+	+		Alemtuzumab+	Triamcinolone+	5	fatigue	SD	CR	PR	NI	SD	7
9	69	IVb	F	W	+		+	+	+			Triamcinolone+ Tacrolimus+	23	rash	R	CR	R	NI	R	25
10	51	IV	F	W	+		+					Triamcinolone+ budesonide+	9		PR	PR	CR	NI	PR	4

*: Previous treatments; +: Concurrent treatments; ‡ Initiated following Moga completion Abbreviations: M: Male; F: Female; AA: African America; NB-UVB: Narrowband UV-B phototherapy; CHOP: (C) cyclophosphamide, (H) doxorubicin hydrochloride, and (O) vincristine sulfate, and (P) prednisolone; PUVA: Psoralen plus ultraviolet A; ILK: intralesional Kenalog; DOR: Duration of Response; CR: Complete Response; PR: Partial Response; SD: Stable Disease; R: Relapse; NI: Not Indicated;

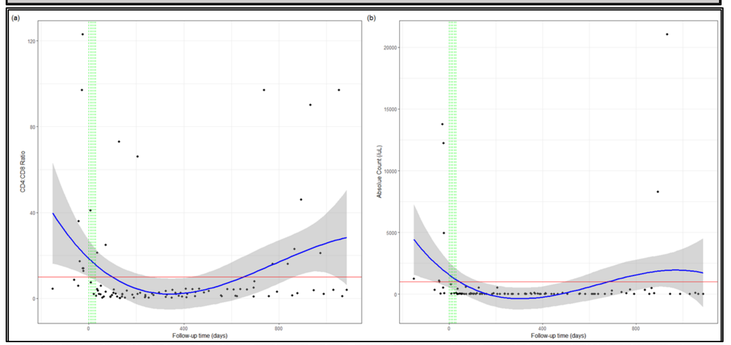

Figure 1. Laboratory values of blood cell counts from Mogamulizumab-treated patients. The green lines correspond to the first month of treatment in which the patients received mogamulizumab (days 0, 7, 14, 21, and 28). The red line represents the reference range threshold (Sezary count < 1000/uL; CD4:CD8 ratio < 10:1). The blue line represents a polynomial regression model used to display changes over time. The grey area represents the 95% confidence interval (CI). (a) The mean CD4:CD8 ratio decreased from 37.9 at baseline to 4.9 after at least one cycle of Mogamulizumab therapy. (b) The mean absolute Sézary count decreased from 3,509.9/uL at baseline to 69.1/uL after at least one cycle of Mogamulizumab therapy. This data is derived from the observation of 10 patients.

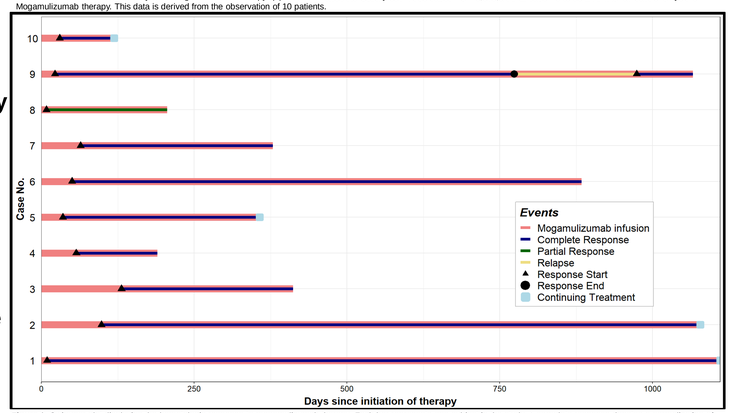

Figure 2. Swimmer plot displaying the hematologic response to mogamulizumab therapy. Each bar represents one subject in the study. A complete response denotes a normalization of absolute Sezary count to < 1000/mm3 and a CD4/CD8 ratio to < 10. A partial response is representative of a decrease in a patients absolute Sezary count or CD4/CD8 ratio from the start of treatment that is not below 1000/mm3 or 10:1 respectively. Relapse describes patients that had a return in their absolute Sezary count or CD4/CD8 ratio to > 1000/mm3 or > 10:1.

DISCUSSION

- **In our cohort, treatment with Mogamulizumab in combination with additional systemic therapies is effective and well tolerated.**
- **Median response of duration was 21.5 months.**
  - **A maximum median response time has yet to be reached with patients 1, 2, 5, and 10 continuing the same treatment protocol.**
- **A hematologic response was seen in all 10 patients with a median time to response of 1.2 months.**
- **Subjects showed decreased erythema and pruritus with combination treatment.**
- **The most commonly used combination in our patient population was bexarotene and interferon (9/10) [3].**
- **Patients with complete response were treated with bexarotene and photopheresis.**
- **Rash was the most common reaction observed (50%).**
  - **2 of these patients remained in stable disease state and one showed complete response.**
- **Relapse was seen in one patient after 26 months of complete hematologic response.**

CONCLUSION

- **A multiagent approach using mogamulizumab in R/R CTCL is not only effective but also tolerable with a subset of patients still showing ongoing response.**

References

1. Kim YH, Bagot M, Pinter-Brown L, Rook AH, Porcu P, Horwitz SM, et. al.. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. Lancet Oncol. 2018 Sep;19(9):1192-1204. doi: 10.1016/S1470-2045(18)30379-6. Epub 2018 Aug 9. Erratum in: Lancet Oncol. 2018 Nov;19(11):e581. PMID: 30100375.
2. Olsen EA, Whittaker S, Kim YH, Duvic M, Prince HM, Lessin SR, et. al; International Society for Cutaneous Lymphomas; United States Cutaneous Lymphoma Consortium; Cutaneous Lymphoma Task Force of the European Organisation for Research and Treatment of Cancer. Clinical end points and response criteria in mycosis fungoides and Sézary syndrome: a consensus statement of the International Society for Cutaneous Lymphomas, the United States Cutaneous Lymphoma Consortium, and the Cutaneous Lymphoma Task Force of the European Organisation for Research and Treatment of Cancer. J Clin Oncol. 2011 Jun 20;29(18):2598-607. doi: 10.1200/JCO.2010.32.0630. Epub 2011 May 16. PMID: 21576639; PMCID: PMC3422534.
3. Teoli, M., Mandel, V. D., Franceschini, C., Saraceni, P. L., Cicini, M. P., & Ardigò, M. (2022). Mogamulizumab and bexarotene are a promising association for the treatment of advanced cutaneous T-cell lymphomas: a case series. *European review for medical and pharmacological sciences*, *26*(21), 8118–8128. doi: 10.26355/eurrev_202211_30166