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Single Institution Experience of Pembrolizumab for Patients with Relapsed or Refractory Mycosis Fungoides or Sézary Syndrome

Omar Elghawy[1] Jonathan Sussman[1] Austin Yang[1] Colin J. Thomas[1] Jordan S. Carter[1] Daniel J. Landsburg[1] Jakub Svoboda[1] Ellen Kim[2], Alain Rook[2], Jina Chung[2] John P. Plastaras[3], Michael LaRiviere[3], Harper Huebeling[3], Monica Chelius[3] Sunita D. Nasta[1] Elise A. Chong[1] Stephen J. Schuster[1] Stefan K. Barta[1]

[1] Lymphoma Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

[2] Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

[3] Department of Radiation Oncology, University of Pennsylvania Perelman School of Medicine, Philadelphia

Penn Medicine

INTRODUCTION

- Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common types of cutaneous T-cell lymphomas (CTCLs) representing 60% and 5% of cases respectively.
- Response for advanced SS/MF is moderate with intravenous agents such as mogamulizumab, romidepsin, and single-agent chemotherapy representing standard of care.
- A recent phase 2 clinical CITN trial using pembrolizumab demonstrated an ORR of 38% in a heavily pretreated CTCL population.
- Further trials have continued to investigate the utility of pembrolizumab with combination therapies including brentuximab vedotin and interferon gamma with mixed results.

AIM

- Real world data for checkpoint inhibition in CTCL is sparse and limited to case reports or small series.
- We aimed to assess real-world survival, response rate and tolerability of pembrolizumab for R/R MF/SS at our institution.

METHODS

- A single-institution retrospective cohort study of patients with a diagnosis of MF/SS who received pembrolizumab between January 1, 2017, and January 1, 2023, was performed.
- Patients were identified through query of the University of Pennsylvania Cancer Center database.
- Treatment response was determined using 2022 consensus criteria for cutaneous lymphomas (*Olsen EA, et al. 2022*).
- Immune related adverse events (IRAEs) were graded using CTCAE v5.0 criteria by chart review.
- Overall survival (OS) and progression free survival (PFS) were co-primary end points, measured from time of first dose of pembrolizumab to death (OS) and/or progression (PFS), respectively, and censored at date of last follow up.

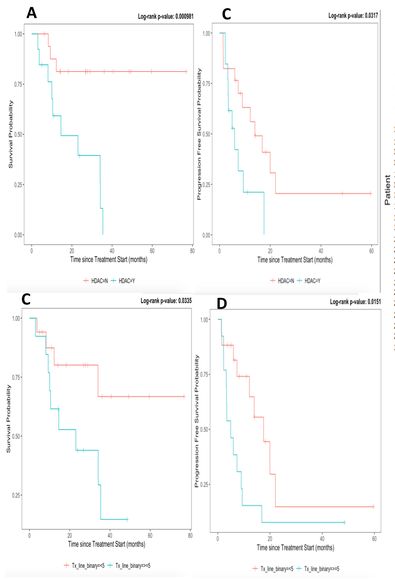
RESULTS

- Eleven patients with SS and 19 with MF were included within this study.
- Median duration of treatment was 4.5 (range: 1.6-11.1) months. Median length of follow-up was 20.4 months.
- Median PFS for the cohort was 7.4 (95% CI 3.5-14.1) months and median OS was 20.6 (95% CI 10.0-34.2) months.
- Overall response rate was evaluable in 29 (97%) patients and 48% had a global response ((CR, 5 [31%], PR, 9 [69%]) with a median duration of response of 13.1 months.
- Nineteen (65%) patients derived clinical benefit (SD, PR or CR) from treatment.
- Overall survival was significantly decreased with prior HDAC treatment and more than 4 prior lines of treatment (HR 3.36 [95% CI 1.03-10.96] p=0.03).
- However, on multivariate analysis, these associations were no longer significant.
- Most IRAEs (11/13, 85%) observed were Grade 1-2. No grade 4 or 5 IRAEs were observed.

Table 1: Patient Demographics and disease characteristics of patients within study cohort

Characteristic	*N*=30 (%)
Median Age (Range)	68 (52-79)
Sex	
Male	17 (56.7%)
Race	
White	24 (80%)
ECOG	
<2	24 (80%)
Diagnosis at Treatment	
Mycosis Fungoides	19 (63.3%)
Sezary Syndrome	11 (36.7%)
Stage	
IA-IB	7(23.3%)
IIA-IIB	8(26.7%)
III	4(13%)
IVA-IVB	11(36.7%
Treatment line	
<5	17 (56.7%)
>=5	13 (43.3%)
Median Cycles of Pembrolizumab (IQR)	5 (3-11.5)
Prior HDACi	
Yes	13 (43.3%)
Radiation during treatment	
Yes	6 (20%)
Assessable compartments	
Skin	29 (97%)
Nodes	13 (43%)
Viscera	4 (13%)
Blood	9 (30%)

For continuous values, median is shown with interquartile range in parentheses.



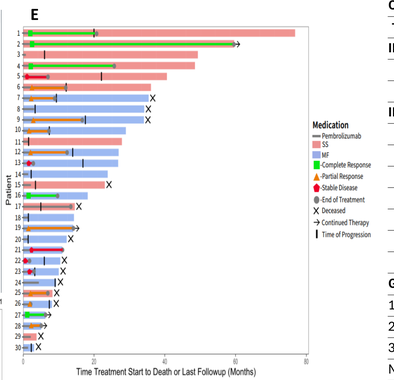


Figure 1: Kaplan Meier curves showing overall survival (A and C) and progression free survival (B and D) for patients with prior HDAC exposure and greater than 5 prior treatment lines. E) Swimmers plot showing individual patient responses to treatment. Length of bar representing total length of followup.

Characteristic	Value (%)
Table 2. IRAEs within patient cohort and ICI retrial	n=30
IRAE occurrence	
Yes	14 (46.7%)
No	16 (53.3%)
IRAE Type	
Derm	5 (16.7%)
MSK	1 (3.3%)
Hypothyroidism	3 (10%)
Colitis	2 (6.7%)
Hepatic	1 (3.3%)
Hypophysitis	1 (3.3%)
None	16 (53.3%)
Grade	
1	4 (13.3%)
2	8 (26.7%)
3	2 (6.7%)
N/A	16 (53.3%)
Treatment of IRAE	
Steroids	5 (16.7%)
Supp	9 (30%)
N/A	16 (53.3%)
ICI Retrial after hold for IRAE	
Yes	4 (13.3%)
No	3 (10%)
N/A	23 (76.7%)

For continuous values, median is shown with interquartile range in parentheses.

CONCLUSIONS

- This case series is, to our knowledge, the first large real-world study to assess the efficacy and tolerability of pembrolizumab specifically in MF/SS.
- Our results suggest that pembrolizumab has a significant therapeutic role in MF/SS, with a response rate of 48%.
- The efficacy of pembrolizumab observed within this cohort appears to exceed that of several other routine therapies including mogamulizumab, brentuximab, and traditional chemotherapy.
- Pembrolizumab exhibited efficacy across all compartments of MF/SS and even in heavily pre-treated patients.
- This study is limited due to its small sample size and heterogeneity within the study cohort in terms of disease characteristics and prior treatment.

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CONTACT INFORMATION

ElghawyO@pennmedicine.upenn.edu

University of Pennsylvania
The Perelman Center for Advanced Medicine TRC-2 West
3400 Civic Center Blvd
Philadelphia, PA 19104, United States