

Sociodemographic, Access to Care and Survival Outcomes for Patients with Mantle Cell Lymphoma: A National Cancer Database Analysis with Focus on Hispanics

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ABSTRACT

Mantle cell lymphoma (MCL) predominantly affects men and represents 3% of all non-Hodgkin's lymphomas. Ethnicity and age at diagnosis may influence prognosis, but the differences between Hispanic (HI) and Non-Hispanic (NH) patients with MCL remain unclear. This National Cancer Database (NCDB) analysis, 2004 to 2019, evaluates how sociodemographic factors impact presentation and survival of HI versus NH patients with MCL. The study included 32,515 MCL patients, with 1,729 being HI. HI patients were diagnosed at a younger median age (65 vs. 68 years, $P < 0.001$) and had a higher incidence of Stage IV disease. HI patients had a higher rate of unknown/uninsured status (13% vs. 4%, $P < 0.001$). Despite these differences, HI patients had better survival outcomes at 2, 5, and 10 years (74%, 57%, 44% for HI vs. 72%, 54%, 36% for NH). The median survival was 7.0 years for HI versus 5.8 years for NH ($P < 0.001$). Propensity score weighting confirmed the survival benefit for HI patients, likely due to their younger age and fewer comorbidities. Despite socioeconomic disadvantages, HI patients seem to access effective care, particularly at academic centers. Further research is needed to explore genetic and disease-specific factors contributing to this observed survival difference.

KEYWORDS: Lymphoma Mantle-Cell; Healthcare Disparities; Access to Care; Minority Groups; Hispanics.

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Introduction

Mantle cell lymphoma (MCL) represents 3% of all new diagnoses of non-Hodgkin lymphomas (NHL). MCL is a heterogeneous disease, possessing characteristics of both indolent and aggressive NHL which makes it a challenging malignancy to diagnose and treat [1]. Despite multiple advances in treatment, MCL remains a disease with variable prognosis, with a median overall survival of 4 to 5 years [2,3]. It is known that incidence is three times higher in males; as well as white Non-Hispanic (NH) compared to black NH patients [4]. Previous database analyses have identified several variables that can affect disease presentation and survival; including gender, age, stage at presentation, race, and ethnicity [5]. Retrospective analysis in Hispanics (HI) have speculated an improved overall survival (OS) as an effect of ethnicity in this population [4]. The purpose of this National Cancer Database (NCDB) analysis is to investigate and clarify racial differences, patient characteristics, disease-specific features, access to care, and whether these variables have any influence on survival in MCL patients in the United States (US), specifically HI compared to NH. Shah and colleagues performed a similar NCDB analysis evaluating outcomes between both populations with MCL; their database analysis was conducted between 2004-2013; our study aims to update the information in this cancer registry, with data being analyzed from 2004-2019 [4]. This article is a revised and expanded version of a paper and paper presentation entitled "Abstract 3818: Sociodemographic, access to care and survival outcomes for patients with mantle cell lymphoma: A national cancer database analysis with focus on Hispanics", which was presented at the American Association for Cancer Research (AACR) 2024 Annual Meeting [6].

Methods

Data were analyzed for MCL patients in the US reported to the NCDB between 2004 and 2019.[7] The most updated dataset included patients until 2019 at the time of analysis. The NCDB is a nationwide oncology outcomes database representing more than 1,500 Commission-accredited programs in the US and Puerto Rico. Approximately Seventy-two percent of all newly diagnosed cancer cases in the US are captured at the institutional level and reported to this database, containing approximately 40 million records from hospital cancer registries, where data on different types of cancer are tracked and analyzed [8]. Demographic and treatment characteristics were compared between racial groups. Kaplan-Meier and Cox regression analyses were used to compare OS between HI and HN populations. Multivariate analysis and propensity score weighting was performed to balance the covariates, adjusting for age, stage, comorbidity score, insurance status, type of facility, and great circle distance. Significance was assessed with t-tests and Fisher's Exact as appropriate. All testing in this study was two-sided with a significance level of 5%.

Study Population

Patient Characteristics

A total of 32,515 patients were included, with 1,729 patients being HI and 29,309 NH. In this cohort, majority of patients were male in both groups, with 1,260 (73%) for HI and 20,795 (71%) for NH. Median age at diagnosis was 65 years for HI and 68 years for NH. Most HI patients (49%) were diagnosed in the age category of less than 65 years, while NH patients (44%) were diagnosed between 65-79 years, with a notable increase in the number of cases diagnosed from 2016-2019 for both groups. Regarding race, for HI and NH most patients were white, 1,546 (89%) and 27,248

(93%), respectively. In terms of comorbidities, 3% of HI and 5% of NH had a Charlson-Deyo score of

2, and 3% of HI and 3% of NH had a score of 3 (Table 1).

Table 1. Mantle Cell Lymphoma Patient Characteristics.

Variable		Hispanics (HI) (N=1,729) (%)	Non-Hispanics (NH) (N=29,309) (%)	Unknown (N=1,477) (%)	Total (N=32,515) (%)	P-Value
Sex	Male	1,260 (73)	20,795 (71)	1,023 (69)	23,078 (71)	P=0.077
	Female	469 (27)	8,514 (29)	454 (31)	9,437 (29)	
Median Age at diagnosis	Years	65	68	69	68	P<0.001
Median age categories	<65 years	841 (49)	11,347 (39)	551 (37)	12,739 (39)	P<0.001
	65-79 years	663 (38)	12,889 (44)	635 (43)	14,187 (44)	
	≥80 years	225 (13)	5,073 (17)	291 (20)	5,589 (17)	
Race	American Indian, Aleutian, or Eskimo	3 (0)	86 (0)	5 (0)	94 (0)	P<0.001
	Asian Indian	0 (0)	22 (0)	0 (0)	22 (0)	
	Asian Indian or Pakistani, NOS	0 (0)	43 (0)	4 (0)	47 (0)	
	Black	24 (1)	1,275 (4)	45 (3)	1,344 (4)	
	Chinese	0 (0)	97 (0)	0 (0)	97 (0)	
	Filipino	0 (0)	75 (0)	1 (0)	76 (0)	
	Guamanian, NOS	0 (0)	1 (0)	0 (0)	1 (0)	
	Hawaiian	0 (0)	15 (0)	2 (0)	17 (0)	
	Hmong	0 (0)	3 (0)	0 (0)	3 (0)	
	Japanese	1 (0)	26 (0)	0 (0)	27 (0)	
	Kampuchean (including Khmer and Cambodian)	0 (0)	3 (0)	0 (0)	3 (0)	
	Korean	0 (0)	17 (0)	0 (0)	17 (0)	
	Laotian	0 (0)	1 (0)	0 (0)	1 (0)	
	Micronesia, NOS	0 (0)	1 (0)	0 (0)	1 (0)	
	Other	118 (7)	116 (0)	13 (1)	247 (1)	
	Other Asian, Including Asian, NOS and Oriental, NOS	3 (0)	118 (0)	1 (0)	122 (0)	
	Pacific Islander, NOS	1 (0)	4 (0)	0 (0)	5 (0)	
	Pakistani	0 (0)	6 (0)	0 (0)	6 (0)	

	Samoan	0 (0)	3 (0)	0 (0)	3 (0)	
	Thai	0 (0)	3 (0)	0 (0)	3 (0)	
	Unknown	33 (2)	101 (0)	163 (11)	297 (1)	
	Vietnamese	0 (0)	45 (0)	0 (0)	45 (0)	
	White	1,546 (89)	27,248 (93)	1,243 (84)	30,037 (92)	
Charlson-Deyo score	0	1,337 (77)	22,504 (77)	1,142 (77)	24,983 (77)	P=0.046
	1	285 (17)	4,469 (15)	228 (15)	4,982 (15)	
	2	57 (3)	1,428 (5)	72 (5)	1,557 (5)	
	3	50 (3)	908 (3)	35 (2)	993 (3)	

Disease and Treatment Characteristics

Most of the cases for both the HI and NH population were diagnosed between 2016-2019. The majority of patients with MCL presented with an advanced stage; 1,050 (61%) of HI and 18,101 (62%) of NH patients had stage IV disease at presentation. For most of the patient in both groups their HIV status was unknown. The

tendency for both HI and NH was towards receiving systemic therapy, however, there was a significant number of patients in which therapy received was unknown. The median time from diagnosis to chemotherapy initiation was 30 days for HI vs 29 days for NH. For immunotherapy initiation, the median time for HI was 35 days vs 32 days for NH (Table 2).

Table 2. Mantle Cell Lymphoma Disease Presentation and Treatment Characteristics.

Variable		Hispanics (HI) (N=1,729) (%)	Non-Hispanics (NH) (N=29,309) (%)	Unknown (N=1,477) (%)	Total (N=32,515) (%)	P-Value
Number of cases in years of diagnosis	2004-2007	256 (15)	5,205 (18)	566 (38)	6,027 (19)	P<0.001
	2008-2011	373 (22)	6,590 (23)	517 (35)	7,480 (23)	
	2012-2015	483 (28)	8,282 (28)	213 (14)	8,978 (28)	
	2016-2019	617 (36)	9,233 (32)	181 (12)	10,030 (31)	
Stage	Not applicable or unknown	199 (12)	2,672 (9)	193 (13)	3,064 (9)	P<0.001
	1	131 (8)	2,253 (8)	135 (9)	2,519 (8)	
	2	123 (7)	2,079 (7)	102 (7)	2,304 (7)	
	3	226 (13)	4,195 (14)	224 (15)	4,645 (14)	
	4	1,050 (61)	18,108 (62)	823 (56)	19,981 (62)	
HIV status	Associated/ Positive	2 (0)	8 (0)	0 (0)	10 (0)	P<0.001

	Not associated/ Negative	173 (10)	2,069 (7)	48 (3)	2290 (7)	
	Unknown	1,554 (90)	27,232 (93)	1,429 (97)	30,215 (93)	
Treatment status	Treatment given	1091 (85)	17,525 (83)	483 (81)	19,099 (83)	P<0.001
	No treatment given	132 (10)	1,881 (9)	83 (14)	2,096 (9)	
	Active surveillance	52 (4)	1,381 (7)	22 (4)	1,455 (6)	
	Unknown	12 (1)	217 (1)	12 (2)	241 (1)	
Median time from diagnosis to start chemotherapy	Days	30	29	28	29	P=0.192
Median time from diagnosis to start immunotherapy	Days	35	32	32	32	P=0.373

Facility, Payer, Income, Education and Geographic Characteristics

The most common facility where patients were treated for both HI and NH were Academic/Research programs (including National Cancer Institute (NCI) designated centers). HI tend to live closer to a treatment center, with a median great circle distance of 8.2 miles compared to 11.3 miles for NH (Table 3). For primary payer type at

the time of diagnosis, government sponsored insurance was the most frequent for HI and NH, covering 935 patients (54%) and 17,370 (60%), respectively. HI had a higher percentage of patients that were uninsured compared to NH, 9% versus 2%. According to census median income quartiles from 2008 to 2012, 22% of HI and 13% of NH patients fell into the quartile of less than \$38,000 dollars.

Table 3. Facility, Payer, and Area Characteristics.

Variable		Hispanics (HI) (N=1,729) (%)	Non-Hispanics (NH) (N=29,309) (%)	Unknown (N=1,477) (%)	Total (N=32,515) (%)	P-Value
Facility	Academic/Research Program (include NCI-designated comprehensive cancer centers)	839 (50)	11,323 (39)	436 (30)	12,598 (40)	P<0.001
	Community Cancer Program	88 (5)	1,875 (7)	87 (6)	2,050 (6)	
	Comprehensive Community Cancer	474 (28)	10,573 (36)	571 (40)	11,618 (36)	

	Program					
	Integrated Network Cancer Program	288 (17)	5,263 (18)	367 (25)	5,918 (18)	
Patients in metropolitan area	Counties in metro areas of 1 million population or more	1,219 (72)	13,856 (50)	663 (48)	15,738 (51)	P<0.001
Great circle distance	Median	8.2 miles	11.3 miles	10.3 miles	11.1 miles	P<0.001
Payer	Government Sponsored	935 (54)	17,370 (59)	872 (59)	19,177 (59)	P<0.001
	Private Insurance / Managed Care	577 (33)	10,723 (37)	519 (35)	11,819 (36)	
	Insurance Status Unknown	57 (3)	705 (2)	52 (4)	814 (3)	
	Not insured	160 (9)	511 (2)	34 (2)	705 (2)	
Census Median Income Quartiles 2008-2012	\$38,000<	351 (22)	3,415 (13)	224 (16)	3,990 (15)	P<0.001
	\$38,000-\$47,999	376 (24)	5,872 (22)	347 (25)	6,595 (23)	
	\$48,000-\$62,999	391 (25)	7,201 (27)	377 (27)	7,969 (27)	
	\$63,000≥	448 (29)	9,757 (37)	447 (32)	10,652 (37)	
Percent No High School Degree 2008-2012	21% or more	710 (45)	3,080 (12)	145 (10)	3,935 (14)	P<0.001
	13%-20.9%	357 (23)	6,139 (23)	325 (23)	6,821 (23)	
	7%-12.9%	306 (20)	9,155 (35)	496 (36)	9,957 (34)	
	Less than 7%	193 (12)	7,887 (30)	430 (31)	8,510 (29)	

Results

The HI cohort tends to have an earlier presentation than NH, with a median age of diagnosis that is 3 years earlier than NH, $P<0.001$. For both HI and NH, white males are the most affected population with MCL. Regarding Charlson-Deyo comorbidity score, the cohorts had a similar distribution. MCL often presents at late stages; regardless of being HI or NH, as almost 62% of the total patients presented as stage IV, $P<0.001$.

For the median time from diagnosis to starting treatment, no differences were noted between HI and NH, $P=0.192$. However, this studied cohort showed delays in starting systemic treatment (chemotherapy and immunotherapy) in the HI patients. A total of 59% of patients with MCL had government sponsored payer, however the HI had a higher percentage of uninsured and unknown insurance statuses, $P<0.001$. There is a notable gap in census median income quartiles from 2008-2012, showing a higher representation of NH patients in the higher income quartiles, with the majority of NH falling in the quartile of census

median income greater than or equal to \$63,000 dollars. Education was also noted to be a variable with statistical significance, with outstanding gaps between HI and NH.

In this cohort, the OS time in MCL patients differed between HI and NH (Figure 1). OS in the database was defined as the patient's vital status from the

time of initial diagnosis to the date recorded on the database as date of last contact or death. HI patients had a superior median overall survival of 7.0 years, compared to 5.8 years for NH, with a $P < 0.001$ (Table 4). On survival analysis, the survival probability at 2, 5, and 10 years for HI patients was 74%, 57%, and 44%; compared to 72%, 54%, and 44% for NH, respectively.

Figure 1. Mantle Cell Lymphoma, Hispanics Vs. Non-Hispanics Survival Curves

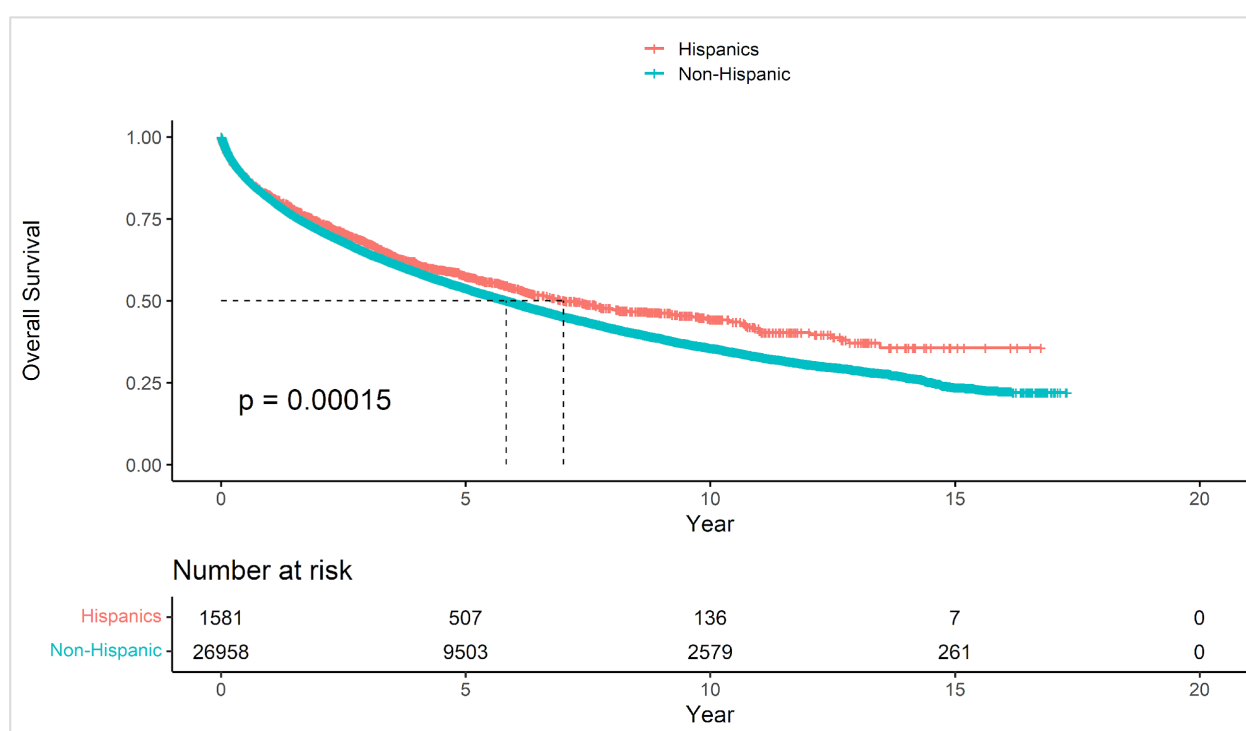


Table 4. Mantle Cell Lymphoma Survival Analysis.

Variable		Hispanics (HI) (N=1,729) (%)	Non-Hispanics (NH) (N=29,309) (%)	Unknown (N=1,477) (%)	Total (N=32,515) (%)	P-Value
Median overall survival	years	7.0	5.8	-	-	$P < 0.001$
Survival probability at 2, 5, and 10 years						
2 years	Number at risk	1,031	17,831	-	-	
	Survival Probability, CI	0.739, [0.717-0.761]	0.716, [0.711-0.722]	-	-	

5 years	Number at risk	507	9,503	-	-	
	Survival Probability, CI	0.574, [0.547-0.602]	0.538, [0.531-0.544]	-	-	
10 years	Number at risk	136	2,579	-	-	
	Survival Probability, CI	0.442, [0.409-0.477]	0.355, [0.347-0.363]	-	-	

Abbreviations: CI, Confidence Interval; OS, Overall Survival.

On multivariate analysis, uninsured status was independently associated with worse OS (hazard ratio of 1.29, with a 95% confidence interval (CI) 1.08-1.55, $P=0.01$). The propensity matched analysis showed significant OS difference between HI vs NH (5.8 years vs. 5.6 years), $P<0.001$.

Discussion

In this NCDB analysis from 2004-2019, HI patients with MCL, it was noted that HI patients diagnosed with MCL had better OS than NH diagnosed with MCL in the US. Interestingly, despite HI presenting at a younger age, with a similar profile in terms of comorbidities, both races presented with advanced disease at diagnosis. This study is consistent with what has been previously described in the literature; MCL being a malignant hematologic neoplasm of those that are older than 60, with a white male predominance [9]. Access to care for HI at academic/research programs seems to be irrespective of census median income, high school education, and primary payer; as the majority of HI and NH received treatment at these types of centers. Government sponsored payer is a common denominator among HI and NH, and this seems to be a constant for states with a high representation of the HI population in the US [10].

Survival in MCL has improved throughout the years along with better diagnostic approaches, which is consistent with a greater number of cases diagnosed in the later years – from 2016 to 2019.

In this analysis, immunotherapy and chemotherapy were the systemic therapies reported, however, no details on the specific regimens were available or how the decision process took place from the provider to determine what was the most appropriate treatment for the patient. In our cohort, it is unclear the difference between patients who received “no treatment” vs “active surveillance”, and there is no distinction on those patients who opted for palliative care treatment. Understanding that there is a MCL subtype called Leukemic Non-Nodal MCL which is an indolent variant and treatment is characterized by active surveillance. Currently, the treatment arsenal has continued to expand, which now includes Bruton Tyrosine Kinase (BTK) inhibitors, stem cell transplantation, and cellular therapy [11]. It is unclear in our analysis what percent of HI compared to NH received stem cell transplant or additional lines of therapy, and how would the outcomes of such treatment might have differed among cohorts. Although in our study there was no statistical difference in the type of facility where the patients were mostly treated, it is known that advanced therapies will most commonly take place at academic facilities and this specialized care is noted to be predictor of the outcome [12]. Additionally, in 2022, with newer data from the Triangle study, the use of BTK inhibitors during induction and maintenance, with or without transplantation, creates a new paradigm as to whether stem cell transplant is still needed and how this change in practice might affect the HI

population and their overall survival [13]. Therefore, information from Real World Outcomes (RWO) becomes relevant, as access to autologous stem cell transplant and cellular immunotherapies is not uniform [14,15].

In the current era of immunotherapy and BTK inhibitors, evaluating how these novel therapies have influenced the rates of stem cell transplantation among HI and NH patients with MCL is essential. A comparative analysis of transplant rates between these groups may uncover significant disparities, particularly regarding access to advanced treatments [16]. Furthermore, examining survival outcomes among HI and NH patients who undergo stem cell transplants, especially after treatment with immunotherapy or BTK inhibitors, could provide valuable insights into the efficacy of these approaches in different populations. Socioeconomic factors and access to care should also be considered as potential contributors to these differences in MCL outcomes.

Previous studies and models have attempted to look at economic evaluations, costs and resource use, as well as health-related quality of life in MCL. Results from this study are hard to interpret as data were compared across different disease settings: first line vs relapse/refractory setting, and also due to quality of life surveys based on treatment received[17]. Our database and study does not focus on these factors specifically, however with newer and potentially less toxic therapies in MCL, knowing the population's socio-demographic background might assist the physician in choosing the most appropriate treatment option as toxicity from treatment is known to increase adverse effects, hospital use and total costs [18]. In the US, it is estimated that the mean monthly costs during treatment can go as high as \$24,719 dollars during treatment; and a

difference of mean monthly cost during follow-up of \$13,650 dollars among patients with ≥ 6 adverse effects compared to \$5,131 dollars among those without adverse effects[19,20].

This study raises the question as to what specific sociodemographic factors truly influence survival in MCL among HI, what are the specific intrinsic biological and cellular factors in HI as well as the external environmental exposures for HI; causing HI to have an earlier presentation, different survival patterns, but a tendency to an increased overall survival. Lastly, a critical aspect of research is exploring the biological differences in tumors between HI and NH patients with MCL. Tumor biology, including molecular markers and genetic mutations, may vary between these populations, potentially influencing treatment response and survival outcomes [21]. The broad categorization of HI may mask specific subgroups with unique biological characteristics and survival patterns. Therefore, redefining the HI category based on factors such as ancestry or geographical location may be necessary to identify which subgroups are most affected by these disparities in MCL. Recognizing these differences could lead to more personalized treatment strategies and improved outcomes for HI patients with MCL. Understanding the impact of diagnosis, treatment and follow up on these population could inform policy changes aimed at reducing disparities in care.

Study limitations

Our retrospective analysis does have some limitations. As mentioned above, the treatment paradigm has continued to evolve in the last years, since our analysis is until 2019, it will be important to determine if the survival outcomes discussed above are still present and valid in future years. Additionally, from the database, we do not know what where the exact chemoimmunotherapy regimens used among the different groups. This is

important, as we do not know if different regimens can potentially have different response outcomes in minorities; or if HI are being treated different than NH. In terms of comorbidities, the Charlson-Deyo score, is a comorbidity score; it would be important to know what comorbidities HI have compared to NH, as these could be associated with better survival. Lastly, factors such as lactate dehydrogenase at presentation, white count at presentation, and Ki-67; all variables used to calculate Mantle Cell Lymphoma International Prognostic Index (MIPI) and TP53 status, were not examined, and these are important to determine survival outcomes in MCL.

Conclusion

In this NCDB cohort of patients diagnosed with MCL, focusing on HI and NH, multiple sociodemographic differences were noted as well as an advantage in survival outcomes favoring the HI population. Despite major variations seen regarding income and education, HI patients seem to access effective care, particularly at academic centers where they seem to get the standard of care treatment, even though, having more uninsured patients. HI survival advantage may be due to their younger age at diagnosis and fewer comorbidities, however, biological markers, genetic and disease-specific factors contributing to this observed survival difference are yet to be studied. Survival has improved in MCL with use of newer therapies; the role of BTK-inhibitors and stem cell transplantation will need to be assessed as it is important to compare the types of treatments HI are being offered with the treatments they end up receiving. In the HI cohort, it would be important to know if a specific molecular profile favors certain treatments with less toxicity but maintains survival outcomes. Despite advances in the management of hematologic malignancies, MCL remains a

complex disease, where it is crucial to tailor the treatment that patients receive; knowing the demographic variables can assist the decision-making process to ensure adequate and timely initiation of treatment. In these exciting times with several treatment options, access to care and consideration of demographic characteristics remain of paramount importance.

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Conflicts of Interest

The authors declare no conflicts of interest.

Authors' contributions

Study Concept & Design: ETV, AK, AEDD.

Data Acquisition, Analysis & Interpretation: ETV, QL, JEM.

Writing of the Manuscript: ETV, CVM, DR, QL, JEM, AK, AEDD

Study Supervision: AEDD

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