Uludağ Üniversitesi Tıp Fakültesi Dergisi
Journal of Uludağ University Medical Faculty
51 (3) 411-417, 2025
DOI: https://doi.org/10.32708/uutfd.1757844

ORIGINAL RESEARCH

Efficacy of Chemotherapy Regimens in Mantle Cell Lymphoma: A Single Center Experience

Mehmet Ali AŞIK[1], Fahir ÖZKALEMKAŞ[2], Vildan ÖZKOCAMAN[2]

[1] Medical Park Adana Hastanesi, Adana, Türkiye.
[2] Bursa Uludağ University Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Bursa, Türkiye.

ABSTRACT

This single-center study evaluates the clinical characteristics, treatment responses, and survival outcomes of patients with Mantle Cell Lymphoma (MCL). We retrospectively analyzed 25 patients with MCL treated at the Hematology Department of Bursa Uludag University between January 2000 and December 2014. The median follow-up was 37 months min-max=6-132). The cohort was predominantly male (84%), with 92% presenting with advanced-stage disease. The overall response rate to first-line chemotherapy was 72%, with 9 patients (36%) achieving complete remission. The median progression-free survival (PFS) was 17 months (range, 2–39), and the 3- and 5-year overall survival (OS) rates were 52% and 28%, respectively. Among nine patients requiring second-line therapy, three (33%) achieved partial remission, while three (33%) had no response; the remaining three patients died before response assessment. The median PFS with second-line treatment was 6 months. Seven (28%) patients underwent autologous hematopoietic stem cell transplantation (AHSCT). The AHSCT cohort was significantly younger (p=0.047) and demonstrated a significantly longer median OS (p<0.05) compared to non-transplanted patients. These real-life data confirm that despite therapeutic advances, MCL remains a challenging malignancy with poor outcomes after relapse.

Keywords: Mantle Cell Lymphoma. Chemotherapy. Autologous hematopoietic stem cell transplantation.

Mantle Hücreli Lenfomada Kemoterapi Rejimlerinin Etkinliği: Tek Merkez Deneyimi

ÖZET

Bu tek merkezli çalışma, Mantle Hücreli Lenfoma (MHL) hastalarının klinik özelliklerini, tedavi yanıtlarını ve sağkalım sonuçlarını değerlendirmektedir. Ocak 2000 ile Aralık 2014 tarihleri arasında Bursa Uludağ Üniversitesi Tıp Fakültesi Hematoloji bölümünde tedavi edilen 25 MCL hastasını retrospektif olarak analiz ettik. Hastaların median takip süresi 37 (min-max=6-132) aydı. Kohortun çoğunluğu erkekti (%84) ve %92'si ileri evre hastalıkla başvurdu. Birinci basamak kemoterapiye genel yanıt oranı %72 idi ve 9 (%36) hastada tam remisyon sağlanmıştı. Progresyonsuz sağkalım (PFS) medyan 17 (min-max=2–39 ay) aydı ve 3 ve 5 yıllık genel sağkalım (OS) oranları sırasıyla %52 ve %28 idi. İkinci basamak tedavi gerektiren dokuz hastadan üçü (%33) kısmi remisyonda iken, üçü (%33) yanıtsızdı; kalan üç hasta ise yanıt değerlendirmesi yapılmadan önce hayatını kaybetmişti. İkinci basamak tedavi ile medyan progresyonsuz sağkalım (PFS) 6 ay olarak saptandı. Yedi (%28) hastaya otolog hematopoietik kök hücre nakli (OHKHN) yapılmıştı. OHKHN uygulanan grup, nakil yapılmayan hastalara kıyasla anlamlı derecede daha gençti (p=0,047) ve medyan genel sağkalım (OS) süresi anlamlı olarak daha uzundu (p<0,05). Bu gerçek yaşam verileri, terapötik ilerlemelere rağmen MHL'nin nüks sonrası kötü prognoza sahip olan zorlu bir malignite olmaya devam ettiğini doğrulamaktadır.

Anahtar Kelimeler. Mantle hücreli lenfoma. Kemoterapi. Otolog hematopoietik kök hücre nakli.

Date Received: 4.August.2025
Date Accepted: 23.September.2025

Title, Given Name, Family Name: Dr. Mehmet Ali Aşık
Institution and Address: Adana Medical Park Hastanesi, Adana, Türkiye.
E-mail: maasik06@gmail.com

AUTHORS' ORCID INFORMATION
Mehmet Ali AŞIK:0000-0001-7336-2342
Fahir ÖZKALEMKAŞ:0000-0001-9710-134X
Vildan ÖZKOCAMAN:0000-0003-0014-7398

Mantle Cell Lymphoma (MCL), a subtype of non-Hodgkin lymphoma, originates from B cells and is characterized by cyclin D1 overexpression due to the t(11;14)(q13;q32) translocation, generally exhibiting an aggressive clinical course[1,2]. MCL exhibits significant clinical and molecular heterogeneity, with its aggressive course, histopathological variants, and molecular subtypes leading to considerable variations in treatment response and prognostic outcomes[3,4]. This heterogeneity complicates the establishment of standard treatment approaches, thereby necessitating the development of personalized strategies. Despite recent advances in treatment protocols, high

recurrence rates and treatment resistance underscore the continuing need for novel therapeutic approaches. Advances in molecular biology, cytogenetics, and immunology have enabled a better understanding of lymphoma pathogenesis and the development of more effective and personalized strategies in the treatment of MCL[5]. Given the absence of a universally superior treatment approach for MCL, clinical departments typically develop treatment protocols tailored to each patient's individual risk profile, considering factors such as age, performance status, and comorbidities[6]. In this study, we aimed to share our clinical experience by evaluating the clinical features, responses to chemotherapy regimens, and survival outcomes of patients with MCL followed in our clinic.

Material and Method

A total of 25 patients diagnosed with MCL who were followed in the Department of Hematology at Bursa Uludag University between January 2000 and December 2014 were included in the study. Data collected included patient gender, date and age at diagnosis, presenting complaints, presence of B symptoms, laboratory data, administered chemotherapy regimens, treatment responses, remission and relapse durations, treatment-related side effects, histological subtypes (from pathology reports), Ki-67 index, and immunohistochemical staining results. The Ann-Arbor staging system was used for disease staging. B symptoms were defined as unexplained weight loss exceeding 10% of baseline body weight within six months, unexplained and recurrent fever of ≥38.3∘C, or drenching night sweats. Systemic symptoms were categorized as present (B) or absent (A) accordingly. The simplified Mantle Cell Lymphoma Prognostic Index (MIPI) and International Prognostic Index (IPI) scores were calculated for each patient. The simplified MIPI score, ranging from 0 to 11 points, classified risk as low (0-3 points), moderate (4-5 points), or high (6-11 points). The Eastern Cooperative Oncology Group (ECOG) performance status scale was used to measure the patients' functional status.

Categorical variables were presented as numbers (n) and percentages (%). Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed continuous variables were summarized as means ± standard deviations and compared using the Student's t-test, while non-normally distributed variables were expressed as medians (minimum–maximum) and compared using the Mann-Whitney U test. The association between categorical variables was evaluated using the Chi-square test when the expected cell counts were ≥5; Fisher's Exact Test was applied when expected counts were <5 to ensure validity. Median survival time was calculated using the Kaplan-Meier method, and Cox regression analyses were performed to identify prognostic factors affecting survival. A p-value < 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics version 21.

The study protocol was approved by the Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee (decision number 2015-8/7).

Results

Of the patients included in the study, 21 (84%) were male and 4 (16%) were female. The median follow-up was 37 months (min-max=6-132 months). The median age at diagnosis was 54 years (min-max=43-80 years), with both male and female patients having a median age of 54 years. The most common presenting complaint (11 patients, 44%) was lymphadenomegaly, followed by gastrointestinal complaints (5 patients, 20%). Thirteen (52%) patients had one of the B symptoms. At the time of diagnosis, 23 (92%) patients had advanced-stage (Stage III-IV) disease. Twelve (48%) patients presented with extranodal involvement. Five patients (20%) had gastrointestinal involvement, 12 patients (48%) had bone marrow involvement, and 6 (24%) patients had spleen involvement.

Patients in our study were categorized as low, moderate, and high risk based on the MIPI score. Given the limited number of patients in the low-risk group, the low- and intermediate-risk groups were combined. Upon comparison with the high-risk group, no significant difference was observed in median overall survival (OS) (p>0.05).

Of the 21 patients with available cyclin D1 results, 18 (85.7%) were positive. The Ki-67 proliferation index was categorized as low/moderate in 12 (48%) patients and high in 7 (28%) patients. Data on the Ki-67 index were missing for six (24%) patients. No significant association was found between the Ki-67 proliferation index (high vs. low/moderate) and median OS (p=0.773) when comparing the 7 patients with a high index to the 12 patients with a low/moderate index.

Regarding histological variants, the classic form was reported in 5 patients (20%), the blastoid form in 6 patients (24%), and lymphomatous polyposis in 1 patient (4%). Histological variant information was not available for 13 (52%) patients. The clinical and pathological characteristics of patients diagnosed with mantle cell lymphoma are summarized in Table I.

LDH levels at diagnosis were available for 22 patients, with a mean of 251.9 ± 66.7 U/L. In the performed statistical analysis, elevated LDH was identified as a prognostic factor adversely affecting OS (p=0.021, HR:1.017, 95% CI:1.003–1.032).

Table I. Clinical and Pathological Characteristics of Patients Diagnosed with Mantle Cell Lymphoma

Characteristic	No. of patients *n* (%)
Sex	
Female	4 (16)
Male	21 (84)
Median age, years (range)	54 (43–80)
B symptoms	
Present	13 (52)
Absent	12 (48)
Stage (Ann Arbor)	
I–II	2 (8)
III–IV	23 (92)
Extranodal involvement	
Present	12 (48)
Absent	13 (52)
Gastrointestinal involvement	
Present	5 (20)
Absent	20 (80)
Splenic involvement	
Present	6 (24)
Absent	19 (76)
ECOG performance status	
0–1	14 (56)
> 2	8 (32)
Unknown	3 (12)
MIPI score	
Low (0–3)	1 (4)
Intermediate (4–5)	12 (48)
High (6–11)	9 (36)
Unknown	3 (12)
IPI score	
Low (0–1)	3 (12)
Low-Intermediate (2)	7 (28)
Intermediate-High (3)	6 (24)
High (4–5)	6 (24)
Unknown	3 (12)
Bone-marrow involvement	
Present	12 (48)
Absent	6 (24)
Not performed	4 (16)
Unknown	3 (12)
Ki-67 index	
Low (< 10 %)	3 (12)
Intermediate (10–40 %)	9 (36)
High (> 40 %)	7 (28)
Unknown	6 (24)
Cellular subtype	
Classical	5 (20)
Blastoid	6 (24)
Other	1 (4)
Unknown	13 (52)
Immunohistochemistry†	
CD5 (tested = 22)	22 (100)
CD20 (tested = 22)	22 (100)
CD23 (tested = 19)	1 (5.2)
Cyclin D1 (tested = 21)	18 (85.7)

† Percentages for immunohistochemical markers refer to the number of positive cases among the samples tested.

ECOG: Eastern Cooperative Oncology Group, **IPI:** International Prognostic Index, **MIPI:** Mantle International Prognostic Index.

The cohort received four distinct first-line chemotherapy protocols, with a median of 6 cycles (min-max=2–8). All patients commenced systemic chemotherapy immediately following diagnosis. The regimens administered were R-CHOP in 16 (64%) patients, R-CHOP/R-DHAP in 5 (20%) patients, R-hyperCVAD in 2 (8%) patients, and CVP in 2 (8%) patients. After completion of induction therapy, 9 patients (36 %) achieved complete remission, 9 (36 %) partial remission, 1 (4 %) exhibited stable disease, and 6 (24 %) showed disease progression. Toxicity assessment revealed grade ≥ 3 haematological adverse events in 7 patients (28 %) and grade ≥ 3 non-haematological toxicities in 6 (24 %). Across the whole group, median progression-free survival (PFS) following first-line chemotherapy was 17 months (min-max= 2–39); the Kaplan–Meier curve is depicted in Figure 1. OS at 3 and 5 years was 52 % and 28 %, respectively, with the corresponding survival curve presented in Figure 2.

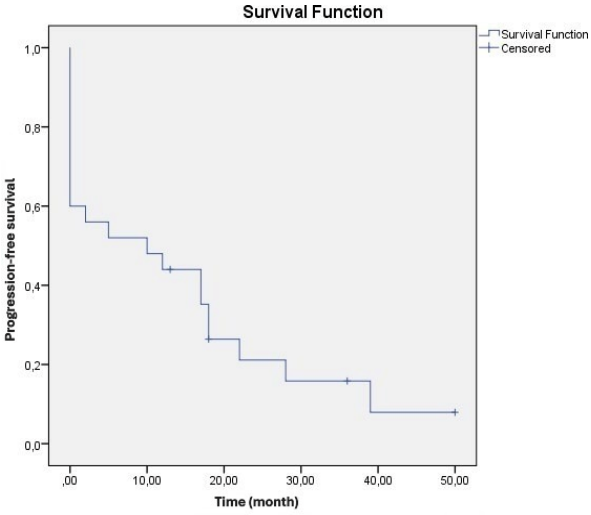

Figure 1:
Progression-free survival curves of the patients

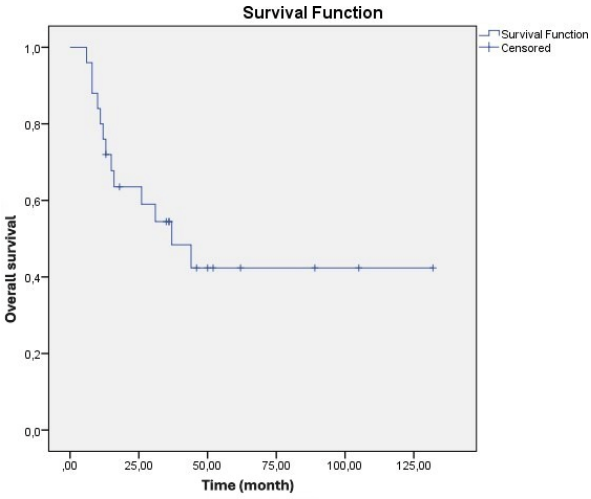

Figure 2:
Median overall survival curves of the patients

Nine patients underwent second-line chemotherapy. The chemotherapy regimens administered were as follows: hyperCVAD in 2 patients, fludarabine–cyclophosphamide in 1 patient, bortezomib–fludarabine–cyclophosphamide in 1 patient, R-bortezomib–dexamethasone in 2 patients, cyclophosphamide–prednisolone in 2 patients, and R-vincristine–dexamethasone in 1 patient (Table II). Among these, partial remission was achieved in 3 (33%) patients. No objective response was observed in another 3 (33%), and 3 patients died before response assessment. Grade ≥ 3 toxicities were observed in three patients, encompassing both hematological and non-hematological adverse events. Median PFS after second-line therapy was 6 months. Due to the heterogeneity of regimens and the limited sample size, meaningful comparisons between protocols could not be made. The individual regimens and corresponding responses are summarized in Table II.

Table II. Distribution of Chemotherapy Regimens and Response Rates

Regimen	No. of patients	Complete response	Partial response	Stable disease	Progressive disease
First-line therapy					
R-CHOP	16	4	5	1	6
R-CHOP→R-DHAP (sequential)	5	4	1	0	0
R-hyperCVAD	2	1	1	0	0
CVP	2	0	2	0	0
Second-line therapy					
HyperCVAD	2 (1†)	0	1	0	0
Fludarabine+ Cyclophosphamide	1	0	0	0	1
Bortezomib+ Fludarabine+ Cyclophosphamide	1	0	1	0	0
R-Bortezomib+ Dexamethasone	2	0	1	0	1
Cyclophosphamide + Prednisolone	2 (2†)	0	0	0	0
R-Vincristine+ Dexamethasone	1	0	0	0	1

† refers to patients who died before response assessment.

R: Rituximab, CHOP: Cyclophosphamide,Hydroxydaunorubicin, Vincristine, Prednisone, CVAD: Cyclophosphamide, Vincristine, Adriamycin, Dexamethasone, DHAP: Dexamethasone, High-dose Cytarabine, Cisplatin

Autologous hematopoietic stem-cell transplantation (AHSCT) was performed in 7 patients (28 %). Based on the evaluations, patients aged ≤65 years, with an ECOG performance status ≤2, and without comorbidities limiting AHSCT were considered eligible for AHSCT. Five patients underwent AHSCT following the R-CHOP/DHAP chemotherapy protocol, and 2 patients after the HyperCVAD protocol. The median age of transplanted patients was 50 years, whereas the median age of those who did not undergo AHSCT was 62 years; this difference was statistically significant (p=0.047). Of the seven recipients, four underwent AHSCT as consolidation after completing first-line chemo-immunotherapy, and three proceeded to AHSCT following salvage therapy for relapsed or refractory disease. During post-transplant follow-up, disease relapse was documented in three patients, with a median time to recurrence of 12 months (range, 6–72 months); by contrast, no relapse was detected in three other transplanted patients at last assessment. One patient died from septic shock secondary to febrile neutropenia one month after AHSCT. Kaplan–Meier analysis demonstrated that median OS was significantly longer in the AHSCT group than in patients managed without transplantation (p<0.05). Comparison between patients who underwent AHSCT and those who did not revealed statistically significant differences in age (p=0.03), MIPI score (p=0.04), and LDH level (p=0.027). No significant differences were observed in gender (p = 0.884), histological variant (p=0.182), and Ki-67 index (p=0.603). ECOG performance status showed a borderline significance (p=0.051). The comparison between patients who underwent AHSCT and those who did not is summarized in Table III. In the univariate analysis of overall survival, statistically significant associations were found with AHSCT (p=0.017, HR=0.083, 95% CI:0.11–0.642), age (p=0.026, HR=1.063, 95% CI:1.007–1.122), and LDH level (p=0.021, HR=1.017, 95% CI:1.003–1.103). However, in the multivariate analysis, none of these variables showed a statistically significant association with overall survival: AHSCT (p=0.144), age (p=0.582), and LDH level (p=0.192).

Table III. Comparison of patients who underwent AHSCT and those who did not

Characteristics	AHSCT performed		p
	Yes (n:7)	No (n:18)	
Age (year) (min-max)	50 (43-61)	62 (46-80)	**0.03**
Gender (n) (Female/Male)	1/6	3/15	0.884
MIPI (n) (Low+Intermediate/High)	6/0	7/9	**0.046**
ECOG (n) (≤ 2 />2)	6/0	8/8	0.051
LDH (U/L) (min-max)	200 (142-267)	260 (117-437)	**0.027**
Ki-67 index (n) (<40%/>40%)	4/1	8/6	0.603
Histological variant (n) (Classic/blastoid)	2/0	3/6	0.182

ECOG:Eastern Cooperative Oncology Group, LDH:Lactate Dehydrogenase, MIPI: Mantle International Prognostic Index.

Across the entire cohort, 15 patients (60%) died during follow-up. Five deaths were attributed to treatment-related infections—three febrile neutropenia and two pneumosepsis—whereas ten deaths resulted

from complications associated with disease progression or relapse.

Discussion and Conclusion

This single-centre series contributes real-world data on MCL, a rare non-Hodgkin lymphoma lacking a universally accepted treatment algorithm. The disease typically presents in older adults (median 60-70 years) and shows a marked male predominance (male-to-female ratio ≈ 3–4:1); B symptoms occur in roughly half of cases[7,8]. In our cohort the median age was 54 years (range 43–80), the male-to-female ratio was 5:1, and B symptoms were documented in 13 of 25 patients (52%), findings in line with published epidemiology.

Consistent with reports that lymphadenopathy is the leading presenting complaint and that >80 % of patients have advanced-stage disease with frequent extranodal spread, 11 patients (44%) sought care for lymphadenopathy and 23 (92%) had stage III–IV disease at diagnosis; extranodal involvement, most often gastrointestinal tract or bone marrow, was confirmed in 12 patients (48%)[9].

Prognostic assessment commonly relies on the MIPI, first validated by Hoster et al. in 455 advanced-stage cases, where distinct risk groups correlated with OS. Incorporation of the Ki-67 proliferation index in the subsequent MIPI-c improved risk stratification[10,11]. However, Shah et al. later failed to reproduce the discriminatory power of MIPI in a uniformly treated, cytarabine-intensive cohort, suggesting that aggressive regimens may blunt the impact of baseline high-risk features[12]. In our series, MIPI-defined risk categories likewise did not predict median OS ($p>0.05$), a result that may reflect the small sample size and the inclusion of several patients treated with intensive chemo-immunotherapy—circumstances echoing those described by Shah et al.

LDH level is a reliable prognostic factor for predicting survival in MCL. In the study conducted by Andersen et al., a significant association between LDH levels and OS was reported. Similarly, our study also found a significant relationship between LDH levels and OS[13].

The Ki-67 index, the most commonly used proliferation marker, is a negative prognostic indicator. A study by Hoster et al. reported significantly reduced overall survival in patients with a Ki-67 index exceeding 30%[11]. In contrast, our study found no significant difference in median OS when comparing patients with a high Ki-67 proliferation index to those with a lower index ($p=0.773$). This lack of significance may be attributable to the limited sample size of our study.

Multiple first-line therapeutic options are available for MCL, and the choice of treatment is tailored to the patient's age, performance status, and comorbidities[14,15,16]. The TP53 mutation is a critical biomarker that predicts a poor prognosis and treatment resistance in MCL. Current guidelines recommend incorporating TP53 mutation status into treatment planning[17,18]. Similar to low-grade lymphomas, it is generally accepted that select patients with MCL can be initially managed with active surveillance. This approach is typically reserved for individuals presenting with a good performance status, an absence of B symptoms and bulky disease, normal LDH levels, a low Ki-67 index, and non-aggressive cytomorphology. Indeed, a single-center study that deferred systemic chemotherapy in low-risk, asymptomatic patients found no significant difference in OS compared to patients who received systemic chemotherapy at diagnosis[19]. In our study, all patients were classified as high-risk and therefore commenced systemic chemotherapy immediately following diagnosis.

A total of four different chemotherapy regimens were used in the first-line setting (Table II). A comparison of these regimens revealed that cytarabine-containing intensive chemotherapy (e.g., hyperCVAD/MA, R-DHAP) yielded significantly higher complete remission rates than other regimens (71% vs. 22%; $p=0.02$). This finding suggests that cytarabine-containing protocols are highly effective treatment options for MCL[20].

Significant improvements in survival rates for MCL have been observed over time. Recently, the introduction of novel agents and advanced therapeutic strategies has greatly enhanced clinical outcomes. A retrospective, 15-year, real-world study by Gencini et al. reported a significant improvement in OS for patients treated between 2016 and 2020 compared to earlier periods, with 5-year OS rates of 91% (2016–2020), 44% (2011–2015), and 33% (2006–2010), respectively. In the TRIANGLE study evaluating the BTK inhibitor ibrutinib, the 3-year PFS rate was higher in the ibrutinib treatment arm compared to the high-dose consolidation and AHSCT treatment arm. (86–88% vs. 72%; $p = 0.0008$; HR 0.52)[21,22]. In our study, the median PFS after first-line treatment was 17 months (range, 2–39), and 3-year and 5-year survival rates were 52% and 28%, respectively. Our findings suggest that patients in the past had more limited access to supportive care and contemporary regimens, and that the protocols currently implemented have positively influenced survival outcomes. Therefore, when evaluating treatment outcomes from earlier periods, the benefits offered by current therapeutic options should be taken into account. Due to the small patient cohort and regimen heterogeneity, comparison

of the effects of different first-line chemotherapy regimens on survival was not feasible.

In past years, for transplant-eligible patients, intensive cytarabine-based chemoimmunotherapy followed by AHSCT had become the standard of care[23]. The benefit of AHSCT consolidation is supported by randomized trials demonstrating improved PFS. AHSCT consolidation after salvage therapy is controversial and provides benefit only to a minority of patients with relapsed disease[24]. In our study, seven patients underwent AHSCT: four as consolidation after first-line therapy and three after salvage therapy. One patient died from treatment-related febrile neutropenia and septic shock. During follow-up, three patients relapsed post-AHSCT; notably, all three had received AHSCT as consolidation after salvage therapy, a strategy with limited reported efficacy. The median time to relapse was 12 months (range, 6–72). A significant association between AHSCT and overall survival was observed in the univariate analysis (p=0.017, HR=0.083, 95% CI:0.011–0.642); however, this association was not confirmed in the multivariate analysis (p=0.144). This finding may be attributable to the limited sample size and the insufficient statistical power of the model. In systematic analyses evaluating the role of AHSCT in first-line therapy, findings have shown that rituximab maintenance is superior to AHSCT in terms of both PFS and OS, particularly in the treatment of MCL. These results suggest that in the modern treatment era, especially with the widespread use of intensive induction regimens and rituximab, the absolute value of AHSCT has diminished. The advantages of rituximab maintenance therapy, such as its lower toxicity and lack of need for hospitalization, have made it the preferred option for many patients[25,26].

The prognosis for patients with relapsed MCL is poor, with short median survival times. Studies have reported a median PFS of 5.3–6.5 months for patients receiving bortezomib-based therapy[27]. Consistent with these reports, the majority of relapsed patients in our cohort received bortezomib-based therapy, and the median PFS was 6 months. An analysis of outcomes (e.g., treatment response, OS, PFS) by specific regimen was not feasible for the relapsed cohort due to the small sample size and heterogeneity of treatments.

Myelosuppression is a significant and common chemotherapy-related toxicity. Rates of Grade ≥ 3 myelosuppression vary depending on the chemotherapy regimen and are particularly common with intensive protocols, such as those containing high-dose cytarabine[28]. In our study, 7 (28%) patients developed Grade ≥ 3 hematologic toxicity. Notably, the majority of these events (85%) occurred in patients receiving intensive chemotherapy regimens.

Bacterial infections are among the most frequent chemotherapy-related complications, with pulmonary infections occurring at a rate of 5–20%[29]. The risk of infection is correlated with the type and intensity of the chemotherapy protocol and the degree of associated myelosuppression. In our cohort, chemotherapy-related pulmonary infections were detected in five patients, including one case of invasive pulmonary aspergillosis (IPA). All affected patients had received intensive chemotherapy and experienced Grade ≥ 3 myelosuppression.

This study has several limitations, including its single-center, retrospective design and small sample size. Due to the limited number of patients over the 14-year period, the statistical power is restricted, and caution should be exercised when generalizing these results. Small changes in prognosis or treatment effects may not be detectable in this cohort. Since our data covers the years 2000-2014, it may not fully reflect current clinical practice considering the significant developments in MCL management in recent years. Clinical practice for MCL has evolved considerably, especially with the introduction of novel targeted therapies. This means that the obtained results may not be applicable to patients currently undergoing treatment.

However, a key strength is the presentation of real-world clinical data for MCL, a rare malignancy with heterogeneous treatment approaches and no single standard of care.

In conclusion, although overall survival in MCL has improved with novel therapeutic approaches, it remains a challenging disease. Ongoing advances in molecular biology, cytogenetics, and immunology are expected to drive significant improvements in future treatment modalities and further refine the management of patients with MCL.

Researcher Contribution Statement:
Idea and design: M.A.A., F.Ö., V.Ö.; Data collection and processing: MA.A.; Analysis and interpretation of data: M.A.A., F.Ö., V.Ö.; Writing of significant parts of the article: M.A.A.

Support and Acknowledgement Statement:
This study received no financial support
Conflict of Interest Statement:
The authors of the article have no conflict of interest declarations.
Ethics Committee Approval Information:
Approving Committee: Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee
Approval Date: 31.03.2015
Decision No: 2015-8/7

References

1. Cortelazzo S, Ponzoni M, Ferreri AJ, Dreyling M. Mantle cell lymphoma. Crit Rev Oncol Hematol 2012; 82(1):78-101.
2. Wiestner A, Tehrani M, Chiorazzi M, et al. Point mutations and genomic deletions in CCND1 create stable truncated cyclin D1 mRNAs that are associated with increased proliferation rate and shorter survival. Blood. 2007 Jun 1;109(11):4599-606.

3. Bernard M, Gressin R, Lefrère F, et al. Blastic variant of mantle cell lymphoma: a rare but highly aggressive subtype. Leukemia 2001;15: 1785-1791.
4. Mozos A, Royo C, Hartmann E, et al. SOX11 expression is highly specific for mantle cell lymphoma and identifies the cyclin D1-negative subtype. Haematologica. 2009 Nov;94(11):1555-62.
5. Smith MR. Should there be a standard therapy for mantle cell lymphoma?. Future Oncol. 2011 Feb;7(2):227-37.
6. Dreyling M. Therapy of mantle cell lymphoma: new treatment options in an old disease or vice versa?. Semin Hematol. 2011 Jul;48(3):145-7.
7. Smith A, Howell D, Patmore R, et al. İncidence of haematological malignancy by sub-type: report from the Haematological Malignancy Research Network. Br J Cancer 2011;105:1684-92.
8. Cortelazzo S, Ponzoni M, Ferreri AJ, Dreyling M. Mantle cell lymphoma. Crit Rev Oncol Hematol 2012;82:78-101.
9. Pileri SA, Falini B. Mantle cell lymphoma. Haematologica 2009 Nov;94(11):1488-92.
10. Hoster E, Dreyling M, Klapper W, et al. German Low Grade Lymphoma Study Group (GLSG); European Mantle Cell Lymphoma Network. A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. Blood. 2008 Jan 15;111(2):558-65.
11. Hoster E, Rosenwald A, Berger F, et al. Prognostic Value of Ki-67 Index, Cytology, and Growth Pattern in Mantle-Cell Lymphoma: Results From Randomized Trials of the European Mantle Cell Lymphoma Network. J Clin Oncol. 2016 Apr 20;34(12):1386-94.
12. Shah JJ, Fayad L, Romaguera J. Mantle Cell International Prognostic Index (MIPI) not prognostic after R-hyper-CVAD. Blood. 2008 Sep 15;112(6):2583.
13. Andersen NS, Jensen MK, Brown PN, Geisler CH. A Danish population-based analysis of 105 mantle cell lymphoma patients: incidences, clinical features, response, survival and prognostic factors. European Journal of Cancer. Volume 38, Issue 3, 2002, 401-408.
14. Dreyling M, Campo E, Hermine O, et al. ESMO Guidelines Committee. Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017 Jul 1;28(suppl_4):62-71.
15. Hermine O, Hoster E, Walewski J, et al. European Mantle Cell Lymphoma Network. Addition of high-dose cytarabine to immunochemotherapy before autologous stem-cell transplantation in patients aged 65 years or younger with mantle cell lymphoma (MCL Younger): a randomised, open-label, phase 3 trial of the European Mantle Cell Lymphoma Network. Lancet. 2016 Aug 6;388(10044):565-75.
16. Kluin-Nelemans HC, Hoster E, Hermine O, et al. Treatment of Older Patients With Mantle Cell Lymphoma (MCL): Long-Term Follow-Up of the Randomized European MCL Elderly Trial. J Clin Oncol. 2020 Jan 20;38(3):248-256.
17. Eskelund CW, Dahl C, Hansen JW, et al. *TP53* mutations identify younger mantle cell lymphoma patients who do not benefit from intensive chemoimmunotherapy. Blood. 2017 Oct 26;130(17):1903-1910.
18. Zelenetz AD, Gordon LI, Abramson JS, et al. NCCN Guidelines® Insights: B-Cell Lymphomas, Version 6.2023. J Natl Compr Canc Netw. 2023 Nov;21(11):1118-1131.
19. Martin P, Chardbun A, Christos P, et al. Outcome of deferred initial therapy in mantle-cell lymphoma. J Clin Oncol. 2009 Mar 10;27(8):1209-13.
20. Chihara D, Cheah CY, Westin JR, et al. Rituximab plus hyper-CVAD alternating with MTX/Ara-C in patients with newly diagnosed mantle cell lymphoma: 15-year follow-up of a phase II study from the MD Anderson Cancer Center. Br J Haematol. 2016 Jan;172(1):80-8.
21. Cencini E, Calomino N, Franceschini M, et al. Survival Outcomes of Patients with Mantle Cell Lymphoma: A Retrospective, 15-Year, Real-Life Study. Hematol Rep. 2024 Jan 18;16(1):50-62.
22. Dreyling M, Doorduijn J, Giné E, et al. Ibrutinib combined with immunochemotherapy with or without autologous stem-cell transplantation versus immunochemotherapy and autologous stem-cell transplantation in previously untreated patients with mantle cell lymphoma (TRIANGLE): a three-arm, randomised, open-label, phase 3 superiority trial of the European Mantle Cell Lymphoma Network. Lancet. 2024 May 25;403(10441):2293-2306.
23. Munshi PN, Hamadani M, Kumar A, et al. American Society of Transplantation and Cellular Therapy, Center of International Blood and Marrow Transplant Research, and European Society for Blood and Marrow Transplantation Clinical Practice Recommendations for Transplantation and Cellular Therapies in Mantle Cell Lymphoma. Transplant Cell Ther. 2021 Sep;27(9):720-728.
24. Eskelund CW, Kolstad A, Jerkeman M, et al. 15-year follow-up of the Second Nordic Mantle Cell Lymphoma trial (MCL2): prolonged remissions without survival plateau. Br J Haematol. 2016 Nov;175(3):410-418.
25. Liu H, Shi X, Fang H, et al. First-Line Autologous Stem Cell Transplantation for Mantle Cell Lymphoma: A Systematic Analysis and Treatment Recommendation. Front Oncol. 2022 May 11;12:881346.
26. Zoellner AK, Unterhalt M, Stilgenbauer S, et al. European Mantle Cell Lymphoma Network. Long-term survival of patients with mantle cell lymphoma after autologous haematopoietic stem-cell transplantation in first remission: a post-hoc analysis of an open-label, multicentre, randomised, phase 3 trial. Lancet Haematol. 2021 Sep;8(9):e648-e657.
27. Robak T, Huang H, Jin J, et al. Bortezomib-based therapy for newly diagnosed mantle-cell lymphoma. N Engl J Med. 2015 Mar 5;372(10):944-53.
28. Lyman GH, Poniewierski MS, Culakova E. Risk of chemotherapy-induced neutropenic complications when treating patients with non-Hodgkin lymphoma. Expert Opin Drug Saf. 2016;15(4):483-92.
29. Ohmoto A, Fuji S. Infection profiles of different chemotherapy regimens and the clinical feasibility of antimicrobial prophylaxis in patients with DLBCL. Blood Rev. 2021 Mar;46:100738.