NEU PRESS

Mevlana Tıp Bilimleri Dergisi
Mevlana Medical Sciences
eISSN:2757-976X

ARAŞTIRMA MAKALESİ/RESEARCH ARTICLE DOI:http:/dx.doi.org/10.56752/Mevmedsci.2025.91
Mev Med Sci, 2025; 5(2): 65-71

Impact of CD30 positivity on the Clinical Characteristics of Diffuse Large B-Cell Lymphoma

Yaygın Büyük B-Hücreli Lenfomada CD30 Pozitifliğinin Klinik Özellikler Üzerine Etkisi

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Makale Tarihleri/Article Dates:
Geliş Tarihi/Received: 30 January 2025
Kabul Tarihi/Accepted: 24 July 2025
Yayın Tarihi/Published Online: 08 August 2025

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Açıklama/Disclosure: Yazarların hiçbiri, bu makalede bahsedilen herhangi bir ürün, aygıt veya ilaç ile ilgili maddi çıkar ilişkisine sahip değildir. Araştırma, herhangi bir dış organizasyon tarafından desteklenmedi. Yazarlar çalışmanın birincil verilerine tam erişim izni vermek ve derginin talep ettiği takdirde verileri incelemesine izin vermeyi kabul etmektedirler.

ÖZET

Amaç: Yaygın Büyük B Hücreli Lenfoma (YBBHL) tanılı hastalarda, CD30 pozitifliğinin klinik bulgular ile ilişkisinin değerlendirilmesi amaçlanmaktadır.
Yöntem: Çalışmamızda Ocak 2005-Kasım 2022 tarihleri arasında Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hematoloji kliniğine başvuran YBBHL tanısı ile takip edilen hastalar incelendi. Hastalar immunhistokimyasal özelliklerine göre CD30 (+) ve (-) olmak üzere iki gruba ayrıldı. Gruplar klinik, laboratuvar parametreler ve sağ kalımlar açısından karşılaştırıldı.
Bulgular: Çalışmamıza 111 hasta dahil edildi. Hastaların 18'i CD30(+), 93'ü CD30(-)'ti. CD30(+) hastalarda medyan kalsiyum 8.8 mmol/L iken CD30(-)'lerde 9,2 mmol/L bulundu (p:0,013). Diğer laboratuvar parametreleri ve klinik özellikler iki grup arasında benzerdi. Medyan TSK, CD30 (+) hastalarda düşük bulundu (36,9 aya karşın 100,9 ay, p=0,155). Medyan PSK da CD30(+) hastalarda istatistiksel olarak anlamlı olmamakla birlikte düşüktü (37 aya karşın 100,9 ay, p=0,849). İki yıllık TSK sırayla CD30 (+) ve (-) hastalarda %70'e karşın %84, 3 yıllık TSK ise %42'ye karşın %67 oranında bulundu. İki yıllık PSK ise sırayla %50'ye %80 oranında hesaplandı. Beş yıllık PSK, CD30(+) hastalarda hesaplanamazken, CD30(-) hastalarda %60 bulundu.
Sonuç: Çalışmamız, YBBHL hastalarında CD30 pozitifliğinin klinik bulgular ve sağ kalım üzerine herhangi bir etkisinin olmadığını göstermiştir.

Anahtar Kelimeler: Yaygın Büyük B Hücreli Lenfoma, CD30, Toplam Sağ Kalım, Progresyonsuz Sağ Kalım

ABSTRACT

Objective: This study aims to analyze the relationship between CD30 positivity and clinical findings in patients diagnosed with Diffuse Large B-Cell Lymphoma (DLBCL).
Method: Patients diagnosed DLBCL between January 2005 and November 2022 at Necmettin Erbakan University, Meram Faculty of Medicine, were evaluated. Patients were classified into CD30(+) and CD30(-) groups based on the immunohistochemical features. Groups were compared regarding clinical, laboratory parametres and survival outcomes.
Results: Among 111 patients, 18 were CD30(+) and 93 were CD30 (-). Median calcium were lower in the CD30 (+) group (8.8 mmol/L vs. 9.2 mmol/L, p=0.013). Other parameters showed no significant differences. The median OS was lower in CD30(+) patients (36.9 months vs. 100.9 months, p=0.155). Similarly, median progression-free survival (PFS) was lower in CD30(+) patients (37 months vs. 100.9 months, p=0.849). Two-year OS rates were 70% for CD30(+) and 84% for CD30(-) patients, while three-year OS rates were 42% and 67%, respectively. Two-year PFS rates were 50% for CD30(+) and 80% for CD30(-) patients. Five-year PFS could not be calculated for CD30 (+) patients but was 60% in the CD30 (-) group.
Conclusion: This study suggests that CD30 positivity does not have a significant impact on clinical characteristics or survival outcomes in patients with DLBCL.

Key words: Diffuse Large B-Cell Lymphoma, CD30, Overall Survival, Progression-Free Survival

Atıf yapmak için/ Cite this article as: Pektas Alpsoy H, Tekinalp A, Demircioglu S, Kilinc F, Ceneli O. Impact of CD30 positivity on the Clinical Characteristics of Diffuse Large B-Cell Lymphoma. Mev Med Sci. 2025; 5(2): 65-71

INTRODUCTION

Diffuse Large B-Cell Lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL) in adults (1). It originates from B cells within the germinal centers of lymphoid tissues and is marked by a rapid proliferation rate alongside an aggressive clinical course. Despite these common characteristics, DLBCL exhibits substantial clinical and molecular diversity. Immunohistochemical and molecular markers have increasingly become pivotal in diagnosing and managing this disease (1,2).

CD30 is a transmembrane glycoprotein among the tumor necrosis factor receptor superfamily. It consists of intracellular and extracellular domains and was initially identified in Hodgkin lymphoma. Subsequent studies have demonstrated its expression in various NHL subtypes, including anaplastic large cell lymphoma and DLBCL (3-7). The presence of CD30 can be upregulated due to mitogenic or viral activation of B and T cells, playing a role in cellular proliferation and apoptosis regulation (8-10). Additionally, CD30 expression has been documented in activated B, T, and natural killer (NK) cells, as well as in lymphocytes affected by viruses such as Epstein-Barr virus (EBV), hepatitis C virus, Human Immunodeficiency Virus (HIV), and Human T-cell Lymphotropic Virus Type 1 (HTLV-1) (3,11-14).

The potential implications of CD30 expression in DLBCL concerning clinical characteristics and treatment responses have attracted increasing attention. Several studies suggest that CD30-positive DLBCL cases exhibit distinct clinical traits compared to CD30-negative cases. Some findings indicate that CD30 positivity in DLBCL may influence patient prognosis, potentially correlating with improved overall survival (OS) and progression-free survival (PFS) in certain cohorts. However, ongoing research continues to evaluate the prognostic significance of CD30 and its role in innovative treatment strategies, including targeted therapies. While some studies have suggested that CD30 expression in DLBCL may be associated with a better response to treatment, particularly with targeted agents such as brentuximab vedotin, others have reported no significant impact on treatment outcomes. (15-17).

This study aims to compare CD30-positive and CD30-negative DLBCL patients in terms of their baseline characteristics, disease progression, and survival outcomes.

MATERIALS AND METHODS

This study was designed retrospectively. The medical

Table 1. Epidemiological and Disease-Related Characteristics of All Patients

Parameter		n (%)
Sex (Female/Male)		47 (42,3) / 64 (57,7)
CD30 (Positive/Negative)		18 (16,2) / 93 (83,8)
Subtype	Activated B Cell	26 (23,4)
	Germinal Center	22 (19,8)
	Unknown	63 (56,8)
Stage	I	6 (5,4)
	II	24 (21,6)
	III	19 (17,1)
	IV	62 55,9)
IPI[1]	Low Risk	20 (18)
	Low-Intermediate Risk	32 (28,8)
	High-Intermediate Risk	40 (36)
	High Risk	19 (17,1
R-IPI[2]	Low Risk	6 (5,4)
	Low-Intermediate Risk	46 (41,4)
	High-Intermediatte Risk	0
	High Risk	59 (53,2)
NCCN-IPI[3]	Low Risk	7 (6,3)
	Low-Intermediate Risk	39 (35,1)
	High-Intermediate Risk	51 (45,9)
	High Risk	14 (12,6)
Bone Marrow Involvement (Yes/No)		18 (16,2) / 93 (83,8)
Extranodal Involvement (Yes/No)		68 (61,3) / 43 (38,7)
CNS[4] Involvement (Yes/No)		3 (2,7) / 108 (97,3)
CNS Prophylaxis (Yes/No)		10 (9,0) / 101 (91,0)
ASCT[5] (Yes/No)		8 (7,2) / 103 (92,8)
allo-SCT (Yes/No)		1 (0,9) / 110 (99,1)

[1]International Prognostic Index; [2]Revised International Prognostic Index
[3]National Comprehensive Cancer Network International Prognostic Index
[4]Central Nervous System; [5]Autologous Stem Cell Transplantation

records of patients diagnosed, treated, and monitored for non-Hodgkin lymphoma (NHL) at the Hematology Department of Necmettin Erbakan University Faculty of Medicine between January 1, 2005, and June 1, 2022, were reviewed. A total of 418 patients ≥18 years old, diagnosed with various NHL subtypes. Among them, 111 cases confirmed as DLBCL and assessed for CD30 expression through immunohistochemical staining were included in this study.

Demographic variables such as age and gender, along with laboratory parameters at the time of diagnosis—including complete blood count, renal function tests, transaminase levels, serum electrolytes, beta-2 microglobulin, lactate dehydrogenase (LDH), albumin, total protein, vitamin B12, ferritin, and erythrocyte sedimentation rate—were collected. Disease-related parameters, including disease stage, risk scoring, and extranodal involvement, were also recorded. Furthermore, details of first-line treatment regimens, responses to initial therapy, progression during follow-up, stem cell transplantation history, and survival outcomes were analyzed.

Patients were classified into two groups—CD30-positive and CD30-negative—based on immunohistochemical staining results. These groups were then compared concerning their baseline clinical and laboratory characteristics, disease progression, and survival outcomes.

Statistical Analysis

Data were analysed using IBM SPSS Statistics version 22.0. The Kolmogorov-Smirnov test was performed for distribution of continuous numerical variables. As descriptive statistics, mean ± standard deviation and median (minimum–

Table 2. Epidemiological and Clinical Features Based on CD30 (+) and CD30 (-) Status

Characteristics n (%)		CD30 pozitive (n:18)	CD30 negative (n:93)	p
Sex	Female	8 (44,4)	39 (41,9)	0,844[a]
	Male	10 (55,6)	54 (58,1)	
Subtype	GM	2 (22,2)	20 (51,3)	0,151[b]
	Non-GM	7 (77,8)	19 (48,7)	
Stage	I	0	6 (6,5)	-[c]
	II	5 (27,8)	19 (20,4)	
	III	2 (11,1)	17 (18,3)	
	IV	11 (61,1)	51 (54,8)	
Stage	Early (I-II)	5 (27,8)	25 (26,9)	1,0[b]
	Late (III-IV)	13 (72,2)	68 (73,1)	
Progression	Yes	6 (33,3)	35 (37,6)	0,729[a]
	No	12 (66,7)	58 (62,4)	
IPI Risk Group	Low	4 (22,2)	16 (17,2)	-[c]
	Low-Intermediate	3 (16,7)	29 (31,2)	
	High-Intermediate	8 (44,4)	32 (34,4)	
	High	3 (16,7)	16 (17,2)	
Response (≥PR)	Yes	17 (100,0)	85 (92,4)	0,593[b]
	No	0	7 (7,6)	
R-IPI	Low	2 (11,1)	4 (4,3)	-[c]
	Low-Intermediate	5 (27,8)	41 (44,1)	
	High	11 (61,1)	48 (51,6)	
NCCN-IPI	Low	2 (11,1)	5 (5,4)	-[c]
	Low-Intermediate	4 (22,2)	35 (37,6)	
	High-Intermediate	8 (44,4)	43 (46,2)	
	High	4 (22,2)	10 (10,8)	
Bone Marrow Involvement	No	13 (72,2)	80 (86)	0,166[b]
	Yes	5 (27,8)	13 (14)	
Extranodal Involvement	No	8 (44,4)	35 (37,6)	0,587[a]
	Yes	10 (55,6)	58 (62,4)	
CNS Involvement	No	18 (100,0)	90 (96,8)	1,0[a]
	Yes	0	3 (3,2)	
ASCT	No	16 (88,9)	87 (93,5)	-[c]
	Yes	2 (11,1)	6 (6,5)	
allo-SCT	No	17 (94,4)	93 (100)	-[c]
	Yes	1 (5,6)	0	

*Two patients was not evaluated for initial response analysis

GM: Germinal Center, IPI: International Prognostic Index, R-IPI: Revised International Prognostic Index, NCCN-IPI: National Comprehensive Cancer Network International Prognostic Index, ASCT: Autologous Stem Cell Transplantation, allo-SCT: Allogeneic Stem Cell Transplantation

[a]Pearson's chi-square; [b]Fisher's exact test; [c]P value not available

Table 3. Laboratory Finding in CD30 (+) and CD30 (-) Groups

Parameter	CD30-pozitive (n:18)	CD30-negative (n:93)	p
Hemoglobulin (g/dL)	12,3±1,9	12,4±2,0	0,928[a]
White Blood Cell (/µL)	7.870 (2.740-14.400)	7.810 (600-23.000)	0,666[b]
Neutrophil count(/µL)	600 (950-13.100)	5.150 (210-17.700)	0,603[b]
Lymphocyte count(/µL)	1.250 (650-2.510)	1.610 (200-12.520)	0,121[b]
Monocyte count(/µL)	680±374	630±324	0,585[a]
Platelet count (10^3xµL)	254 (20-441)	287 (24-655)	0,337[b]
Urea (mg/dL)	31 (7-121)	32 (12-107)	0,581[b]
Creatinine (mg/dL)	0,7 (0,5-7,2)	0,7 (0,4-2,0)	0,930[b]
Sodium (mmol/L)	139 (125-142)	139 (127-145)	0,717[b]
Potassium (mmol/L)	4,6±0,4	4,5±0,5	0,544[a]
Calcium (mmol/L)	8,8 (7,5-10,3)	9,2 (7,4-15,0)	0,013[b]
Phosphorus (mmol/L)	3,6 (2,8-5,2)	3,6 (2,2-5,1)	0,955[b]
Lactate Dehyrogenase (U/L)	337 (206-1205)	279 (134-1337)	0,206[b]
Uric Acid (mg/dL)	5,8 (1,9-8,9)	5,4 (1,7-13,2)	0,567[b]
Aspartate Aminotransferase (U/L)	24,5 (8-77)	20 (9-193)	0,396[b]
Alanine Aminotransferase (U/L)	18 (5-58)	18 (5-176)	0,826[b]
Total Protein(g/L)	66 (53-79)	70 (44-82)	0,066[b]
Albumin (g/L)	3,7±0,7	3,9±0,5	0,138[a]
C-Reactive Protein (mg/L)	33 (1-231)	16 (1-33)	0,767[b]
Sedimentation (mg/h)	40 (3-90)	32 (2-117)	0,914[b]
Ferritin (ng/mL)	174 (9-5960)	796 (30-1530)	0,231[b]
Beta-2 Microglobulin (mg/L)	2,5 (1,8-6,4)	3,1 (0,7-11,1)	0,476[b]
Vitamin B12 (n:68) (ng/L)	373 (250-1412)	365 (56-2000)	0,957[b]

[a]Student's T-Test; [b]Mann-Whitney U Test

Table 4. Initial treatment and The response of patients

Treatment	n (%)
CHOEP-1	1 (0.9)
DA-R-EPOCH	5 (4.5)
MATRIX	3 (2.7)
R-BENDAMUSTINE	2 (1.8)
R-CHOP	84 (75.7)
R-GVCP	1 (0.9)
R-MINI-CHOP	14 (12.6)
None	1 (0.9)
Response to the Initial Treatment	
Non-assessable	5 (4.5)
Complete Response	34 (30.6)
Partial Response	68 (61.3)
Stable	2(1.8)
Progressive	2(1.8)

CHOEP-1: Cyclophosphamide, Doxorubicin, Vincristine, Etoposide, Prednisone
DA-R-EPOCH: Dose-Adjusted EPOCH (Etoposide, Prednisone, Vincristine, Doxorubicin, Cyclophosphamide)
MATRIX: Methotrexate, Cytarabine, Doxorubicin, Rituximab
R-Bendamustine: Rituximab + Bendamustine
R-CHOP: Rituximab + Cyclophosphamide, Doxorubicin, Vincristine, Prednisone
R-GVCP: Rituximab + Gemcitabine, Vincristine, Cyclophosphamide, Prednisone
R-MINI-CHOP: Rituximab + Mini CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone)

maximum) were utilized for normally and abnormally distritubed data, respectively. The Student T-Test and Mann-Whitney U test were performed to compare of two independent groups.

Categorical variables were raported as percentages (%) and compared using the chi-square test. Survival analyses were performed using the Kaplan–Meier method and compared using the long rank test. P-value of <0.05 was considered statistically significant.

RESULTS

This study included 111 patients with a mean age of 58.2 ± 1.4 years. Of the patients, 47 (42.3%) were female, while 64 (57.7%) were male. The epidemiological and disease-related characteristics of the patients were summarized in Table 1.

Based on CD30 expression analysis, 18 patients (16.2%) were classified as CD30-positive, whereas 93 (83.8%) were CD30-negative. The mean age for CD30-positive patients was 56.5 ± 17.8 years, compared to 58.5 ± 15.1 years for CD30-negative patients (p = 0.611). A detailed comparison of epidemiological and clinical characteristics between the two groups were presented in Table 2.

In laboratory evaluations, a statistically significant difference was observed in median calcium levels between CD30-positive and CD30-negative groups (8.8 vs. 9.2 mmol/L, p = 0.013). However, other parameters given in table-3 were similar between two groups. In terms of first-line treatment, 84 patients (75.7%) received R-CHOP therapy (Table-4). One patient from each group was excluded from the treatment response evaluation due to death prior to the initiation of therapy.

Survival Analysis

The estimated median PFS and OS for all patients were both calculated at 100.9 months (95% confidence interval [CI]: 3.831–198.157 for PFS and 24.141–177.846 for OS). Two-year and five-year PFS rates were 65% and 57%, respectively, while OS rates were 74% and 60%. Although statistical significance was not reached, CD30-positive patients had a lower estimated median OS (36.9 months vs. 100.9 months, p = 0.155) and PFS (37 months vs. 100.9 months, p = 0.849) compared to CD30-negative patients.

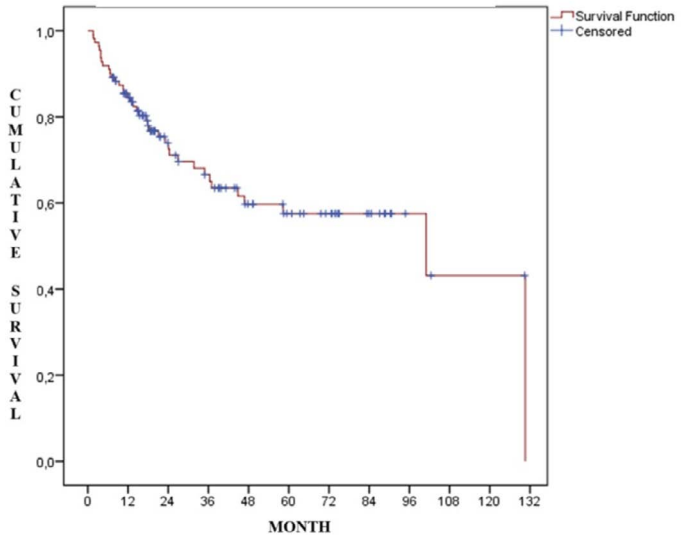

Figure 1. Overall Survival Graph of All Patients Diagnosed with DLBCL

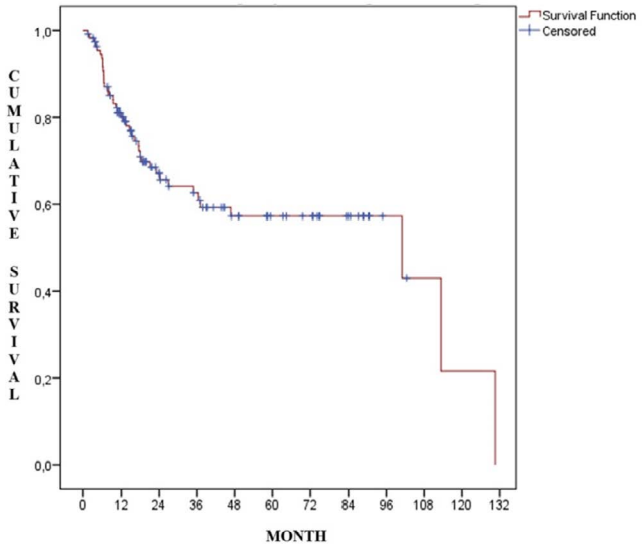

Figure 2. Progression-Free Survival Graph of All Patients Diagnosed with DLBCL

DISCUSSION

DLBCL is a heterogeneous group of tumors characterized by transformed B-cells, a diffuse growth pattern, and a high proliferation fraction (1).

The literature contains limited studies evaluating CD30 expression in DLBCL. Zuluaga et al. reported that the frequency of CD30 positivity was 33% in patients aged ≤47 years, significantly higher than the 15% observed in patients aged >47 years (18). The mean age were 49.3 and 56.5 years CD30 (+) and (-) groups, respectively. In contrast to our findings, where the mean age of CD30-positive and negative patients was similar, the study by Zuluaga et al. reported a higher mean age of 56.5 ± 17.8 years for CD30-positive patients. Similarly, Salas et al., in a study with a comparable sample size, found that nearly half of CD30-positive patients were over 60 years old (7). These findings suggest that no definitive relationship between CD30 positivity and age can be established.

Studies on CD30-positive DLBCL patients reveal differences in gender distribution. In the study by Salas et al., the rate of female patients was 57.4%, while the study by Zuluaga the majority of patients was male with the rate of 55.1% (7,18). In our study, the rate of male patients was also higher with no significant difference between CD30 (+) and (-) groups.

The serum calcium level was significantly lower in CD30 (+) group compared to CD30 (–) group in our study. In human cell culture studies, it has been shown that the intracellular calcium level increases with the stimulation of CD30 in gamma delta T cells. However, in the literature, no relationship has been observed between serum calcium levels and CD30 in lymphomas (19). Calcium levels may be lower in patients with tumor lysis due to disease burden; however, the presence of tumor lysis at diagnosis was not evaluated in our study. On the other hand, there are few studies investigating the relationship between CD30 expression and LDH levels indicating tumor burden. Among these, Salas et al., Zhao et al., and Gong et al. found no significant relationship between CD30 and LDH (7,20,21). In our study, similar to the literature, LDH levels were found to be similar between CD30 (+) and (–) patients.

In the study by Rodrigues-Fernandes et al., which examined CD30 (+) in DLBCL in terms of disease stage and extranodal involvement, 64.4% of the CD30 (+) patient group was found to be at an advanced stage, and this rate was significantly high. In the same study, the rate of patients with <2 extranodal sites in CD30 (+) patients was 70.8%, which was also significantly high (22). On the other hand, no significant correlation was found between CD30 expression and extranodal involvement and stage in the studies of Zhao et al. and Gong et al. (20,21). In our study, the frequency of early and advanced stage and

the presence of extranodal involvement were similar in CD30 (+) and (–) patients.

The cell of origin of DLBCL affects its clinical presentation. Rodrigues-Fernandes et al. showed that most of the CD30 (+) patients (57.1%) were in the Activated B cell (ABC) group, with statistical significance (22). In the study by Salas et al., the CD30 (+) patient rate in the ABC subtype was 78.7%, which is significantly high (7). In the analysis by Zhao et al., included 149 patients, no significant relationship was shown between CD30 (+) and DLBCL subtypes (20). In our study, the ABC subtype was 77.8% in CD30 (+) patients, which was higher, although not statistically significant. In CD30 (–) patients, the frequencies of ABC and Germinal Center-Derived B cell (GCB) subtypes were found to be similar. However, in our study, the number of patients with known cell origin was 48, which is less than half of all patients. This makes it difficult to evaluate the relationship between cell origin and CD30.

Varies outcomes related to survival have been reported in the literature. Hao et al., analized 146 patients. In the study OS and event-free survival (EFS) were found to be significantly lower in CD30 (+) patients (5-year OS 12.9% vs. 58.4%, p = 0.041). This difference was seen more clearly in patients in the high-intermediate and high-risk IPI groups (5-year OS 42.9% vs. uncalculated, p = 0.001). All patients were treated with R-CHOP or similar regimens (23). In the study by Hu et al., included 461 patients 5-year OS and PFS were found to be higher in CD30 (+) patients (79% vs. 59%, p = 0.0013; 73% vs. 57%, p = 0.003). Although the reason for this has not yet been fully explained, it has been suggested that it may be due to the antiproliferative effects of CD30 (3). In another the study by Salas et al., OS and PFS were similar between the CD30 (+) and (–) groups at an median follow of 15 months (7). In our study OS and PFS were lower in the CD 30 (+) group however the difference was not statistically significant (2-year OS 70% vs. 84%, 2-year PFS 50% vs. 80%).

These studies also evaluated IPI risk scoring; however, no significant difference was observed between CD30 (+) and (–) patients (3,7,20,21,23). In contrast, CD30 (+) patients showed a low survival advantage in the study by Hao et al. and a high survival advantage in the study by Hu et al. (3,23). This suggests that CD30 affects survival independently of IPI. However, the fact that it has both positive and negative effects on survival makes it difficult to establish a definitive relationship.

In addition to CD30 expression, various biomarkers have been studied to evaluate their prognostic implications in DLBCL. A recent retrospective study by Ciftciler et al. investigated the prognostic impact of serum danger-associated molecules, such as fibrinogen and uric acid levels, at the time of diagnosis. Their findings demonstrated that elevated levels of these molecules were associated with significantly poorer 5-year OS and PFS (24). Although our study did not identify CD30 positivity as a statistically significant prognostic marker, the results by Ciftciler et al. support the notion that host response to cellular stress and systemic inflammation may contribute to disease progression and survival outcomes in DLBCL.

Bone marrow involvement, one of the prognostic criteria in DLBCL, increases the stage and negatively affects prognosis. In previous studies, no significant relationship was found between CD30 expression and bone marrow involvement (20). In our study, bone marrow involvement in CD30 (+) patients was 27%, while in the CD30 (–) patient group, bone marrow involvement was 14%, and there was no significant difference.

There is no standard treatment approach in the first line of CD30 (+) DLBCL. In nearly all studies, the first-line treatment is R-CHOP. These studies do not examine treatment response in detail. Bartlett et al. combined R-CHOP with anti-CD30 Brentuximab Vedotin (BV) in the first-line setting, reporting a complete response rate of 92% in 13 CD30 (+) patients, compared to 69% in 16 CD30 (–) patients. However, survival analysis was not included in this study (25). In our study, it was observed that 84 (75.7%) of the patients received R-CHOP as the first-line treatment, and at least a partial response was achieved in 91.9% of all patients.

In DLBCL, features such as testicular, breast, and uterine involvement from extranodal sites and the ABC type are risky in terms of CNS involvement, regardless of stage. In these cases, prophylactic systemic methotrexate is preferred to prevent intraparenchymal involvement (26). In our study, no CNS involvement was observed in any of the 18 CD30 (+) patients. CNS involvement was observed in 3 (3.2%) of the CD30 (–) patients. The number of patients, in our opinion, were not sufficient to establish a relationship between CD30 and CNS involvement.

Brentuximab Vedotin (BV), an anti-CD30 antibody indicated for Hodgkin lymphoma and anaplastic large cell lymphoma, is a drug approved for treatment based on clinical studies (15). The important prognostic value in these studies is that CD30 is a therapeutic target for BV. This opens the idea of examining CD30 (+) DLBCL as a separate subgroup of DLBCL. Evaluating the potential for anti-CD30 therapy in DLBCL and conducting more comprehensive studies that incorporate anti-CD30 antibodies into the treatment regimen for this group is necessary (3). However BV was not administered to our patients due to the lack of approval for this indication in our country.

The main limitations of our study are that the number of CD30 (+) patients is lower than in the literature, the molecular expressions of DLBCL cannot be evaluated, and it was not designed to establish a molecular link between

serum calcium and CD30. Moreover, no pathophysiological association between calcium levels and CD30 expression has been identified in the literature.

On the other hand, our study examined CD30 (+) DLBCL patients in terms of clinical features and survival. Although not statistically significant, lower OS and PFS rates were found in these patients compared to CD30 (–) patients.

In conclusion, CD30 expression in DLBCL is associated with a variety of clinical and prognostic factors, although no definitive relationships have been established. While our study highlights some notable trends, such as the potential impact on survival and serum calcium levels, further comprehensive research is needed to clarify these findings. Incorporating targeted therapies like Brentuximab Vedotin into treatment regimens for CD30-positive DLBCL may offer promising avenues for improving patient outcomes.

Etik Kurul: Ethical approval for this study was obtained from the Necmettin Erbakan University Non-Pharmaceutical and Non-Medical Device Research Ethics Committee (approval number: 2022/3881).

Çıkar Çatışması: Çalışmada herhangi bir çıkar çatışması yoktur.

Finansal Çıkar Çatışması: Çalışmada herhangi bir finansal çıkar çatışması yoktur.

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