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# The Effect of Bone Marrow CD4/CD8 Ratio on Lymphoma Response and Survival: Single Center Experience

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## ABSTRACT

**Introduction:** A minor subset of CD4+ T cells, known as regulatory T cells (Tregs), makes up 1-4% of lymphocytes in circulation. These cells are responsible for regulating excessive immune responses, promoting immune tolerance, and suppressing anti-tumor immunity. This study aimed to investigate how the CD4/CD8 ratio influences treatment outcomes and survival rates in patients newly diagnosed with lymphoma. The research involved analyzing samples extracted from bone marrow aspirates.

**Methods:** Our study included individuals diagnosed with lymphoma at the Clinic of Hematology in University of Health Sciences Türkiye, İstanbul Training and Research Hospital from January 2010 to January 2021. These patients underwent flow cytometric analysis of bone marrow aspiration samples at the time of their initial diagnosis.

**Results:** In the statistical analysis performed to reveal the effect of CD4/CD8 ratio on the interim response to treatment, the ratio was found to be significantly higher in patients with a response of complete response "(CR)" compared to others (p=0.003). The statistical analysis performed to reveal the effect of the ratio on the end-of-treatment response found higher in patients with a CR response compared to others (p=0.008). CD4/CD8 ratio did not have a significant effect on survival.

**Conclusion:** According to the literature review, the increase in the ratio of non-Treg CD4+ cells, and the high CD4/CD8 ratio contributes positively to the response. It will shed light on new studies evaluating the effect of subtypes of CD4+ T cells on response and survival in lymphomas.

**Keywords:** Lymphoma, CD4+ T cells, CD4/CD8 ratio, response, survival

## Introduction

T lymphocytes can be categorized into two main groups: CD4+ helper T cells and CD8+ cytotoxic T cells. CD4+ T cells identify antigenic epitopes displayed by major histocompatibility complex (MHC) II molecules and undergo differentiation upon antigenic stimulation (1). In contrast, CD8+ T cells recognize antigens presented on MHC class I molecules and transform into cytotoxic CD8+ T cells when activated. Although CD8+ Tregs produce various cytokines, their primary function is to eliminate infected host cells. The activation of CD8+ T cells requires mediator stimuli, which can occur with or without CD4+ T cells involvement (1-4).

A small subset of CD4+ T cells, known as regulatory T cells (Tregs), comprises 1-4% of circulating lymphocytes (1). These cells play a crucial role in regulating excessive immune activity and promoting immune tolerance (3). Tregs are characterized by their expression of surface interleukin 2 receptors and are identified by CD25 and FOXP3+ (3,4). They have been shown to promote tumor progression and suppress antitumoral immune responses (5,6) and negatively impact survival rates (6-10). Despite the potential anti-cancer effects of CD4+ T lymphocytes through the activation of CD8+ cytotoxic T lymphocytes, evidence suggests that the current increased CD4+ T cell ratio has a detrimental role in cancer pathogenesis and adversely affects treatment response and survival.

The role of the CD4/CD8 ratio in hematological malignancies differs significantly from that in solid tumors, making it a relatively new area of research for prospective studies. This study aims to investigate the impact of the CD4/CD8 ratio on treatment response and survival in newly diagnosed lymphoma patients by analyzing bone marrow aspirate samples.

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## Methods

Our study included patients diagnosed with lymphoma at the Clinic of Hematology, University of Health Sciences Türkiye, İstanbul Training and Research Hospital from January 2010 to January 2021, whose bone marrow aspirations underwent flow cytometric analysis at diagnosis. We collected data on patient demographics (age and gender at diagnosis), lymphoma subtypes, initial staging, bone marrow involvement status based on pathological evaluation, initial laboratory values (leukocyte counts, neutrophil counts, lymphocyte counts, hemoglobin counts, platelet counts), bone marrow CD4/CD8 ratios, treatment responses, and survival outcomes. Treatment response was evaluated at two points: interim and end-of-treatment, using the Lugano criteria (11).

We excluded patients with Tregs lymphoma and bone marrow involvement due to potential effects on the bone marrow CD4/CD8 ratio. Furthermore, we omitted patients lacking initial evaluation, bone marrow samples, or continued follow-up or treatment in our department. Those whose treatment response could not be assessed for any reason were also excluded from the study.

### Samples and Analysis

Patients' bone marrow samples were collected in EDTA tubes and examined within 2 hours using the XN 9000 (Sysmex, Kobe, Japan). A 3-laser, 10-color FACSLyric flow cytometry analyzer (BD Biosciences, San Jose, United States of America) was utilized for flow-cytometric analysis. Prior to running samples, calibration controls and compensation adjustments were conducted. The system's performance was verified using standardized beads. EDTA-containing samples were maintained at room temperature and analyzed within 24 hours. The antibodies employed were CD4 V450 (SK3 clone) and CD8 FITC (SK1 clone). Analysis was carried out using BD FACSSUITE software. The research was reviewed and approved by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital Ethics Committee (approval number: 2573, date: 13.11.2020) and was conducted according to the principles of the Declaration of Helsinki.

### Statistical Analysis

In the data analysis, descriptive statistics for continuous variables included the mean, standard deviation, and range (minimum and maximum values). Categorical variables were described using frequencies and percentages. To compare means between two independent groups, Student's t-test and the Mann-Whitney U test were utilized. The relationship between categorical variables was assessed using chi-square or Fisher's Exact test statistics. Survival curves were estimated using the Kaplan-Meier method, and the log-rank test was used to identify differences based on risk factors. Hazard ratios were reported with 95% confidence intervals (CI). To determine optimal cut-off values, the receiver operating characteristic (ROC), area under the curve (AUC) was calculated, with significance evaluated through sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio statistics. ROC curves were plotted to quantify the AUCs with 95% CI. The AUC values were categorized as follows: 0.90-1 (excellent), 0.80-0.90 (good), 0.70-0.80 (fair), 0.60-0.70 (low), and 0.50-0.60 (fail). Statistical significance was set at $p<0.05$. Data analysis was conducted using IBM SPSS version 25 and MedCalc statistical software.

## Results

A total of 126 patients were included in the study. 79.4% of the patients were diagnosed with B cell lymphoma (n=100), 8.7% with T cell l lymphoma (n=11), and 11.9% with Hodgkin lymphoma (HL). The mean age was 52.1±15.9 years (range: 19-88). The number of patients with stage 4 disease at the time of diagnosis was 56 (44.4%). The number of patients with bone marrow involvement was 47 (n=37.3%). The number of patients with complete response (CR) in the interim evaluation was 47 (37.7%) and with CR + partial response (PR) was 104 (82.5%). At the end-of-treatment evaluation, the number of patients with a CR was 57 patients (45.2%), and with (CR + PR) was 102 patients (81%) (Table 1).

Flow cytometric analysis revealed a mean CD4/CD8 ratio of 1.08±1.01 at diagnosis. Statistical evaluation of the ratio's impact on interim treatment response showed a significantly higher value in patients achieving CR compared to others (p=0.003). The mean ratio was 1.48±1.16 in CR patients and 0.85±0.67 in non-CR patients. No significant differences

**Table 1. Descriptive statistics of socio-demographic characteristics, clinical and laboratory data**

| | | $\bar{x} \pm SD$ | Min.-Max. |
|---|---|---|---|
| **Age** | | 52.1±15.9 | 19-88 |
| | | n | % |
| **Gender** | Female | 45 | 35.7 |
| | Male | 81 | 64.3 |
| **Lymphoma subtypes** | Hodgkin | 15 | 11.9 |
| | B-cell | 100 | 79.4 |
| | T-cell | 11 | 8.7 |
| **Stage at the time of diagnosis** | 1 | 12 | 9.5 |
| | 2 | 19 | 15.1 |
| | 3 | 39 | 31 |
| | 4 | 56 | 44.4 |
| **Bone marrow involvement** | (-) | 79 | 62.7 |
| | (+) | 47 | 37.3 |
| **Progression** | (-) | 94 | 74.6 |
| | (+) | 32 | 25.4 |
| **Interim response** | CR | 47 | 37.3 |
| | Others | 79 | 62.7 |
| **Interim response** | CR + PR | 104 | 82.5 |
| | Others | 22 | 17.5 |
| **End-of-the-treatment response** | CR | 57 | 45.2 |
| | Others | 69 | 54.8 |
| **End-of-the-treatment response** | CR + PR | 102 | 81 |
| | Others | 24 | 19 |
| **Mortality** | Alive | 93 | 73.8 |
| | Exitus | 33 | 26.2 |
| **CD4/CD8** | | 1.08±1.01 | 0.11-5.1 |

SD: Standard deviation, CR: Complete response, PR: Partial response, Min.: Minimum, Max.: Maximum

were observed when grouping patients as CR + PR compared to others, with p=0.17 (Table 2).

Analysis of the ratio's effect on end-of-treatment response indicated higher values in CR patients compared to others (p=0.008). CR patients had a mean ratio of 1.36±1.02, while others had 0.86±0.71. The mean CD4/CD8 ratio was notably higher in patients with CR + PR compared to others (p<0.001) (1.19±1.01 and 0.65±0.38, respectively) (Table 2).

Regarding the ratio's effect on interim response, cut-off values for CD4/CD8 did not yield significant results. Neither statistical analysis of CR nor CR + PR treatment response groups yielded significant outcomes (p>0.05) (Table 3, Graphics 1, 2).

The statistical analysis of end-treatment response revealed significant findings. For the 0.38 cut-off value indicating end-of-treatment unresponsiveness (excluding CR), sensitivity was 35.29% and specificity was 89.47%. The positive predictive value reached 80%, while the negative predictive value was 53.7% (95% CI: 0.56-0.73, AUC: 0.65, p=0.002). Regarding the 0.87 cut-off value for CR + PR response, sensitivity and specificity were 79.17% and 54.46%, respectively. The positive predictive value was 29.2%, and the negative predictive value was 91.7% (95% CI: 0.59-0.76, AUC: 0.68, p=0.004) (Table 3, Graphics 3, 4).

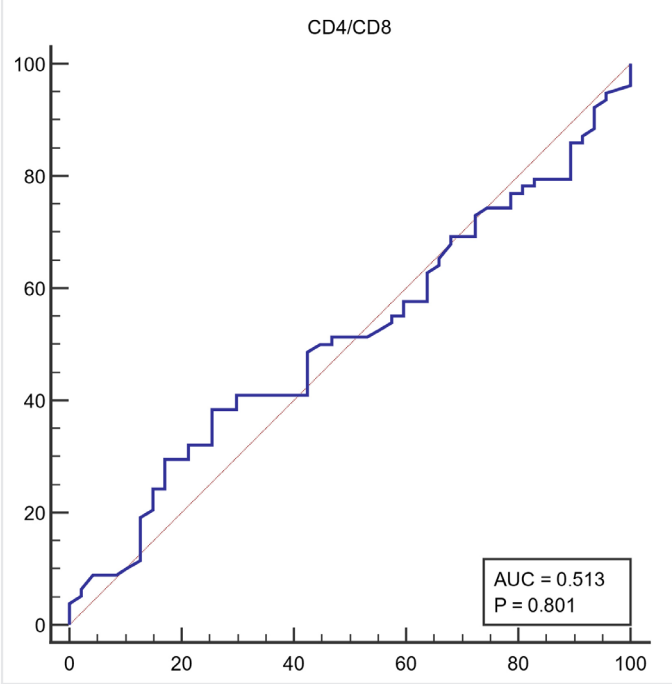
**Table 2. The effect of CD4/CD8 ratio on the interim and end-of-treatment response**

| | | $\bar{x} \pm SD$ | p-value |
|---|---|---|---|
| **Interim response** | CR | 1.48±1.16 | **0.003** |
| | Others | 0.85±0.67 | |
| | CR + PR | 1.15±1.01 | 0.17 |
| | Others | 0.82±0.73 | |
| **End-of-treatment response** | CR | 1.36±1.02 | **0.008** |
| | Others | 0.86±0.71 | |
| | CR + PR | 1.19±1.01 | **<0.001** |
| | Others | 0.65±0.38 | |

(p<0.05 significance), Student's t-test, SD: Standard deviation, CR: Complete response, PR: Partial response

During the 0-90 month period, 33 patients (26.9%) died. Among those with a CD4/CD8 ratio ≤0.87, 18 (27.7%) died, while 48 (72.73%) survived. Analysis of overall survival (OS) revealed no significant difference in survival curves, indicating that the CD4/CD8 ratio did not significantly impact mortality (p>0.05) (Table 4 and Graphic 5).

Disease progression occurred in 32 patients (25.4%) within the 0-90 month timeframe. For patients with a CD4/CD8 ratio ≤0.87, 22 (33.3%) experienced progression, while 44 (66.7%) did not. In the group with a CD4/CD8 ratio >0.87, 10 patients (16.67%) progressed, and 50 (83.33%) remained progression-free. The CD4/CD8 ratio showed no significant effect on progression-free survival (PFS) (p>0.05) (Table 4 and Graphic 6).




**Graphic 1.** Interim evaluation: patients with a response of CR and others
CR: Complete response, AUC: Area under the curve

**Table 3. Evaluation of the diagnostic accuracy of CD4/CD8 ratio in distinguishing treatment response**

| | AUC | Cut-off | Sensitivity % | Specificity % | AUC 95% CI | p | PPV % | NPV % |
|---|---|---|---|---|---|---|---|---|
| **Interim evaluation** | | | | | | | | |
| No response: 78<br>Response (CR): 47 | 0.51 | ≤0.52 | 38.46 | 74.47 | 0.42-0.61 | 0.81 | 71.4 | 42.2 |
| No response: 22<br>Response (CR + PR): 103 | 0.52 | >2.03 | 22.73 | 91.26 | 0.43-0.61 | 0.76 | 35.7 | 84.7 |
| **End-of-treatment** | | | | | | | | |
| No response: 68<br>Response (CR): 57 | 0.65 | ≤0.38 | 35.29 | 89.47 | 0.56-0.73 | **0.002** | 80 | 53.7 |
| No response: 24<br>Response (CR + PR): 101 | **0.68** | ≤0.87 | 79.17 | 54.46 | 0.59-0.76 | **0.004** | 29.2 | 91.7 |

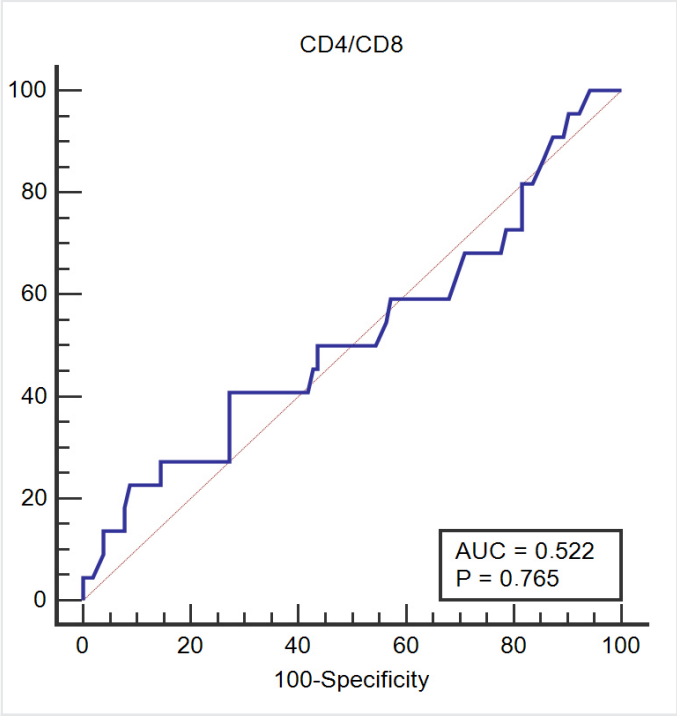
CR: Complete response, PR: Partial response, AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

## Discussion

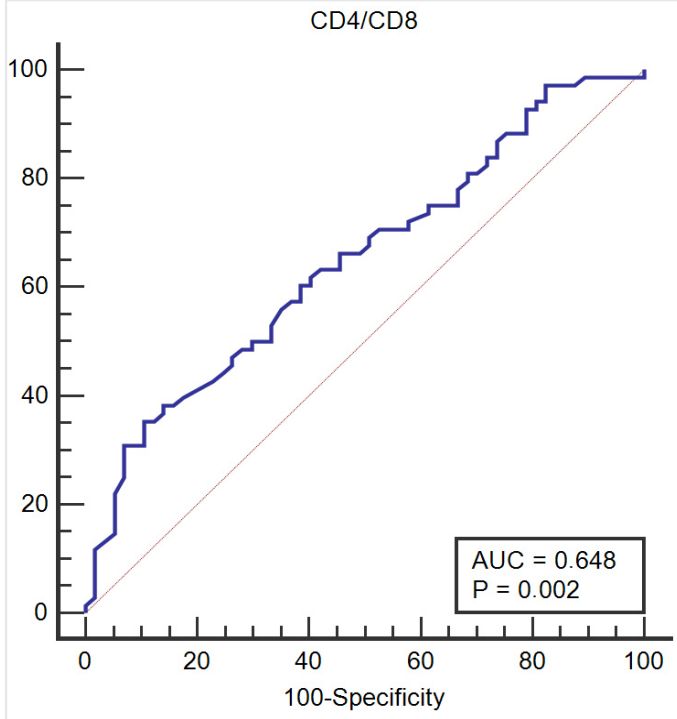
Our research revealed that the CD4/CD8 ratio had a significant impact on treatment responses. For the interim response, patients achieving CR showed a notably higher rate compared to other response groups. Similarly, for the end-of-treatment response, the ratio was elevated in CR patients relative to others. Additionally, patients with either CR or PR demonstrated a significantly higher mean CD4/CD8 ratio than those with other outcomes. Analysis of end-of-treatment response indicated that a CD4/CD8 ratio cut-off of 0.38 for non-CR responses yielded 35.29% sensitivity and 89.47% specificity. For CR + PR responses, a cut-off value of 0.87 provided 79.17% sensitivity and 54.46% specificity. However, the CD4/CD8 ratio did not significantly influence patient survival.

Although literature data evaluating lymphoma and the CD4/CD8 ratio is quite limited, the role of the ratio in different hematological malignancies has been evaluated and analyses have been presented. Generally, the increase in CD4+ cells and the "Tregs" among them had a negative effect on the treatment of malignancy due to the immunosuppressive effects; however, in our study, it was revealed that the increase in the ratio was found to be associated with a treatment response of CR in lymphomas. Our results may seem different from the literature when evaluated over the ratio; they are actually aligned with the literature data.

There are very few studies examining CD4+, CD8+, and other Tregs distributions, especially in bone marrow aspiration materials. In one of them, Braga et al. (12) evaluated Tregs in bone marrow aspirates of a total of 46 patients diagnosed with multiple myeloma (MM), 4 patients with monoclonal gammopathy of undetermined significance, and solitary plasmacytoma. When compared to the healthy controls, it




**Graphic 2.** Interim evaluation: Patients with a response of CR + PR and others
CR: Complete response, PR: Partial response, AUC: Area under the curve




**Graphic 3.** End-of-treatment evaluation: patients with a response of CR and others
CR: Complete response, AUC: Area under the curve

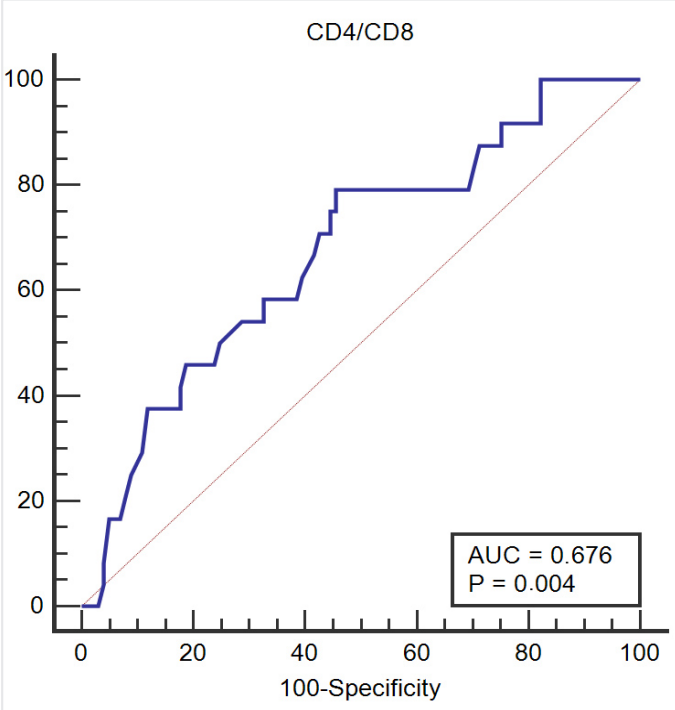
**Table 4. Survival analyses: Overall survival and progression-free survival**

| CD4/CD8 | Exitus n (%) | Non-exitus n (%) | Median survival (95% CI) | Hazard ratio (95% CI) | Log rank p-value |
|---|---|---|---|---|---|
| ≤0.87 (n=66) | 18 (27.27) | 48 (72.73) | 61 (32-64) | 1.001 (0.49-2.03) | 0.98 |
| >0.87 (n=60) | 15 (25) | 45 (75) | 71 (30-79) | | |
| Total | 33 (26.19) | 93 (73.81) | 64 (49-79) | | |
| | Progressed n (%) | Non-progressed n (%) | | | |
| ≤0.87 (n=66) | 22 (33.3) | 44 (66.7) | 34 (24-53) | 1.81 (0.89-3.68) | 0.09 |
| >0.87 (n=60) | 10 (16.67) | 50 (83.33) | 66 (54-78) | | |
| Total | 32 (25.4) | 94 (74.6) | 70 (31-70) | | |

CI: Confidence interval

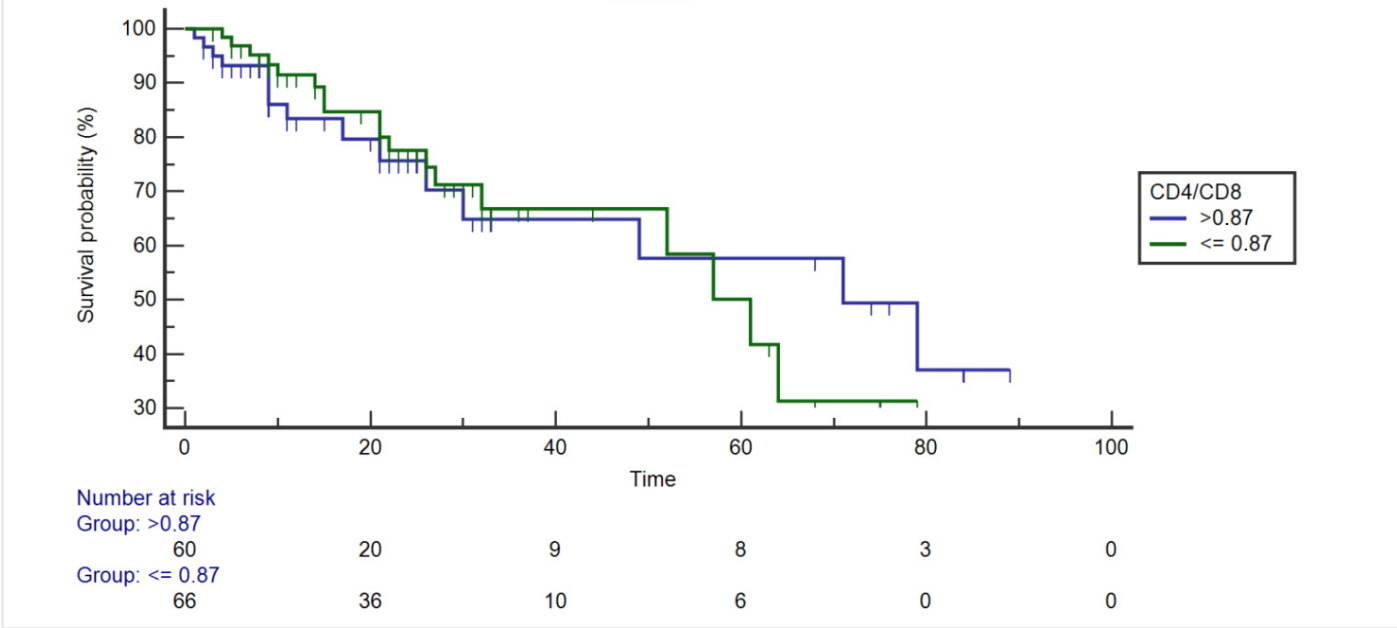
was observed that the FOXP3+ group was 30 times higher in patients diagnosed with MM. Based on that, it has been suggested that immune dysregulation may play a role in the pathogenesis of MM.

A lymph node study investigating the proportion of FOXP3+ cells (13) revealed that an increased number of these cells correlated with improved PFS in follicular lymphoma and diffuse large B-cell lymphoma (DLBCL), as well as better OS in HL and germinal-center DLBCL. However, it was associated with poorer OS in non-germinal DLBCL. Another investigation focused on CD4+ and CD25+ cell percentages in DLBCL lymph node biopsies, finding that higher levels of these cells were linked to worse survival outcomes and International Prognostic Index scores (14). Additionally, a separate lymph node analysis of relapsed/refractory HL patients showed that low regulatory Treg levels were connected to reduced OS (15). These investigations concentrate on affected lymph nodes, or "tumor tissue," and varying results may occur due to potential differences in disease mechanisms. Conversely, examining bone marrow aspirates, which may indicate systemic immune responses, can yield distinct findings, as observed in our research when compared to existing literature. While no significant survival correlations were found, the ratio proved influential in both interim and end-of-treatment responses. The response improves as the ratio increases, a finding not previously reported in the literature.

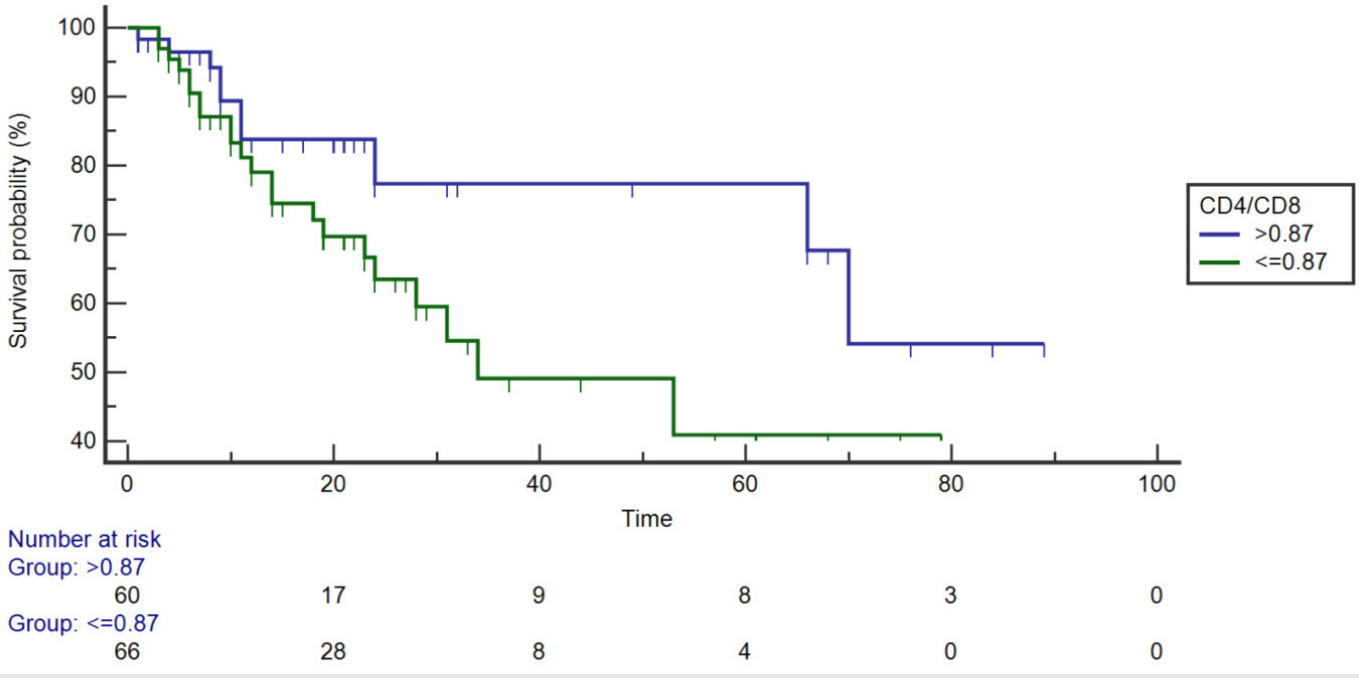



**Graphic 4.** End-of-treatment evaluation: patients with a response of CR + PR and others
CR: Complete response, PR: Partial response, AUC: Area under the curve

In another study (16), researchers performed bone marrow sampling and evaluated the effect of subtyping on response and survival. Patients diagnosed with B-acute lymphoblastic leukemia were examined, and an increase in Treg was found to be associated with disease progression. Another study (17) evaluated 39 patients with acute lymphoblastic leukemia (ALL). The high CD4/CD8 ratio in bone marrow aspirates taken before treatment with the pediatric ALL regimen showed a positive correlation with the 15$^{th}$ day response. When the CD4+ cell subgroups were evaluated separately, non-Treg cells were found to be higher compared to others, excluding CD4+, CD25+, FOXP3+ Treg cells. Therefore, the interpretation is that the increase in the ratio of non-Treg CD4+ cells and the high CD4/CD8 ratio contributes positively to the response. We think that a similar mechanism was effective in our study; however, the fact that subtyping could not be studied was an important limitation.




**Graphic 5.** Overall survival probabilities (%)




**Graphic 6.** Progression-free survival probabilities (%)

### Study Limitations

There were important additional limitations of our study. Subtyping of CD4+ cells could not be studied in our flow cytometry laboratory. For this reason, subtyping could not be performed. In another study, the evaluation of CD25+, FOXP3+ cells using appropriate subtyping methods will be much more accurate. Another important limitation was the restricted patient population, as it included single-center data.

## Conclusion

In conclusion, in our study, the CD4/CD8 ratio was found to be significantly higher in patients with a CR response compared to others, in terms of the interim response to treatment. In the statistical analysis performed to reveal the effect of the ratio on the end-of-treatment response, it was found to be higher in patients with response of CR, compared to others. The CD4/CD8 ratio did not have a significant effect on OS and PFS. It was revealed that the ratio was effective both in the interim and at the end-of-treatment response. The response increases as the ratio increases. It will shed light on new studies evaluating the effect of subtypes of CD4+ Tregs on response and survival in lymphomas.

### Ethics

**Ethics Committee Approval:** The research was reviewed and approved by the University of Health Sciences Türkiye, İstanbul Training and Research Hospital Ethics Committee (approval number: 2573, date: 13.11.2020) and was conducted according to the principles of the Declaration of Helsinki.

**Informed Consent:** Prospective studies.

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### Footnotes

**Authorship Contributions:** Concept - D.S., B.O., H.S., O.Y.; Design - D.S., B.O., H.S., O.Y.; Data Collection or Processing - V.C.Ç., İ.S.; Analysis or Interpretation - V.C.Ç., İ.S.; Literature Search - V.C.Ç., İ.S.; Writing - V.C.Ç., İ.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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## References

1. Hobbs MV, Ernst DN. T cell differentiation and cytokine expression in late life. Dev Comp Immunol. 1997; 21: 461-70.
2. Actor JK. T Lymphocytes. Introductory Immunology. 1st ed. Academic Press; 2014, p.42-58.
3. Sakaguchi S, Wing K, Miyara M. Regulatory T cells - a brief history and perspective. Eur J Immunol. 2007; 116-23.
4. D'Arena G, Vitale C, Coscia M, Festa A, Di Minno NMD, De Feo V, et al. Regulatory t cells and their prognostic relevance in hematologic malignancies. J Immunol Res. 2017; 2017: 1832968.
5. Beyer M, Schultze JL. Regulatory T cells in cancer. Blood. 2006; 108: 804-11.
6. Whiteside TL. The role of regulatory T cells in cancer immunology. Immunotargets Ther. 2015; 4: 159-71.

7. Takeuchi Y, Nishikawa H. Roles of regulatory T cells in cancer immunity. Int Immunol. 2016; 28: 401-9.

8. Wang J, Ke XY. The four types of Tregs in malignant lymphomas. J Hematol Oncol. 2011; 4: 50.

9. Farinha P, Al-Tourah A, Gill K, Klasa R, Connors JM, Gascoyne RD. The architectural pattern of FOXP3-positive T cells in follicular lymphoma is an independent predictor of survival and histologic transformation. Blood. 2010; 115: 289-95.

10. Droeser R, Zlobec I, Kilic E, Güth U, Heberer M, Spagnoli G, et al. Differential pattern and prognostic significance of CD4+, FOXP3+ and IL-17+ tumor infiltrating lymphocytes in ductal and lobular breast cancers. BMC Cancer. 2012; 12: 134.

11. Hoppe RT, Advani RH, Ai WZ, Ambinder RF, Armand P, Bello CM, et al. NCCN Guidelines® insights: hodgkin lymphoma, version 2.2022. J Natl Compr Canc Netw. 2022; 20: 322-34.

12. Braga WM, da Silva BR, de Carvalho AC, Maekawa YH, Bortoluzzo AB, Rizzatti EG, et al. FOXP3 and CTLA4 overexpression in multiple myeloma bone marrow as a sign of accumulation of CD4(+) T regulatory cells. Cancer Immunol Immunother. 2014; 63: 1189-97.

13. Tzankov A, Meier C, Hirschmann P, Went P, Pileri SA, Dirnhofer S. Correlation of high numbers of intratumoral FOXP3+ regulatory T cells with improved survival in germinal center-like diffuse large B-cell lymphoma, follicular lymphoma and classical Hodgkin's lymphoma. Haematologica. 2008; 93: 193-200.

14. Chang C, Wu SY, Kang YW, Lin KP, Chen TY, Medeiros LJ, et al. High levels of regulatory T cells in blood are a poor prognostic factor in patients with diffuse large B-cell lymphoma. Am J Clin Pathol. 2015; 144: 935-44.

15. Koreishi AF, Saenz AJ, Persky DO, Cui H, Moskowitz A, Moskowitz CH, et al. The role of cytotoxic and regulatory T cells in relapsed/refractory Hodgkin lymphoma. Appl Immunohistochem Mol Morphol. 2010; 18: 206-11.

16. Bhattacharya K, Chandra S, Mandal C. Critical stoichiometric ratio of CD4(+) CD25(+) FoxP3(+) regulatory T cells and CD4(+) CD25(-) responder T cells influence immunosuppression in patients with B-cell acute lymphoblastic leukaemia. Immunology. 2014; 142: 124-39.

17. Lustfeld I, Altvater B, Ahlmann M, Ligges S, Brinkrolf P, Rosemann A, et al. High proportions of $CD4^+$ T cells among residual bone marrow T cells in childhood acute lymphoblastic leukemia are associated with favorable early responses. Acta Haematol. 2014; 131: 28-36.