Open Access Original Article

Outcomes of Patients Treated with Brentuximab Vedotin in Relapsed or Refractory CD30 Positive Lymphomas; A Single Center Experience

***Salman Arif*[1]**
***Natasha Ali*[2]**
***Usman Shaikh*[2]**
***Salman Adil*[2]**

[1]Department of Oncology, Aga Khan University Hospital, Karachi, Pakistan
[2]Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

Abstract

Objective: To assess the efficacy of Brentuximab Vedotin ± Bendamustine in the management of relapsed or refractory CD30-positive lymphomas, including classic Hodgkin lymphoma (cHL) and systemic anaplastic large cell lymphoma (sALCL).

Methodology: An observational retrospective study was conducted at Aga Khan University Hospital, Pakistan, from January 2021 to June 2022. Eligible participants were aged 17 or older with CD30-positive disease (cHL or sALCL), having undergone at least one prior chemotherapy regimen and experiencing relapse or refractory disease. Treatment involved Brentuximab Vedotin ± Bendamustine, and patients were assessed using PET-CT scans.

Results: Twenty-two patients received chemotherapy with Brentuximab Vedotin ± Bendamustine, comprising 19 with Hodgkin lymphoma and 3 with sALCL. Among them, 6 were in relapse, and 16 were refractory. At the end of treatment, 17 patients achieved complete response, 3 achieved partial response, and 1 had stable disease, yielding an overall response rate (ORR) of 90.9%. Nineteen patients survived, while 3 deceased. The median overall survival was 30 months. Commonly encountered side effects, including nausea, neutropenia, peripheral neuropathy, gastrointestinal disturbances, infusion reactions, and rash, were generally well tolerated.

Conclusions: Brentuximab Vedotin ± Bendamustine demonstrates effectiveness and tolerability in patients with relapsed or refractory cHL and sALCL, even in heavily pretreated individuals. In middle-income countries like Pakistan, affordability and accessibility play pivotal roles in determining patient eligibility for this treatment regimen.

Keywords: Brentuximab Vedotin; relapsed or refractory; Hodgkin lymphoma; Anaplastic large cell lymphoma.

\

Address for Correspondence
Dr. Salman Arif
Department of Oncology, Aga Khan University Hospital, Karachi, Pakistan.
Email: salmanarif77@gmail.com

Introduction

Lymphomas are a type of neoplasm that arises from lymphocytes and other lymphatic system organs. Lymphomas are divided into two types: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).[1, 2] The NHLs are a diverse group of neoplastic diseases. They are classified as B, T, or natural killer (NK) cell lymphomas. According to the World Health Organization (WHO).

Of all lymphomas, Hodgkin lymphoma makes up 25%, and non-Hodgkin lymphoma makes up 75%.[3] The disease primarily affects young adults aged 15–30 years 4 and 20–40 years 3; a second surge is seen in those over 55 years.[3, 4] There are two main forms of HL: nodular lymphocyte-predominant Hodgkin lymphoma, which accounts for only 5% of cases, and classical Hodgkin lymphoma (cHL), which accounts for 95% of cases. A subclass of peripheral T-cell lymphomas, cutaneous and systemic anaplastic large-cell lymphomas (sALCL), make up 2–8% of all lymphoid neoplasms. [2, 3] Approximately 2% to 8% of non-Hodgkin lymphomas in adults and 20% to 30% of large-cell lymphomas in children are caused by primary sALCL.[5]

Most younger individuals with Hodgkin's lymphoma (HL) can be effectively treated with front-line medications currently available; however, up to 30% of them experience refractory disease or relapse following initial therapy.[6] The standard treatment protocol for these patients involves second-line chemotherapy followed by autologous stem cell transplantation (ASCT), which boasts a cure rate of 50% to 55%. After completing front-line therapy, between 40% and 65% of individuals with systemic anaplastic large cell lymphoma (sALCL) experience disease recurrence.[7] Patients with recurrent or refractory disease often undergo high-dose chemotherapy followed by autologous stem

Authorship Contribution: [1,3]Conceived and planned the idea of the study, final approval of the version to be published, [2,4]Collecting the data, drafting the work or revising it critically for important intellectual content,

Funding Source: none
Conflict of Interest: none

Received: June 13, 2023
Accepted: Nov 20, 2023

cell transplantation, which offers a 5-year progression-free survival (PFS) rate of up to 56%.[8]

Since its approval in the late 1990s, rituximab (anti-cluster of differentiation CD 20), the first monoclonal antibody used in cancer treatment, has marked the emergence of antibody-based immunotherapy as a pivotal component in cancer therapies. These monoclonal antibodies induce complement-dependent cytotoxicity (CDC) and antibody-dependent cell-mediated cytotoxicity (ADCC), while also impeding the signalling cascade initiated by target molecules through specific recognition of antigens on the surface of target cells. However, unconjugated monoclonal antibodies typically exhibit poor single-agent effectiveness and must be used in combination with additional chemotherapy drugs.[9]

Numerous alterations have been made to increase the activity of monoclonal antibodies. One method is to produce antibody-drug conjugates by coupling cytotoxic medications to tumor antigen-specific antibodies (ADCs). Theoretically, ADCs can deliver cytotoxic medications to tumor cells while considerably reducing systemic toxicity.

A promising target for ADC-based therapy is the cell membrane protein CD30, which is significantly expressed on a subset of malignancies, including cHL and sALCL, but not on most normal cells. Both aggressive lymphomas (cHL and sALCL) carry a poor prognosis for individuals with refractory or relapsed disease after initial therapy. Antibody-based therapy using the CD30 antigen was tried to treat refractory or relapsed cHL and sALCL considering the expression profile of CD30. Despite the promising outcomes in preclinical studies on unconjugated anti-CD30 antibodies in cHL and sALCL[10], the evidence was supported by further research, leading to the creation of the anti-CD30 ADC, Brentuximab Vedotin (BV), which opened up new therapy options for CD30-positive malignancies.

Because of the recent studies' encouraging outcomes and ongoing research. In our institution, relapsed refractory cHL and sALCL patients were given the option of receiving BV, which was only introduced in January 2021. In this study, we explore the outcomes of patients treated with BV either alone or in combination with other chemotherapy (Bendamustine). This study will serve as a foundation for future projects on the drug.

Methodology

An observational retrospective study was conducted among patients with classical Hodgkin lymphoma (cHL) or systemic anaplastic large cell lymphoma (sALCL) treated with Brentuximab Vedotin (BV) outside of clinical trials at the Aga Khan University Hospital, Pakistan from January 2021 to June 2022. The patient list was retrieved from our institute's electronic database. The study received approval from our institutional board and ethical committee, and it was carried out in compliance with the ethical principles outlined in the 1964 Helsinki Declaration and its later amendments. Patients were consecutively enrolled to avoid selection bias and retrospectively collect their data.

All eligible patients aged 17 and older with histologically confirmed CD30-positive disease (either cHL or sALCL), of either relapsed or refractory nature, and who had received at least one prior line of chemotherapy were included. Patients who were CD30 positive but treatment naive were excluded from the study. No exclusion criteria were determined regarding bone marrow and other organ function, Eastern Cooperative Oncology Group (ECOG) performance status, or the total number of previous therapies received.

Procedures and assessment: All patients underwent pre-BV assessments, including physical examination, routine hematology, and biochemistry testing, as well as PET-CT imaging, before therapy. Response to treatment was assessed every three to four cycles (clinician preference) with PET-CT and at the end of treatment. Patients thereafter were monitored with close follow-up every 1-2 months.

Participants received an infusion of Brentuximab at a dose of 1.8 mg/kg on the first day of every three weeks, either by itself or in conjunction with Bendamustine at a dose of 90 mg/m2 on the first and second days of a 21-day cycle (BV±B). Conversely, when Bendamustine and Brentuximab were coupled, the number of cycles was limited to six.

The determination of tumor response was based on the revised response criteria for malignant lymphoma and the Lugano classification.[11] Patients who achieved remission, defined as complete remission (CR) or partial remission (PR), were offered an autologous stem cell transplant and further maintenance therapy with BV (based on patient and physician preference). To investigate the effectiveness of using the BV ± B combination to treat patients with relapsed or refractory (no complete remission or relapse within 3 months of front-line therapy) cHL or sALCL, we measured the complete response (CR) and overall response rates (ORR), as well as the median overall survival time. Additionally, we recorded the common adverse events that occurred during the study.

Statistical analysis using Fisher's exact test and calculated

survival data using the Kaplan-Meier method. Descriptive variables were expressed as means and percentages. SPSS 25.0 software was utilized for this purpose.

Results

A retrospective analysis of 22 patients with confirmed CD30-positive lymphoma who underwent chemotherapy with Brentuximab Vedotin either alone or in combination with Bendamustine were enrolled from January 2021 to June 2022. Of the patients, 59.1% were male and 40.9% were female, with a median age of 37.5 years (SD±17.6 years, range 17–75 years) (Table I).

Histological confirmation of the type of lymphoma revealed that 19 patients (86.4%) had Hodgkin lymphoma. While 3 patients (13.6%) had sALCL. 6 (27.3%) were in the relapsed category, while 16 (72.7%) were of a refractory nature. PET-CT evaluation before the start of therapy showed 13 (59.1%) patients were classified as stage 4, 5 (22.7%) patients as stage 3, 2 (9.1%) patients as stage 2, and 2 (9.1%) patients as stage 1. Out of these, 15 (68.2%) patients had non-bulky disease and 7 (31.8%) patients had bulky disease (Table I).

Table : Patient characteristics. (n=22)	
Parameters	Value
Gender	n (%)
Male	13 (59.1)
Female	9 (40.9)
Age, median (SD), years	37.5 (17.6)
Histological confirmation	
Hodgkin	19 (86.4)
sALCL	3 (13.6)
Response to frontline therapy	
Refractory	16 (72.7)
-Relapsed (CR > 1 year)	6 (27.3)
PET-CT	
Stage 1	2 (9.1)
Stage 2	2 (9.1)
Stage 3	5 (22.7)
Stage 4	13 (59.1)
Disease status upon **relapse**	
Non-bulky	15 (68.2)
Bulky	7 (31.8)

Treatment Regimen and Response Evaluation:

All patients received Brentuximab Vedotin as standard chemotherapy alone in 6 (27.3%) cases and combined with Bendamustine in 16 (72.0%) cases (Table Ⅱ). The average number of cycles received was 6, with a range of 1–9 cycles. In terms of response evaluation, 16 (72.7%) patients had undergone interim PET-CT for response evaluation, while 6 (27.3%) patients did not undergo this evaluation. The response was 12 (75%) patients in CR and 4 (25%) patients in PR. Upon completion of the cycles, an end-of-treatment PET was done for 21 (95.5%) patients, while 1 (4.54%) patient did not undergo this evaluation. The response at the end of treatment was CR in 17 (77.3%) of patients, PR in 3 (13.6%) of patients, and SD in 1 (4.5%) of patients, while the overall response rate (ORR) was 90.9%.

Of 22 patients, 8 underwent autologous stem cell transplant (Table II) 19 (86.4%) survived, with 3 (13.6%) deaths. Median overall survival was 30 months (24–36 months) (Figure 1). Disease status upon last hospital visit was CR in 14 (63.6%) patients, PR in 2 (9.1%) patients, SD in 1 (4.5%) patient, relapsed in 4 (18.2%) patients, and 1 (4.5%) patient was lost to follow up.

Table I: Patient characteristics. (n=22)	
Parameters	Value
Gender	n (%)
Male	13 (59.1)
Female	9 (40.9)
Age, median (SD), years	37.5 (17.6)
Histological confirmation	
Hodgkin	19 (86.4)
sALCL	3 (13.6)
Response to frontline therapy	
Refractory	16 (72.7)
Relapsed (CR > 1 year)	6 (27.3)
PET-CT	
Stage 1	2 (9.1)
Stage 2	2 (9.1)
Stage 3	5 (22.7)
Stage 4	13 (59.1)
Disease status upon relapse	
Non-bulky	15 (68.2)
Bulky	7 (31.8)

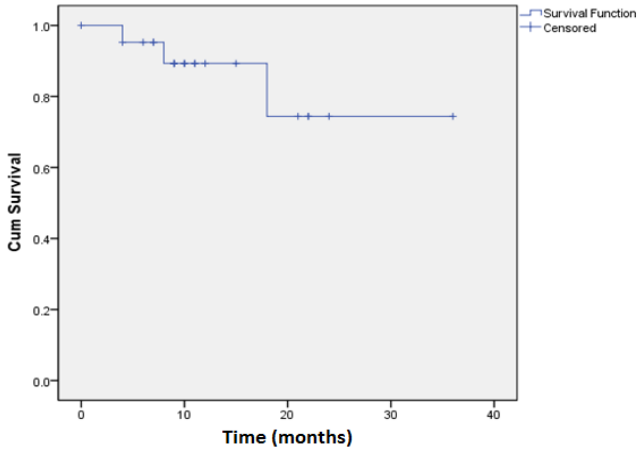

Figure 1: Median overall survival. (n=22)

Table III lists the frequent adverse events that took place during the study. 31.8% of the patient group, or 7 out of 22 patients, reported having nausea. Similarly, 10 (45.5%) had neutropenia, 8 (36.4%) had peripheral neuropathy, 6 (27.3%) had GI problems, 3 (13.6%) had an infusion-related reaction, and 1 (4.5%) had a rash. None of the patients had grade 3 or 4 toxicity, and no therapy related deaths occurred while on treatment.

Table III: Treatment related adverse events.

Adverse Events	Patients	%
Nausea	7	31.8
Fatigue	8	36.4
Neutropenia	10	45.5
P. Neuropathy	8	36.4
GI	6	27.3
Rash	1	4.5
Infusion related reactions	3	13.6
Death during therapy	0	0

Discussion

Our single-center experience of patients treated with Brentuximab Vedotin yielded the results that Brentuximab Vedotin, either alone or in combination with Bendamustine, is effective in treating CD30-positive lymphoma. Brentuximab Vedotin (BV) and immune checkpoint inhibitors (CPIs), two innovative therapeutic alternatives that have recently been accessible for patients with relapsed or refractory cHL, have led to significant CMR rates prior to ASCT, particularly when paired with chemotherapy.[12] As a salvage regimen and a bridging therapy before transplant, there have been various attempts to combine BV with other chemotherapies, each of which has demonstrated a varying success rate in treating both refractory and relapsed Hodgkin lymphoma.[13-16] Our study explored the option of combining it with Bendamustine or using it alone. The results of previous studies and clinical trials employing the same medication (BV±B) mainly matched the overall response rate (ORR) of our study, which was 90.9% with a CR rate of 77.3%. [15-18]

Approximately 87% of our study population had classical Hodgkin lymphoma, and 13% had systemic anaplastic large cell lymphoma (sALCL). Anaplastic large cell lymphoma is rare, especially in our population, though it is the most common peripheral T-cell lymphoma (PTCL) among our demographic.[19, 20] Bouabdallah et al observed a 71% overall response rate (ORR) and 51% complete response rate (CR) of BV+B as salvage treatment for relapsed or refractory PTCL (26% sALCL).[21] Our study showed 3 sALCL patients (13.6%), of whom one was ALK positive and two were ALK negative. All three had refractory stage 4 bulky disease, except one patient with stage 1 non-bulky disease. They all received a combination therapy of BV+B and achieved complete remission as observed on PET-CT at the end of treatment. The patients-maintained remission until their last follow-up visits and survived without disease relapse.

The study enrolled heavily treated patients who had relapsed or were refractory to prior chemotherapy regimens. Research has shown that primary refractory disease and a short duration between first-line therapy and relapse can negatively impact the response to salvage therapy and progression-free survival.[22, 23] Despite these factors, most patients in our study responded positively to Brentuximab Vedotin, either alone or in combination with Bendamustine. Specifically, 77.3% of patients achieved a complete response (CR) by the end of treatment, and 13.6% achieved a partial response (PR). Of those who achieved a CR, 82.3% maintained that response until the final follow-up, demonstrating the effectiveness of this salvage treatment option for this patient population.

The use of Brentuximab Vedotin (BV) in combination with chemotherapy as the initial salvage treatment has been extensively investigated in numerous trials, demonstrating promising results in terms of complete metabolic response (CMR) rates prior to autologous hematopoietic stem cell transplantation (ASCT) of up to 83% and 2-year progression-free survival (PFS) rates ranging from 63% to 81%.[13, 15, 16] Obtaining CMR before ASCT is a crucial factor for improved PFS.[13, 15, 16] To further consolidate the disease, we offered ASCT to all patients who achieved durable remission (either CR or PR). In our study, all eight patients who underwent ASCT had Hodgkin lymphoma. Prior to the transplant, five of these patients were in CR, and three were in PR. Following the transplant, six patients remained in remission and were alive, while two experienced relapse and died at the time of the last follow-up.

Regarding the feasibility of stem cell collection during or after chemotherapy that includes Bendamustine, we had no difficulties with our patients. After only a few cycles of treatment, we were able to mobilize and harvest stem cells from eight patients from whom no stem cells had been obtained during prior therapy lines.

Post-transplant, BV maintenance was shown to prolong progression-free survival (PFS) and event-free survival (EFS) in high-risk Hodgkin lymphoma.[24] Of 8 patients treated with autologous stem cell transplantation, 3 received BV maintenance and achieved full survival, with 1 relapse of the primary disease.

The chemotherapy treatment combined with Bendamustine was well tolerated by the patients, with only mild to moderate side effects observed (listed in Table III), none of which were severe enough to require stopping treatment or modifying the dose in the long term. The most common side effects included nausea, fatigue, peripheral neuropathy, GI upset and neutropenia, which were treated with symptomatic therapy and GCSF to boost cell counts for the following cycles. However, another study[25] found that Bendamustine and BV treatment caused more severe toxicity in patients over the age of 60, and we observed that toxicities were more pronounced in patients over 50 years old. The relatively low level of side effects made this regimen an ideal choice for outpatient chemotherapy, with no long-term toxicity observed during the follow-up period.

The study has certain limitations, which include the collection of data in a retrospective manner. Additionally, the research has a narrow focus with a small number of participants and a short follow-up period, which reduces the applicability of the findings to other lymphoma types, as most participants had Hodgkin lymphoma and only a few had sALCL. While the treatment regimen is expensive, it may be more appropriate for use in relapsed or refractory settings in underprivileged countries like the one where the study was conducted than for upfront treatment, although it is also used for the latter. However, the study's strength lies in the inclusion of patients of all ages with no consideration for co-morbidities, which reflects real-world experience. Despite its limitations, this study provides valuable information on ORR and median OS and is the first of its kind to be conducted in the local population.

Conclusion

In conclusion, our study offers evidence that Brentuximab Vedotin, whether administered alone or in combination with Bendamustine, represents an effective and well-tolerated treatment option for patients diagnosed with relapsed or refractory CD30-positive lymphomas.

References

1. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO classification of tumours of haematopoietic and lymphoid tissues: International agency for research on cancer Lyon; 2008.
2. Singh R, Shaik S, Negi BS, Rajguru JP, Patil PB, Parihar AS, et al. Non-Hodgkin's lymphoma: A review. Fam. Med. Prim. Care Rev.2020;9(4):1834-40. https://doi.org/10.4103/jfmpc.jfmpc_1037_19
3. Shahid R, Gulzar R, Avesi L, Hassan S, Danish F, Mirza T. Immunohistochemical Profile of Hodgkin and Non-Hodgkin Lymphoma. J Coll Physicians Surg Pak: JCPSP. 2016;26(2):103-7.
4. Eichenauer DA, Engert A, André M, Federico M, Illidge T, Hutchings M, et al. Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology. 2014;25 Suppl 3:iii70-5. https://doi.org/10.1093/annonc/mdu181
5. Stein H, Foss H-D, Dürkop H, Marafioti T, Delsol G, Pulford K, et al. CD30+ anaplastic large cell lymphoma: a review of its histopathologic, genetic, and clinical features. Blood, The Journal of the Am. J. Hematol. 2000;96(12):3681-95. https://doi.org/10.1182/blood.V96.12.3681
6. Voorhees TJ, Beaven AW. Therapeutic Updates for Relapsed and Refractory Classical Hodgkin Lymphoma. Cancers. 2020;12(10). https://doi.org/10.3390/cancers12102887
7. Savage KJ, Harris NL, Vose JM, Ullrich F, Jaffe ES, Connors JM, et al. ALK- anaplastic large-cell lymphoma is clinically and immunophenotypically different from both ALK+ ALCL and peripheral T-cell lymphoma, not otherwise specified: report from the International Peripheral T-Cell Lymphoma Project. Blood. 2008;111(12):5496-504. https://doi.org/10.1182/blood-2008-01-134270
8. Smith SM, Burns LJ, van Besien K, Lerademacher J, He W, Fenske TS, et al. Hematopoietic cell transplantation for systemic mature T-cell non-Hodgkin lymphoma. Journal of clinical oncology. 2013;31(25):3100-9. https://doi.org/10.1200/JCO.2012.46.0188
9. Chen X, Soma LA, Fromm JR. Targeted therapy for Hodgkin lymphoma and systemic anaplastic large cell lymphoma: focus on brentuximab vedotin. Onco Targets and therapy. 2013;7:45-56. https://doi.org/10.2147/OTT.S39107
10. Forero-Torres A, Leonard JP, Younes A, Rosenblatt JD, Brice P, Bartlett NL, et al. A Phase II study of SGN-30 (anti-CD30 mAb) in Hodgkin lymphoma or systemic anaplastic large cell lymphoma. Br J Hematol..2009;146(2):171-9. https://doi.org/10.1111/j.1365-2141.2009.07740.x
11. Younes A, Hilden P, Coiffier B, Hagenbeek A, Salles G, Wilson W, et al. International Working Group consensus response evaluation criteria in lymphoma (RECIL 2017). Annals of oncology. 2017;28(7):1436-47. https://doi.org/10.1093/annonc/mdx097
12. Chen R, Zinzani PL, Lee HJ, Armand P, Johnson NA, Brice P, et al. Pembrolizumab in relapsed or refractory Hodgkin lymphoma: 2-year follow-up of KEYNOTE-087. Blood. 2019;134(14):1144-53. https://doi.org/10.1182/blood.2019000324
13. Moskowitz CH. Highlights in Lymphoma From the 2017 American Society of Clinical Oncology Annual Meeting and the 14th International Conference on Malignant Lymphoma. Clinical advances in hematology & oncology : H&O. 2017;15 Suppl 11 9:1-24.
14. Herrera AF, Palmer J, Martin PJM, Armenian SH, Tsai N, Kennedy N, et al. Autologous stem-cell transplantation after second-line brentuximab vedotin in relapsed or refractory Hodgkin lymphoma. Annals of Oncology. 2017;29:724-30. https://doi.org/10.1093/annonc/mdx791
15. LaCasce AS, Bociek RG, Sawas A, Caimi P, Agura E, Matous J, et al. Brentuximab vedotin plus bendamustine: a highly active first salvage

regimen for relapsed or refractory Hodgkin lymphoma. Blood, The Journal of the Am. J. Hematol. 2018;132(1):40-8. https://doi.org/10.1182/blood-2017-11-815183

16. Broccoli A, Argnani L, Botto B, Corradini P, Pinto A, Re A, et al. First salvage treatment with bendamustine and brentuximab vedotin in Hodgkin lymphoma: a phase 2 study of the Fondazione Italiana Linfomi. Blood Cancer J. 2019;9(12):100. https://doi.org/10.1038/s41408-019-0265-x

17. Wagner SM, Melchardt T, Egle A, Magnes T, Skrabs C, Staber P, et al. Treatment with brentuximab vedotin plus bendamustine in unselected patients with CD30-positive aggressive lymphomas. Eur J Haematol. 2020;104(3):251-8. https://doi.org/10.1111/ejh.13368

18. Sawas A, Connors JM, Kuruvilla JG, Rojas C, Lichtenstein R, Neylon E, et al. The Combination of Brentuximab Vedotin (Bv) and Bendamustine (B) Demonstrates Marked Activity in Heavily Treated Patients with Relapsed or Refractory Hodgkin Lymphoma (HL) and Anaplastic Large T-Cell Lymphoma (ALCL): Results of an International Multi Center Phase I/II Experience. Blood. 2015;126(23):586-. https://doi.org/10.1182/blood.V126.23.586.586

19. Resham S, Khan R, Ashraf S, Rizvi A, Altaf S. Clinical Features and Treatment Outcomes of Children With Anaplastic Large Cell Lymphoma in Pakistan: A Multicenter Study. J Pediatr Hematol Oncol. 2019;41(4):298-302. https://doi.org/10.1097/MPH.0000000000001451

20. Syed S, Khalil S, Pervez S. Anaplastic large cell lymphoma: the most common T-cell lymphoma in pakistan. Asian Pac J Cancer Prev. 2011;12(3):685-9.

21. Bouabdallah K, Aubrais R, Chartier L, Herbaux C, Banos A, Brice P, et al. Salvage Therapy with Brentuximab-Vedotin and Bendamustine for Patients with Relapsed/Refractory T Cell Lymphoma. a Multicenter and Retrospective Study. Blood. 2021. https://doi.org/10.1182/blood-2021-150953

22. Moskowitz CH, Matasar MJ, Zelenetz AD, Nimer SD, Gerecitano J, Hamlin P, et al. Normalization of pre-ASCT, FDG-PET imaging with second-line, non-cross-resistant, chemotherapy programs improves event-free survival in patients with Hodgkin lymphoma. Blood. 2012;119(7):1665-70. https://doi.org/10.1182/blood-2011-10-388058

23. Moskowitz CH, Yahalom J, Zelenetz AD, Zhang Z, Filippa DA, Teruya-Feldstein J, et al. High-dose chemo-radiotherapy for relapsed or refractory Hodgkin lymphoma and the significance of pre-transplant functional imaging. Br J Hematol. 2010;148. https://doi.org/10.1111/j.1365-2141.2009.08037.x

24. Akay OM, Ozbalak M, Pehlivan M, Yıldız B, Uzay A, Yiğenoğlu TN, et al. Brentuximab vedotin consolidation therapy after autologous stem-cell transplantation in patients with high-risk Hodgkin lymphoma: Multicenter retrospective study. Hematological Oncology. 2021;39:498 - 505. https://doi.org/10.1002/hon.2897

25. Friedberg JW, Forero-Torres A, Bordoni RE, Cline VJM, Patel Donnelly D, Flynn PJ, et al. Frontline brentuximab vedotin in combination with dacarbazine or bendamustine in patients aged ≥60 years with HL. Blood. 2017;130(26):2829-37. https://doi.org/10.1182/blood-2017-06-787200