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Original Article

A Prospective Study Comparing Treatment Outcomes of Brentuximab Vedotin Plus AVD versus ABVD in Egyptian Patients with Advanced Classical Hodgkin Lymphoma

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Abstract

Background: Classical Hodgkin lymphoma (cHL) is a malignancy that is readily amenable to treatment, but still advanced–stage disease (stage III/IV) carries a significant therapeutic challenge. While ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) is a standard frontline regimen, its efficacy is limited by toxicity and relapse rates. Brentuximab Vedotin (BV), an anti–CD30 antibody–drug conjugate, concurrent with AVD (BV+AVD) has emerged as a promising alternative. This study compares the effectiveness and tolerability of BV+AVD versus ABVD in Egyptian patients with advanced cHL.

Methodology: A prospective, randomized, open–label study was conducted at Helwan University Hospitals (March 2023–February 2025). A total of sixty patients with newly diagnosed stage III/IV cHL were randomized to receive either BV combined with AVD (BV+AVD; n = 30) or standard ABVD (n = 30). The primary endpoint was PFS, while secondary endpoints included PET negativity after two cycles, overall response rate (ORR), overall survival (OS), and treatment–related toxicity.

Results: Interim analysis demonstrated superior 2–year PFS for BV+AVD (80.0%) versus ABVD (53.3%). BV+AVD showed higher PET negativity rates post–cycle 2 (83.3% vs. 76.6%) and reduced pulmonary toxicity (6.7% vs. 23.3%). Hematologic toxicity (neutropenia: 60% vs. 40%) and neuropathy (43.3% vs. 16.7%) were more frequent with BV+AVD but mainly low grade and manageable.

Discussion: Limitations of this study encompass that it is a single–center study with a relatively small sample size that reduces the statistical power and makes it challenging to detect rare side effects. The population of the study represents the young and middle age group of patients with cHL so the treatment effect on older population was not studied. The limited follow–up duration restricts further knowledge about late relapses or delayed toxicities.

Conclusion: BV+AVD significantly improves PFS and reduces bleomycin–associated toxicity, supporting its adoption as a frontline regimen for advanced cHL. Extended follow–up is required to validate the observed survival benefits.

Keywords: Hodgkin Lymphoma, ABVD, Brentuximab Vedotin, AVD, PET/CT

Introduction:

Hodgkin lymphoma (HL) is known to have dual age distribution. Around two–thirds of HL patients are younger individuals of working age, while the remaining one–third are older adults over the age of 55 [1]. Worldwide in 2022, HL occupied the 26th rank in cancer incidence among other cancer types with approximately 82,409 new cases. Males had higher incidence by affecting 48,753 cases. For females, the number of cases reached 33,656 [2]. According to the WHO estimated cancer incidence for countries, HL occupied the 17th rank among cancer types in Egypt with 1684 new cases [3]. Between 24% and 39% of patients with advanced HL demonstrate refractory

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disease or relapse after initial ABVD therapy [4]. BV is an antibody–drug conjugate that selectively targets CD30 expressed on Reed–Sternberg cells. This drug, when combined with AVD, has shown a superior outcome as relative to ABVD in newly diagnosed individuals with advanced cHL [5].

The primary objective of this study was to compare progression–free survival (PFS) between Egyptian patients receiving BV+AVD and those receiving ABVD as first–line therapy for advanced cHL. Secondary objectives included the complete metabolic response (CMR) rate assessed by positron emission tomography (PET) after two cycles, overall response rate (ORR) at the end of treatment, and overall survival (OS) at two years. Safety endpoints involved evaluation of treatment–emergent adverse events from the administration of the first dose until 30 days following completion of frontline therapy

Patients and methods:

This is a randomized open label prospective clinical study which encompassed 60 participants with advanced stage cHL and was carried out at clinical oncology department, Helwan university hospitals from March 2023 to February 2025. The inclusion creiteria were patients between 18 and 60 years. 2) ECOG performance status ≤ 2. Diagnosed with cHL in accordance with the most recent World Health Organization (WHO) classification. CD30 positive by immunohistochemistry. Stage III or IV HL by Ann Arbor classification system. Treatment–naïve.

Approval was obtained from the ethical committee of the faculty of medicine at Helwan University. The Declaration of Helsinki, the international Medical Association's guideline of ethics for studies involving humans, was adhered to throughout the conduct of this study. Informed consent was obtained from the study participants, addressing risks, benefits, compensation, and withdrawal rights. Research involving the analysis of data from existing samples or documents, provided either without identifiers or not containing private information, was coded and kept in department files. In our study, we protected patients' privacy with an adequate level of confidentiality. Participants were informed by the results of our study. This study was registered at clinical trial.gov (ID: NCT07171827).

The exclusion criteria included: nodular lymphocyte–predominant HL and non–Hodgkin lymphoma. Cerebral/meningeal disease. Prior treatment with chemotherapy, radiotherapy, or any immunotherapy within 12 weeks of randomization. Individuals with a known human immunodeficiency virus (HIV) infection, positive hepatitis B surface antigen, or active hepatitis C infection were excluded. Known organ failure.

Study Procedure:

All enrolled patients with Histopathologic confirmation of classical Hodgkin disease underwent baseline: Full labs including CBC, LDH (U/L), serum Albumin (g/L), Liver enzymes, Renal function tests and virology lab, pulmonary function test, echocardiography and whole–body FDG–PET/CT scan. The patients were subsequently randomized into two treatment arms. In Arm A, patients received the ABVD regimen, consisting of Doxorubicin (25 mg/m²), Bleomycin (10 units/m²), Vinblastine (6 mg/m²), and Dacarbazine (375 mg/m²) administered via intravenous infusion on Days 1 and 15 of each 28–day cycle. In Arm B, patients received the BV+AVD regimen, comprising BV (1.2 mg/kg), Doxorubicin (25 mg/m²), Vinblastine (6 mg/m²), and Dacarbazine (375 mg/m²) administered intravenously on Days 1 and 15 of each 28–day cycle.

PET/CT reassessment was performed after two cycles, and treatment continued up to a total of six cycles. Patients achieving a complete response (CR) on PET/CT after cycle six were followed up with PET/CT evaluations at three months and subsequently every six months for two years. Outcomes assessed included PFS, PET, CMR rate at cycle two, ORR at the end of treatment, and two–year OS.

Patients who did not achieve CR underwent re–biopsy and received second–line chemotherapy, with additional lines of therapy administered as indicated to achieve CR, followed by consideration for bone marrow transplantation. Treatment–related toxicity was evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI–CTCAE), version 4.03.

Randomization method:

Simple Randomization with overall ratio 1:1 to BV+AVD or ABVD without blinding was followed. Prior to dosing, a randomization number was assigned to each patient. Study specific identifiers including treatment arm, protocol name and date of randomization were generated and recorded for each patient.

Statistical analysis of the data

Data collected from historical records, clinical examinations, laboratory investigations, imaging studies, and treatment outcomes were coded, entered, and initially analyzed via Microsoft Excel. Subsequently, the data were imported into the Statistical Package for the Social Sciences (SPSS, version 26.0) for further analysis. Qualitative variables were shown as frequencies and percentages, whereas quantitative variables were summarized using range (minimum and maximum), mean, standard deviation (SD), median, and interquartile range (IQR).

Associations and differences in qualitative variables were assessed via the Chi–square test (χ^2). Differences between independent quantitative groups were evaluated using the independent t–test, and paired measurements were compared using the paired t–test. Statistical significance was set at $p < 0.05$. The Shapiro–Wilk test was applied to assess the normality of data distribution.

Survival analyses were executed via Kaplan–Meier curves, and Cox regression analysis was performed for variables showing a significant relationship with PFS and OS. PFS was defined as the time from initiation of frontline therapy to disease relapse, progression, death, or last follow–up. OS was defined as the time from the start of frontline therapy to death or last follow–up. Patients alive at the end of the follow–up period were censored at their last follow–up date.

Results:

In this study, 60 patients met the eligibility criteria and accepted to participate. The participants were randomly allocated into two equal groups (30 patients in each). Patients in arm A received ABVD while patients in arm B received BV+ AVD.

The baseline characteristics of the study population. Patients were generally well balanced between the two treatment arms. There were no statistically significant differences in gender, age, weight, height, BMI, performance status, histopathologic subtype, disease stage, presence of B symptoms, family history, nodal involvement, or extra–lymphatic disease. **Table 1**

Interim PET/CT response rates following 2 treatment cycles in both arms and the combined patient cohort. Although the BV+AVD arm exhibited a higher CMR rate of 83.3% compared to 76.6% in the ABVD arm, this difference was not statistically significant ($p = 0.817$). CMR was defined as PET negativity after 2 cycles. Overall, 80% of patients achieved CMR, indicating a favorable early metabolic response across both treatment groups. **Table 2**

Patients in Arm B who achieved a CMR had the highest mean progression–free survival (21.00 months), with 88.0% survival at 1 year and 84.0% at the end of the study, followed by those who achieved CMR in Arm A. Patients in Arm A who did not achieve CMR had the lowest progression–free survival by the end of the study. Although the BV+AVD group with a complete metabolic response showed a trend toward better outcomes, the difference was not statistically significant ($p = 0.122$). **Table 3**

The toxicity profiles of both treatment arms, showed a significantly higher incidence of fatigue in the BV+AVD arm, as reported by physicians using CTCAE criteria. Although neutropenia and neuropathy rates were also higher in the BV+AVD arm, these differences were not statistically significant. Conversely, pulmonary toxicity was more frequent in the ABVD arm, but this difference did not reach statistical significance. Treatment duration was longer in the BV+AVD arm compared to the ABVD arm, while the incidence of anemia was similar between the two groups. **Table 4**

Arm A (ABVD) experienced one event (death), while Arm B (BV+AVD) had no events. Median survival has not been reached in either group because the survival curves have not fallen below 50%.

The significant superior performance of arm B (BV+AVD). compared to arm A (ABVD) in terms of both reducing the number of progression events and extending the duration of progression–free survival. **Table 5**

The comparison of ORR of two treatment arms. The data shows that the BV+AVD arm had a higher overall response rate (83.3%) compared to the ABVD arm (63.6%) however no statistically significant difference. **Table 6**

Discussion

Following frontline treatment with ABVD Duggan et al., [4] reported that about one third of participants with advanced cHL will become refractory or manifest relapse. Straus et al., [5] found that the strong expression of CD30 on the tumor cell surface is an attractive therapeutic target that would maximize efficacy and minimize toxicity of initial therapy among those patients.

In this study, we aimed to evaluate the efficacy of BV, an anti–CD30 agent, as part of first–line therapy for advanced–stage Hodgkin lymphoma. A total of 60 patients were included, with ages ranging from 18 to 39 years and a median age of 26 years (interquartile range: 21–29 years).

In this study, BV+AVD showed significantly superior PFS achieved at 1 year (84% in BV+AVD arm relative to 65% in ABVD arm. The PFS benefit was maintained in BV+AVD arm with 80% vs. 53.3% in ABVD at the end of the study at 2 years (p=0.032). The PFS achieved in our study at 1year in BV+AVD arm was less than that was reached by Steiner et al., [6] after offering BV+AVD to 41 participants with stage III and IV. They documented 96 % PFS at 1 year. In the same way, the 2–year PFS in our study is different from that documented by Ramchandren et al., [7] as they included 497 patients treated with BV+AVD (n = 250) and ABVD (n = 247). The 2–year PFS was 84.3% in the BV+AVD arm while it was higher than what we reached in ABVD am (73.7%). The variations in PFS from other studies could be related to differences in numbers and criteria of the enrolled patients.

	Total (n = 60)		Arm A (ABVD) (n = 30)		Arm B (BV+ AVD) (n = 30)	
	No.	%	No.	%	No.	%
Sex						
Male	35	58.3	17	56.7	18	60.0
Female	25	41.7	13	43.3	12	40.0
Age (years)						
Min. – Max.	18.0 – 39.0		18.0 – 39.0		19.0 – 36.0	
Mean ± SD.	25.92 ± 5.42		24.80 ± 6.02		27.03 ± 4.57	
Median (IQR)	26.0 (21.0 – 29.0)		22.0 (20.0 – 29.0)		26.50 (24.0 – 30.0)	
Weight (kg)						
Min. – Max.	56.0 – 95.0		56.0 – 95.0		57.0 – 95.0	
Mean ± SD.	75.83 ± 10.35		78.20 ± 9.76		73.47 ± 10.55	
Median (IQR)	76.50 (68.0 – 84.5)		79.0 (72.0 – 85.0)		10.55 (67.0 – 83.0)	
Height (cm)						
Min. – Max.	157.0 – 186.0		157.0 – 186.0		158.0 – 183.0	
Mean ± SD.	169.9 ± 8.01		169.8 ± 8.39		169.9 ± 7.75	
Median (IQR)	168.5 (163.0 – 177.0)		169.0 (163.0 – 176.0)		168.5 (163.0 – 178.0)	
BMI (kg/m^2)						
Min. – Max.	19.84 – 32.39		19.84 – 32.39		20.90 – 29.34	
Mean ± SD.	26.23 ± 2.70		27.09 ± 2.63		25.37 ± 2.54	
Median (IQR)	26.02 (24.7 – 28.3)		26.85 (25.5 – 29.0)		25.48 (23.4 – 27.4)	
ECOG						
0	26	43.3	15	50.0	11	36.7
1	30	50.0	13	43.3	17	56.7
2	4	6.7	2	6.7	2	6.7
Histopathology (HP) type						
Nodular sclerosis	44	73.3	21	70.0	23	76.7
Mixed cellularity	13	21.7	7	23.3	6	20.0
Lymphocyte predominant	3	5.0	2	6.7	1	3.3
Lymphocyte depleted	0	0.0	0	0.0	0	0.0
PET/CT stage						
Stage III	33	55.0	16	53.3	17	56.7
Stage IV	27	45.0	14	46.7	13	43.3
IPS ≤2	38	63.3	20	66.6	18	60.0
≥3	22	36.7	10	33.3	12	40.0
B symptoms	28	46.7	12	40.0	16	53.3
Family history	3	5.0	1	3.3	2	6.7
Progression	20	33.3	14	46.7	6	20.0
Died	1	1.7	1	3.3	0	0.0

Table 1: Distribution of the studied cases according to patient characteristics in total and separately in each arm

IQR: Inter quartile range. SD: Standard deviation

	ABVD (n = 30) (%)	BV+AVD (n = 30) (%)	Total arm (n = 60) (%)	χ^2	P
PETCT after 2 cycles					
CMR	23 (76.6)	25 (83.3)	48 (80)	0.418	0.817
Incomplete metabolic response	7 (23.3)	5 (16.6)	12 (20)		

Table 2: PET/CT response after 2 cycles in each arm and total patients

PETCT response	Mean	% 1 year	% End of study	Log rank	
				χ^2	p
ABVD, (+1)	17.91	69.6%	57.2%	5.787	0.122
BV+AVD, (+1)	21.00	88.0%	84.0%		
ABVD, (+2)	17.14	57.1%	52.1%		
BV+AVD, (+2)	17.40	60.0%	60.0%		

Table 3: Kaplan–Meier survival table for PFS in both arms with interim PETCT CMR(+1) or inCMR(+2)

+1 complete metabolic response. +2 incomplete metabolic response.

In this study interim PET/CT response was evaluated; twenty–five (83.3%) patients in BV+AVD arm who attained CMR by interim PETCT after 2 cycles group showed better PFS rates at both 1–year (88.0%) and at the end of the study (84.0%) compared to 23 (76.6%) patients in ABVD arm who achieved CMR by interim PETCT (69.6%) PFS at 1 year and 57.2% at the end of the study). There was also PFS benefit in patients who had residual metabolic activity in BV+AVD arm (60%) at 1 year and was maintained till the end of the study vs (57%) at 1 year and (52%) at the end of the study for those with in CMR in with incomplete metabolic response in ABVD arm. This is matched with the 3–year follow–up of Straus et al., [5] has shown 83.1% PFS for interim PET with CMR in BV+AVD arm vs 76.0% for

	Total (n = 60)		Arm A (ABVD) (n = 30)		Arm B (BV+ AVD) (n = 30)		Test of Sig.	p
	No.	%	No.	%	No.	%		
Anaemia								
No	43	71.7	22	73.3	21	70.0	χ^2= 0.082	0.774
Yes	17	28.3	8	26.7	9	30.0		
Neutropenia								
No	30	50.0	18	60.0	12	40.0	χ^2= 2.817	0.421
Grade 1	19	31.7	8	26.7	11	36.7		
Grade 2	7	11.7	3	10.0	4	13.3		
Grade 3	4	6.7	1	3.3	3	10.0		
Thrombocytopenia								
No	55	91.7	28	93.3	27	90.0	χ^2= 0.2182	0.64
Yes	5	8.3	2	6.7	3	10.0		
Neuropathy								
No	42	70.0	25	83.3	17	56.7	χ^2= 6.142	0.105
Grade 1	11	18.3	4	13.3	7	23.3		
Grade 2	5	8.3	1	3.3	4	13.3		
Grade 3	2	3.3	0	0.0	2	6.7		
Pulmonary toxicity								
No	51	85.0	23	76.7	28	93.3	χ^2= 3.268	^{FE}p= 0.145
Yes	9	15.0	7	23.3	2	6.7		

Table 4: Comparison between the two studied groups according to toxicity and duration of treatment

IQR: Inter quartile range. SD: Standard deviation. t: t–test χ^2: Chi square test. FE: Fisher Exact test. p: p value for comparing between the two studied groups. *: Statistically significant at $p \leq 0.05$

	Total No.	No. of Events	Mean	% End of study	Log rank	
					χ^2	p
OS						
Arm A (ABVD)	30	1	23.77	96.7%	1.000	0.317
Arm B (BV+ AVD)	30	0	24.0	100.0%		
PFS						
Arm A (ABVD)	30	14	17.73	53.3%	4.578	0.032*
Arm B (BV+ AVD)	30	6	21.10	80.0%		

Table 5: Kaplan–Meier survival table for OS and PFS in each arm

χ^2: Chi square test. FE: Fisher Exact test. *: Statistically significant at $p \leq 0.05$.

	Patients who responded	Total patients	ORR	Odds	χ^2	^{FE}p
BV+AVD	25	30	83.3%	5	2.9	0.143
ABVD	19	30	63.6%	1.72		

Table 6: ORR to the treatment line given to each group

χ^2: Chi square test. FE: Fisher Exact test.

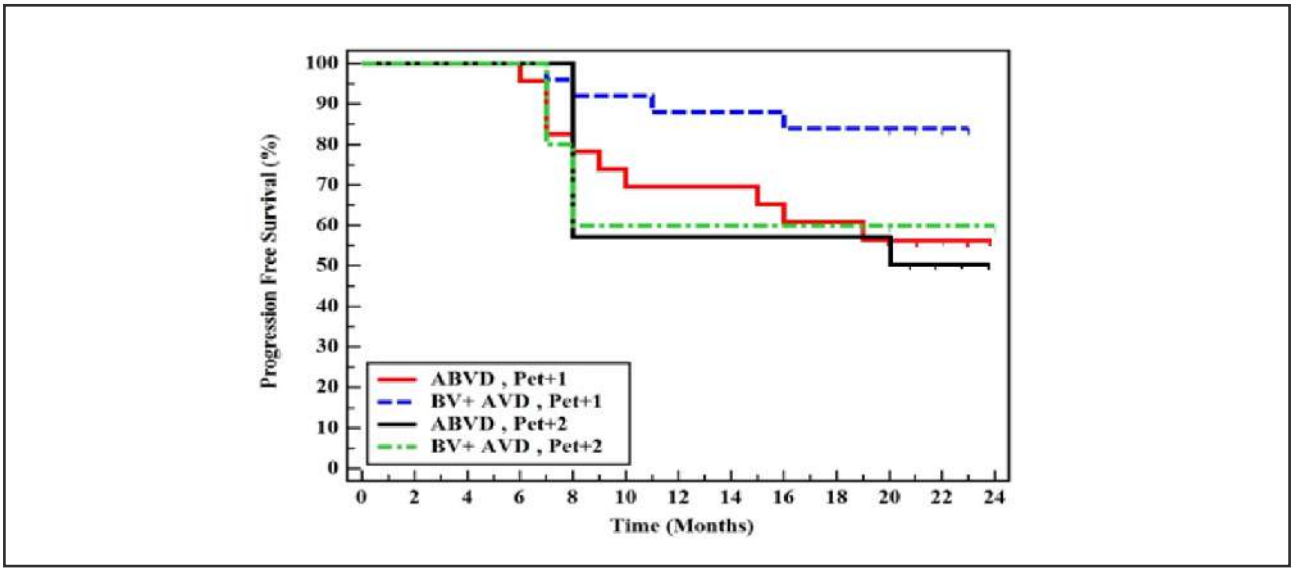


Figure 1: Kaplan–Meier survival curve for PFS in both arms with interim PETCT CMR(+1) or inCMR(+2)

ABVD arm. A trend with favorable impact on participants with interim PET residual treated with BV+AVD was also noted, with a 3–year PFS of 69.2% vs 54.7% with ABVD. In the same way another PET–guided treatment study by Lynch & Advani [8] 519 patients with advanced cHL were treated by ABVD. PFS at 3 years was 67.5% for interim PET residual metabolic activity patients compared to a PFS of 81% for interim PET CMR patients.

On the other hand Romano et al., [9] had a retrospective study executed at a single institution in newly diagnosed patients with HL treated upfront using an interim PET–based risk–adapted approach, those with PET–positive results were escalated from the ABVD regimen to the BEACOPP regimen.. This group of patients had 5–year PFS of 40.1% . So, the added toxicity was not translated into better survival. In another study Herrera et al., [10] assessed the effect of adding Nivolumab (N) to AVD vs BV+AVD in 976 eligible patients with advanced cHL. One–year PFS was higher (94%) in N+AVD vs 86% in BV+AVD. The results of studies built on upfront integration of targeted and immunotherapy in management of advanced HL are showing better outcome than only escalation of chemotherapy combinations.

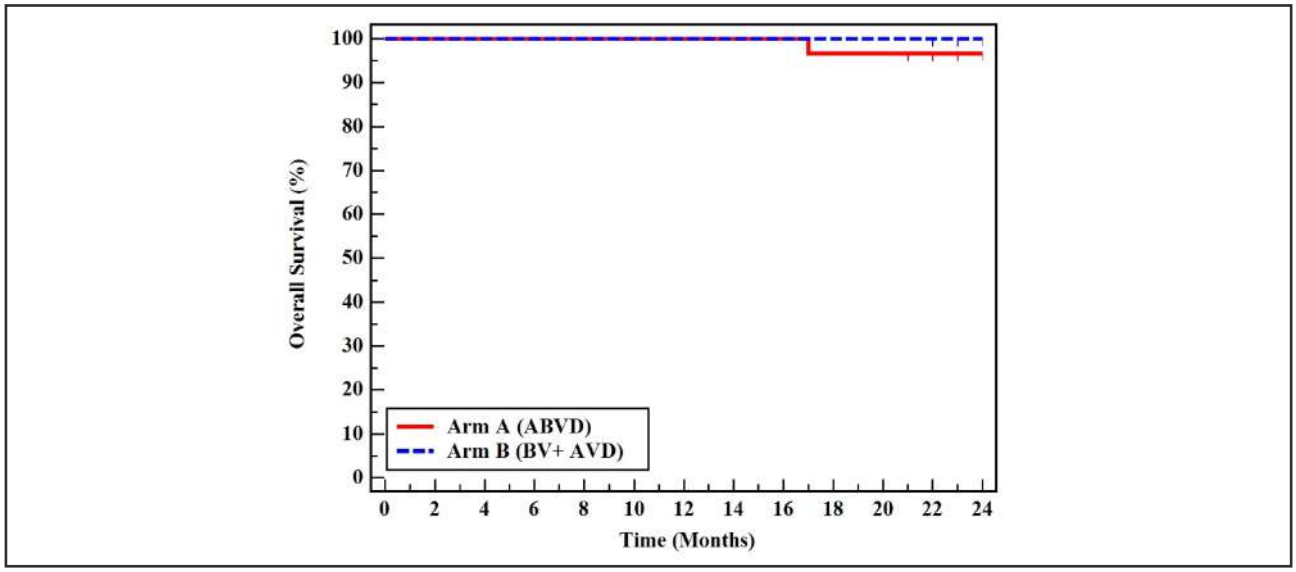


Figure 2: Kaplan–Meier survival curve for OS in both arms

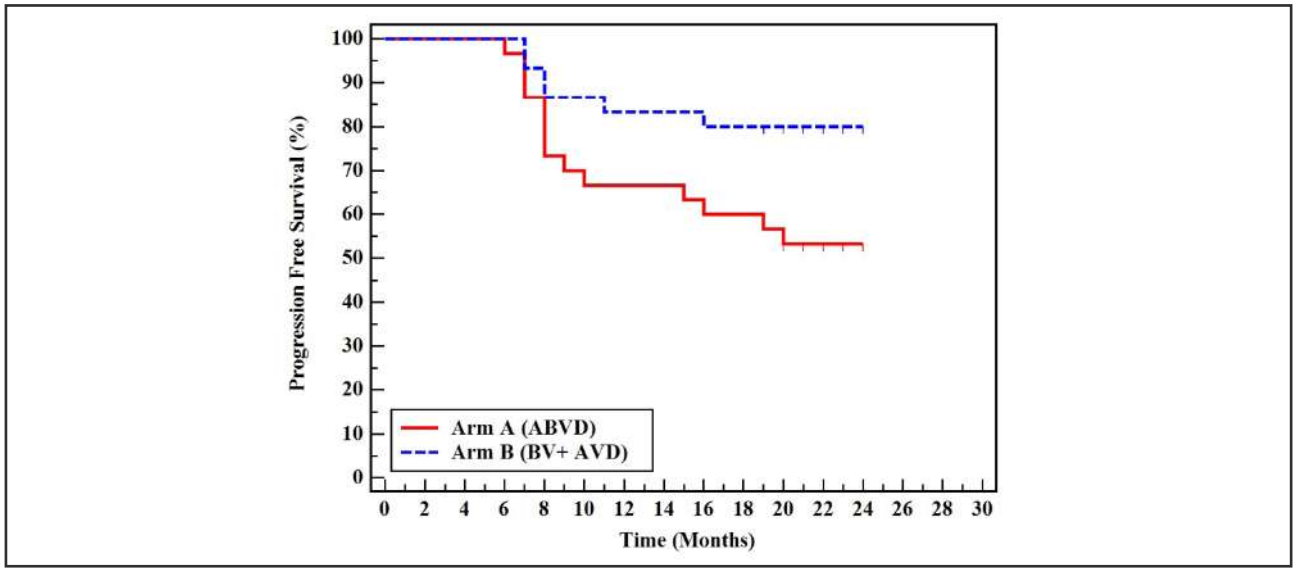


Figure 3: Kaplan–Meier survival curve for PFS in each arm

In this study the ORR in arm BV+AVD arm was higher response rate (83.3%) compared to the ABVD arm (63.6%). This is less than that reached by Evens et al., [11] study encompassed 812 cases of advanced cHL. The ORR was 70% in ABVD arm. In a study by Bowers et al., [12] including a total of 153 newly diagnosed cHL participants who had 6 cycles of BV+ AVD. The ORR was 89%. This is slightly higher than what is achieved in our study. Similarly, Zhang et al., [13] reported a consistent ORR of 80% after studying BV+ AVD in treatment naïve Chinese population compared to 73% in patients treated with ABVD.

This study showed 96.7% OS in ABVD arm vs 100% in BV+AVD arm. One mortality was reported for a female patient who died at 17 months from the beginning of the study. The patient died with viral encephalitis following BMT.

Our results varied slightly from real–world analysis by Winter et al., [14] for upfront BV+AVD in advanced cHL, 2–year OS was 94.4%. In a different way, Straus et al., [5] study reported OS of 96 % after a median follow–up of two years in patients who were randomized to ABVD vs 97.3 % in BV+AVD arm. In this study treatment toxicity was compared between both arms; BV+AVD arm had a higher proportion of patients who developed neutropenia (60.0%) with 3 (10 %) of those patients had grade 3 compared to (40.0%) in ABVD arm with 1 (3.3%) patient had grade 3. These data are in line with that retrieved by Phillips et al., [15] from a real world prospective clinical study including 1002 participants with stage III and IV cHL treated with frontline BV+AVD vs ABVD. Sixty five percent of participants managed with BV+AVD developed all

grades neutropenia vs 44% of patients with cHL treated with ABVD. The results also had some variation from that reported by Ansell et al., [16], the occurrence of neutropenia was 58% in BV+AVD arm and 45% in ABVD arm.

In this study neuropathy levels showed a noticeable difference between the two groups. Thirteen (43.3 %) patients in BV+AVD arm had all grades of neuropathy including 2 patients with Grade 3 sensory peripheral neuropathy compared to 5 (16.7 %) patients in ABVD arm. The last patient reported achieving full recovery 6 months post–treatment during follow–up. The results in our study were lower than that reported by Connors et al., 2018 [17] who reported occurrence of peripheral neuropathy 60 % in BV+AVD arm and 43 % in ABVD arm. A higher rate of neuropathy was reported in a study by Bowers et al ., [12] including total of 153 patients with newly diagnosed cHL who received 6 cycles of BV + AVD. Peripheral neuropathy was diagnosed in 80% of them. Grade 1 neuropathy was observed in 39%, grade 2 in 31%, and grade 3 in 15 (10%).

Similarly, Zhang et al., [13] reported neuropathy as the most occurring toxicity with (50.0%) in patients receiving BV, however most of the cases had peripheral neuropathy which was moderate and reversible. Gibb et al., [18] prospectively studied BV monotherapy in old age patients with untreated cHL (median age 77 years). By the end of therapy over 50% of patients demonstrated peripheral neuropathy. This variation can be accounted for by the presence of older patients within these study populations, so prober selection of patients is needed to avoid more toxicity. In our study there was no statistically significant difference in pulmonary toxicity among the two groups. However, ABVD Arm has a slightly higher incidence of pulmonary toxicity in 7 patients compared to 2 patients in BV+AVD arm.

These results were in line with Ansell et al., [16] who documented the most notable toxicity in the ABVD arm was pulmonary toxicity, which occurred in 9 % in ABVD compared with 3% with BV+AVD. This finding is also supported by Evens et al., [11] study that compared the outcome of patients receiving ABVD vs bleomycin free Stanford V protocol. The incidence of pulmonary toxicity was 17% vs 0%, respectively. The results were also matched with a retrospective study by Andersen et al., [19] who reported that the prevalence of bleomycin–induced pulmonary toxicity was 8% in 412 participants managed with ABVD or BEACOPP in the interval from 1990–2014.

In the current study more patients in ABVD arm (14 patients) received subsequent lines of treatment compared to 6 patients in BV+AVD arm. BMT was also done for 7 patents in ABVD arm compared to 2 participants in BV+AVD arm. The higher percentages in the ABVD arm could point to a less effective initial treatment for advanced stage cHL. These results are also aligned with Ansell et al., [16] which reported a less frequent use of subsequent therapy in BV+AVD than with ABVD (in 135 of 662 participants vs. 157 of 659). Fewer autologous transplantations were also reported (in 44 vs. 59) respectively. BV, either as monotherapy or in combination with other agents, represented the most frequently administered subsequent therapy in the ABVD group, being used in 69 patients (10.5%). Immunotherapy was less commonly employed in the BV+AVD group compared with the ABVD group, with use reported in 18 patients (2.7%) versus 28 patients (4.2%), respectively. Similarly, Winter et al., [14] study included 167 participants who treated with frontline ABVD. Ninety–two (55.1%) of the participants had subsequent systemic therapy. Median time to next line of therapy was 10.5 months. A BV–based therapy was offered to 43.5% of those patients. Among all participants managed with frontline ABVD, 31.7% of patients underwent subsequent SCT.

Limitations of this study encompass that it is a single–center study with a relatively small sample size that reduces the statistical power and makes it challenging to detect rare side effects. The population of the study represents the young and middle age group of patients with cHL so the treatment effect on older population was not studied. The limited follow–up duration restricts further knowledge about late relapses or delayed toxicities.

Recommendations: Long–term data is needed to validate survival benefits in diverse populations. BV+AVD's cost may limit use in low–income countries, but reduced relapse rates would justify its cost–effectiveness.

Conclusion:

In conclusion, this study demonstrated that BV+AVD is an effective frontline management for Egyptian patients with advanced cHL, with superior PFS and ORR outcomes compared to ABVD. BV+AVD also showed a favorable toxicity profile, with manageable adverse events such as neuropathy and neutropenia compared to long lasting Bleomycin related to pulmonary toxicity. Further studies, including bigger number of participants with extended follow–up are required to confirm these results and assess long–term outcomes.

Strengths of this study encompass that it is a prospective randomised clinical study using the standard of care chemotherapy regimen vs newly FDA approved treatment protocol and the exclusion of participants with chronic diseases limited the effect of confounding factors which enhanced the validity of treatment response outcomes.

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