The efficacy and safety of BV-ICE salvage therapy for relapsed/refractory Hodgkin lymphoma: A single center

Ghid Amhaz,MD1, Ammar Zahreddine, MSN, RN2, Ali Bazarbachi,MD,PhD1, Iman Abou Dalle,MD1, Jean El Cheikh,MD1

1 Division of Hematology-Oncology, American University of Beirut Medical Center, Beirut, Lebanon

2 Department of Nursing, American University of Beirut Medical Center, Beirut, Lebanon

Abstract

Context: Autologous stem-cell transplantation (ASCT) is still considered the standard of care in relapsed/refractory (R/R) Hodgkin Lymphoma (HL). Despite the high remission rates, patients require salvage therapy prior to ASCT to achieve CR. Brentuximab-vedotin (BV) has been studied as maintenance therapy post ASCT, also is used as single agent after failure of at least two lines of chemotherapy or in combination with different chemotherapy protocols as a sequential agent or combined. Objective: The aim of this study is to evaluate the complete metabolic response post salvage BV-ICE in patients with R/R HL prior to ASCT. The secondary end-points would include progression free survival, overall survival, response rate and safety profile as well as the delay to platelets and neutrophils engraftment post ASCT. Methods: This is a retrospective study including patients with R/R HL treated and followed at the American University of Beirut Medical Center (AUBMC) between 2018 and 2021.Results: We identified 14 R/R HL patients, with a median age of 29.5 (23-54) years. 13 patients were of Nodular sclerosis (NS) subtype and 1 patient had mixed cellularity HL. All patients received ABVD as initial therapy. The median duration from diagnosis to relapse was 9.6 month (4.3 -66.7 months). Patients with R/R HL were divided into 3 categories 43% (n=6) primary refractory, 21% (n=3) relapsed within 3 to 12 month and 23% (n=5) relapsed after 12 month from initial therapy. Two (14%) patients received E-BEACOPP and 1 (7%) patient received DHAP as 1st salvage therapy. Those 3 (21%) received BV-ICE as second salvage and 11 (79%) received BV-ICE as 1st salvage. BV was given on day 1 with a dose of 1.8mg/kg intravenously (IV) , Etoposide 100 mg/m2 IV from day 1 to day 3 and Ifosfamide 5mg/m2 plus mesna 5 g/m² intravenously over 24 h on day 2 and carboplatin IV AUC5 on day 2 for 2 cycles every 21 days cycle. The median duration from relapse to BV-ICE initiation was 1 month (0-11 months). Response rate after 2 cycles of BV-ICE using PET-FDG showed 93 % (n=13) complete remission (CR) and 7% (n=1) partial response (PR). All 14 patients underwent single SCC after cycle 2 without the need to plexifor initiation and received 3rd BV-ICE cycle and went into ASCT using BEAM conditioning protocol. At day 100, 79% (n=11) had CR, 14% (n=2) PR, 7% (n=1) had progression. Median days to ANC engraftment was 9 days (8-18 days) and median days to platelets engraftment was 16.5 days (12-46 days). After a median follow up on 12.3 month (16.7-57.2 months) the overall survival (OS) was 100% and progression- free survival of 77% . 50% (n=7) had grade 3 anemia, 71.6% (n=10) had grade 3 thrombocytopenia, 35.8% (n=5)had grade 3 neutropenia and 71.6% (n=10) developed febrile neutropenia (FN) without any septic shock or the need for intensive care transfer. 2 patients (14.2%) had increase in their transaminases and 14.2% (n=2) developed grade 2 peripheral neuropathy where 1 patient (7%) developed grade 4 peripheral neuropathy with reversible symptoms. BV dose required reduction to 1.2 mg/kg in 2 patients and to 1.5 mg/kg in 1 patient due to grade 2-4 peripheral neuropathy. Conclusion: BV-ICE as first salvage in R/R HL showed high overall response rates of 100% to be translated into significant improvement in disease free survival with acceptable toxicity profile.

Background

- **HL is one of highly curable type of lymphoma with frontline chemotherapy where early stages can achieve a complete response rates of 85–90, where in those with advanced-stage disease the response rates range between 75 to 80%[1].**
- **Relapsed/refractory (R/R) cases can still be cured using combination chemotherapy to be followed by auto-stem cell transplant (ASCT) [1].**
- **In R/R cases what is crucial is the status of the diseases prior to ASCT which predicts the long-term remission post ASCT[1].**
- **Brentuximab-vedotin (BV) has been studied as maintenance therapy post ASCT, also it is used as single agent after failure of at least two lines of chemotherapy or in combination with different chemotherapy protocols as a sequential agent or combined[1].**

Objective

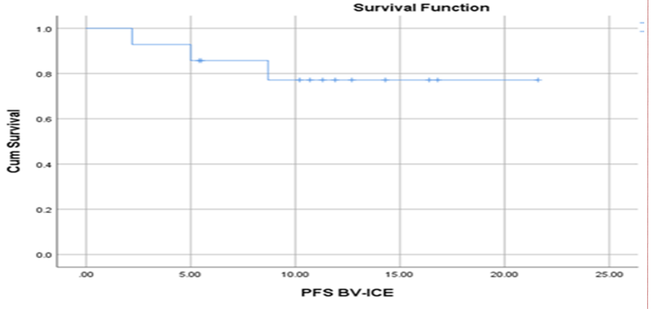
- **Evaluate the complete metabolic response post salvage BV-ICE in patients with R/R HL prior to ASCT**
- **Evaluate the progression free survival, overall survival rate, response rate and safety profile as well as the delay to platelets and neutrophils engraftment post ASCT**

Materials & Methods

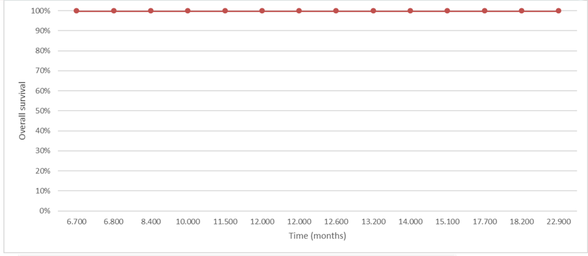
- **This is a retrospective study including all R/R HL treated at AUBMC from 2018-2020**

Results

Patient Characteristics	StudyPopulation (n=14)
Age	29.5 (23-54)
Sex	
Male	9 (64%)
Female	5 (36%)
Stage at Diagnosis	
I	1 (7%)
II	5 (36%)
III	5 (36%)
IV	3 (21%)
Stage on relapse	
I	0
II	8 (57%)
III	1 (7%)
IV	5(36%)
IPS-score on relapse	
0	2 (14%)
1	3 (21%)
2	5 (36%)
3	4 (29%)
4	0
>5	
Relapse Disease Characteristics	
B- symptoms	8 (57%)
Bone marrow involvement	3 (21%)
Bulky disease	6 (43%)
Median Duration from Diagnosis to Relapse	10.5 months (4-65)
Primary Therapy received	
ABVD	14 (100%)
Radiation therapy	3 (21%)
Response to frontline Therapy	
primary refractory	6 (43%)
relapse 3 to 12 month after treatment completion	3 (21%)
relapse after more than 12 month of treatment completion	5 (36%)
Subsequent therapies	
2nd line E-BEACOPP	2
2nd line DHAP	1
2nd line BV-ICE	11
3rd Line BV-ICE	3
Median Duration from Relapse to BV-ICE	30.8 (16.7-57.2) days
PET 2 after BV-ICE	
CR	13
PR	1
Duration from Last BV-ICE to SCT	1 month
Mozobil	0
No Of collection 1	14 (100%)
PBSC	
Collected	14.7 x10^6 (2.94-28.05x10^6)
Infused	10.96x10^6 (2.94- 14.02 x10^6)
ASCT	14 100%
Conditioning	
BEAM	14 (100%)
Median Follow up	30.8 (16.7-57.2)



Days to ANC engraftement	9 (8-18)
Days to platelets engraftement	16.5 (12-46)



Adverse events	n	%
Anemia		
No anemia		
Grade 1	1	7
Grade2	6	43
Grade 3	7	50
Neutropenia		
Grade 1	3	21.4
Grade2	3	21.4
Grade 3	5	35.8
Grade 4	3	21.4
Thrombocytopenia		
Grade 1	1	7
Grade 2	3	21.4
Grade 3	10	71.6
Grade 4	0	
Febrile Neutropenia	10	71.6
Sepsis/ICU Transfer	0	0
Increase in Liver enzymes	2	14.2
Peripheral neuropathy		
Non	7	50
Grade 1	4	28.8
Grade 2	2	14.2
Grade 3	0	
Grade 4	1	7
Reversible	1	7

Conclusion

BV in combination with ICE protocol showed promising results with fast and efficacious effects as salvage treatment for R/R Hodgkin lymphoma. Our results are similar to previously published data regarding the response rates and safety data, but it shows that we can reach the same target with one single dose of BV of 1.8 mg/kg.

References

Lynch, R. etal, Dose-dense Brentuximab Vedotin plus ICE second-line treatment of relapsed or refractory classical Hodgkin lymphoma: A Single centre, phase 1/2 study. *The Lancet Haematology*, 2021.