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DOES INTERIM PET ASSESSMENT AFTER TWO CYCLES OF TREATMENT WITH BRENTUXIMAB VEDOTIN STILL HAVE A PREDICTIVE VALUE IN HODGKIN LYMPHOMA?

Ravand Samaeekia MD MS[1,2], Joel M. Brothers MD[1], Hamid Mirshahidi MD[1], Mojtaba Akhtari MD[1]
1. Division of Hematology and Medical Oncology, Loma Linda University Medical Center, Loma Linda, CA, USA
2. Loma Linda Veterans Affairs Medical Center, Loma Linda, California

LOMA LINDA UNIVERSITY

INTRODUCTION

- An interim PET-CT scan after two cycles of chemotherapy (PET2) has become the standard of care in treatment of Hodgkin lymphoma (HL) due to its prognostic value and its utility in PET-adapted treatment protocols.
- Implementing a PET-guided approach can be challenging as it is costly, requires timely availability, may be affected by variability in scan interpretation, can have low negative and positive predictive values, and PET2-based escalation of treatment often increases the risk of acute and late toxicities.
- Since the incorporation of brentuximab vedotin (Bv) into frontline treatment, the value of PET2 imaging is uncertain.

AIM

Evaluate the predictive value of PET2 by reviewing frontline trials that incorporated Bv and reported interim PET data (between 12/2018 and 12/2022), as well as retrospective review of PET2 and end-of-treatment PET (EOT-PET) results of HL patients treated with BvAVD (i.e AAVD) in the same time period from Loma Linda University Cancer Center (LLUCC).

METHOD

- We performed a review of frontline trials that incorporated BV and reported interim PET data between 12/2018 and 12/2022.
- We also reviewed the PET2 and end-of-treatment PET (EOT-PET) results of HL patients treated with BvAVD (i.e AAVD) in the same time period from Loma Linda University Cancer Center (LLUCC).

RESULTS

- In the ECHELON-1, AHOD1331, and BREACH trials, the magnitude of benefit with Bv treatment in terms of either PFS or OS was significantly higher in both PET2-negative and PET-2 positive patients (Table 3).
- The ongoing ACCRU-LY study incorporating nivolumab and BV into frontline treatment reports a 97% rate of interim PET negativity with a 100% 2-year PFS.
- The review of LLUCC patients showed that among the 40 patients who received BvAVD, 24 patients were PET2 negative and 12 patients PET2 positive (Table 2).
- All the PET2 negative patients had a negative EOT-PET indicating no progression in cancer. Four out of 12 PET2 positive patients had a positive EOT-PET.
- The results of PET2 scans did not have any meaningful impact on management of patients as only 1 patient had a change in chemotherapy regimen after PET2 among all 40 patients who initially started on BvAVD.
- There were no differences between the outcomes of PET2 positive patients who had negative EOT-PET compared to PET2 negative patients as all the 24 patients with negative PET2 as well as all the 8 patients with positive PET2 and negative EOT-PET remained in complete remission at the end of treatment.

Table 1: Patient Demographic and Clinical Characteristics

Characteristic	BvAVD
Total patients — no.	40
Male sex — no. (%)	19 (48)
Age — yr	
Median	22
Range	11 - 83
Age categories — no. (%)	
≤ 21	17
22-45	18
> 45	5
Ethnicity	
Hispanic	17
Non Hispanic white	18
Non Hispanic black	5
Ann Arbor stage at initial diagnosis — no. (%)	
Stage II	11 (28)
Stage III	15 (37)
Stage IV	14 (35)
International Prognostic Score — no. (%)	
Low (0-2)	19
High (3-7)	21
ECOG performance status — no. (%) Adults	
0-1	15 (68)
1-2	6 (27)
>2	1 (5)
Extranodal involvement at diagnosis — no. (%)	
Yes	26 (65)
1 extranodal site	16
>1 extranodal site	10
No	14
Patients with any B symptom — no. (%)	24 (60)

Table 2: Summary of Response

Measure	BvAVD
Median follow up (range) in months	14 (6 - 43)
≥ 22 yr	14 (6 - 43)
≤ 21 yr	21 (6 - 36)
Death — no./total no. (%)	2 / 40
≥ 22 yr	2 / 23
≤ 21 yr	0 / 17
Deauville score at PET2 (%)	
Available	36 (90)
Unavailable	4
0-3 (PET positive)	24 (66)
≥ 22 yr	14
≤ 21 yr	10
> 3 (PET negative)	12 (34)
≥ 22 yr	6
≤ 21 yr	6
Deauville score at EOT PET (%)	
Available	33 (83)
Unavailable	7
0-3	29 (88)
≥ 22 yr	13
≤ 21 yr	15
> 3	4 (12)
≥ 22 yr	2
≤ 21 yr	2
Complete response at end of frontline therapy (%)	32 (80)
≥ 22 yr	17 (77)
≤ 21 yr	15 (83)

Table 3. Summary of clinical trials

Trial Name	Population	Trial Design	Interim PET negative	Outcome
ECHELON-1	Adult HL, Stage III/IV	BV+AVD (n=664) v. ABVD (n=670), 6 cycles	89 v. 86%	6-year PFS: PET2 negative 85.0% vs 78.1%; HR 0.66 PET2 positive 62% vs 46%; HR 0.70
AHOD1331	Pediatric HL, Stage IIB (bulky)-IV	BV+AVE-PC (n=298) v. ABVE-PC (n=289) 5 cycles	82 v. 81%	3-year EFS: PET2 negative: 92.3% vs 85.7%; HR 0.48 PET2 positive: 90.7% vs 68.3%; HR 0.28
BREACH	Adult HL, early stage unfavorable	BV+AVD x4 cycles (n=113) v. ABVD x 4 cycles (n=57) followed by 30 Gy ISRT	82 v. 75%	2-year PFS: PET2 negative: 97.8% v. 97.7% PET2 positive: 93.8% v. 71.6%
ACCRU-LY1601	Adult HL, early stage, non-bulky	BV-AVD x3 cycles followed by nivo x8 cycles if PET negative (single arm, n=75)	97% (PET3)	N/A

CONCLUSIONS

Incorporation of brentuximab into frontline treatment results in superior efficacy regardless of PET2 results. Our data along with previous studies point to the **loss of predictive value and therefore redundancy of an interim PET2 scan**, providing evidence for safe omission of PET2 in treatment regimens containing BV.

REFERENCES

- ECHELON-1 trial: N Engl J Med 2018; 378:331-344 DOI: 10.1056/NEJMoa1708984
- AHOD1331 trial: N Engl J Med 2022; 387:1649-1660 DOI: 10.1056/NEJMoa2206660
- BREACH trial: Journal of Clinical Oncology 41, no. 2 (January 10, 2023) 327-335. DOI: 10.1200/JCO.21.01281
- ACCRU-LY1601 trial: Blood 2022; 140 (Supplement 1): 1751–1752. doi: https://doi.org/10.1182/blood-2022-159258

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CONTACT INFORMATION

Ravand Samaeekia MD. MS.
Rsamaeekia@llu.edu
Ravand.Samaeekia@va.gov
@RavandSK