Efficacy of Brentuximab Vedotin Combination Treatment in Patients With Relapsed or Refractory Diffuse Large B-Cell Lymphoma With CD30 <1% Expression

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Objective

To examine whether the presence of trace amounts of CD30 staining are necessary for patients with CD30 expression <1% to derive clinical benefit from brentuximab vedotin (BV) + lenalidomide (Len) + rituximab (R)

Conclusions

- Results from this updated analysis indicate that visible CD30 detection by IHC (<1% vs no staining) is not required for response to BV + Len + R in patients with relapsed or refractory DLBCL
- Treatment with BV + Len + R showed efficacy benefit compared with placebo + Len + R regardless of CD30 expression level, including in patients with no visible CD30 IHC staining
- These results are consistent with those from the overall ECHELON-3 study population

Background

- BV is a CD30-directed antibody-drug conjugate approved for the treatment of patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) in combination with Len and R[1]
  - DLBCLs have variable expression of CD30[2]
- In the phase 3 ECHELON-3 study (NCT04404283), BV + Len + R showed statistically significant overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) benefits vs placebo + Len + R in patients with relapsed or refractory DLBCL[3]
  - This study showed that BV + Len + R provided clinical benefit regardless of CD30 expression level (≥1% or <1%)
- We hypothesize that BV may exert antitumor activity in patients whose CD30 expression is undetectable by immunohistochemistry (IHC)

Methods

- In the ECHELON-3 study, patients with relapsed or refractory DLBCL were randomized 1:1 to receive BV + Len + R or placebo + Len + R
  - Primary endpoint was OS
  - Key secondary endpoints were PFS and ORR per Lugano 2014
  - CD30 expression was assessed by IHC by central and/or local testing
    - CD30 positivity was scored as the percentage of CD30-positive cells out of neoplastic cells or total lymphocytes, when neoplastic cells could not be distinguished
- In this updated analysis, patients with CD30 <1% staining by central laboratory IHC were further grouped into CD30 <1% without trace staining and CD30 <1% with trace staining
- Analyses described here are post hoc, and results are descriptive

Results

PATIENTS AND TRACE STAINING

- **Figure 1** shows the distribution of patients in both treatment arms with CD30 <1% without and with trace staining and representative IHC staining for these patients

EFFICACY

OS

- In patients with CD30 <1%, a greater OS benefit was observed with BV + Len + R vs placebo + Len + R (hazard ratio [HR], 0.57; 95% CI, 0.36-0.89) (**Figure 2**)
  - The OS benefit was maintained regardless of trace staining

PFS

- In patients with CD30 <1%, a greater PFS benefit was observed with BV + Len + R vs placebo + Len + R (HR, 0.53; 95% CI, 0.34-0.82) (**Figure 3**)
  - The PFS benefit was maintained regardless of trace staining

ORR

- In patients with CD30 <1%, the ORR was higher with BV + Len + R (60%) vs placebo + Len + R (35%) (**Figure 4**)
  - The ORR benefit was maintained regardless of trace staining

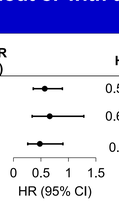
Figure 1. Representative CD30 IHC staining in patients without or with trace staining

	BV + Len + R (n=60)	Placebo + Len + R (n=63)	CD30 IHC Staining		
			H&E	CD30	Negative IgG Control
Patients without trace staining, n (%)	26 (43)	27 (43)			
Patients with trace staining, n (%)	34 (57)	36 (57)			

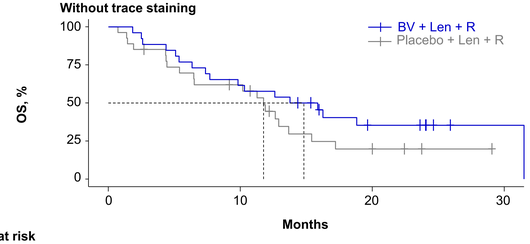
All images at 40× magnification. BV=brentuximab vedotin; H&E=hematoxylin and eosin; IgG=immunoglobulin G; IHC=immunohistochemistry; Len=lenalidomide; R=rituximab.

Figure 2. OS in CD30 <1% patients without or with trace staining

Patients with CD30 <1%	BV + Len + R OS, median (n/N)	Placebo + Len + R OS, median (n/N)	HR (95% CI)
Overall	13.8 mo (35/60)	6.9 mo (45/63)	0.57 (0.36-0.89)
Without trace staining	14.8 mo (17/26)	11.8 mo (19/27)	0.66 (0.34-1.28)
With trace staining	15.6 mo (18/34)	5.2 mo (26/36)	0.48 (0.26-0.9)

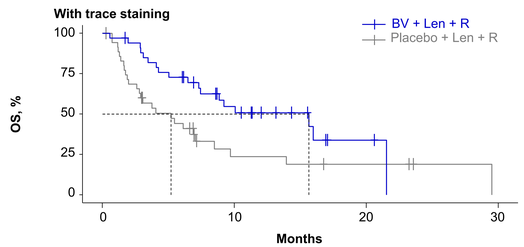


Without trace staining



No. at risk				
BV + Len + R	26	16	6	1
Placebo + Len + R	27	15	4	0

With trace staining

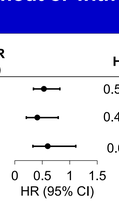


No. at risk				
BV + Len + R	34	14	2	0
Placebo + Len + R	36	5	3	0

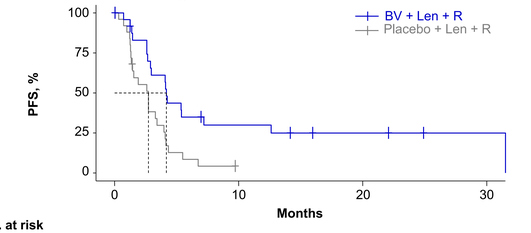
BV=brentuximab vedotin; HR=hazard ratio; Len=lenalidomide; OS=overall survival; R=rituximab.

Figure 3. PFS in CD30 <1% patients without or with trace staining

Patients with CD30 <1%	BV + Len + R OS, median (n/N)	Placebo + Len + R OS, median (n/N)	HR (95% CI)
Overall	4.1 mo (39/60)	1.9 mo (46/63)	0.53 (0.34-0.82)
Without trace staining	4.2 mo (18/26)	2.7 mo (23/27)	0.41 (0.21-0.79)
With trace staining	2.8 mo (21/34)	1.5 mo (23/36)	0.6 (0.33-1.11)

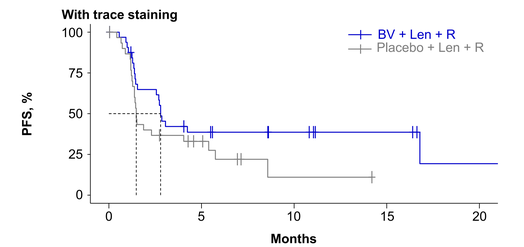


Without trace staining



No. at risk				
BV + Len + R	26	6	3	1
Placebo + Len + R	27	0	0	0

With trace staining



No. at risk					
BV + Len + R	34	11	7	4	1
Placebo + Len + R	36	7	1	0	0

BV=brentuximab vedotin; HR=hazard ratio; Len=lenalidomide; PFS=progression-free survival; R=rituximab.

Figure 4. ORR in CD30 <1% patients without or with trace staining

BV=brentuximab vedotin; Len=lenalidomide; ORR=objective response rate; R=rituximab.

Supplementary Materials

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