Abstract 4483

Outcomes in Older Patients With Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL) From the ECHELON-3 Study

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Conclusions

- Brentuximab vedotin (BV) + lenalidomide (Len) + rituximab (R) demonstrated a clinically meaningful improvement in all key efficacy outcomes in patients aged ≥65 years and patients aged ≥75 years
  - Overall survival (OS) was improved with BV+Len+R vs placebo+Len+R in both age groups
    - 15.9 vs 8.5 months (*P*=.0043) in patients aged ≥65 years
    - 21.5 vs 8.5 months (*P*=.0189) in patients aged ≥75 years
  - Progression-free survival (PFS) was also improved with BV+Len+R vs placebo+Len+R in both age groups
    - 5.7 vs 2.8 months (*P*=.0003) in patients aged ≥65 years
    - 7.1 vs 4.0 months (*P*=.0136) in patients aged ≥75 years
  - Complete response (CR) rate was consistent with the overall study results (40.2% in the BV+Len+R group and 18.6% in the placebo+Len+R group regardless of age) with response typically occurring at the first assessment (6 weeks)
- No clinically meaningful safety trends in patients aged ≥65 years and patients aged ≥75 years were identified
  - Differences in some safety endpoints are likely attributable to longer duration of treatment in the BV+Len+R group
- The results from these subgroup analyses show that BV+Len+R is a safe, tolerable, and efficacious regimen in elderly patients, including those who are ≥75 years of age

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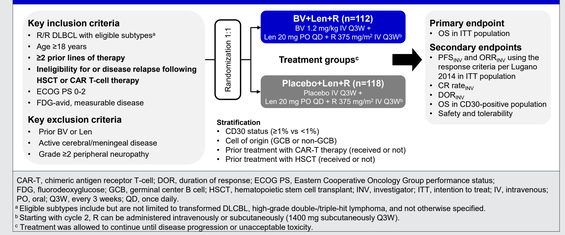
Background

- Age correlates with survival in patients with diffuse large B-cell lymphoma (DLBCL), which has a median age at diagnosis of 67 years[1,2]
- Recent therapeutic advances, including bispecifics and cell therapy, have promising efficacy, but safety and accessibility continue to be challenges for older patients
- BV is an antibody-drug conjugate targeting CD30[3] that is being evaluated in the randomized, global, phase 3 ECHELON-3 study (NCT04404283) of BV+Len+R vs placebo+Len+R in patients with relapsed/refractory (R/R) DLBCL after ≥2 prior systemic therapies who were ineligible for hematopoietic stem cell transplant and/or chimeric antigen receptor T-cell therapy[4]
- In ECHELON-3, BV+Len+R demonstrated a statistically significant improvement in OS, PFS, and objective response rate (ORR) vs placebo+Len+R[4]
- We present safety and efficacy in patients aged ≥65 years and patients aged ≥75 years

Methods

- The ECHELON-3 study design is summarized in **Figure 1**
- The data cutoff for this subgroup analysis, comprising patients aged ≥65 years and patients aged ≥75 years at baseline, was January 22, 2024
  - Statistical methods are similar to those presented previously,[4] with the exception that analyses are unstratified and *P* values are descriptive

Figure 1: ECHELON-3 study design



CAR-T, chimeric antigen receptor T-cell; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; GCB, germinal center B cell; HSCT, hematopoietic stem cell transplant; INV, investigator; ITT, intention to treat; IV, intravenous; PO, oral; Q3W, every 3 weeks; QD, once daily.
[a] Eligible subtypes include but are not limited to transformed DLCBL, high-grade double-/triple-hit lymphoma, and not otherwise specified.
[b] Starting with cycle 2, R can be administered intravenously or subcutaneously (1400 mg subcutaneously Q3W).
[c] Treatment was allowed to continue until disease progression or unacceptable toxicity.

Results

PATIENTS

- Between April 2021 and November 2023, 155 patients aged ≥65 years were randomized to BV+Len+R (n=79) or placebo+Len+R (n=76)
  - 86 of these patients were ≥75 years
- Patient demographics and baseline disease characteristics are shown in **Table 1** and **Table 2**, respectively

Table 1: Patient demographics

	Aged ≥65 years		Aged ≥75 years	
	BV+Len+R (n=79)	Placebo+Len+R (n=76)	BV+Len+R (n=48)	Placebo+Len+R (n=38)
Age, median (range), years	76 (65-87)	74.5 (65-89)	79 (75-87)	78.5 (75-89)
Age ≥80 years, n (%)	23 (29.1)	15 (19.7)	23 (47.9)	15 (39.5)
Male, n (%)	42 (53.2)	41 (53.9)	26 (54.2)	22 (57.9)
ECOG PS 2, n (%)[a]				
0	25 (31.6)	26 (34.2)	13 (27.1)	14 (36.8)
1	45 (57.0)	45 (59.2)	28 (58.3)	21 (55.3)
2	9 (11.4)	5 (6.6)	7 (14.6)	3 (7.9)
Race, n (%)				
White	51 (64.6)	40 (52.6)	28 (58.3)	21 (55.3)
Asian	14 (17.7)	16 (21.1)	12 (25.0)	7 (18.4)
Other/unknown/not reportable	14 (17.7)	20 (26.3)	8 (16.7)	10 (26.3)

[a] Values presented are the last nonmissing values on or before the first dose date. If a patient did not receive any dose, the randomization/enrollment date is used in place of the first dose date.

Table 2: Baseline disease characteristics

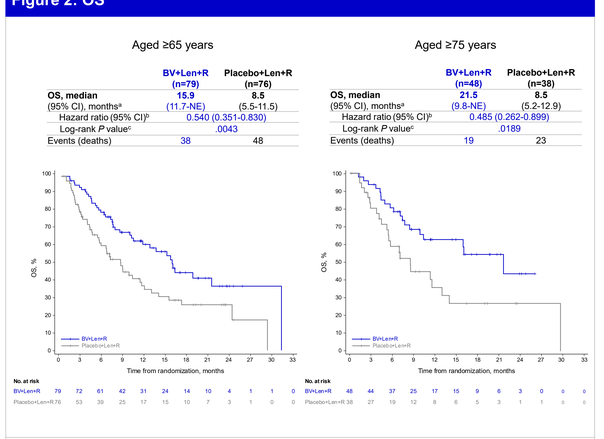
	Aged ≥65 years		Aged ≥75 years	
	BV+Len+R (n=79)	Placebo+Len+R (n=76)	BV+Len+R (n=48)	Placebo+Len+R (n=38)
Disease diagnosis, n (%)				
DLBCL NOS	63 (79.7)	57 (75.0)	38 (79.2)	28 (73.7)
Double-/triple-hit lymphoma[a]	9 (11.4)	8 (10.5)	6 (12.5)	4 (10.5)
Transformed DLBCL, n (%)	24 (30.4)	21 (27.6)	13 (27.1)	11 (28.9)
GCB cell origin, n (%)[b]	37 (46.8)	37 (48.7)	22 (45.8)	16 (42.1)
CD30 status, n (%)[c]				
≥1%	27 (34.2)	20 (26.3)	17 (35.4)	13 (34.2)
<1%	52 (65.8)	56 (73.7)	31 (64.6)	25 (65.8)
Extranodal disease involvement at study entry, n (%)				
No involvement	19 (24.1)	23 (30.3)	12 (25.0)	13 (34.2)
1 site	22 (27.8)	25 (32.9)	12 (25.0)	13 (34.2)
>1 site	38 (48.1)	28 (36.8)	24 (50.0)	12 (31.6)
Other disease characteristics, n (%)				
Ann Arbor stage III at study entry	13 (16.5)	23 (30.3)	8 (16.7)	13 (34.2)
Ann Arbor stage IV at study entry	46 (58.2)	37 (48.7)	27 (56.3)	18 (47.4)
IPI score ≥3 at time of enrollment	51 (64.6)	48 (63.2)	33 (68.8)	25 (65.8)
Primary refractory[d]	42 (53.2)	34 (44.7)	25 (52.1)	12 (31.6)
Refractory to last prior DLBCL therapy[d]	67 (84.8)	59 (77.6)	41 (85.4)	27 (71.1)
Prior CAR T-cell therapy, n (%)	17 (21.5)	17 (22.4)	5 (10.4)	4 (10.5)
Prior HSCT, n (%)	5 (6.3)	9 (11.8)	1 (2.1)	3 (7.9)
Time from initial DLBCL diagnosis to randomization, median (range), months	22.2 (3.3-169.5)	23.4 (3.6-218.7)	22.2 (4.2-169.5)	27.9 (6.5-218.7)
Elevated LDH at study entry, n (%)	45 (57.0)	48 (63.2)	26 (54.2)	25 (65.8)
Bulky disease at study entry, n (%)[e]	10 (12.7)	19 (25.0)	4 (8.3)	8 (21.1)

EBV, Epstein-Barr virus; IPI, International Prognostic Index; LDH, lactate dehydrogenase; NOS, not otherwise specified.
[a] High-grade B-cell lymphoma with translocations of MYC or BCL2 and/or BCL6.
[b] Based on post-randomization corrected values.
[c] CD30 status per central result. When central result is not available, local result is used.
[d] Refractory was defined as no response or a response lasting <6 months from the last treatment end date.
[e] Bulky disease is defined as ≥1 target lesion with longest diameter of >7.5 cm by investigator assessment.

EFFICACY

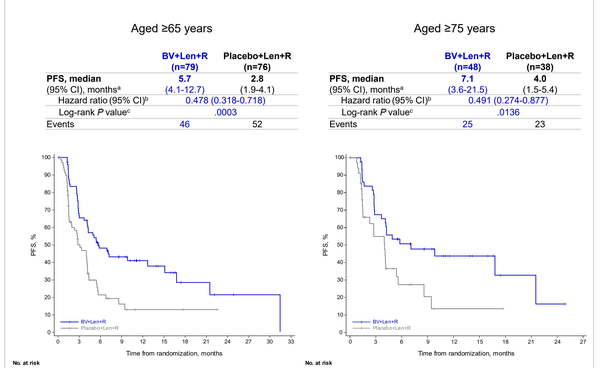
- OS and PFS were improved with BV+Len+R vs placebo+Len+R in both age groups (**Figure 2** and **Figure 3**)
- ORR and CR rates were greater with BV+Len+R vs placebo+Len+R (**Figure 4**)

Figure 2: OS



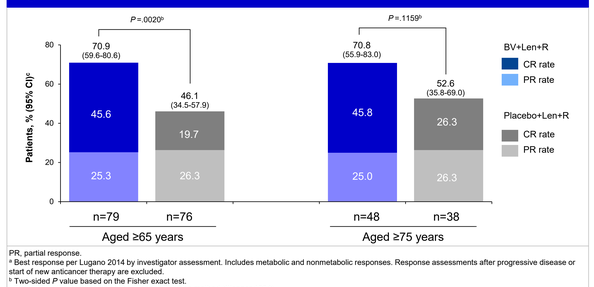
NE, not estimable.
[a] OS is time from randomization to death due to any cause. OS is estimated using the Kaplan-Meier method.
[b] Hazard ratio and 95% CI are based on an unstratified Cox regression model.
[c] Two-sided *P* value from an unstratified log-rank test.

Figure 3: PFS



[a] PFS is the time from randomization to the earliest occurrence of progressive disease per Lugano 2014 or death. PFS is estimated using the Kaplan-Meier method.
[b] Hazard ratio and 95% CI are based on an unstratified Cox regression model.
[c] Two-sided *P* value from an unstratified log-rank test.

Figure 4: ORR[a]



PR, partial response.
[a] Best response per Lugano 2014 by investigator assessment. Includes metabolic and nonmetabolic responses. Response assessments after progressive disease or start of new anticancer therapy are excluded.
[b] Two-sided *P* value based on the Fisher exact test.
[c] Exact 95% CI computed using the Clopper-Pearson method (Clopper 1934).

Table 3: Time to and duration of CR

	Aged ≥65 years		Aged ≥75 years	
	BV+Len+R (n=79)	Placebo+Len+R (n=76)	BV+Len+R (n=48)	Placebo+Len+R (n=37)
Time to CR, median (range), months	1.6 (1.2-7.3)	1.6 (0.7-4.6)	1.6 (1.2-7.3)	1.6 (0.7-4.2)
Duration of CR, median (95% CI), months[a]	18.9 (12.4-NE)	5.4 (2.8-NE)	18.9 (12.4-NE)	NE (1.4-NE)

[a] Calculated using the complementary log-log transformation method (Collett, 1994).

SAFETY

- The median duration of treatment and median number of cycles were greater with BV+Len+R vs placebo+Len+R in both age groups (**Table 4**)
- The percentage of patients with any treatment-emergent adverse event (TEAE) was similar between groups
- Serious TEAEs and TEAEs leading to death were reported more frequently in the BV+Len+R group than the placebo+Len+R group
- More patients discontinued study treatment due to TEAEs in the BV+Len+R group than the placebo+Len+R group
- The majority of peripheral neuropathy cases were grade 1

Table 4: Safety

	Aged ≥65 years		Aged ≥75 years	
	BV+Len+R (n=79)	Placebo+Len+R (n=75)	BV+Len+R (n=48)	Placebo+Len+R (n=37)
Treatment duration, median (range), months	4.4 (0.5-26.4)	2.1 (0.4-23.4)	4.5 (0.7-26.4)	2.1 (0.7-19.1)
No. of cycles, median (range)	5 (1-34)	3 (1-31)	6 (1-33)	3 (1-24)
Any dose modification, n (%)	63 (79.7)	44 (58.7)	39 (81.3)	22 (59.5)
Any dose modification due to AE, n (%)	63 (79.7)	40 (53.3)	39 (81.3)	19 (51.4)
Any BV/placebo dose modification due to AE	52 (65.8)	27 (36.0)	32 (66.7)	14 (37.8)
Any Len dose modification due to AE	60 (75.9)	38 (50.7)	37 (77.1)	18 (48.6)
Any TEAE, n (%)	77 (97.5)	74 (98.7)	46 (95.8)	37 (100)
Grade ≥3 TEAE, n (%)	70 (88.6)	57 (76.0)	41 (85.4)	28 (75.7)
Serious TEAE, n (%)	49 (62.0)	35 (46.7)	30 (62.5)	17 (45.9)
TEAE leading to death, n (%)	10 (12.7)	6 (8.0)	5 (10.4)	3 (8.1)
Discontinued all study Tx due to TEAE, n (%)	16 (20.3)	6 (8.0)	9 (18.8)	4 (10.8)
Any-grade peripheral neuropathy, n (%)[a]	31 (39.2)	20 (26.7)	17 (35.4)	10 (27.0)
Grade 1	17 (21.5)	13 (17.3)	10 (20.8)	5 (13.5)
Grade 2	8 (10.1)	7 (9.3)	2 (4.2)	5 (13.5)
Grade 3	6 (7.6)	0	5 (10.4)	0

AE, adverse event; TEAE, treatment-emergent adverse event; Tx, treatment.
[a] Based on the standardized MedDRA query, broad.