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ACALABRUTINIB ± OBINUTUZUMAB VS OBINUTUZUMAB + CHLORAMBUCIL IN TREATMENT-NAÏVE CHRONIC LYMPHOCYTIC LEUKEMIA: ELEVATE-TN 4-YEAR FOLLOW-UP

Topic: 06. Chronic lymphocytic leukemia and related disorders - Clinical

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Background: Early results from ELEVATE-TN (NCT02475681) at a median follow-up of 28.3 months demonstrated superior efficacy of acalabrutinib (A) ± obinutuzumab (O) compared with O + chlorambucil (Clb) in patients with treatment-naïve (TN) chronic lymphocytic leukemia (CLL) (Sharman et al. Lancet 2020;395:1278-91).

Aims: To report the updated efficacy and safety results from the ELEVATE-TN study after a median follow-up duration of 4 years.

Methods: Patients received A±O or O+Clb. Crossover to A monotherapy was permitted in patients who progressed on O+Clb. Investigator-assessed (INV) progression-free survival (PFS), INV overall response rate (ORR), overall survival (OS), and safety were evaluated. Informed consent was obtained from all patients prior to trial enrollment.

Results: A total of 535 patients (A+O, n=179; A, n=179; O+Clb, n=177) were randomized. The median patient age was 70 years; 63% of patients had unmutated IGHV and 9% had del(17p). At a median follow-up of 46.9 months (range, 0.0–59.4; data cutoff: Sept 11, 2020), the median PFS was not reached (NR) for A+O and A patients versus 27.8 months for O+Clb patients (both $P<0.0001$). In patients with unmutated IGHV, the median PFS was NR (A+O and A) versus 22.2 months among O+Clb patients (both $P<0.0001$). In patients with del(17p), the median PFS was NR (A+O and A) versus 17.7 months for O+Clb ($P<0.005$). Estimated 48-month PFS rates were 87% for A+O, 78% for A, and 25% for O+Clb. Median OS was NR in any treatment arm with a trend towards significance in the A+O group (A+O vs O+Clb, $P=0.0604$); estimated 48-month OS rates were 93% (A+O), 88% (A), and 88% (O+Clb). ORR was significantly higher with A+O (96.1%; 95% CI 92.1–98.1) versus O+Clb (82.5%; 95% CI 76.2–87.4; $P<0.0001$); ORR with A was 89.9% (95% CI 84.7–93.5; $P=0.035$ vs O+Clb). Complete response/complete response with incomplete hematologic recovery (CR/CRi) rates were higher with A+O (26.8%/3.9%) versus O+Clb (12.4%/0.6%); 10.6%/0.6% had CR/CRi with A. Common adverse events (AEs) and AEs of interest are shown in the Table. Overall treatment discontinuation rates were 25.1% (A+O), 30.7% (A), and 22.6% (O+Clb); the most common reasons were AEs (12.8%, 12.3%, 14.7%, respectively) and progressive disease (4.5%, 7.8%, 1.7%). Most patients (77.4%) completed O+Clb treatment.

Image:

	A+O (n=178)		A (n=179)		O+Clb (n=169)	
	Any grade	G≥3	Any grade	G≥3	Any grade	G≥3
Common AEs (in ≥30% of patients [any grade] in any group), n (%)						
Diarrhea	73 (41.0)	9 (5.1)	72 (40.2)	1 (0.6)	36 (21.3)	3 (1.8)
Headache	71 (39.9)	2 (1.1)	68 (38.0)	2 (1.1)	20 (11.8)	0
Neutropenia	60 (33.7)	55 (30.9)	22 (12.3)	20 (11.2)	76 (45.0)	70 (41.4)
Nausea	41 (23.0)	0	41 (22.9)	0	53 (31.4)	0
Infusion-related reaction	25 (14.0)	5 (2.8)	0	0	68 (40.2)	10 (5.9)
Selected AEs of interest, n (%)						
Bleeding	84 (47.2)	5 (2.8)	75 (41.9)	5 (2.8)	20 (11.8)	0
Hypertension	14 (7.9)	6 (3.4)	13 (7.3)	5 (2.8)	7 (4.1)	6 (3.6)
Atrial fibrillation	7 (3.9)	1 (0.6)	11 (6.1)	2 (1.1)	1 (0.6)	0

Summary/Conclusion: With a median follow-up of 46.9 months (~4 years) in the ELEVATE-TN study, the efficacy and safety of A+O and A monotherapy was maintained, with an increase in CR since the interim analysis (from 21% to 27% [A+O] and from 7% to 11% [A]) and low rates of discontinuation.

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