(S113) IMPROVING EFFICACY AND SAFETY OUTCOMES IN PATIENTS (PTS) WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA IN MORPHOLOGIC REMISSION TREATED WITH OBECABTAGENE AUTOLEUCEL (OBE-CEL)

Topic: 02. Acute lymphoblastic leukemia - Clinical

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Background

Low disease burden (<5% bone marrow [BM] blasts) prior to chimeric antigen receptor (CAR) T-cell therapy is associated with longer survival compared with high disease burden (≥5% BM blasts) in pts with relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL; Roddie et al, *NEJM* 2024). Obe-cel is an autologous, fast off-rate 4-1BB-ζ CD19-directed CAR T-cell therapy that demonstrated efficacy in adult R/R B-ALL in the Phase Ib/II FELIX study (NCT04404660). Characterization of the effect of bridging therapy (BT) and outcomes in pts based on morphologic response at the time of obe-cel infusion is required.

Aims

To report a post-hoc analysis characterizing long-term EFS and safety in adults with R/R B-ALL in FELIX by disease burden at both screening and lymphodepletion (LD) following BT.

Methods

All pts provided informed consent. Following leukapheresis, pts received BT at the discretion of the investigator to reduce BM blasts prior to LD. Disease burden was assessed at screening and within seven days prior to LD by local morphology. Following LD, obe-cel was administered using tumor burden-guided dosing to minimize immunotoxicities. EFS was analyzed using Kaplan-Meier methodology.

Results

Of 127 pts treated with obe-cel, ten (7.9%) had low disease burden at both screening and LD (Low/Low [LL]), nine (7.1%) had low disease burden at screening and high disease burden at LD (Low/High [LH]), 26 (20.5%) had high disease burden at screening and low disease burden at LD (High/Low [HL]), and 82 (64.6%) had high disease burden at both screening and LD (High/High [HH]). Overall, 118/127 (92.9%) pts received BT (**Fig. A**). Most (85.4%) pts in the HH group received BT containing chemotherapy; 38.5% of pts in the HL group received BT containing inotuzumab ozogamicin. At 32.8 months' median follow-up (range 19.9–52.8), median EFS (95% CI) was not yet reached in the LL, LH, and HL groups, and was 9.0 months (5.1–12.3) in the HH group (**Fig. B**). The 24-month EFS probabilities (95% CI) were 90.0% (47.3–98.5), 66.7% (28.2–87.8), 57.6% (35.3–74.7), and 29.3% (18.3–41.1) in the LL, LH, HL, and HH groups, respectively. At last follow-up, ≥50% of pts in the LL, LH, and HL groups and 20% of pts in the HH group, were in ongoing remission without additional anti-cancer therapies, excluding tyrosine kinase inhibitors. No pts in the LH group received post obe-cel stem-cell transplant (SCT); 40.0%, 11.5%, and 13.4% of pts in the LL, HL, and HH groups received post obe-cel SCT, respectively. Grade ≥3 cytokine release syndrome (CRS) incidence was 0% in the LL, LH, and HL groups, and 3.7% in the HH group. Grade ≥3 immune effector cell-associated neurotoxicity syndrome (ICANS) incidence was 0%, 11.1%, 0% and 9.8% in the LL, LH, HL, and HH groups, respectively. Incidence of any-grade CRS and ICANS was lower in pts with low disease burden, particularly those with low disease burden at LD, compared with pts with high disease burden.

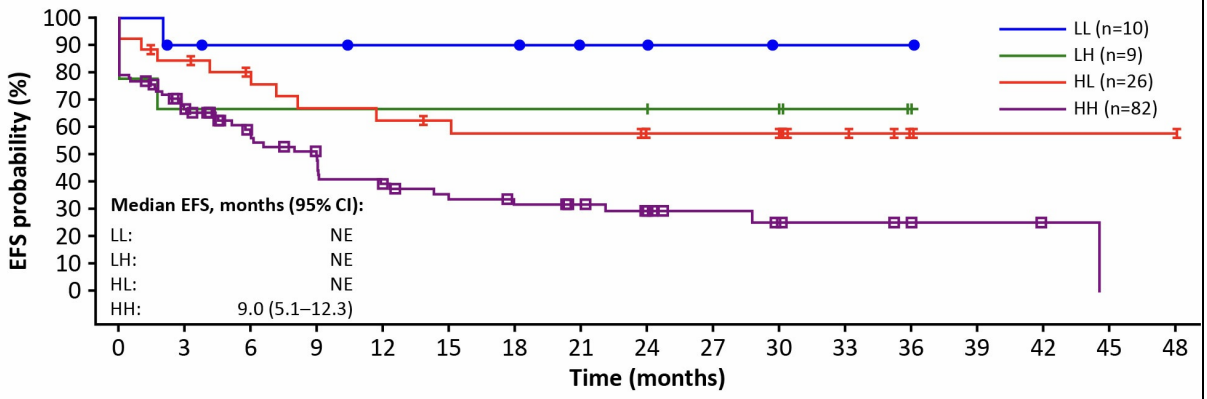
Summary/Conclusion

Obe-cel treatment demonstrated a therapeutic effect in pts regardless of disease burden at screening or LD. Comparable EFS and low incidence of CRS/ICANS were observed in pts who achieved low disease burden before or after BT. The greatest effect appeared to be in pts with low disease burden at both screening and LD. These data suggest that best outcomes are achieved with obe-cel when disease burden is low or can be effectively reduced. Outcomes in pts in the HH group may indicate high-risk biology or a need to further optimize their BT.

Figure A. Patient and disease characteristics by disease burden group

	LL (n=10)	LH (n=9)	HL (n=26)	HH (n=82)
Age in years, median (range)	34.5 (21–73)	43.0 (23–67)	42.5 (21–72)	50.5 (20–81)
BM blasts, median (range)				
Screening	0.5 (0–3)	1.6 (0–3)	53.6 (5–96)	64.5 (6–100)
LD	0.7 (0–3)	40.0 (5–96)	1.0 (0–5)	65.5 (5–100)
Bridging therapy received, n (%)	9 (90.0)	7 (77.8)	26 (100)	76 (92.7)
Chemotherapy	6 (60.0)	5 (55.6)	8 (30.8)	61 (74.4)
Chemotherapy + TKI	1 (10.0)	0	4 (15.4)	5 (6.1)
Chemotherapy + InO	0	1 (11.1)	4 (15.4)	4 (4.9)
InO	0	0	6 (23.1)	3 (3.7)
TKI	2 (20.0)	1 (11.1)	3 (11.5)	1 (1.2)
Steroids	0	0	1 (3.8)	1 (1.2)
Other	0	0	0	1 (1.2)

Figure B. Event-free survival* by disease burden group



Patients at risk

LL (n=10)	10	7	6	6	5	5	5	3	3	2	1	1	1	0	0	0	0
LH (n=9)	9	6	5	5	5	5	5	5	5	4	3	2	1	0	0	0	0
HL (n=26)	26	21	18	15	14	13	12	12	9	9	8	5	2	1	1	1	1
HH (n=82)	82	51	36	29	22	18	16	14	11	7	5	4	3	2	1	0	0

*Event-free survival, censoring new, non-protocol anti-cancer therapies, including stem cell transplant.
BM, bone marrow; CI, confidence interval; HH, high disease burden at screening and LD; HL, high disease burden at screening and low disease burden at LD; InO, inotuzumab ozogamicin; LD, lymphodepletion; LH, low disease burden at screening and high disease burden at LD; LL, low disease burden at screening and LD; NE, not estimable; TKI, tyrosine kinase inhibitor.