Abstract: P1391

Title: VARNIMCABTAGENE AUTOLEUCEL (VAR-CEL) IN RELAPSED / REFRACTORY CD19+ NON-HODGKIN LYMPHOMA

Abstract Type: Poster Presentation

Session Title: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

Varnimcabtagene autoleucel (var-cel, ARI-0001 cells), an academic second generation anti-CD19 CAR T-cell, has been granted hospital exemption use by the AEMPS and PRIME designation by the EMA for patients >25 years old with relapsed or refractory (R/R) B cell acute lymphoblastic leukaemia (B-ALL) based on the results of the CART19-BE-01 clinical trial (NCT03144583). Currently, var-cel is also being used as a compassionate use (CU) for adult patients with R/R CD19+ non-Hodgkin lymphoma (NHL).

Aims:

Here we report outcomes from all consecutive patients with R/R CD19+ NHL referred for treatment with var-cel either within the clinical trial or in the CU program.

Methods:

Fifty-one consecutive patients signed the consent form at our institution from July/17 to September/22. Ten patients were enrolled in the original trial and the subsequent 41 in the CU program. Patients underwent lymphodepletion with fludarabine (30mg/m^2) and cyclophosphamide (300mg/m^2). Target dose was 1-5 x10^6 CAR T cells/kg which was split in 3 fractions (10%, 30% and 60%).

Results:

Apheresis was performed in all 51 patients, 45 patients received at least one dose of var-cel: 45% were female; median age was 55 years (range 19-74); median prior lines was 4 (range 2-9); and 35% had a prior autologous stem cell transplant. Median follow-up was 12.8 months (range 3.9-44.6). Specific histologic subtypes are displayed in Table 1.

Median vein-to-vein time was 29 days (range 18-182) and median time from screening to infusion was 40 days (range 23-195). Forty-one patients (80%) received bridging therapy.

CRS rate was 84%, only 2 cases (4%) had grade ≥3 CRS. ICANS occurred in 3 patients (7%), one patient (2%) had grade ≥3 ICANS. 43 patients (96%) had grade ≥3 neutropenia and 24 (56%) grade ≥3 thrombocytopenia, but only one patient required a CD34+ boost for persistent cytopenia. One patient died due to severe sepsis and toxic epidermal necrolysis.

The pre-specified overall response rate (ORR) (at day +100) was 73% (95% CI: 58-85%), with a complete response rate (CRR) of 64% (49-78%). Median duration of response (DOR) from response assessment (day +100) had not been reached, and was 56% (39-81%) at 3 years. Median progression-free survival (PFS) was 10.4 months (6.48-NE) and median overall survival (OS) had not been reached. At 3 years, estimated PFS and OS were 40% (26-61%) and 52% (36-76%), respectively. Median duration of absolute B-cell aplasia (BCA) had not been reached and was estimated as 69% (52-91%) at 3 years. The cumulative incidence of relapse/progression was 53% at 3 years (37-71%). Table 1 shows efficacy results by histological subtype.

Univariate analysis revealed that both histology (indolent vs. aggressive) and serum LDH (normal vs. abnormal) had a significant impact on PFS. However, in multivariate analysis only LDH retained its prognostic impact. Patients with increased LDH had a shorter median PFS compared to those with normal LDH (6.1 months vs not reached, p = 0.006).

Summary/Conclusion:

High percentage of included patients received var-cel treatment. Var-cel had an acceptable safety profile in adult patients with R/R CD19+ NHL. Efficacy results may be comparable to other commercial CD19 CAR T cell products. Long-term persistent absolute BCA was achieved in the majority of patients. In multivariate analysis, only abnormal LDH had a significant impact on PFS.

Table 1

Subtype		ORR at day +100, % (95% CI)	CRR at day +100, % (95% CI)	DOR at 3y, % (95% CI)	PFS at 3y, % (95% CI)	OS at 3y, % (95% CI)
Aggressive NHL	DLBCL, PMLBCL and tFL (n = 7)	57 (18-90)	43 (10-81)	25 (46-100)	14 (2-88)	14 (2-88)
	Richter's transformation (n = 9)	56 (21-86)	44 (14-79)	80 (52-100)	44 (21-92)	56 (31-99)
	Mantle-cell lymphoma (n = 7)	86 (42-99)	86 (42-99)	67 (30-100)	56 (23-100)	67 (30-100)
	Other (HGL, GZL, PEL, PCNSL, BL) (n = 8)	63 (24-91)	63 (24-91)	40 (14-100)	19 (4-98)	75 (50-100)
Indolent NHL	Follicular lymphoma (n = 11)	100 (72-100)	82 (48-98)	62 (35-100)	62 (35-100)	72 (44-100)
	Other (MZL, SDRPBL) (n = 3)	67 (9-99)	67 (9-99)	NE	67 (30-100)	50 (13-100)

Abbreviations: NHL, non-Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; PMLBCL, primary mediastinal large B-cell lymphoma; tFL, transformed follicular lymphoma; HGL, high-grade lymphoma; GZL, grey-zone lymphoma; PEL, primary effusion lymphoma; PCNSL, primary central nervous system lymphoma; BL, Burkitt's lymphoma; MZL, marginal zone lymphoma; SDRPBL, splenic diffuse red pulp B-cell lymphoma; ORR, overall response rate; CI, confidence interval; CRR, complete response rate; DOR, duration of response; PFS, progression-free survival; OS, overall survival; not estimable.

Keywords: CAR-T, Cellular therapy, NHL