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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Loncastuximab in High-Risk and Heavily-Pretreated Relapsed/Refractory Diffuse Large B-Cell Lymphoma: A Real World Analysis from 21 US Centers

Emily Ayers, MD[1], *Viktoriya Zelikson, MD*[1], *Ashwath Gurumurthi, MBBS*[2], *Yazeed Sawalha, MD*[3], *Kaitlin Annunzio, DO*[3], *Aditi Saha, MBBS*[4], *Ning Dong, MD*[5], *David Augustus Qualls, MD*[6], *Behzad Amoozgar, MDMPH*[7], *Brad S. Kahl, MD*[7], *John H. Baird, MD*[8], *Pavan Challa, MD*[9], *Scott F. Huntington, MD MPH, MSc*[9], *Jennifer Santos, MD*[10], *Steven M. Bair, MD*[10], *Mayur S. Narkhede, MBBS*[11], *Shuning Li, MD*[12], *Zachary AK Frosch, MD MSHP*[13], *Carrie I Ho, MD*[14], *Stephen D Smith, MD*[14], *Allison Winter, MD*[15], *Daniel J. Landsburg, MD*[16], *Fateeha Furqan, MBBS*[17], *Mehdi Hamadani, MD*[18], *Katelin Baird, BS*[19], *Jason T. Romancik, MD*[19], *Hanan Alharthy, MBBS*[20], *Jennie Law, MD*[20], *Leyla Bojanini, MD*[21], *Ranjana H. Advani, MD*[21], *Boyu Hu, MD*[22], *Patrick Connor Johnson, MD*[23], *Natalie S. Grover, MD*[24], *Debamita Kundu, PhD*[25], *Mwanasha Hamuza Merrill, MD*[26], *Jennifer L Crombie, MD*[26], *Nazila Shafagati, MD*[27], *Cole Sterling, MD*[27], *Loretta J. Nastoupil, MD*[28], *Narendranath Epperla, MDMS*[3]

[1] University of Virginia, Charlottesville, VA
[2] Department of Lymphoma & Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX
[3] The James Cancer Center, The Ohio State University Wexner Medical Center, Columbus, OH
[4] Department of Malignant Hematology, H Lee Moffitt Cancer Center and Research Institute, Tampa, FL
[5] Department of Malignant Hematology, Moffitt Cancer Center, Tampa, FL
[6] Dana Farber Cancer Institute, Boston
[7] Siteman Cancer Center, Division of Oncology, Washington University School of Medicine in St. Louis, Saint Louis, MO
[8] Department of Hematology and HCT, City of Hope National Medical Center, Duarte, CA
[9] Division of Hematology, Yale University, New Haven, CT
[10] Division of Hematology, University of Colorado - Anschutz Medical Campus, Aurora, CO
[11] Department of Hematology Oncology, University of Alabama at Birmingham, Birmingham, AL
[12] Fox Chase Cancer Center, Philadelphia, PA
[13] Department of Hematology/Oncology; Cancer Prevention and Control Research Program, Fox Chase Cancer Center, Philadelphia, PA
[14] Fred Hutchinson Cancer Center, Seattle, WA
[15] Department of Hematology and Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH
[16] Department of Medicine, University of Pennsylvania, Philadelphia, PA
[17] Division of Hematology/Oncology, Medical College of Wisconsin, Milwaukee, WI
[18] Division of Hematology and Oncology, The Medical College of Wisconsin Inc, Milwaukee, WI
[19] Department of Hematology and Medical Oncology, Winship Cancer Institute at Emory University, Atlanta, GA
[20] University of Maryland, Baltimore
[21] Division of Oncology, Stanford University Institute, Stanford, CA
[22] Huntsman Cancer Institute, University of Utah, Salt Lake City, UT
[23] Cancer Center, Massachusetts General Hospital, Boston, MA
[24] Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC
[25] Division of Biostatistics, University of Virginia, Charlottesville
[26] Dana Farber Cancer Institute, Boston, MA
[27] Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD
[28] MD Anderson Cancer Center, Houston, TX

Background: In the LOTIS-2 study, patients (pts) with relapsed/refractory (R/R) DLBCL treated with loncastuximab-tesirine (lonca), a CD19 directed antibody-drug conjugate, demonstrated an overall response rate (ORR) and complete response rate (CRR) of 48.3 % and 24.1%. However, there is a paucity of data evaluating outcomes with lonca in the real-world setting (RWS).

Hence, we performed a multicenter retrospective study to describe pt characteristics and clinical outcomes in R/R DLBCL pts receiving lonca in this setting.

Methods: This retrospective study included pts with R/R DLBCL treated with commercial lonca at 21 academic centers in USA. Clinicopathologic data, treatment outcomes and adverse event (AE) data were collected. Progression-free survival (PFS) and overall survival (OS) were estimated using Kaplan-Meier method and characteristics associated with survival and CR calculated using Cox proportional hazards model and logistic regression. Response was assessed per institutional standards.

Results: 187 pts were analyzed with a median follow-up of 12.5 months (mo). Median age was 68 years (range 22-95), 64% male, and 85% white (**Table 1)**. Most common histology was DLBCL (55% *de novo*, 22% transformed from low-grade) and 19% were double hit (DH). Thirty-two percent (n=59) had primary refractory disease, 17% (n=31) prior autologous transplant, and 60% (n=112) prior CAR T-cell therapy (CART). Median number of treatment lines before lonca was 4 (1-11) with 81% (n=151) receiving lonca in 4 th line (4L) or later and 8 pts treated off-label in 2 nd line. More pts receiving lonca in ≥4L had prior CART (72% vs 8%, p <0.001). CD19 status was confirmed prior to lonca in 128 pts (68%) with 109 (58%) confirmed CD19+.

The ORR/CRR were 33% and 14%, respectively. Median PFS was 2.1 mo (95%CI=1.8-2.6) and median OS 4.6 mo (95%CI=3.7-5.8). 12-month PFS and OS were 12% and 20%. The CRR in 2L/3L, 4L, and >4L were 15%, 13%, and 15% with ORR of 44%, 26%, and 33%, respectively. **Figure 1** shows PFS stratified by response with median PFS not reached in those achieving CR. Patients with a CR to last therapy prior to lonca had superior median PFS (8.8 vs 2.0 mo, p<0.01) and OS (10.8 vs 4.5 mo, p =0.01). Factors associated with achieving CR to lonca included CR to last prior therapy (OR 8.3, p<0.01) and nonGCB subtype (OR 3.9, p=0.02). No pts with bulky disease (>10 cm) had objective response. In multivariable analysis (MVA) including factors in Table 1, elevated LDH (HR 1.8, p=0.02; 95%CI=1.1-2.9) and bulky disease (HR 1.7, p=0.03; 95%CI=1.1-2.6) were associated with inferior PFS while CR to last therapy was associated with superior PFS (HR 0.2, p=0.02; 95%CI=0.05-0.76). Bulky disease (HR 2.3, p<0.01; 95%CI=1.4-3.5), HGBL histology (HR 6.1, p<0.01; 95%CI=2.6-14.5), and elevated LDH (HR 2.0, p<0.01; 95%CI=1.2-3.3) were associated with inferior OS, while CR to last therapy (HR 0.4, p=0.05; 95%CI=0.13-0.98) was associated with superior OS in MVA.

Neither CD19 status nor prior CART were associated with PFS, OS, or CR. In pts receiving lonca after CART, ORR/CRR were 31% and 15%, respectively, and median PFS/OS were 2.0mo (95%CI=1.6-2.7) and 4.6mo (95%CI=3.2-6.1). In pts who received tafasitamab (n=15) and CART (n=7) after lonca, CR was 13% and 29%, respectively.

The most commonly documented AE was cytopenias (45%), followed by peripheral edema, and rash (27% and 27% respectively). Infection was seen in 5% and AEs led to lonca discontinuation in 14%, including peripheral edema (24%) and rash (28%).

Conclusions: In this heavily pre-treated population enriched with prior CART exposure, HGBL, and DHL, ORR and CRR to lonca were lower than previously reported. Nonetheless, we found that pts who achieve a CR to lonca have favorable outcomes and factors associated with achieving a CR include lack of bulky disease, nonGCB subtype, and achieving a CR to most recent therapy prior to lonca. Receipt of prior CART did not negatively impact outcomes to lonca. Furthermore, responses were seen with CD19-directed therapies following lonca failure, suggesting sequencing of CD19 therapy pre and post lonca was successful.

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Table 1

		Total N=187	LOTIS-2 N=145
Sex	Male	119 (63.6%)	85 (59%)
Age, years	<65	76 (40.6%)	65 (45%)
	65-75	62 (33.2%)	59 (41%)
	>75	49 (6.2%)	21 (14%)
Race	Asian	11 (6.5%)	
	African American/Black	14 (8.3%)	
	White	144 (85.2%)	
Histology	*de novo* DLBCL	102 (54.5%)	98 (67.6%)
	HGBL	33 (17.6%)	11 (8%)
	Transformed DLBCL	41 (21.9%)	29 (20%)
	Other	11 (5.9%)	
Stage	I-II	23 (12.5%)	33 (23%)
	III-IV	161 (87.5%)	112 (77%)
Cell of Origin	GCB	61 (32.6%)	48 (33%)
	nonGCB	96 (51.3%)	23 (16%)
	Missing	30 (16.0%)	74 (51%)
Double Hit	No	123 (65.8%)	
	Yes	36 (19.3%)	15 (10%)
	Missing	28 (15.0%)	
ECOG PS	0-1	111 (74.0%)	
	2-4	39 (26.0%)	
Elevated LDH at Lonca Initiation	No	47 (25.1%)	
	Yes	139 (74.3%)	
	Missing	1 (0.5%)	
Bulky disease >10cm	No	154 (82.8%)	137 (94%
	Yes	32 (17.2%)	8 (6%)
CD19+ at Lonca initiation	No	19 (10.2%)	
	Yes	109 (58.3%)	
	Unknown	59 (31.6%)	
Lonca line of therapy	2nd or 3rd	36 (19.3%)	63 (43%)
	4th	39 (20.9%)	35 (24%)
	>4th	112 (59.9%)	47 (32%)
Response to 1st Line Therapy:	Relapsed	126 (68.1%)	99 (68%)
	Refractory	59 (31.9%)	29 (20%)
Response to most recent therapy	< CR	171 (91.4%)	84 (58%)
	CR	16 (8.6%)	43 (30%)
Previous CAR	No	75 (40.1%)	132 (91%)
	Yes	112 (59.9%)	13 (9%)

Figure 1

Figure 1