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Efficacy and Safety of Loncastuximab tesirine and Rituximab (Lonca-R) Followed by DA-R-EPOCH in Previously Untreated High-Risk DLBCL: Preliminary Results from UCDCC#303, a UCHMC Phase II Trial

Jacqueline Hsieh-Wong[1], Naseem Esteghamat[1], Rasmus Hoeg[1] , Mehrdad Abedi[1], Sheila Firoozan[1], Aaron Rosenberg[1], Ashley Trane[2], Aneeqa Zafar[1], Shuai Chen[1], Siyao Li[1] , Matthew Wieduwilt[3], Lloyd Damon[4], Benjamin Heyman[5], Haifaa Abdulhaq[6], Elizabeth Brem[7], Deepa Jeyakumar[7] , Gary Schiller[8], Joseph Tuscano[1]

[1]University of California, Davis, Sacramento, CA, United States; [2]Intermountain Health, St. George, UT, United States; [3]Wake Forest University, Winston-Salem, NC, United States; [4]University of California, San Francisco, San Francisco, CA, United States; [5]City of Hope, Duarte, CA, United States; [6]University of California, San Francisco – Fresno, Fresno, CA United States; [7]University of California, Irvine, Irvine, CA, United States; [8]University of California, Los Angeles, Los Angeles, CA, United States

BACKGROUND

Newly-diagnosed diffuse large B-cell lymphoma (DLBCL) is a potentially curable malignancy[1]. However, there are high-risk subsets that respond poorly to and have worse outcomes using standard first-line immunochemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Double-expressor/double-hit DLBCL (DEL/DHL) is one such subset[2]. Both loncastuximab tesirine and dose-adjusted rituximab with etoposide, doxorubicin, cyclophosphamide, vincristine and prednisone (DA-R-EPOCH) have previously demonstrated efficacy in this subgroup[3-4].

AIMS

- To evaluate the safety and also efficacy of Lonca-R followed by DA-R-EPOCH in patients aged ≥ 18 with previously untreated DEL/DHL confirmed via histology or cytology using 2016 World Health Organization (WHO) criteria.

METHODS

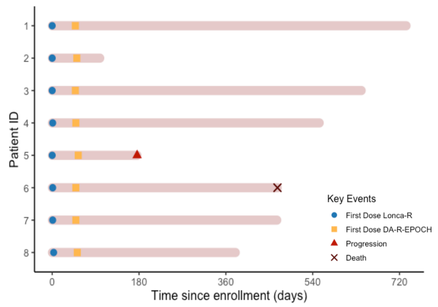
- Patients received 2 three-week cycles of Lonca-R via a "smart start" approach followed by up to six cycles of DA-R-EPOCH, starting at the level 1 dose.
- Computed tomography (CT) of the chest, abdomen, pelvis and positron emission tomography/CT scans were obtained at baseline, every 2 cycles during treatment, and at the end of treatment to assess response using the 2014 Lugano classification.
- Toxicity was assessed each cycle as per the Common Terminology Criteria for Adverse Events Version 5 (CTCAEv5.0).
- Progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan-Meier curves.
- Patients discontinued therapy at completion of 6 cycles of DA-R-EPOCH, progressive disease, unacceptable toxicity, withdrawal of consent, treatment non-adherence, or administrative reasons.

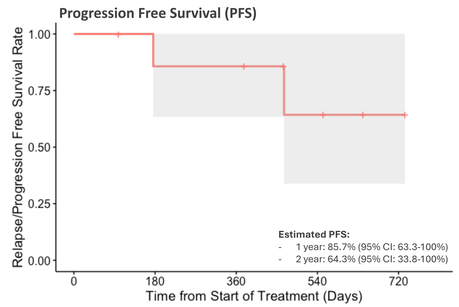
RESULTS

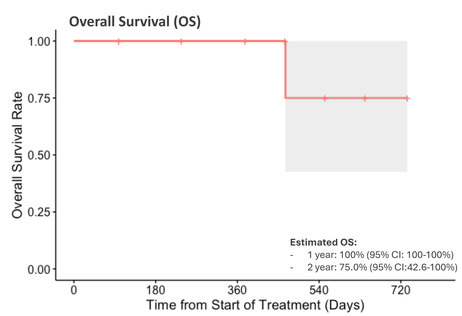
Patient Characteristics (n=8*)

CHARACTERISTIC	NUMBER OF PATIENTS (PERCENTAGE)
Age at Diagnosis (years)	
30-40	2 (25%)
40-50	0 (0.0%)
50-60	1 (12.5%)
60-70	4 (50%)
70-80	1 (12.5%)
Gender	
Female	1 (12.5%)
Male	7 (87.5%)
Performance Status (ECOG score)	
0	2 (25%)
1	6 (75%)
Baseline Disease Status	
Nodal	4 (50%)
Extranodal	1 (12.5%)
Both	3 (37.5%)
R-IPI Score	
0	1 (12.5%)
1	0 (0.0%)
2	3 (37.5%)
3	3 (37.5%)
4	1 (12.5%)
DEL/DHL Status	
DEL	6 (75%)
DHL	1 (12.5%)
Both	1 (12.5%)
Number of DA-R-EPOCH Cycles Completed	
1-4	1 (12.5%)
5-8	7 (87.5%)

* Although a total of 9 patients had been enrolled in the study, data was available for only 8 patients at the time of interim analysis.





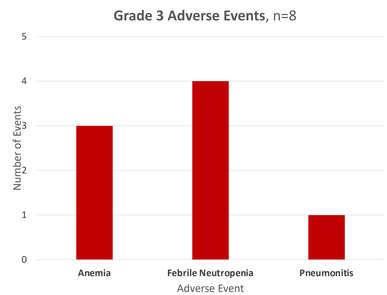


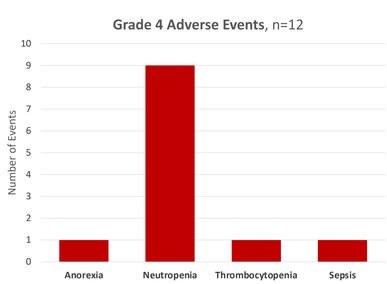
Best Response After 2 Cycles of Lonca-R

RESPONSE TYPE	NUMBER OF PATIENTS (PERCENTAGE)
Progressive disease	0 (0.0%)
Stable disease	1 (12.5%)
Partial response	6 (75%)
Complete response	1 (12.5%)
Overall response	8 (87.5%)

Best Overall Response

RESPONSE TYPE	NUMBER OF PATIENTS (PERCENTAGE)
Progressive disease	0 (0.0%)
Stable disease	0 (0.0%)
Partial response	3 (37.5%)
Complete response	5 (62.5%)
Overall response	8 (100%)





CONCLUSIONS

Lonca-R followed by DA-R-EPOCH appears to be a promising regimen for patients with DHL and/or DEL. ORR was >80% in patients after completing the first 2 cycles of Lonca-R alone, and 100% if all 8 cycles were completed. Median PFS and OS were not reached. Although not shown on the figures here, the regimen is well-tolerated as most AEs (89%) are either G1 or G2. Compared to DA-R-EPOCH alone, the ORR with Lonca-R followed by DA-R-EPOCH is improved with fewer G3/G4 AEs[5]. As the trial is ongoing, these results will be explored further within a larger cohort and with longer follow up time.

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CONTACT INFORMATION

Correspondence may be directed to the principal investigator, Dr. Joseph Tuscano, MD, at jtuscano@health.ucdavis.edu.

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