Abstract: P2085

Title: NOVEL TARGETED AGENTS IN COMBINATION WITH R-ICE (R-ICE-X) BASED ON GENOTYPING IN RELAPSED/REFRACTORY DLBCL

Abstract Type: e-Poster Presentation

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of aggressive non-Hodgkin lymphoma, which is characterized by high heterogeneity, rapid progression and poor prognosis. 30%-40% of the patients are relapsed or refractory to R-CHOP treatment, and only about 40% patients get benefits from second-line regimens including R-ICE. The outcomes of these relapsed/refractory (R/R) DLBCL remain to be improved.

Aims:

This prospective, single-arm study aims to investigate the efficacy and safety of a new targeted agent in combination with R-ICE (R-ICE-X) based on different molecular subtypes in R/R DLBCL patients, providing a new treatment for improving clinical efficacy in DLBCL patients with poor prognosis.

Methods:

In this study, patients with R/R DLBCL aged 18-75 years were enrolled. All patients were assigned and stratified by genetic subtypes and received different targeted agents combined with R-ICE. The efficacy was evaluated after 3 courses of R-ICE-X (every 21 days). Patients with complete remission or partial remission (CR/PR) were subsequently treated with autologous hematopoietic stem cell transplantation (ASCT) or 3 courses of R-ICE-X consolidation and lenalidomide maintenance for up to 12 months. The primary endpoint was the overall response rate (ORR), and the secondary endpoints were the 2-year progression-free survival (PFS) rate, 2-year overall survival (OS) rate, and safety evaluation. This trial is registered with ClinicalTrials.gov, NCT05348213.

Results:

At the time of data cut off, a total of 76 patients were enrolled, with a median age of 61 (20-75) years. Among 71 patients who completed treatment, the end of induction CR rate was 59.2%, and ORR was 78.9%. In the patients with R-ICE-zanubrutinib group (n=34), the ORR was 78.8%, with 18 patients (18/33, 54.6%) achieved CR and 8 patients (8/33, 24.2%) achieved PR. The 1-year PFS rate and OS rate were 70.2% and 86.5%, respectively. In the patients with lenalidomide combined with R-ICE (n=30), 17 patients (17/30, 56.7%) achieved CR, 6 (6/30, 20.0%) patients achieved PR, and the ORR was 76.7%. The 1-year PFS and OS rates were 84.0% and 100.0%, respectively. 5 patients (5/8, 62.5%) with decitabine plus R-ICE achieved CR. 2 patients received R-ICE-chidamide and got CR as well. Only one patient in R-ICE-tofacitinib considered other clinical studies due to poor treatment efficacy. Furthermore, we found the proportion of *SOCS1* mutation was increased in patients with poor response to R-ICE-X regimen. In univariate analysis, we also revealed that *CD70*, *SOCS1* and *TMSB4X* mutations indicated poor survival outcomes. Subsequent analyses of poor prognosis genes in each treatment group will be performed.

Summary/Conclusion:

Novel targeted agents in combination with R-ICE (R-ICE-X) regimen was well tolerated and efficacy in R/R DLBCL patients, being a promising bridging regimen for ASCT, especially R-ICE-zanubrutinib and R-ICE-lenalidomide therapy. The study is ongoing and further results will be continuously released.

Keywords: Targeted therapy, Diffuse large B cell lymphoma, relapsed/refractory, Gene mutation