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POSTER ABSTRACTS

626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Zanubrutinib Combined with R-CHOP in Previously Untreated Non-Germinal Center B-Cell (GCB) Diffuse Large B-Cell Lymphoma (DLBCL) Patients with BCL2 and MYC Protein Co-Expression: A Multicenter, Phase II Study

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Introduction

DLBCL is the most common subtype of lymphoma, accounting for up to 40% of lymphoma cases worldwide and can be classified into GCB and non-GCB by immunohistochemistry (IHC). Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) chemotherapy is the standard first-line treatment of DLBCL. Patients with non-GCB DLBCL or co-expression of BCL2 and MYC have a worse outcome with R-CHOP treatment. Previous study has showed that ibrutinib combined with R-CHOP had improved event free survival (EFS) compared with placebo plus R-CHOP in non-GCB DLBCL patients with BCL2 and MYC co-expression (Johnson et al., Blood 2019). This study aimed to investigate the efficacy and safety of the new-generation BTKi zanubrutinib combined with R-CHOP in previously untreated non-GCB DLBCL patients with BCL2 and MYC protein co-expression. Here, we report the preliminary results of this study.

Methods

Eligible patients were previously untreated non-GCB DLBCL confirmed by Hans' algorithm
age 18 years or older, MYC positive (defined as ≥40% of tumor cells showed any level of MYC nuclear staining above background) and BCL-2 positive (defined as ≥50% of tumor cells showed a cytoplasmic intensity score of 2+ or 3+) determined by IHC, and Eastern Cooperative Oncology Group performance status of 0-2.Patients were treated with R-CHOP combined with zanubrutinib (160 mg oral BID per day) of each 21-day cycle for six cycles. After 4 cycles, response was assessed by CT per Lugano 2014 criteria. Patients who were progression disease (PD) would discontinue the treatment. After completion of 6 cycles treatment, patients who were assessed with complete response (CR) (by PET-CT) would proceed to zanubrutinib (160 mg oral BID) maintenance treatment for one year, or until PD, intolerance of toxicity, loss of follow-up, withdrawal of informed consent, or death. Patients who were not CR would receive subsequent anti-tumor therapies determined by investigator. The primary endpoint was 3-year EFS rate assessed by investigator, Secondary endpoints included overall response rate (ORR), CR rate, 3-year progression free survival rate, 3-year overall survival rate and safety.

Results

From Jan 2022 to Jun 2023, 27 patients were enrolled with a median age of 58, and 40.7% (11/27) were with IPI ≥3. At the data cut-off date of 30 Jun 2023, all 27 patients received at least one cycle of R-CHOP plus zanubrutinib and included in safety evaluation. Seventeen patients have received 4 cycles treatment and were assessed by CT with CR (n=1) or partial response (n=16); 2 patients withdrew the study before the first assessment. Among the 17 patients, 11 patients completed 6 cycles of treatment and achieved a response (11/11), with a CR (CR and complete metabolic response) of 10/11 (**Table**). Two patients discontinued after 4 cycles treatment (1 due to outbreak of COVID 19 and 1 due to AE, infectious pneumonia). Ten patients with CR are in the zanubrutinib maintenance treatment, while 1 patient with PR had received salvage therapy decided by the investigator. The most common hematologic TEAEs were neutropenia (33.3% in Grade 1-2, 18.5% in Grade ≥3) and thrombocytopenia (7.4% in Grade 1-2, 11.1% in Grade ≥3), and non-hematologic TEAE includes alanine aminotransferase increased, aspartate aminotransferase increased, rash, hypokalemia, anemia, diarrhea, infectious pneumonia and hemorrhage **(Figure)**. Hypertension and atrial fibrillation/flutter were not observed during the treatment. Four patients experienced SAE of infectious pneumonia (n=1), neutropenia (n=1), and thrombocytopenia (n=2, Grade 3), and were recovered.

Conclusions

At the time of data cut-off 30 Jun 2023, 6 cycles of zanubrutinib combined with R-CHOP regimen was well tolerated and showed a promising response result in untreated non-GCB double-expression DLBCL patients. The study is ongoing and further results will be continuously released.

Disclosures No relevant conflicts of interest to declare.

Table Response after 4 cycles and 6 cycles treatment

	4 cycle, assessed by CT, N=17	6 cycle, assessed by PET-CT, N=11
ORR	17/17	11/11
CR + CMR	1/17	10/11
PR	16/17	1/11

CR: Complete Response; CMR: Complete Metabolic Response; PR: Partial Response

Figure Most common TEAE in the treatment duration.

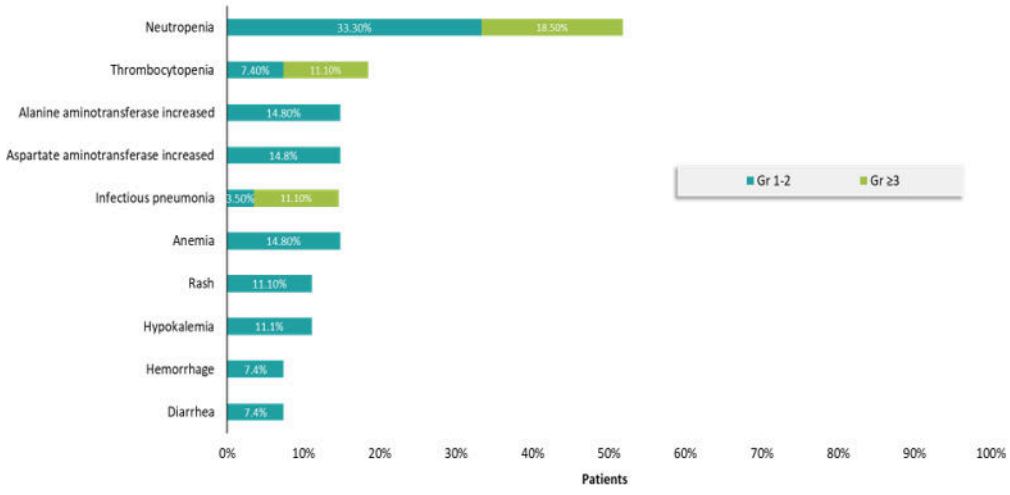

Figure 1

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