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626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Preliminary Results from a Phase I/II Study of Pomalidomide Plus Rituximab, Ifosfamide, Carboplatin, and Etoposide for Relapsed or Refractory Diffuse Large B-Cell Lymphoma (PRIDE)

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Background: Relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) patients have limited treatment options and are associated with poor prognosis. Outcomes are particularly poor following immunochemotherapy failure or relapse within 12 months of induction. The addition of the immunomodulatory agent lenalidomide (Len) to rituximab plus ifosfamide-carboplatin-etoposide (RICE) was shown to be feasible with promising efficacy in some studies. Pomalidomide (Pom) is a third-generation immunomodulatory drug that has shown excellent therapeutic activity against relapsed/refractory primary central nervous system lymphoma (PCNSL) with an acceptable toxicity profile. We conducted a phase I/II study combining Pom with RICE (PRICE) as a salvage regimen in first-relapse or primary refractory DLBCL (ChiCTR2100049327). Here we report the phase I results of the study.
Methods: In phase I of the study, patients receive escalating doses of pomalidomide (2 mg, 3 mg, or 4 mg daily on d1-10) along with R-ICE therapy every 21 days by 3+3 design. Patients with CR or PR but not eligible for ASCT receive continuous pomalidomide as maintenance therapy for 12 months. The primary objective was to determine the maximum tolerated dose (MTD) or recommended dose, based on the occurrence of treatment-related DLTs. Secondary objectives included tumor response and safety.
Results: At data cut-off (July 11, 2023), 14 patients were screened and 10 eligible patients were enrolled. 9 patients had been treated in the first 2 dose-escalation cohorts: 6 patients at 2 mg and 6 patients at 3 mg. Patient characteristics at baseline are shown in Table I. DLT was observed in two patients in the 3 mg cohort (grade 4 thrombocytopenia and grade 4 rash). MTD was determined as 2 mg. Grade (G) $\geq$ 3 TRAEs were leukopenia (4 patients), lymphopenia (3 patients), thrombocytopenia (3 patients), neutropenia (3 patients), rash (1 patient) and myelosuppression (1 patient). No death was related to the treatment. Five patients (55.6%) achieved an objective response including four patients (44.4%) with CR. ORR for the MTD dose level was (4/6) 66.7% with 3 CR and 1 PR. Notably, among the 7 patients with MYD88 mutations, which are associated with enhanced NF-κB activity, 4 achieved CR and 1 achieved PR.
Conclusion: The addition of pomalidomide to the widely used RICE salvage regimen is feasible, and results in promising response rates in this DLBCL population that mostly with non-GCB subtype and double expression. MTD was reached and RP2D was determined to be 2 mg. Further studies are needed to evaluate the efficacy of this regimen, particularly in patients with MYD88 mutations.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Pomalidomide is indicated for the treatment of adult patients: in combination with dexamethasone, for patients with multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy in China. The abstract presents the use of generic pomalidomide in combination with R-ICE, a combination that is not approved in China at present.

Table 1 Disease characteristics and clinical responses

Characteristic	Patients, n (%)
No. of patients	9 (100.0)
Sex	
Male	5 (55.6)
Female	4 (44.4)
Age, years	
Median	66
Range	25-74
ECOG Performance Status	
0-1	9 (100)
GCB vs non-GCB subtype	1 (11.1)/8 (88.8)
Double-expression	8 (88.8)
Ann-Arbor Stage	
I-II	3 (33.3)
III-IV	6 (66.7)
IPI at relapse	
Low, low-intermediate	3 (33.3)
High-intermediate, high	6 (66.7)
Primary refractory	4 (44.4)
Relapse occurred <12 months after initial therapy	2 (22.2)
Relapse occurred >12 months after initial therapy	3 (33.3)
Response	
ORR	5 (55.6)
CR	4 (44.4)

Abbreviations: CR, complete response; ECOG, Eastern Clinical Oncology Group; GCB, germinal B-cell; IPI, International Prognostic Index; ORR, objective response rate.

Figure 1

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