P1243 RUXOLITINIB COMBINED WITH DEXAMETHASONE IN ADULT PATIENTS WITH NEWLY DIAGNOSED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: INTERIM ANALYSIS OF A PROSPECTIVE, SINGLE-CENTER, SINGLE-ARM, PHASE 2 CLINICAL TRIAL

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background: Hemophagocytic lymphohistiocytosis (HLH) in adults is a major clinical challenge due to its rapid progress and high mortality. The current first-line therapy strategies such as HLH-94 or HLH-2004 regimens are largely extrapolated from paediatric HLH; however, the prognosis of adult HLH is worse than that of children. Ruxolitinib (an oral JAK inhibitor) has shown favorable efficacy and safety in murine models and clinical trials in adult HLH. Moreover, Lauren K. Meyer et al. demonstrate that ruxolitinib can reverse the resistance of CD8 positive T cells to dexamethasone in hypercytokinemia of HLH. We were very interested in these results and preliminarily revealed the high response rate and good short-term survival of ruxolitinib combined with dexamethasone (Ru-D) in a pilot study involving 8 adult HLH patients. On these bases, we conducted this prospective, single-center, single-arm, Phase 2 clinical study.

Aims: This phase 2 clinical trial (ChiCTR2100049996) aims to evaluate the efficacy and safety of Ru-D regimen as first-line therapy in adults with newly diagnosed HLH.

Methods: This is an interim analysis of an ongoing phase 2 clinical trial of a planned 28 newly diagnosed adult HLH patients. Inclusion criteria were patients who met HLH-2004 diagnostic criteria, older than 18 years old, and had not received HLH first-line therapy. Patients in this study received an 8-week period of treatment. The Ru-D regimen consists of ruxolitinib (15 mg twice daily for 8 weeks) and dexamethasone (initially 10 mg/m² for 2 weeks followed by 5 mg/m² for 2 weeks, 2.5 mg/m² for 2 weeks, 1.25 mg/m² for one week, and one week of tapering). The primary endpoint is the 2-month overall survival rate (OS), and the secondary endpoints are overall response rate (ORR), progression-free survival (PFS), safety and changes in biomarkers.

Results: From August 15, 2021 to January 15, 2022, there were 15 patients enrolled in this study with a median follow-up of 78 (31-171) days. The 15 patients included 8 cases of lymphoma-associated HLH (LAHS), five case of Epstein-Barr virus-associated HLH (EBV-HLH), and 2 cases of unknown etiology. It should be mentioned that 4 of 15 patients carried heterozygous HLH-related gene mutations. Patients were followed up until February 15, 2022 or until death, with none lost to follow-up. The primary endpoint, 2-month OS, was 83.3% in 12 evaluable patients, both patients died due to lymphoma progression. The overall mortality rate was 26.7% (4/15), 75% (3/4) deaths occurred in LAHS patients and there was no death directly related to HLH until data cutoff. The ORR to Ru-D regime was 86.7% (13/15), with 13.3% (2/15) in complete response (CR), 73.3% (11/15) in partial response (PR), and 13.3% (2/15) in no response (NR). The treatment was well tolerated, with no toxicities leading to dose reduction or discontinuation of treatment. All LAHS patients were successfully bridged to chemotherapy after Ru-D therapy. Table 1 shows the response outcomes in detail.

Image:
Summary/Conclusion: In our study, the Ru-D regimen initially demonstrated favorable efficacy in newly diagnosed adult patients with HLH. For patients with LAHS, it is an efficient and safe bridging therapy while waiting for pathological diagnosis. Therefore, Ru-D represents a novel and promising therapeutic option for HLH patients that may provide clinical benefit.