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POSTER ABSTRACTS

624.HODGKIN LYMPHOMAS AND T/NK CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Brentuximab Vedotin in Combination with Methotrexate, L-Asparaginase, and Dexamethasone (B-MAD) As Frontline Treatment for Patients with Extranodal NK/T-Cell Lymphoma

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Introduction

Extranodal natural killer/T-cell lymphoma (ENKTL) is a unique lymphoma associated with Epstein-Barr virus infection. It is more common in Asia than in the Western. The prognosis is usually poor, especially in advanced disease, and no standard treatment exists. Brentuximab vedotin (BV) is a drug-conjugated monoclonal antibody which targets the cell-membrane protein CD30 linked to the potent anti-tubulin agent. Due to frequent expression of CD30 in ENKTL, we investigated the safety and efficacy of BV in combination with methotrexate, L-asparaginase, and dexamethasone (B-MAD) as frontline treatment in Thai patients with ENKTL.

Methods

The Thai Lymphoma Study Group conducted a prospective, multicenter phase I/II study and enrolled patients aged 18-60 years with newly diagnosed ENKTL between December 2018 and December 2021 from 9 hospitals in Thailand. Patients with localized ENKTL (stage I/II) received concurrent weekly cisplatin and involved-field radiation (IFRT) 40-50 Gy, followed by 3 cycles of B-MAD. Patients with advanced ENKTL (stage III/IV) received only B-MAD for 6 cycles. BV in combination with standard dose MAD chemotherapy was given every 21 days. The primary objective was to determine the safety and optimal dose of BV in B-MAD regimen using a 3+3 dose escalation design. The secondary objective was to evaluate the overall response rate (ORR) at the end of B-MAD treatment, safety, progression-free survival and overall survival. An analysis was performed at the data cutoff date of June 30, 2023.

Results

Thirty-four patients (pts.) were enrolled; 23 had localized and 11 had advanced diseases. The median age was 42 years (range, 18-59). Four pts. in the localized group did not receive B-MAD due to disease progression during concurrent cisplatin and IFRT (n=3) and consent withdrawal (n=1). Six pts. received B-MAD in phase I study (3 pts. at 1.2 mg/kg and 3 pts. at 1.8 mg/kg of BV). No dose-limiting toxicity was observed among six patients, therefore the recommended dose of BV in phase II study was 1.8 mg/kg. Of 30 evaluable pts., 20 (66.7%) achieved complete response (CR), 5 (16.7%) had partial response, and 5 (16.7%) progressed after treatment. The response rates (ORR/CR rate) in localized and advanced diseases were 89.5%/78.9% and 72.7%/45.5%, respectively.

A total of 190 adverse events (AEs) were reported. The most common AEs were anemia 19/190 (10%), leukopenia 9/190 (4.7%), neutropenia 9/190 (4.7%), hypoalbuminemia 9/190 (4.7%), peripheral neuropathy 7/190 (3.7%), elevated ALT 7/190 (3.7%), and elevated serum creatinine level 5/190 (2.6%), respectively. Twenty-four events were classified as grade ≥ 3 including

anemia (4/24), leukopenia (7/24), neutropenia (7/24), and elevated ALT (1/24), respectively. A total of 21 serious adverse events (SAEs) were reported. The causes of SAE were varied as follows: acute kidney injury 2/21, pneumonia 2/21, leukopenia 1/21, neutropenia 1/21, and thrombocytopenia 1/21. Most of the SAEs were suspected to be related to the treatment. Two cases of acute kidney injury related to methotrexate and one case of hypersensitivity reactions to L-asparaginase were reported as SAEs. They were manageable and completely resolved upon follow-up. There were no treatment-related deaths. At the data cutoff date, after the median follow up of 11.6 months, 25 pts. were alive, 7 experienced progressions, and 5 had died. Two pts. had progression in the central nervous system.

Conclusion

Treatment with standard-dose of BV in combination with MAD chemotherapy was well tolerated and showed encouraging efficacy in patients with newly diagnosed ENKTL. Evaluation of long-term survival data is ongoing. (ClinicalTrials.gov identifier: NCT03246750)

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Brentuximab vedotin in combination with chemotherapy for treatment of extranodal NK/T cell lymphoma

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