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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Efficacy and Safety of BTK Inhibitors in Vitreoretinal Lymphoma: A Single-Center, Retrospective Analysis of 24 Patients

Jing Gao[1], *Liang Wang*[2]

[1] HEMATOLOGY, BEIJING TONGREN HOSPITAL, BEIJING, China
[2] Beijing Tongren Hospital, Guangzhou, China

Background: Vitreoretinal lymphoma (VRL) is a special subtype of rare central nervous system lymphoma (PCNSL). Most of the pathologic types are diffuse large B-cell lymphoma of non-germinal central origin. Currently, the optimal treatment strategy for VRL is not clear, and the traditional treatment usually includes about 20 repeated intravitreal injections of low doses of methotrexate or intraocular local radiotherapy. Eventually, however, 60-90% of VRL will progress to PCNSL. Therefore, CNS prophylaxis of VRL patients is very important. A previous prospective clinical study of our research group (including 10 VRL patients) confirmed that single-drug BTK inhibitors can replace repeated intravitreal injection of low doses of methotrexate, with rapid effect, high safety, and certain value in preventing CNS progression.
Methods: In order to further clarify the efficacy and safety of BTK inhibitors in VRL patients, we included 24 VRL patients who were consecutively admitted to the Hematology Department of Beijing Tongren Hospital from May 2020 to December 2022, and retrospectively analyzed their clinical features, treatment methods, treatment outcomes, survival status and treatment-related adverse reactions.
Results: Of the 24 patients, 14 were female and 10 were male, with a median age of 62 years old (36-75). There were 18 patients with primary VRL (PVRL) and 6 patients with secondary VRL (SVRL) to PCNSL. The IL-10 in aqueous humor/vitreous fluid at baseline was significantly increased in all patients (362.1±89.5pg/mL), and the IL-10/IL-6 ratio was greater than 1. Except for one patient with both uncontrolled PCNSL and VRL, the other 23 VRL patients showed no evidence of CNS involvement by brain MRI and cerebrospinal fluid detection. All 24 patients were treated with a BTK inhibitor (Zanubrutinib 160mg bid, or Orelabrutinib 150mg qd), of whom, 9 VRL patients were also treated with intravitreal methotrexate injection (0.4mg/ time, weekly ×12 times → monthly ×9 times) concurrently, and the remaining 15 patients did not receive any antitumor therapy other than BTK inhibitors. After 1 month of treatment with BTK inhibitors, the efficacy was evaluated by slit lamp microscope, optical coherence tomography (OCT), and aqueous humor cytokines. 21 patients achieved CR (87.5%), 2 PR (8.3%), and 1 PD (progression of CNS lesion but improvement of intraocular disease). The IL-10/IL-6 levels in aqueous humor were lower than 1 in all 24 patients 1 month after treatment, and the IL-10 levels in aqueous humor were slightly higher than the normal range in two patients. The median duration of BTK inhibitors use was 10 months (1.5-23.0 months). At a median follow-up of 17 months (5.4-31.5 months), 15 patients (62.5%) developed disease progression, including 11 patients (45.8%) with CNS progression and 4 patients (16.7%) with intraocular recurrence. The median progression-free survival (PFS) time was 11.9 months, and the median overall survival (OS) time was not reached. The 1-year and 2-year PFS rates were 34% and 26%, and the 1-year and 2-year OS rates were 96% and 82%, respectively. The recurrence rate was 33.3% in the combined treatment group and 80.0% in the BTK inhibitors monotherapy group. A total of three patients died, all due to CNS progression. BTK inhibitors were generally well tolerated in VRL patients, with no adverse reactions that led to treatment discontinuation. 4 patients had grade 1-2 hypertension (16.7%), 1 patient had grade 1 hypotension (4.2%), 2 patients had grade 1 joint pain (8.5%), and 6 patients had grade 1 subcutaneous hemorrhage and ecchymosis (25.0%). Four patients developed COVID-19 infection while taking the drug and the drug was suspended. All four patients recovered from COVID-19 infection within 2 weeks and did not develop significant pneumonia.
Conclusion: This is the largest report regarding the use of BTK inhibitors in VRL patients. BTK inhibitor has a rapid local control effect on VRL and is well tolerated. However, BTK inhibitors monotherapy has unsatisfied preventive effect on the CNS, and it is still necessary to explore the value of combinational therapy, such as combined BTK inhibitors and high-dose methotrexate.

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