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POSTER ABSTRACTS

614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

To Reverse Sensitization By Co-Administration of Bortezomib and Rituximab with Conventional Chemotherapy for Patients Who Developed Neutralizing Hypersensitivity Reactions Against Asparaginase

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Background:
Acute lymphoblastic leukemia (ALL) patients undergoing Pegylated asparaginase (Peg-asp) or Erwinia-asparaginase (Erw-asp) preparation therapy may experience silent inactivation and allergy to asparaginase (ASP), leading to decreased therapeutic efficacy. How to treat ASP sensitized patients, especially those who are allergic to both Peg-asp and Erw-asp, without compromising the treatment outcome remains a problem for hematologists.This study aims to investigate whether the sensitization to Peg-asp can be reversed through the co-treatment of bortezomib and rituximab with conventional chemotherapy for patients hypersensitive to both Peg-asp and Erw-asp.
Method:
ALL Patients who developed silent inactivation and allergic reaction to both Peg-asp and Erw-asp enrolled in the study. The study featured 2 courses of combined conventional chemotherapy with rituximab and bortezomib co-treatment. In the second course of desensitization, Peg-asp was re-exposed according to the severity of previous allergic reaction against Peg-asp. For those with silent inactivation or previous allergic reactions of grade $\leq$ III, a split intramuscular injection was administered (the first dose was given at 1/10th of the required dosage, and then the remaining dose was given at an interval of 2 hours if there was no allergic reaction). Patients with grade IV previous allergic reactions underwent a standard 3-bag desensitization procedure. ASP activity was measured on days 1, 3, 7, 10, 14, and 21 after the first Peg-asp re-challenge. If re-exposure to the first dose did not result in an allergic reaction, a subsequent intramuscular single full dose was administered based on the results of ASP activity monitoring. Primary endpoint: to observe the percentage of allergic reaction on re-exposure and the duration of sustained ASP activity.
Result:
From August 2020 to May 2023, 10 patients of ALL who developed a neutralizing allergy or silent inactivation to both Peg-asp and Erw-asp preparation were recruited to the study. Among them, six cases were B-ALL, and four were T-ALL. The median age of the participants was 8 years, with seven boys and three girls. Seven children experienced Peg-asp neutralizing allergy or silent inactivation during remission induction, while three children experienced it during the interphase treatment. Eight of them had clinical manifestations of allergy and two had silent inactivation. During the second desensitization course, none of the children showed any allergic reaction after the first re-exposure to Peg-asp. Three children maintained >3 weeks of therapeutic activity after the first Peg-asp re-exposure, while one child maintained 14 days, and three children maintained 10 days. Three children detected Asp activity below 100U/L on day 3 monitoring.
After two courses of desensitization, the patients returned to the original chemotherapy regimen. Nine patients (90%) maintained activity above 0.1IU/ML for more than three weeks after subsequent Peg-asp administration. One child developed pancreatitis after the last dose of Peg-asp but recovered soon. Another child experienced silent inactivation and was discontinued from all ASP administration.
During desensitization therapy, eight children developed febrile neutropenia. Three were recovered with outpatient antibiotic treatment, while five required hospitalization for 5-7 days. As of July 30, 2023, all ten children survived without any adverse events, with a median follow-up time of 28 months from the start of desensitization therapy.
Conclusion:
Rituximab and bortezomib co-treatment effectively reverse ASP sensitization and restore the sustained potent activity of Peg-asp. This co-treatment is a safe and promising desensitization therapy after ASP sensitization in ALL patients.

Disclosures No relevant conflicts of interest to declare.

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