Clinical and Subclinical Hypersensitivity to Asparaginase in Acute Lymphoblastic Leukemia

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Asparaginase is an essential element of acute lymphoblastic leukemia treatment. It depletes serum asparagine (an amino acid necessary for synthesis of cellular proteins), deprives leukemic blast cells of asparagine, and eventually results in cell death. To gain benefit from asparaginase, asparagine depletion must be ensured by giving intensive therapy and completing the full course of treatment. Three formulations of asparaginase exist; two are derived from Escherichia coli, a native form and pegylated form, and one is derived from Erwinia chrysanthemi (Erwinia asparaginase). Like many large proteins, asparaginases are immunogenic, and some patients develop antibodies to asparaginase. Antibodies may result in clinical hypersensitivity or subclinical hypersensitivity without symptoms, and both can result in a reduction in asparaginase activity and may affect therapeutic benefit. Clinical hypersensitivity is the most common reason for patients to stop asparaginase treatment. Subclinical hypersensitivity can only be identified by laboratory testing; therapeutic monitoring of asparaginase activity is used as a surrogate measure for asparagine depletion.

Asparaginase is a naturally occurring enzyme in animals, plants, and microorganisms. It hydrolyzes asparagine to aspartic acid and ammonia, removing asparagine from the serum. Leukemic blast cells are unable to synthesize asparagine and, therefore, in treatment identifies patients with an extremely high risk of relapse (Pui & Evans, 2006). The use of MRD in terms of methodology, time points of testing, and appropriate cutoffs to identify different groups is an area of active investigation among all cooperative groups and continues to evolve.

Asparaginase is a cornerstone of treatment for ALL and is used in all treatment protocols (Pieters et al., 2011). To gain clinical benefit from asparaginase, patients must receive intensive therapy and complete the full course of treatment. A number of studies have shown significant benefit in terms of event-free survival (EFS), disease-free survival, and continuous complete remission rate with intensive asparaginase therapy (Rizzari et al., 2013).

Asparaginase Products

Mode of Action

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