UPDATED OUTCOMES OF AN INDIVIDUALIZED HIGH-DOSE METHOTREXATE PROTOCOL FOR PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: High-dose methotrexate (HD-MTX), an essential component of acute lymphoblastic leukemia (ALL) therapy, is associated with adverse events including mucositis, neurotoxicity, and myelosuppression. We previously described success of an intensive monitoring protocol to safely administer HD-MTX to patients with history of, or at risk for, severe toxicity. Per provider discretion, some patients have been treated per an institutional best practice standard using the protocol examined in the prospective study since study closure in November 2016. The purpose of this analysis is to describe the real-world application of our institutional practice since the study closure, to examine the use of the standard versus fixed dose reductions, and to better describe patients eligible who may benefit from intensive monitoring of HD-MTX.

Materials/Methods: This is a retrospective chart review of patients who received at least one dose of HD-MTX at Texas Children's Hospital (TCH) from 12/2016-12/2020 per the intensive monitoring protocol or with a fixed-dose reduction. Data abstraction included the rationale for selecting the intensive monitoring protocol or fixed dose reduction, number and severity of clinical adverse events, errors encountered implementing the protocol, and criteria used by the clinician to follow the intensive monitoring protocol.

Results: We identified 79 patients for inclusion. 23 patients received HD-MTX via the intensive monitoring protocol due to prior course of delayed clearance or severe toxicity. Of the 56 patients identified with fixed dose reductions most had a prior course with severe toxicity. Feasibility and implementation concerns of the intensive monitoring protocol included: methotrexate extending beyond pre-defined infusion time, misinterpretation of the protocol with pre-infusion fixed dose reductions, non-adherence for all courses, and inconsistent use of the institutional practice.

Conclusions: HD-MTX is a critical part of ALL therapy; as such, we continue to support use of the intensive monitoring protocol. Our investigation revealed opportunities for improvement in translating the protocol from one administered in the context of a clinical study to one provided in the real world. In addition, we identified a significant number of patients in our center who may have benefitted from the intensive monitoring protocol, but for whom a fixed dose reduction was selected. Each of these issues will be addressed with relevant stakeholders to improve our ability to deliver HD-MTX at TCH.

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