MTXPK.org: A clinical decision support tool evaluating high-dose methotrexate pharmacokinetics to inform post-infusion care and use of glucarpidase

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Background: At high-doses, MTX is intravenously infused over 3-36 hours and is accompanied by therapeutic drug monitoring and meticulous supportive care. However, some patients experience delayed renal elimination of MTX, leading to an increased risk for severe nephrotoxicity and possibly death. Glucarpidase is a rescue agent for MTX overexposure but knowing when to administer the drug is challenging due to ambiguity in the labeled indication and clinical interpretation of the consensus guideline. Our goal was to develop a web-based clinical decision support tool, MTXPK.org, that could help clinicians understand MTX PK and when to use glucarpidase.

Methods: MTXPK.org uses a three-compartment population pharmacokinetic (PK) model developed using 31,717 MTX plasma concentrations obtained from 772 pediatric patients with acute lymphoblastic leukemia receiving MTX on Nordic Society of Hematology and Oncology protocols. Model fitting was validated on two external datasets with diverse age range, indication, and dosing schedules prior its integration into MTXPK.org. A module for Bayesian estimation is included in the MTXPK.org platform. The Edsim++ model designer compatible PK-engine runtime enables the Bayesian estimation of individual PK parameters.

Results: The web-based clinical decision support tool works by allowing the user to enter the patient's demographics, dose administered, infusion duration, MTX plasma concentrations, and serum creatinine levels. Then, the tool uses the model parameters from the default population PK model as reliable, prior knowledge for a posteriori Bayesian estimation of the individual patient's elimination profile. MTXPK.org then plots it over top of the population's average concentration-time curve and shaded ± 2 SD, to illustrate the labeled indication of glucarpidase, and glucarpidase guideline thresholds at static time points to facilitate model-informed supportive care and use of glucarpidase based on real-time feedback of a patient's MTX clearance. Since its launch in December 2019, the webtool has been used by >900 unique users in at least 35 countries.

Conclusion: MTXPK.org is a free, web-based clinical decision support tool that is designed to help clinicians understand MTX PK and when to use glucarpidase in individual patients. This tool has the capability to improve the quality of care for all patients receiving high-dose MTX treatment.

Key Words: Clinical Decision Support Tool, Glucarpidase, Methotrexate, Oncology, Pharmacometrics, Therapeutic Drug Monitoring