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:
- Glucarpidase is a FDA-approved exogenous enzyme administered as a rescue agent for severe methotrexate (MTX) toxicity for patients with delayed MTX clearance following an intravenous infusion of high-dose MTX
- However, appropriate administration is challenging due to the ambiguity in the labeled indication and clinical interpretation of the consensus guideline

Methods:
- Use NONMEM to perform population PK modeling of 31,672 MTX plasma concentrations from 772 pediatric patients with acute lymphoblastic leukemia (ALL)
- Two external data sets with diverse age range, indication, and dosing schedules were used to validate the model.
- The model’s predictive performance as a Bayesian estimator was compared to previously published population PK models using a windows stand-alone prototype, MtxSim

Results:
- The user loads their patient demographics, treatment details, MTX plasma concentrations, and serum creatinine as clinical covariates to estimate the patient’s elimination profile.
- MTXPK.org will plot 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.
- Visual and numeric interpretation facilitate model-informed supportive care and use of glucarpidase.

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