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Reply to: Glucarpidase for the Treatment of Methotrexate-Induced Renal Dysfunction and Delayed Methotrexate Excretion

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To the Editor: Dr. Meyers suggests in his letter [1] and in a similar communication in the past [2] that the administration of glucarpidase is unnecessary for the treatment of high-dose methotrexate (HDMTX) induced renal dysfunction, as glucarpidase (i) only addresses reduction of methotrexate (MTX) in the intravascular compartment, (ii) does not impact the intracellular or urinary collecting system, and (iii) does not obviate the need for continued administration of leucovorin.

The risk for the development of life-threatening toxicities in HDMTX-related renal dysfunction is directly linked to the degree of elevation of plasma MTX concentrations. Rescue with pharmacokinetically guided doses of leucovorin is the standard treatment in this situation [3] and essential for the reasons outlined by Dr. Meyers.[1] However, while critical to the treatment of HDMTX-induced renal dysfunction, leucovorin has no impact on MTX clearance or removal. By hydrolyzing plasma MTX to inactive metabolites, glucarpidase greatly decreases the magnitude (median decreases in plasma MTX concentrations 98.7% within 15 min) and duration of systemic exposure to MTX.[4] Thus, glucarpidase eliminates the risk resulting from elevated plasma MTX concentrations within minutes and allows for safe continued rescue with leucovorin until renal function recovers sufficiently to clear MTX. For these reasons, glucarpidase was approved as an adjunct treatment in addition to leucovorin. With this in mind, the question should not be whether HDMTX-related renal dysfunction could be treated with leucovorin rescue alone but why one would not utilize glucarpidase as noninvasive and highly effective means of drug removal in addition to leucovorin.

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Conflict of interest: Nothing to declare.

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