On behalf of BTG, I respectfully request the NCCN Acute Lymphoblastic Leukemia panel review the enclosed publications as support for revision to the recommendation on use of glucarpidase currently included in the NCCN guideline for ALL.

Currently, the NCCN Guideline for ALL includes a recommendation for use of glucarpidase in the Supportive Care section on page ALL-C 1 of 4:

“Consider use of glucarpidase in patients with significant renal dysfunction and toxic plasma methotrexate concentrations with delayed methotrexate clearance (plasma methotrexate concentrations >2 standard deviations of the mean methotrexate excretion curve specific for the dose of methotrexate administered).”

The specific change we are requesting is to modify the recommendation language based on the consensus guidelines published (Ramsey LB et al. The Oncologist 2017, enclosed).

We propose that the recommendation on page ALL-C 1 of 4 in the Supportive Care section be revised to the following:

“Glucarpidase is strongly recommended in the context of a rising serum creatinine if the 36-hour plasma methotrexate level is above 30 μM, 42-hour level is above 10 μM, or 48-hour level is above 5 μM. Optimal administration of glucarpidase is within 48 to 60 hours from the start of methotrexate infusion."

The guideline also includes a recommendation in the discussion section of the guideline pertaining to NCCN Recommendations for Supportive Care, on page MS-52 and we request that similar additional or revised language be included within this section.

Rationale: In support of the proposed change, an international panel of clinicians convened to provide expert consensus guidelines for the use of glucarpidase in patients who develop acute kidney injury and delayed methotrexate excretion during methotrexate therapy. The guideline provides specific methotrexate plasma concentrations and times that would indicate when glucarpidase should be given, and recommend administration optimally within 48 to 60 hours from start of methotrexate infusion. These guidelines have been adopted by the Children's
Oncology Group, and are also referenced in UpToDate, and therefore should be reflected in the NCCN guidelines as well.

The following articles are submitted in support of this proposed change.


2. LaCasce AS. Therapeutic use and toxicity of high-dose methotrexate. In: UpToDate, Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com

Sincerely,

Suzanne Ward
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BTG International Inc.