National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Marie C. Rush, PharmD, CPP, BCOP
Wake Forest Baptist Health
Updated 8/10/20

Positive Quality Intervention: Use of Rasburicase (Elitek) for Treatment of Tumor Lysis Syndrome

Description: The purpose of this PQI is to identify appropriate dosing and utilization of rasburicase based on uric acid levels

Background: Rasburicase is an FDA approved intravenous medication for the management of serum uric acid levels in the setting of anticancer therapy that is expected to result in tumor lysis.[1,2]

While rasburicase breaks down uric acid that has already formed in the body, allopurinol prevents the formation of additional uric acid. The two medications work concomitantly to actively decrease elevated uric acid levels while also preventing hyperuricemia in the future.[3]

In general, the risk of a patient developing TLS is higher with hematologic malignancies. Risk stratification can be found in the modified chart below, adapted from TLS stratification[5] and prophylaxis[10] references.[5,10,12]

Type of Malignancy	High Risk	Intermediate Risk	Low Risk
Non-Hodgkin lymphoma (NHL)[5]	Burkitt lymphoma	DLBCL	Indolent NHL
Acute lymphoblastic leukemia (ALL)[10]	WBC ≥ 100,000 OR WBC <100,000 and/or LDH ≥ 2X ULN	WBC <100,000 and LDH <2X ULN	WBC <100,000
Acute myeloid leukemia (AML)[10]	WBC ≥ 100,000, monoblastic	WBC >25,000 but <100,000 OR WBC <25,000 and LDH >/=2X ULN	WBC <25,000 and LDH <2X ULN
Chronic lymphocytic leukemia (CLL)[10,12]	Venetoclax use (lymph node ≥ 10 cm or ALC ≥ 25,000 and lymph node ≥ 5 cm)	WBC 10,000 – 100,000 and treatment with targeted and/or biologic Therapy (ex. Fludarabine or Venetoclax) (lymph node 5-<10 cm or ALC ≥ 25,000)	WBC < 10,000 and using only alkylating agents Venetoclax use (all lymph nodes < 5 cm and ALC < 25,000)
Other hematologic malignancies (chronic myeloid leukemia, multiple myeloma) and solid tumors (small cell lung cancer)[5]	---	Rapid proliferation with expected rapid response to therapy	Remainder of patients

While FDA approved dosing of rasburicase is weight-based (0.2 mg/kg daily for up to 5 days), several studies have been performed that evaluated the use of single, fixed doses of rasburicase.[1,4,6,7,8,9] Trifilio and colleagues demonstrated that rasburicase 3 mg effectively lowered uric acid levels to ≤ 7 mg/dL in 72% of patients at 24 hours; uric acid levels continued to decrease without additional doses of rasburicase. Of note, patients with higher baseline uric acid levels (defined as ≥ 12 mg/dL) were found to be at risk of rasburicase failure. This patient population may require a higher initial dose of rasburicase at 6 mg, or a repeated dose of 3 mg if uric acid levels begin to rise again.[6] McBride and colleagues found similar success with the 3 mg dose in their study. However, it is worth noting that patients who received 3 mg of rasburicase had lower baseline uric acid levels compared to the patients who received 6 mg of rasburicase.[7]

National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Marie C. Rush, PharmD, CPP, BCOP
Wake Forest Baptist Health
Updated 8/10/20

PQI Process:

- Confirm the patient has an order/prescription for allopurinol
- Confirm the patient is maintaining adequate oral hydration or initiated on IV hydration
- Baseline and follow-up TLS labs (potassium, serum creatinine, uric acid, phosphorus, calcium, lactate dehydrogenase) should be obtained pre- and post-rasburicase administration
- Rasburicase dosing may vary per institution guidelines/policies
    - Patients with malignancies that are classified as having a high risk for TLS may require upfront dosing of rasburicase
    - Consider rasburicase 3 mg for patients with baseline uric acid <12 mg/dL
        - Encourage use of allopurinol and aggressive hydration prior to initiation of rasburicase
    - Consider rasburicase 6 mg for patients with baseline uric acid ≥12 mg/dL OR consider an initial dose of 3 mg and monitor the patient's uric acid levels closely to determine if a repeat dose of 3 mg is warranted
    - If warranted, repeated rasburicase dosing can be considered 24 hours after the initial dose
- Ensure uric acid levels obtained after rasburicase administration are immediately put on ice. If left at room temperature, the enzymatic activity of rasburicase will continue to break down uric acid and can result in a falsely low uric acid level

Patient Centered Activities:

- Patient Education
    - Although rare, hypersensitivity reactions have been reported with rasburicase
    - Methemoglobinemia can occur as a result of rasburicase administration
    - Hemolysis can occur after rasburicase administration in patients with G6PD deficiency
    - Counsel patients to maintain increased oral hydration

References:

1. Elitek (rasburicase) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; July 2019.
2. Cairo MS, Coiffier B, Reiter A, et al. Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: an expert TLS panel consensus. Br J Haematol. 2010;149:578-586.
3. Cairo MS and Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol 2004;127:3-11.
4. Hutcherson DA, Gammon DC, Bhatt MS, et al. Reduced-Dose Rasburicase in the Treatment of Adults With Hyperuricemia Associated With Malignancy. Pharmacother. 2006;26(2):242-7.
5. Coiffier B, Altman A, Pui C et al. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. *J Clin Oncol*. 2008;26:2767-78.
6. Trifilio SM, Pi J, Zook J, et al. Effectiveness of a single 3-mg rasburicase dose for the management of hyperuricemia in patients with hematological malignancies. Bone Marrow Transplant 2011;46:800-805.
7. McBride A, Lathon SC, Boehmer L, et al. Comparative evaluation of a single fixed dosing and weight-based dosing of rasburicase for tumor lysis syndrome. Pharmacother. 2013;33(3):295-303.
8. McDonnell AM, Lenz KL, Frei-Lahr DA, et al. Single-Dose Rasburicase 6 mg in the Management of Tumor Lysis Syndrome in Adults. Pharmacother. 2006;26(6):806-12.
9. Yu X, Liu L, Nie X et al. The optimal single-dose regimen of rasburicase for management of tumour lysis syndrome in chlidren and adults: a systematic review and meta-analysis. J Clin Pharm Ther. 2017;42:18-26.
10. Cairo MS, Coiffier B, Reiter A, Younes A. BJH 2010; 149;578-586
11. Howard N Eng J Med 2011;2011;364(19):1844-54
12. Itchaki G, Brown JR. The potential of venetoclax (ABT-199) in chronic lymphocytic leukemia. Ther Adv Hematol. 2016 Oct; 7(5): 270-287

National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Marie C. Rush, PharmD, CPP, BCOP
Wake Forest Baptist Health
Updated 8/10/20

Supplemental Information

Table 1: Diagnosis of Tumor Lysis (Cairo-Bishop Classification)[3,5]

Laboratory Tumor Lysis	Clinical TLS
Two or more of the following occurring in a patient with cancer within 3 days prior to or 7 days following initiation of cancer treatment: • Uric acid ≥ 8 mg/dL or 25% increase from baseline • Potassium ≥ 6 mmol/L (6 mg/L) or 25% increase from baseline • Phosphate ≥ 4.5 mg/dL or 25% increase from baseline • Calcium ≤ 7 mg/dL or 25% decrease from baseline	Laboratory tumor lysis plus one of the following: • Serum creatinine ≥ 1.5 x ULN • Cardiac arrhythmia/sudden death • Seizure

Image 1: TLS Risk Assessment regarding tumor mass[11]