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

Description: The purpose of this PQI is to identify appropriate dosing of rasburicase based upon 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] Rasburicase enzymatically metabolizes uric acid into allantoin, a highly soluble compound that can be renally eliminated. Allopurinol inhibits xanthine oxidase and the formation of uric acid but does not remove existing 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 laboratory or clinical TLS is higher with hematologic malignancies.

Risk Stratification for the development of TLS[5]

Type of Malignancy	High Risk	Intermediate Risk	Low Risk
Non-Hodgkin lymphoma (NHL)	Burkitt lymphoma	DLBCL	Indolent NHL
Acute lymphoblastic leukemia (ALL)	WBC ≥ 100,000	WBC 50,000 – 100,000	WBC < 50,000
Acute myeloid leukemia (AML)	WBC ≥ 50,000, monoblastic	WBC 10,000 – 50,000	WBC < 10,000
Chronic lymphocytic leukemia (CLL)	Venetoclax (lymph node ≥ 10 cm or ALC ≥ 25,000 and lymph node ≥ 5 cm)	WBC 10,000 – 100,000 Fludarabine Venetoclax (lymph node 5-<10 cm or ALC ≥ 25,000)	WBC < 10,000 Venetoclax (all lymph nodes < 5 cm and ALC < 25,000)
Other hematologic malignancies (chronic myeloid leukemia, multiple myeloma) and solid tumors (small cell lung cancer)	---	Rapid proliferation with expected rapid response to therapy	Remainder of patients

Diagnosis of Tumor Lysis[3]

Laboratory Tumor Lysis	Clinical TLS
Two or more of the following occurring in a patient within 3 days prior to or 7 days following initiation of cancer treatment: • Uric acid ≥ 8 mg/dL or 25% increase from baseline in adults; above ULN for age in children • Potassium ≥ 6 mg/dL or 25% increase from baseline • Phosphate ≥ 4.5 mg/dL or 25% increase from baseline in adults; >6.5 mg/dL in children • Corrected calcium ≤ 7 mg/dL or 25% decrease from baseline; ionized calcium <4.5 mg/dL	Laboratory tumor lysis plus one of the following: • Hyperkalemia leading to cardiac dysrhythmia/sudden death • Hypocalcemia leading to cardiac dysrhythmia/sudden death/seizure, neuromuscular irritability/hypotension/ heart failure • Acute kidney injury - increase in serum creatinine of 0.3 mg/dL (or a single value >1.5 times ULN of age-appropriate normal range, if no baseline available) or presence of oliguria (average urine output of <0.5 ml/kg/hr for 6 hr)

Risk and Preventive Treatment of TLS with ≤ 1 Abnormal Laboratory Value[10]

Risk	**Negligible Risk**		**Low Risk**		**Intermediate Risk**		**High Risk**	
Cancer Mass	**Small/resected localized tumor**	**Medium Mass**	**Medium Mass**	**Large Mass**	**Medium Mass**	**Large Mass**	**Medium Mass**	**Large Mass**
Cell Lysis Potential	--	Low	Medium	Low	Medium/Unknown	Medium/Unknown	High	High
Preexisting nephropathy, dehydration, acidosis, hypotension, or nephrotoxin exposure	--	None	None	--	Yes	--	--	--
Treatment	No Prophylaxis		• Allopurinol • IV Fluids • Daily labs		• Allopurinol or Rasburicase • IV Fluids • Inpatient Monitoring • Labs every 8-12 hours		• Rasburicase • IV Fluids • Cardiac Monitoring • Labs every 6-8 hours	

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]

PQI Process:

- Confirm the patient has an order/prescription for allopurinol
- Confirm the patient is maintaining adequate oral hydration or initiated on IV hydration
- Screen for G6PD deficiency
    - Hemolysis can occur after rasburicase administration in patients with G6PD deficiency
- 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 high risk TLS 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 uric acid levels to determine if a repeat dose of 3 mg if 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:

- Provide written and verbal patient education
  - Educate patients that although rare, hypersensitivity reactions have been reported
  - Ensure patients know the signs and symptoms of methemoglobinemia and TLS
  - Counsel patients to maintain increased and adequate oral hydration
- Patient Assistance: NCODA Financial Assistance Tool

References:

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