MEET SARAH: NEWLY DIAGNOSED PATIENT WITH CLL WHO IS AT RISK OF TLS

Not an actual patient

Medical History

- 65-year-old woman of Caucasian descent
- No family history of blood and bone marrow cancers
- Treated 4 months ago for a cold that progressed to recurrent sinusitis
- Presented with fatigue, weight loss, night sweats, and a fever
- Upon examination, Sarah's lymph nodes and spleen were enlarged
- Diagnosed with stage IV CLL and International Prognostic Index score 4[1]

Diagnostic workup[1]	Laboratory workup[1-4]
CT: showed cervical lymphadenopathy ~6 cm	Elevated WBC: 46,000 cells/mm^3 (normal range: 4500–11,000 cells/mm^3)
Spleen: palpable 8 cm below the costal margin	Elevated LDH: 320 U/L (normal range: 140–280 U/L)
Kidney function: normal	Normal creatinine: 0.65 mg/dL (normal range: 0.6–1.1 mg/dL)
	Normal eGFR: 97 mL/min/1.73 m^2 (normal range: 90–120 mL/min/1.73 m^2)
	Elevated uric acid: 8.7 mg/dL (normal range: 2.4–6.0 mg/dL)
	Low Hgb: 8.8 g/dL (normal range: 12.1–15.1 g/dL)
	Low platelets: 105 × 10^9/L (normal range: 150–400 × 10^9/L)
	Elevated beta-2 microglobulin: 4.1 mg/L (normal range: <2.4 mg/L)

- **Disease status: Sarah's workup shows that she has high tumor burden and high uric acid level at baseline. Her laboratory results show an elevated WBC count, elevated LDH, elevated uric acid, low Hgb and platelets, and elevated beta-2 microglobulin**
- **Treatment plan: Venetoclax in combination with obinutuzumab for 12 months[5]**

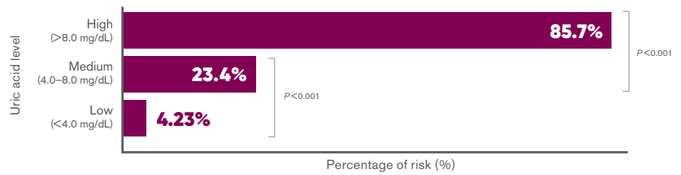
Are patients like Sarah with high tumor burden and elevated uric acid at baseline at high risk of developing tumor lysis syndrome?

CLL=chronic lymphocytic leukemia; TLS=tumor lysis syndrome; CT=computed tomography; WBC=white blood cell count; LDH=lactate dehydrogenase; eGFR=estimated glomerular filtration rate; hgb=hemoglobin.

PATIENTS WITH A HIGH URIC ACID LEVEL (>8 mg/dL) AT BASELINE HAD AN 85.7% INCREASED RISK OF DEVELOPING TLS[6]

In a retrospective analysis, 1198 patients diagnosed with a hematologic malignancy were admitted for inpatient chemotherapy. Those with baseline hyperuricemia (>8.0 mg/dL) had an 85.7% increased risk of developing TLS versus patients with a uric acid level of 4.0–8.0 mg/dL (*P*<0.001).[6]

Relationship between uric acid level and development of TLS in patients with hematologic malignancies[6]



ELITEK® (rasburicase) is indicated for the initial management of plasma uric acid levels in pediatric and adult patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of uric acid. ELITEK is indicated only for a single course of treatment.

Important Safety Information

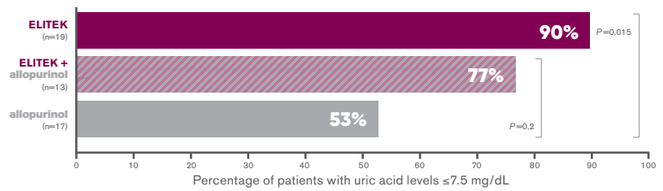
WARNING: HYPERSENSITIVITY REACTIONS, HEMOLYSIS, METHEMOGLOBINEMIA, AND INTERFERENCE WITH URIC ACID MEASUREMENTS

- **Hypersensitivity Reactions: ELITEK can cause serious and fatal hypersensitivity reactions including anaphylaxis. Immediately and permanently discontinue ELITEK in patients who experience a serious hypersensitivity reaction.**
- **Hemolysis: Do not administer ELITEK to patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Immediately and permanently discontinue ELITEK in patients developing hemolysis. Screen patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) prior to starting ELITEK.**

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

ELITEK (rasburicase) GIVEN PROPHYLACTICALLY MAINTAINED NORMAL URIC ACID LEVELS IN SIGNIFICANTLY MORE PATIENTS WITH BASELINE HYPERURICEMIA VS ALLOPURINOL[7]

Hyperuricemic patients (%) who maintained normal uric acid levels (≤7.5 mg/dL) from days 3–7 after initiating antihyperuricemic treatment[7,8]



- Results were consistent with the overall study population of intermediate and high-risk patients[7]
- **Primary endpoint:** 87% (n=92) of patients receiving ELITEK prophylactically maintained uric acid levels ≤7.5 mg/dL vs 66% (n=91) of patients receiving allopurinol (*P*=0.001)[7]
  - ELITEK + allopurinol maintained normal uric acid in 78% (n=92) of patients (*P*=NS vs allopurinol)[7]

ELITEK HAS A PROVEN SAFETY PROFILE[8]

Per-patient incidence of selected adverse reactions[8]

	ELITEK % (n=92)		ELITEK + allopurinol % (n=92)		allopurinol % (n=91)	
Adverse Reaction*	**All grades**	**Grades 3/4**	**All grades**	**Grades 3/4**	**All grades**	**Grades 3/4**
Nausea	57.6	1.1	60.9	1.1	54.9	2.2
Peripheral edema	50	2.2	43.5	3.3	42.9	6.6
Vomiting	38	1.1	37	0	30.8	1.1
Anxiety	23.9	3.3	17.4	0	17.6	0
Abdominal pain	21.7	3.3	33.7	4.3	25.3	2.2
Hypophosphatemia	17.4	4.3	22.8	6.5	16.5	6.6
Hyperbilirubinemia	16.3	3.3	14.1	2.2	7.7	4.4
Pharyngolaryngeal pain	14.1	1.1	20.7	0	9.9	0
Sepsis	12	5.4	7.6	6.5	4.4	4.4
Fluid overload	12	0	6.5	0	3.3	1.1
Increased ALT	10.9	3.3	27.2	4.3	17.6	2.2
Hyperphosphatemia	9.8	0	15.2	0	8.8	1.1

ALT=alanine aminotransferase.
*Events were reported and graded according to NCI-CTC Version 3.0 and presented as preferred terms MedDRA version 10.1.

Overall incidence of adverse reactions ≥10% in any ELITEK arm and the difference between any ELITEK arm vs allopurinol ≥5%[8]

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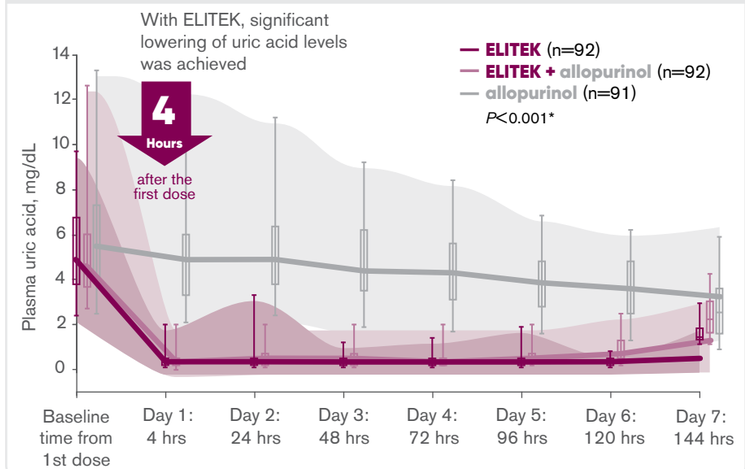
ELITEK GIVEN PROPHYLACTICALLY SIGNIFICANTLY AND RAPIDLY LOWERED URIC ACID LEVELS, INCLUDING PATIENTS WITH BASELINE HYPERURICEMIA (>7.5 mg/dL)[8]

- 96% of ELITEK patients achieved uric acid levels ≤2 mg/dL within 4 hours after their first dose vs 0% with allopurinol[7,8]

Reduction in uric acid levels[7,8]



*Plasma uric acid AUC from day 1 through day 7 was significantly lower for ELITEK and ELITEK + allopurinol than for allopurinol alone (*P*<0.001).

AUC=area under the curve.

Important Safety Information cont'd

CONTRAINDICATIONS

ELITEK is contraindicated in patients with a history of anaphylaxis or severe hypersensitivity to rasburicase or in patients with development of hemolytic reactions or methemoglobinemia with rasburicase. ELITEK is contraindicated in individuals deficient in glucose-6-phosphate dehydrogenase (G6PD).

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

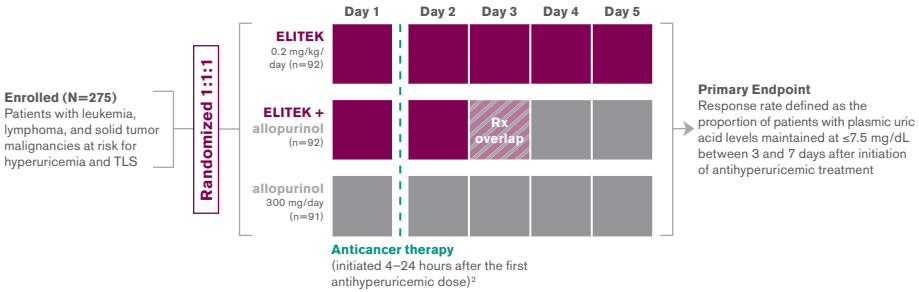
ELITEK® rasburicase IV Infusion

ELITEK GIVEN PROPHYLACTICALLY WAS STUDIED IN HIGH-RISK PATIENTS, SOME WITH BASELINE HYPERURICEMIA (>7.5 mg/dL)[7]

Antihyperuricemic therapy in all 3 arms was initiated prior to anticancer therapy[7]

Phase 3, randomized, multicenter, open-label study

Pivotal trial design[7,8]



18% of patients were hyperuricemic (>7.5 mg/dL) at baseline and therefore considered at high risk of developing TLS.[8]

NCCN CLL/SLL Guidelines: Consider prophylaxis with rasburicase in patients receiving venetoclax with high tumor burden and elevated baseline uric acid[1]

Important Safety Information cont'd

- **Methemoglobinemia: ELITEK can result in methemoglobinemia in some patients. Immediately and permanently discontinue ELITEK in patients developing methemoglobinemia.**
- **Interference with Uric Acid Measurements: ELITEK enzymatically degrades uric acid in blood samples left at room temperature. Collect blood samples in prechilled tubes containing heparin and immediately immerse and maintain sample in an ice water bath. Assay plasma samples within 4 hours of collection.**

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

ELITEK® rasburicase IV Infusion

ELITEK® rasburicase IV Infusion

PROTECT PATIENTS PRESENTING WITH HIGH URIC ACID WHO ARE AT RISK OF DEVELOPING TLS[8]

Consider ELITEK: The only recombinant urate-oxidase FDA approved for the initial management of uric acid in patients with leukemia and lymphoma who are receiving anticancer therapy[8]

Recommended: For patients at high and intermediate (potential) risk for development of TLS associated with hyperuricemia[1]

Important Safety Information cont'd

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥20%), when used concomitantly with anticancer therapy, are vomiting, nausea, fever, peripheral edema, anxiety, headache, abdominal pain, constipation, diarrhea, hypophosphatemia, pharyngolaryngeal pain, and increased alanine aminotransferase.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Consider the benefits and risks of ELITEK and possible risks to the fetus when prescribing ELITEK to a pregnant woman.
- **Lactation:** Because of the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with ELITEK and for 2 weeks after the last dose.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed WARNING.

References: 1. NCCN Guidelines. Chronic lymphocytic leukemia/small lymphocytic lymphoma. V5.2019. Accessed June 27, 2019. **2.** US National Library of Medicine. Medical encyclopedia. MedlinePlus website. https://medlineplus.gov/encyclopedia.html. Accessed July 10, 2019. **3.** Fischbach FT et al. Chemistry studies. In: Fischbach FT et al, eds. *A Manual of Laboratory and Diagnostic Tests.* 10th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2017:325-456. **4.** Thompson PA et al. *Cancer.* 2016;122(4):565-573. **5.** Venclexta [prescribing information]. South San Francisco, CA: Genentech USA, Inc; 2019. **6.** Cairo MS. *Clin Lymphoma.* 2002;3(suppl1):S26-S31. **7.** Cortes J et al. *J Clin Oncol.* 2010;28(27):4207-4213. **8.** Elitek [prescribing information]. Bridgewater, NJ: sanofi-aventis US, LLC; 2017.

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