MEET VICTOR: NEWLY DIAGNOSED PATIENT WITH DLBCL WHO IS AT RISK OF TLS

Not an actual patient

Medical History

- 58-year-old man of Caucasian descent
- Active in retired life
- Recently found palpable lump under right armpit
- Has been experiencing night sweats and weight loss of 10 pounds over the last 6 weeks
- Upon examination, Victor had nodal masses, with the largest measuring up to 8 cm in diameter
- Diagnosed with stage III bulky DLBCL and International Prognostic Index score

Diagnostic workup[1,2]	Laboratory workup[3-5]
PET-CT: showed multiple nodal lesions, including in the spleen	Elevated WBC: 20,000 cells/mm^3 (normal range: 4500–11,000 cells/mm^3)
ECOG PS score: 0	Elevated LDH: 600 U/L (normal range: 140–280 U/L)
Kidney function: impaired	Elevated creatinine: 1.9 mg/dL (normal range: 0.7–1.3 mg/dL)
	Low eGFR: 39 mL/min/1.73 m^2 (normal range: 90–120 mL/min/1.73 m^2)
	Normal uric acid: 6.8 mg/dL (normal range: 3.4–7.0 mg/dL)
	Low Hgb: 8.8 g/dL (normal range: 13.8–17.2 g/dL)
	Low platelets: 105 × 10^9/L (normal range: 150–400 × 10^9/L
	Normal beta-2 microglobulin: 2.1 mg/L (normal range: <2.4 mg/L)

- **Disease status: Victor's workup shows that he has bulky disease with nodal involvement. His laboratory results show an elevated WBC count, elevated LDH, elevated creatinine, low eGFR and low Hgb and platelets**
- **Treatment plan: R-CHOP* for 6 cycles[2]**

According to his workup, what is Victor's risk level for developing tumor lysis syndrome (TLS) and hyperuricemia?

DLBCL=diffuse large B-cell lymphoma; PET-CT=positron-emission tomography–computed tomography; ECOG PS=Eastern Cooperate Oncology Group Performance Status; WBC=white blood cell; LDH=lactate dehydrogenase; eGFR=estimated glomerular filtration rate; hgb=hemoglobin.
*R-CHOP=rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone (combined therapy with rituximab 375 mg/m^2 IV on day 1 plus cyclophosphamide 750 mg/m^2 IV on day 1 or 3 plus doxorubicin 50 mg/m^2 IV on day 1 or 3 plus vincristine 1.4 mg/m^2 [maximum dose, 2 mg] IV on day 1 or 3 plus prednisone 40 mg/m^2 orally on days 1-5 or 3-8).

THE CHARACTERISTICS OF VICTOR'S DISEASE PUT HIM AT HIGH RISK OF DEVELOPING TLS[2,6]

☑ Bulky disease	☑ Elevated LDH	☑ Renal involvement or insufficiency
☑ Lymph node involvement	☑ Elevated creatinine levels	☐ Reduced eGFR
☐ Bone marrow involvement	☑ Elevated WBC count	☐ Elevated uric acid

ADDITIONALLY, VICTOR'S TREATMENT REGIMEN PUTS HIM AT RISK[7-10]

Anticancer agents associated with elevated uric acid or TLS[7-26,*]

☐ Bendamustine HCl	☑ Doxorubicin HCl†	☐ Pomalidomide
☐ Bortezomib	☐ Ibrutinib	☑ Rituximab†
☐ Brentuximab vedotin	☐ Imatinib	☐ Romidepsin
☐ Carfilzomib	☐ Ixazomib	☐ Thalidomide
☑ Cyclophosphamide†	☐ Lenalidomide	☐ Venetoclax
☐ Cytarabine	☐ Obinutuzumab	☑ Vincristine sulfate†
☐ Dasatinib	☐ Omacetaxine	

*This is not a comprehensive list of agents.
†Components of the R-CHOP regimen.

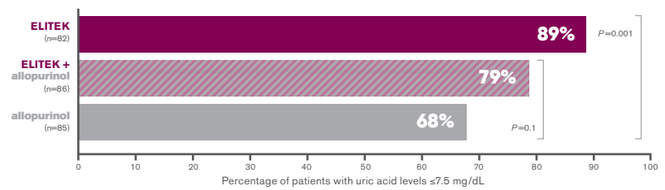
ELITEK® (rasburicase) is recommended for patients at high and intermediate (potential) risk for development of TLS associated with hyperuricemia[27]

ELITEK 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.

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 HIGH-RISK PATIENTS VS ALLOPURINOL[28]

High-risk patients (%) who maintained normal uric acid levels (≤7.5 mg/dL) from day 3 to day 7 after initiating antihyperuricemic treatment[28,32]



- Results were consistent with the overall study population of intermediate and high-risk patients[28]
- **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). ELITEK + allopurinol maintained normal uric acid in 78% (n=92) of patients (*P*=NS vs allopurinol)[28]
- **Phase 3 study:** randomized, multicenter, open-label study in adults (N=275) with leukemia, lymphoma, and solid tumor malignancies at risk for hyperuricemia and TLS[28]
- **3 study arms:** patients in Arm A received ELITEK (0.2 mg/kg/day) for 5 days (n=92). Patients in Arm B received ELITEK (0.2 mg/kg/day) from day 1 through day 3 followed by oral allopurinol (300 mg/day) from day 3 through day 5 (overlap on day 3: ELITEK [0.2 mg/kg/day] and allopurinol [300 mg/day] administered approximately 12 hours apart) (n=92). Patients in Arm C received oral allopurinol (300 mg/day) for 5 days(n=91)[28]
  - Anticancer therapy was initiated 4–24 hours after the first antihyperuricemic dose[28]
- **Primary endpoint:** response rate defined as the proportion of patients with plasma uric acid levels maintained at ≤7.5 mg/dL between 3 and 7 days after initiation of antihyperuricemic treatment[28]

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.**

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UNLIKE ALLOPURINOL, ELITEK MAINTAINED NORMAL URIC ACID LEVELS IN 100% OF ASSESSABLE PATIENTS[32]

Documented failure rate in hyperuricemic and nonhyperuricemic patients[32]

✓	✓	✗
0%	0%	11%
ELITEK (n=92)	ELITEK + allopurinol (n=92)	allopurinol (n=91)

- The ELITEK, ELITEK + allopurinol, and allopurinol arms had 13%, 15%, and 19% missing uric acid samples, respectively. The uric acid failure status in those patients is unknown[32]

ELITEK HAS A PROVEN SAFETY PROFILE[32]

Per-patient incidence of selected adverse reactions[32]

	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%.

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ELITEK® rasburicase IV Infusion

ELITEK WAS STUDIED IN PATIENTS AT HIGH RISK OF TLS AND HYPERURICEMIA LIKE VICTOR[28,29]

9 out of 10 patients were at high risk

82% of patients had normal uric acid levels ≤7.5 mg/dL

Patients meeting at least one of the following criteria were enrolled in the pivotal trial[28]:

High Risk[28,30,31]	Intermediate (Potential) Risk[28]
Aggressive lymphoma/leukemia (defined by REAL) • DLBCL • Anaplastic large cell lymphoma • Peripheral T-cell lymphomas • Burkitt lymphoma • Lymphoblastic lymphoma • CLL	Aggressive lymphoma/leukemia, not limited to the REAL definition, with LDH ≥2× the upper limit of normal
AML	Any stage III to IV lymphoma or leukemia
Elevated plasma uric acid levels at baseline (>7.5 mg/dL)	Stage I or II disease with bulky lymph node/tumor (>5 cm) involvement
High-grade MDS with >10% bone marrow blast involvement	
CML in blast crisis	

AML=acute myeloid leukemia; CLL=chronic lymphocytic leukemia; CML=chronic myeloid leukemia; MDS=myelodysplastic syndromes; REAL=Revised European American Classification of Lymphoid Neoplasms.

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 IV Infusion

ELITEK®
rasburicase
IV Infusion

PROTECT PATIENTS AT HIGH RISK FROM RISING URIC ACID LEVELS

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[32]

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).

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.

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