ELITEK® rasburicase IV Infusion

HEAD-TO-HEAD TRIAL VS ALLOPURINOL DEMONSTRATING SUPERIOR EFFICACY IN MAINTAINING NORMAL URIC ACID LEVELS[1]*

*Significantly (*P*=0.001) more patients receiving ELITEK (87% [n=92]) prophylactically maintained normal uric acid levels ≤7.5 mg/dL vs those receiving allopurinol (66% [n=91]). More patients receiving ELITEK + allopurinol (78% [n=92]) maintained normal uric acid (*P*=NS vs allopurinol).[1] See these results as a bar chart on page 2.

ELITEK was studied in adult patients at high and intermediate (potential) risk of TLS[1]

92% of adult patients were at high risk for tumor lysis syndrome (TLS)[1]

82% of adult patients had normal uric acid levels (≤7.5 mg/dL)[1]

Patients meeting at least 1 of the following criteria were enrolled in the pivotal trial[1]:

HIGH RISK[1-3]	
Aggressive lymphoma/leukemia (defined by REAL) • DLBCL • Anaplastic large cell lymphoma • Peripheral T-cell lymphomas • Burkitt lymphoma • Lymphoblastic lymphoma • CLL	AML
	Elevated plasma uric acid levels (>7.5 mg/dL) at baseline
	High-grade MDS with >10% bone marrow blast involvement
	CML in blast crisis
INTERMEDIATE (POTENTIAL) RISK[1]	
Aggressive lymphoma/leukemia, not limited to the REAL classification, with LDH ≥2x the upper limit of normal	Any stage III to IV aggressive lymphoma or leukemia
	Stage I or II aggressive disease with bulky lymph node/tumor (>5 cm) involvement

AML=acute myeloid leukemia; CLL=chronic lymphocytic leukemia; CML=chronic myeloid leukemia; DLBCL=diffuse large B-cell lymphoma; LDH=lactate dehydrogenase; MDS=myelodysplastic syndrome; REAL=Revised European American Classification of Lymphoid Neoplasms.

ELITEK is indicated for the initial management of plasma uric acid levels in patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of plasma 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

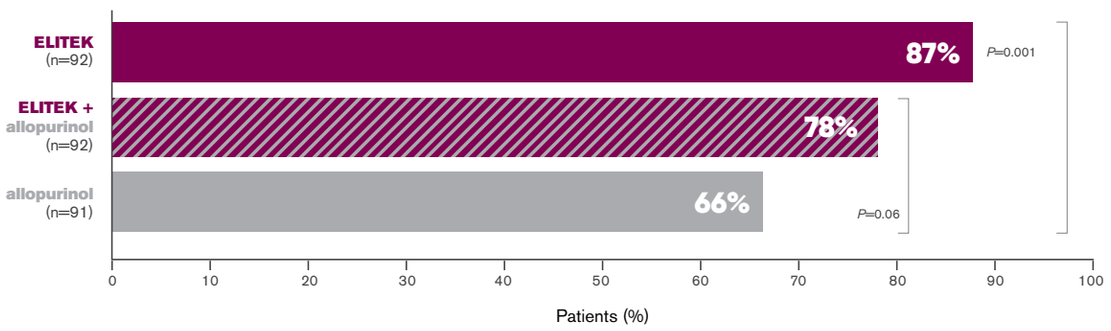
- **Hypersensitivity Reactions: ELITEK can cause serious and fatal hypersensitivity reactions including anaphylaxis. Immediately and permanently discontinue ELITEK in patients who experience a serious hypersensitivity reaction.**
- **Hemolysis: Do not administer ELITEK to patients with glucose-6-phosphate 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 IV Infusion

ELITEK GIVEN PROPHYLACTICALLY MAINTAINED NORMAL URIC ACID LEVELS IN SIGNIFICANTLY MORE PATIENTS VS ALLOPURINOL[1]

Proportion of patients with normal uric acid levels ≤7.5 mg/dL from Day 3 to Day 7 after initiating antihyperuricemic treatment (primary endpoint)[1]



Study design:

ELITEK was studied in a multicenter, randomized, open-label, 3-arm, phase 3 study in 275 patients with leukemia, lymphoma, and solid tumor malignancies at risk for hyperuricemia and TLS. Patients were randomized 1:1:1 to 1 of 3 arms. Patients in Arm A received ELITEK 0.2 mg/kg/d for 5 days (n=92). Patients in Arm B received ELITEK 0.2 mg/kg/d from Day 1 through Day 3, followed by oral allopurinol 300 mg/d from Day 3 through Day 5 (overlap on Day 3: ELITEK 0.2 mg/kg/d and allopurinol 300 mg/d administered approximately 12 hours apart) (n=92). Patients in Arm C received oral allopurinol 300 mg/d for 5 days (n=91). Anticancer therapy was initiated 4 to 24 hours after the first antihyperuricemic dose in each arm.[1,4]

ELITEK is recommended for patients at high and intermediate (potential) risk for development of TLS associated with hyperuricemia[5]

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.**

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.

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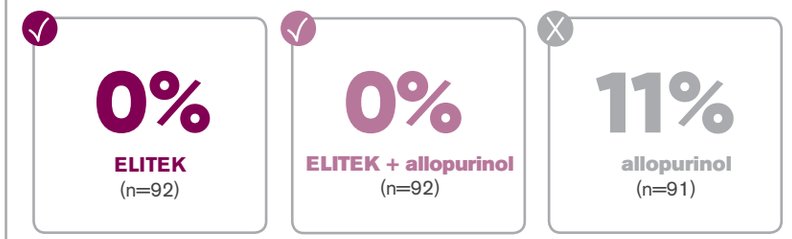
FAILURE RATE FOR ELITEK WAS 0% IN ASSESSABLE PATIENTS

Proportion of assessable patients failing to maintain normal uric acid levels[4]



- 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[4]

- 18% of patients (n=275) were hyperuricemic (>7.5 mg/dL) at baseline and therefore considered at high risk of developing TLS[1]
- 96% of ELITEK patients (n=275) achieved uric acid levels ≤2 mg/dL within 4 hours after their first dose vs 0% with allopurinol[1,4]

Not all patients who are at risk for TLS have elevated uric acid levels before starting anticancer therapy; there are other high-risk factors to consider[6]

Per-patient incidence of selected adverse reactions by study arm in Study 4:

All Grades ARs in Study 4 (ELITEK alone; ELITEK plus oral allopurinol; oral allopurinol alone) were nausea (57.6%, 60.9%, 54.9%), peripheral edema (50%, 43.5%, 42.9%), vomiting (38%, 37%, 30.8%), anxiety (23.9%, 17.4%, 17.6%), abdominal pain (21.7%, 33.7%, 25.3%), hypophosphatemia (17.4%, 22.8%, 16.5%), hyperbilirubinemia (16.3%, 14.1%, 7.7%), pharyngolaryngeal pain (14.1%, 20.7%, 9.9%), sepsis (12%, 7.6%, 4.4%), fluid overload (12%, 6.5%, 3.3%), increased ALT (10.9%, 27.2%, 17.6%), and hyperphosphatemia (9.8%, 15.2%, 8.8%).[4]

ALT=alanine aminotransferase; AR=adverse reaction.

References: 1. Cortes J, Moore JO, Maziarz RT, et al. Control of plasma uric acid in adults at risk for tumor lysis syndrome: efficacy and safety of rasburicase alone and rasburicase followed by allopurinol compared with allopurinol alone–results of a multicenter phase III study. *J Clin Oncol.* 2010;28(27):4207-4213. **2.** Jakić-Razumović J, Aurer I. The World Health Organization classification of lymphomas. *Croat Med J.* 2002;43(5):527-534. **3.** Nicolaides C, Dimou S, Pavlidis N. Prognostic factors in aggressive non-Hodgkin's lymphomas. *Oncologist.* 1998;3(3):189-197. **4.** ELITEK [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC. **5.** Howard SC, Jones DP, Pui C-H. The tumor lysis syndrome. *N Engl J Med.* 2011;364(19):1844-1854. **6.** Edeani A, Shirali A. Tumor lysis syndrome. Onco-Nephrology Curriculum. American Society of Nephrology. 2016. https://www.asn-online.org/education/distancelearning/curricula/onco/Chapter4.pdf. Accessed February 26, 2020. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for T-Cell Lymphomas. V.1.2020. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 20, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas. V.1.2020. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 20, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **9.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia. V.1.2020. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 20, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **10.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. V.4.2020. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 20, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **11.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia. V.3.2020. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 20, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

TLS IN NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®)

Consider TLS prophylaxis for patients with certain lymphomas or leukemias and the following risk factors[7-11]

T-cell lymphomas risk factors[7]	
• Pre-existing elevated uric acid • Elevated WBC count • Renal disease or renal involvement by tumor	• Spontaneous TLS • Bone marrow involvement • High tumor burden or bulky disease

B-cell lymphomas and ALL risk factors[8,9]	
• Pre-existing elevated uric acid • Elevated WBC count • Renal disease or renal involvement by tumor	• Spontaneous TLS • Histologies of Burkitt lymphoma and lymphoblastic lymphoma; occasionally patients with DLBCL • Ineffectiveness or intolerance of allopurinol

CLL/SLL risk factors[10]	
• Pre-existing elevated uric acid • Elevated WBC count • Renal disease or renal involvement by tumor • Spontaneous TLS	• Patients receiving treatment with venetoclax, chemoimmunotherapy, lenalidomide, and obinutuzumab • Progressive disease after small-molecule inhibitor therapy • Bulky lymph nodes

NCCN Guidelines recommend tumor lysis prophylaxis for patients with AML[11]

AML considerations[11]
Tumor lysis prophylaxis: hydration with diuresis, and allopurinol or rasburicase. Rasburicase should be considered as initial treatment in patients with rapidly increasing blast counts, high uric acid, or evidence of impaired renal function.

Please note that these do not represent all potential risk factors for the development of TLS.

NCCN Guidelines recommend ELITEK for first-line treatment of hyperuricemia in patients with T-cell lymphomas, B-cell lymphomas, ALL, CLL/SLL, or AML[7-11]

ALL=acute lymphoblastic leukemia; NCCN=National Comprehensive Cancer Network; SLL=small lymphocytic lymphoma; WBC=white blood cell.

Important Safety Information (cont'd)

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 accompanying full Prescribing Information, including Boxed WARNING.

SANOFI GENZYME

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