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

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ABSTRACT

Purpose

Rasburicase is effective in controlling plasma uric acid in pediatric patients with hematologic malignancies. This study in adults evaluated safety of and compared efficacy of rasburicase alone with rasburicase followed by oral allopurinol and with allopurinol alone in controlling plasma uric acid.

Patients and Methods

Adults with hematologic malignancies at risk for hyperuricemia and tumor lysis syndrome (TLS) were randomly assigned to rasburicase (0.20 mg/kg/d intravenously days 1-5), rasburicase plus allopurinol (rasburicase 0.20 mg/kg/d days 1 to 3 followed by oral allopurinol 300 mg/d days 3 to 5), or allopurinol (300 mg/d orally days 1 to 5). Primary efficacy variable was plasma uric acid response rate defined as percentage of patients achieving or maintaining plasma uric acid ≤ 7.5 mg/dL during days 3 to 7.

Results

Ninety-two patients received rasburicase, 92 rasburicase plus allopurinol, and 91 allopurinol. Plasma uric acid response rate was 87% with rasburicase, 78% with rasburicase plus allopurinol, and 66% with allopurinol. It was significantly greater for rasburicase than for allopurinol ($P = .001$) in the overall study population, in patients at high risk for TLS (89% v 68%; $P = .012$), and in those with baseline hyperuricemia (90% v 53%; $P = .015$). Time to plasma uric acid control in hyperuricemic patients was 4 hours for rasburicase, 4 hours for rasburicase plus allopurinol, and 27 hours for allopurinol.

Conclusion

In adults with hyperuricemia or at high risk for TLS, rasburicase provided control of plasma uric acid more rapidly than allopurinol. Rasburicase was well tolerated as a single agent and in sequential combination with allopurinol.

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INTRODUCTION

Tumor lysis syndrome (TLS), a life-threatening metabolic disorder that may occur spontaneously or in response to anticancer chemotherapy or bi-therapy, is particularly prevalent among patients who have hematologic malignancies with a high proliferative rate, large cellular burden, and high sensitivity to chemotherapy or cytolytic antibody therapy.¹⁻⁴ TLS is characterized by massive release of tumor cell contents into the bloodstream.¹ Resulting metabolic derangements, including hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, may lead to serious clinical complications,

such as renal dysfunction, cardiac failure, seizures, or death.¹

Hyperuricemia, the most frequently recognized clinical manifestation of TLS, is caused by breakdown of purine-containing nucleic acids released from tumor cells.² Oxidation of hypoxanthine and xanthine to uric acid is the final step of purine catabolism in humans.⁵ In most other mammalian organisms, the enzyme urate oxidase further converts uric acid to allantoin.⁵ Uric acid is five to 10 times less soluble in water than allantoin and may precipitate in renal tubules at concentrations ≥ 7 mg/dL,¹ causing renal insufficiency that may progress to acute renal failure.¹ Acute renal failure is

one of the most immediate, serious, and costly TLS-related complications of treatment for hematologic malignancies.⁶⁻¹⁰

Current treatment options for managing hyperuricemia include oral or intravenous (IV) allopurinol, with or without alkaline hydration, and possibly diuretics. Allopurinol, a xanthine oxidase inhibitor,^{11,12} requires 24 to 72 hours to effectively prevent de novo formation of uric acid¹³ and does not actively reduce existing plasma uric acid concentrations.^{1,2} In contrast, rasburicase (Elitek, sanofi-aventis U.S., Bridgewater, NJ), a recombinant urate oxidase produced in genetically modified *Saccharomyces cerevisiae*,¹ can both prevent and rapidly reverse hyperuricemia.² Rasburicase, compared with allopurinol, provided superior control of plasma uric acid in a randomized trial of pediatric patients with cancer.¹⁴ In the United States, rasburicase is approved for initial management of plasma uric acid in pediatric patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis and hyperuricemia.¹⁵ Here, we present, to the best of our knowledge, the first randomized, controlled study of adult patients with hematologic malignancies at risk for hyperuricemia and TLS that compares efficacy in controlling plasma uric acid and safety between rasburicase alone, allopurinol alone, and rasburicase followed by allopurinol.

PATIENTS AND METHODS

Study Design

This was a multicenter, open-label, randomized, parallel-group, comparative phase III study with three treatment arms: single-agent rasburicase (0.20 mg/kg/d IV infusion over 30 minutes) for 5 days, sequential treatment with rasburicase (0.20 mg/kg/d IV infusion over 30 minutes) from days 1 through 3 followed by oral allopurinol (300 mg/d orally) from days 3 through 5 (overlap on day 3), and single-agent oral allopurinol (300 mg/d orally) for 5 days.

The primary objective was to compare the adequacy of plasma uric acid control between the three treatment arms and to evaluate safety. The primary efficacy measure was rate of plasma uric acid response. Treatment success was assessed if plasma uric acid was ≤ 7.5 mg/dL for all measurements (ie, no hyperuricemia) from days 3 to 7. Treatment failure was assessed if at least one plasma uric acid measurement showed a value > 7.5 mg/dL, if antihyperuricemic treatment was extended beyond the planned duration, or if the day 7 plasma sample or two or more consecutive samples from days 3 to 6 were missing. Secondary objectives included area under the plasma uric acid concentration-time curve (AUC) from baseline (day 1) to day 7, time to plasma uric acid control in patients with hyperuricemia, and immunogenicity to rasburicase. Time to plasma uric acid control was defined as the time from first administration of study drug to first measurement showing plasma uric acid ≤ 7.5 mg/dL in patients with hyperuricemia at baseline.

Patients

Each patient provided fully informed, written consent before enrollment. The study was approved by local institutional review boards and was conducted in accordance with Good Clinical Practice and the Helsinki Declaration of the World Medical Assembly. Eligible patients were age ≥ 18 years, had an Eastern Cooperative Oncology Group performance status of 0 to 3, life expectancy of > 3 months, active leukemia/lymphoma, and were at high or potential risk for TLS. High risk for TLS was defined by the presence of at least one of the following characteristics: hyperuricemia at baseline (plasma uric acid > 7.5 mg/dL), aggressive lymphoma/leukemia (on the basis of the Revised European American Lymphoma classification),¹⁶⁻¹⁸ acute myeloid leukemia (AML), chronic myeloid leukemia in blast crisis, or high-grade myelodysplastic syndrome with $> 10\%$

bone marrow blast involvement. Potential risk for TLS was defined as aggressive lymphoma/leukemia with lactate dehydrogenase concentration at least twice the upper limit of normal, stage III to IV disease, or stage I to II disease with one lymph node/tumor > 5 cm in diameter.

Main exclusion criteria were history of asthma or severe, life-threatening atopic allergy, hypersensitivity to uricases (or excipients), known glucose-6-phosphate dehydrogenase (G6PD) deficiency, concomitant treatment with any investigational drug, history of uricolytic therapy, and relapsed or refractory leukemia, lymphoma, or solid tumors.

Study Treatment and Assessments

Patients stratified by TLS risk (high or potential) were randomly assigned to three treatment arms at a ratio of 1:1:1 using a random permutation block design. Cytoreductive chemotherapy was initiated within 4 to 24 hours after the first dose of antihyperuricemic treatment (ie, all patients received study medication before or during the first cycle of chemotherapy). The regimen for optimal hydration was at the investigator's discretion. It was recommended to start intravenous administration of normal or half-normal saline at a rate of 4 to 5 L of fluid per day 24 to 48 hours before the initiation of chemotherapy. Plasma samples for uric acid levels were collected at baseline (within 4 hours before the start of antihyperuricemic treatment) and at 4, 24, 48, 72, 96, 120, and 144 hours after the first dose of antihyperuricemic treatment. Adverse event (AE) reports and hematology and clinical chemistry data were collected throughout treatment and on days 14 and 35. Using quantitative immunoassays, antirasburicase antibodies (plasma immunoglobulin E [IgE], IgG, and neutralizing IgG) were measured centrally at baseline, and at day 14, day 35, 3 months, and 6 months. For patients positive for antibodies at 6 months, measurements continued every 6 ± 1 months or at 1 year, whichever came first.

Statistical Analyses

Safety and primary efficacy analyses were performed for all patients who received at least one dose of study drug (safety or modified intent-to-treat population [mITT]). The plasma uric acid response rate was determined along with its 95% CI. Statistical comparison of plasma uric acid response rates was conducted through the CI approach. One arm was considered superior to another if the lower one-sided 97.65% confidence limit of the difference in response rates between two arms was greater than 0% (type I error rate = 4.695%). Confidence limits were constructed using Wilson's method.¹⁹ Differences in plasma uric acid AUC between treatment arms were determined by one-way analysis of variance; median time to plasma uric acid control in hyperuricemic patients was summarized with a 95% CI. For safety assessments, descriptive statistics were used.

RESULTS

Patients

Of 280 patients randomly assigned, 275 received at least one dose of study medication; 92 were treated with rasburicase, 92 with rasburicase plus allopurinol, and 91 with allopurinol (Fig 1). Treatment arms overall were well matched regarding demographics, disease characteristics at baseline, and type of chemotherapy received (Table 1), although more patients on the rasburicase arm had been diagnosed with leukemia (76%; AML, 71%) than on the rasburicase plus allopurinol (59%; AML, 56%) or allopurinol arm (62%; AML, 59%). Approximately 90% of patients in each arm were classified as being at high risk for TLS, and 14% to 21% in each arm had hyperuricemia at baseline. From 98% to 100% of patients received at least one cytotoxic anticancer therapy after the first dose of study drug. The most commonly used cytotoxic agents—anthracyclines (86% to 97%) and cytarabine (80% to 86%)—were frequently used in combination with other agents, including steroids. All but four

Fig 1. CONSORT diagram. Patient disposition.

patients were hydrated during the study (all patients on rasburicase, 91 of 92 patients on rasburicase plus allopurinol, and 88 of 91 patients on allopurinol).

Plasma Uric Acid Response Rate

Plasma uric acid response rates were 87% (95% CI, 80% to 94%) for rasburicase alone, 78% (95% CI, 70% to 87%) for rasburicase plus allopurinol, and 66% (95% CI, 56% to 76%) for allopurinol alone (Fig 2). The plasma uric acid response rate for rasburicase was significantly higher than for allopurinol ($P = .001$). Although the response rate was higher for rasburicase plus allopurinol than for allopurinol alone, the difference was not statistically significant ($P = .06$). Missing samples were the only reason for treatment failure in the rasburicase arm and the major reason for treatment failure in the other two treatment arms (missing samples in rasburicase arm, 13%; rasburicase plus allopurinol, 15%; allopurinol, 19%). Treatment failure attributable to hyperuricemia (plasma uric acid > 7.5 mg/dL) during the postbaseline evaluation period from days 3 to 7 occurred only in patients treated with allopurinol (11%). Treatment failure because hyperuricemic treatment was extended beyond the planned period occurred in 7% of patients treated with rasburicase plus allopurinol and 4% of those treated with allopurinol.

Plasma Uric Acid Response Rates in Patients at High Risk of TLS and Baseline Hyperuricemia

Treatment-related differences in plasma uric acid response rates observed in the mITT population were essentially preserved in subgroups defined by high TLS risk or hyperuricemia at baseline (Fig 2). Plasma uric acid response rate was significantly higher for rasburicase than for allopurinol among patients with high TLS risk (89% ν 68%; $P = .001$) and among those with hyperuricemia at baseline (90% ν 53%; $P = .015$). Plasma uric acid response rate was also higher for rasburicase plus allopurinol than for allopurinol alone among patients with high risk of TLS (79% ν 68%; $P = .1$) and among those with baseline hyperuricemia (77% ν 53%; $P = .2$), but the differences were not statistically significant.

Plasma Uric Acid Profile Over Time

Changes in plasma concentration of uric acid over time are shown in Figure 3. In the rasburicase and rasburicase plus allopurinol arms, uric acid concentrations were rapidly reduced by hour 4 (mean reduction of 88% for each arm) after the first dose and were maintained at low levels throughout treatments. In the allopurinol arm, mean plasma uric acid reduction within the first 4 hours of treatment initiation was only 14%; plasma uric acid concentrations

continued to decline slowly, but overall remained high compared with those observed in the other two treatment arms. Consequently, plasma uric acid AUC from day 1 through day 7 was significantly lower for rasburicase and rasburicase plus allopurinol than for allopurinol ($P < .001$; Fig 3). Median time to plasma uric acid control in patients with baseline hyperuricemia was 4 hours for rasburicase, 4 hours for rasburicase plus allopurinol, and 27 hours for allopurinol.

Safety

Drug-related AEs (number [percent] of patients) were infrequent (rasburicase, four [4%]; rasburicase plus allopurinol, five [5%]; and allopurinol, one [1%]) and mainly immunoallergic in nature (Table 2). No drug-related life-threatening events or deaths occurred. The most common AEs across all arms, regardless of causality, were those of the blood and lymphatic system (thrombocytopenia, neutropenia, anemia), general disorders and administration site conditions (pyrexia, peripheral edema), and those of the GI system (nausea, vomiting, diarrhea); they reflected mainly known toxicities of the concomitant chemotherapy. The most common serious AEs across all arms, regardless of causality, were neutropenic infection (4% to 9%), febrile neutropenia (3% to 6%), and neutropenic sepsis (1% to 5%).

Eight patients discontinued study treatment because of an AE. One patient in the rasburicase arm discontinued because of hyperbilirubinemia and neutropenic sepsis. Five in the rasburicase plus allopurinol arm discontinued for various reasons: tachycardia, pulmonary hemorrhage, hypersensitivity reaction (rasburicase-related), respiratory failure, and confusional state. Two patients in the allopurinol arm discontinued because of TLS.

The incidence of clinical TLS was 3% for rasburicase, 3% for rasburicase plus allopurinol, and 4% for allopurinol (Table 3); all events were considered unrelated to study medication. The incidence of laboratory TLS (Table 3) was 21% for rasburicase (rasburicase ν allopurinol: $P = .003$), 27% for rasburicase plus allopurinol (rasburicase plus allopurinol ν allopurinol: $P = .054$), and 41% for allopurinol. The percentage of patients who experienced acute renal failure was 2% each for rasburicase and for allopurinol, and 5% for rasburicase plus allopurinol (Table 3).

Drug-related events of potential hypersensitivity were reported in five patients: four (4%) in the rasburicase arm and one (1%) in the rasburicase plus allopurinol arm (Table 2). Most of these events were grade 1 or 2. In the rasburicase arm, one patient had irritation at the injection site; one had arthralgia, myalgia, and rash; one had peripheral edema; and the fourth patient had grade 3 hypersensitivity. In the

Table 1. Baseline Characteristics of All Randomly Assigned Patients (N = 280) and Patients Who Received at Least One Dose of Study Drug (mITT; n = 275)

Baseline Characteristic	Rasburicase (%) (n = 94)	Rasburicase Plus Allopurinol (%) (n = 93)	Allopurinol (%) (n = 93)
Sex			
Male	63	55	69
Female	37	45	31
Age, years			
Mean	57	53	52
SD	16	17	16
Median	59	54	54
Range	18-89	18-85	18-84
≥ 65	33	30	26
Race/ethnicity			
White	85	74	80
Black	10	11	10
Asian	2	4	0
Other	3	11	11
ECOG performance score			
0	28	24	30
1	39	51	46
2	26	22	17
3	6	4	5
Missing	1*	0	1†
Leukemia	76‡	59	62
Acute myeloid	71	56	59
Chronic myeloid	0	2	0
Other	4	1	3
WBC count, % of leukemia patients			
≥ 50,000/μL	21	18	16
≥ 10,000 to < 50,000/μL	28	22	26
Lymphoma	20	34	33
Aggressive (including diffuse large) B-cell	11	6	6
Very aggressive B-cell	7	19	16
Aggressive or very aggressive T-cell or natural killer cell	2	8	11
Other	1		
Myelodysplastic syndrome	3	5	4
Other: multiple myeloma	0	1	0
Missing	1§	0	0
Tumor lysis syndrome risk			
High	89	94	93
Potential	11	6	5
Low	0	0	2
Hyperuricemia			
Plasma uric acid ≤ 7.5 mg/dL	79	86	82
Acute myeloid leukemia	60	54	53
Burkitt lymphoma/B-cell acute lymphoblastic leukemia	1	4	3
Other leukemia/lymphoma	15	24	23
Myelodysplastic syndrome	3	4	3
Plasma uric acid > 7.5 mg/dL	21	14	18
Acute myeloid leukemia	12	4	7
Burkitt lymphoma/B-cell acute lymphoblastic leukemia	1	3	1
Other leukemia/lymphoma	7	6	9
Myelodysplastic syndrome	0	1	1

Abbreviations: mITT, modified intent-to-treat; SD, standard deviation; ECOG, Eastern Cooperative Oncology Group.

*One patient in the rasburicase arm was randomly assigned but was not treated and did not have an ECOG performance status reported.

†One patient in the allopurinol arm did not have an ECOG performance status reported.

‡Percentages may not add up to 100 because of rounding.

§One patient in the rasburicase arm was randomly assigned but was not treated because of a diagnosis that did not meet inclusion criteria.

Fig 2. Uric acid response rates. RSB, rasburicase; ALLP, allopurinol; mITT, modified intent-to-treat population; TLS, tumor lysis syndrome. * $P < .05$.

rasburicase plus allopurinol arm, one patient reported a rash and grade 3 drug hypersensitivity possibly due to rasburicase, which led to treatment discontinuation on day 1. No anaphylaxis or grade 4 hypersensitivity AEs were reported. No event of hemolytic reaction or methemoglobinemia occurred.

No patients were positive for antirasburicase IgG or IgE; only 2% were positive for antirasburicase neutralizing IgG. Overall, the incidence of antirasburicase antibody development in rasburicase-containing arms was low, indicating that treatment with rasburicase was not highly immunogenic.

DISCUSSION

The incidence of TLS is a function of TLS risk and the cytoreductive nature of the chemotherapy. A retrospective study found

Fig 3. Plasma uric acid profile over time. Error bars indicate standard error of the mean. AUC, area under the plasma concentration time curve; ALLP, allopurinol; RSB, rasburicase; SD, standard deviation.

Table 2. Rasburicase- or Allopurinol-Related Adverse Events

Adverse Event*	Percent of Patients in Study Arm		
	Rasburicase (n = 92)	Rasburicase Plus Allopurinol (n = 92)	Allopurinol (n = 91)
Any drug-related adverse event	4	5	1
Fatigue	1	1	1
Upper abdominal pain	1	0	0
Anorexia	1	0	0
AST increased	1	0	0
Blood ALP decreased	1	0	0
Diarrhea	1	0	0
Hyponatremia	1	0	0
Thrombocytopenia	1†	0	0
Increased blood LDH	0	1‡	0
Decreased appetite	0	1	0
Dysphagia	0	1	0
Dysuria	0	1	0
Abnormal liver function	0	1†	0
Muscle twitching	0	1	0
Pain	0	1	0
Paresthesia	0	0	1
Related hypersensitivity reaction			
Any drug-related hypersensitivity reaction	4	1	0
Rash	1	1	0
Arthralgia	1	0	0
Hypersensitivity	1‡	0	0
Injection site irritation	1	0	0
Myalgia	1	0	0
Edema, peripheral	1	0	0
Drug hypersensitivity	0	1‡	0

Abbreviations: ALP, alkaline phosphatase; LDH, lactate dehydrogenase.

*One patient may experience multiple adverse events.

†Grade 4.

‡Grade 3.

that 5% of adult patients with AML developed clinical TLS after receiving induction chemotherapy, even with prophylactic hydration and allopurinol treatment.²⁰ Renal failure occurred in 98% of patients with clinical TLS, and dialysis was necessary in 18% of patients.²⁰ The prevention and treatment of TLS are becoming more important with increasing use of potentially nephrotoxic chemotherapy agents, such as ifosfamide or methotrexate,²¹ that may increase the risk of TLS. Some immunomodulating agents, including rituximab and lenalidomide, have been reported to cause hyperuricemia and TLS in patients with chronic lymphocytic leukemia and other lymphoproliferative disorders.^{22,23}

Reduction of hyperuricemia may reduce the incidence of clinical TLS, because hyperuricemia is an important component of this syndrome. Consistent with results of a previous study in pediatric patients with lymphoma and leukemia,¹⁴ this study conducted in adult patients with hematologic malignancies found that rasburicase was more rapid and more effective than allopurinol in reducing and normalizing plasma concentrations of uric acid. The uric acid response rate of 87% with rasburicase was significantly higher than that observed with allopurinol (66%; $P = .001$; Fig 2), although the percentage of patients with AML was higher in the rasburicase group (71%) than in the allopurinol group (59%).

Table 3. Incidence of Tumor Lysis Syndrome and Renal Events

Event	Percent of Patients in Study Arm		
	Rasburicase (n = 92)	Rasburicase Plus Allopurinol (n = 92)	Allopurinol (n = 91)
Clinical tumor lysis syndrome ^a	3	3	4
Laboratory tumor lysis syndrome ^b	21 ^c	27	41
Hyperuricemia ^d	8	12	29
Hyperphosphatemia ^e	49	58	57
Hypocalcemia ^f	16	19	25
Hyperkalemia ^g	21	14	17
Renal events			
Increased blood creatinine ^h	8	10	10
Renal failure/impairment	4	9	2
Acute renal failure	2	5	2

^aClinical tumor lysis syndrome was defined by changes in two or more laboratory parameters for hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia and at least one of the following events occurring within 7 days of treatment: renal failure/injury, need for renal dialysis and/or increase in serum creatinine > 1.5× upper limit of normal, arrhythmia, or seizure. No formal statistical comparisons were performed because of the small number of patients experiencing the events.

^bTwo or more laboratory changes within 7 days after cytotoxic therapy according to the Cairo-Bishop definition.³

^c $P < .05$, rasburicase v allopurinol.

^dPlasma phosphate ≥ 1.45 mmol/L or 25% increase from baseline.

^ePlasma uric acid ≥ 8 mg/dL or 25% increase from baseline.

^fPlasma calcium ≤ 1.75 mmol/L or 25% decrease from baseline.

^gPlasma potassium ≥ 6.0 mmol/L or 25% increase from baseline.

^hDefined as blood creatinine levels > 1.4 mg/dL.

Similar improvements in plasma uric acid levels were observed in clinically relevant subgroups of patients at high TLS risk or with hyperuricemia at baseline (Fig 2). Rasburicase reduced plasma uric acid levels to ≤ 7.5 mg/dL at about 4 hours after the first dose, compared with 27 hours for allopurinol. During rasburicase administration, plasma uric acid levels should be monitored regularly,¹ but urine alkalization is not required.¹ In addition, no drug-drug interactions are known, and there is no indication that adjustment of rasburicase dose is required for patients with renal impairment.¹⁵ Rasburicase does not interfere with cytochrome P450 activity and should not alter P450-related drug metabolism.¹⁵

In this study, rasburicase generally was well tolerated and no new safety concerns for adult patients were identified. Although no patients were screened for G6PD deficiency, among 28 black patients who were at potential risk for G6PD deficiency, no cases of hemolysis or methemoglobinemia were reported. No major differences in the frequencies of AEs, treatment-related AEs, serious AEs, treatment discontinuations due to AEs, and deaths were observed between rasburicase and allopurinol groups. Most AEs were attributable to underlying disease and/or to concurrent chemotherapy.

Rasburicase plus allopurinol and rasburicase alone were similarly effective in controlling plasma uric acid. Rasburicase followed by allopurinol rapidly reduced uric acid concentrations by hour 4 after the first dose and maintained uric acid at low levels throughout treatments (Fig 3). Response rate (mITT population) with rasburicase plus allopurinol (78%) was higher than with allopurinol (66%; Fig 2), but the difference was not statistically significant ($P = .06$). It should be emphasized that “missing uric acid samples” and “antihyperuricemic treatment extending be-

yond 5 days” were the primary parameters affecting the results of this analysis, not lack of uric acid control. Treatment failure attributable to lack of uric acid control occurred only with allopurinol (11%), not with rasburicase-containing treatments. As part of the management of TLS, sequential therapy of rasburicase for 3 days followed by allopurinol for 3 days may be beneficial for patients who are at risk for the syndrome.

This study was not designed to demonstrate a reduction in clinical or laboratory TLS. The number of patients with clinical TLS was too low to allow firm conclusions regarding treatment effects; however, the incidence of laboratory TLS, which can be regarded as an indicator of the risk of clinical TLS, was significantly lower with rasburicase than with allopurinol.

Rasburicase was well tolerated and was significantly better than allopurinol in controlling plasma uric acid in terms of rapidity and efficacy. The superiority of rasburicase over allopurinol was observed in patients at high risk for TLS and also in those with hyperuricemia at baseline. The rasburicase plus allopurinol regimen was rapid and effective in controlling plasma uric acid and could be an alternative for patients who are at risk for TLS or who are not hyperuricemic. In summary, rasburicase has a more favorable risk-benefit ratio than allopurinol for the initial management of uric acid plasma concentrations in adult patients with hematologic malignancies who are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid. On the basis of the results from this phase III study, rasburicase was recently approved by the US Food and Drug Administration for use in adults. From our experience, the rapid reduction in uric acid to less than 1.0 mg/dL with rasburicase simplifies uric acid control by reducing the need for urinary alkalization in patients who are often critically ill with compromised organ function.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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