Fatalities from Tumor Lysis Syndrome (TLS) After Anti-Hyperuricemic Monotherapy – Nationally Representative, Propensity Score Matched, Retrospective Study Comparison of Rasburicase and Allopurinol

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INTRODUCTION

- Treatment outcome comparisons in randomized control trials (RCTs) versus observational studies can yield different results.
- Distortions in observational studies may occur because of differences in factors other than those being studied (confounders).
- RCTs minimize confounder effects by random assignment to each treatment group.
- Quasi-experimental observational study methods intending to control confounders are available.
- Here we present the first US representative, real-world observational study using a quasi-experimental confounder minimizing method to compare tumor lysis syndrome (TLS)-associated morbidities in patients with hematological malignancies at risk for TLS, following rasburicase monotherapy versus allopurinol monotherapy.
- We have previously found that rasburicase significantly and rapidly reduces uric acid exposure (area under curve) compared with allopurinol in patients with or at risk of TLS.[1]

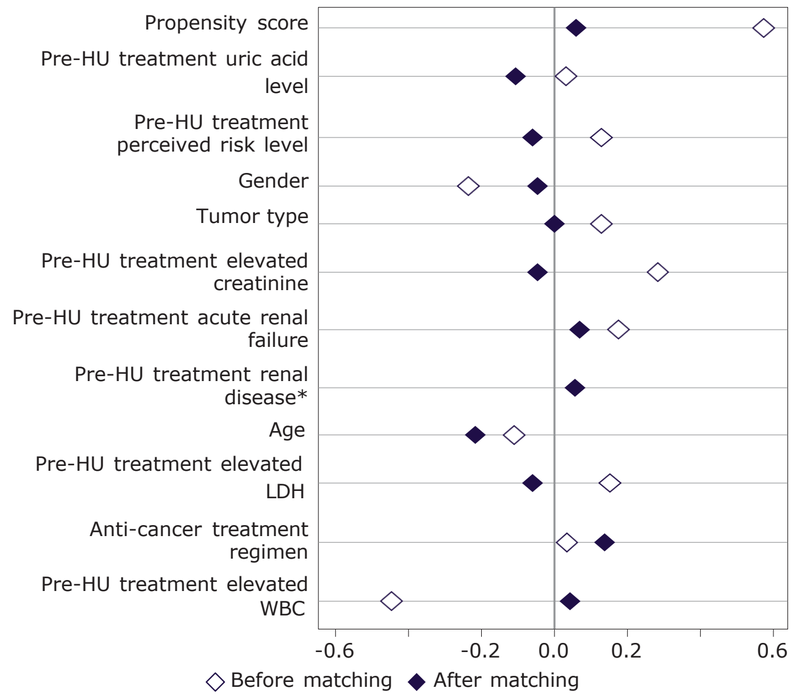
METHODS

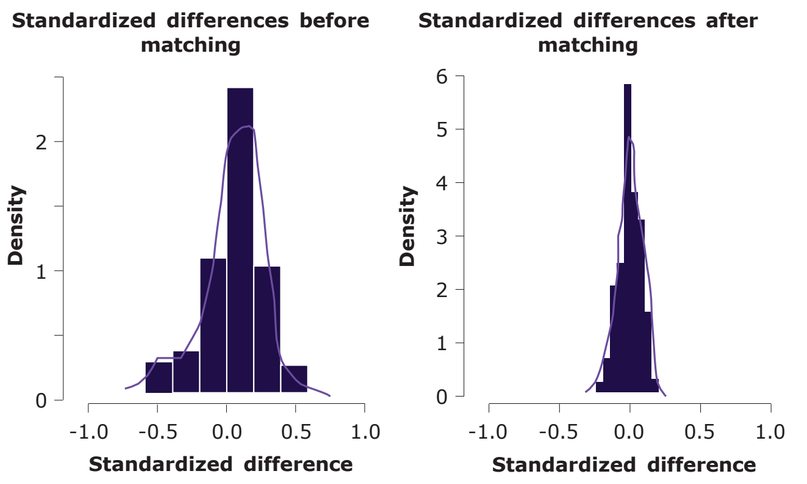
- In 2021, 266 oncologists from US physician practices, academic and non-academic hospitals, and outpatient clinics provided anonymized information about 715 randomized liquid-tumor patients treated in the past year for hyperuricemia (HU) risk and TLS potential.
- From this group, 282 rasburicase and allopurinol patients without spontaneous TLS or TLS before anti-HU treatment were propensity score (PS) matched for TLS risk using 11 predictive covariates: acute renal failure, age, anti-cancer regimen, creatinine, gender, lactate dehydrogenase, perceived risk, renal disease, tumor type, uric acid, and white blood cell count (**Figure 1**).
- Matched patients met the 1:1, nearest neighbor, caliper matching requirements using calipers of width equal to 0.2 of the standard deviation of the logit of the PS (d score) on the covariates, regardless of whether they later developed post-HU treatment TLS.

RESULTS

- The overall PS was almost 0.6 before matching but near zero afterward.
- No covariate exhibited a large imbalance ($|d| > 0.25$), nor did the overall relative imbalance difference of the groups (0.077) before and after matching. There was significant improvement in the density of overall standardized differences before and after (**Figure 1**).
- TLS-associated mortality was significantly less likely among rasburicase patients (2.1% vs. 7.1%, $p = 0.047$, 71% reduction) (**Figure 2A**).
- Analyzing the 63-patients subset who developed TLS after anti-HU treatment, TLS-associated fatalities were even less likely among rasburicase patients, 3 of 36 rasburicase TLS patients versus 10 of 27 allopurinol TLS patients (8.3% vs. 37.0%, $p = 0.005$, 78% reduction) (**Figure 2B**).

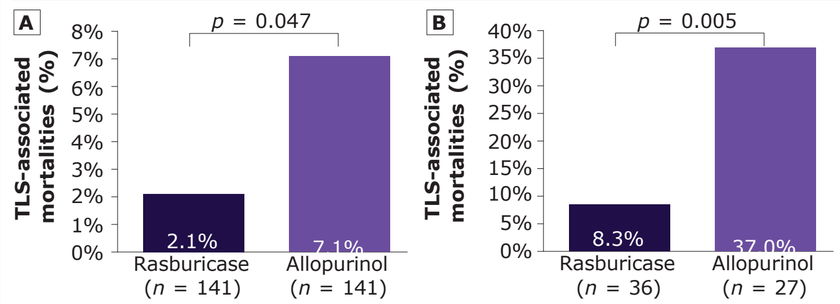
Figure 1. Pre- and Post-Matching Reduction of Differences in 11 Covariates and Propensity score ($n = 282$)





*Renal disease before/after values equal and overlap.
HU, hyperuricemia; LDH, lactate dehydrogenase; WBC, white blood cells

Figure 2. TLS-Associated Mortality, Post-Hyperuricemia Treatment in All Matched Patients ($n = 282$)* (A); and in Subset Who Developed TLS ($n = 63$)* (B)



*Excluding pre-HU treatment TLS and spontaneous TLS.
HU, hyperuricemia; TLS, tumor lysis syndrome

DISCUSSION

- The potential for vital advancements in the understanding of medical therapeutics based on observational studies is almost unimaginable, partially because of the explosive growth of individual patient health data and other developing metrics.
- The arrival of quasi-experimental methods to minimize the distorting effects of study confounders, the Achilles heel of observational studies, is an important step forward.
- This presentation alerts and attempts to educate readers/attendees on the use of an important quasi-experimental methodology.
- In the initial presentation of these data, the focus was on the comparison of two therapeutics with the methodology described only as a tool for analysis.
- The focus of this presentation is on the usefulness of the methodology, with the comparison used as a demonstration. We believe that any readers/attendees of both presentations will be well served.

CONCLUSIONS

Results indicate (1) PS matching successfully corrects before and after overall covariate and individual baseline covariate imbalances and (2) rasburicase compared with allopurinol significantly reduces TLS-associated mortality.

REFERENCE

1. Goldman SC, et al. *Blood*. 2001;97(10):2998–3003.

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QUESTIONS

If you have questions about this poster, please email Dr. Mitchell S. Cairo (Mitchell_Cairo@NYMC.EDU) or Edward Drea (Edward.Drea@sanofi.com).