Comparison of Nationally Representative Samples of Rasburicase vs. Allopurinol Post-Hyperuricemia Monotherapy in Patients with Hematological Malignancies: Significant Reduction in Tumor Lysis Syndrome Mortality with Rasburicase

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INTRODUCTION

- Treatment outcome comparisons in randomized control trials (RCTs) vs. 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 for 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 vs. allopurinol monotherapy.
- We have previously found rasburicase significantly and more rapidly reduces uric acid exposure compared to allopurinol in patients with or at risk of TLS.[1]

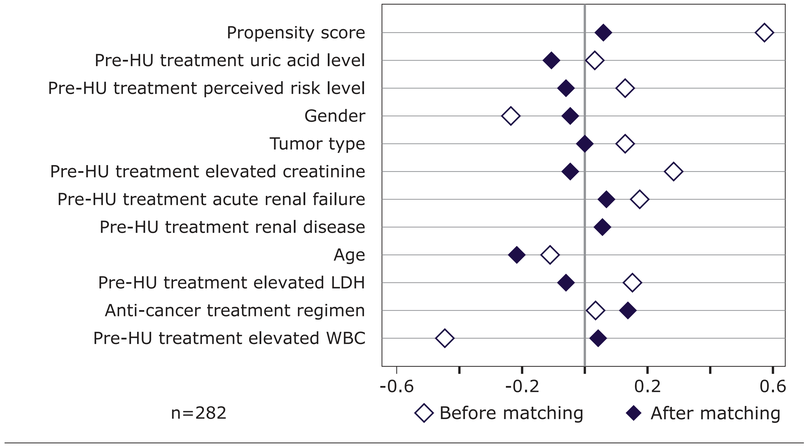
METHODS

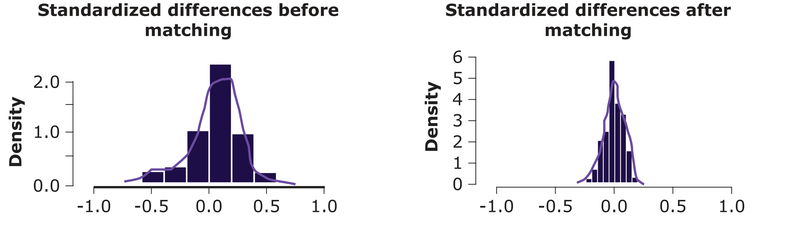
- In 2021, 266 oncologists from US physician practices, academic and non-academic hospitals, and outpatient clinics provided anonymized information for 715 randomized liquid-tumor patients treated in the past year for hyperuricemia (HU) risk and TLS potential.
- From this group, 282 rasburicase and allopurinol patients without spontaneous TLS or TLS before HU treatment were propensity score (PS) matched for TLS risk using eleven 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 ($|d| > .25$), nor did the overall relative imbalance difference of the groups (.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-value=0.047]) (71% Reduction) (**Figure 2**).
- Analyzing the 63-patients subset who developed TLS after HU treatment, TLS-associated fatalities were even less likely among rasburicase patients, 3 of 36 rasburicase TLS patients vs. 10 of 27 allopurinol TLS patients [P-value=0.005].

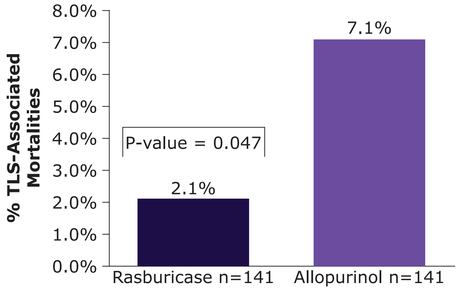
Figure 1. Pre- and Post-Matching Reduction of Differences in 11 Covariates and Propensity Score





LDH, lactate dehydrogenase; HU, hyperuricemia; WBC, white blood cells

Figure 2. TLS-Associated Mortality, Post-Hyperuricemia Treatment*



*Excluding pre-HU treatment TLS and spontaneous TLS

HU, hyperuricemia; TLS, tumor lysis syndrome

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.

REFERENCES:

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

DISCLOSURES

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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).

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