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### Rasburicase Utilization After Protocol Implementation Focused on Fixed Dosing by Limiting Use of Weight-Based Dosing to Oncology Providers

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## OBJECTIVE

Evaluate the change in rasburicase use pre- and post-implementation of dosing restriction protocol.

## BACKGROUND

- Tumor Lysis Syndrome (TLS) is a life-threatening complications that can occur in patients with a high tumor burden.<sup>1</sup>
- The lysis of tumor cells after chemotherapy leads to the release of intracellular materials which causes multiple electrolyte abnormalities and hyperuricemia leading to acute renal failure, seizures, and arrhythmias.<sup>1,2</sup>
- Reducing crystallization and precipitation of uric acid is a way to prevent renal failure in TLS.
- Rasburicase is a recombinant urate-oxidase enzyme that is used to breakdown uric acid in the blood and reduce the risk of renal failure in TLS.<sup>3</sup>
- Xanthine oxidase inhibitors are recommended in patients at lower risk of TLS and can be used in addition to rasburicase in high-risk patients.
- Rasburicase is labeled to be dosed via weight, but evidence has shown that fixed-dosing is effective and may lead to decreased cost.<sup>4,5</sup>
- Based on a study in 2010, there was a cost savings of \$4,637.52 per patient that received a fixed dose of 6 mg.<sup>5</sup>
- One institution implemented various interventions to reduce inappropriate use of rasburicase as well as decrease cost by defaulting the rasburicase dose to 3 mg.<sup>6</sup>
- A protocol was implemented at our community health center to utilize fixed dosing of rasburicase and limit weight-based dosing to oncology providers in specific patients.
- The end goal is for appropriate indication of use which would lead to majority of ordering to be completed by oncology providers.

## METHODS

- Community health system involving two hospitals and outpatient infusion center
- Two separate time frames with a four-month crossover period
  - Pre-implementation: November 1, 2018 – October 31, 2019
  - Post-implementation: March 1, 2020 – February 28, 2021
- Protocol defaulted rasburicase dose to 3 mg or 6 mg and limited the use of weight-based dosing to hematology and oncology providers and prompted other providers to include the name of the approving oncology provider to use a weight-based dose (0.05-0.20 mg/kg).
- Inclusion Criteria
  - ≥18 years old and received at least one dose of rasburicase
- Information collected from electronic health record
  - Patient demographics
  - Medication details including dose, administration time, ordering provider specialty, and location of given dose.
  - Baseline laboratory values from within 48 hours of rasburicase dose
  - Follow-up laboratory values from between 8-24 hours after rasburicase dose
- Manual collection included determining patient risk for TLS and cancer diagnosis (if applicable) along with overall indication of use.
  - Patient risk for TLS was determined using recommendations from a TLS expert panel.<sup>7</sup>
  - Determination of indication and cancer diagnosis were determined by review of the ordering provider's notes prior to rasburicase administration and ICD-10 codes.
  - Appropriate indications for rasburicase use were considered prevention of TLS in patients at high risk or treatment of TLS.
- Cost of rasburicase was determined using AWP of \$1,149.64 per 1.5mg vial as of September 2021.<sup>3</sup>
- The primary endpoint was the rate of appropriate dosing strategy meaning a fixed-dose of rasburicase was used.
- Secondary endpoints included average cost per dose, average dose, appropriate ordering provider, ordering provider specialty, TLS risk category, appropriate indication, average change in uric acid (UA), cancer diagnosis, and indication for use.
- This data was analyzed using descriptive statistics.
- The data from the post-implementation time frame was compared to the pre-implementation time frame to determine the value of this protocol at limiting use of weight-based dosing of rasburicase.

## RESULTS

- Rasburicase was administered 168 times during the prespecified time frame; 93 administrations pre-implementation and 75 administrations post-implementation.

| Table 1: Baseline Characteristics |                    |                     |
|-----------------------------------|--------------------|---------------------|
|                                   | Pre-Implementation | Post-Implementation |
| Median Age (IQR)                  | 72 (62.5-78)       | 66 (56-75)          |
| Cancer Diagnosis                  |                    |                     |
| Diffuse Large B-Cell Lymphoma     | 22%                | 32%                 |
| Mantle Cell Lymphoma              | 22%                | 9%                  |
| Acute Lymphocytic Leukemia        | 2%                 | 7%                  |
| Acute Myeloid Leukemia            | 6%                 | 11%                 |
| Chronic Lymphocytic Leukemia      | 6%                 | 5%                  |
| Chronic Myeloid Leukemia          | 1%                 | 4%                  |
| Multiple Myeloma                  | 5%                 | 1%                  |
| Other Cancers                     | 21%                | 20%                 |
| No Cancer                         | 15%                | 11%                 |

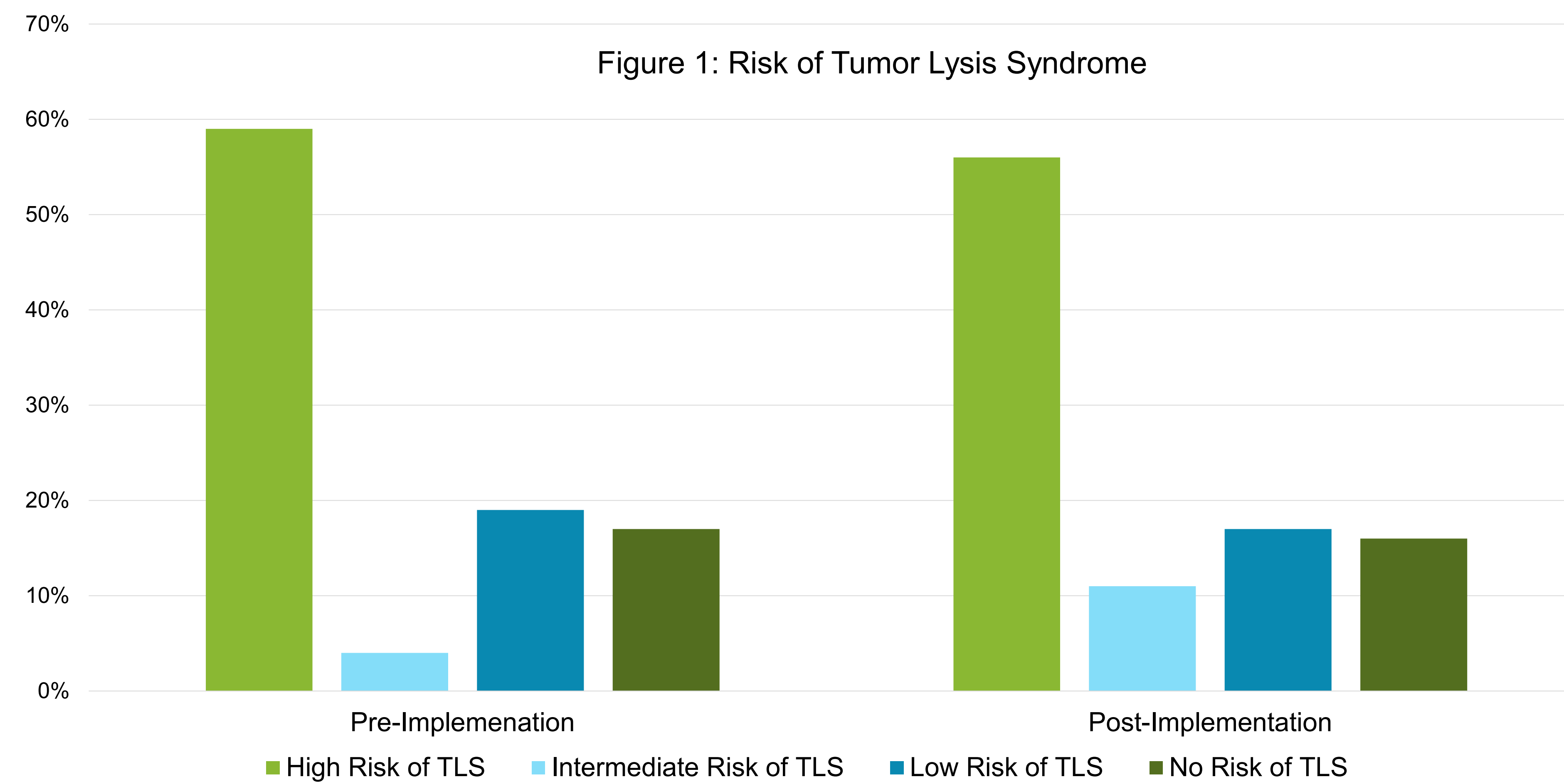


Figure 3: Pre-Implementation Ordering Provider Specialty

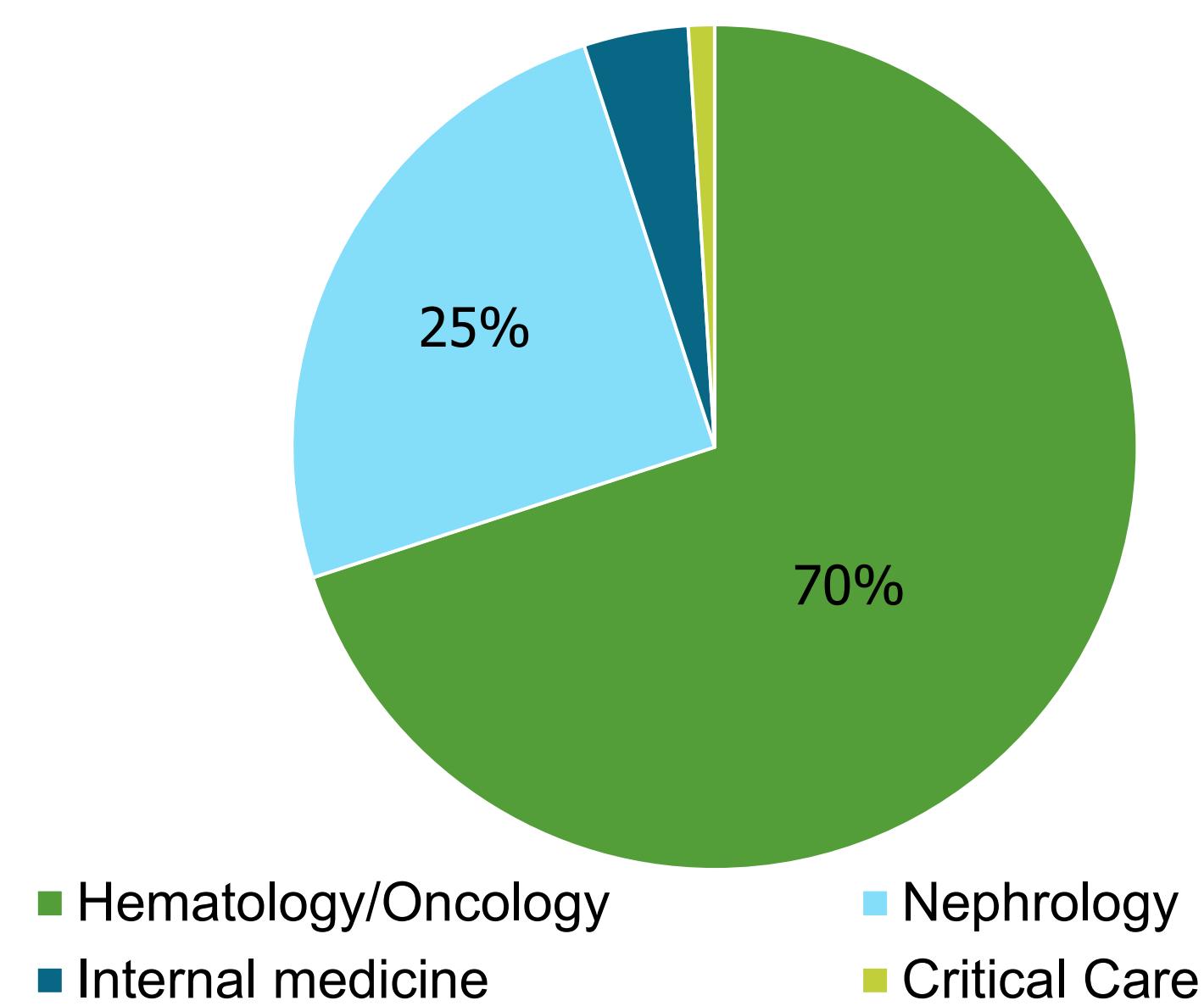
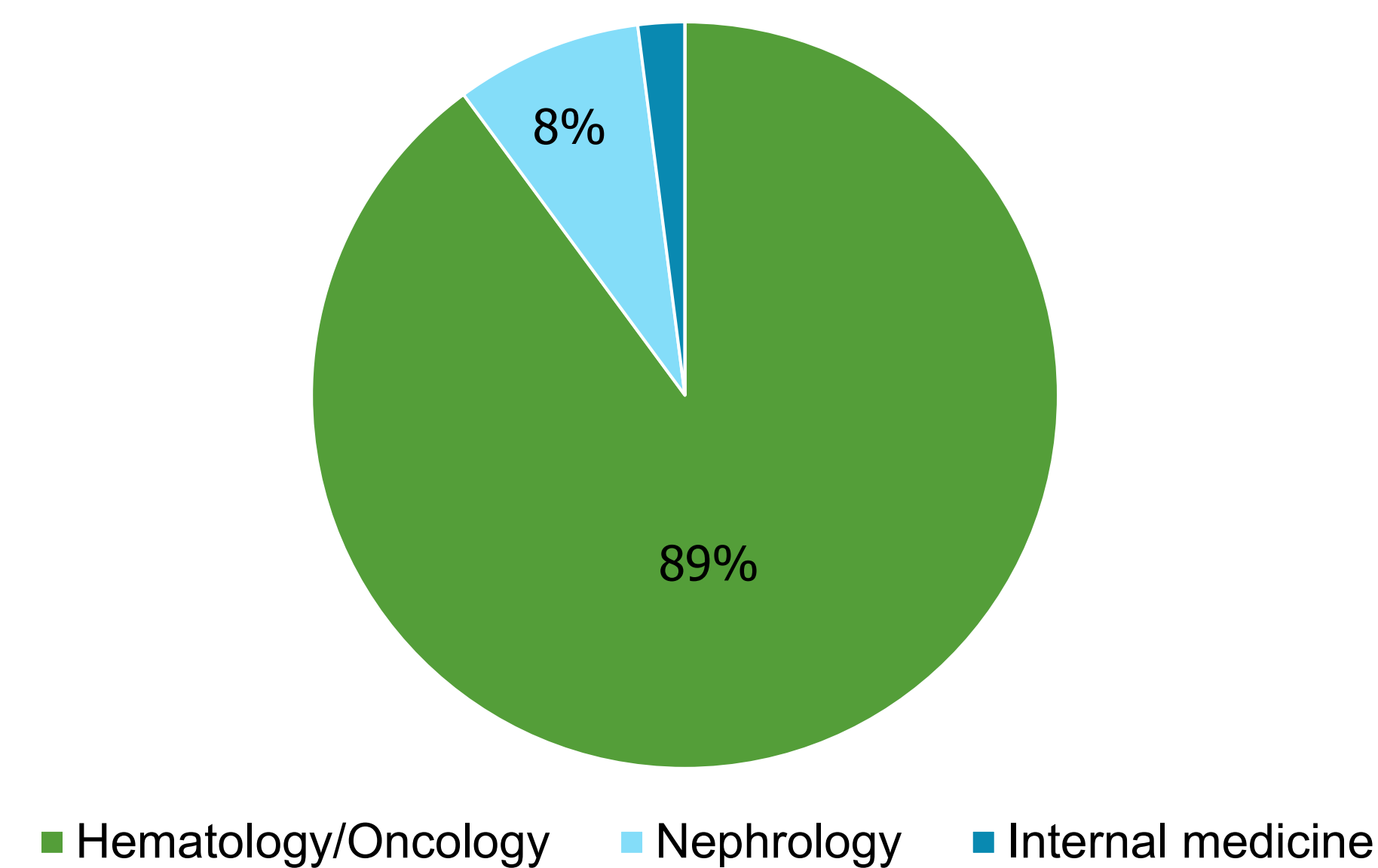


Figure 4: Post-Implementation Ordering Provider Specialty



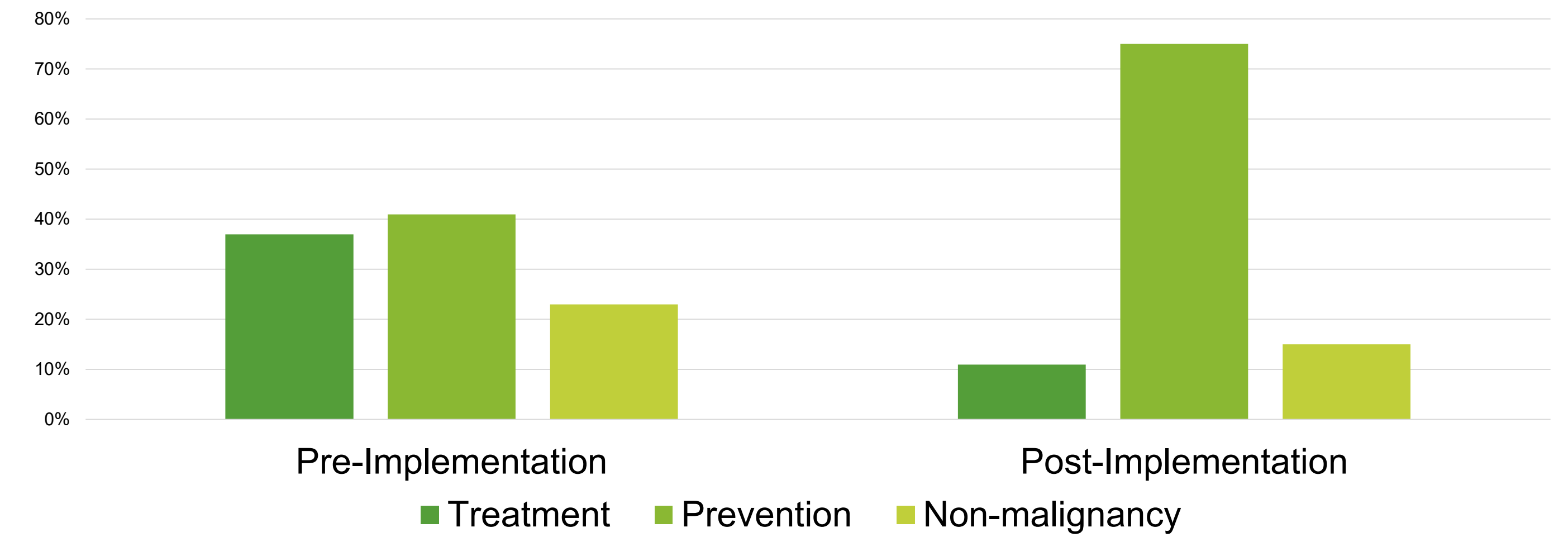
## RESULTS

Table 2: Results

|                               | Pre-Implementation | Post-Implementation |
|-------------------------------|--------------------|---------------------|
| Appropriate Dosing Strategy   | 61%                | 96%                 |
| Appropriate Indication        | 63%                | 59%                 |
| Appropriate Ordering Provider | 70%                | 89%                 |
| Average Dose                  | 9.11 mg            | 6.10 mg             |
| Average Cost per Dose         | \$6,980.29         | \$4,672.95          |
| Average Reduction in UA       | 7.95 mg/dL         | 6.55 mg/dL          |

- The use of xanthine oxidase inhibitors was similar between groups; 67% of patient pre-implementation and 56% post-implementation.
- Of those who were given xanthine oxidase inhibitors, 72% in the pre-implementation group and 69% in the post-implementation group received them prior to rasburicase administration.

Figure 4: Indication for Use



## DISCUSSION & CONCLUSIONS

- The implementation of our protocol saw a drastic increase in fixed dosing and a change in ordering providers that favored oncology providers.
- The increased usage of fixed dosing led to a decrease in average dose per administration and a significant decrease in cost was attributed to this adjustment.
- The use by non-oncology providers for alternative indications was also reduced despite that not being the primary goal; however, it is preferred that only oncology providers order rasburicase.
- Increased preventative use post-implementation may have led to less treatment use.
- Previous studies have shown that fixed doses are effective, and this study displays a cost reduction associated with using fixed-doses.<sup>4,5</sup>
- Single, fixed doses have been shown to be non-inferior to daily dosing and rarely results in the need for multiple doses for treatment of TLS.<sup>8</sup>
- Limitations
  - Cost was determined based on average wholesale cost and cost may differ for each facility
  - Patient population and physician training may impact usage patterns
- This protocol will continue to be in use at Parkview Health and may in the future move toward only hematology or oncology providers being allowed to order rasburicase.
- The protocol is effective at reducing cost by increasing the use of fixed-doses and may also lead to changes in the distribution of ordering providers.

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### Disclosure

The authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:  
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