Impact on healthcare resource utilization and cost of care of concomitant prescribing of Acid Reducing Agents with Tyrosine Kinase inhibitors: A US Payer Perspective

CML-628

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Introduction

- Tyrosine kinase inhibitors represents a paradigm shift in Chronic myeloid leukemia (CML) turning CML into a manageable chronic condition.
- The first TKI, imatinib (Gleevec)[1], was approved in 2001 with 2nd-generation TKIs such as dasatinib (Sprycel) and nilotinib (Tasigna) subsequently developed.
- Studies have shown that dasatinib and nilotinib can induce faster and deeper molecular responses compared to imatinib[2].
- 2nd generation TKIs have some advantages, however their solubility is significantly influenced by pH, which can impact absorption and bioavailability and may lead to a negative impact on disease control[3-5].
- Therefore, conditions that increase pH, such as use of acid-reducing agents (ARAs: proton pump inhibitors (PPIs), H2-antagonist and antacids) influence TKI-bioavailability, potentially leading to suboptimal therapeutic levels[6].
- Despite this, the concomitant use of TKIs with ARAs is common in clinical practice: Studies indicate that up to 50% of cancer patients receiving TKIs are also prescribed ARAs[7] with potentially more patients using over the counter preparations.

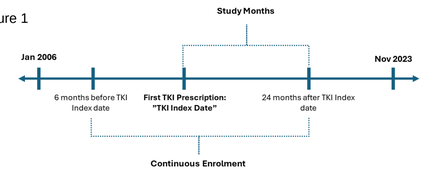
Objectives

- Despite the potential impact of concomitant TKI and ARAs on disease control, there is a lack of data examining any negative impact in terms of healthcare resource utilization in US patients.
- We therefore analyzed the Merative Research claims database to estimate the potential impact of concomitant prescribing of TKI and ARAS vs TKIs alone on patient healthcare costs from a US payer perspective ext

Methods

- We used the Merative Research closed claims Database (derived from health insurance providers 2006-2023) to identify adult patients with a CML diagnosis (ICD-10 CML code C92.1X or an ICD-9 CML code 205.1X) and at least 1 paid and dispended claim for a CML-Indicated TKI
- Each patient had to have continuous enrolment (CE) 6 months before and 24 months after the date of first TKI prescription (TKI index date) (figure 1)

Figure 1



- Entropy balancing was applied to adjust for covariates: age at index, sex, insurance, region, 1st or 2nd generation TKI initiation and Elixhauser Comorbidity index score.
- Observations were re-weighted for covariates in each group.
- Re-weighted observations are the observations "adjusted" for the covariates.
- Cost of Care and HCRU analyses were adjusted for inflation and reported in 2023 dollars paid to provider.
- Costs are reported in total cost per patient per month (PPPM), both for patients with code and normalized over total patient study cohort.
- Hospitalization readmission and total cost of care were analyzed by Major Diagnostic Categories (MDC), Revenue Codes, Diagnosis Related Groups (DRG) and by Place of Service. ER visits were identified using revenue, place of service or observation status Current Procedural Terminology (CPT).

Results

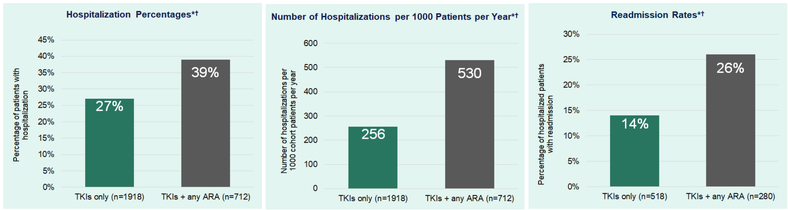
Overview

18,818 Adult TKI Patients with a CML Code were identified with 2,630 fulfilling the criteria of CE 6 months before and 24 months after TKI Index Date. Of these, 1,918 (73%) were in te TKI-Only cohort and 712 (23%) in the TKI+ARA cohort. Baseline characteristics

Hospitalization Rates

In the 24 months following the TKI Index date, 27% of patients in TKI-Only were hospitalized compared to 39% of patients in TKI+ARA cohorts (Fig 2). Hospitalizations per 1000 cohort patients per year were 2.1 times higher for the TKI+-ARA cohort (256 vs 530). Of patients who required hospitalization, 14% of TKI-Only patients required readmission within 30 days, compared to 26% of TKI+-ARA patients, a 2.6 fold increase.

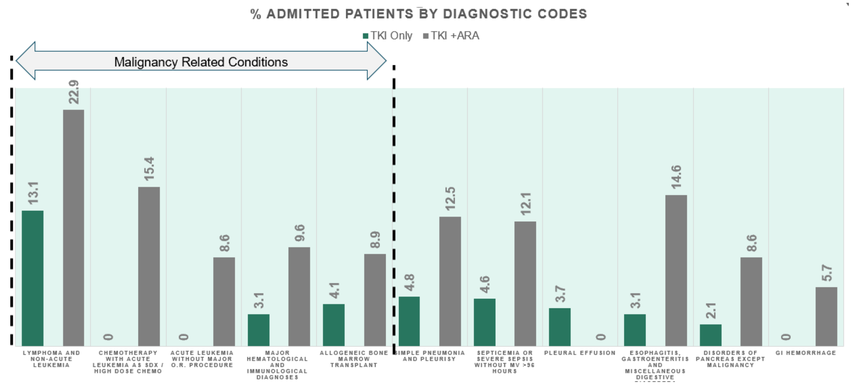
Figure 2



Diagnostic codes at Hospitalization

The DRG codes on hospitalization demonstrated an increase in malignancy-related conditions including allogeneic bone marrow transplant and requirement for chemotherapy in TKI-ARA patients. In these patients there was also an increase in GI related admissions (Figure 3).

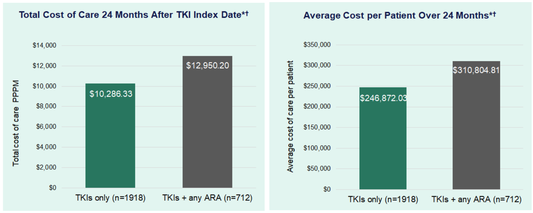
Figure 3



Cost of care

The total mean cost per patient over the 24-month period was $246,872 for TKI-Only patients and $310,805 for TKI-ARA patients, an average cost PPPM of $10,286 vs $12,950 respectively (Fig. 4).

Figure 4



The average total cost of hospitalizations per patient over 24 months was also higher in TKI+ARA patients, costing $151,950 vs $95,168, a PPPM cost of $6,331 vs $3,965 of hospitalized patients. The average cost per patient of outpatient procedures was greater in the TKI-ARA cohort at $52,236 compared to $33,391 in the TKI-Only cohort with a cost PPPM of $2176 vs $1389.

Conclusions

These data are consistent with the body of clinical evidence suggesting the concomitant use of TKIs with ARAs results in poorer outcomes for patients.

Additionally, concomitant ARA's appear to result in suboptimal disease control and need for hospital admission and treatment adjustments with a resultant increase in healthcare costs. This may translate into a more negative experience for patients and impacting quality of life.

Given that entropy balancing was applied, differences in comorbibities, age at index, sex, insurance, region or 1st or 2nd generation TKI are unlikely to explain the differences observed. These differences may be attributable to reduced bioavailability of active drug when pH is increased by ARAs. This aspect warrants further exploration.

There is also a need for the development of TKIs with minimal pH-dependent absorption which can offer better treatment options for CML patients requiring ARAs. Guidelines need to be updated in order that they can recommend specific drugs or formulations of drugs tailored to the patients need that will ensure the optimal experience and outcome.

References

1. 21-335S003_Gleevec_Approv.pdf (fda.gov)
2. Bidikian A, et al. Am J Hematol. 2023 Apr;98(4):639-644..
3. SPRYCEL® (dasatinib) [Prescribing Information]. Princeton, NJ. Bristol-Myers Squibb; 2023.
4. BOSULIF® (bosutinib) [Prescribing Information]. New York, NY. Pfizer Inc; 2023.
5. TASIGNA® (nilotinib) [Prescribing Information]. East Hanover, NJ. Novartis Pharmaceuticals Corporation; 2024
6. Van Leeuwen RW, et al. Lancet Oncol. 2014;15(8):e315-26
7. Larfors G, et al. Eur J Haematol. 2023;111(4):644-654

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