Concomitant acid reducing agents with TKI's increases time to achieve remission in CML patients: A real world analysis of a US claims database

CML-627

Pierantonio Russo[1], Charlotta Liljebris[2], Ramaa Nathan[1], Carlton Anderson[1], Michael Sicilia[1], Alex Moore[1], Sudarshan Prasad[1], Per Anderson[2]

[1]Eversana, Milwakuee, MI, US, [2]Xspray, Solna, Sweden

Introduction

Over the past 2 decades, oral Tyrosine Kinase Inhibitors (TKI's) have revolutionized the outcomes for patients with CML. However, the oral administration of many TKIs presents therapeutic challenges including significant inter and intra-subject variability in plasma exposure resulting in the need for frequent dose reductions and treatment interruptions[1]. One of the key drivers of the observed inconsistency in plasma exposure of currently available TKI's is their highly pH dependant bioavailability. This has led to warnings related to the concomitant use of acid reducing agents (ARA's) [2-4]. Despite label warnings, data has demonstrated that approximately half of all CML patients receiving TKI's also receive PPI's. In these patients the risk of death was observed to be significantly increased.

Objectives

As next generation formulations of existing TKI's with reduced gastric pH dependency and without warnings of concomitant pH altering medication treatment become available, we assess the real world scale and impact of concomitant pH altering therapy use in CML patients on TKI's with a warning or contraindication related to their use in the United States using available claims databases.

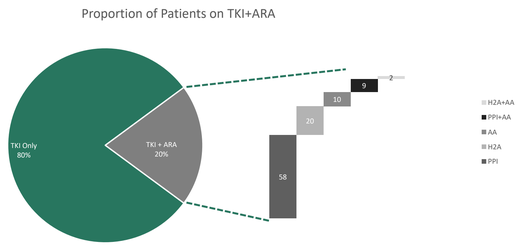
Methods

The Symphony open claims database (July 18-Sep 23) was analyzed and CML patients new to TKI's with a label warning or recommendation to avoid concomitant ARA's were selected. Patients with at least one ICD 10 claim coded "not having achieved remission" and a subsequent ICD 10 code of "achieved remission" were included in the analysis. Time to remission at 3 , 6 and 12 months post TKI initiation was compared based on concomitant use of ARA's. Confounding factors were controlled for using the Elixhauser Comorbidity Index (ECI). In order to balance the distribution of covariates, entropy balancing was applied. The set of balance conditions provided were: age at index, sex, insurance, region, 1st or 2nd generation TKI initiation and Elixhauser Comorbidity index score. The observations were reweighted so that the distribution of covariates in each group is as similar as possible. For patients with available data for 5 years, remission code rate were compared between both cohorts.

Results

4267 patients on a TKI with a specific warning in the label related to concomitant ARA's were identified. 862 (19%) were prescribed concomitant gastric acid reducing agents including PPI alone (58%), H2 antagonist alone (20%) and Antacid (21%) which included antacid alone (10%), PPi + Antacid (9%) and H2A + antacid (2%) (Figure 1).

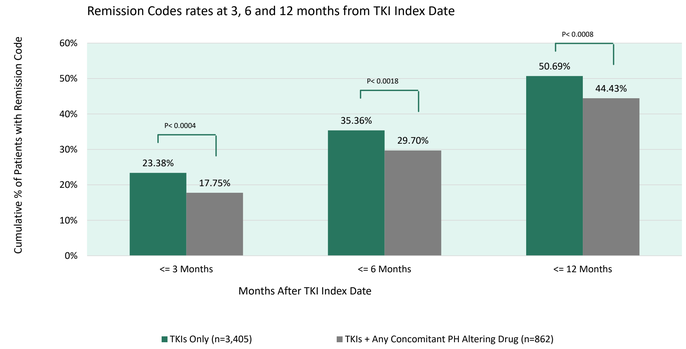
Figure 1



Remission Rates at 6 and 12 months Rates

The time to achieve a remission code in patients on TKI's alone at 3, 6 and 12 months was 23.4%, 35.4% and 50.7% respectively compared to 18.2%, 30% and 44.4% in patients on GARA' s. These differences were statistically significant at all 3 timepoints (p= 0.0004, p=0.0018 and p=0.0008) (Figure 2).

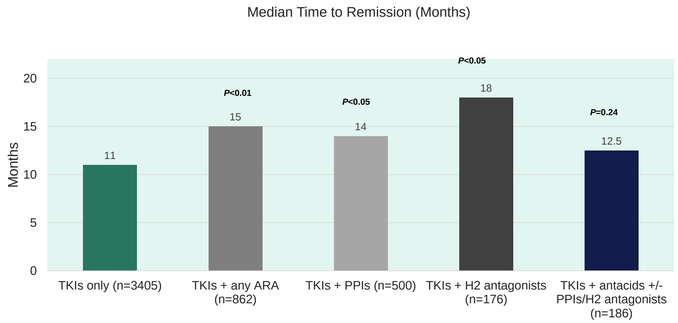
Figure 2



Time to Remission Code

Of those patients who achieved a remission code, the median time to achieve this was longer in the patients taking ARA group at 15 months compared to 11 months in the patients on TKI's alone but as long as 18 months in patients taking H2 antagonists. There was a similar trend irrespective of the ARA being administered

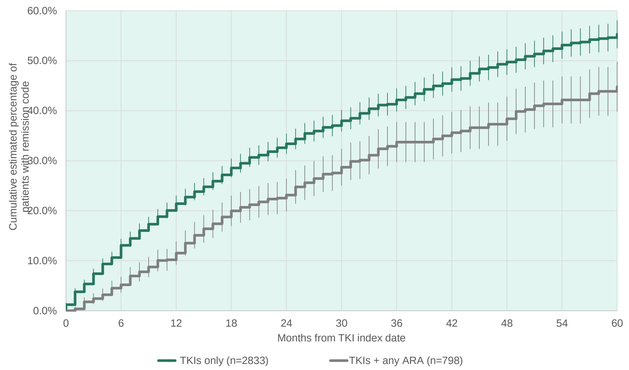
Figure 3



Remission rates at 5 years

3631 patients had 5 year follow up data available. Of these 2833 (78%) were on TKIs only and 798 (22%) on TKI + ARA. Kaplan Meier analysis up to 5 years demonstrated the significantly lower remission code rates were observed in patient's taking concomitant antacids (54.6% vs 43.9%)

Figure 4



Conclusions

Despite warnings and contraindications, a significant proportion of patients continue to be prescribed ARA's while taking TKI's with a specific contraindication or warning related to concomitant use. Based on these data, comedication with a TKI and ARA may result in :

- **Lower rates of remission codes** at 3, 6 and 12 months of starting TKI treatment
- **Increased median time to remission** for those aptients who achieve a remission code
- **Reduced remission code rate at 5 years** which becomes apparent early in the treatment process

There is a need for therapeutic options whose bioavailability is less pH dependent to allow concomitant use of pH altering treatments without compromising consistent bioavailability and remission rates. .

References

1. Lennernäs H, et al. Poster presented at: the 64th ASH Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA
2. SPRYCEL® (dasatinib) [Prescribing Information]. Princeton, NJ. Bristol-Myers Squibb; 2023.
3. BOSULIF® (bosutinib) [Prescribing Information]. New York, NY. Pfizer Inc; 2023.
4. TASIGNA® (nilotinib) [Prescribing Information]. East Hanover, NJ. Novartis Pharmaceuticals Corporation; 2024.
5. Larfors G, et al. Eur J Haematol. 2023;111(4):644-654.

Presented at the SOHO Annual Meeting 20204, 03 September 2024, in Houston, Texas