

## **Abstract: P725**

### **Title: PROPENSITY SCORE MATCHING ANALYSIS COMPARING ASCIMINIB VERSUS PONATINIB FOR ITS TREATMENT OUTCOMES IN CHRONIC MYELOID LEUKEMIA PATIENTS**

**Abstract Type: Poster Presentation**

**Topic: Chronic myeloid leukemia - Clinical**

#### **Background:**

Asciminib (ASC) is approved for chronic myeloid leukemia (CML) patients who have failed to 2 or more tyrosine kinase inhibitors (TKIs). Its efficacy compared to Ponatinib (PON) remains a subject of debate due to the absence of direct comparison. This study, conducted without pharmaceutical industry funding to eliminate potential bias, retrospectively assessed treatment outcomes. Our data have been updated, broadened, and analyzed across a larger patient cohort to compare the efficacy of ASC versus PON. A propensity score matching (PSM) analysis was utilized to address potential differences in baseline characteristics between patients treated with ASC and PON

#### **Aims:**

To assess the therapeutic efficacy of ASC compared to PON in CML pts who have failed prior TKIs

#### **Methods:**

607 CML pts who had been treated with ASC or PON in 9 countries (Canada, the Netherlands, Czech Republic, France, Argentina, Italy, Japan, South Korea, and Spain) were included. The primary endpoint was FFS at 1 year, calculated from the date of start of the TKI of interest until treatment failure. Treatment failure was defined as loss of complete hematologic response, loss of major cytogenetic response, transformation to accelerated or blast phase, or death from any cause. MR2 (BCR::ABL1 <1%IS), MMR (BCR::ABL <0.1%IS), MR4 (BCR::ABL1 <0.01%IS), progression, and overall survival (OS) were assessed. For PSM, the following pre-treatment variables were selected using a binary logistic regression model: age, history of cardiovascular disease (CVD), disease phase, T315I mutation (mut), and reason for failure to prior TKI line. 270 pts (i.e. 135 case-control pairs) were extracted through the PSM process within 0.2 of caliper difference.

#### **Results:**

In the overall population, treatment outcomes were as follows: FFS rate at 12 months was 39.8% [95% CI, 35.7-43.9], MR2 48.6% [44.1-53.4], MMR 39.3% [34.8-44.2], MR4 21.4% [22.2-30.6], and OS 91.0% [88.1-93.2]. Significant differences on various pre-treatment factors were observed in the overall population between ASC and PON, which was balanced out following the PSM.

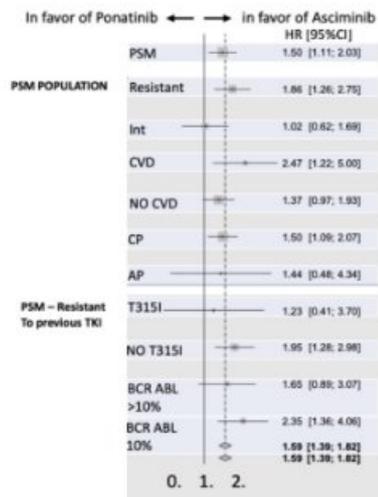
In the overall population, the ASC group exhibited a higher FFS rate compared to the PON group. This difference persisted when the analysis was confined to the PSM-selected subgroup with FFS rates at 12 months 45.4% (36.0-54.4%) for ASC and 29.85% (22.3-37.7%) for PON, HR for PON 1.5 (1.1 - 2.0, p = 0.009). In other words, PON had a 50 % higher risk of failure than ASC. Better MR2 and MR3 were observed in favor of PON in the overall group but this finding was not replicated in the PSM subgroup. No significant differences were found between the 2 groups for other outcomes.

In the PSM subgroup analysis, ASC showed significant FFS benefits over PON, particularly in patients resistant to prior TKI therapy (HR 1.8, 1.2-2.7, p=0.002), those with a history of CVD (HR 2.4, 1.2-5.0, p=0.011), and patients diagnosed in the chronic phase (HR 1.5, 1.09-2.0, p=0.012). Additionally, for TKI-resistant patients without T315I mutation or with a BCR::ABL1 ratio <10%, ASC offered therapeutic advantages in FFS, with PON's HRs at 1.9 (1.2-2.9, p=0.002) and 2.35 (1.3-4.0, p=0.002), respectively.

#### **Conclusion:**

From our results, it can be established that provided the absence of ASC-resistant mutation and prescription at a proper dose, ASC has at least an equal efficacy to PON. Treatment with ASC was associated with a higher FFS compared to PON in the overall cohort and PSM-selected subgroup. The benefit of ASC for FFS was particularly seen in those subgroups of patients who had been previously resistant, had a history of CVD, or those in CP at diagnosis. It is worth highlighting that within the resistant group patients who benefited were only those with BCR::ABL<10% and with no T315I mutation. Although this analysis does not provide a direct comparison, these findings could help clinical practice.

Figure 1. Forest plot summarizing FFS in ASC vs PON



Int: intolerant to previous TKI therapy, CVD: cardiovascular risk, CP: Chronic phase, AP: accelerated phase.

**Keywords:** Treatment, Tyrosine kinase inhibitor, Chronic myeloid leukemia