Background

Mastocytosis (MC) is a clonal myeloproliferative disorder of mast cells that can present in various clinical subtypes, including indolent systemic mastocytosis (ISM). The majority of ISM patients have low-risk disease; however, up to 20% present with more aggressive disease, including severe symptoms and patient QoL. 

Methods

PIONEER is a phase 2, multi-part, randomized, placebo-controlled, double-blind trial investigating avapritinib, an oral, oral KIT (CD117) inhibitor, in patients with ISM. The primary endpoint was response rate to avapritinib 25 mg QD, and patients were randomized to avapritinib 25 mg once daily (QD) and 71 patients were randomized to placebo.

As of June 23, 2022, there were 212 patients enrolled in Part 2 of the PIONEER trial; 141 patients were randomized to avapritinib 25 mg QD and 71 patients were randomized to placebo.

A median of 31.1 months (range, 0.3–78.1) from diagnosis to study entry and a median of 11.8 months (range, 2.2–62.1) from initial diagnosis to protocol treatment were observed. Median D816V VAF was 11% (n=12/109) in the avapritinib group and 6% (n=3/54) in the placebo group. Of patients with detectable D816V VAF in peripheral blood, 68% (80/118) were undetectable at baseline, with 11% (12/109) in the avapritinib group and 6% (3/54) in the placebo group.

Results

Avapritinib reduced mast cell burden in bone marrow and skin biopsies, as assessed via central pathology review (Figures 1 and 2). Table 1 summarizes the baseline characteristics of avapritinib and placebo patients. Significant findings include:

- Median serum tryptase was reduced from 43.7 ng/mL at baseline to 15.2 ng/mL at Week 24 in the avapritinib group (vs 50.1 ng/mL at baseline to 46.0 ng/mL at Week 24 in the placebo group; p=0.003).
- Most severe symptom score was improved from 7.9 to 5.2 in the avapritinib group, compared to 7.7 to 7.6 in the placebo group (p=0.004).
- Reductions in bone marrow mast cell aggregates were observed in the avapritinib group (36% [n=33/91] vs placebo 6% [n=6/96]; p=0.001).
- Mast cell number was reduced from 0.02% of the total cell population at baseline to undetectable levels (<0.02%) at Week 24 in the avapritinib group.

Table 2 summarizes the summary of safety data:

Conclusions

Avapritinib treatment led to significant reductions in serum tryptase and most severe symptom score, and improvements in ISM symptoms and patient QoL were observed. A safety profile was seen with avapritinib (Table 2).

Figure 1. Baseline characteristics

Table 1. Baseline characteristics

Table 2. Summary of safety

References

4. AYVAKIT® (avapritinib). Prescribing Information. May 2023. Blueprint Medicines Corporation; Sumitomo Oncology Pharma; and honoraria from AbbVie, Blueprint Medicines Corporation, Karyopharm, Novartis, Pharma Essentia, and GSK. Full disclosures for all authors are available in the article. ©2023 Blueprint Medicines, Inc. All rights reserved.

Disclosures

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