Real-World Experience of Patients with Indolent Systemic Mastocytosis Treated with Avapritinib in a Community Oncology Setting

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Background

- Indolent systemic mastocytosis (ISM) is a clonal mast cell disease driven by the *KIT* D816V mutation in ~95% of cases and is associated with symptoms of mast cell activation and tissue infiltration.
- It can cause chronic, debilitating symptoms − including life-threatening anaphylaxis and impaired bone health.
- ISM is a chronic disease, and patients experience symptoms such as flushing, pruritus, diarrhea and headaches. Treatment has historically been symptom-directed, and patients may be on 6+ therapies at a time.
- Avapritinib (AVA) is an oral, potent, selective inhibitor of KIT D816V. It is the first approved therapy for the treatment of ISM.
- Therapies targeting KIT D816V mutations may have disease modifying effects and the potential to alter the natural history of the disease.
- This is the first study to describe real-world patient profiles, treatment patterns, resource use and clinical outcomes among ISM patients treated with AVA in a U.S. community hematology network.

Study Objectives

- To describe the demographic and clinical characteristics of ISM patients receiving AVA within the ONCare Alliance Network.
- To evaluate AVA treatment patterns and duration of therapy.
- To assess health care resource use (HCRU) in ISM patients receiving AVA.

Methods

- The ONCare Alliance Network real world database was reviewed for adult patients who started AVA as treatment for ISM.
- Data collection consisted of patient demographics, disease characteristics, existing comorbidities, performance status, and biochemistry/hematology parameters at the initiation of AVA.
- Data were also collected on biomarker profiles, presenting symptoms, AVA dosage and duration, supportive care use, treatment response, symptom changes, reasons for treatment discontinuation, and clinical outcomes.
- Patient and disease related data were presented descriptively as means, medians, or proportions, with interquartile range (IQR) or 95%CIs.
- In an exploratory analysis, duration of AVA therapy and time to symptom improvement were assessed using the Kaplan-Meier (KM) method.

Results

- The final sample consisted of 18 ISM patients who started AVA between October 1, 2022, and October 1, 2024.
- Patients had a median age of 46 (IQR: 41-60) and a median Charlson Comorbidity Index score of 0 (IQR: 0-1).
- 83.3% were female, 94.4% were white and approximately 72.2% of patients had an ECOG of 0-1 **(Table 1)**.
- Of the 94.4% of patients tested for KIT mutation, the D816V mutation was detected in 64.7%.
- Mean serum tryptase levels at the start of AVA were elevated (39.1 ng/mL).
- Approximately 94.4% of patients reported symptoms within 90 days prior to AVA initiation.
- Osteopenia was reported in 4 patients (22.2%) and osteoporosis was reported in 2 patients (11.1%) within 90 days prior to AVA initiation **(Table 1)**.
- Two patients (11.1%) experienced anaphylaxis in the 6 months pre-treatment compared to zero patients (0.0%) during AVA therapy.
- The median time from ISM diagnosis to the start of AVA was 17.4 months.
- The median AVA starting dose was 25 mg daily (range: 25 to 200 mg) **(Table 4)**.
- During AVA therapy initiation, patients reported an average of 5.0 symptoms per patient **(Table 2)**.
- On AVA, symptom improvement was documented in a mean of 2.2 symptoms per patient, with a median time to improvement of 36.5 days **(Figure 1, Table 3)**. Improvements in gastrointestinal, skin, abdominal pain, and headache symptoms were most common.
- Over the course of AVA therapy, there were no anaphylaxis events reported.

Table 1. Demographic and clinical characteristics

Parameter	Indolent SM (n=18)
Median age [IQR]	46 [41-60]
Female sex (%, n)	83.3% (15)
White race (%, n)	94.4% (17)
Median Charlson comorbidity score [IQR]	0 [0-1]
ECOG Performance Status (%,n)	
0	50.0% (9)
1	22.2% (4)
Not documented	27.8% (5)
KIT D816V mutation at start of avapritinib (%, n)	61.1% (11)
Serum tryptase at baseline (%, n)	
Serum tryptase ≤ 20 ng/mL	16.7% (3)
Serum tryptase > 20 ng/mL	61.1% (11)
Not documented	22.2% (4)
Osteopenia at the start of avapritinib	22.2% (4)
Osteoporosis at the start of avapritinib	11.1% (2)
Median time from diagnosis to the start of avapritinib [IQR]	17.4 months [2.7-51.3]

Abbreviations: ECOG: Eastern Oncology Cooperative Group, IQR = interquartile range, SM = systemic mastocytosis
[1]The weighted comorbidity classes were: Low = 0 points, Medium = 1 to 2, High = 3 to 4 and Very high = ≥ 5.

Table 2. Provider documented symptoms during therapy initiation

Parameter	Indolent SM (n=18)
Anaphylaxis during avapritinib therapy (%, n)	0.0% (0)
Reported symptoms during AVA therapy initiation (%, n)	
Abdominal pain	33.3% (6)
Bone pain	22.2% (4)
Brain fog	27.8% (5)
Diarrhea	33.3% (6)
Dizziness	33.3% (6)
Fatigue	83.3% (15)
Flushing	16.7% (3)
Headache	38.9% (7)
Hypertension	11.1% (2)
Lymphadenopathy	5.6% (1)
Nausea/vomiting	50.0% (9)
Pruritus/itching	44.4% (8)
Rash	55.6% (10)
Skin lesions	16.7% (3)
Splenomegaly	11.1% (2)
Unintentional weight loss	11.1% (2)
Mean number of symptoms per patient (range)	5.0 (2-12)

Abbreviations: SM = systemic mastocytosis

Table 3. Provider documented symptom improvement during therapy[1]

Parameter	Indolent SM (n=18)
Abdominal pain	3 of 6 (50.0%)
Bone pain	1 of 4 (25.0%)
Brain fog	2 of 5 (40.0%)
Diarrhea	4 of 6 (66.7%)
Dizziness	3 of 6 (50.0%)
Fatigue	3 of 15 (20.0%)
Flushing	1 of 3 (33.3%)
Headache	4 of 7 (57.1%)
Nausea/vomiting	5 of 9 (55.6%)
Pruritis/itching	5 of 8 (62.5%)
Rash	6 of 10 (60.0%)
Skin lesions	1 of 3 (33.3%)
Weight gain	1 of 2 (50.0%)
Mean number of symptoms improved per patient	2.2
Median time to first reported symptom improvement [IQR]	36.5 days [12.2-79.0]

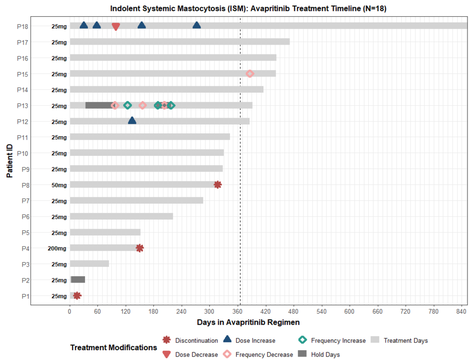
Abbreviations: IQR = interquartile range
[1]Symptom improvement during avapritinib therapy was assessed based on documentation in the medical record (Yes/No).

Table 4. Avapritinib treatment patterns

Parameter	Indolent SM (n=18)
Median starting daily starting dose (range)	25 mg (25 to 200)
Total number of patients with any therapy modifications (%, n)	27.8% (5)
Mean duration of therapy in months (95%CI)	23.5 (19.0-28.1)
Total number who remained on therapy at end of record (%, n)	83.3% (15)
Reason therapy was DC (%, n)	
Disease progression	0.0% (0)
Toxicity	11.1% (2)
Patient choice	5.6% (1)

Abbreviations: CI = confidence interval, DC = discontinued, SM = systemic mastocytosis

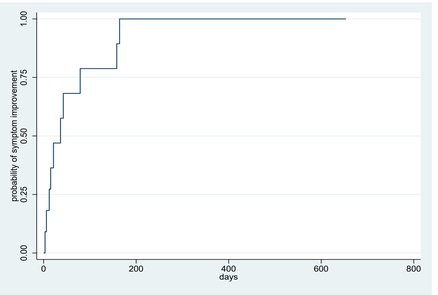
Patient level treatment



Results Contd.

- In the 18 ISM patients, there were 5 patients with any AVA modifications, including only two patients (11.1%) discontinued AVA due to intolerance **(Table 4)**.
- The two events leading to discontinuation consisted of panic attacks and a combination of diarrhea, edema and brain fog.
- The median duration of follow-up from the start of AVA was 14.2 months but median AVA duration was not reached in the sample. At the end of follow-up, 83.3% of patients remained on treatment.

Figure 1. Time to symptom improvement[1]



[1]Median time to first reported symptom improvement [IQR] was 36.5 days [12.2-79.0]

Study Limitations

- Given the retrospective nature of the study, there was undocumented data on some key endpoints (e.g., markers of bone health, biomarker status, symptom improvement, clinical outcomes).
- Additionally, since this study was designed to be descriptive in nature, results should be interpreted as directional in nature and are not intended to suggest causation.

Conclusions

- In this real-world community cohort, avapritinib was well tolerated and associated with meaningful and rapid symptom improvement in patients with ISM.
- Of the 16 patients who started on recommended label dose of 25 mg, 14 of 16 (87.5%) remained on therapy by end of record.
- These findings support the clinical utility of AVA 25 mg daily as a treatment option for SM in everyday hematology practice.
- Relatively low D816V detection rates highlight the need for more widespread high sensitivity testing in real-world practice.

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Disclosures

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