Long-Term Treatment With Pacritinib on a Compassionate Use Basis in Patients With Advanced Myelofibrosis

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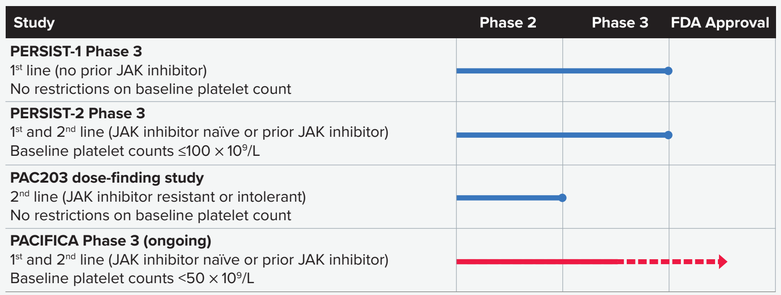
INTRODUCTION

Pacritinib Therapy for Cytopenic Myelofibrosis

- Pacritinib, an oral Janus kinase (JAK) 2/interleukin-1 receptor-associated kinase 1 (IRAK1) inhibitor that does not inhibit JAK1[1], is in development for the treatment of patients with cytopenic myelofibrosis (MF).
- The efficacy and safety of pacritinib in patients with MF has been evaluated in multiple studies (**Figure 1**), including patients with moderate and severe thrombocytopenia (platelet counts ≤100 and <50 × 10^9/L, respectively).[2-4]

Figure 1. Clinical Studies of Pacritinib in MF



- When these completed studies closed, physicians with patients who were receiving pacritinib could apply for their patients to continue treatment on a compassionate use basis.

OBJECTIVE

- To describe the experience of patients treated with compassionate use pacritinib after receiving pacritinib on a clinical trial, with a focus on patients with cytopenic MF.

METHODS

- Patients who were treated with pacritinib on PERSIST-1, PERSIST-2, or PAC203 (**Figure 1**) were provided the option to continue receiving pacritinib if they were eligible for the compassionate use program (**Table 1**).

Table 1. Eligibility for Pacritinib Compassionate Use

Inclusion	Exclusion
• Previously treated with pacritinib on a completed clinical trial • Benefitted from pacritinib in the opinion of the treating physician • Unmet medical need	• Progression to acute leukemia • High-grade bleeding or cardiac event on study • Unable to tolerate pacritinib

- Dosing regimens for pacritinib included 200 mg twice daily (BID), 100 mg BID, and 100 mg daily. Patients treated at lower doses during the original clinical study could escalate to 200 mg BID at the discretion of the treating physician.
- Monitoring on the compassionate use program included blood counts every 3 months, electrocardiogram every 3 months, and assessment of left ventricular ejection fraction every 6 months.
- Patient characteristics are reported based on data obtained from the original pacritinib study. All longitudinal data updated as of 09-July-2021.

RESULTS

Patient Characteristics

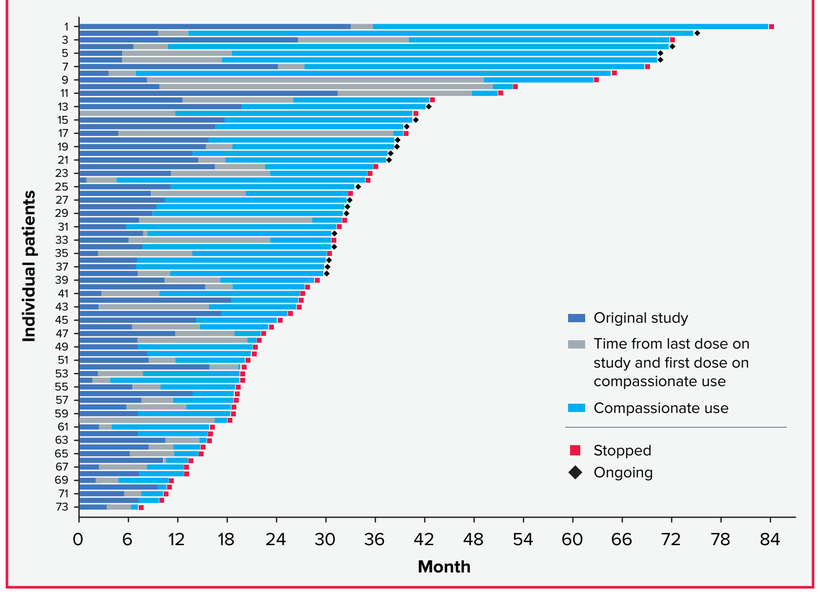
- After receiving pacritinib on an original clinical trial, 75 patients continued to receive pacritinib on a compassionate use basis (**Table 2**). Twenty patients were still on treatment as of the data cutoff date.
- Most patients had advanced disease, characterized by cytopenias and circulating blasts.

Table 2. Characteristics of Compassionate Use Population

Patient Characteristics	Pacritinib (N=75 total, denominators based on n with available data)[a]	
Prior study participation		
PERSIST-1	8% (6/75)	
PERSIST-2	47% (35/75)	
PAC203	45% (34/75)	
Age at start of original study (median, range)	69 (37-84) years	
Cytopenias (%)	**At original study start**	**Prior to compassionate use**
Platelets <50 × 10^9/L	34% (24/70)	40% (29/72)
Platelets <100 × 10^9/L	69% (48/70)	74% (53/72)
Hemoglobin <10 g/dL	49% (36/73)	52% (38/73)
Peripheral blasts ≥1%	60% (37/62)	
Prior JAK inhibitor exposure	70% (51/73)	

- Of 69 patients with dosing data, 67% received compassionate use pacritinib at a starting dose of 200 mg BID, whereas the rest received lower doses; 97% received the same or higher doses on compassionate use as they had received on study.
- Data on total treatment duration (original study + compassionate use) is available on 73 patients (**Figure 2**).

Figure 2. Time on Pacritinib in Compassionate Use Population



Long-Term Treatment Experience

- Median total combined treatment duration (original study + compassionate use) was 21.1 months (range: 0.8-80.9 months, **Figure 2, Table 3**).
  - Treatment duration was similar in patients with baseline cytopenias compared to the overall population. In particular, patients with baseline platelet counts <50 and 50-100 × 10^9/L had similar total exposure time.
  - Patients who were JAK inhibitor-naïve had longer treatment duration compared to those with prior exposure (median 29.4 vs 18.4 months).

Table 3. Duration of Compassionate Use Pacritinib Treatment

	Original Study[a]	Compassionate Use	Total Treatment
All patients (N=75), median (range), months	7.8 (0 – 32.9)	11.6 (0.3 – 61.3)	**21.1 (0.8 – 80.9)**
PLT <50 × 10^9/L (n=24)	8.7 (2.3 – 24.2)	11.6 (0.4 – 57.7)	**20.6 (6.0 – 65.6)**
PLT 50-100 × 10^9/L (n=24)	7.0 (0.9 – 19.7)	14.4 (0.9 – 60.7)	**24.9 (8.1 – 67.3)**
Hb <10 g/dL (n=36)	7.3 (0 – 24.2)	10.9 (0.3 – 60.7)	**20.4 (1.5 – 67.3)**
PLT <50 × 10^9/L & Hb <10 g/dL (n=16)	8.4 (2.3 – 24.2)	13.2 (2.5 – 57.7)	**21.8 (9.7 – 65.4)**
Prior JAK inhibitor (n=51)	7.6 (0 – 19.7)	9.8 (0.3 – 23.7)	**18.4 (1.5 – 42.1)**
No prior JAK inhibitor (n=22)	8.4 (0.2 – 32.9)	16.4 (0.9 – 61.3)	**29.4 (8.1 – 80.9)**

[a]Data on the original study is based on n=73 patients, as 2 patients had missing study data.
Hb=hemoglobin; PLT=platelet count.

- Among patients with prior JAK inhibitor exposure, median time from prior JAK inhibitor discontinuation to last known treatment with compassionate use pacritinib was 27.2 months.
  - This duration compares favorably to median survival reported in patients discontinuing ruxolitinib: 14 months overall, ~8 months if platelet count <100 × 10^9/L.[5]
  - Median time from prior JAK inhibitor to start of pacritinib was 20 days.

Safety

- Of 75 patients treated on compassionate use, 44% experienced a serious adverse event (SAE). Most SAEs were considered unlikely to be related to pacritinib and were consistent with advanced MF, including infection (13%, n=10), bleeding (19%, n=14), cytopenias (4%, n=3), and heart failure (4%, n=3).
  - Among infections, one was considered potentially opportunistic (actinomyces pneumonia in a patient with baseline neutropenia).
  - One case of skin cancer was reported (squamous cell carcinoma in a patient with an extensive history of both squamous and basal cell carcinoma prior to starting pacritinib).

CONCLUSIONS

- **Prolonged treatment with pacritinib is well-tolerated in patients with advanced MF, including those with cytopenias.**
- **Reported SAEs were consistent with those expected in advanced MF patient population and with treatment in a compassionate use setting.**

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