Outcomes of Patients with Myelofibrosis and Elevated Peripheral Blood Blasts Treated with Pacritinib on Phase 2/3 Trials

Pankit Vachhani,[1] Bart Scott,[2] Prithviraj Bose,[3] Sarah Buckley,[4] Karisse Roman-Torres,[4] Marta Sobas[5]

[1]O'Neal Comprehensive Cancer Center at the University of Alabama at Birmingham, AL, [2]Fred Hutchinson Cancer Research Center, Seattle, WA; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]CTI BioPharma Corp., a Sobi company, Seattle, WA; [5]Wroclaw Medical University, Wroclaw, Poland

INTRODUCTION

- Myelofibrosis is a clonal myeloproliferative neoplasm that can progress to blast phase disease with ≥20% bone marrow or peripheral blood blasts (PBBs).
- The presence of PBBs is associated with poor prognosis, with worse outcomes in those with 5-19% PBBs.[1]
- Pacritinib, a JAK2/IRAK1/ACVR1 inhibitor,[2,3] has been studied in patients with cytopenic MF, including those with elevated PBBs, in a phase 3 (PERSIST-2) and a phase 2 (PAC203) study.

AIM

- Describe hematological outcomes in myelofibrosis patients with elevated PPBs (≥5%) treated with pacritinib 200 mg twice daily (BID) or best available therapy (BAT).

METHODS

- Myelofibrosis patients with baseline PBBs ≥5% treated with pacritinib 200 mg BID (pooled from PERSIST-2 and PAC203) or BAT (PERSIST-2) were included in this analysis (safety population).
- In the BAT group the treatments received were categorized by:
  - Ruxolitinib only (no other treatment)
  - Chemotherapy agents (alone or in combination): cytarabine, hydroxyurea, mercaptopurine, clofarabine or idarubicin or decitabine,
  - Other: lenalidomide, prednisone, wait and watch, or ruxolitinib in combination
- Data was summarized in a tabular or graphical form using descriptive statistics.

RESULTS

- There were 16 patients (n=12 from PERSIST-2; n=4 from PAC203) in the pacritinib 200 mg BID group and 12 patients in BAT group (PERSIST-2) who had elevated baseline PBBs ≥5%.
  - In the BAT group there were 4 patients in each treatment category (ruxolitinib only, chemotherapy agents, and other).
- 94% of patients in pacritinib group had prior JAK2 inhibitor exposure vs 67% in BAT.

Table 1. Baseline Characteristics

Baseline characteristics	PAC 200 mg BID n=16	BAT n=12
Age, median years	66.5	62.5
DIPSS high risk n, (%)	8 (50)	4 (33.3)
PLT count (x10^9/L), median	52	30
Hemoglobin (g/dL), median	10.0	9.4
Grade 2 or greater fibrosis staging n, (%)	10 (62.5)	7 (58.3)
Requires RBC transfusion n, (%)	6 (37.5)	7 (58.3)
Primary Myelofibrosis n, (%)	14 (87.5)	6 (50)
JAK2^{V617F} positive n, (%)	7 (43.8)	9 (75)
Prior JAK2 inhibitor n, (%)	15 (93.8)	8 (66.7)
Palpable spleen length (cm), median	17.5	17.5

RESULTS

- Median treatment duration for patients receiving pacritinib was 5.3 months, with an average dose intensity of 92.5%.
- Pacritinib-treated patients had a consistent trend in decreasing median absolute blast count and blast percentage over time (**Table 2**).

Table 2. Median Absolute Blast Counts and Blasts Percentage for Pacritinib and BAT

Treatment	Median Absolute Blast Count (/mL)				Median Blast Percentage (%)			
	Baseline	Week 4	Week 12	Week 24	Baseline	Week4	Week 12	Week 24
Pacritinib 200 mg BID	2500	500	350	190	6.5	3.0	2.0	1.5
BAT	600	500	200	200	7.5	5.0	3.0	2.0

- In the pacritinib group 69% of patients experienced a ≥50% decrease in blast count by week 4 (**Figure 1**).
- In the BAT group, 33% of patients experienced a ≥50% decrease in blast count by week 4 (**Figure 2**).

Figure 1. Absolute (a) Blasts Count and (b) Blast Percentage Over Time for Pacritinib

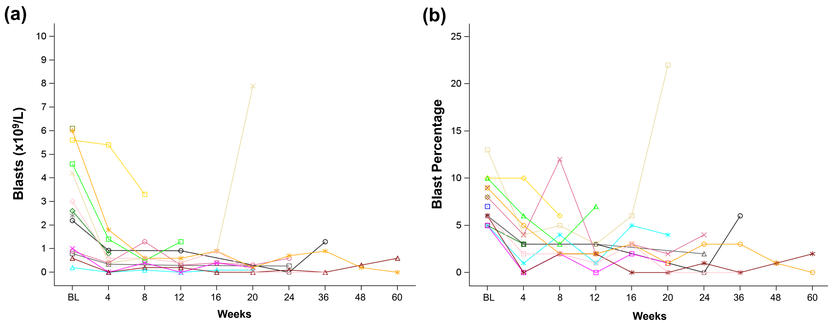
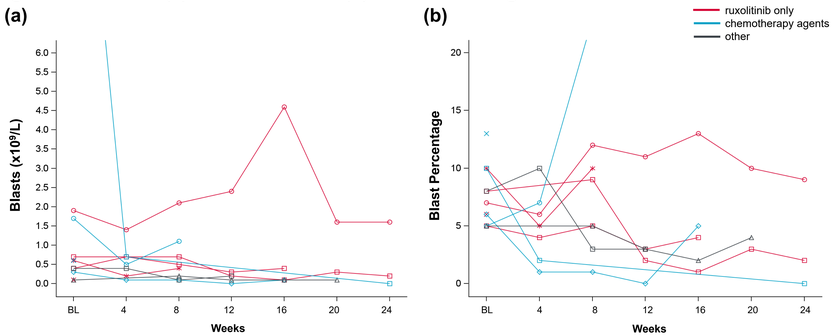
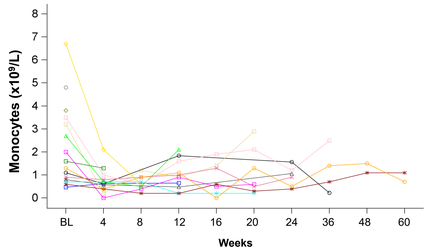


Figure 2. Absolute (a) Blast Count and (b) Blast Percentage Over Time for BAT



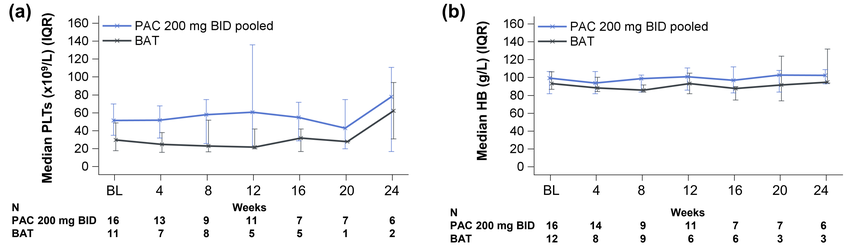
*One patient had a baseline absolute blast count outside of rate at 14.9 x 10^9/L (2a) and one patient had a spike outside of range to 23% at week 4 (2b). 2 patients that had ruxolitinib in addition to watch and wait were classified as ruxolitinib only.

Figure 3. Monocytes Count for Pacritinib



- Pacritinib-treated patients experienced a notable decrease in monocyte counts over the first 4 weeks before stabilizing over time (**Figure 3**).
  - Median monocyte count decreased from 1450/mL at baseline to 630/mL at week 4.
- Median platelet count remained generally stable for pacritinib and BAT groups **(Figure 4a).**
- Median hemoglobin remained stable over time (through week 24) for pacritinib and BAT groups **(Figure 4b).**

Figure 4. Median (a) Platelet Count and (b) Hemoglobin Over Time



- Of the 12 patients from the PERSIST-2 study, 4 patients in the pacritinib group and 2 patients in the BAT group had baseline and post-week 24 bone marrow fibrosis (BMF) grading data.
  - Of the 4 patients in the pacritinib-treated group, one patient had a ≥1 BMF grade improvement and 1 patient had a ≥2 BMF grade improvement and 2 had no BMF grade improvement.
  - Neither of the 2 patients in the BAT-treated group experienced BMF grade improvement.

CONCLUSIONS

- In myelofibrosis patients with elevated PBBs, treatment with pacritinib 200 mg BID led to a dramatic decline in blasts starting within 4 weeks, as well as decreases in BMF among evaluable patients.
- These patients also had initial decreases in monocytes at week 4 before stabilizing, while the platelet counts, and hemoglobin remained stable over time.
- Further studies are warranted to assess the efficacy of pacritinib, either alone or in combination with other agents, as a disease-modifying therapy for treatment of accelerated or blast phase MF.

ACKNOWLEDGEMENTS: This study is supported by CTI BioPharma Corp, a Sobi company.

ABBREVIATIONS: BAT, best available therapy; BL, baseline; BID, twice daily; HB, hemoglobin; IQR, interquartile range; PAC, pacritinib, PBB, peripheral blood blasts; PLT, platelet.

REFERENCES: 1. Masarova L, et al. *Cancer.* 2020;126(19):4322-31. 2. Singer J, et al. *Oncotarget.* 2018;9(70):33416-33439. 3. Oh et al. *Blood Adv.* 2023; doi.org/10.1182/bloodadvances.2023010151.

DISCLOSURES: PV has received honoraria from AbbVie, Amgen, Blueprint Medicines, Cogent Biosciences, Incyte, CTI BioPharma., a Sobi company, Daiichi Sankyo, GSK, Karyopharm, Novartis, Pfizer, Genetech, Inc., Servier, Stemline, MorphoSys, and LAVA Therapeutics; and has participated in speaker's bureaus for Incyte, CTI BioPharma Corp., a Sobi company, and Blueprint Medicines. **BS** participated on the data and safety monitoring board for Nektar and Johnson and Johnson; has participated in advisory panels for BMS, Celgene, Jazz Pharmaceuticals, and Novartis; has consulted for Alexion, Celgene, BMS, and Incyte; has received honoraria from Celgene, and BMS; and has received research funding from BMS and Novartis. **PB** has consulted for AbbVie, and Karyopharm; has consulted for and received honoraria from Blueprint, BMS, Cogent, CTI BioPharma Corp., a Sobi company, GSK, Incyte, Jubilant, Karyopharm, Morphic, MorphoSys, Novartis, PharmaEssentia, and Sumitomo; has received honoraria and research funding from Blueprint, BMS, Cogent, CTI BioPharma Corp., a Sobi company, Incyte, and MorphoSys; and has received research funding from Blueprint, BMS, Cogent, CTI BioPharma Corp., a Sobi company, DISC Medicine, Geron, Incyte, Ionis, Janssen, Kartos, MorphoSys, Sumitomo, and Telios. **SB** and **KR-T** are employed by and have received unvested equity awards from CTI BioPharma Corp., a Sobi company. **MS** has received honoraria from BMS/Celgene and Novartis.

Presenter: Dr. Pankit Vachhani; pvachhani@uabmc.edu