Abstract #7011

PACRITINIB (PAC) VS BEST AVAILABLE THERAPY (BAT) IN MYELOFIBROSIS (MF): OUTCOMES IN PATIENTS (PTS) WITH BASELINE (BL) THROMBOCYTOPENIA

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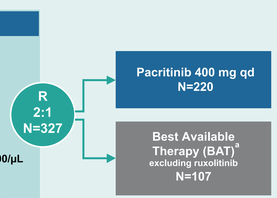
INTRODUCTION

- Myelofibrosis (MF) is a myeloproliferative neoplasm characterized by clonal myeloproliferation, dysregulated kinase signaling, and release of abnormal cytokines[1]
  - Frequent symptoms include fatigue, night sweats, pruritus, abdominal pain, early satiety, inactivity, bone pain, left subcostal margin pain[2]
- From the time of diagnosis, the incidence of disease-related thrombocytopenia increases dramatically within as early as 1 year[3]
  - In a retrospective study of 1000 pts with primary MF treated at the Mayo Clinic, the incidence of thrombocytopenia increased from 18% at diagnosis to 28% within 1 year after diagnosis and 31% in pts seen >1 year from diagnosis[3]
  - Patients (pts) with thrombocytopenia have significantly greater symptom burden, distinct clinical characteristics, and thrombocytopenia is a prognostic factor for shorter overall survival (OS)[4,5]
- Pacritinib is an oral kinase inhibitor with specificity for JAK2, FLT3, IRAK1, and CSF1R[6,7]
- In the phase 3 PERSIST-1 study, treatment with pacritinib resulted in consistent reductions in spleen volume and symptom burden, irrespective of baseline characteristics, including platelet count[8]
- This analysis examines outcomes at 72 weeks among pts in the PERSIST-1 trial with baseline platelets <100,000/μL treated with pacritinib vs BAT
- On February 8, 2016, the U.S. Food and Drug Administration notified the sponsor that the IND for pacritinib has been placed on full clinical hold due to concerns over interim survival results, bleeding and cardiovascular events (discussed in Mesa et al. Abstract 7065, ASCO 2016)

METHODS

Figure 1. PERSIST-1 Study Design



Hgb, hemoglobin; JAK, Janus kinase; PET-MF, post-essential thrombocythemia myelofibrosis; PMF, primary myelofibrosis; PPV-MF, post-polycythemia vera myelofibrosis; R, randomized.
[a]Crossover from BAT allowed after progression or after Week 24 assessment.

- Stratification at randomization: platelet count category, risk category, and region (North America, Europe, Russia, Oceania)
- Study endpoints
  - **Primary:** proportion of pts achieving a ≥35% reduction in spleen volume (by MRI/CT) from baseline to Week 24
  - **Secondary:** proportion of pts with ≥50% reduction in TSS from baseline to Week 24 on the MPN-SAF v2.0

RESULTS

Baseline Characteristics

- The majority of pts had primary MF, MF 2-3 stage disease, >50% had baseline hemoglobin <10 g/dL, and approximately 25% were red blood cell transfusion dependent by stringent Gale criteria[a]; 106 (PAC [n=72] and BAT [n=34]) had platelet counts <100,000/μL (**Table 1**)

Table 1. Baseline Characteristics for Pts With Platelets <50,000/μL and <100,000/μL

Characteristic	PAC <50,000/μL (n=35)	PAC <100,000/μL (n=72)	BAT <50,000/μL (n=16)	BAT <100,000/μL (n=34)
Median age, years (range)	71 (65-75)	69 (64-74)	66 (60-73)	62 (58-69)
≥65 years, n (%)	27 (77)	52 (72)	9 (56)	15 (44)
Male, n (%)	24 (69)	50 (69)	10 (63)	22 (65)
ECOG PS, n (%)				
0-1	26 (74)	58 (81)	13 (81)	26 (76)
2-3	9 (26)	14 (19)	3 (19)	8 (24)
MF diagnosis, n (%)				
Primary MF	**28 (80)**	**54 (75)**	**10 (63)**	**25 (74)**
Post-polycythemia vera MF	4 (11)	11 (15)	5 (31)	8 (24)
Post-essential thrombocythemia MF	3 (9)	6 (8)	1 (6)	1 (3)
Missing	0	1 (1)	0	0
DIPSS score, n (%)				
Int-1	13 (37)	29 (40)	3 (19)	7 (21)
Int-2	11 (31)	25 (35)	7 (44)	19 (56)
High	11 (31)	17 (24)	6 (36)	8 (24)
Median spleen length by physical exam, cm (range)	15 (12-19)	15 (4-33)	16 (10-19)	15 (8-17)
Median spleen volume by MRI/CT, cm^3 (range)	2604 (912-4940)	2571 (553-5278)	2930 (1543-5404)	2368 (1041-5404)
*JAK2*V617F positive, n (%)	26 (74)	54 (75)	14 (88)	25 (74)
BM biopsy completed, n (%)	34 (97)	71 (99)	16 (100)	34 (100)
Reticulin and collagen fibrosis staging				
MF 0-1	6 (18)	8 (11)	3 (19)	5 (15)
MF 2-3	**25 (74)**	**59 (83)**	**11 (69)**	**26 (77)**
Missing	3 (9)	4 (6)	2 (13)	3 (9)
Peripheral blasts, n (%)				
<1%	11 (31)	21 (29)	5 (31)	11 (32)
≥1%	16 (46)	37 (51)	7 (44)	13 (38)
<5%	27 (77)	53 (74)	10 (63)	20 (59)
≥5%	0	5 (7)	2 (13)	4 (12)
Missing	8 (23)	14 (19)	4 (25)	10 (29)
White blood cell count, n (%)				
<25 ×10⁹/L	30 (86)	54 (75)	11 (69)	27 (79)
>25 ×10⁹/L	5 (14)	18 (25)	4 (25)	6 (18)
Hemoglobin, n (%)				
<10 g/dL	**23 (66)**	**41 (57)**	**10 (63)**	**22 (79)**
≥10 g/dL	12 (34)	31 (43)	5 (31)	6 (18)
RBC transfusion status (Gale criteria)[a], n (%)				
Dependent (≥6 units/90 days)	**12 (34)**	**19 (26)**	**4 (25)**	**9 (27)**
Independent (None)	15 (43)	40 (56)	8 (50)	17 (50)
Indeterminate (50% decrease)	8 (23)	13 (18)	3 (19)	7 (21)

[a]Gale et al. *Leuk Res*. 2011;35:8-11.

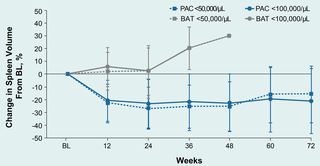
Spleen Volume Reduction (SVR)

Table 2. Proportion of Pts with SVR ≥35%[a]

Time point	Overall Population, %			Platelets <100,000/μL, %			Platelets <50,000/μL, %		
	PAC	BAT	BAT Crossover[b]	PAC	BAT	BAT Crossover[b]	PAC	BAT	BAT Crossover[b]
Week 12	16	1	NA	14	0	NA	21	0	NA
Week 24	25	6	NA	24	0	NA	33	0	NA
Week 36	31	NA	16	27	NA	25	33	NA	10
Week 48	23	NA	16	25	NA	30	31	NA	29
Week 60	24	NA	19	26	NA	33	21	NA	50
Week 72	24	NA	–	21	NA	25	17	NA	20

[a]Evaluable population; [b]Time points for crossover pts refer to time following the crossover event, e.g. Week 36 refers to 12 weeks from the time of crossover from BAT to pacritinib (at Week 24).
BAT, best available therapy; NA, not applicable; PAC, pacritinib; SVR, spleen volume reduction.

Figure 2. Mean Percent Change in Spleen Volume With Pacritinib vs BAT Among Pts[a] With Platelets <50,000/μL and <100,000/μL



[a]Patients had both baseline and each timepoint spleen assessment by MRI or CT.
BAT, best available therapy; BL, baseline; CT, computed tomography; MRI, magnetic resonance imaging; PAC, pacritinib; pt, patient.

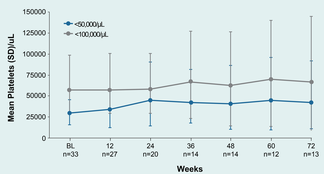
Duration of SVR ≥35%

- Among pacritinib treated pts, median duration (95% CI) of SVR ≥35% was 48 weeks (24, NA) and 57 weeks (25, NA), respectively, for pts with baseline platelets <50,000/μL and <100,000/μL
- For BAT-treated pts who crossed over to receive pacritinib, duration of SVR ≥35% (95% CI) was 73 weeks (NA, NA) and 46 weeks (21, 73), respectively, for pts with baseline platelets <50,000/μL and <100,000/μL

Hematological Parameters Over Time

- Among pts with baseline (BL) thrombocytopenia treated with pacritinib, mean platelet counts remained stable through Week 72 (**Figure 3**)
- There were no evaluable pts with baseline thrombocytopenia in the BAT arm beyond Week 36

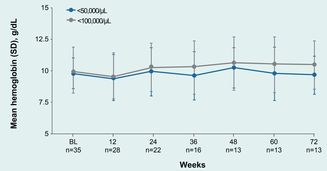
Figure 3. Mean Change in Platelet Counts from BL to Week 72 Among Pacritinib-Treated Pts



BL, baseline; SD, standard deviation

- Among pts with baseline (BL) thrombocytopenia treated with pacritinib, mean hemoglobin levels remained stable through Week 72 (**Figure 4**)
- There were no evaluable pts with baseline thrombocytopenia in the BAT arm beyond Week 36

Figure 4. Mean Change in Hemoglobin Levels from BL to Week 72 Among Pacritinib-Treated Pts

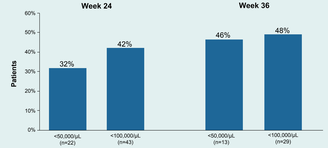


BL, baseline; SD, standard deviation

Symptom Burden Reduction

- At Week 36, 46% (6 of 13) and 48% (12 of 28) of evaluable pacritinib-treated pts with baseline platelets <50,000/μL or <100,000/μL achieved ≥50% reduction in TSS (increased from 32% and 42% at Week 24; Figure 5)

Figure 5. Pacritinib-Treated Pts[a] Achieving TSS Reduction[b] ≥50% at Week 48 by Baseline Platelet Count

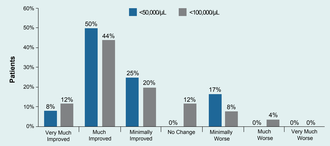


[a]Evaluable patients with baseline, Week 24, and Week 48 TSS values. [b]Using 6 common symptoms between MPN-SAF and MPN-SAF v2.0
MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form; TSS, total symptom score.

Patient Global Impression of Change (PGIC)

- 58% (7 of 12) and 56% (14 of 25) of pacritinib-treated pts with platelets <50,000/μL or <100,000/μL, respectively, reported being "much improved" or "very much improved" at Week 72 by PGIC (**Figure 6**)

Figure 6. PGIC Among Pacritinib-Treated Pts at Week 72 by Baseline Platelet Count



PGIC, Patient Global Impression of Change

Overall Survival

- No difference noted in median OS among pacritinib- and BAT-treated pts with baseline platelets <50,000/μL and <100,000/μL (**Figure 7A, B**)

Figure 7. Overall Survival in Pts With Baseline Platelets <50,000/μL (A) and <100,000/μL (B)

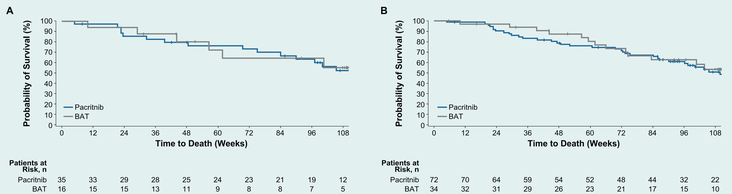


Table 3A. Incidence of Bleeding Events Over Time (All Grades)

All Grades	Platelets <50,000/μL			Platelets <100,000/μL		
Time Interval	PAC (n=35) n/n at risk (%)	BAT Initial Treatment (n=15) n/n at risk (%)	BAT Crossover (n=13) n/n at risk (%)	PAC (n=72) n/n at risk (%)	BAT Initial Treatment (n=33) n/n at risk (%)	BAT Crossover (n=29) n/n at risk (%)
Week 1 – Week 8	9/35 (26)	6/15 (40)	3/13 (23)	11/72 (15)	9/33 (27)	6/29 (21)
Week 8 – Week 16	7/32 (22)	3/15 (20)	3/11 (27)	11/68 (16)	4/32 (13)	5/27 (19)
Week 16 – Week 24	7/29 (24)	2/13 (14)	1/7 (14)	8/62 (13)	1/30 (3)	2/21 (10)
Week 24 – Week 32	1/25 (4)	1/12 (8)	1/7 (14)	5/55 (9)	1/26 (4)	1/21 (5)
Week 32 – Week 40	3/22 (14)	1/5 (20)	1/7 (14)	5/48 (10)	1/10 (10)	1/18 (6)
Week 40 – Week 48	3/18 (17)	0/4	1/7 (14)	3/40 (8)	0/4	1/17 (6)

Table 3B. Incidence of Bleeding Events Over Time (Grades 3/4)

Grades 3/4	Platelets <50,000/μL			Platelets <100,000/μL		
Time Interval	PAC (n=35) n/n at risk (%)	BAT Initial Treatment (n=15) n/n at risk (%)	BAT Crossover (n=13) n/n at risk (%)	PAC (n=72) n/n at risk (%)	BAT Initial Treatment (n=33) n/n at risk (%)	BAT Crossover (n=29) n/n at risk (%)
Week 1 – Week 8	2/35 (6)	0/15	0/13	2/72 (3)	1/33 (3)	1/29 (3)
Week 8 – Week 16	2/32 (6)	1/15 (7)	1/11 (9)	3/68 (4)	1/32 (3)	2/27 (7)
Week 16 – Week 24	0/29	0/13	0/7	0/62	0/30	0/21
Week 24 – Week 32	0/25	0/12	0/7	1/55 (2)	0/26	0/21
Week 32 – Week 40	1/22 (5)	1/5 (20)	1/7 (14)	1/48 (2)	1/10 (10)	1/8 (6)
Week 40 – Week 48	1/18 (6)	1/18 (6)	0/7	1/40 (3)	0/4	0/17

CONCLUSIONS

- In pts with MF and baseline thrombocytopenia (platelets <50,000/μL and <100,000/μL), treatment with pacritinib led to durable reductions in spleen volume and symptom burden
- Patients treated with pacritinib had stable mean platelet counts and hemoglobin levels through end of treatment and increased platelet counts in patients with platelets <50,000/μL
- At 24 weeks, bleeding events occurred at a similar rate in pacritinib- and BAT-treated patients; following crossover to pacritinib, BAT patients had a similar rate of events

References

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Disclosures

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