PACIFICA: A Randomized Phase 3 Study of Pacritinib vs. Physician’s Choice in Patients with Myelofibrosis and Severe Thrombocytopenia

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BACKGROUND

Myelofibrosis with Severe Thrombocytopenia

- Patients with myelofibrosis (MF) and severe thrombocytopenia (platelet count <50,000/µL) have advanced disease and poor prognosis1,2
- These patients represent an area of serious unmet medical need. Effective treatment options are limited, as approved JAK2 inhibitors generally cannot be given at optimally effective doses due to drug-induced myelosuppression3

Pacritinib Development

- Pacritinib is a JAK2/IRAK1 inhibitor with minimal activity against JAK1,4
- Pacritinib has demonstrated efficacy in two Phase 3 trials in patients with MF (PERSIST-1 and PERSIST-2),5,6 including in patients with severe thrombocytopenia (Abstract #1495 – Monday)
- The PAC203 Phase 2 dose-finding study was conducted in patients with MF who did not respond to or were unable to tolerate prior ruxolitinib
- Based on results from PAC203, as well as dose-response / exposure-response analysis (Oral abstract #667 – Monday), the 200mg BID dose has demonstrated efficacy and will be used in patients with MF and severe thrombocytopenia in the Phase 3 PACIFICA trial

STUDY DESIGN

Key Eligibility

- Platelet count <50,000/µL
- DIPSS Int 1-2 or High Risk
- Palpable spleen ≥35cm
- TSS ≥10 (MPN SFS v2.0)
- Prior JAK inhibitor s90 days
- PC therapy includes any one of: low-dose ruxolitinib (5mg BID or 5mg QD starting), hydroxyurea, thalidomide, lenalidomide, or corticosteroids
- Patients treated until disease progression, toxicity, or withdrawal of consent
- All patient followed for survival until 2.5 years after randomization

Randomize 51:1, N=180

Key Exclusion Criteria

- Prior splenectomy or allogeneic stem cell transplantation
- Any myelofibrosis therapy within 14 days prior to Day 1
- Any prior JAK2 inhibitor treatment for >90 days
- Grade ≥2 bleeding within prior 3 months unless precipitated by an inciting event
- Medications that increase bleeding risk within 14 days prior to Day 1
- Grade ≥2 cardiac conditions within 6 months prior to Day 1 (asymptomatic and stable grade 2 conditions may be considered for inclusion)
- QTC >450 ms or medications that prolong QT interval within 14 days prior to Day 1
- NYHA Class II, III, or IV heart failure
- Active or uncontrolled bowel disorders
- Non-myelofibrosis malignancy within prior 3 years other than curatively treated basal or squamous skin cancer, cervical carcinoma in situ, breast carcinoma in situ, or non-metastatic prostate cancer (prostate cancer under watch and wait strategy may be considered for inclusion)

STRATIFICATION

- PCR selection
- Prior JAK inhibitor
- Physician’s Choice (P/C)

1° Endpoint

- SVR at 52 weeks

2° Endpoints

- TSS at 24 weeks
- Overall Survival
- PGIC at 24 weeks

STUDY OBJECTIVES

Primary Objective

- To compare efficacy of pacritinib vs. P/C therapy based on the proportion of patients with ≥35% spleen volume response at Week 24.

Secondary Objectives

- To compare the proportion of patients treated with pacritinib vs. P/C with ≥50% reduction in Total Symptom Score at Week 24.

OS

- To compare the overall survival of patients treated with pacritinib vs. P/C therapy.

PGIC

- To compare the proportion of patients treated with pacritinib vs. P/C who self-assess as “very much improved” or “much improved” at Week 24 as measured by the Patient Global Impression of Change.

Tertiary Objectives

- Hematologic improvement (in transfusions, anemia, and thrombocytopenia)
- Improvement in fatigue (PROMIS – Fatigue – Short Form 7a)
- Changes in mutated allelic burden and gene expression

MAJOR ELIGIBILITY CRITERIA

Key Inclusion Criteria

1. Adults with primary or secondary myelofibrosis
2. Platelet count <50,000/µL
3. DIPSS Intermediate-1, Intermediate-2, or High-Risk disease
4. Palpable spleen ≥35 cm below costal margin
5. TSS ≥10 (MPN-SFS v2.0) or 1 symptom ≥5 or 2 symptoms ≥3 including only the symptoms of left upper quadrant pain, bone pain, itching, night sweats
6. ECOG performance status 0-2
7. Left ventricular ejection fraction ≥50%
8. Peripheral blasts <10%
9. Adequate hepatic and renal function, coagulation parameters, and neutrophil count

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STATISTICAL ANALYSIS

- Variable: Plan
- Sample Size
- Randomization: 2:1 (pacritinib:P/C)
- Primary Endpoint: SVR
- Power: >80%
- Alpha: Two-sided 0.05

CONCLUSIONS

- There is a serious unmet need for safe and effective therapies for patients with MF and severe thrombocytopenia
- The Phase 3 PACIFICA trial will compare efficacy and safety of pacritinib 200mg BID vs. Physician’s Choice therapy in this patient population
- The PACIFIC trial is currently open to enrollment

REFERENCES


CONTACT INFORMATION

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Clinicaltrials.gov Identifier: NCT03165734
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