Essai Clinique

Généré le 26 avr. 2025 à partir de

Titre	A Randomized, Controlled Phase 3 Study of Pacritinib Versus Physician's Choice in Patients With Primary Myelofibrosis, Post Polycythemia Vera Myelofibrosis, or Post-Essential Thrombocythemia Myelofibrosis With Severe Thrombocytopenia (Platelet Count
Protocole ID	PACIFICA
ClinicalTrials.gov ID	NCT03165734
Type(s) de cancer	NMP : Vaquez , Thrombocythémie essentielle, Métaplasie myéloide
Phase	Phase III
Type étude	Clinique
Médicament	Pacritinib versus traitement au choix du clinicien
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Ville	
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Statut	Actif en recrutement
Date d'activation	03-08-2022
But étude	This study (study ID PAC203 North America; PAC303 ex-North America) is evaluating 200 mg BID of pacritinib compared to physician's choice (P/C) therapy in patients with MF and severe thrombocytopenia (platelet count <50,000/µL). Approximately 399 patients in total will be enrolled, randomized 2:1 to either pacritinib (approximately 266 patients) or to P/C therapy (approximately 133 patients).Condition or disease: Primary Myelofibrosis/Post-Polycythemia Vera Myelofibrosis/ Post-essential Thrombocythemia MyelofibrosisIntervention/treatment: Drug-Pacritinib

Critères d'éligibilité	• PMF (including pre-fibrotic MF), PPV-MF, or PET-MF (Tefferi and Vandiman 2008)
	• Average platelet count of <50,000/µL at Screening (Day -35 to Day -3) based on two measurements taken on different days; both measurements must be <50,000/µL
	• DIPSS Intermediate-1, Intermediate-2, or High risk (Passamonti et al 2010)
	• Palpable splenomegaly ≥5 cm below the lower costal margin (LCM) in the midclavicular line as assessed by physical examination
	• TSS of ≥10 on the MPN-SAF TSS 2.0 or a single symptom score of ≥5 or two symptoms of ≥3, including only the symptoms of left upper quadrant pain, bone pain, itching, or night sweats
	• If the patient has received prior JAK2 inhibitor treatment, this treatment must meet at least one of the following criteria:
	  • Prior treatment with any JAK2 inhibitor, irrespective of dose, with a duration of 90 days or less. The 90-day period starts on the date of first administration of JAK2 inhibitor therapy and continues for 90 calendar days, regardless of whether therapy is administered continuously or intermittently during that interval.
	  • Prior treatment with ruxolitinib, at no more than 10 mg total daily dose on any day, with a duration of 270 days or less. The 270-day period starts on the date of first ruxolitinib administration and continues for 270 calendar days, regardless of whether therapy is administered continuously or intermittently during that interval.The patient may not have received >10 mg of ruxolitinib on any day during that interval
	• Age ≥18 years
	• Eastern Cooperative Oncology Group performance status 0 to 2

	• Peripheral blast count of <10% throughout the Screening period and at baseline • Absolute neutrophil count of ≥500/μL • Left ventricular cardiac ejection fraction of ≥50% by echocardiogram or multigated acquisition (MUGA) scan • Adequate liver and renal function, defined by liver transaminases (aspartate aminotransferase [AST]/serum glutamic-oxaloacetic transaminase [SGOT] and alanine aminotransferase [ALT]/serum glutamic pyruvic transaminase [SGPT]) ≤3 × the upper limit of normal (ULN) (AST/ALT ≤5 × ULN if transaminase elevation is related to MF), total bilirubin ≤4 x ULN (in cases where total bilirubin is elevated, direct bilirubin ≤4 × ULN, is required) and creatinine ≤2.5 mg/dL • Adequate coagulation defined by prothrombin time/international normalized ratio and partial thromboplastin time ≤1.5 × ULN • If fertile, willing to use effective birth control methods during the study • Willing to undergo and able to tolerate frequent MRI or CT scan assessments during the study • Able to understand and willing to complete symptom assessments using a patient-reported outcome instrument • Provision of signed informed consent
Critères d'exclusion	• Life expectancy <6 months • Completed allogeneic stem cell transplant (allo-SCT) or are eligible for and willing to complete other approved available therapy including allo-SCT • History of splenectomy or planning to undergo splenectomy • Splenic irradiation within the last 6 months • Previously treated with pacritinib • Treatment with any MF-directed therapy within 14 days prior to treatment Day 1 • Any prior treatment with more than one JAK2 inhibitor • Treatment with an experimental therapy within 28 days prior to treatment Day 1 • Systemic treatment with a strong CYP3A4 inhibitor or a strong cytochrome P450 (CYP450) inducer within 14 days prior to treatment Day 1. Shorter washout periods may be permitted with approval of the Medical Monitor, provided that the washout period is at least five half-lives of the drug prior to treatment Day 1 • Significant recent bleeding history defined as National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) grade ≥2 within 3 months prior to treatment Day 1, unless precipitated by an inciting event (e.g., surgery, trauma, or injury) • Systemic treatment with medications that increase the risk of bleeding, including anticoagulants, antiplatelet agents (except for aspirin dosages of ≤100 mg per day), anti-vascular endothelial growth factor (anti-vascular endothelial growth factor [anti-VEGF]) agents, and daily use of cyclooxygenase-1 (COX-1) inhibiting nonsteroidal anti- inflammatory drugs (NSAIDs) within 14 days prior to treatment Day 1 • Systemic treatment with medications that can prolong the QT interval within 14 days prior to treatment Day 1. Shorter washout periods may be permitted with approval of the Medical Monitor, provided that the washout period is at least five half-lives of the drug prior to treatment Day 1 • Any history of CTCAE grade ≥2 non-dysrhythmia cardiac conditions within 6 months prior to treatment Day 1. Patients with asymptomatic grade 2 non- dysrhythmia cardiovascular conditions may be considered for inclusion, with the approval of the Medical Monitor, if stable and unlikely to affect patient safety. • Any history of CTCAE grade ≥2 cardiac dysrhythmias within 6 months prior to treatment Day 1. Patients with non-QTc CTCAE grade 2 cardiac dysrhythmias may be considered for inclusion, with the approval of the Medical Monitor, if the dysrhythmias are stable, asymptomatic, and unlikely to affect patient safety. • QT corrected by the Fridericia method (QTcF) prolongation >450 ms or other factors that increase the risk for QT interval prolongation (e.g., hypokalemia [defined as serum potassium <3.0 mEq/L that is persistent and refractory to correction], or history of long QT interval syndrome • New York Heart Association Class II, III, or IV congestive heart failure • Any active gastrointestinal or metabolic condition that could interfere with absorption of oral medication • Active or uncontrolled inflammatory or chronic functional bowel disorder such as Crohn's Disease, inflammatory bowel disease, chronic diarrhea, or chronic constipation • Other malignancy within 3 years prior to treatment Day 1. The following patients may be eligible despite having had a malignancy within the prior 3 years: patients with curatively treated squamous or basal cell carcinoma of the skin; patients with curatively treated non-invasive cancers; patients with organ-confined prostate cancer with prostate-specific antigen (PSA) <20 ng/mL and National Comprehensive Cancer Network risk of Very Low, Low, or Favorable Intermediate; and patients with curatively treated non-metastatic prostate cancer with negative PSA. • Uncontrolled intercurrent illness, including, but not limited to, ongoing active infection, psychiatric illness, or social situation that, in the judgment of the treating physician, would limit compliance with study requirements • Known seropositivity for human immunodeficiency virus • Known active hepatitis A, B, or C virus infection • Women who are pregnant or lactating • Concurrent enrollment in another interventional trial • Severe thrombocytopenia due to vitamin B12 deficiency, folate deficiency, or viral infection in the opinion of the investigator • Known hypersensitivity to pacritinib or any of the following inactive ingredients: microcrystalline

	cellulose, polyethylene glycol, and magnesium stearate; any contraindication to the "physician's choice" medicinal product selected by the investigator to be used as the comparator or to loperamide or equivalent antidiarrheal medication.