GRN163LMYF3001

Randomized Open-Label, Phase 3 Study to Evaluate Imetelstat (GRN163L) Versus Best Available Therapy (BAT) in Patients with Intermediate-2 or High-risk Myelofibrosis (MF) Refractory to Janus Kinase (JAK)-Inhibitor

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Trattamento: Imetelstat

Sindromi MIELOPROLIFERATIVE CRONICHE target: Myelofibrosis

Principali Criteri Inclusione:

1. ≥18 years of age.

2. Diagnosis of PMF according to the revised WHO criteria or PET-MF or PPV-MF according to the IWG-MRT criteria confirmed by local pathology report. DIPSS intermediate-2 or high-risk MF.

4. Refractory to JAK-inhibitor treatment as defined in either inclusion 4.1 or 4.2:

4.1: Treatment with JAK-inhibitor for ≥ 6 months duration, including at least 2 months at an optimal dose as assessed by the investigator for that participant and ONE of the following:

a) no decrease in spleen volume (< 10% by MRI or CT) from the start of treatment with JAK-inhibitor.

b) no decrease in spleen size (< 30% by palpation or length by imaging) from start of treatment with JAK-inhibitor

c) no decrease in symptoms (< 20% by MFSAF or myeloproliferative neoplasm SAF) from start of treatment with JAK-inhibitor.

d) a score of at least 15 on TSS assessed using the MFSAF v4.0 (adapted as the MF Symptom Recall Form, Section 18.6) during screening. For patients on JAK-inhibitor at time of signing the informed consent form (ICF), this symptom assessment should be performed prior to tapering.

4.2: Treatment with JAK-inhibitor treatment for ≥ 3 months duration with maximal doses (e.g., 20-25 mg twice daily ruxolitinib) for that participant and no decrease in spleen volume/size or symptoms as defined in inclusion criterion 4.1 (a, b, or c).

5. Measurable splenomegaly demonstrated by a palpable spleen measuring ≥ 5 cm below the left costal margin or a spleen volume ≥ 450 cm3 by MRI or CT.

6. Active symptoms of MF on the MFSAF v4.0 (adapted as the MF Symptom Recall Form) demonstrated by a symptom score of at least 5 points (on a 0 to 10 scale) on at least 1 of the symptoms or a score of 3 or greater on at least 2 of the following symptoms: fatigue, night sweats, itchiness, abdominal discomfort, pain under ribs on left side, early satiety, and bone pain.

9. Eastern Cooperative Oncology Group Performance Status score of 0-2

Principali Criteri Esclusione:

1. Peripheral blood blast count of ≥ 10% or bone marrow blast count of ≥ 10%.

2. Known allergies, hypersensitivity, or intolerance to imetelstat or its excipients.

3. Prior treatment with imetelstat.

4. Any chemotherapy or MF directed therapy, including investigational drug regardless of class or mechanism of action, immunomodulatory or immunosuppressive therapy, corticosteroids > 30 mg/day prednisone or equivalent, and JAK-inhibitor treatment ≤ 14 days prior to randomization.

6. Diagnosis or treatment for malignancy other than MF except: • Malignancy treated with curative intent and with no known active disease present for ≥ 3 years before randomization.

• Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.

• Adequately treated cervical carcinoma in situ without evidence of disease.

7. Clinically significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months of screening, or any Class 3 (moderate) or Class 4 (severe) cardiac disease as defined by the New York Heart Association Functional Classification.