KARTA BADANIA
NAZWA BADANIA A 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
NUMER PROTOKOŁU: **GRN163LMYF3001**
WSKAZANIE: C94.5 - Ostre zwłóknienie szpiku

WŁĄCZENIA

1. ≥18 years of age.

2. Diagnosis of PMF according to the revised WHO criteria (Section 18.2); or PET-MF or PPV-MF according to the IWG-MRT criteria (Section 18.3) confirmed by local pathology report.

3. Dynamic International Prognostic Scoring System 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:

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

    2. no decrease in spleen size (< 30% by palpation) from start of treatment with JAK-inhibitor

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

    4. 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 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.

7. Hematology laboratory test values within the following limits:

1. absolute neutrophil count (ANC) ≥ 1.5 x 109/L (i.e., ≥ 1,500/mm3) independent of growth factor support, AND

2. platelets ≥ 75 x 109/L (i.e., ≥ 75,000/mm3) independent of platelet transfusion support.

8. Biochemical laboratory test values must be within the following limits:

1. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 2.5 x upper limit of normal (ULN);

2. Alkaline phosphatase (ALP) ≤ 5 x ULN;

3. Serum creatinine ≤ 2 x ULN;

4. Total bilirubin ≤ 3 x ULN; and direct bilirubin ≤ 2 x ULN (unless due to Gilbert's syndrome or underlying MF).

9. Eastern Cooperative Oncology Group Performance Status score of 0, 1, or 2

10. Women of childbearing potential and men who are sexually active must use a highly effective method of birth control during and after the study consistent with local regulations regarding the use of birth control methods for participants participating in clinical trials. Men must use a highly effective method of birth control and agree not to father a child or donate sperm during and after the study. For females, these restrictions apply for 1 month after the last dose of study drug. For males, these restrictions apply for 3 months after the last dose of study drug.

11. A woman of childbearing potential must have a negative serum (β-human chorionic gonadotropin) or urine pregnancy test at screening.

12. Each participant (or their legally acceptable representative) must sign an ICF indicating the participant understands the purpose of and procedures required for the study and are willing to participate in the study.

WYŁĄCZENIA

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 (refer to the current IB).

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.

5. Persistent unresolved toxicity from prior treatment, i.e., has not returned to Grade ≤1 or pre-treatment baseline.

6. Diagnosis or treatment for malignancy other than MF except:

    1. Malignancy treated with curative intent and with no known active disease present for ≥ 3 years before randomization.

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

    3. 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.

8. Known history of human immunodeficiency virus or any uncontrolled active systemic infection requiring IV antibiotics.

9. Active systemic hepatitis infection requiring treatment (carriers of hepatitis virus are permitted to enter the study), or any known acute or chronic liver disease unless related to underlying hepatosplenomegaly due to MF.

10. Major surgery within 28 days prior to randomization.

11. Female participants who are pregnant or are currently breastfeeding or planning to become pregnant while enrolled in this study or within 30 days after the end of dosing.

12. Male participants who plan to father a child while enrolled in this study or within 90 days after the end of dosing.

13. Any life-threatening illness (e.g., COVID-19), medical condition, or organ system dysfunction which, in the investigator's opinion, could compromise the participant's safety, interfere with the imetelstat metabolism, or put the study outcomes at undue risk; if participant has any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (e.g., compromise the well- being) or that could prevent, limit, or confound the protocol-specified assessments.