A Phase 3, Randomized, Open-label, Active-Comparator-Controlled Clinical Study to Evaluate the Safety and Efficacy of Bomedemstat (MK-3543/IMG-7289) versus Best Available Therapy (BAT) in Participants With Essential Thrombocythemia who have an Inadequate Response to or are Intolerant of Hydroxyurea.

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Sindromi MIELOPROLIFERATIVE CRONICHE target: TROMBOCITEMIA ESSENZIALE

Studio di fase 3

Principali Criteri Inclusione:

1. Has a diagnosis of ET per WHO 2016 diagnostic criteria for myeloproliferative neoplasms (Appendix 9).

2. Has a bone marrow fibrosis score of Grade 0 or Grade 1, as per a modified version of the European Consensus Criteria for Grading Myelofibrosis (Appendix 11)

3. Has a history of inadequate response to or intolerance of hydroxyurea per at least 1 of the following criteria, based on modified ELN criteria for hydroxyurea resistance or intolerance [Barosi, G., et al 2007]

- Hydroxyurea Resistance (or Inadequate Response):

- Platelet count >600 × 109/L after 3 months of at least 2 g/day or MTD of hydroxyurea, or

- Platelet count >400 × 109/L and WBC <2.5 ×109/L at any dose and duration of hydroxyurea, or

- Platelet count >500 × 109/L and Hb <10 g/dL at any dose and duration of hydroxyurea, or

- Platelet count >450 × 109/L at any dose and duration of hydroxyurea if the above criteria are not met.

• Hydroxyurea Intolerance:

- ANC <1 × 109/L, or platelet count <150 × 109/L, or Hb <10 g/dL at the lowest dose of hydroxyurea to achieve a hematologic remission, defined as platelet count ≤400 × 109/L and WBC <10 × 109/L

- Unacceptable hydroxyurea-related non-hematologic toxicities (eg, pulmonary toxicities such as pneumonitis, fibrosis and allergic alveolitis; hepatotoxicity; hemolytic anemia; vasculitic toxicities; mucocutaneous manifestations; precancerous or cancerous skin lesions; gastrointestinal symptoms; or fever) at a dose of hydroxyurea needed to achieve CHR defined as:

◦ Toxicity that recurred after rechallenge with hydroxyurea

◦ Toxicity requiring permanent discontinuation of hydroxyurea

◦ Toxicity with intensity of Grade 4 (CTCAE v5.0) lasting >1 week

◦ Toxicity with intensity of Grade 3 (CTCAE v5.0) lasting >2 weeks

4. Has an inadequate or loss of response to their most recent prior ET therapy, requiring a change of cytoreductive therapy, as demonstrated by one of the following [National Comprehensive Cancer Network 2022]:

• Intolerance or inadequate response to hydroxyurea, formulations of interferon alfa, or anagrelide

• New thrombosis or disease-related major bleeding (eg, acquired Von Willebrand's disorder)

• Progressive thrombocytosis (platelet count >600 × 109/L)

• Progressive leukocytosis (WBC >11 × 109/L)

• Uncontrolled disease-related symptoms (for study purposes this has been defined as a single symptom score of MFSAF v4.0 ≥4)

• Vasomotor/microvascular disturbances not responsive to aspirin (eg, headaches, chest pain or erythromelalgia)

5. Has a platelet count > 450 × 109/L (450k /μL) assessed up to 72 hours before first dose of study intervention

6. Has an ANC ≥0.75 × 109/L assessed up to 72 hours before first dose of study intervention

7. Has a life expectancy of >52 weeks

8. Participants may have received up to 3 prior lines of therapy including hydroxyurea.

15. Has an ECOG Performance Status of 0 to 1 assessed within 7 days before the start of study intervention.

Principali Criteri Esclusione:

3. Evidence at the time of Screening of increased risk of bleeding, including any of the following:

- History of severe thrombocytopenia or platelet dysfunction unrelated to a myeloproliferative disorder or its treatment.

- Known hereditary bleeding disorder (eg, dysfibrinogenemia, factor IX deficiency, hemophilia, VWD, disseminated intravascular coagulation, fibrinogen deficiency, or other clotting factor deficiency).

- Active or chronic bleeding within 8 weeks before randomization.

- An autoimmune disorder causing bleeding.

4. History of a malignancy, unless potentially curative treatment has been completed with no evidence of malignancy for 2 years