MK3543-006: A Phase v3, randomized, active-comparator-Controlled Clinical Study to Evaluate the Safety and Efficacy fo Bomedemstat (MK-3543/IMG-7289) versus Best Available Therapy (BAT) in participants with Essential Thrombocytemia who have An inadequate response to or are intollerant of hydroxyurea

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Sindromi MIELOPROLIFERATIVE CRONICHE target: Trombocitemia essenziale

Trattamento: Bomedemstat vs BAT (anagrelide o interferone)

Criteri inclusione:

1) Has a diagnosis of ET per WHO 2016 diagnostic criteria for myeloproliferative neoplasms
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
3) Has a history of inadequate response to or intolerance of hydroxyurea per at least 1 of the following criteria:
• 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:
• 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) Participants may have received up to 3 prior lines of therapy including hydroxyurea.
8) Has an ECOG Performance Status of 0 to 1

Criteri esclusione:

1) Evidence at the time of Screening of increased risk of bleeding
2) Use of prohibited medication within 14 days of first dose of study intervention (eg, all hematopoietic growth factors, MAOIs, strong inhibitors and inducers of CYP3A4 or CYP2D6, drugs such as chloroquine whose metabolites are known to inhibit CYP3A4 or CYP2D6, Class 1c antiarrhythmics such as propafenone that are known to cause thrombocytopenias, etc) or expected to require any of these medications during study treatment