Öffentlicher Titel: Eltrombopag bei MDS-Patienten mit Gabe von Azacitidin

Wissenschaftl. Titel: Randomisierte, doppelblinde, placebokontrollierte, multizentrische Studie der Phase III zu Eltrombopag bzw. Placebo in Kombination mit Azacitidin bei Patienten mit IPSS INT-1, IPSS INT-2 und Hochrisiko-MDS (myelodysplastisches Syndrom)

Kurztitel: SUPPORT: StUdie zu EltromboPag bei myelodysPlastischen SyndrOmen bei VerabReichung von AzaciTidin

Studiennummer KN/ELN: LN_MDSIG_2015_581

Studiengruppe: MDS-IG

Studienart: multizentrisch, randomisiert, doppelblind

Studienphase: Phase III

Erkrankung: Myelodysplastisches Syndrom (MDS) - Alle Subtypen

Leukämiestadium: de novo/non-treated

Ziele:
- The primary objective of this study is to determine the effect of eltrombopag versus placebo on the proportion of subjects who are platelet transfusion free during the first 4 cycles of azacitidine therapy.
- Secondary objectives compare the following in subjects treated with eltrombopag/azacitidine versus placebo/azacitidine: Overall survival (OS) Disease Response Hematologic improvement (HI) Platelet and red blood cell (RBC) transfusions Bleeding adverse events (AEs) greater than Grade 3 Bleeding AEs Azacitidine treatment Safety and tolerability Health related quality of life (HRQoL) Medical resource utilization (MRU) Pharmacokinetic
  - Characterize the pharmacokinetics of steady-state eltrombopag in subjects with MDS treated with azacitidine
  - Characterize the effect of eltrombopag on the PK of azacitidine in a subset of subjects.

Einschlusskriterien:
- Age ≥ 18 years. (For subjects in Taiwan, Age ≥ 20 years).
- 2. MDS by World Health Organization (WHO) or French-American-British (FAB) classification.
- Intermediate 1, intermediate 2 or high risk MDS by IPSS. • A bone marrow for the determination of IPSS must be completed during the screening period, or within 3 months prior to randomization. Assessment of bone marrow blasts must be completed by bone marrow slide review.
- At least one platelet count < 75 Gi/L.
- Eastern Cooperative Oncology Group (ECOG) Status 0-2.
- Adequate baseline organ function defined by the criteria below • total bilirubin less than 1.5x the upper limit of normal (ULN) except for Gilbert’s syndrome or cases clearly not indicative of inadequate liver function (i.e. elevation of indirect [haemolytic] bilirubin in the absence of ALT abnormality) • alanine aminotransferase (ALT) less than 2.5xULN • creatinine less than 2.5xULN
- Subjects with a QTc <450msec or <480msec for subjects with bundle branch block. The QTc is the QT interval corrected for heart rate according to Fridericia’s formula (QTcF), machine or manual overread. For subject eligibility and withdrawal, QTcF will be used. For purposes of data analysis, QTcF will be used. The QTc should be based on single or averaged QTc values of triplicate electrocardiograms (ECGs) obtained over a brief recording period
- Subject is able to understand and comply with protocol requirements and instructions.
- Subject has signed and dated informed consent.
- Women must be either of non-child bearing potential, or women with child-bearing potential and men with reproductive potential must be willing to practice acceptable methods of birth control during the study.
Women of childbearing potential must have a negative serum or urine pregnancy test within 7 days of first dose of study treatment and agree to use effective contraception (as defined in Section 7.3.3) during the study and for 3 months following the last dose of study treatment.

Men with a female partner of childbearing potential must have either had a prior vasectomy or agree to use effective contraception (as described in Section 7.3.3) from time of randomization until 16 weeks after the last dose of study treatment.

French subjects: In France, a subject will be eligible for inclusion in this study only if either affiliated to or a beneficiary of a social security category.

Ausschlusskriterien

- Previous treatment with hypomethylating agent or induction chemotherapy for MDS.
- Proliferative type chronic myelomonocytic leukemia with white blood cell count >12 Gi/L at any time during the 28 days before Day 1.
- History of treatment with eltrombopag, romiplostim or other TPO-R agonists.
- Previous allogeneic stem-cell transplantation.
- Known thrombophilic risk factors. Exception: Subjects for whom the potential benefits of participating in the study outweigh the potential risks of thromboembolic events, as determined by the investigator.
- Treatment with an investigational drug within 30 days or 5 half-lives (whichever is longer) preceding the first dose of investigational product (eltrombopag/placebo).
- Active and uncontrolled infections, including hepatitis B or C.
- Human Immunodeficiency Virus (HIV) infection.
- Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to eltrombopag or its excipient, or azacitidine, that contraindicates the subjects’ participation.
- Pregnant or lactating female.
- Any serious and/or unstable pre-existing medical (including any advanced malignancy other than the disease under study), psychiatric disorder, or other conditions that could interfere with subject’s safety, obtaining informed consent or compliance with the study procedures.
- French subjects: the French subject has participated in any study using an investigational drug during the previous 30 days.

Alter

>= 18 Jahre

Status

Geschlossen

Beginn der Rekrutierung

11.03.2015

Fallzahl

350

Studienleiter/in

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KURZPROTOKOLL

SUPPORT: Studie zu EltromboPag bei myelodysPlastischen SyndrOmen bei VerabReichung von AzaciTidin

Sponsoren: Novartis Pharma GmbH

Registrierung in anderen Studienregistern: European Clinical Trials Database - EUDRACT2013-000918-37