SAMENVATTING SHINE, PCI-32765MCL3002

TITEL

Een gerandomiseerd, dubbelblind, placebogecontroleerd fase 3 onderzoek in fase 3 van de Brutons Tyrokinase (BTK) remmer, PCI32765 (Ibrutinib), in combinatie met Bendamustine en Rituximab bij patiënten met pas gediagnosticeerd mantelcellymfoom (≥65 jaar)

DOEL/ ACHTERGROND

Vergelijken doeltreffendheid (verlengen progression free survival) en veiligheid van Ibrutinib in combinatie met Bendamustine en Rituximab.

POPULATIE

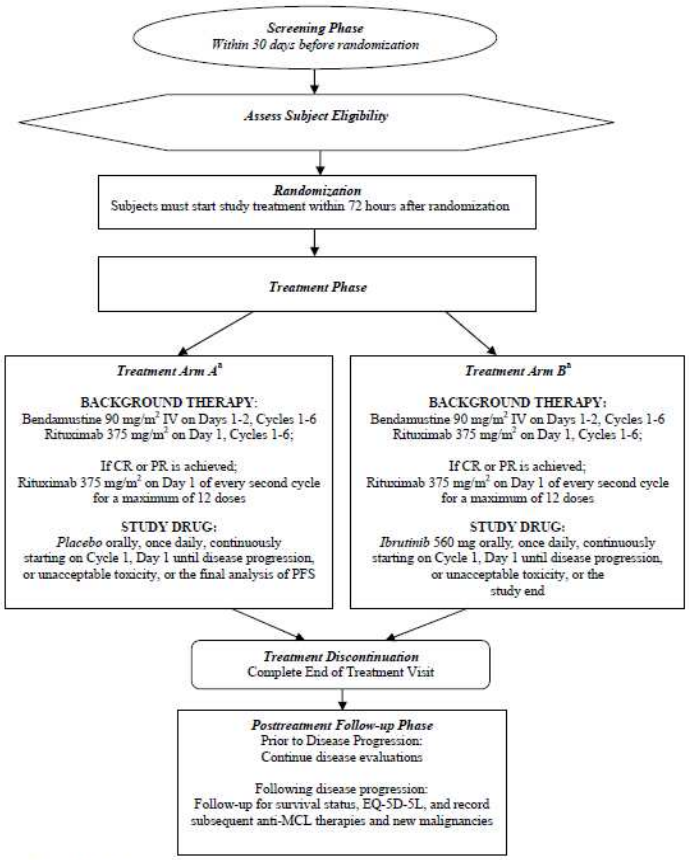
Patiënten ≥65 jaar, met bevestigde diagnose van mantelcellymfoom stadium II, III of IV (AnnArbor-classificatie)

ONDERZOEKSGENEESMIDDEL

Ibrutinib : Brutons tyrosinekinase (BTK)-remmer, PCI-32765
Ibrutinib wordt geleverd als capsule, patiënt neemt dagelijks op ongeveer hetzelfde tijdstip het voorgeschreven aantal capsules in met een glas water. Inname dient minimaal 30 minuten voor of ten minste 2 uren na een maaltijd plaats te vinden.
Meest voorkomende bijwerkingen; diarree, vermoeidheid, misselijkheid, infectie.

STUDIEOPZET/ BEHANDELPLAN

Figure 1: Study Diagram



[a]A cycle is defined as 28 days.

INCLUSIECRITERIA (verkorte weergave)

1. Subject is 65 years of age or older
2. Criterion modified per Amendment INT-1:
    2.1 Diagnosis of MCL must include morphology and expression of either cyclin D1 in association with other relevant markers (eg, CD19, CD20, PAX5, CD5) or evidence of t(11;14) as assessed by cytogenetics, fluorescent in situ hybridization (FISH), or polymerase chain reaction (PCR).
3. Clinical Stage II, III, or IV by Ann Arbor Classification
4. At least 1 measurable site of disease according to Revised Response Criteria for Malignant Lymphoma. The site of disease must be greater than 1.5 cm in the long axis regardless of short axis measurement or greater than 1.0 cm in the short axis regardless of long axis measurement, and clearly measurable in 2 perpendicular dimensions
5. No prior therapies for MCL
6. Eastern Cooperative Oncology Group (ECOG) performance status grade 0 or 1
7. Criterion modified per Amendment INT-1:
    7.1 Hematology values must be within the following limits within 14 days prior to randomization:
    a. Absolute neutrophil count (ANC) □ 1000/mm3 independent of growth factor support
    b. Platelets □100,000/mm3 or □50,000/mm3 if bone marrow involvement independent of transfusion support in either situation
8. Criterion modified per Amendment INT-1:
    8.1 Biochemical values within the following limits within 14 days prior to randomization:
    a. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 3 x upper limit of normal (ULN)
    b. Total bilirubin ≤ 1.5 x ULN unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin
    c. Serum creatinine ≤ 2 x ULN or estimated Glomerular Filtration Rate (Cockroft-Gault10) ≥ 40 mL/min/1.73m2
9. Women of childbearing potential and men who are sexually active must be practicing a highly effective method of birth control during and after the study. Men must agree to not donate sperm during and after the study.
10. Women of childbearing potential must have a negative serum (beta-human chorionic gonadotropin [□-hCG]) or urine pregnancy test at Screening. Women who are pregnant or breastfeeding are ineligible for this study.

EXCLUSIECRITERIA (verkorte weergave)

1. Major surgery within 4 weeks of randomization.
2. Known central nervous system lymphoma.
3. Diagnosed or treated for malignancy other than MCL, except:
    a. Malignancy treated with curative intent and with no known active disease present for ≥ 3 years before randomization
    b. Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.
    c. Adequately treated cervical carcinoma in situ without evidence of disease.
4. Subjects for whom the goal of therapy is tumor debulking prior to stem cell transplant.
5. History of stroke or intracranial hemorrhage within 6 months prior to randomization.
6. Requires anticoagulation with warfarin or equivalent vitamin K antagonists (eg, phenprocoumon).
7. Criterion modified per Amendment INT-1.
    7.1 Requires treatment with strong CYP3A inhibitors:
8. Clinically significant cardiovascular disease
9. Vaccinated with live, attenuated vaccines within 4 weeks of randomization.
10. Criterion modified per Amendment INT-1
    10.1 Known history of human immunodeficiency virus (HIV) or active Hepatitis C Virus or active Hepatitis B Virus infection or any uncontrolled active systemic infection requiring intravenous (IV) antibiotics
11. Any life-threatening illness, medical condition, or organ system dysfunction which, in the investigator's opinion, could compromise the subject's safety, interfere with the absorption or metabolism of ibrutinib capsules, or put the study outcomes at undue risk.