SAMENVATTING HOVON 133

TITEL

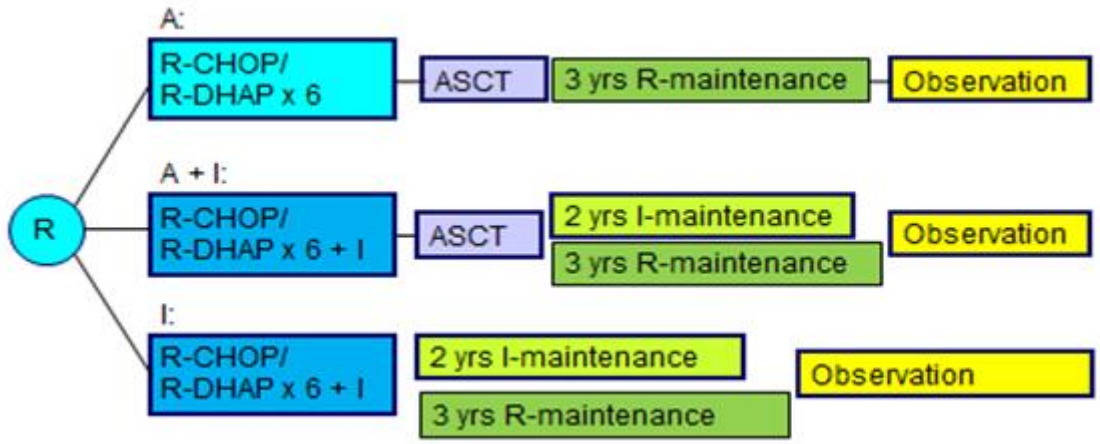
TRIANGLE

autologous Transplantation after a Rituximab/Ibrutinib/Ara-c containing iNduction in Generalized mantle cell Lymphoma – a randomized European mcl network trial

INDICATIE

Untreated patients (≥ 18 and ≤ 65 years) with mantle-cell lymphoma (MCL)

SCHEMA



INCLUSIE CRITERIA

All patients must meet the following criteria:

- Histologically confirmed diagnosis of MCL according to WHO classification
- suitable for high-dose treatment including high-dose Ara-C
- Stage II-IV (Ann Arbor)
- Age ≥ 18 years and ≤ 65 years
- Previously untreated MCL
- At least 1 measurable lesion; in case of bone marrow infiltration only, bone marrow aspiration and biopsy is mandatory for all staging evaluations.
- ECOG/WHO performance status ≤ 2
- The following laboratory values at screening (unless related to MCL):
  - Absolute neutrophil count (ANC) ≥1000 cells/μL
  - Platelets ≥100,000 cells/μL
  - Transaminases (AST and ALT) ≤3 x upper limit of normal (ULN)
  - Total bilirubin □2 x ULN unless due to known Morbus Meulengracht [Gilbert-Meulengracht-Syndrome])
  - Creatinine ≤2 mg/dL or calculated creatinine clearance ≥ 50 mL/min
- Written informed consent form according to ICH/EU GCP and national regulations
- Sexually active men and women of child-bearing potential must agree to use one of the highly effective contraceptive methods (combined oral contraceptives using two hormones, contraceptive implants, injectables, , intrauterine devices, sterilized partner)

together with one of the barrier methods (latex condoms, diaphragms, contraceptive caps) while on study; this should be maintained for 90 days after the last dose of study drug

EXCLUSIE CRITERIA

Any potential subject who meets any of the following criteria will be excluded from participating in the study.

- Major surgery within 4 weeks prior to randomization.
- Requires anticoagulation with warfarin or equivalent vitamin K antagonists (e.g. phenprocoumon).
- History of stroke or intracranial hemorrhage within 6 months prior to randomization.
- Requires treatment with strong CYP3A4/5 inhibitors.
- 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.
- Vaccinated with live, attenuated vaccines within 4 weeks prior to randomization.
- Known CNS involvement of MCL
- Clinically significant hypersensitivity (e.g., anaphylactic or anaphylactoid reactions to the compound of ibrutinib itself or to the excipients in its formulation)
- Known anti-murine antibody (HAMA) reactivity or known hypersensitivity to murine antibodies
- Previous lymphoma therapy with radiation, cytostatic drugs, anti-CD20 antibody or interferon except prephase therapy outlined in this trial protocol
- Serious concomitant disease interfering with a regular therapy according to the study protocol:
    - Cardiac (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 or LVEF below LLN)
    - Pulmonary (chronic lung disease with hypoxemia)
    - Endocrinological (severe, not sufficiently controlled diabetes mellitus)
    - Renal insufficiency (unless caused by the lymphoma): creatinine > 2x normal value and/or creatinine clearance < 50 ml/min)
    - Impairment of liver function (unless caused by the lymphoma): transaminases > 3x normal or bilirubin > 2,0 mg/dl unless due to Morbus Meulengracht (Gilbert-Meulengracht-Syndrome)
- Patients with unresolved hepatitis B or C infection or known HIV positive infection (mandatory test)
- Prior organ, bone marrow or peripheral blood stem cell transplantation
- Concomitant or previous malignancies within the last 3 years other than basal cell skin cancer or in situ uterine cervix cancer
- Pregnancy or lactation
- Any psychological, familiar, sociological, or geographical condition potentially hampering compliance with the study protocol and follow up schedule
- Subjects not able to give consent
- Subjects without legal capacity who are unable to understand the nature, scope, significance and consequences of this clinical trial
- Participation in another clinical trial within 30 days before randomization in this study.