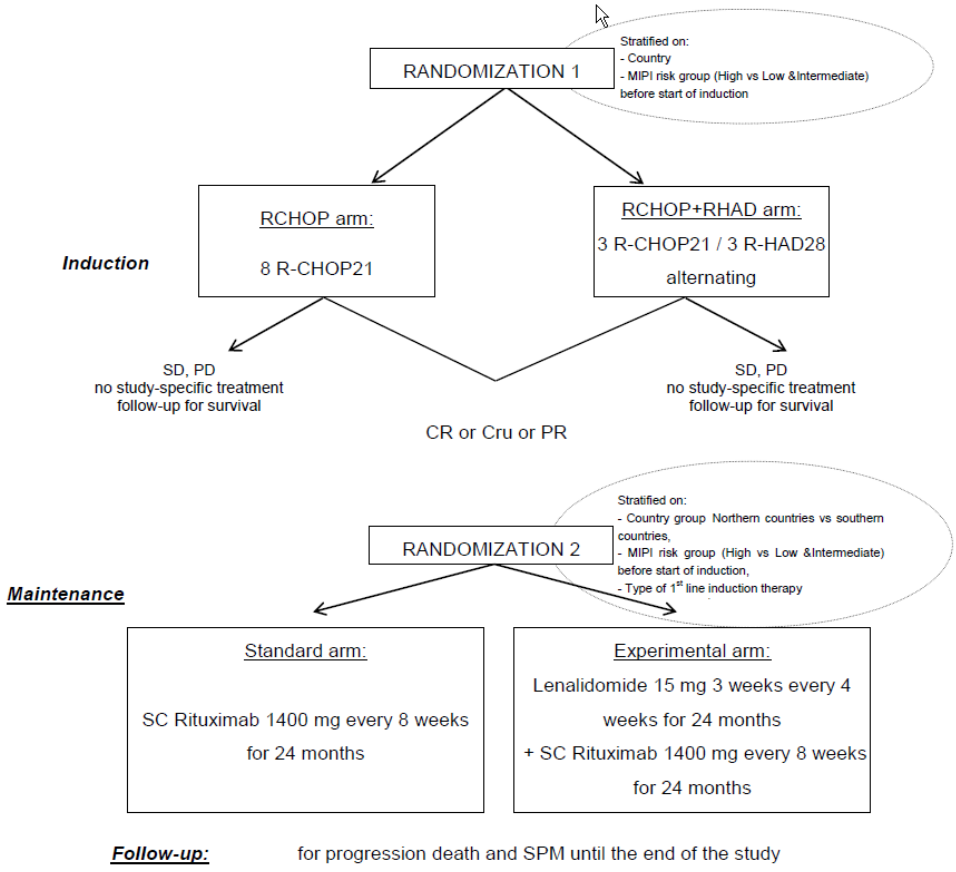
SAMENVATTING HOVON 119

Efficacy of alternating immunochemotherapy consisting of R-CHOP + R-HAD *versus* R-CHOP alone, followed by maintenance therapy consisting of additional lenalidomide with rituximab *versus* rituximab alone for older patients with mantle cell lymphoma

INDICATION

Untreated patients with Mantelcel lymfoom ≥ 60 years and ineligible for autologous transplant



Key Inclusion Criteria

• signed informed consent form
• Biopsy-proven mantle cell lymphoma according to WHO classification, including evidence of cyclin D1 overexpression or the translocation t(11;14)(q13;q32),
• ≥ 60 years of age and ineligible for autologous transplant
• Ann Arbor stage II-IV

• previously untreated (except for patients randomized directly for maintenance treatment who will receive 8 RCHOP before registration in the trial)
• ECOG performance status ≤ 2

Male subjects must:
- agree to use a condom during sexual contact with a woman of childbearing potential, even if they have had a vasectomy, throughout lenalidomide therapy
- agree to not donate semen during lenalidomide therapy.
• All subjects must:
- have an understanding that the lenalidomide could have a potential teratogenic risk.
- agree to abstain from donating blood while taking lenalidomide therapy
- agree not to share study medication with another person.
- be counselled about pregnancy precautions and risks of foetal exposure.

Key Exclusion Criteria
• Female of child-bearing potential (without natural menopause for at least 24 consecutive months, a hysterectomy or bilateral oophorectomy)
• Any of the following laboratory abnormalities, if not related to lymphoma:
- Absolute neutrophils count (ANC) <1,000 /mm^3 (1.0 x 10^9/L) if not result of a BM infiltration.
- Platelet counts < 75,000/mm^3 (75 x 10^9/L) if not result of a BM infiltration.
- Serum aspartate transaminase (AST/SGOT) or alanine transaminase (ALT/SGPT) >3.0 x upper limit of normal (ULN).
- Serum total bilirubin > 1.5 ULN (except if due to Gilbert's syndrome)
• Calculated creatinine clearance (Cockcroft-Gault formula or MDRD) < 30 mL /min.
• Central nervous system involvement by lymphoma
• Contraindication for medicamentous DVT prophylaxis for patients at high risk for DVT
• Prior history of malignancies other than MCL unless the subject has been free of the disease for ≥ 5 years (Exceptions: Basal or squamous cell carcinoma of the skin, Carcinoma in situ of the cervix or of the breast, Incidental histologic finding of prostate cancer (TNM stage of T1a or T1b).
• Any serious medical condition, laboratory abnormality, or psychiatric illness that would prevent the patient to receive the study medication as planned.
• Poor cardiac function (LVEF < 50%) on echocardiography
• Seropositivity for human immunodeficiency virus (HIV, mandatory test)
Seropositivity for hepatitis C virus (HCV, mandatory test),
Active viral infection with hepatitis B virus (HBV, mandatory test):
- HBsAg positive
- HBsAg negative, anti-HBs positive and anti-HBc positive
• Uncontrolled illness including, but not limited to:
- Active infection requiring parenteral antibiotics
- Uncontrolled diabetes mellitus
- Chronic symptomatic congestive heart failure (Class NYHA III or IV).
- Unstable angina pectoris, angioplasty, stenting, or myocardial infarction within 6 months
- Clinically significant cardiac arrhythmia that is symptomatic or requires treatment, or asymptomatic sustained ventricular tachycardia.
• Prior ≥ Grade 3 allergic hypersensitivity to thalidomide.
• Prior ≥ Grade 3 rash or any desquamating (blistering) rash while taking thalidomide.
• Subjects with ≥ Grade 2 neuropathy.
• Known anti-murine antibody (HAMA) reactivity or known hypersensitivity to murine antibodie
• Prior use of lenalidomide.

•Participation in another clinical trial within three weeks before randomization in this study.

Additional criteria for randomization in maintenance phase :

Inclusion criteria

- CR, CRu or PR after induction treatment, determined as per Cheson 1999 criteria by investigator
- During the run-in period of 6 months starting from the date of the first patient randomized in the trial: in case of direct randomization into maintenance phase, patient must have been treated in first line by 6-8 cycles of R-CHOP.

Exclusion criteria

- SD or PD after induction treatment determined as per Cheson 1999 criteria assessed by investigator.
- Patients who had not received at least 6 cycles of R-CHOP21 or 2 cycles of R-CHOP21 / 2 cycles of R-HAD28 (alternating)
- Patients with serious underlying medical conditions, which could impair the ability to receive maintenance treatment
- Calculated creatinine clearance (Cockcroft-Gault formula or MDRD) of < 30 mL /min at screening for maintenance.
- ANC < 1,000 cells/mm^3 (1.0 X 10^9/L) at screening for maintenance;
- Platelet count < 50,000 cells/mm^3 (50 X 10^9/L) at screening for maintenance.

Benefit/Risk imbalance of treatment program