Summary HOVON 109

Title

Efficacy and safety of first-line therapy with chlorambucil, rituximab and lenalidomide (Revlimid®) (CR_2) in elderly patients and young frail patients with advanced Chronic Lymphocytic Leukemia (CLL): a phase I/II trial

Background

For elderly and young FCR unfit patients, response rates and duration of chlorambucil monotherapy is limited. Addition of rituximab improves ORR, but not CR rate. Lenalidomide is active in CLL mainly by interaction in crosstalk between the microenvironment and leukemic cells.
Hypothesis: Addition of lenalidomide to chlorambucil and rituximab will result in better response rates with acceptable toxicity.

Population

Elderly (65 years – 80 years, inclusive) patients and patients 18 - 64 years, inclusive, with CIRS ≥7 with advanced previously untreated Chronic Lymphocytic Leukemia

Inclusion Criteria

- Diagnosis of CLL without prior treatment;
- Patients with symptomatic (according to IWCLL guidelines56) Binet stage A / Rai stage 0 or Binet stage B or C / Rai I, II, III or IV (appendix A);
- Age 65 - 80 years, inclusive, at the time of signing the informed consent form, or age 18 – 64, inclusive, and CIRS ≥ 7 57 (appendix E);
- Able to adhere to the study visit schedule and other protocol requirements;
- WHO performance status of ≤ 2;
- Laboratory test results within these ranges: absolute neutrophil count ≥ 1.0 x 109/l, platelet count ≥ 30 x 109/l, creatinine clearance ≥ 60 ml/min, total bilirubin ≤ 25 µmol/L, AST & ALT ≤ 2 x ULN;
- Females of childbearing potential must have a negative serum or urine pregnancy test within 10 - 14 days prior to and again within 24 hours of starting lenalidomide;
- Patients who are willing and capable to use adequate contraception during the therapy (all men, all women of childbearing potential). Patients must be able to adhere to the requirements of the Lenalidomide Pregnancy Prevention Risk Management Plan;
- Written informed consent.

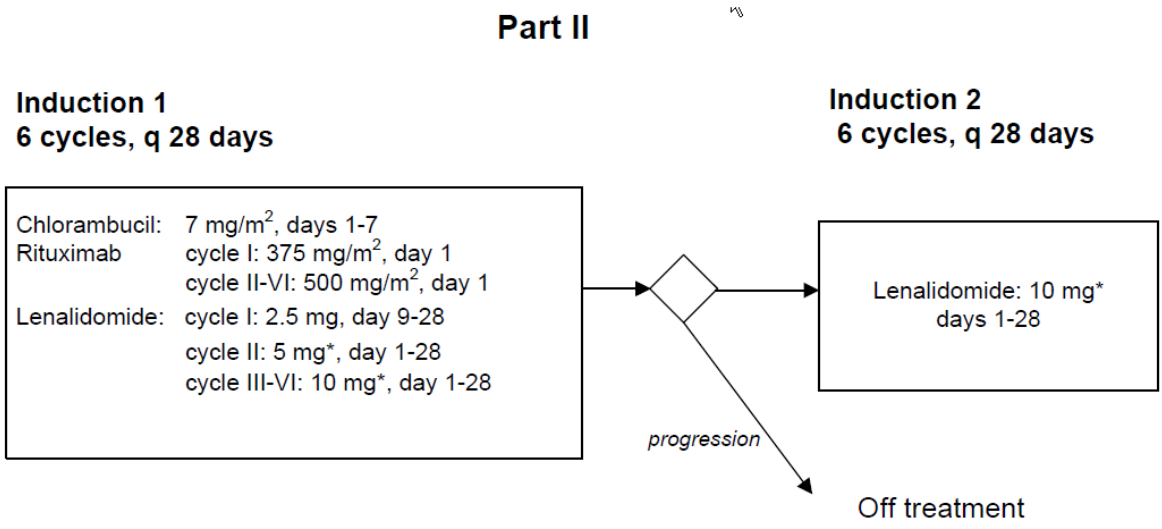
Exclusion Criteria

- Patients that are unable or unwilling to adhere to the requirements of the Lenalidomide Pregnancy Prevention Risk Management Plan;
- Intolerance of exogenous protein administration;

- Hepatitis B Ag positive, Hepatitis C positive and/or HIV positive patients;
- Patients with uncontrolled Autoimmune Hemolytic Anemia (AIHA) or autoimmune thrombocytopenia (ITP);
- Active fungal, bacterial, and/or viral infection;
- Pregnant or breast-feeding females (lactating females must agree not to breast feed while taking lenalidomide);
- Use of any other experimental drug or therapy within 28 days of baseline;
- Known hypersensitivity and/or serious adverse reactions to lenalidomide or similar drugs;
- Any prior use of lenalidomide;
- Concurrent use of other anti-cancer agents or treatments;
- Uncontrolled hyperthyroidism or hypothyroidism;
- Patients with history of idiopathic deep venous thrombus and/or pulmonary embolism within last three years;
- Neuropathy ≥ grade 2;
- History of active malignancy during the past 5 years with the exception of basal carcinoma of the skin; squamous cell carcinoma of the skin, carcinoma in situ of the cervix, carcinoma in situ of the breast, prostate cancer (TNM stage of T1a or T1b)
- Current inclusion in other clinical trials;
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule.

Scheme of study

Since 7NOV2013 fase II is open for inclusion of new patients.



* Dose reduction of Lenalidomide in case of toxicity according to chapter 9.2.2.