Département d'oncologie
Plateformes du DO
Bâtiment Maternité PAV1
Avenue Pierre Decker 2
CH-1011 Lausanne

Indication	**Lymphomes diffus à grandes cellules B,** patients âgés de 60-80 ans, après réponse par chimiothérapie initiale
Title	Double blind randomized phase III study of lenalidomide (REVLIMID®) maintenance versus placebo in responding elderly patients with DLBCL and treated with R-CHOP in first line
Protocol ID	**REMARC**
Phase	Phase III
Sponsor	GELA (Groupe d' Etude des Lymphomes Adultes)
Local Principal Investigator	Dr Grégoire Berthod
Primary Objective	The primary objective is to determine the benefit estimated by the progression free survival associated with lenalidomide maintenance compared to placebo in responding patients treated in first line with R-CHOP for diffuse large B-cell lymphoma.
Inclusion/exclusion criteria	**Inclusion Criteria include the following :** **For patients registered at time of initial diagnosis:** • **Initial diagnosis of histologically confirmed CD20+ diffuse large B-cell Lymphoma** based on the World Health Organization 2008 classification Lymphoma → FL grade 3b is allowed →De novo transformed FL is allowed • Patients with some small cell infiltration in bone marrow (suspicion of de novo transformed indolent lymphoma) may be included • **Previously untreated with chemo- or radiotherapy** **For patients registered after response evaluation to first line treatment with R-CHOP:** • **Diagnosis of histologically confirmed CD20+ diffuse large B-cell Lymphoma** based on the World Health Organization 2008 classification Lymphoma ➔ FL grade 3b is allowed ➔ De novo transformed FL is allowed • **Have reached a CR or PR (Cheson 2007) after first line treatment with at least 6 cycles of R-CHOP 14 or up to 8 cycles of R-CHOP 21** • **Previously untreated with radiotherapy** For all patients: • Aged from 60 to 80 years at time of initial diagnosis • Eastern Cooperative Oncology Group [ECOG] performance status 0, 1 or 2 • Ann Arbor stages II-IV at time of initial diagnosis • aaIPI > 1 at time of initial diagnosis • Minimum life expectancy of 3 months • Voluntary signed informed consent before performance of any

study related procedure not part of normal medical care, with the understanding that consent may be withdrawn by the subject at any time without prejudice to future medical care

- The following laboratory values at screening
  - ➔ Absolute neutrophil count (ANC) □□1 000.10^6/L and Platelets □60 000.10^6/L, unless these abnormalities are related to bone marrow infiltration.
  - ➔ Aspartate transaminase (AST) □5 x ULN; Alanine transaminase (ALT) □□5 x ULN; Total bilirubin □1.5 x ULN; > Creatinine clearance > 30 ml/min (as calculated by the Cockcroft-Gault formula)
- Females of childbearing potential (FCBP)† must:
  →Have a negative medically supervised pregnancy test prior to starting of study therapy. She must agree to ongoing pregnancy testing during the course of the study, and after end of study therapy. This applies even if the patient practices complete and continued sexual abstinence.
  →Either commit to continued abstinence from heterosexual intercourse (which must be reviewed on a monthly basis) or agree to use, and be able to comply with, effective contraception without interruption, 28 days prior to starting study drug, during the study therapy (including dose interruptions), and for 28 days after discontinuation of study therapy.
- Male patients must:
  →Agree to use a condom during sexual contact with a FCBP, even if they have had a vasectomy, throughout study drug therapy, during any dose interruption and after cessation of study therapy.
  →Agree to not donate semen or sperm during study drug therapy and for a period after end of study drug therapy.
- All patients must:
  → Have an understanding that the study drug could have a potential teratogenic risk.
  → Agree to abstain from donating blood while taking study drug therapy and following discontinuation of study drug therapy.
  → Agree not to share study medication with another person.
  → Be counseled about pregnancy precautions and risks of fetal exposure.

Exclusion Criteria include the following :

For all patients:

- **Any other type of lymphoma.**
- **Any previous history of low grade lymphoma**
- **Central nervous system or meningeal involvement by lymphoma**
- **Contraindication to any drug contained in the chemotherapy regimen**. *For example: "cardiac contraindication to anthracyclines (alteration of Left Ventricular Function defined by LVEF<50%) neurological contra-indication to vincristine (peripheral neuropathy of WHO grade ≥ 2)*.
- **Myocardial infarction during last 3 months or unstable**

	coronary disease or uncontrolled chronic symptomatic congestive heart insufficiency NYHA III-IV • **Uncontrolled hypertension** • **Uncontrolled diabetes mellitus as defined by the investigator** • **Active systemic infection requiring treatment.** • **Previously known HIV positive serology** • **Active hepatitis B or C** • **Prior history of malignancies other than lymphoma within 3 years** (except for complete resection of basal cell carcinoma, squamous cell carcinoma of the skin, or in situ malignancy. Patients previously diagnosed with prostate cancer are eligible if (1) their disease was T1-T2a, N0, M0, with a Gleason score □7, and a prostate specific antigen (PSA) □10 ng/mL prior to initial therapy, (2) they had definitive curative therapy (ie, prostatectomy or radiotherapy) □2 years before Day 1 of Cycle 1, and (3) at a minimum 2 years following therapy they had no clinical evidence of prostate cancer, and their PSA was undetectable if they underwent prostatectomy or <1 ng/mL if they did not undergo prostatectomy. • **Serious medical or psychiatric illness** likely to interfere with participation in this clinical study.