SAMENVATTING LYMRIT-37-01 (PARADIGME)

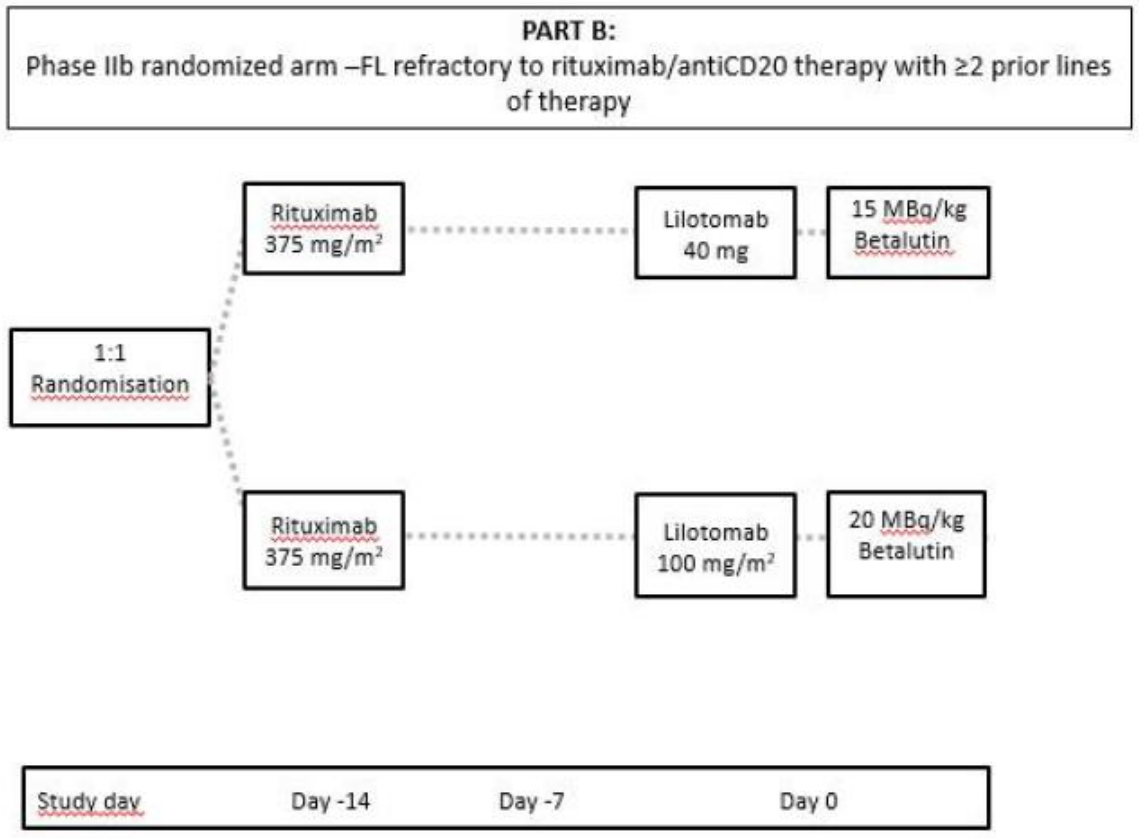
TITEL

A phase I/II study of lutetium (177Lu)-lilotomab satetraxetan (Betalutin®) antibodyradionuclide-conjugate for treatment of relapsed non-Hodgkin lymphoma.

INDICATIE

Adult patients with relapsed, rituximab/anti-CD20 refractory FL who have received ≥2 prior lines of therapy.

SCHEMA



INCLUSIE CRITERIA

1. Histologically confirmed (by WHO classification) relapsed non-Hodgkin B-cell FL (follicular grade I-IIIA).
2. Male or female aged ≥ 18 years.

3. Received at least 2 prior anti-neoplastic or immunotherapy-based regimens (maintenance therapy following a CR/PR is not considered to be a separate line of therapy).
4. Prior therapy must include a rituximab/anti-CD20 agent and an alkylating agent. Prior exposure to other systemic anti-neoplastic agents (including idelalisib or other PI3K inhibitors, etc.) is also allowed.
5. Patients must be refractory to any previous regimen containing rituximab or an anti-CD20 agent, defined as:
    a. no response (no CR or PR) during therapy, or
    b. a response (CR/PR) lasting less than 6 months after the completion of a regimen including rituximab/anti-CD20 therapy (including occurrence of progressive disease (PD) during rituximab/anti-CD20 maintenance therapy, or within 6 months of completion of maintenance therapy).
6. WHO performance status of 0-2.
7. Life expectancy of ≥ 3 months.
8. Bone marrow tumour infiltration < 25% (in biopsy taken from a site not previously irradiated).
9. Measurable disease by CT or MRI: longest diameter (LDi) > 1.5 cm for nodal lesion, LDi > 1.0 cm for extra nodal lesion within 28 days prior to start of treatment.
10. ANC ≥ 1.5 x 10^9/L.
11. Platelet count ≥ 150 x 109/L.
12. Haemoglobin ≥ 9.0 g/dL.
13. Total bilirubin ≤ 1.5 x upper limit of normal (ULN) (except patients with documented Gilbert's syndrome [< 3.0 mg/dL]).
14. Liver enzymes: Aspartate transaminase (AST); Alanine transaminase (ALT) or ALP ≤ 2.5 x ULN (or ≤ 5.0 x ULN with liver involvement by primary disease).
15. Adequate renal function as demonstrated by a serum creatinine < 1.5 x ULN.
16. Women of childbearing potential must:
    a. understand that the study medication is expected to have teratogenic risk.
    b. have a negative serum beta human-chorionic gonadotropin (ß-HCG) pregnancy test at screening.
    c. commit to continued abstinence from heterosexual intercourse (excluding periodic abstinence or the withdrawal method) or begin a highly effective method of birth control with a Pearl-Index < 1%. without interruption from 4 weeks before starting study medication, throughout study medication therapy and for 12 months after end of study medication therapy, even if she has amenorrhoea. Apart from abstinence, highly effective methods of birth control are:
        I. Combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal).
        II. Progestogen-only hormonal contraception associated with inhibition of ovulation. (oral, injectable, implantable)
        III. Intrauterine device (IUD).
        IV. Intrauterine hormone-releasing system (IUS).
        V. Bilateral tubal occlusion.
        VI. Vasectomised partner.
17. Male patients must agree to use condoms during intercourse throughout study medication therapy and the following 12 months.
18. The patient is willing and able to comply with the protocol, and agrees to return to the hospital for follow-up visits and examination.

19. The patient has been fully informed about the study and has signed the informed consent form.
20. Negative HAMA test at screening.
21. Negative test at screening for Hepatitis B (negative HBsAG and anti-HBC), Hepatitis C and HIV.

EXCLUSIE CRITERIA

1. Prior hematopoietic allogenic stem cell transplantation.
2. Prior autologous stem cell transplantation.
3. Evidence of histological transformation from FL to DLBCL at time of screening.
4. Previous total body irradiation.
5. Prior anti-lymphoma therapy (chemotherapy, immunotherapy or other investigational agent) within 4 weeks prior to start of study treatment (corticosteroid treatment at doses of ≤ 20 mg/day, topical or inhaled corticosteroids, G-CSF or GM-CSF are permitted up to 2 weeks prior to start of study treatment). Note: excludes pre-treatment with rituximab as part of this study.
6. Patients who are receiving any other investigational medicinal products.
7. Patients with known or suspected CNS involvement of lymphoma.
8. History of a previous treated cancer except for the following:
    a. adequately treated local basal cell or squamous cell carcinoma of the skin.
    b. cervical carcinoma in situ.
    c. superficial bladder cancer.
    d. localised prostate cancer undergoing surveillance or surgery.
    e. localised breast cancer treated with surgery and radiotherapy but not including systemic chemotherapy.
    f. other adequately treated Stage 1 or 2 cancer currently in CR.
9. Pregnant or breastfeeding women.
10. Exposure to another CD37 targeting drug.
11. A known hypersensitivity to rituximab, lilotomab, Betalutin or murine proteins or any excipient used in rituximab, lilotomab, or Betalutin.
12. Has received a live-attenuated vaccine within 30 days prior to enrolment.
13. Evidence of severe or uncontrolled systemic diseases:
    a. Uncontrolled infection including evidence of ongoing systemic bacterial, fungal, or viral infection (excluding viral upper respiratory tract infections) at the time of initiation of study treatment.
    b. Pulmonary conditions e.g. unstable or uncompensated respiratory disease.
    c. Hepatic, renal, neurological, or metabolic conditions - which in the opinion of the investigator would compromise the protocol objectives.
    d. Psychiatric conditions e.g. patients unlikely to comply with the protocol, e.g. mental condition rendering the patient unable to understand the nature, scope, and possible consequences of participating in the study.
    e. History of erythema multiforme, toxic epidermal necrolysis, or Stevens-Johnson syndrome.
    f. Cardiac conditions, including:
        I. history of acute coronary syndromes (including unstable angina).
        II. class II, III, or IV heart failure as defined by the NYHA functional classification system.
        III. known uncontrolled arrhythmias (except sinus arrhythmia) in the past 24 weeks.