

In en exclusie criteria Genmab

fase 1 first in man studie GEN3013-01 (epcoritamab)

Expansion phase (stage 1)

Inclusion Criteria

Each potential patient must satisfy all of the following criteria to be enrolled in the trial.

1. Patient must be 18 years of age or older
2. Documented mature CD20 positive B-cell neoplasm according to WHO classification Swerdlow et al., 2016 (Swerdlow et al., 2016) or WHO classification 2008, depending on time of diagnosis
 - Diffuse large B-cell lymphoma – de novo or transformed from all types indolent lymphoma
 - Follicular lymphoma grade 1-3A
3. DLBCL: relapsed, progressive and/or refractory disease (Cheson et al., 2007). Previously treated with at least 2 therapies including:
 - an anti-CD20 monoclonal antibody-containing chemotherapy combination regimen
 - either failed prior autologous hematopoietic stem cell transplantation (HSCT), or ineligible for autologous HSCT due to age or comorbidities
4. FL grade 1-3A: relapsed, progressive and/or refractory disease (Cheson et al., 2007).
 - previously treated with at least 2 prior lines of therapy including at least 1 prior anti CD20 monoclonal antibody-containing chemotherapy combination
 - previously treated with an alkylating agent or lenalidomide
 - relapsed or refractory to the last prior line therapy. Previous lymphoma therapy is defined as 1 of the following: At least 2 months of single-agent therapy, at least 2 consecutive cycles of combination therapy, autologous HSCT, immunomodulatory therapy, or radioimmunotherapy

Patients with follicular lymphoma must have a need for treatment initiation based on symptoms and/or disease burden
5. CD20 positivity at most recent (previous or current) representative tumor biopsy based on the pathology report
6. Scanning with measurable disease
 - At least **1 measurable site of disease** based on computed tomography (CT) or magnetic resonance imaging (MRI) with involvement of 2 or more clearly demarcated lesions/nodes with a long axis >1.5 cm and short axis >1.0 cm or 1 clearly demarcated lesion/node with a long axis >2.0 cm and short axis ≥1.0 cm AND baseline FDG positron emission tomography (PET) scans must demonstrate positive lesion compatible with CT (or MRI) defined anatomical tumor sites
7. ECOG performance status 0 or 1
8. Lymphocyte counts < 5 x 10⁹/L
9. Platelet counts ≥ 75 x 10⁹/L (bone marrow infiltration or splenomegaly ≥ 50 x 10⁹/L)
10. Hemoglobin level ≥ 9 g/dL (≥ 5.6 mmol/L) with or without transfusion
11. Absolute neutrophil counts ≥ 1.0 x 10⁹/L; growth factor support allowed in case of bone marrow involvement
12. Patient must meet the following criteria regarding time since **previous neoplastic agent(s)**
 - at least 4 weeks from last dose of non-investigational chemotherapy

- at least 2 weeks or 5 half-lives from last dose of other non-investigational antineoplastic agents, whichever is longer
- at least 5 half-lives from last dose of investigational agents except for CAR-T cell therapy (described in exclusion criterion #11)

13. Resolution of toxicities from prior therapy to a grade that does not contraindicate trial participation in the opinion of the investigator

14. If receiving **glucocorticoid treatment at screening**, treatment must be tapered down and administered with a maximum of 25 mg daily in the last 14 days before the first dose of GEN3013

15. Before the first dose of IMP, during the trial and for 12 months after last administration of GEN3013, a woman must be either

a. Not of childbearing potential*: premenarchal; postmenopausal (> 45 years of age with amenorrhea for at least 12 months or any age with amenorrhea for at least 6 months and a serum follicle stimulating hormone [FSH] level > 40 IU/L or mIU/mL); permanently sterilized (*e.g.* bilateral tubal occlusion [which includes tubal ligation procedures as consistent with local regulations], hysterectomy, bilateral salpingectomy, bilateral oophorectomy); or otherwise be incapable of pregnancy

b. Of childbearing potential and practicing a highly effective method of birth control (as defined by the EU Clinical Trial Facilitation Group) consistent with local regulations regarding the use of birth control methods for patients participating in clinical trials: *e.g.* established use of oral, injected or implanted combined (estradiol and progesterone containing) hormonal contraception; placement of an intrauterine device (IUD) or intrauterine system (IUS); male partner sterilization (the vasectomized partner should be the sole partner for that patient); true abstinence (when this is in line with the preferred and usual lifestyle of the patient)

*If the childbearing potential changes after start of the trial (*e.g.* woman who is not heterosexually

active becomes active, premenarchal woman experiences menarche) a woman must begin a highly effective method of birth control, as described under 15b.

16. A man who is sexually active with a woman of childbearing potential must agree to use a barrier method of birth control (that is the use of condom) during the trial and for 12 months after receiving the last dose of IMP

17. Women must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the trial and for 12 months after receiving the last dose of IMP. Men must also not donate sperm during the trial and for 12 months after receiving the last dose of IMP

18. The patient understands the purpose of the trial and procedures required for the trial and is capable of giving signed informed consent as which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in this protocol

19. Each patient must sign a separate informed consent form if he or she agrees to provide sample(s) for evaluation of DNA. Refusal to give consent for the optional DNA research samples does not exclude a patient from participation in the trial

Exclusion Criteria

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

1. Primary central nervous system (CNS) lymphoma or known CNS involvement by lymphoma
2. Prior history of malignancy other than NHL, except basal cell or squamous cell carcinoma of the skin or carcinoma in situ of the uterine cervix or breast with curative therapy. The patient must have been free of disease and without treatment for at least 3 years
3. AST, and/or ALT > 3 x upper limit of normal
4. Total bilirubin > 1.5 x upper limit of normal
5. Creatinine clearance < 45 mL/min (see [Appendix 1](#))
6. Known clinically significant cardiac disease, including:
 - a. Onset of unstable angina pectoris within 6 months of signing ICF
 - b. Acute myocardial infarction within 6 months of signing ICF
 - c. Congestive heart failure (grade III or IV as classified by the New York Heart Association (see [Appendix 2](#)) and/or known decrease ejection fraction of < 45%
7. Chronic ongoing infectious diseases (except hepatitis B or hepatitis C) requiring treatment (excluding prophylactic treatment) at the time of enrolment or within the previous 2 weeks prior to the first dose of GEN3013
8. Confirmed history or current autoimmune disease or other diseases resulting in permanent immunosuppression or requiring permanent immunosuppressive therapy
9. Seizure disorder requiring therapy (such as steroids or anti-epileptics)
10. Any prior therapy with a compound targeting CD3
11. Eligible for curative salvage therapy with high dose therapy followed by stem cell rescue
12. Previous allogeneic stem cell transplant
13. Active hepatitis B or hepatitis C. If laboratory evidence for a chronic infection with hepatitis B close monitoring and prophylactic therapy is required (see [Section 6.5.1.3](#))
14. Known human immunodeficiency virus (HIV) infection
15. Exposed to live or live attenuated vaccine within 4 weeks prior to signing ICF
16. Pregnancy or breast feeding
17. Patient has any condition for which, in the opinion of the investigator, participation would not be in the best interest of the patient (*e.g.* compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments