In en exclusie criteria Genmab

fase 1 first in man studie GEN3013

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 B-cell neoplasm according to WHO classification Swerdlow et al., 2016 (Swerdlow et al., 2016) or WHO classification 2008, depending on time of diagnosis
a. Diffuse large B-cell lymphoma – de novo or transformed
b. High-grade B-cell lymphoma (Swerdlow et al., 2016)
c. Primary mediastinal large B-cell lymphoma
d. Follicular lymphoma
e. Mantle cell lymphoma
f. Small lymphocytic lymphoma
g. Marginal zone lymphoma (nodal, extranodal or mucosa associated)
3. Relapsed, progressive and/or refractory disease (Cheson et al., 2007) following treatment with an anti-CD20 monoclonal antibody (*e.g.* rituximab) potentially in combination with chemotherapy and/or relapsed after autologous stem cell rescue
a. Patients must have exhausted or are ineligible for all standard therapeutic options
b. Patients with indolent lymphoma (follicular, marginal zone or small lymphocytic lymphoma) must have a need for treatment initiation based on symptoms and/or disease burden
4. CD20 positivity at most recent (previous or current) representative tumor biopsy based on the pathology report
5. Relapsed, progressive or refractory disease and ineligible for or have exhausted standard therapeutic options that are expected to prolong survival
6. Scanning
a. For dose-escalation part: computer 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
b. For expansion part: CT (or 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, 1 or 2 (see Appendix 5)
8. Lymphocyte counts < 5 x 109/L

9. Platelet counts ≥ 75 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. At least 4 weeks from last dose of unconjugated anti-CD20 targeting therapy till first dose of GEN3013
13. At least 12 weeks from last dose of radio-conjugated or toxin-conjugated compound till first dose of GEN3013
14. Resolution of toxicities from prior therapy to a grade that does not contraindicate trial participation in the opinion of the investigator
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