PROTOCOL SUMMARY

Study Title

A Phase 1b Open-label Study to Evaluate the Safety and Efficacy of CC-122 in Combination with Obinutuzumab (GA101) in Subjects with Relapsed/Refractory Diffuse Large B-Cell Lymphoma and Indolent Non-Hodgkin's Lymphoma

Indication

Relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and indolent Non-Hodgkin's Lymphoma (iNHL)

Inclusion Criteria

Subjects must satisfy the following criteria to be enrolled in the study:

1. Understand and voluntarily sign an informed consent document prior to any study related assessments/procedures are conducted.
2. $\geq$ 18 years of age or older at the time of signing the informed consent document.
3. Subjects with CD20 positive, histologically or cytologically-confirmed, DLBCL (including transformed low grade lymphoma) who have relapsed or refractory disease following at least two prior standard treatment regimens (eg, R-CHOP or similar first-line regimen and at least one second-line salvage regimen) and ASCT in chemotherapy-sensitive patients, with the following ASCT EXCEPTIONS:
   - Subjects in the pre-ASCT setting with poor prognosis, defined as primary refractory disease, that have relapsed within 12 months following first-line treatment;
     "double-hit" lymphomas with Bcl-2/Myc gene rearrangements or, overexpression or high IPI score (2,3) at relapse.
   - Subjects refusing ASCT or for whom ASCT is not appropriate based on the Investigator's judgment.
4. Subjects with CD20 positive, histologically confirmed (by WHO 2008 classification [Jaffe, 2009]), FL (Grade 1, 2, or 3a) or MZL who have relapsed or refractory disease following at least one prior standard systemic treatment regimen including systemic chemo-, immune-, or chemoimmunotherapy.
   - Systemic therapy includes treatments such as rituximab monotherapy, chemotherapy given with or without rituximab, radio-immunoconjugates such as 90Y-ibritumomab tiuxetan and 1311-tositumomab. Systemic therapy does not include, for example,
     H. pylori eradication or antibiotic treatment.
5. Bi-dimensionally measurable disease on cross sectional imaging by CT or MRI with at least one lesion > 1.5 cm in the transverse diameter, as defined by the IWG NHL criteria (Cheson, 2007; refer to Section 6.4).
   - Measurable disease cannot be previously irradiated.
6. ECOG PS of 0 to 1.

7. Subjects must have the following laboratory values at screening:

   - Absolute Neutrophil Count (ANC) $\geq 1.5 \times 10^9$/L without growth factor support for 7 days (14 days if subject received pegfilgrastim).
   - Hemoglobin (Hgb) ≥ 8 g/dL.
   - Platelets (plt) $\geq 50 \times 10^9$/L without transfusion for 7 days.
   - Potassium within normal limits or corrected with supplements.
   - AST/SGOT and ALT/SGPT ≤ 2.5 x Upper Limit of Normal (ULN) or ≤ 5.0 x ULN if liver tumor is present.
   - Serum bilirubin ≤ 1.5 x ULN except in cases of Gilberts Syndrome, then ≤ 2.0 x ULN
   - Estimated serum creatinine clearance of ≥ 60 mL/min using the Cockcroft-Gault equation.

8. Per the Pregnancy Prevention Risk Management Plan (Appendix B):

   a. Females of childbearing potential (FCBP)[1] must undergo pregnancy testing based on the frequency outlined in PPRMP and pregnancy results must be negative.

   b. Unless practicing complete abstinence from heterosexual intercourse, sexually active FCBP must agree to use adequate contraceptive methods as specified in PPRMP.

      – Complete abstinence is only acceptable in cases where this is the preferred and usual lifestyle of the subject.

      – Periodic abstinence (calendar ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable.

   c. Males (including those who have had a vasectomy) must use barrier contraception (condoms) when engaging in sexual activity with FCBP as specified in PPRMP.

   d. Males must agree not to donate semen or sperm for the duration specified in PPRMP.

   e. All subjects must:

      – Understand that the study drugs could have a potential teratogenic risk.

      – Agree to abstain from donating blood while taking study drugs and following discontinuation of investigational product.

      – Agree not to share study drugs with another person.

   f. Other than the subject, FCBP and males able to father a child should not handle the study drugs or touch the capsules, unless gloves are worn.

   g. Be counseled about pregnancy precautions and risks of fetal exposure (refer to PPRMP, Appendix B)

9. Able to adhere to the study visit schedule and other protocol requirements.

[1] A female of childbearing potential is a sexually mature woman who 1) has not undergone a hysterectomy (the surgical removal of the uterus) or bilateral oophorectomy (the surgical removal of both ovaries) or 2) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (ie, has had menses at any time during the preceding 24 consecutive months).

Exclusion Criteria

The presence of any of the following will exclude a subject from enrollment:

1. Any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study.
2. Any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study.
3. Any condition that confounds the ability to interpret data from the study.
4. Symptomatic central nervous system involvement.
5. Known symptomatic acute or chronic pancreatitis.
6. Persistent diarrhea or malabsorption ≥ NCI CTCAE Grade 2, despite medical management.
7. Peripheral neuropathy ≥ NCI CTCAE Grade 2
8. Impaired cardiac function or clinically significant cardiac diseases, including any of the following:
   - LVEF < 45% as determined by MUGA or ECHO.
   - Complete left bundle branch or bifascicular block.
   - Congenital long QT syndrome.
   - Persistent or clinically meaningful ventricular arrhythmias.
   - QTcF > 460 msec on Screening ECG (mean of triplicate recordings as assessed by central read).
   - Unstable angina pectoris or myocardial infarction ≤ 6 months prior to starting study drugs.
   - Troponin T value > 0.4 ng/mL or BNP > 300 pg/mL
     – Subjects with baseline troponin T > ULN or BNP > 100 pg/mL are eligible but must have a cardiologist evaluation prior to enrollment in the trial for baseline assessment and optimization of cardioprotective therapy.
9. Prior ASCT ≤ 3 months before first dose.
10. Prior allogeneic stem cell transplant with either standard or reduced intensity conditioning.
11. Prior systemic cancer-directed treatments or investigational modalities ≤ 5 half lives or
    1 month prior to starting study drugs, whichever is shorter, with the exception of:

a. CD20-directed therapies (eg, rituximab, ofatumumab) or any investigational monoclonal antibody within 3 months prior to starting study drugs.

b. Radioimmunotherapy (eg, ibritumomab tiuxetan, tositumomab) within 6 months prior to starting study drugs.

12. Prior radiotherapy within 1 month prior to starting study drugs.
13. A major surgery ≤ 2 weeks prior to starting study drugs. Subjects must have recovered from any effects of recent surgery or therapy that might confound the safety evaluation of study drug.
14. Prior treatment with CC-122 or obinutuzumab (GA101).
15. History of severe allergic or anaphylactic reactions to humanized monoclonal antibodies. a. Allergic to any excipients in obinutuzumab.
16. Known human immunodeficiency virus (HIV) infection.
17. Known seropositivity for or history of active viral infection with HBV or HCV. a. Subjects who are seropositive due to HBV vaccination are eligible.
18. Need for current chronic systemic corticosteroid therapy (≥ 10 mg of prednisone per day or an equivalent dose of other anti-inflammatory corticosteroids).
    a. Stable use of inhaled corticosteroids is allowed.
19. Treatment-related myelodysplastic syndrome.
20. Prior history of secondary malignancies (except for basal cell or squamous cell carcinoma of the skin or carcinoma in situ of the cervix or breast) unless the subject has been free of the disease for ≥ 1 year prior to starting study drugs.
21. Prior immunization with live virus vaccines (within 3 months prior to starting study drug) or anticipated immunization with live virus vaccines during the duration of the study.
22. Pregnant or nursing females.
23. Unwilling or unable to comply with the protocol, in the opinion of the Investigator.