4. Study population

This study will enroll adult patients with aggressive or indolent forms of relapsed or refractory B-cell non-Hodgkin lymphoma (r/r NHL).

4.1 Inclusion Criteria

Each potential subject must satisfy all of the following criteria to be enrolled in the study:

1. Signed informed consent form
2. Age ≥ 18 years
3. Histologically confirmed diagnosis of one of the following non-Hodgkin lymphoma subtypes:
    a) Aggressive diffuse large B-cell lymphoma (DLBCL), refer to Appendix 1 for all included subtypes defined by WHO 2016
    b) Follicular lymphoma (FL) grade 1, 2 or 3A (FL grade 3B is considered under the subtypes of DLBCL)
    c) Marginal zone lymphoma (MZL)
    d) Mantle cell lymphoma (MCL)
4. Relapsed or refractory disease defined as one of the following:
    a) DLBCL:
        - Primary refractory disease, defined as patients failing to achieve CR to first-line anti-CD20 and anthracycline-based chemoimmunotherapy and having either stable disease or primary progression
        - Relapse within 12 months of completion of first line therapy and not eligible for transplant (ASCT). Transplant ineligible subjects will include those who are deemed ineligible for high-dose chemotherapy and ASCT due to age, performance status or comorbidity, while having adequate organ function for CAR T-cell treatment
        - No response to second or greater lines of therapy, defined as one of the following:
            - PD as best response to most recent therapy regimen
            - SD as best response after at least 2 cycles of last line of therapy with SD duration no longer than 6 months from last dose of therapy
        - Relapsed or refractory disease post-ASCT, defined as one of the following:
            - Disease progression or relapse post-ASCT (must have biopsy proven recurrence in relapsed subjects)
            - If salvage therapy is given post-ASCT, the subject must have had no response to or relapsed after the last line of therapy, as defined above
    b) FL and MZL: Relapsed/refractory disease after at least 2 prior lines of therapy
    c) MCL: Relapsed/refractory disease after at least 2 prior lines of therapy, including a BTK inhibitor
5. Measurable disease according to the Lugano Classification

6. ECOG performance status of 0 or 1 (ECOG 2 may be allowed if due to underlying disease and after discussion with the Medical Monitor)
7. Adequate bone marrow function defined as:
   - Absolute neutrophil count (ANC) ≥ 500/µL or ≥ 0.5 × 10^9/L (without G-CSF support within 7 days of the laboratory test or pegylated G-CSF support within 14 days of the laboratory test)
   - Platelet count ≥ 50,000/µL or ≥ 50 x 10^9/L (without prior platelet transfusion within 7 days before the laboratory test)
   - Absolute lymphocyte count (ALC) ≥ 300/µL or ≥ 0.3 × 10^9/L
   - Absolute number of CD3+ T cells ≥ 150/µL or ≥ 0.15 × 10^9/L
8. Adequate renal, hepatic and pulmonary function defined as:
   - Serum albumin ≥ 3.4 g/dL
   - Creatinine clearance (Cockcroft Gault) ≥ 30 mL/min
   - Aspartate aminotransferase (AST) ≤ 3 × upper limit of normal (ULN)
   - Alanine aminotransferase (ALT) ≤ 3 × ULN
   - Total bilirubin ≤ 2 x ULN, except in subjects with Gilbert's syndrome
   - No clinically significant pleural effusion
   - Baseline oxygen saturation > 92% on room air
9. Women of childbearing potential must have a negative serum pregnancy test at screening and prior to the first dose of cyclophosphamide and fludarabine
10. Women of childbearing potential and all male subjects must agree to use highly effective methods of contraception (failure rate of < 1% per year when used consistently and correctly) and agree to remain on a highly effective method of contraception from the time of signing the informed consent form until at least 12 months after 19CP02 infusion. Subjects must agree to not donate eggs or sperm during this period. Refer to Appendix 4 for detailed information on definitions and contraceptive guidance

4.2 Exclusion criteria

Each potential subject should not satisfy any of the following criteria to be enrolled in the study:

1. Primary CNS B-cell lymphoma, Burkitt lymphoma, or Richter's transformation
2. Prior treatment:
   - Any anti-CD19 targeted therapy
   - Salvage systemic therapy within 2 weeks or 5 half-lives (whichever is shorter) prior to leukapheresis
   - Allogeneic stem cell transplant within 6 months before leukapheresis. Subjects who received an allogeneic transplant must have stopped all immunosuppressive medications for 6 weeks without signs of graft-versus-host disease. Subjects with active graft-versus-host disease are excluded
   - Corticosteroid therapy at a pharmacologic dose (> 5 mg/day of prednisone or equivalent doses of other corticosteroids) and other immunosuppressive drugs are not allowed for 7 days prior to leukapheresis and > 72 hours prior to 19CP02 infusion (if restarted)
3. History of malignancy other than lymphoma, except:
   - Adequately treated non-melanoma skin cancer without evidence of disease

- Curatively treated localized prostate cancer
- Carcinoma in situ (e.g. cervix, bladder, breast) and disease free for at least 3 years prior to screening

4. Toxicity from previous anticancer therapy must resolve to baseline levels or to Grade 1 or less
5. Active CNS involvement (with neurological changes) by disease under study, except if the CNS involvement has been effectively treated (i.e. patient is asymptomatic) and local treatment was > 4 weeks before screening
6. Clinically significant cardiac disease within 12 months of screening such as:
   - Impaired cardiac function (LVEF < 45%) as assessed by echocardiogram performed ≤ 4 weeks prior to screening
   - Evidence of pericardial effusion as determined by echocardiogram
   - New York Heart Association Class III or IV congestive heart failure
   - Clinically significant arrhythmias
7. Primary immunodeficiency
8. Stroke or seizure within 6 months of screening
9. History of autoimmune disease resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within 2 years prior to screening
10. Infection with HIV, hepatitis B or hepatitis C virus. A history of hepatitis B or C is permitted if the viral load is undetectable per quantitative PCR and/or nucleic acid testing.
11. Uncontrolled infection or infection requiring antimicrobials for management, at screening
12. Vaccinated with live attenuated vaccine ≤ 6 weeks prior to the start of lymphodepleting chemotherapy
13. Pregnant or nursing women, or planning to become pregnant within 12 months after 19CP02 infusion
14. No major surgery ≤ 2 weeks prior to leukapheresis
15. Known allergy or hypersensitivity to tocilizumab
16. In the investigator's judgment, the subject is unlikely to complete all protocol-required study visits or procedures, including follow-up visits, or comply with the study requirements for participation