Official Title: A Phase I/II Trial of MB-dNPM1-TCR.1 in HLA-A*02:01-positive Patients with Relapsed or Refractory NPM1-mutated AML to Determine Safety and Obtain First Data on Efficacy

Short title: MB-dNPM1-TCR.1 in Relapsed/refractory AML

Eligibility criteria

Inclusion criteria:

1. Age ≥ 18 years
2. Patients must be able to understand and be willing to give signed informed consent
3. Relapsed or refractory acute myeloid leukemia without standard treatment options defined as:
    - No morphological CR after at least two courses of intensive chemotherapy, decitabine or other standard therapy or
    - MRD positive after at least two courses of intensive chemotherapy and not eligible for allogeneic stem cell transplantation or
    - Relapsed bone marrow or blood disease after CR after first line treatment and not eligible to undergo allogeneic stem cell transplantation or
    - Bone marrow or blood relapse, non-response or MRD positivity after allogeneic stem cell transplantation and not eligible to receive Donor Lymphocyte Infusion (DLI) according to local standards, relapse after DLI.
4. Positive for HLA-A*02:01 according to genotyping results*.
5. AML has NPM1 mutation encoding CLAVEEVSL or CMAVEEVSL which is recognized by dNPM1-TCR.1 and for which a specific Q-PCR is available for disease monitoring*.
6. Number of circulating WBC above 1x109/L with less than 20% leukemic blasts and at least $0.3x10^9$ T cells/L and 0.03×10^9 CD8+ T cells/L.
7. Life expectancy of at least 3 months.
8. ECOG performance status 0-3.
9. Negative pregnancy test in women of childbearing potential.
10. For fertile men and women, agreement to use highly effective contraceptive methods during the trial.

*for this inclusion criterion, the use of laboratory assessment which was done before inclusion in the trial is permitted.

Exclusion Criteria

1. Pregnant or breast feeding women.
2. Active infection with HIV-1, HIV-2, HBV, HCV, HTLV-I, HTLV-II, SARS-CoV-2 or Treponema Pallidum.
3. Any clinically significant, advanced or unstable disease or inadequate main organ function that may put the patient at increased risk for severe complications of trial participation at the discretion of the investigator.
4. Use of systemic immune suppression including, but not limited to: immunosuppressive agents such as cyclosporine or corticosteroids (at an equivalent dose of 0.5 mg

prednisone/kg body weight per day, or higher). Inhaled steroid and physiological replacement for adrenal insufficiency are allowed.

5. Unwillingness or inability to comply with procedures required in this clinical trial protocol.
6. Uncontrolled central nervous system (CNS) disease.
7. Uncontrolled life-threatening infections or uncontrolled disseminated intravascular coagulation; however, if these problems resolve, the start of treatment can be initiated on a delayed schedule.
8. Subjects currently on any other IMP (including within the last 30 days before start of treatment).
9. Current use of high dose immunosuppression for immune disorders interfering with T cell function (on discretion of the investigator).
10. Known hypersensitivity against any drug of the mandatory trial procedures.
11. Serum creatinine = 2.0 × ULN or eGFR < 30 mL/min calculated according to the modified MDRD formula.
12. BMI ≥ 40
13. Has received vaccination with live vaccines 6 weeks prior to treatment
14. Major surgery less than 30 days before start of treatment.
15. Committal to an institution on judicial or official order.