7 TRIAL POPULATION

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

7.1 Inclusion Criteria

Patients are eligible to be included in the trial only if all of the following criteria apply (for both Part 1 and 2 of the trial):

1. Patient must be 18 years of age inclusive or above, at the time of signing the informed consent.

2. Confirmed tumor cell CD1d positivity/expression.

3. Patients with documented diagnosis of CLL, MM, or AML who have failed to respond to or who have relapsed after prior therapy and are not amenable to standard treatments or for whom no standard treatments are available. Patients may have undergone prior cell therapy.

3.1. CLL/ Small Lymphocytic Lymphoma (SLL) patients:

3.1.1. Proven disease by the presence of CD5+CD19+CD23+ clonal B cells in blood, bone marrow and/or lymph nodes.
3.1.2. Patients should meet criteria for requiring therapy (the most recent iwCLL guidelines (39)) and must have measurable disease (measurable lesion > 1.5 cm diameter in at least one dimension) and/or lymphocytosis.
3.1.3. Patients must have failed at least one line of targeted therapy (ibrutinib or venetoclax or similar) and not be amenable to- or for whom no further standard treatment is available.
3.1.4. Patients with Richter's transformation can be included in Part 1 of the trial but not in Part 2 of the trial.

3.2. MM patients:

3.2.1. Documented diagnosis of MM and measurable disease (see Appendix 6, Section 13.6.2; measurable disease is defined as serum monoclonal paraprotein (M-protein) ≥ 5 g/L or urine M-protein ≥ 200 mg/24 hours or abnormal free light chain (FLC) ratio with involved FLC > 100 mg/L or proven plasmacytoma by biopsy*).
3.2.2. Documented progression or refractory multiple myeloma as per the IMWG uniform response criteria (see Appendix 6, Section 13.6.3) following ≥3 prior regimens that include at least one immunomodulatory drug, a proteasome inhibitor, and an anti-CD38 monoclonal antibody in any order.
* *If plasmacytoma is the only measurable parameter, the patient is not allowed to be included in the trial, because of difficult response evaluation.*

3.3. AML patients:

3.3.1. Patients with relapsed/refractory AML (defined using World Health Organization [WHO] 2016 criteria, WHO classification definition of ≥ 20% blasts) of any type with the exception of acute promyelocytic leukemia (APL; AML M3). [Patients with a myelomonocytic or monocytic lineage (M4, M5) are most likely to be positive for the CD1d expression].

3.3.2. Patients with relapsed/refractory AML (defined using either recurrence of disease after a CR, or failure to achieve CR with initial therapy) after at least one prior AML therapy.

4. Males or non-pregnant, non-breastfeeding females who are:
a. Surgically sterile (hysterectomy, bilateral oophorectomy or bilateral salpingectomy, vasectomy).
b. Female of childbearing potential with a negative pregnancy test prior to first dosing and compliant with a highly effective contraceptive regimen (i.e., pregnancy rate of <1% per year: oral contraceptives, intrauterine device (IUD), intrauterine hormone-releasing systems; refer to Appendix 4, Section 13.4 for more details) from signing of the informed consent form (ICF) through 90 days after the last IMP administration. Abstinence is not considered an adequate contraceptive regimen.
c. Female, postmenopausal defined as continuous amenorrhea for at least 12 consecutive months without an alternative medical cause and a serum follicle-stimulating hormone (FSH) measurement of > 40 IU/L).
d. Male, compliant with an effective contraceptive regimen (i.e., use of male condom with female partner and assuring use of an additional highly effective contraceptive method with a failure rate of <1% per year when having sexual intercourse with a woman of childbearing potential who is not currently pregnant following from signing of the ICF through 90 days after the last IMP administration; refer to Appendix 4, Section 13.4 for more details) from signing of the ICF through 90 days after the last IMP administration). Abstinence is not considered an adequate contraceptive regimen.
e. Male, refraining from donating sperm following from signing of the ICF through 90 days after the last IMP administration.

5. Predicted life-expectancy of ≥ 3 months.

6. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

7. Adequate renal function (estimated glomerular filtration rate [eGFR] per local laboratory > 40 mL/min/1.73m2), hepatic function [(total bilirubin ≤ 2 times upper limit of normal (ULN), unless in patients with known Gilbert's syndrome who must have total bilirubin ≤ 3 times ULN; AST and ALT ≤ 3.0 times ULN] and hematological function (neutrophils ≥ 1 x109/L; platelet count ≥ 75x109/L, unless due to bone marrow tumor infiltration, in which case it must be ≥ 50x109/L).

8. Capable of giving signed and dated informed consent prior to initiation of any trial-related procedure that is not considered Standard of Care which includes compliance with the requirements and restrictions listed in the ICF and in the protocol.

7.2 Exclusion Criteria

Patients are excluded from the trial if any of the following criteria apply:
1. Prior allogeneic bone marrow transplant as long as the patient still has active acute or chronic graft versus host disease requiring >10 mg prednisone or equivalent corticosteroids.

2. Concomitant malignancies except carcinoma in situ, basal or squamous cell skin carcinoma. Patients who had no evidence of disease from another primary cancer for 2 or more years are allowed to participate in the trial. Localized non-metastatic prostate cancer, not requiring systemic treatment, and for which no local treatment is planned, is allowed.

3. Uncontrolled or severe intercurrent medical condition.

4. Known uncontrolled central nervous system involvement.

5. Patient has any active-, uncontrolled-, or suspected infection.

6. A significant history of renal, neurologic, psychiatric, pulmonary, endocrinologic, metabolic, immunologic, cardiovascular, or hepatic disease that in the opinion of the investigator would adversely affect his/her participating in this trial.

7. Unstable cardiovascular function defined as: (a) symptomatic ischemia, or (b) uncontrolled clinically significant conduction abnormalities (i.e., ventricular tachycardia on antiarrhythmic agents are excluded; 1st degree atrioventricular block or asymptomatic left anterior fascicular block/right bundle branch block (left anterior fascicular block /right bundle branch block) will not be excluded), or (c) congestive heart failure New York Heart Association Class ≥ 3, or (d) myocardial infarction within 3 months.

8. Previous treatment with radiotherapy, immunotherapy, or chemotherapy in the 2 weeks prior to initial IMP administration.

9. Previous treatment with biological therapy or with an investigational product in the 4 weeks prior to initial IMP administration.

10. Previous treatment with an aminobisphosphonate IV (e.g., ibandronate, pamidronate, zoledronate etc) within 4 weeks prior to initial IMP.

11. Previous treatment of any systemic immunosuppressant within 2 weeks prior to initial IMP administration, with the exception of systemic corticosteroid use up to oral dose of 10 mg prednisolone daily (or equivalent for other steroids).

12. Previous treatment with live or live attenuated vaccines within 2 weeks prior to initial IMP administration. Other (new) types of vaccines need to be evaluated as to their mode of action.

13. Known non-CLL/MM/AML related pre-existing clinically relevant immunodeficiency disorders.

14. Positive serological testing for Human Immunodeficiency Virus (HIV) antibody, hepatitis B surface antigen [HBsAg] and hepatitis B core antibody (anti-HBc) negative, and hepatitis C virus antibody. Patients who are positive for anti-HBc or hepatitis C antibody may be included if they have a negative PCR within 6 weeks prior to initial IMP administration. Those who are PCR positive will be excluded.

15. Known allergies, hypersensitivity, or intolerance to the excipients of the IMP.

16. Major surgery within 4 weeks of initial IMP administration or planned surgery during the time the patient is expected to participate in the trial.

17. Known ongoing drug and alcohol abuse in the opinion of the investigator.

NOTE: Investigators should ensure that all trial inclusion/exclusion criteria have been met at screening and prior to the first dose of IMP.