SAMENVATTING ADVANCE II

TITEL

AN INTERNATIONAL, MULTICENTRE, OPEN-LABEL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF TWO DIFFERENT VACCINATION REGIMENS OF IMMUNOTHERAPY WITH ALLOGENEIC DENDRITIC CELLS, DCP-001, IN PATIENTS WITH ACUTE MYELOID LEUKAEMIA THAT ARE IN REMISSION WITH PERSISTENT MRD.

Allogeneic Dendritic cell Vaccination in AML oNgoing Clinical Evaluation II (ADVANCE II)

INDICATIE

Patients with a confirmed diagnosis of AML that are in CR1 or CRi with MRD, greater than 18 years of age.

SCHEMA

Weken	0	0	2	4	6	6	11	14	18	18	20	32
Dagen	0	2	14	28	42	44	77	98	126	128	140	224
Visite Nr	2	3	4	5	6	7	8	9	10	11	12	13
Ziekte evaluatie	■		■	■	■			■	■		■	■
Beenmerg afname voor analyse effect DCP-001	■							■			■	■
DCP-001 vaccinatie	■		■	■	■			■	■			
Bloed afname voor analyse effect DCP-001 op het immuunsysteem	■	■				■	■			■	■	■
Huid biopsie		■				■				■		

International, multicenter, open-label proof of concept study without randomization and stratification. Two different dose groups are included.
Group 1 consists of 10 patients that will receive 25E6 DCP-001 cells per vaccination with two additional booster vaccinations of 10E6 cells.
Group 2 consists of 10 patients who will receive 50E6 DCP-001 cells per vaccination with two additional booster vaccinations of 10E6 cells.
Patients will be screened for eligibility for the study and evaluated at baseline, at each vaccination visit and every 8 weeks during follow up.
Each patient will be followed up for 12 months after the 4th vaccination.
Sera and cell samples (blood and bone marrow) will be collected when indicated for efficacy (MRD evaluation) and immune response monitoring.

Main Inclusion Criteria:

1. Confirmed diagnosis of AML according to WHO2016 criteria, including cytological, molecular and cytogenetic criteria (except acute pro-myelocytic leukemia/APL).
2. In CR1 (first complete remission) or CRi (incomplete blood count recovery) documented by bone marrow examination up to one month before vaccination; CR defined as less than 5% blasts in normo-cellular bone marrow, ANC >1*E9/L, platelet count 100*E9/L, no evidence of extra-medullary disease. Patients in CRi (patients with <5% blasts but with incomplete blood count recovery) should have platelets >50 E9/L.
3. MRD as defined by multicolor flow cytometry (MFC) at a value of > 0.1%, or detection of

specific molecular abnormalities such as NPM1 mutation.
4. Patients that are in CR1 or Cri. Patients not having undergone consolidation therapy must have been in CR1 for at least 1 month prior to enrolment.
5. Expected and willing to undergo all study procedures, including outpatient evaluations for clinical and immunological monitoring.
6. Male or female of > 18 years of age.
7. Women of childbearing potential must be on anti-conceptive therapy or use two (2) barrier contraceptive methods (one by each partner and at least one of the barrier methods must include spermicide (unless spermicide is not approved in the country or region). See section 12.8 for birth control methods deemed acceptable for this study.
8. ECOG (WHO) performance status 0-2.
9. Willing and able to provide written informed consent for participation in the study

Main Exclusion Criteria:

1. Acute Promyelocytic (APL; M3) type of AML.
2. Patients who have undergone or are scheduled for allogeneic stem cell transplantation.
3. History of previous allogeneic bone marrow or solid organ transplantation.
4. Uncontrolled or serious infections
5. Ongoing immunosuppressive therapy, other than short use of low dose steroids, i.e. equivalent to an average dose of ≤10mg of prednisone/day.
6. Chemotherapy and antineoplastic hormonal therapy within 28 days prior to the screening visits.
7. Active autoimmune disease.
8. Inadequate liver function (AST and ALT > 3 x ULN, serum bilirubin >3 x ULN).
9. Other active Malignancies within the last 5 years, except for adequately treated carcinoma in situ of the cervix or squamous carcinoma of the skin or adequately controlled limited basal cell skin cancer.
10. Pregnant or lactating females.
11. Major surgical procedure (including open biopsy) within 28 days prior to the first study treatment, or anticipation of the need for major surgery during the course of the study treatment.
12. Uncontrolled hypertension (systolic > 150 mm Hg and/or diastolic > 100 mm Hg) or clinically significant (i.e. active) cardiovascular disease.
13. Evidence of any other medical conditions (such as psychiatric illness, physical examination or laboratory findings) that may interfere with the planned treatment, affect patient compliance or place the patient at high risk from treatment-related complications.
14. Known HIV, Hepatitis B and/or Hepatitis C infections.
15. History of hypersensitivity to the investigational medicinal product or to any excipient present in the pharmaceutical form of the investigational medicinal product.