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 leukemia that are in remission with persistent MRD.

Published: 13-09-2017
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Primary:• To assess the effect of DCP-001 on MRD. MRD will be measured by flow cytometry pre and post vaccination as a surrogate marker for established clinical endpoints in AML.• To assess the effect of DCP-001 on immune responses in AML patients...

Ethical review	Approved WMO
Status	Completed
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON52641

Source
ToetsingOnline

Brief title
ADVANCE II

Condition

- Leukaemias

Synonym
Acute Myeloid Leukemia, Blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Immunicum AB (voorheen DCprime bv)
Source(s) of monetary or material Support: Immunicum AB (voorheen DCprime bv)

Intervention

Keyword: allogeneic dendritic cells, AML, Immunotherapy, Minimal Residual Disease (MRD)

Outcome measures

Primary outcome

- Any change in MRD (flow cytometric) as compared to baseline MRD

- Any change in immunoreactivity (specific and non-specific) as compared to

baseline.

Secondary outcome

Secondary Efficacy Endpoints

- To document safety and tolerability.

- To quantify any lag time between initiation of treatment & onset of effect.

- To determine the effect of DCP-001 on Time to Relapse (TTR).

- To determine the effect of DCP-001 on Overall Survival (OS).

- To document the difference between the two vaccination regimens based on MRD

outcome and immunological parameters.

Exploratory Endpoints

- To document the number and duration of subsequent remissions.

- To identify subgroups of patients most likely to benefit from treatment.

- To identify surrogate (immunological) markers that might correlate with

clinical outcome.

- To quantify any lag time between initiation of treatment & onset of effect

- To identify surrogate (immunological) markers that might correlate with clinical outcome.

Safety endpoints:

- Treatment emergent adverse events (TEAEs) will be collected in first 48 hours after the first vaccination to determine (acute) toxicity due to intradermal injection.

- All TEAEs will be collected during the study period for each patient and the grade of toxicity (CTCAE v.4.0, see Appendix B) and relationship to product determined.

- A DSMB will meet after every 5 patients complete treatment to evaluate safety; written reports will be made of each meeting.

- All SAEs will be reported by the investigator within 24 hours of the first knowledge. All SAEs will be reported in a timely manner to the appropriate regulatory body, consistent with existing regulations. Information on relevant SAEs will be disseminated between sites in a timely manner. Processes are described in detail in the study specific safety plan.

Study description

Background summary

Immunotherapy offers promise in AML and has created opportunities for improved outcomes. Dendritic cell (DC)-based immunotherapy has shown to be a promising

strategy for the elimination of minimal residual disease (MRD) in patients with acute myeloid leukemia (AML).
DCP-001 is an allogeneic dendritic cell based immunotherapeutic vaccine that expresses a number of tumor antigens that are expressed in AML and have shown clinical results when applied as peptide vaccines or loaded onto patient derived DC's.
Evidence for DCP-001 mediated safety, feasibility and immunological responses have been demonstrated in a Phase I study; the current study aims to generate evidence for clinical efficacy.

Study objective

Primary:
• To assess the effect of DCP-001 on MRD. MRD will be measured by flow cytometry pre and post vaccination as a surrogate marker for established clinical endpoints in AML.
• To assess the effect of DCP-001 on immune responses in AML patients in first complete remission (CR1) and persistent MRD.
• To document safety and tolerability.

Secondary:
• To identify surrogate (immunological) markers that might correlate with clinical outcome.
• To quantify any lag time between initiation of treatment & onset of effect.
• To determine the effect of DCP-001 on Time to Relapse (TTR).
• To determine the effect of DCP-001 on Overall Survival (OS) during the study.
• To document the difference between the two vaccination regimens based on MRD outcome and immunological parameters.

Study design

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, and will subsequently be asked to prolong the follow up up until five years after first vaccination. Sera and cell samples (blood and bone marrow) will be collected when indicated for efficacy (MRD evaluation) and immune response monitoring.

Intervention

Patients will receive 25E6 DCP-001 cells per vaccination (Group 1; 10 patients) or 50E6 DCP-001 cells (Group 2; 10 patients) per vaccination. Both groups will receive two additional booster vaccination of 10E6 cells.
The first treatment for both dose groups is given at Day 0 (Baseline), the second, third and fourth treatments are given at 2 weekly intervals. A total of 4 treatments will be administered in a 6 week timeframe followed by a booster vaccination at 8 and 12 weeks after the 4th vaccination at week 6. A summary of the treatment schedule is given below:

Study burden and risks

The Phase I study with DCP-001 has not generated any safety concerns.
This study involves administration of a therapeutic agent which could provide an efficacious treatment for patients. Both active treatment arms are expected to provide therapeutic benefit for patients. It is therefore concluded that the risk-benefit ratio for patients entering this study is favorable.
Risk of infection:
Risk is considered low/absent as the DCOne cell line from which DCP-001 derived has been extensively tested for multiple viruses according to applicable regulatory guidelines (see IB/IMPD). Upon release the DCP-001 product is confirmed to be sterile.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Confirmed diagnosis of AML according to WHO2016 criteria, including cytological, molecular and cytogenetic criteria (except acute promyelocytic leukemia/APL).
2. In CR1 or CRi 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*10E9/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 G/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 or CRi for at least 1 month prior to enrolment. . Patients treated with hypomethylating agents must have been given at least two cycles and up to a maximum of nine cycles of hypomethylating agents.
5. Expected to be willing and able to undergo all study procedures, including outpatient evaluations for clinical and immunological monitoring.
6. Male or female > 18 years of age.
7. Women of childbearing potential must be on anti-conceptive therapy, or using an intrauterine device, 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), or underwent tubal ligation, or the partner was vasectomized, or is sexually abstinent.
8. ECOG (WHO) performance status 0-2.
9. Willing and able to provide written informed consent for participation in the study and for tissue sample biobanking..

Exclusion criteria

1. APL (M3) type of AML.
2. Patients who have undergone or are scheduled/eligible 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 therapy within 28 days prior to the

screening visit, with the exception of hypomethylating agents such as azacitidine and decitabine, or midostaurin for FLT3 mutations, or patients treated with IDH1/2 inhibitors in mIDH1/2.
7. Current or past medical history of autoimmune disease.
8. Inadequate liver function (AST and ALT > 3 x ULN, serum bilirubin >3x 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 or 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

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-11-2018
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	13-09-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-12-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-10-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-11-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	15-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-11-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	2017-003426-17
EudraCT	EUCTR2017-003426-32-NL
CCMO	NL62714.000.17