A Phase 1, Multinational Study of MCLA-117 in Acute Myelogenous Leukemia

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Primary:To assess the safety and tolerability of MCLA-117, in order to determine the MTD/RP2D and frequency of administration.Secondary:- To assess the pharmacokinetic (PK) profile of MCLA-117 i.v. infusion- To investigate the pharmacodynamic (PD)…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON47785

Source
ToetsingOnline

Brief title
MCLA-117-CL01

Condition

- Leukaemias

Synonym
Acute Myelogenous Leukemia OR Leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Merus N.V.
Source(s) of monetary or material Support: Merus

Intervention

Keyword: Acute Myelogenous Leukemia, MCLA-117, Phase 1

Outcome measures

Primary outcome

Preliminary clinical efficacy will be evaluated according to the international working group revised criteria of response for AML (Cheson et al, 2003). Assessments and assignment of efficacy will be done at investigational sites. Samples of blood and BM will be obtained at Screening and during and post treatment at intervals specified in the study protocol*s schedule of assessments.

Secondary outcome

PK assessments

In Part 1 and 2, samples will be collected at pre-specified time points from pre-dose at Day 1 up to 6 days after EOI of Day 22 during cycle 1 and pre-dose and at 5 minutes prior to end-of-infusion (EOI) at Day 1 and Day 15 during all other cycles.

PK sampling will be performed by the investigating site. PK sample analysis will be performed at a central laboratory. In case of changes in frequency of administration during the study, timing and number of sampling may be modified per amendment.

Cytokine panel

In cycle 1 a panel of cytokines will be measured in serum samples obtained pre-infusion and at a number of predefined time points following MCLA-117

administrations.

Cytokine sampling will be performed by the investigating site. The analysis of the cytokines will be performed at a central laboratory.

Anti-drug antibody assessment (Part 1 and Part 2)

Serum titers of anti-MCLA-117 antibodies will be determined pre-dose at Day 1 and at Day 28 of each cycle. Additional sampling within individual patients is allowed if a suspected delayed hypersensitivity reaction is observed. In case ADA blood sampling and MCLA-117 administration are scheduled for the same day, ADA blood sampling should be performed prior to MCLA-117 administration. Anti-drug antibody sampling will be performed by the investigating site and analysis will be performed at a central laboratory.

Study description

Background summary

Acute myelogenous leukemia (AML) is the third most common leukemia worldwide with little progress in disease outcomes for the last four decades. In the majority of patients who have achieved remission upon induction chemotherapy, disease relapse is observed within 3 years. Thus, improving response rate and prolonging duration of complete response (CR), preventing relapse, improving disease-free survival and overall survival in both younger and older AML patient population, are unmet medical needs. Similar to AML patients, high-risk MDS patients have very limited therapeutic options once failed standard therapies.

MCLA-117, a human bispecific IgG antibody which targets CLEC12A and CD3, has demonstrated preclinical proof of concept using AML patient samples. Targeting CLEC12A-expressing cells by MCLA-117 results in eradication of malignant blasts and their leukemic stem cells in the BM, which might be effective in eliminating minimal residual disease (MRD) and preventing disease recurrence. The CD3 arm of MCLA-117 recruits T-cells to the AML cells coated with the

antibody through CLEC12A binding, triggering T-cell activation, proliferation and subsequently lysis of the antigen-positive tumor cells. Similar to AML patients, CLEC12A is expressed in myeloblasts in the majority of patients with high-risk MDS. The full-length IgG1 immunoglobulin format of MCLA-117 enables administration as a conventional intravenous infusion without the necessity of a continuous infusion. In addition, the silencing of the Fc portion of MCLA-117 might mitigate to some extent the risk of severe cytokine release symptoms in the absence of binding to the tumor-associated antigen (CLEC12A).

MCLA-117 has the potential of being developed as an induction or consolidation therapy for AML, or to treat Minimal Residual Disease (MRD), and as a rescue therapy for the relapsed/refractory target patient population. Clinical development can be explored both as single agent and in combination with chemotherapy agents in AML. The safety profile of MCLA-117 is expected to be acceptable with manageable neutropenia and infusion-related reactions.

Study objective

Primary:
To assess the safety and tolerability of MCLA-117, in order to determine the MTD/RP2D and frequency of administration.
Secondary:
- To assess the pharmacokinetic (PK) profile of MCLA-117 i.v. infusion
- To investigate the pharmacodynamic (PD) effects of MCLA-117 in adult AML patients
- To determine incidence and serum titer of ADAs against MCLA-117
- To determine the cytokine profile of MCLA-117 in adult AML patients
- To evaluate the preliminary efficacy/ anti-leukemic activity of MCLA-117 in adult AML patients

Study design

This First-in-Human, single arm, open-label, multi-national study is designed to determine the safety, tolerability and preliminary efficacy of MCLA-117, a full-length human IgG1 T cell redirecting bispecific antibody targeting CLEC12A in patients with AML. The dose and frequency of the administration of MCLA-117 to be used in further clinical studies will be determined. In addition, the preliminary PK profile, anti-drug antibodies (ADA) incidence and titer, cytokine profile will be determined. Relevant biomarker identification will be explored.
The study consists of two parts:
Part 1-Dose Escalation
Dose escalation cohorts with single agent MCLA-117 are planned to determine the safety and tolerability of MCLA-117 and identify the maximum tolerated dose (MTD) and/or recommended phase 2 dose schedule (RP2DS). Dose escalation starts with two-patient cohorts, allowing intra-patient dose escalations until a PD

effect is observed (e.g., treatment-related adverse events, or a reduction in BM cellularity or blast count, or reaching a dose level at which a clinically meaningful response could be expected). From cohort 3, the design switches to a 3+3 dose escalation method with at least 33% dose increments until dose-limiting toxicity (DLT) occurs or the RP2DS is defined. From cohort 7 onwards, patients are not preselected for CLEC12A expression level *10%. Therefore, a modified 3+3 design is used, termed the "A+B" design (Lin and Shih, 2001; Le Tourneau et al, 2009) with initial patient enrollment per cohort of 3-6 patients upfront to ensure the representation of patients with CLEC12A expression level *10%. Patients who do not complete the DLT observation period will be replaced unless treatment discontinuation is due to DLT. DLTs will be determined based on predefined criteria for hematologic and non-hematologic toxicities. Adverse events (AEs) will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 4.03.

A cohort review session by a Data Review Committee (DRC) with attendance of study Investigators and relevant study team members will take place at completion of the DLT observation period of each dose cohort. Additional experts may be invited to attend when deemed necessary by the Sponsor or study investigators. At this review session, a decision will be made on whether to open the next cohort and at which dose level and dosing frequency. In addition, the DRC will recommend measures to be taken to optimize the medical management of possible IRRs following administration of MCLA-117.

Part 2-Expansion Cohort

Part 2 will begin once the MTD or RP2DS is determined in Part 1. This part will consist of 2 cohorts of approximately 15 evaluable patients each (evaluable for the first efficacy assessment), recruited in parallel. Cohort A will include patients without prior hematopoietic stem cell transplantation, and Cohort B will include patients with prior hematopoietic stem cell transplantation (see exclusion criterion #3).

The following safety evaluation rules will be applied to each cohort separately. Part 2 consists of two steps in each cohort, to further characterize the safety, tolerability, PK, PD, cytokine profile, and immunogenicity, and to assess preliminary efficacy of MCLA-117. The first 9 patients in each Part 2 cohort will be evaluated for safety. If in the first cycle of treatment, * 2 out of the 9 patients experience AEs that meet the criteria of DLT, after

discussion between Investigators and the Sponsor, the enrollment will continue up to 15 patients in each cohort. For each Part 2 cohort, once 15 patients have been enrolled, a new assessment of DLTs will be performed, and if * 4 out of 15 patients meet the criteria for DLT, expansion will continue in that population, following submission and approval of a substantial protocol amendment. In this case, it is anticipated that Part 2 of the study could be expanded up to approximately 100 patients. If >2/9 or >4/15 patients in either of the 2 cohorts meet the criteria for DLT in either of these two DLT evaluation steps, the Sponsor and the Investigators will discuss further exploration at the dose level below or another intra-patient dose escalation regimen in the applicable

cohort(s).
MCLA-117 will be evaluated as a single agent in Part 2. Based on the available data from Part 1, new preclinical data, scientific data or medical information, the Sponsor may enroll additional patients in the expansion cohort, and/or open additional patient cohorts either as a single agent or as a combination treatment with standard or commonly used AML treatments or other investigational agents (following submission of a protocol amendment).

Intervention

The starting dose level was estimated based on a minimum anticipated biological effect level (MABEL) approach. The starting dose is 25 *g flat dose (equal to approximately 0.4 *g/kg). The MTD or the RP2DS will be established based on incidence of DLTs in the DLT observation period only, as well as MCLA-117 PK properties and cytokine profile, potentially supported by correlative biomarker and ADA data.
Patients without a response may remain on treatment until disease progression, unacceptable toxicity or discontinuation for any other reason. Patients in CR, CRi or CRp will receive up to 6 additional cycles. MCLA-117 will be administered intravenously over approximately 2 hours. Prolonging the duration of infusion to up to 4 hours is permitted. The DRC may propose an increased duration of infusion based on the data becoming available after completing each cohort.
One treatment cycle is approximately 4 weeks and patients will be hospitalized for the first treatment cycle. According to the investigator*s discretion, patients may be discharged 48 hours after the C1D15 and C1D22 infusions, provided that the patient is clinically stable and there are no signs of CRS or other safety concerns at the time of discharge and the patient has immediate access to medical attention. The investigator will decide if following cycles can be completed on an outpatient basis. The study drug will be administered on a weekly basis. However, during the first 2 weeks of administration in cycle 1 (including Day 15), a gradual intra-patient dose escalation will be applied (ramp up).
On Day 28 of the first cycle, a BM aspiration (BMA) and BM biopsy (BMB) will be performed. Based on BM blast count and/or based on peripheral blood cell counts, the treating investigator will decide to continue dosing orto introduce a pause for that patient.
Up to 13 dose levels are anticipated. A combination of an accelerated dose escalation approach and the 3+3 dose escalation study design will be used for the first 6 cohorts. The first two cohorts will enroll two patients per cohort with at least one evaluable patient for the full cycle including protocol-specified intra-patient dose escalation in consecutive doses over the course of the first cycle. The second patient in each of these first two cohorts will only be enrolled after the first patient in the same cohort has completed at least 7 days of the planned treatment. Beginning at cohort 3 a minimum of 3 evaluable patients will be required. From cohort 7 onwards with the A+B design, a maximum of 6 patients can be enrolled at any given time

depending on the number of patients who are already considered evaluable within that dose level.
All dose escalation decisions in Part 1 of the study and the definition of the MTD and the RP2DS, will be made by a DRC who will convene to review all available data. The DRC includes participation of principal investigators (or their qualified representatives), the Sponsor*s medical director, the study pharmacovigilance physician, the study project managers and other relevant study team members. When required, external independent experts will be invited. The DRC will also decide about expansion of sample size for part 2 of the study.
The DRC could recommend alternative dose and frequency schedules before moving to the A+B design. Starting with cohort 3, all cohorts will enroll at least 3 evaluable patients with dose increments of a minimum of 33% percent. However, all cohorts will enroll a minimum of 3 patients with * 10% of blasts expressing CLEC12A measured by flow cytometry at baseline (in BMA, BMB or peripheral blood sample). The dose increments are predetermined as shown in Table 1, however, for safety reasons, the DRC may determine a lower or intermediate dose level not previously defined prior to opening the next cohort. The target dose per cohort as predetermined in Table 1 cannot be exceeded. The intra-patient dose escalation during the first 2 weeks of treatment (including the dose on Day 15) is subject to change, based on decisions made by the DRC.
During Part 1, the starting dose (C1D1) of patients within the same cohort (from cohort 3 and onwards) will be separated by a minimum of 24 hours between each new patient starting treatment. Dose escalation (opening of a new cohort of patients) will occur only after the last patient in the previous cohort has completed at least 1 full cycle of MCLA-117 at the planned dose. During Part 2, patients can start treatment with the RP2DS in parallel.
The decision to continue treatment for each patient depends on the results of BMA and BMB on Day 28 of Cycle 1, according to the recommendation of the treating investigator. From cohort 3 onwards, the protocol plans to reduce the frequency of administration during the first cycle, given that the MCLA-117 serum half-life will increase with increasing doses.
De-escalation to an intermediate level (e.g., between the level at which DLT occurred and the immediately lower one) will be carried out if recommended by the DRC. Patients will be permitted to receive subsequent cycles at higher dose levels provided such dose levels have been established as safe by the DRC. This intra-patient dose escalation can be initiated at each next scheduled administration upon DRC approval of that dose level.
The following dose escalation rules will apply for Cohorts 1 and 2:
1) No DLT for the first two patients and no non-disease related toxicity * Grade 2: the dose for the next cohort will be escalated according to the proposed scheme in Table 1.
2) No DLT but * 1 Grade 2 non-disease related toxicity for either of the first 2 patients: the dose for the next cohort will be escalated with a reduced increment than that proposed in Table 1, which will be recommended by the DRC.
Upon switching to the 3+3 scheme, the following dose escalation rules will apply:

1) No DLT for the first three patients: the dose for the next cohort will be escalated according to the proposed scheme in Table 1.
2) At least 1 of the first 3 patients experiences DLT: the cohort of three patients will be expanded to six patients at the same dose level. Subsequently, if no other patient within the dose level experiences a DLT, dose escalation will proceed to the next dose level according to Table 1. If two or more patients (of the 3 to 6 patients) in the dose level experience DLT then the MTD has been exceeded. A previous dose level will be declared the MTD. Alternatively, an intermediate dose level could be recommended by the DRC and tested in an additional cohort of patients.
From cohort 7 onwards the following dose escalation rules will apply:
1) no DLTs are seen in 3-6 evaluable patients or a maximum of 1 patient with DLT is observed in 6 evaluable patients: the next dose level will be tested.
2) 1 DLT is seen in the initial cohort of 3-5 evaluable patients: additional patients will be enrolled with up to 6 evaluable patients at that dose level.
3) 2 or more DLTs are seen at the dose level: the MTD will be declared to be the preceding dose level. Alternatively, an intermediate dose level could be recommended by the DRC and tested in an additional cohort of patients.
From cohort 9, the following dose escalation rules will apply:
1) no DLTs are seen in 3-6 evaluable patients: the next dose level will be tested.
2) DLT in the ramp up period, i.e. before the highest dose in the cohort: consider DLT information from all patients treated at this ramp up in the current or preceding cohorts. If the posterior probability that the true DLT rate does not exceed 33% is at least 75% then this ramp up is considered safe. A number of DLTs and the minimum number of patients required to declare ramp up as safe are: - 1 DLT and minimum 5 patients treated at this ramp up - 2 DLTs and minimum 8 patients treated at this ramp up - 3 DLTs and minimum 12 patients treated at this ramp up - 4 DLTs and minimum 15 patients treated at this ramp up
3) DLTs at the highest dose for the cohort:
3.1) 1 DLT at the highest dose for the cohort in 6 evaluable patients: proceed to the next dose level
3.2) 2 or more DLTs are seen at the dose level: the MTD will be declared to be the preceding dose level. Alternatively, an intermediate dose level could be recommended by the DRC and tested in an additional cohort of patients.
3.3) 1 DLT at the highest dose for the cohort in the initial cohort of 3-5 evaluable patients: additional patients will be enrolled with up to 6 evaluable patients at that dose level.
Patients will be permitted to receive subsequent doses beyond Cycle 1 if:
a) no significant drug-related toxicity occurs (e.g., meeting definition of DLT),
b) in the opinion of the Investigator the patient is experiencing clinical benefit.

Study burden and risks

Adverse events (side effects) complications and/or injury (both expected and

unexpected) are possible with any experimental medicinal products. As this is the first time that MCLA-117 is tested in humans, there may be side effects that cannot be predicted yet.
Based on information from laboratory tests and other anticancer drugs with some similarity with this compound, the following adverse reactions might occur:
* Risks of administering the drug through an infusion
Symptoms like fever, chills, phlebitis, hypotension (low blood pressure), shortness of breath, skin rash, nausea and/or vomiting can occur. These reactions might be mild or moderate or serious. These reactions typically occur during or after the first infusion of the drug, with incidence and severity decreasing with subsequent infusions.
* Cytokine release syndrome and neurotoxicity
This specific reaction to the administration of the drug through an infusion is known to occur in patients receiving treatments similar to MCLA-117. Symptoms include: fever, fatigue, loss of appetite, muscle and joint pain, vomiting, diarrhea, rashes, fast breathing, rapid heart rate, low blood pressure and neurotoxicity (seizures, headache, confusion, delirium (confusion or madness), encephalopathy (abnormal brain function), hallucinations, tremor and loss of coordination). You will be monitored closely during and following each infusion to observe possible signs or symptoms of this cytokine release syndrome. Due to the possible risk of neurotoxicity (when a drug has an adverse effect on your nervous system), it is important that you do not drive or operate heavy machinery while on treatment with MCLA-117 and for at least 30 days after discontinuation of treatment.
* Risk of allergic reactions
There is potential for allergic reactions with administration of MCLA-117. This risk is considered to be low. Symptoms are similar to those described above for infusion related reactions.
* Risk of neutropenia (reduced number of neutrophils, a subset of white blood cells responsible to fight against infections) with an associated risk of immune impairment and infection. Usually this is already present due to the leukemia.
* Risk of hepatic toxicities, including liver function test abnormalities.

Pregnancy/Birth Control
The risks of taking MCLA-117 to pregnant women or an unborn baby are unknown. Females must have a pregnancy test before the study starts and again just before receiving the first dose of MCLA-117 (unless the previous test is done less than 3 days ago), and again if there is an indication that you might be pregnant. The patient will also have pregnancy test at the final study visit.
The Patient must not become pregnant during this study. If the patient is a female of childbearing potential, the patient must use a highly effective form of birth control during this study and until 6 months thereafter. The study doctor will discuss with the patient which contraception methods are acceptable.
The effects of MCLA-117 on a nursing infant are unknown; if the patient is is breastfeeding, the patient cannot participate in the study.

If the patient is a male and can father a child, it is recommended that both the patient and the partner use contraception until 6 months after completion of the study.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

To be eligible to participate in this study, all candidates must meet all the following criteria:
1. Male or female age *18 years old;
2. Understand and voluntarily sign the informed consent form prior to any study specific screening procedures;
3. One of the two following:
i) Documented diagnosis of AML either de novo or secondary [any subtype except

acute promyelocytic leukemia (APL)] according to World Health Organization (WHO) classification who either:
a) are in relapse to standard therapy following an initial response;
b) failed primary induction therapy with no CR (failed *2 courses of intensive induction therapy. Intensive chemotherapy defined as an intensity of * 5+2);
c) newly diagnosed untreated AML in patients * 65 years of age with high risk cytogenetics, if they are not candidates for standard available induction chemotherapy;
d) AML secondary to MDS, either relapsed or refractory, previously treated with hypomethylating agents for at least 4 cycles;
e) Relapsed or refractory AML unfit for intensive chemotherapy previously treated with a low intensity regimen (e.g. low dose Ara-c, hypomethylating agent, etc.) including Venetoclax for at least 2 cycles;
Or
ii) MDS patients who meet the following criteria: very high-risk disease (IPSS-R score > 6, Greenberg et al., 2012), either relapsed or refractory, previously treated with hypomethylating agents for at least 4 cycles;
4. Baseline BM sample taken by BMA and BMB (unless there is a contraindication) within 28 days prior to first dose of MCLA-117 for CLEC12A detection. In case of a dry tap by BMA a peripheral blood sample will be acceptable;
5. Estimated life expectancy of at least 8 weeks;
6. Eastern Cooperative Oncology Group (ECOG) performance status * 2;
7. Significant toxicities incurred as a result of previous anti-cancer therapy must have resolved to * Grade 1 or baseline before enrollment as defined by NCI-CTCAE version 4.03. Note: alopecia and stable neuropathy (* Grade 2) are allowed;
8. Acceptable laboratory values:
a. Serum creatinine * 3.0 × ULN (upper limit of normal);
b. Total serum bilirubin * 1.5 × ULN, except for patients with Gilbert syndrome in which case it should be * 3 x ULN;
c. Serum aspartate transaminase (AST) and alanine transaminase (ALT) * 2.5 × ULN;
d. Serum potassium, magnesium and calcium levels within institutional normal limits;
9. Male patients must agree to use an adequate and medically accepted method of contraception throughout the study and for at least 6 months after if their sexual partners are women of child bearing potential (WOCBP);
10. WOCBP must be using highly effective and medically accepted method of contraception to avoid pregnancy throughout the study and for at least 6 months after the study in such a manner that the risk of pregnancy is minimized. WOCBP includes any female that has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation or bilateral oophorectomy) or is not post- menopausal (defined as amenorrhea >12 consecutive months; or women on hormone replacement therapy with documented serum follicle stimulating hormone level > 35 mIU/mL). Women who are using oral, implanted or injectable contraceptive hormones or mechanical products such as an intrauterine device or barrier methods (diaphragm, condoms,

spermicides) to prevent pregnancy or are practicing abstinence or where the partner is sterile (e.g., vasectomy), should be considered to be of childbearing potential. Highly effective and medically accepted methods of contraception are:
* combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
o oral
o intravaginal
o transdermal
* progestogen-only hormonal contraception associated with inhibition of ovulation:
o oral
o injectable
o implantable
* intrauterine device (IUD)
* intrauterine hormone-releasing system (IUS)
* bilateral tubal occlusion
* vasectomized partner
* sexual abstinence;
11. WOCBP must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin) within 72 hours prior to the start of study drug;
12. Peripheral blast count on Cycle 1 Day 1;
13. Able and willing to comply with all study procedures.

Exclusion criteria

Candidates will be excluded from study entry if any of the following exclusion criteria exist:
1. Diagnosis of chronic myelogenous leukemia in blast crisis;
2. Prior hematopoietic stem cell transplantation (this exclusion applies for dose escalation Part 1 and Cohort A of Part 2);For patients in Cohort B of Part 2, prior hematopoietic stem cell transplantation if any of the following applies:
a) transplant within 60 days
b) history of acute GVHD
c) evidence of active chronic GVHD
d) need for immunosuppressive therapy (refer to exclusion criterion #7)
3.
4. Treatment with anticancer medications, investigational drugs or radiotherapy within the following intervals before the first dose of MCLA-117:
a) 14 days or 5 half-lives for anticancer medications or investigational drugs. For agents with long half-lives (e.g., > 5 days), enrollment before the fifth half-life requires medical monitor approval. Note: the concomitant use of hydroxyurea is allowed up to Day 7 (including) during Cycle 1;

b) 14 days for radiotherapy. Note: a 1-week washout period is permitted for palliative radiation to non-CNS disease with Sponsor approval;
5. Previous receipt of live vaccines in the 4 weeks prior to study drug administration (Cycle 1 Day 1);
6. Chronic concurrent need for corticosteroids > 10 mg/day of oral prednisone or the equivalent, except topical preparations (e.g., topical creams, steroid inhaler, nasal spray or ophthalmic solution);
7. Use of immunosuppressant medications within 4 weeks of MCLA-117 administration (Cycle 1 Day 1);
8. Clinically active central nervous system (CNS) leukemia. Patients with CNS leukemia, which is controlled, but who are still receiving intrathecal therapy at study entry may be considered eligible and continue receive IT therapy at the discretion of the Investigator and with agreement of the Sponsor. The CNS leukemia controlled state should have been documented with at least two consecutive negative spinal fluid assessments and with negative imagining studies if previously positive;
9. Patients who are pregnant or lactating;
10. Patients with an active infection or with an unexplained fever greater than 38.5°C during screening visits or on the first scheduled day of dosing. (At the discretion of the investigator, patients with tumor fever may be enrolled; patients with recent infections should have temperature < 38.5°C for at least 48 hours prior to first administration of MCLA-117);
11. Patients with known hypersensitivity to any of the components of MCLA-117 or who have had prior hypersensitivity reactions to human or humanized monoclonal antibodies;
12. Patients with known HIV, hepatitis B or C. Patients who have previously been treated for HCV and have undetectable viral loads, could be considered eligible for the trial;
13. Patients with NYHA Class III or IV congestive heart failure or known left ventricular ejection fraction (LVEF) < 50%, or significant uncontrolled cardiac disease, current diagnosis of unstable angina, uncontrolled CHF, new myocardial infarction, or ventricular arrhythmia requiring medication;
14. Prior malignancy (other than basal cell carcinoma and cervical in situ carcinoma) unless treated with a curative intent and without evidence of malignant disease for 1 year before screening. Patients with prior hematologic malignancies that have progressed to AML (such as MDS, MPN, bi-phenotypic leukemias, ALL) or AML that has relapsed are eligible;
15. Urinary protein >2+ possibly indicative of renal disease. If the 24 hours urine protein shows a result of < 100 mg protein, subject can be eligible;
16. Patients with any other medical or psychological condition deemed by the Investigator to be likely to interfere with a patient's ability to sign informed consent, cooperate and participate in the study, or interfere with the interpretation of the results;
17. WOCBP or males with a WOCB partners not willing to use highly effective and medically accepted methods of contraception for 6 months after last study drug administration (see inclusion criterion #10 for allowed contraceptive methods);

18. Need for concurrent other cytoreductive chemotherapy.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-04-2016
Enrollment:	43
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MCLA-117
Generic name:	MCLA-117

Ethics review

Approved WMO

Date:	15-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	01-03-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date: 05-04-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 11-04-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 26-07-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 28-07-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 04-11-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 07-11-2016

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 13-02-2018

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 20-02-2018

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO
Date: 18-04-2018

Application type: Amendment

Review commission: METC Amsterdam UMC

Approved WMO

Date:	30-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-06-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2015-003704-23-NL
CCMO	NL55829.029.15