# Accuracy Testing of the Chromosomal Aberration and Gene Mutation Markers of the AMLProfiler

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The objective of the study is to demonstrate the accuracy (positive and negative percent agreement) by comparing AMLProfiler results from fresh and banked, AML, APL and RAEB bone marrow samples at multiple participating clinical sites with results...

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Leukaemias |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON57165

**Source**
ToetsingOnline

**Brief title**
AMLProfiler accuracy study

### Condition

- Leukaemias

**Synonym**
Leukemia (Acute Myeloid Leukemia and Acute Promyelocytic Leukemia)

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Skyline Diagnostics B.V.
**Source(s) of monetary or material Support:** Industrie en indirect de overheid

## Intervention

**Keyword:** Accuracy, AMLProfiler, diagnostic, In-vitro

## Outcome measures

### Primary outcome

The positive and negative percent agreement of the AMLProfiler to the reference

result will be calculated for the t(8;21), t(15;17) (APL), inv(16)/t(16;16),

NPM1 mutants (A, B or D) and CEBPA double mutants.

### Secondary outcome

NA

# Study description

### Background summary

Acute myeloid leukemia is a bone marrow malignancy of progenitor cells of the myeloid cell lineage it includes APL (Acute Promyelocytic Leukemia) and MDS which resembles AML, and is the most common type of leukemia in adults. There are multiple varieties of acute myeloid leukemia with characteristic prognosis. Estimated new cases from acute myeloid leukemia (AML) in the western world in 2009 amount to 31.500 cases annually.

The World Health Organization (WHO) classification of AML incorporates and interrelates morphology, cytogenetics, molecular genetics, and immunologic markers as a classification that is universally applicable and prognostically valid. An important part of this classification is based on genetic analysis of the blast cells from the patients. Amongst others, CBFB-MYH11 fusion, AML1-ETO fusion, PML-RARA fusion, NPM1 mutations, and CEBPA mutations are frequent and clinically relevant genetic aberrations in AML and APL .

Molecular classification of AML, APL and MDS patients is performed using gene profiles of bone marrow aspirates collected at the time of diagnosis. Three markers for chromosomal aberrations, one for the detection of CEBPA double mutants, and one for NPM1 mutation detection are included in the AMLProfiler. Collectively these markers allow the identification of inv(16) / t(16;16), t(15;17), t(8;21), NPM1 mutant and CEBPA double mutant cases(see table 2). The incidence of these aberrations and mutations in the patient population are

summarized below.

Incidence rate of genetic aberrations involved in AML and APL
t(8;21): 8 % Prevalentie
t(15;17): 5 - 10 % Prevalentie
inv(16)/t(16;16): 5 - 10 % Prevalentie
NPM1 mutanten (A, B or D): 25 - 40 % Prevalentie
CEBPA dubbel mutanten: 4 - 5 % Prevalentie

Intended use of the AMLprofiler assay:
The AMLProfiler assay is a qualitative in vitro diagnostic test for the detection of AML,APL and RAEB specific chromosomal aberrations (specific recurrent translocations and inversions), as well as expression of specific genetic markers in RNA extracted from bone marrow aspirates of patients with Acute Myeloid Leukemia. The results of the AMLProfiler assay may be used to aid in the diagnosis or the assessment of prognosis of AML, APL and RAEB.

Markers associated with the AMLProfiler are:
Chromosomal abberations: t(8;21), t(15;17) en inv(16) / t(16;16)
Mutations: CEBPA gen (dubbel mutaties), NPM1 gen
Gene expression: BAALC, EVI1

The AMLProfiler is intended for professional use only. For in vitro diagnostic use.

**Study objective**

The objective of the study is to demonstrate the accuracy (positive and negative percent agreement) by comparing AMLProfiler results from fresh and banked, AML, APL and RAEB bone marrow samples at multiple participating clinical sites with results from the sequencing reference lab.
The AMLProfiler molecular diagnostic assay also contains expression markers in the array that will be evaluated in the protocol Prognostic value of the Expression Markers of the AMLProfiler, and are not covered in this study.

**Study design**

The design is a comparison study in which AMLProfiler results for the markers t(8;21), t(15;17), inv(16) / t(16;16), CEBPA double mutants and NPM1 mutation will be compared to those obtained using standard sequencing methods generated at the sequencing reference lab.
The positive and negative percent agreement of the AMLProfiler to the molecular result will be calculated using results generated from 109 positive samples for each marker derived from 200 prospective (fresh), uncharacterized bone marrow samples, from 4 participating clinical sites in the EU (3) and US (1) with

additional banked samples (total of 545 samples).

**Study burden and risks**

Problems associated with diagnostic bone marrow aspiration are highly uncommon. Bone marrow punctures may be associated with local discomfort or pain at site of aspiration and infrequently with:
• Bleeding at the sample collection site.
• Local infection at the sample collection site.
There are no potential benefits to the subject

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

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

### Inclusion criteria

1) Newly diagnosed subjects with a cytopathologically confirmed diagnosis of AML, APL, or refractory anemia with excess of blasts (RAEB) according to the WHO 2008 classification prior to start of antileukemic treatment
2)Subjects with a cytopathologically confirmed relapse diagnosis of AML, APL, or refractory anemia with excess of blasts (RAEB) according to the WHO 2008 classification prior to start of antileukemic treatment
3) subjects >= 18 years
4) Written informed consent available

### Exclusion criteria

Subjects who received chemotherapy or hematopoietic stem cell transplantation within 3 months before bone marrow aspiration for PROT-015.

## Study design

### Design

**Study type:** Observational invasive

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

### Recruitment

NL

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| Recruitment status: | Completed |
| Start date (anticipated): | 12-04-2011 |
| Enrollment: | 50 |
| Type: | Actual |

## Ethics review

Approved WMO

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| Date: | 04-02-2011 |

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| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 07-12-2011 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 02-04-2012 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 11-07-2012 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# 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 |
|---|---|
| CCMO | NL31800.078.10 |