# Assessing Overall Survival, Quality of Life, Frailty, Comorbidity Indexes, Healthcare Usage, and Pharmacoeconomics in Elderly Patients with Acute Myeloid Leukemia

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Primary Objective:- To assess and describe Quality of Life throughout a patients treatment trajectorySecondary Objective(s):- To assess and describe how frail unselected real world AML patients are at diagnosis using geriatric screening tools (G8, 6...

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|---|---|
| **Ethical review** | Not approved |
| **Status** | Will not start |
| **Health condition type** | Leukaemias |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON51315

**Source**
ToetsingOnline

**Brief title**
ZEALOUS-AML

### Condition

- Leukaemias

**Synonym**
AML, bloodcancer

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Medisch Centrum Leeuwarden
**Source(s) of monetary or material Support:** Medisch Centrum Leeuwarden

## Intervention

**Keyword:** AML, Frailty, Pharmacoeconomics, Quality of Life

## Outcome measures

### Primary outcome

• Quality of Life reported by patient

• Overall survival

### Secondary outcome

• Rate of Complete Remission or Complete Remission with incomplete count

recovery CR/CRi

• Early Death (30-day mortality)

• Ferrara Criteria treatment advice

• Wheatley Score

• HCT-CI Score

• AML-CM Score

• ECOG Performance Status

• Cytogenetica / molecular risk profile

• ELN classification

• Other parameters necessary for scoring such as eGFR, LDH, RBC, BMI, Albumine,

Serum Creatinine

• Treatment regimen as per 2 weeks after diagnosis

• Healthcare usage such as antibiotic prescription events or receiving blood

transfusion

• Quality of Life as reported posthumous by relatives

A complete list of datapoints collected and how they will be formatted in our research database can be found in the excel file *Databasestructure ZEALOUS-AML*.

# Study description

**Background summary**

Acute myeloid leukemia (AML) is a malignant disease of the bone marrow with a poor prognosis, especially in elderly patients [1][2]. With a year incidence of 3 - 4,5 cases per 100.000 people AML is a rare disease although it is the most frequently diagnosed leukemic disease [3]. As the median age at diagnosis is 68 years, AML at a young age is viewed as a different disease entity [1][2][3]. Patients aged below 65 are commonly treated by intensive induction chemotherapy until remission or remission with minimal residual disease is reached. Remission, if reached, is then consolidated with an allogenic or autologic stem cell transplant. Elderly patients are often times not in a good enough baseline health state to undergo this highly intensive, somewhat risky, and overall expensive treatment trajectory [1][3]. In 2012 and 2015 respectively the Hypomethylating agents Azacitidine and Decitabine were introduced to the market and offer less intensive treatment options for elderly patients [4][5]. Because of this, stratifying de novo AML patients into the follow three groups became common practice: Fit for intensive chemotherapy, not fit for intensive chemotherapy but fit enough for HMA based therapy, and unfit even for HMA based therapy [6]. After a period in which Azacitidine monotherapy was the first choice of treatment for patients deemed ineligible for intensive induction therapy, the combination of Azacitidine AZA with Venetoclax VEN was proven to lead to superior outcomes and has been promoted to first choice of treatment for this patient group in March 2022 [7]. In the near future, multiple other agents currently in phase III clinical trials are expected to make it into treatment guidelines [8][9].
The superiority in terms of OS of the HMA with VEN combination regimens over HMA comes with more side effects, adverse events, nights stayed in the hospital (time toxicity), as well as increasing healthcare costs. It is unknown how Quality of Life (QOL) develops in AML patients under the novel regimens in the real world setting [10]. It would be highly desirable to be able to predict

which patients develop toxicity to better identify patients that might benefit from regimens such as AZA+VEN There are multiple prognostic tools for evaluation of certain conditions and interventions already validated in AML populations (Ferrara criteria, Wheatley Index, HCT-CI, AML-CM, and more being developed) [6][11][12]. It is unknown however how valuable these tools are for aiding clinical decision-making. It is also not well known what other costs -besides the substantial cost of agents such as Venetoclax- the new regimens creates through increases in healthcare usage.

**Study objective**

Primary Objective:
- To assess and describe Quality of Life throughout a patients treatment trajectory

Secondary Objective(s):
- To assess and describe how frail unselected real world AML patients are at diagnosis using geriatric screening tools (G8, 6-CIT) and comorbidity tools (HCT-CI, AML-CM, Ferrara criteria lists, Wheatley Index, Charlson Comorbidity Index CCI)
- To determine of what predictive quality of clinical scoring tools (Ferrara, Wheatley, HCT-CI, AML-CM) are for endpoints such as overall survival, 1-year survival, remission rates, rates of treatment related mortality, and early death (within 30 days)
- To evaluate the potential of the Wheatley Index, the HCT-CI, and the AML-CM for usage as a tool to support choosing between non-intensive chemotherapy and best supportive care in AML
- To analyze how an AML patients QOL changes in respect to time and in respect to treatment regimens
- To quantify healthcare usage (transfusions, antibiotics, other) of elderly patients with AML.
- To evaluate the AZA+VEN regimen from a pharmaco-economical perspective (ICER, price per QALY) by combining the survival-, quality of life-, and healthcare usage data and comparing it to existing data on Azacitidine monotherapy

**Study design**

The ZEALOUS-AML study is a prospective, observational, single-centre, real world study. The investigators are exploring options for collaboration with other STZ hospitals. The inclusion period of the study is 2,5 years (between 01-01-2023 and 31-06-2025). The design was chosen for its real world representativeness, aiming for inclusion of at least 50 patients in the Medisch Centrum Leeuwarden. Assessment of comorbidity scores requires access to a patients full medical history. Quantification of healthcare usage and pharmacoeconomic evaluation require extensive data gathering during a patients trajectory. All datapoints collected are required for the analysis. An interim

pharmacoeconomic analysis may commence as early as when the 15th included patient passed away.

### Study burden and risks

The study is mainly observational in nature with questionnaires for patients (before cycle 1, after cycle 1, after cycle 2, after cycle 4, 6, 8, *) and family (2-4 weeks after death of the patient) being the only interventions. AML patients spend considerable time in the hospital anyways, especially during the first cycle. We deem the risk for patients to be zero and the burden for patients to be acceptable with each questionnaire taking approximately 30 minutes of their time. The burden for the family is potentially significant as they are approached with an optional request in a difficult time of their life, that however only takes 5-15 minutes to answer.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Elderly (65 years and older)

### Inclusion criteria

Patients in the Dutch province of Friesland may present at any of the 4 Frisian Hospitals. Complicated cases such as elderly patients with AML are referred to the MCL. Patients from outside of the province of Friesland are uncommon.

### Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Age upon diagnosis <= 65 years
• Patients diagnosed with APL (t(15;17), WHO 2016)

## Study design

### Design

**Study type:** Observational non invasive

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Health services research |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 100 |
| Type: | Anticipated |

## Ethics review

Not approved

| | |
|---|---|
| Date: | 03-04-2023 |
| Application type: | First submission |
| Review commission: | RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden) |

# 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 | NL83339.099.22 |