Quality of life, Survival, COmorbidities, and Pharmacoeconomics in Elderly patients with Acute Myeloid Leukemia

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We aim to measure quality of life and overall survival in patients with AML classified as ineligible for intensive chemotherapy and get treated with HMA combination regimens in the Medical Centre Leeuwarden. We also aim to determine the predictive...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Observational non invasive

Summary

ID

NL-OMON53259

Source
ToetsingOnline

Brief title
QSCOPE-AML

Condition

- Leukaemias

Synonym
Bloodcancer, Leukeamia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute Myeloid Leukemia, Pharmacoeconomics, Quality of Life

Outcome measures

Primary outcome

Primary Objective:

• To assess how the quality of life develops throughout a patients journey in an unselected real-world population of AML patients treated with HMA combination regimens

Secondary outcome

Secondary Objectives:

• To assess overall survival of AML patients treated with HMA combination regimens in an unselected real-world population

• To calculate remission (CR/CRi/PR) rates

• To calculate event free survival (time between CR and progression of disease PD)

• To calculate rates of early death (ED, death within 30 days after diagnosis)

• To quantify healthcare usage (length of hospital stay, number of bonemarrow analysis, amount of transfusion usage, number of days under anti-infective treatment)

• To evaluate HMA combination regimens pharmaco-economically by calculating gained QALYs, price per gained QALY, and the ICER of the combination regimens compared against HMA monotherapy

Exploratory Objectives:

• To explore and describe how frail unselected real-world AML patients are at diagnosis using geriatric screening tools (G-8, 6CIT) and comorbidity tools (HCT-CI, AML-CM, Ferrara criteria lists, Wheatley Index, Charlson Comorbidity Index CCI)

• To explore which baseline characteristics such as patient priorities and results of clinical scoring tools (Ferrara, Wheatley, HCT-CI, AML-CM) predict overall survival, 1-year survival, remission rates, rates of treatment related mortality, and rates of ED best

• To explore how much time patients spend in the hospital (planned / unplanned, during first 2 cycles / during rest of treatment trajectory, under various regimens)

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 [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 with 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 rarely in a good enough baseline health state to undergo this highly intensive, somewhat dangerous, and overall expensive treatment trajectory [1][3]. In 2012 and 2015 respectively the hypomethylating agents Azacitidine AZA and Decitabine DEC were introduced to the market and offer less intensive treatment options for these elderly patients [4][5]. Because of this, stratifying de novo AML patients into the following three groups by the so called Ferrara-criteria 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 HMA monotherapy was the first choice of treatment for patients deemed ineligible for intensive induction therapy, the combination of

a HMA 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]. Combination of a HMA with Ivosidenib in patients with a specific cytogenetic lesion has proven even superior to HMA+VEN, but remains a 2nd line of treatment for now [8]. In the near future, a multitude of other agents, currently in phase III clinical trials, are expected to make it into treatment guidelines [8][9][10]. All of these agents have in common that they are researched as additions to either an HMA or even HMA+VEN backbone. These HMA based combination regimens are expected to become the main weapons in the therapeutic arsenal for AML as they seem to improve survival when compared against HMA monotherapy. In the clinical trials investigating these regimens, QOL questionnaires such as the EORTC-QLQ-C30 are commonly collected. Results of this data are however often left unpublished or are only published years later and in lower impact factor journals. Real world experience in the MCL with for example the AZA+VEN regimen points towards a noticeable increase in treatment intensity as patients spend more time in the hospital, undergo more bonemarrow analysis, etc. Data from phase III clinical trials point towards noticeable increases in treatment toxicity (side effects & adverse events) [7][8][9][10][11]. Overall a negative effect on QOL seems plausible. Data of a patients* health state before and at diagnosis can be predictive of outcomes such as survival and quality of life. Such data may include patient related factors such as performance status and comorbidity profile, as well as disease related factors such as mutation profile and bloodvalues. Multiple attempts have been made in the past to construct prognostic tools for various groups of AML patients (Wheatley Index, HCT-CI, AML-CM, ALFA1200, Liu-Index) [6][12][13][14][15][16][17][18]. Being able to predict which patients do or do not develop serious adverse events or decreases in quality of life may aid in identifying patients that may benefit more or may benefit less from HMA combination regimens. The first HMA combination regimen that achieved approval for reimbursement for treatment of AML in the Netherlands is HMA+VEN. The evaluation of novel agents or regiments through the Zorginstituut Nederland ZIN include a detailed pharmacoeconomic model, attempting to quantify both benefits as well as costs. In the case of HMA+VEN, quality of life was calculated based upon the proportional shortfalls method, estimating that the average AML patient loses 8,39 QALYs through the disease [19]. Furthermore they estimate that HMA+VEN will result in a gain of 1,72 QALYs compared to the 0,75 QALYs gained by HMA monotherapy. The data for the HMA+VEN intervention for this model comes solely from patent holder AbbVie. Furthermore, the commencing cost effectiveness calculations are lacking in respect to quantification of time spend in the hospital, and transfusion burden. Therefore it is deemed of high interest to recalculate the QALY data based upon real-world survival and quality of life data, as well as to recalculate the ICER of the HMA+VEN regimen against HMA monotherapy while including prospectively measured additional costs in the form of healthcare consumption (such as transfusion usage and length of hospital stay). For this purpose we aim to measure baseline characteristics, quality of life, healthcare consumption, and survival prospectively in an unselected real-world population of elderly AML patients treated with HMA

combination regimens.

Study objective

We aim to measure quality of life and overall survival in patients with AML classified as ineligible for intensive chemotherapy and get treated with HMA combination regimens in the Medical Centre Leeuwarden. We also aim to determine the predictive potential of various comorbidity indexes and clinical tools for assessing a patients* health state on outcomes such as their survival. Furthermore we aim to gather data on healthcare consumption so that insights into survival, quality of life, and costs can be combined into a pharmacoeconomic analysis of the novel regimens.

Study design

The QSCOPE-AML study is a prospective, observational, single-centre, real world study. All de novo AML patients aged 65 or older that are classified as *not eligible for intensive chemotherapy* by the list 1 of the Ferrara criteria or by assessment of their haematologist and are treated with a HMA combination regimen in the Medical Centre Leeuwarden are included in the study. Patients are approached for participation in the study by the researchers with a patient information leaflet PIL and an informed consent form is signed. Patients are followed prospectively until either loss-to-follow-up or death. The EQ-5D-5L, EORTC-QLQ-C30 and FACIT questionnaires are taken before start of chemotherapy and again after 2, 4, 8, 12, 18, and 24 months. The patients priority questionnaire is taken once before start of chemotherapy. For assessing baseline characteristics and comorbidity scores the patients* medical history the EHR/EPD is reviewed. Time spend in the hospital (planned, unplanned, consultations, nights) is measured per cycle of chemotherapy starting from diagnosis. Transfusion dependence is measured cumulatively over the intervals 0-2, 2-4, 4-8, 8-12, 12-18, and 18-24 months.

Study burden and risks

Patients are approached with the following four questionnaires:
• The general 5 item EQ-5D-5L
• The fatigue focussed 7 item PROMIS-7SFa
• The cancerspecific 30 item EORTC-QLQ-C30
• The question to order 4 possible treatment goals by importance

After inclusion, patients are approached with all 4 questionnaires. For all items of the EQ-5D, PROMIS, and EORTC questionnares patients are asked to rate their life/health now and 1 month prior to diagnosis. For this initial measurement 45 minutes are deemed realistic.

2, 4, 8, 12, 18, and 24 month after diagnosis patients are approached again

with the EQ-5D, PROMIS, and EORTC questionnaires. All 42 questions (5+7+30) are of shot and definitive character and have between 4 and 7 (commonly 5) answering options. The researchers deem 30 minutes per measurement per patient a realistic estimate of timeburden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

• Patient is diagnosed with de novo AML [ICD-10 = C92]
• Patient is treated in the Medical Centre Leeuwarden
• Age upon diagnosis >= 65 years
• Patient is classified as *ineligible for intensive chemotherapy* by the list 1 of the Ferrara criteria or by consideration from the practising haematologist
• Patient receives treatment in the form of a HMA combination regimen

• Patient provides a signed Informed Consent Form

Exclusion criteria

• Bonemarrow analysis did not confirm AML
• Patients diagnosed with APL (t(15;17), WHO 2016) [ICD-10 = C92.4]
• Patients diagnosed with AMML (AML M4 / AML-M4eos) [ICD-10 = C92.5]
• Patients diagnosed with AMBL/AMCL (AML M5 / M5a / M5b) [ICD-10 = C93]

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-10-2023
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	07-08-2023
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	NL85106.099.23