QPiAML 2020 study

Published: 17-09-2020
Last updated: 13-01-2025

A higher percentage of patients with MRD levels <0.1% (MRD negativity) after up to 2 courses of induction chemotherapy plus quizartinib, as measured in the bone marrow using MFCM before start of consolidation therapy, compared to a historical...

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON19921

Source
NTR

Brief title
QPiAML 2020

Health condition

Newly diagnosed, de novo AML with FLT3-ITD and wild-type NPM1

Sponsors and support

Primary sponsor: Prinses Máxima Centrum voor Kinderoncologie
Source(s) of monetary or material Support: Pharmaceutical company

Intervention

Outcome measures

Primary outcome

Primary endpoint: The percentage of patients with MRD levels <0.1% (MRD negativity) after up to 2 courses of induction chemotherapy plus quizartinib, as measured in the bone marrow using MFCM before start of consolidation therapy, in the full analysis population. Primary

endpoint safety run-in: The number of patients with DLTs prior to start of consolidation chemotherapy, in the first 6 patients evaluable for the safety run-in (as defined above).

Secondary outcome

Secondary endpoints: - Other measures of treatment response: o bone marrow blast counts by morphology and MFCM after course #1 and #2 and before allo-SCT; CRc (CR and CRi) and morphologic leukemia-free state (MLFS) rates after course #1 and #2; MRD negativity after course #1 and #2 and before allo-SCT; absolute MRD levels after course #1 and #2, and before allo-SCT; o DFS probability, at least at 1, 2 and 3 years o EFS probability, at least at 1, 2 and 3 years o CIR probability, at least at 1,2 and 3 years o OS probability, at least at 1, 2 and 3 years - Number and percentage of patients actually being treated with an allo-SCT - Toxicity as graded by NCI CTCAE version 5.0 - Acceptability including palatability of quizartinib, as determined by a questionnaire - Population PK analysis to estimate AUC(tau) and Cmax for quizartinib and AC886, and clearance (CL/F) and volume of distribution (Vss/F) for quizartinib

Study description

Background summary

This will be a single-arm, open label, multinational, multicenter phase II study, with a safety run-in, to assess the clinical benefit of quizartinib as measured by the MRD-negativity rate (defined as <0.1%) after up to two courses of conventional chemotherapy plus quizartinib, in newly diagnosed pediatric de novo AML with a FLT3-ITD and without a concurrent NPM1 mutation. Quizartinib will be administered in between courses of chemotherapy and for 12 x 28-day cycles after allo-SCT (or after 3 cycles of consolidation, in patients unable to receive allo-SCT) as continuation treatment.

Study objective

A higher percentage of patients with MRD levels <0.1% (MRD negativity) after up to 2 courses of induction chemotherapy plus quizartinib, as measured in the bone marrow using MFCM before start of consolidation therapy, compared to a historical cohort.

Study design

Primary outcome MRD negativity after 2 courses of induction therapy is measured at screening, end of course 1 (day 29-56), and end of course 2 (day 29-56). For time points of secondary outcomes please refer to the protocol, as this is extensively described in this document.

Intervention

Quizartinib will be administered in between courses of chemotherapy and for 12 x 28-day cycles after allo-SCT (or after 3 cycles of consolidation, in patients unable to receive allo-SCT) as continuation treatment.

Contacts

Public
Prinses Máxima Centrum voor Kinderoncologie
Anne Elsinghorst

06 5000 62 70
Scientific
Prinses Máxima Centrum voor Kinderoncologie
Anne Elsinghorst

06 5000 62 70

Eligibility criteria

Inclusion criteria

For the quizartinib study, patients are eligible if they fulfill the inclusion criteria below, initial work-up as described below is done before start of chemotherapy or quizartinib (depending on item), and none of the exclusion criteria applies. However, they can actually enroll in the quizartinib study until day 12 from start of induction course 1, knowing that status of FLT3 and NPM1 must be known before they can be enrolled on this study. Initial work-up: • Complete initial work-up within 14 days prior to start of quizartinib, including bone-marrow aspiration, assessment of organ function including cardiac function (ultrasound and ECG). A (diagnostic and therapeutic) lumbar puncture with intrathecal therapy is normally done on day 6 of treatment according to this protocol, but if done earlier will not be considered a protocol violation. General conditions: • newly diagnosed, de novo AML with FLT3-ITD and wild-type NPM1 • ≥1 month and ≤ 18 years old at initial diagnosis • Life expectancy > 6 weeks • Calculated creatinine clearance ≥ 50 ml/min/1.73m2 as calculated by the Schwartz formula for estimated glomerular filtration rate (GFR) where GFR (ml/min/1.73 m2) = k*Height (cm)/serum creatinine (mg/dl). k is a proportionality constant which varies with age and is a function of urinary creatinine excretion per unit of body size; 0.45 up to 12 months of age; 0.55 children and adolescent girls; and 0.70 adolescent boys. • Liver function: Serum bilirubin ≤5 × upper limit of normal (ULN) Aspartate transaminase (AST)/alanine transaminase (ALT) ≤10×ULN Other: • Able to comply with scheduled follow-up and with management of toxicity • For female patients with childbearing potential, a test for pregnancy is to be done before start of quizartinib, and to be confirmed as negative every 3

months • Male and female patients must use an highly effective contraceptive method during the study and for a minimum of 6 months after study treatment, as per Clinical Trial Facilitation Group (CTFG) recommendations • Written informed consent/assent from patients and/or from parents or legal guardians for minor patients, according to local law and regulations

Exclusion criteria

General conditions: • Secondary AML • Isolated extramedullary disease • Acute promyelocytic leukemia (APL) • Myeloid leukemia of Down Syndrome (ML-DS) • Other serious illnesses or medical conditions, that will likely make it impossible to complete treatment according to protocol • Evidence of cardiac dysfunction (shortening fraction below 28% and/or QTc >500 ms) • Pregnant or lactating patients Concomitant treatments: Concomitant administration of any other experimental drug under investigation, or concurrent treatment with any other anti-cancer therapy other than specified in the protocol is not allowed. G-CSF will not be used for priming and no routine G-CSF support is allowed in between courses, except for life-threatening infections. Live vaccines within 30 days prior to study start, during the study, and for three months after last dose of chemotherapy or allo-SCT, whichever is latest, is not allowed.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2021
Enrollment:	60
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Not applicable
Application type: Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 53580
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8916
CCMO	NL82495.041.22
OMON	NL-OMON53580

Study results