Trial record **1 of 1** for: AMLSG26-16/AML-ViVA

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Low-dose AZA, Pioglitazone, ATRA Versus Standard-dose AZA in Patients >=60 Years With Refractory AML (AML-ViVA)

ClinicalTrials.gov Identifier: NCT02942758

Recruitment Status : Recruiting
First Posted : October 24, 2016
Last Update Posted : May 4, 2017

See **Contacts and Locations**

Sponsor:
University Hospital Regensburg

Collaborators:
Anticancer Fund, Belgium
Celgene

Information provided by (Responsible Party):
Simone Thomas, University Hospital Regensburg

Study Description

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Brief Summary:

Diagnosis: Acute myeloid leukemia refractory to intensive induction chemotherapy; Age ≥ 60 years, no upper age limit; Study drug: low-dose azacitidine, pioglitazone, ATRA; Safety Run-In Phase; randomized Phase II, open-label

- Safety Run-In Phase: Based on a 3 + 3 modified design, the tolerable dose of ATRA for the randomized phase II is defined.
- Phase II: Experimental Arm: low-dose azacitidine, pioglitazone, ATRA; Standard Arm: standard-dose azacitidine; in both arms patients can receive further cycles (with no limit to the number given) as long as clinically appropriate

Condition or disease	Intervention/treatment	Phase
Acute Myeloid Leukemia	Drug: low-dose Azacitidine Drug: Pioglitazone Drug: ATRA Drug: standard-dose AZA	Phase 2

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	94 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Randomized Phase II Trial With Safety run-in Phase Evaluating Low-dose AZA, ATRA and Pioglitazone Versus Standard Dose Azacitidine in Patients >=60 Years With AML Who Are Refractory to Standard Induction Chemotherapy
Actual Study Start Date :	April 10, 2017
Estimated Primary Completion Date :	February 2020
Estimated Study Completion Date :	February 2020

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics:
- Core binding factor acute myeloid leukemia
- Cytogenetically normal acute myeloid leukemia
- Familial acute myeloid leukemia with mutated CEBPA

MedlinePlus related topics: Acute Myeloid Leukemia

Drug Information available for: Azacitidine Pioglitazone Pioglitazone hydrochloride

Genetic and Rare Diseases Information Center resources: Myeloid Leukemia
- Acute Myeloid Leukemia
- Acute Non Lymphoblastic Leukemia

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: low-dose AZA / ATRA / Pioglitazone low-dose azacitidine (75 mg/d), ATRA, pioglitazone	Drug: low-dose Azacitidine Azacitidine 75 mg/d s.c. for 7 days, repeated 28-day treatment cycle Other Name: Vidaza Drug: Pioglitazone Pioglitazone 45 mg p.o. continuously from day 1 Other Name: Actos Drug: ATRA ATRA *45 mg/m² p.o. from day 1 to 28, 15 mg/m² from day 29 continuously; *this regimen will be chosen for the first dose to be evaluated. Other Name: All-trans-retinoic acid; Vesanoid
Active Comparator: standard-dose AZA standard-dose azacitidine (75mg/m²/d)	Drug: standard-dose AZA Azacitidine 75 mg/m²/d s.c. for 7 days, repeated 28-day treatment cycle Other Name: Vidaza

Outcome Measures

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Primary Outcome Measures :

1. overall Survival [Time Frame: 3 years]

Secondary Outcome Measures :

1. complete remission (CR) rate [Time Frame: 3 years]
2. complete remission with incomplete blood count recovery (CRi) rate [Time Frame: 3 years]
3. partial remission (PR) rate [Time Frame: 3 years]
4. hematological improvement (HI) rate [Time Frame: 3 years]
5. cumulative incidence of relapse (CIR) [Time Frame: 3 years]
6. cumulative incidence of death (CID) [Time Frame: 3 years]
7. cumulative incidence of relapse event free survival (EFS) [Time Frame: 3 years]
8. event free survival (EFS) [Time Frame: 3 years]
9. Quality of Life (QLQ-C30) [Time Frame: 3 years]
10. Incidence and intensity of adverse events (AEs) [Time Frame: 3 years]

Eligibility Criteria

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Information from the National Library of Medicine NIH NLM

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	60 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Patients with confirmed diagnosis of acute myeloid leukemia (AML) who are refractory* to induction therapy and not eligible for further intensive induction therapy based on documented medical reasons (e.g. disease characteristics or patient characteristics), or
2. Patients with confirmed diagnosis of acute myeloid leukemia (AML) who are refractory* to induction therapy and not immediate candidates for allogeneic HSCT (bridge to transplant is allowed)

   *refractory to induction therapy is defined as no CR, no CRi and no PR (according to standard criteria, see Section 11.2.3) after at least one intensive induction therapy including at least 5 days of cytarabine 100-200 mg/m² continuously or an equivalent regimen with cytarabine with total dose not less than 500 mg/m² per cycle and at least 2 days of an anthracycline (e.g. daunorubicin, idarubicin).
3. Age ≥ 60; no upper age limit
4. ECOG performance status of ≤ 2 at screening
5. To control hyperleukocytosis or extramedullary involvement, medication with hydroxyurea is allowed up to 24h before start of study treatment. In case of hyperleukocytosis hydroxyurea should be given and start of study treatment should be delayed until leukocyte counts are < 20 x 10^9/L.
6. Female subjects of childbearing potential* may participate, providing they meet the following conditions:
   - Have a negative pregnancy test (serum or urine with a sensitivity of at least 25 mIU/mL; local laboratory) within 72 hours prior to starting study therapy. They must agree to ongoing pregnancy testing during the course of the study, and after end of study therapy. This applies even if the subject practices true abstinence** from heterosexual contact.
   - Agree to practice true abstinence** from heterosexual contact (which must be reviewed on a monthly basis) or agree to use, and be able to comply with two effective methods of contraception (e.g., oral, injectable, or implantable hormonal contraceptive; tubal ligation; intra-uterine device; barrier contraceptive with spermicide; or vasectomized partner) without interruption during the study therapy (including dose interruptions), and for 3 months after discontinuation of study drugs.
     - A female subject of childbearing potential (FCBP) is a female who: 1) has achieved menarche at some point 2) has not undergone a hysterectomy or bilateral oophorectomy or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for

at least 24 consecutive months (ie, has had menses at any time in the preceding 24 consecutive months).

- True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (eg, calendar, ovulation, symptothermal, postovulation methods) and withdrawal are not acceptable methods of contraception.

7. Male patients with a female partner of childbearing potential must agree to abstain from sexual intercourse or to the use of at least two effective contraceptive methods (e.g., synthetic condoms with spermicide, etc) at screening and throughout the course of the study and should avoid fathering a child during the course of the study and for 3 months following the last study treatment.
8. Signed written informed consent.

Exclusion Criteria:

1. Known or suspected hypersensitivity to the study drugs and/or any excipients
2. Patients with acute promyelocytic leukemia exhibiting t(15;17)(q22;q12); PML-RARA, or with variant translocations
3. Acute myeloid leukemia (AML) with isocitratdehydrogenase (IDH) 1 or 2 mutations if results are available from the central AMLSG reference laboratories
4. ECOG performance status > 2
5. Inadequate cardiac, hepatic and/or renal function at Screening Visit defined as:
    1. heart failure NYHA II-IV
    2. unstable angina pectoris
    3. total bilirubin, ALT, AST > 2.5 x upper normal serum level
    4. Creatinine > 1.5 x upper normal serum level
6. Active central nervous system involvement
7. Uncontrolled infection
8. Uncontrolled diabetes mellitus
9. Patients with a "currently active" second malignancy requiring active therapy other than non-melanoma skin cancers (except for hormonal/antihormonal treatment, e.g. in prostate or breast cancer)
10. Patients with "currently active" bladder cancer or bladder cancer in their history, patients with risk factors for bladder cancer (e.g. exposure to aromatic amines or heavy tobacco smoker), or macrohematuria of unknown origin
11. Severe neurological or psychiatric disorder interfering with ability of giving an informed consent

12. Known or suspected active alcohol or drug abuse
13. Known positive for HIV, active HBV or HCV infection
14. No consent for registration, storage and processing of the individual disease characteristics and course as well as information of the family physician and/or other physicians involved in the treatment of the patient about study participation.
15. Treatment with any other clinical study drug within 14 days before the first administration of the investigational drugs or at any time during the study
16. Breast feeding woman or women with a positive pregnancy test at Screening Visit
17. Male patients with a female partner of childbearing potential not willing to abstain from sexual intercourse or to the use of at least two effective contraceptive methods (e.g., synthetic condoms with spermicide, etc) at screening and throughout the course of the study and for 3 months following the last study treatment.

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02942758***

Contacts

Contact: Simone Thomas, PD Dr. +49-941-9440 simone.thomas@ukr.de

Locations

Germany

University Hospital Regensburg **Recruiting**
Regensburg, Germany, 93053

Sponsors and Collaborators

University Hospital Regensburg

Anticancer Fund, Belgium

Celgene

Investigators

Principal Investigator: Simone Thomas, Dr. University Hospital Regensburg

More Information

Go to

Responsible Party:	Simone Thomas, Dr. med., University Hospital Regensburg
ClinicalTrials.gov Identifier:	NCT02942758 History of Changes
Other Study ID Numbers:	**AMLSG26-16**
First Posted:	October 24, 2016 Key Record Dates
Last Update Posted:	May 4, 2017
Last Verified:	May 2017

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Undecided

Studies a U.S. FDA-regulated Drug Product:	No
Studies a U.S. FDA-regulated Device Product:	No

Additional relevant MeSH terms:

Leukemia, Myeloid, Acute	Physiological Effects of Drugs
Leukemia, Myeloid	Antimetabolites, Antineoplastic
Leukemia	Antimetabolites
Neoplasms by Histologic Type	Molecular Mechanisms of Pharmacological
Neoplasms	Action
Pioglitazone	Antineoplastic Agents
Azacitidine	Enzyme Inhibitors
Tretinoin	Keratolytic Agents
Hypoglycemic Agents	Dermatologic Agents