A Phase 3, Multicenter, Open-label, Randomized Study of SGI-110 versus Treatment Choice (TC) in Adults with Previously Untreated Acute Myeloid Leukemia (AML) Who Are Not Considered Candidates for Intensive Remission Induction Chemotherapy

Published: 02-04-2015
Last updated: 14-04-2024

To assess and compare efficacy (complete response [CR] rate and overall survival [OS]) between SGI-110 and TC in adults with previously untreated AML who are not considered candidates for intensive remission induction chemotherapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON45193

Source
ToetsingOnline

Brief title
SGI-110-04

Condition

- Leukaemias

Synonym
blood- and bone marrow cancer

Research involving
Human

Sponsors and support

Primary sponsor: Astex Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Astex Pharmaceuticals;Inc.

Intervention

Keyword: acute Myeloid Leukemia, open-label, randomized, treatment choice

Outcome measures

Primary outcome

Co-primary Endpoints

* CR rate based on modified International Working Group (IWG) 2003 AML Response Criteria.

* OS, defined as the number of days from randomization to death.

Secondary outcome

Secondary Endpoints

* Composite CR rate (CRc = CR + Complete response with incomplete blood count recovery [CRi] + Complete response with incomplete platelet recovery [CRp])

* Number of days alive and out of the hospital.

* Progression-free survival (PFS), defined as the number of days from randomization to disease progression or death, whichever occurs first.

* Number of red blood cell (RBC) or platelet transfusions (units) over the duration of the study treatment.

* Health-related quality of life (QOL) by EQ-5D (consisting of the EQ-5D-5L descriptive system and the EQ Visual Analogue Scale [EQ VAS]).

* Duration of CR, defined as the time from first CR to time of relapse.

* Incidence and severity of adverse events (AEs).

* 30- and 60-day all-cause early mortality.

Study description

Background summary

See page 16 of the protocol, section 1.0 Introduction and Background

Study objective

To assess and compare efficacy (complete response [CR] rate and overall survival [OS]) between SGI-110 and TC in adults with previously untreated AML who are not considered candidates for intensive remission induction chemotherapy.

Study design

This is a phase 3, multicenter, randomized, open-label study of SGI-110 versus Treatment Choice (TC). Blinded central reading of marrow and disease response will be performed.
Approximately 800 subjects from approximately 100-160 study centers will be randomly assigned (1:1) to 1 of 2 groups:
* SGI-110: 60 mg/m2 SGI-110 given SC daily for 5 days (Days 1-5) in 28-day cycles.
* Treatment Choice: subjects will be assigned (before randomization) by the investigator to 1 of the following treatment regimens:
* 20 mg cytarabine given SC BID on Days 1-10 every 28 days.
* 20 mg/m2 decitabine given IV on Days 1-5 every 28 days.
* 75 mg/m2 azacitidine given IV or SC on Days 1-7 every 28 days.

Data will be reviewed by an independent Data Monitoring Committee (DMC) at regular intervals primarily to evaluate safety during study conduct.

Intervention

* SGI-110: 60 mg/m2 SGI-110 given SC daily on Days 1-5 in 28-day cycles. Treatment should be given for at least 6 cycles in the absence of unacceptable toxicity or disease progression requiring alternative therapy. Beyond 6 cycles, treatment should continue as long as the subject continues to benefit based on investigator judgment.

* TC: before randomization, subjects will be assigned by the investigator to 1

of the following treatment regimens (dose, schedule, and administration route; other treatment parameters, such as duration of treatment and dose adjustment guidelines, should follow locally approved prescribing information and institutional standard practice):
- 20 mg cytarabine given SC BID on Days 1-10 every 28 days.
- 20 mg/m2 decitabine given IV on Days 1-5 every 28 days.
- 75 mg/m2 azacitidine given IV or SC on Days 1-7 every 28 days.

Study burden and risks

Procedure-Related Risks or Discomforts

Subcutaneous Injection (SGI-110, cytarabine, and azacitidine):
Subcutaneous (SC) injection (when the drug is injected just under the skin) may cause local pain, bruising, redness, swelling, or infection.

Intravenous Injection (decitabine and azacitidine):
Intravenous (IV) injection (when the drug is injected into a vein) may cause local pain, bruising, or infection.

Blood Collection:
Blood will be collected at certain times during the study. Possible side effects of blood collection are tenderness, pain, bleeding, bruising, infection at the site where the needle goes into the skin, nausea, or feeling lightheaded.

Bone Marrow Collection:
A bone marrow collection is done once before the patient start treatment and may be repeated to see how the disease is doing and how the patient is responding to the study treatment. A large needle is inserted through the skin until it reaches the bone. Then, with a twisting motion, the needle is inserted through the hard outer layer of the bone and into the marrow. Once the needle is in the marrow, a syringe is attached and used to suck out some liquid bone marrow. If a biopsy is needed, a slightly larger needle is used in a similar manner. For both procedures, anesthetic medicine is injected to numb the area. After the needle is taken out, the patient might be asked to lie flat for 5-10 minutes and to put pressure over the site where the needle went in. After that, if there is no bleeding, the patient can resume normal activities.
The patient may have stinging or burning when the anesthetic is injected, pain when marrow is withdrawn, and soreness or redness or both at the site. Side effects the patient might have are fever, bleeding, swelling, or infection.

Electrocardiogram (ECG):
There may be some pulling on the patient's skin or irritation when the adhesive patches are removed.

The side effects of SGI-110, decitabine, cytarabine and azacitidine are

described in the patient information and informed consent form.

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. Able to understand and comply with study procedures, and provides written informed consent before any study-specific procedure.
2. Cytologically or histologically confirmed diagnosis of AML (except M3 acute promyelocytic leukemia) according to the 2008 World Health Organization (WHO) classification (bone marrow or peripheral blood blast counts *20%).
3. Performance status (ECOG) of 0-3.
4. Adults with previously untreated AML except for hydroxyurea or corticosteroids. Prior hydroxyurea or lenalidomide treatment for myelodysplastic syndrome (MDS) is allowed.
5. Not considered candidates for intensive remission induction chemotherapy at time of

enrollment based on
EITHER:
a. *75 years of age
OR
b. <75 years of age with at least 1 of the following:
i. Poor performance status (ECOG) score of 2-3.
ii. Clinically significant heart or lung comorbidities, as reflected by at least 1 of:
1) Left ventricular ejection fraction (LVEF) *50%.
2) Lung diffusing capacity for carbon monoxide (DLCO) *65% of expected.
3) Forced expiratory volume in 1 second (FEV1) *65% of expected.
4) Chronic stable angina or congestive heart failure controlled with medication.
iii. Liver transaminases >3 × upper limit of normal (ULN).
iv. Other contraindication(s) to anthracycline therapy (must be documented).
v. Other comorbidity the investigator judges incompatible with intensive remission induction chemotherapy, which must be documented and approved by the study medical monitor before
randomization.
6. Creatinine clearance as estimated by the Cockroft-Gault (C-G) or other medically acceptable formulas *30 mL/min.
7. Women of child-bearing potential must not be pregnant or breastfeeding and must have a negative pregnancy test at screening. Women of child-bearing potential and men with female partners of child-bearing potential must agree to practice 2 highly effective contraceptive measures during the study and for at least 3 months after completing treatment and must agree not to become pregnant or father a child while receiving treatment with SGI-110 and for at least 3 months after completing treatment.

Exclusion criteria

1. Candidate for intensive remission induction chemotherapy at the time of enrollment.
2. Candidate for best supportive care only, ie, not a candidate for any active therapy with the TC comparators.
3. Known extramedullary central nervous system (CNS) AML.
4. Second malignancy currently requiring active therapy except breast or prostate cancer stable on or responding to endocrine therapy.
5. Prior treatment with decitabine or azacitidine.
6. Hypersensitivity to decitabine, azacitidine, cytarabine, SGI-110, or any of their excipients.
7. Treated with any investigational drug within 2 weeks of the first dose of study treatment.
8. Total serum bilirubin >2.5 × ULN, except for subjects with Gilbert's Syndrome for whom direct bilirubin is <2.5 × ULN, or liver cirrhosis or chronic liver disease Childs-Pugh B or C.
9. Known active human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) infection. Inactive hepatitis carrier status or low viral hepatitis titer on antivirals is allowed.
10. Known significant mental illness or other condition such as active alcohol or other substance abuse or addiction that, in the opinion of the investigator, predisposes the subject to high risk of noncompliance with the protocol.

11. Refractory congestive heart failure unresponsive to medical treatment; active infection resistant to all antibiotics; or advanced pulmonary disease requiring >2 liters per minute (LPM) oxygen.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-04-2016
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dacogen
Generic name:	Decitabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Depocyt
Generic name:	Cytarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	NA

Generic name:	Sodium (2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1(2H)-yl)-2-(hydroxymethyl)tetrahydrofuran-3-yl ((2
Product type:	Medicine
Brand name:	Vidaza
Generic name:	Azacitidine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-12-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	03-11-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	01-02-2017
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	04-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
EudraCT	EUCTR2014-001233-89-NL
ClinicalTrials.gov	NCT02348489
CCMO	NL51836.041.15