A Study to Evaluate Imetelstat (JNJ-63935937) in Transfusion-Dependent Subjects with IPSS Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS) that is Relapsed/Refractory to Erythropoiesis-Stimulating Agent (ESA) Treatment

Published: 03-11-2015
Last updated: 21-09-2024

This study has been transitioned to CTIS with ID 2024-511348-25-00 check the CTIS register for the current data. Part 1: To evaluate the efficacy and safety of imetelstat in transfusion dependent subjects with low or intermediate-1 risk MDS that is...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON54841

Source
ToetsingOnline

Brief title
63935937MDS3001 / IMerge

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
myelodysplasia, Myelodysplastic Syndrome (MDS)

Research involving
Human

Sponsors and support

Primary sponsor: Geron Corporation
Source(s) of monetary or material Support: door de verrichter

Intervention

Keyword: # Imetelstat, # Myelodysplastic Syndrome, # Relapsed/Refractory to ESA Treatment, # Transfusion-Dependent

Outcome measures

Primary outcome

The (primary) hypothesis is that imetelstat will improve the rate of RBC TI

(transfusion independence) as compared to placebo in transfusion dependent

subjects with low or intermediate-1 risk MDS that is relapsed/refractory to ESA

treatment.

The primary efficacy endpoint is the rate of RBC TI lasting at least 8 weeks.

The 8-week RBC TI rate is defined as the proportion of subjects without any RBC

transfusion during any consecutive 8 weeks starting from Study Day 1.

Secondary outcome

Secondary Objectives (For Part 1 and Part 2)

• To assess the safety of imetelstat in subjects with MDS

• To assess the time to RBC TI and duration of RBC TI

• To assess the rate of hematologic improvement

• To assess the rates of complete remission (CR), partial remission (PR), or

marrow complete remission (mCR)

• To assess overall survival (OS)

• To assess progression free survival (PFS)

• To assess time to progression to acute myeloid leukemia (AML)

• To assess the rate and amount of supportive care, including transfusions and myeloid growth factors (Part 2 only)

• To evaluate the pharmacokinetics and immunogenicity of imetelstat in subjects with MDS

• To assess the effect of imetelstat treatment on patient-reported outcomes (PROs)

• To assess the effect of treatment on medical resource utilization (Part 2 only)

• To assess the effect of imetelstat on corrected QT (QTc) interval in subjects in the Ventricular Repolarization substudy (to be reported separately from Part 2)

Study description

Background summary

IImetelstat (GRN163L) is a covalently-lipidated 13-mer thiophosphoramidate oligonucleotide that acts as a potent specific inhibitor of telomerase. Telomerase inhibition leads to loss of a cancer cell*s ability to maintain telomere length (TL), resulting in cell-cycle arrest, apoptosis, or senescence. Imetelstat binds with high affinity to the template region of the ribonucleic acid (RNA) component of human telomerase reverse transcriptase (hTERT) and is a competitive inhibitor of telomerase enzymatic activity.2,24 Treatment of various cancer cells with imetelstat in vitro increases their sensitivity to radiation, decreases their clonogenic potential, and results in altered expression of stem-cell related genes. Clinical data in a small number of MDS subjects further indicate that treatment with imetelstat resulted in transfusion independence and other measures of hematologic improvement.

Study objective

This study has been transitioned to CTIS with ID 2024-511348-25-00 check the CTIS register for the current data.

Part 1: To evaluate the efficacy and safety of imetelstat in transfusion dependent subjects with low or intermediate-1 risk MDS that is relapsed/refractory to ESA treatment.
Part 2: To compare the efficacy, in terms of red blood cell (RBC) transfusion independence (TI), of imetelstat to placebo in transfusion dependent subjects with low or intermediate-1 risk MDS that is relapsed/refractory to ESA treatment.
Extension Phase: To evaluate the long-term safety, overall survival (OS), and disease progression, including progression to acute myeloid leukemia (AML) in transfusion dependent subjects with low or immediate-1 risk to MDS that is relapsed/refractory to ESA treatment receiving imetelstat.

Study design

This is a multicenter study of imetelstat in transfusion-dependent subjects with low or intermediate-1 risk MDS that is relapsed/refractory to ESA treatment (as per inclusion criteria). The study will consist of 2 parts, and approximately 270 subjects will be enrolled. Part 1 was an open-label, single-arm design to assess the efficacy and safety of imetelstat, which enrolled 57 subjects. Part 2 is a double-blind, randomized, placebo-controlled design to compare the efficacy of imetelstat with placebo. In addition to the approximately 170 subjects to be enrolled in the main study in Part 2, approximately 45 subjects will be enrolled in a separate Ventricular Repolarization substudy. Subjects should be enrolled in the main study of Part 2 until enrollment is complete unless a subject is known to meet criteria that would make the subject ineligible for the main study (eg, del 5 q, prior HMA therapy). The sponsor has reviewed and assessed all available data in Part 1, including blood counts, transfusion requirement, tolerability, pharmacokinetic, and pharmacodynamic biomarker data.

Intervention

Intravenous administration of imetelstat or placebo.

Study burden and risks

Possible Adverse Events include cytopenias (particularly thrombocytopenia and neutropenia), liver function test (LFT) abnormalities (or clinical hepatic adverse events), fatigue, nausea, aPTT prolongation, constipation, cough, anemia, anorexia, dyspnea, diarrhea, dizziness, vomiting and decreased appetite. Refer to the patient information sheet for a complete overview of risks/benefits for participating patients.

Contacts

Public
Geron Corporation

149 Commonwealth Drive Menlo Park, USA
Menlo Park, USA CA 94025
NL
Scientific
Geron Corporation

149 Commonwealth Drive Menlo Park, USA
Menlo Park, USA CA 94025
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Diagnosis of MDS according to WHO criteria confirmed by bone marrow aspirate and biopsy within 12 weeks prior to Randomization
IPSS low or intermediate-1 risk MDS
RBC transfusion dependent
Relapsed/refractory to ESA treatment
ECOG performance status 0, 1 or 2

Exclusion criteria

Prior treatment with imetelstat, or known allergies, hypersensitivity or intolerance to imetelstat or its excipients

Prior treatment with a hypomethylating agent (eg, azacitidine, decitabine)
Prior treatment with lenalidomide
Any ESA, chemotherapy, immunomodulatory or immunosuppressive therapy, corticosteroids (defined dosage, refer to protocol) or growth factor treatment within 4 weeks prior to C1D1 (part 1) or Randomization (Part 2) (8 weeks for long acting ESA)
Prior history of hematopoietic stem cell transplant
Anemia attributed to factors other than MDS
Active systemic hepatitis infection requiring treatment
Previously assessed as having IPSS intermediate-2 or high risk
Del(5q) karyotype
MDS/myeloproliferative neoplasm overlap syndrome

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-12-2015
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Imetelstat
Generic name:	Imetelstat

Ethics review

Approved WMO Date:	03-11-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-11-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-01-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-02-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-03-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-11-2016

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-03-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-06-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-07-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-09-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-10-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-05-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-05-2018

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-10-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-03-2020

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-03-2021

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-03-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-06-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-10-2022

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-11-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-02-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-12-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EU-CTR	CTIS2024-511348-25-00
EudraCT	EUCTR2015-002874-19-NL
ClinicalTrials.gov	NCT02598661
CCMO	NL54768.042.15