

# 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...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Haematopoietic neoplasms (excl leukaemias and lymphomas)
<b>Study type</b>	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

Imetelstat (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.<sup>2,24</sup> 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 intermediate-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

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Menlo Park, USA CA 94025  
NL

### Scientific

Geron Corporation

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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**

<b>Register</b>	<b>ID</b>
EU-CTR	CTIS2024-511348-25-00
EudraCT	EUCTR2015-002874-19-NL
ClinicalTrials.gov	NCT02598661
CCMO	NL54768.042.15