Elixirgen therapeutics: Phase I/II Study to Evaluate the Safety and Tolerability of EXG34217 in Patients with Telomere Biology Disorders with Bone Marrow Failure

elixirgen THERAPEUTICS

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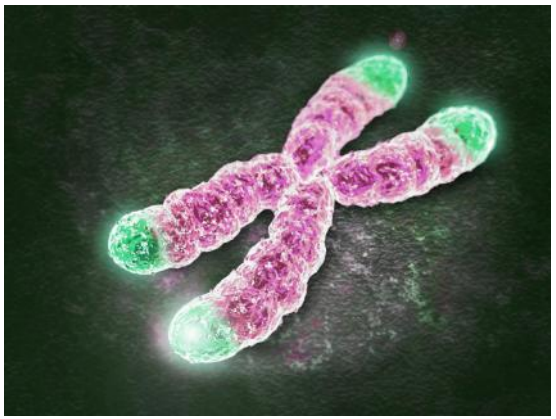
Outline

- Brief Overview of Telomere Biology Disorders
- Study Overview
- Study Eligibility

Telomere Biology Disorders (TBD)

- Characterized by accelerated telomere shortening results in cell loss or dysfunction
- Telomeres are regions of repetitive nucleotide sequences at ends of chromosomes to protect from deterioration or fusion with neighboring chromosomes
- 13 identified genes for TBD



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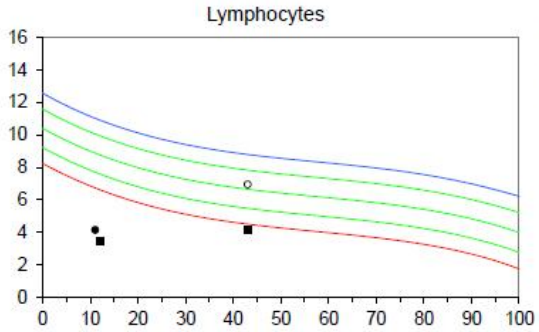


Telomere Biology Disorders

- Classic presentation includes bone marrow failure with
  - Nail dystrophy/changes
  - Skin pigmentation changes
  - Oral leukoplakia (white plaques in the mouth)
- Other common clinical features include
  - Lung fibrosis
  - Liver disease
- Many other organ systems can be affected
- Can appear with age and ***may not be present at diagnosis***

Telomere Biology Disorders

- Symptoms may advance within families
  - Increased lung/liver disease in early generations
  - Increased bone marrow failure in subsequent generations
- Predisposition to cancer
  - AML
  - Head & Neck cancers

EXG34217 Study

- Phase I/II, adult only study
- First in human trial
- 12 subjects with telomere biology disorders with mild or moderate bone marrow failure
- Bone marrow stem cells are collected from participants and treated to try to elongate their telomeres
- Potential survival advantage
- Extends telomeres in a telomerase independent mechanism

EXG34217 Study

- Stem cells are treated in the laboratory using EXG-001
  - A virus that expresses a human protein that normally helps elongate human telomeres during specific phases of development
  - Virus is NOT a known human pathogen – does not infect humans
- After treatment with EXG-001 the treated cells (now called EXG34217) are returned to the participant through an IV infusion

EXG34217 Study

- The treated stem cells with longer telomeres may have a survival advantage that could help them work better
- This may improve the bone marrow and blood count problems associated with their TBD
- This is NOT anticipated to change other TBD related complications like liver or lung disease

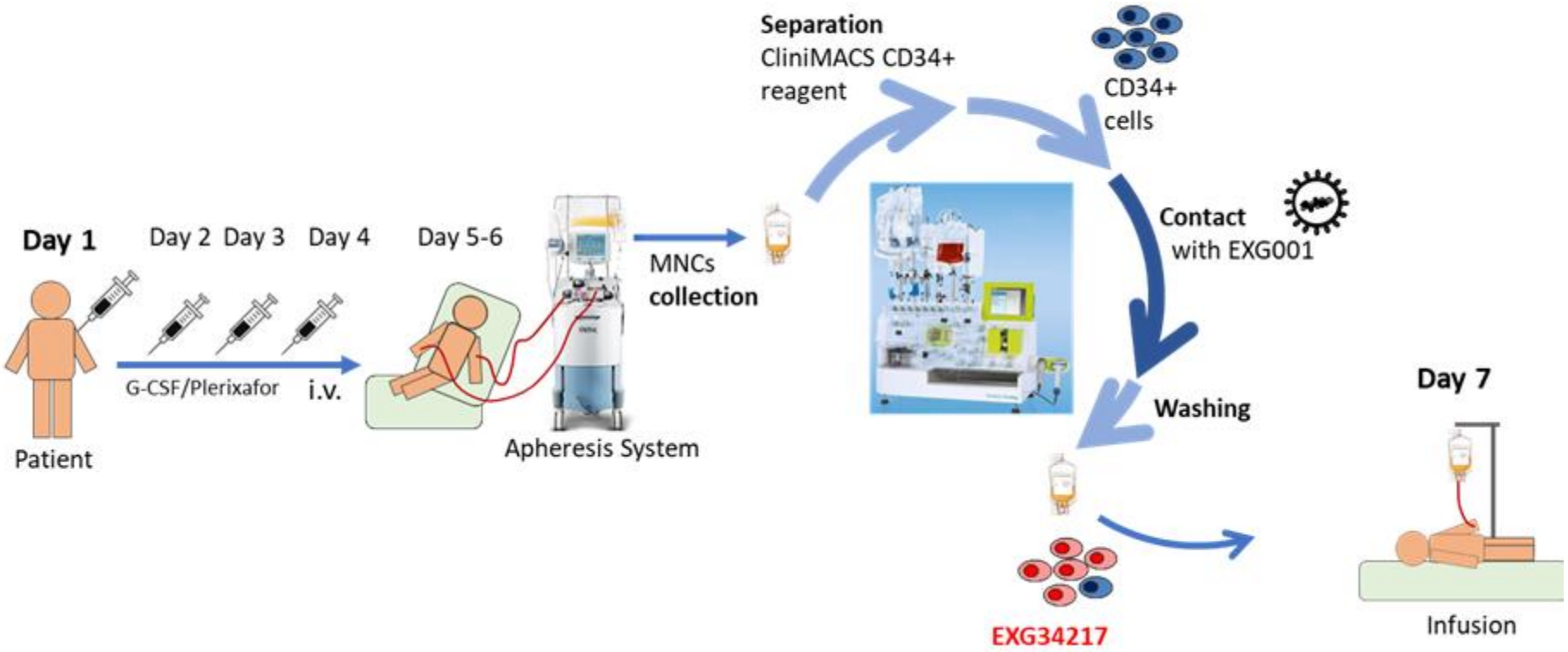
EXG34217 Study Overview

- Subjects for this study will **not** require any chemotherapy or radiation

The study will be conducted in four parts

1. Mobilization and collection of stem cells from the peripheral blood
2. Treatment of the stem cells in the lab with EXG-001
3. Processed cell infusion and post-infusion safety monitoring
4. Follow-up (Weeks 2-5, Months 2, 3, 4, 5, 6, 9, and 12)
   - Some visits may occur locally
   - Travel covered by the study

EXG34217: Study Overview



EXG34217 Study Goals

Primary Goal:

- Assess safety and tolerability of EXG34217 stem cells

Secondary Goals:

- Assess the feasibility of stem cell collection, treatment and reinfusion of EXG34217 stem cells
- Assess the feasibility of telomere extension
- Assess clinical benefit by measuring complete blood count over time.

Study Population - Inclusion

Adult males and females with telomere biology disorders with bone marrow failure.

1) Age ≥ 18 years.
2) Mild or moderate bone marrow failure defined by satisfying both conditions:
   - Peripheral blood neutrophils (ANC) < 1.5×10^9/L; or platelets < 100×10^9/L; or Hemoglobin <10 g/dL
   - Bone marrow hypocellular for age
4) Diagnosis of TBD defined by one of the following:
   - age-adjusted mean telomere length < 1 percentile in all tested peripheral blood cells such as granulocytes, lymphocytes, B-cells, naïve T-cells, memory T-cells, and NK cells
   - a pathogenic mutation in DKC1, TERC, TERT, NOP10, NHP2, TINF2, CTC1, PARN, RTEL1, ACD, USB1, or WRAP53

Study Population - Exclusion

- Women of childbearing potential or breastfeeding
- Patients with cancer who are on active chemotherapeutic treatment
- Patients with severe bone marrow failure
- Clonal cytogenetic abnormalities associated with MDS or AML
- Uncontrolled bacterial, viral or fungal infections
- Prior hematopoietic stem cell transplant
- Patients who are not eligible for G-CSF and plerixafor
- Patients who are not eligible for the apheresis
- Patients currently taking or have taken danazol and androgens within 60 days prior to Day 1
- Patients with any other clinically relevant acute or chronic diseases which could interfere with the patients' safety during the trial, expose them to undue risk, or which could interfere with study objectives
- Patients who have participated in another clinical trial with an investigational drug within the previous 30 days

CONTACT US!

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