Safety and Efficacy of PMT Therapy of hPAP

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 18 years and over
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

Patients must meet all of the following conditions to be eligible for participation in this study:

1. Male or female with a confirmed diagnosis of hPAP defined as:

- Homozygous or compound heterozygous CSF2RA mutations - AND -
- A normal GM-CSF autoantibody test result - AND -
- An abnormal STAT5-PI test result - OR -
- An abnormal GM-CSF 50% effective concentration (EC50) test result
    1. Diffuse ground glass opacification of the lungs visualized on a chest computed tomogram (CT)
    2. History of prior receipt of WLL therapy or moderate hPAP lung disease severity requiring therapy in the opinion of the Clinical Site Investigator and/or Sponsor
    3. Able to undergo bone marrow collection by routine clinical aspiration
    4. 18 years of age or older on the date the Informed consent form (ICF) is signed
    5. Females who have been post-menopausal for >2 years or females of child-bearing potential after a confirmed menstrual period using a highly efficient method of contraception (as described in Section 11.4.2) for the period from 3 months prior to the first administration of gene-corrected macrophages until 12 months after the last administration of gene-corrected macrophages. Females of child-bearing potential must have a negative serum pregnancy test at Screening (Visit 1), at bone marrow collection (Visit 2), and immediately before each administration of gene-corrected macrophages (Visits 3, 5, 7), and must not be lactating.
    6. Males of reproductive potential must agree to use condoms for the period from the 1st administration of gene-corrected macrophages until 12 months after the last dose of gene-corrected macrophages, have a partner who is not of child-bearing potential (i.e. men or females who have been post-menopausal for >2 years), or have a female partner who is using adequate contraception as described in Section 11.4.2.
    7. Signed written informed consent form (ICF)

Exclusion Criteria:

Patients who meet any of the following conditions will not be eligible for participation in this study:

1. History of a confirmed diagnosis of any other PAP-causing disease defined as:
    1. PAP caused by function-altering mutations in CSF2RB, adenosine triphosphate (ATP)-binding cassette subfamily A member 3 (ABCA3), SFTPB, SFTPC, Thyroid Transcription Factor 1 (TTF-1), GATA-binding factor 2 (GATA2), SLC7A7, and methionyl-transfer RNA (tRNA) synthetase (MARS), or other genes demonstrated to cause PAP other than CSF2RA
    2. PAP associated with an abnormal GM-CSF autoantibody test
    3. PAP associated with hematologic disorders including but not limited to myelodysplasia, aplastic anemia, leukemia, multiple myeloma, lymphoma
    4. PAP associated with non-hematologic malignancies
    5. PAP associated with immune deficiency syndromes
    6. PAP associated with chronic inflammatory syndromes
    7. PAP associated with chronic infections including but not limited to human immunodeficiency virus, Mycobacteria tuberculosis or other Mycobacterial species, or other organisms
    8. PAP associated with inhaled materials including but not limited to inorganic dusts (e.g., silica, titanium, indium, aluminum), organic dusts (e.g., sawdust, fertilizer); or gases/vapors (e.g., cleaning products, paints, and welding-related fumes)
2. Pulmonary fibrosis that is clinically significant in the opinion of Clinical Site Investigator and/or Sponsor
3. A confirmed (i.e., repeated) positive serum anti-GM-CSF receptor antibody test and/or a confirmed positive anti-lentiviral antibody test at the time of screening and prior to each administration of gene-corrected macrophages
4. History of receipt of any investigational agent within 3 months of Study Visit 3
5. History of active chronic infection (e.g., HIV, Hepatitis, others) at the time of Screening
6. History of significant alcohol consumption for a period of more than 3 consecutive months within 1 year prior to Study Visit 3, defined as more than 14 drinks/week for females or 21 drinks/week for males (1 drink - 5 ounces (150 ml) of wine or 12 ounces (360 ml) of beer, or 1.5 ounces (45 ml) of hard liquor)
7. History of medication or illicit drug abuse within 1 year prior to Study Visit 3, including but not limited to cocaine, heroin, or other opioids
8. Currently or planning to become pregnant between the Screening visit and Visit 14 and/or currently breast-feeding

9. Any other medical, behavioral, or psychiatric condition that would interfere with the completion of Study Visits or assessments in the opinion of the Clinical Site Investigator and/or Sponsor

Conditions & Interventions

Interventions:
COMBINATION_PRODUCT: Gene-Corrected Macrophages administered by bronchoscopic instillation
Conditions:
Hereditary Pulmonary Alveolar Proteinosis
Keywords:
Pulmonary Alveolar Proteinosis, Pulmonary Macrophage Transplantation

More Information

Description:
The major goal of this study is to evaluate a new type of cell transplantation therapy for individuals with hereditary PAP, study a new treatment that may be useful for treatment of other diseases, and research mechanisms that drive the development and function of lung macrophages.

Contact(s): Brenna Carey - brenna.carey@cchmc.org
Principal Investigator:
Principal Investigator ID:
Phase: PHASE1
IRB Number:
System ID: NCT05761899
