Docket #: S20-361

Hematopoietic Stem Cell Engraftment with Novel Combination of Agents

Researchers at Stanford have developed a clinically applicable method of bone marrow conditioning for stem cell transplantation or treatment of hematologic malignancies. Currently, hematopoietic cell transplantation (HCT) utilizes stem cell replacement therapy to provide curative options for many malignant and non-malignant blood disorders. However, the toxicity of the conditioning regimens used to achieve engraftment of allogeneic donor or autologous gene corrected hematopoietic stem cells (HSC) continues to be a major obstacle. **The researchers have determined that a hypomethylating agent, 5-Azacytidine (AZA), which is widely used in cancer therapy, can cause HSC depletion and permit engraftment of exogenous (donated) HSC**. Furthermore, the combination of AZA and an anti-CD117 antibody results in more profound and prolonged depletion of recipient HSC compared to either agent alone, and treatment can result in robust and stable engraftment of donor HSC in immunocompetent wild type mice.

Stage of Development
Preclinical proof of concept engraftment studies *in vivo* in mice.

Applications

- Conditioning prior to allogeneic HCT to treat:
    - Non-malignant disorders of the blood system including hemoglobinopathies (e.g., sickle cell anemia and thalassemia major), genetic and acquired immune deficiencies (e.g., severe combined immunodeficiency, HIV)
    - Certain genetic disorders affecting the central nervous system (e.g., metachromatic leukodystrophy, Hurler syndrome)
    - Autoimmune non-hematologic (e.g., multiple sclerosis, systemic lupus erythematosus, inflammatory bowel diseases, juvenile idiopathic arthritis)

and hematologic (e.g., immune thrombocytopenia, autoimmune hemolytic anemia, Evans syndrome) diseases
    - Malignant myeloid and lymphoid hematologic disorders
    - Patients with failed or poor hematopoietic graft function
- Conditioning prior to HCT of autologous gene corrected cells for a wide spectrum of diseases (e.g., disorders of the blood and lymphoid system, neurologic disorders)

Advantages

- Substantially safer method for transplanting allogeneic donor or autologous gene corrected HSC
- Potentially more targeted HSC depletion to allow engraftment of allogeneic donor HSC compared to standard-of-care reduced intensity conditioning regimens
- Potentially better efficacy than AZA alone or AZA plus other standard-of-care agents at eliminating diseased myeloid clones from the bone marrow of patients with hematopoietic malignancies
- Potential to make HCT a more acceptable treatment for broader array of conditions

Patents

- Published Application: WO2022081828
- Published Application: 20230310508

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