PRGN-3005 UltraCAR-T®: Multigenic CAR-T cells generated using non-viral gene delivery and rapid manufacturing process for the treatment of ovarian cancer

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PRGN-3005 targets MUC16 on tumor cells

mbl15 expression on PRGN-3005 does not promote bystander proliferation

PRGN-3005 demonstrates MUC16 specific cytotoxic activity and cytokine expression

PRGN-3005 is engineered to simultaneously express MUC16 CAR, mbl15 and Kill Switch

PRGN-3005 demonstrates significant anti-tumor activity, CAR T cell persistence and expansion in vivo in a preclinical ovarian cancer model

Overview of PRGN-3005 UltraCAR-T production with an overnight manufacturing process

Conclusions

• The UltraCAR-T® platform provides a non-viral gene transfer and rapid manufacturing approach to enable improved potency, safety and scalability of CAR-T therapies.

• PRGN-3005 UltraCAR-T cells simultaneously co-express MUC16 CAR, mbl15 and a kill switch to generate a uniform, homogenous cell product and exhibit robust MUC16 specific cytotoxicity to tumor cells.

• Unlike conventional CAR-T cells (mbl15-negative), a single administration of PRGN-3005 UltraCAR-T, even at a lower dose, one day after gene transfer, effectively eliminated tumor cells in an ovarian mouse model.

• PRGN-3005 UltraCAR-T demonstrated significantly higher expansion and persistence in ovarian tumor bearing mice and maintained preferred memory-like T cell phenotype in vivo compared to conventional MUC16 CAR-T cells.

• PRGN-3005, after a single administration, showed long term persistence in vivo and effectively eliminated tumor upon re-challenge more than three months after PRGN-3005 administration.

• The first-in-human Phase 1 clinical trial of PRGN-3005 UltraCAR-T for treatment of patients with advanced, recurrent platinum resistant ovarian, fallopian tube or primary peritoneal cancer is in progress (ClinicalTrials.gov: NCT03907527, scan QR code).

Introduction

• Traditional methods for chimeric antigen receptor (CAR) T cell generation have involved viral vectors and periods of ex vivo cell expansion, prolonging the waiting period between apheresis and administration of CAR-T therapy to a patient and resulting in high manufacturing costs with a centralized manufacturing process.

• Precigen’s UltraCAR-T® platform is based upon an advanced non-viral multigenic delivery system and rapid manufacturing process with high cell scalability for administration of autologous CAR-T cells one day after gene transfer.

• UltraCAR-T® cells offer potential for enhanced potency, safety and scalability:
  • Potency: multigenic expression that includes membrane-bound IL-15 (mbl15) expression to provide improved cell persistence and maintenance of memory and stem cell-like/naïve phenotype.
  • Safety: non-viral gene delivery and ability to eliminate the CAR T cells through expression of a kill switch and mediated by administration of a kill switch activator.
  • Scalability: rapid manufacturing with no ex vivo expansion for treatment of patients one day following gene transfer.

• Ovarian cancers, are often detected at later stages with a high incidence of tumor recurrence. Current treatment options for recurrent ovarian tumors are limited and not specific for a tumor antigen.

• Mucin 16 (MUC16) is overexpressed on over 80% of ovarian tumors with limited expression found in healthy tissues.

• MUC16, a large membrane bound glycoprotein, can shed from tumor cells; however, PRGN-3005 recognizes the non-shed MUC16 retained on cell surface.

• PRGN-3005 UltraCAR-T is a multigenic autologous CAR-T cell treatment simultaneously expressing a CAR optimized to preferentially target MUC16 on tumor cells, mbl15, and a kill switch.