INTRODUCTION

Agonists antibodies and monoclonal cytokines have had limited success in the clinic due to their pharmacokinetic behavior leading to intense therapeutic and off-target activities. Conventional cytokines have a natural ligand and the loss of multiple agonists renders them effectively a blunted agonist. Rubius Therapeutics has developed RTX-240, an allogeneic cellular therapy using genetically modified red blood cells to express rIL-15 and 4-1BB fusion proteins, that allows for broad activation of innate and adaptive immunity to act in concert to drive naive T-cell proliferation. RTX-240 uses the natural ligand and the lack of multiple signals needed to effectively mimic human biology by broadly stimulating adaptive and innate immunity.

OBJECTIVE

To assess the immunomodulatory and cell cytotoxicity of RTX-240 in vitro and in vivo.

BURLUS THERAPEUTICS TECHNOLOGY

• Red Cell Therapeutics (RCT)-TCP™ is a new class of allogeneic, off-the-shelf cellassociated therapeutic for the treatment of cancer and autoimmunediseases.
• RCTs are engineered red blood cells that express hundreds of thousands of copies of biologically active proteins on the cell surface.
• Universal, scalable, and consistent manufacturing process.

RESULTS

• RTX-240 is an allogeneic cellular therapy product candidate that significantly outperforms hundreds of thousands of copies of free cytokines in vitro and in vivo.
• RCT-240 is a permanently modified red cell that co-expresses rIL-15 and 4-1BB in their native forms to activate and expand T and natural killer (NK) cells.
• rIL-15 is a cytokine that induces naive T-cell and NK cell proliferation and activation and induces IFNγ production.
• 4-1BB is a cytokine that bridges innate and adaptive immunity by promoting T and NK cell proliferation, and NK cell cytokine stimulation of 4-1BB is a fusion of IL-15 and 4-1BB receptors.

Figure 1: The RED PLATFORM™ is Designed to Generate Allogeneic, Off-The-Shelf Cellular Therapies

Red Cell Therapeutics (RCT)-TCP™ is a new class of allogeneic, off-the-shelf cell-associated therapeutic for the treatment of cancer and autoimmunediseases. RCTs™ are a new class of allogeneic, off-the-shelf cell-associated therapeutic for the treatment of cancer and autoimmunediseases. RCTs™ are engineered red blood cells that express hundreds of thousands of copies of biologically active proteins on the cell surface. Universal, scalable, and consistent manufacturing process.

Figure 2: RTX-240 Mediates Immunomodulatory Effects Through Simultaneous Presentation of the Costimulatory 4-1BBL and the Cytokine rIL-15

• RTX-240 is a genetically modified red blood cell expressing 4-1BBL and IL-15TP, a known population with cytokine activity, compared to rIL-15.

Figure 3: RTX-240 Promotes Superior Activation and Expansion of NK Cells and CD8 T Cells Compared to Agonistic pBbb Al of IC-Ag5 in Vitro

• RTX-240 increased CD8 T cell and NK cell expansion and activation when compared to positive controls.

Figure 4: RTX-240 Expands CD8+ T Cells in Vitro

• RTX-240 promotes NK cell cytotoxicity, by increasing their ability to kill the myeloid leukemia cell line K562.

Figure 5: RTX-240 Increases CD8 T Cell and NK Cell Expansion and Activation

• RTX-240 increased CD8 T cell and NK cell expansion and activation when compared to positive controls.

Figure 6: RTX-240 Enhances NK Cell Cytotoxicity Against the Myeloid Leukemia Cell Line K562

• RTX-240 increased CD8 T cell and NK cell expansion and activation when compared to positive controls.

CONCLUSIONS

• RTX-240 increased CD8 T cell and NK cell expansion and activation in vitro when compared to agonistic antibody and rIL-15 and this was directly correlated with the percentage of 4-1BB and rIL-15.
• Treatment with mRBC-240 did not lead to an increase in spleen weight as compared to 4-1BB agonistic antibody and rIL-15.
• mRBC-240 induced potent antitumor activity in a B16F10 melanoma model that was directly correlated with the percentage of 4-1BB and rIL-15.

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DISCLOSURES

All authors: Employment and equity ownership in Rubius Therapeutics.

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