VB-111, a Vascular Targeting Viral Therapy, Augments PD-L1 Checkpoint Blockade Anti-tumor Activity

Niva Yacov, Itzhak Mendel and Eyal Breitbart

VBL Therapeutics

Abstract #585

BACKGROUND

Immunotherapy with checkpoint inhibitors demonstrates remarkable efficacy in several cancers; yet, only a low percentage of patients seem to benefit from this class of treatment when given as a monotherapy. Several studies have shown that response rates are increased when checkpoint blockade is combined with other anti-cancer treatments.

Ofranergene obadenovec (VB-111) is a unique biologic agent that uses a dual mechanism to target solid tumors. Based on a non-integrating, non-replicating, Adeno 5 vector, VB-111 utilizes VBL's proprietary Vascular Targeting System (VTS™) to target the tumor vasculature for cancer therapy. In addition, VB-111 induces specific anti-tumor immune response, which is accompanied by recruitment of $CD8^+$ T-cells and apoptosis of tumor cells. VB-111 is currently being studied in a Phase 3 pivotal trial for recurrent glioblastoma, conducted under an FDA Special Protocol Assessment (SPA).

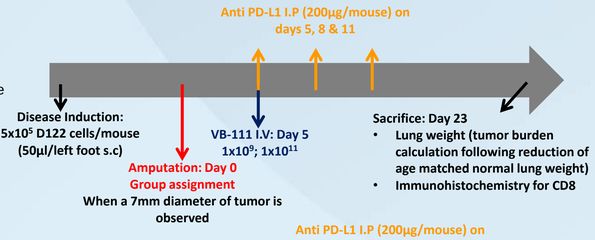
In this study, we tested VB-111 in combination with a PD-L1 checkpoint inhibitor in lung and melanoma cancer models.

METHODS

C57Bl6 male mice 12-14 weeks old were induced with lung or melanoma cancer models as follows:

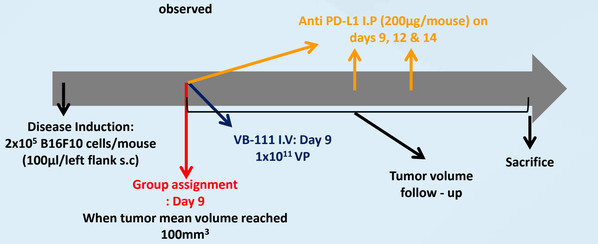
Lewis lung carcinoma (LLC):

- Saline
- VB-111 $1x10^{11}$ viral particles (VPs)/mouse
- VB-111 $1x10^9$ VP/mouse
- Anti PD-L1
- Anti PD-L1 & VB-111 $1x10^9$ VPs/mouse



B16F10 melanoma:

- Saline
- VB-111 $1x10^{11}$ VPs/mouse
- Anti PD-L1
- Anti PD-L1 & VB-111 $1x10^{11}$ VPs/mouse

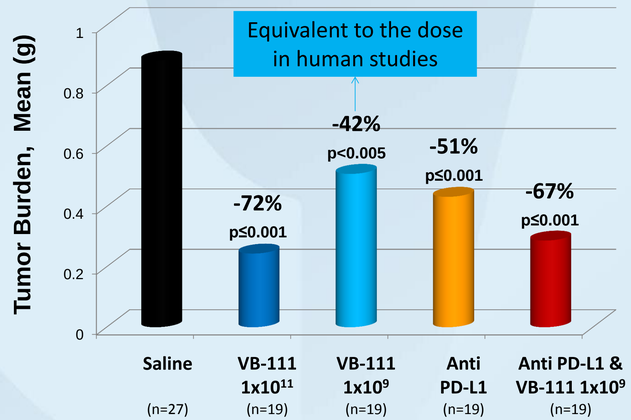


NASDAQ:VBLT

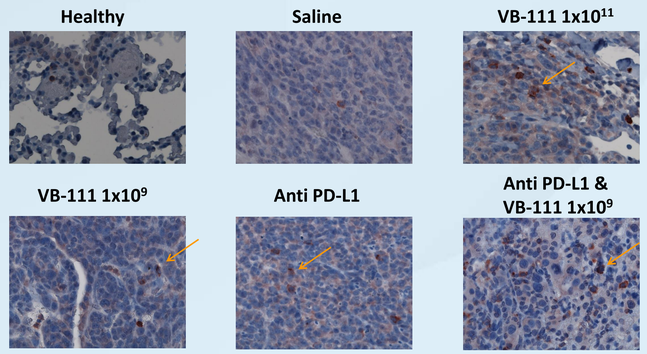
RESULTS

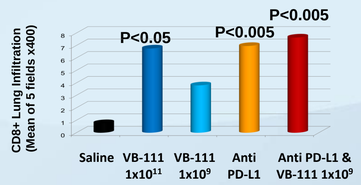
Lewis Lung Carcinoma (LLC) Model

VB-111 Augments PD-L1 Blockade to Advance Reduction of Tumor Burden in Lung Cancer Model



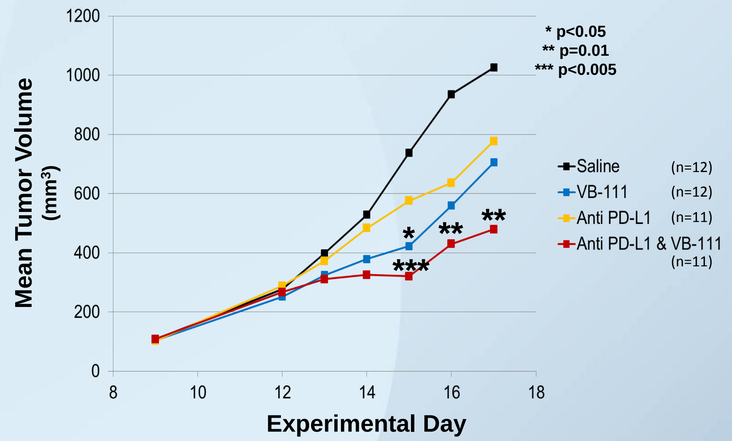
VB-111 and PD-L1 Blockade Increase $CD8^+$ Lung Infiltration in LLC Model





B16F10 Melanoma Model

VB-111 Enhances anti-PD-L1 Inhibition of Tumor Growth in B16F10 Melanoma Model



CONCLUSIONS

- **VB-111 is a novel Phase 3 biologic agent that reduces tumor volume and increases $CD8^+$ T-cell infiltration.**
- **Treatment with VB-111 augments the anti-tumor activity of anti PD-L1 checkpoint inhibitor in lung and melanoma cancer models.**
- **Combination of VB-111 at dose of 10^9 VPs/mouse (equivalent to 10^{13} in humans; therapeutic dose) with anti-PD-L1 mAb resulted in a tumor reduction effect similar to a dose of 10^{11} VPs (100x dose; equivalent to 10^{15} in humans) in a lung cancer model.**
- **The data support VBL's plan to launch an exploratory Phase 2 combination study of VB-111 with checkpoint inhibitor in NSCLC.**