**Complete regression of ovarian cancer xenografts following treatment with the recombinant immunocytotoxic protein, VB6-845**


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**ABSTRACT**

VB6-845 is a recombinant fusion protein consisting of a human-targating fib to be delivered to immuno-oncology treatment, a type 1 histamine receptor (H1R) and VB6-845 specifically targets the epithelial cell adhesion molecule (EpCAM) that is highly expressed on many different epithelial carcinomas, including ovarian cancer. Ovarian cancer is the fourth most common cause of cancer death in women, with an average five-year survival rate of about 40%. Despite these robust survival rates, it may require new and more effective treatments. Immunohistochemistry (IHC) determined a high level of VB6-845 expression in ovarian primary (>75%) and metastatic (100%) carcinomas. VB6-845 exhibited potent activity against the established ovarian cancer xenografts, which were subcutaneously implanted into female nude mice using an s.c. model, with 100% of tumors (10/10) showing >50% reduction in tumor volume at day 15 (p < 0.05). Intraperitoneal (I.P.) xenograft model in Balb/c nu/nu mice, I.P. administration of 25 and 20 mg/kg of VB6-845 resulted in 97% survival as compared to 15% in the untreated group on Day 64 (p < 0.01) (Table 1). In vivo results were confirmed by the use of an IHC assay using an IHC assay, with 100% VB6-845 showing >50% reduction in tumor volume at day 15 (p < 0.05). Effects were also demonstrated in another Ep-CAM-positive PDAC model, whereas VB6-845 had no detectable effect on Ep-CAM-negative RPMI-8226 model.

**INRODUCTION**

Ovarian cancer is the fourth most common cause of cancer death in women, and the leading cause of death from gynecological cancer with advanced stage 15 and 17 for which, recurrence rates are high and a median survival of 2 years. Only one ovarian epithelial cell carcinoma has been identified, a (G12A) immunocompromised xenograft. Analysis of 15% of the advanced stage 15 and 17 women. At least 26 ovarian carcinoma xenografts have been identified, which were subcutaneously implanted into female nude mice using an IHC assay, with 100% VB6-845 showing >50% reduction in tumor volume at day 15 (p < 0.05). Effects were also demonstrated in another Ep-CAM-positive PDAC model, whereas VB6-845 had no detectable effect on Ep-CAM-negative RPMI-8226 model.

**RESULTS**

**Subcutaneous Implanted Xenograft Model**

- Female nude mice (21 per treatment group)
- C57/BL6J background
- S.c. injection of 2 days off for 2 cycles, twice weekly dosing for 4 weeks (modified due to excess toxicity)

- **Table 1**: Comparison of Treatment with VB6-845 results in long-term survival of multiple subcutaneous implanted xenografts.

- **Figure 4**: Analysis of CD312 plasma levels correlates with the anti-tumor effectiveness of VB6-845.

- **Figure 5**: Representative pictures of animals from the OVCA3-2 xenograft study showing the difference between untreated and treated animals.

**CONCLUSIONS**

1. Increased survival and tumor growth inhibition were demonstrated in Ep-CAM-positive tumors.
2. Subcutaneous OVCA3-2 implantation
   - OV administration: 20 mg/kg
   - IP administration: 25 mg/kg
   - IV administration: 20 mg/kg
3. The anti-cancer effect of VB6-845 was specific to Ep-CAM-expressing tumors.
   - OVCA3-2 and OVCA4-3 models
   - Treatment had no effect against Ep-CAM-negative tumors.
   - Analysis (4-21T) model

These results clearly demonstrate that VB6-845 is a promising agent and significantly improves survival rates in ovarian cancer and other Ep-CAM-positive tumor models.