

## Abstracts

### **BMET-26. PHASE 2 STUDY OF VB-111, AN ANTI-CANCER GENE THERAPY, AS MONOTHERAPY FOLLOWED BY COMBINATION OF VB-111 WITH BEVACIZUMAB, IN PATIENTS WITH RECURRENT GLIOBLASTOMA**

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**BACKGROUND:** VB-111 is an anti-angiogenic agent consisting of a non-replicating adenovirus vector (Ad-5) with a modified murine pre-proendothelin promoter leading to apoptosis of tumor-vasculature by

expressing a fas-chimera transgene in angiogenic-endothelial cells. Safety and efficacy of VB-111 alone and in combination with bevacizumab (BEV) were evaluated in recurrent-Glioblastoma (rGBM) patients in this Phase 1-2 dose-escalation study. **METHODS:** VB-111 was administered at  $3 \times 10^{12}$  or  $1 \times 10^{13}$  bimonthly until progression, followed by BEV standard-of-care (SOC). The protocol was amended to add-on BEV 10mg/Kg biweekly combined with VB-111 bimonthly, until further progression. Assessments included safety, pharmacokinetics, overall survival (OS) (Kaplan Meyer) and tumor response (RANO). **RESULTS:** 46 patients at 4 sites (US and Israel) received up to 13 doses of VB-111. Upon further progression, 24 received VB-111 with BEV, 22 were treated with BEV SOC. VB-111 was safe and well-tolerated alone and in combination with BEV. There were 30 grade  $\geq 3$  AEs, of which 6 were considered possibly related to VB-111: thrombocytopenia, pyrexia, brain edema, depressed consciousness, general weakness, pulmonary embolism. Median OS was 16 months for patients receiving combination therapy versus 8 months for those receiving SOC ( $p = 0.05$ ). OS of combination therapy was superior to the historical control BELOB BEV arm, 16 versus 8 months ( $p = 0.003$ ). Of 46 patients who received VB-111, 25 patients spiked a fever post-VB-111 dosing at least once, while 21 didn't. Feverish patients demonstrated a median OS of 16 months, compared to non-feverish patients, with a median OS of 8.5 months ( $p = 0.03$ ). **CONCLUSIONS:** VB-111 was safe and well-tolerated alone and in combination with BEV in rGBM patients. OS of patients who received VB-111 followed by combination therapy almost doubled compared to historical BEV data, and compared to patients who received VB-111 monotherapy. Toxicities were as expected in this population. A phase 3 randomized controlled trial is currently underway.