EVT801: A differentiating anti-tumor approach

Targeting tumor angiogenesis with the selective VEGF-3 Inhibitor EVT801 in combination with cancer immunotherapy

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inhibitor EVT801 in combination with cancer immunotherapy

1. Inhibition of tumor escape & metastasis
   • Stabilization of tumor vasculature
     • Inhibition of lymphangiogenesis
     • Reduction of tumor hypoxia
   • Enhanced anti-tumor immunity
     • No impact on T-cell viability
     • Decrease in immunosuppressive cells
     • Enhanced effector cell infiltration
   • Tumor killing
     • Direct effect on VEGF-3 tumor cells from endothelial therapy

Expression of vascular marker CD34, lymphatic marker D2-40 and VEGF-3 in primary kidney tumors.

Consecutive slices of the same tumor were stained for VEGF-3, CD34 and D2-40. VEGF-3 was expressed in CD34-positive vessels in the tumor and in the normal adjacent tissue, whereas D2-40 staining was mainly observed in normal adjacent tissue. Black arrows indicate lymphatic vessels.

Expression of vascular marker CD34, lymphatic marker D2-40

VEGF-3 expression in kidney cancer cohorts

VEGF3 expression has been validated in multiple indications including non small cell lung cancer, hepatocarcinoma and colorectal cancer

Pleiomorphic sarcomas 20 0%
Kaposi's sarcomas 53 0% 0% 0%
Ewing sarcoma 33% 66%
Pleiomorphic liposarcomas 6 0% 0%
(Lymph) angiosarcomas 7 10% 0% 0%
No Low Medium high

MTD RP2D

STAGE 1 (Ongoing) - Monotherapy Dose escalation, n ≤ 48

Dose Cohort 1 EVT801 monotherapy
Dose Cohort 2 EVT801 monotherapy
Dose Cohort 3 EVT801 monotherapy
Dose Cohort 4 EVT801 monotherapy

MTD: Expatients PD Cohort in Soft Tissue Sarcoma
RP2D: Expatients PD Cohort in Renal Cell Carcinomas

Patient stratification based on VEGF-3 expression on tumor tissues (i.e. pre and post treatment)

• VEGF-3 expression by IHC and IF
• Unbiased biomarkers (CD1 & CD21)
• Total RNA sequencing

PD biomarkers (CD1 & CD21):
• Immunomonitoring
• Based on CD1 and CD21/MSCC ratio
• Protein signature
• Chemokines involved in angiogenesis and inflammation

Unbiased biomarkers (CD1 & CD21):
• Total RNA sequencing
• Remaining blood samples (CD1 & CD21):
• Frozen plasma
• Frozen PBMC

Preliminary results and promising leads

3 high grade serous ovarian carcinoma patients included in the phase I clinical trial exhibited a strong VEGF3 expression associated with a significant tumor regression in one patient

Conclusion

• EVT801 presents a more selective and less toxic profile than two major approved inhibitors of VEGF3 (i.e., sorafenib and pazopanib).
• In monotherapy, EVT801 showed a potent antitumor effect in tumors with VEGF-3-positive microenvironment in preclinical models.
• EVT801 will be evaluated as single agent in patients with kidney cancer and soft tissue sarcomas. Combination with cancer immunotherapies would come next.