A first-in-human phase I study of VGX-100, a selective anti-VEGF-C antibody, alone and in combination with bevacizumab in patients with advanced solid tumors.

G.S Falchuk1, J.W.Goldman2, J. Desai3, I.M. Leitch4, D.S. Hong5, V. Subbiah1, R. Kurzrock1, L.S. Rosen2
1University of Texas MD Anderson Cancer Center, Houston, TX; 2UCLA Hematology-Oncology, Santa Monica, CA; 3Royal Melbourne Hospital, Melbourne, Australia; 4Ceres Oncology / Vegenics, Melbourne, Australia;

INTRODUCTION

VGX-100 (anti-VEGF-C)

- VGX-100 is an investigational first-in-class fully human IgG1 neutralizing antibody targeting VEGF-C, inhibiting its receptor activation of VEGFR2 and VEGFR3.
- VGX-100 is a pro-angiogenic / lymphangiogenic growth factor that may contribute to tumor escape / resistance to anti-VEGF therapy and allow growth of tumor vasculature.1
- VGX-100 is associated with:
  - melanoma, breast, pancreatic, colorectal, lung
  - Poor outcomes including reduced survival
  - Gastric, colorectal, lung, breast, pancreatic, ovarian
- In preclinical models of VGX-100 to bevacizumab co-administration, melanoma or syngeneic knoxin inhibited pulmonary tumor regression2,3.

Clinical combination of VGX-100 with bevacizumab (Avastin®) may result in synergistic effects to targeting multiple VEGF signaling pathways that mediate angiogenesis and lymphangiogenesis.

VGX-100 Inhibition of VEGF-C Signaling in Tumors.

VGX-100 inhibits angiogenesis in vitro on both VEGFR2 and VEGFR3 and lymphangiogenesis in vitro activation of VEGF-C. VGX-100 is a fully human monoclonal antibody that inhibits VEGF-C activity.

Targeted CoTherapy

- Bevacizumab is a humanized monoclonal anti-VEGF-α antibody that binds to and inhibits the biological activity of human VEGF-A.

STUDY DESIGN

Arm A: VGX-100 alone or in combination with bevacizumab.

Arm B: VGX-100 plus bevacizumab.

Each 28 day treatment cycle consists of:

- Arm A (VGX-100 monotherapy):
  - Treatment with bevacizumab is given as an IV infusion weekly at D1, D8, D15 and D22.
  - Patients received treatment until disease progression or intolerable toxicity.

- Arm B (VGX-100 plus bevacizumab):
  - Treatment with bevacizumab is given as an IV infusion at D1, D8, D15 and D22.
  - Bevacizumab is administered with bevacizumab.

RESULTS

Demographics and Patient Characteristics

Fundamental findings:

- Overall incidence rate of grade 3 / 4 events: of progressive disease.
- Drug-related emergent grade 5 events: of progressive disease.
- No MTD was reached.

RESULTS - SAFETY AND TOLERABILITY

Tumor Response

Patients with measurable disease progression and the follow-up assessment and without stable disease / stable disease were evaluated for the following endpoints:

- Best response: was assessed using the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria.
- VGX-100 or bevacizumab.

RESULTS - PHARMACOKINETICS

Mean VEGF-C Concentration-Time Profiles on Days 1 and 15 cycle 1 Arm A & B-3.

CONCLUSIONS

- VGX-100 at weekly doses up to 30 mg/kg alone or up to 20 mg/kg in combination with bevacizumab Q2W for 1 year is safe and tolerable in patients with advanced solid tumors. No MTD was reached.
- VGX-100 plus bevacizumab weekly 10 mg/kg is well tolerated and did not result in any DLT. 2 patients discontinued prior to post-dose tumor assessment (1 patient progression, 1 withdrawal of consent and 1 SAE).

REFERENCES

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