The novel therapeutic monoclonal antibody VGX-100 neutralises VEGF-C and inhibits tumor growth and metastasis in subcutaneous and orthotopic models of human cancer.

Baldwin, M.E., Tester, A., Phelan, D. and Klupacs, R.
Circadian Technologies Limited, Level 1, 10 Wallace Ave, Toorak, 3142, Victoria, Australia.
Email: megan.baldwin@circadian.com.au
www.circadian.com.au

Abstract

Angiogenesis and lymphangiogenesis are important processes facilitating tumor growth and metastases. Growth factors that stimulate blood and lymphatic proliferation within tumors are therefore potential therapeutic targets. VEGF-C, VEGF-D, and their receptors are highly expressed in human tumors, and the VEGF-C ligands are known to be involved in angiogenesis and lymphangiogenesis. The receptor binding specificity of VEGF-C and VEGF-D is distinct to that of VEGF, which blocks VEGF-B but not VEGF-C.

VGX-100 is a highly specific, fully human monoclonal antibody for VEGF-C that blocks VEGF-C binding to both VEGFR-3 and VEGFR-2. Here we demonstrate that VGX-100 has an additive effect in combination with docetaxel and/or anti-VEGF (bevacizumab) in several tumor models, suggesting that VEGF-C may be an important mediator of the resistance to existing anti-VEGF therapies. Further, we demonstrate that an orthotopic model of prostate cancer, the inhibition of VEGF-C by VEGF-C is sufficient to inhibit tumor growth and significantly reduce the incidence of tumor metastasis to local lymph nodes. These data indicate that VGX-100 has excellent potential as a cancer therapeutic by targeting a key factor involved in angiogenesis, lymphangiogenesis and tumor metastasis.

Materials and Methods

For clarity of presentation, the methodological details are not shown. For further information, please refer to the references.

Conclusions

VGX-100 reduces lymph node metastasis in an orthotopic prostate tumor model.

VGX-100 reduces tumor burden by 59% (at day 90) compared to control IgG. There were no toxicities.

Materials and Methods

PC-3, H2B2 and OVCAR-8 subcutaneous tumor models: PC-3 (x 10³), H2B2 (x 10³) or OVCAR-8 (x 10⁵) cells were implanted subcutaneously in mice (n = 10 mice per group). Due to the high level of VEGF-C expression, this model was selected for testing the effect of VGX-100. Tumor burden was measured by caliper measurements at the end of the treatment period (week 6). Antisense antibodies were administered intraperitoneally once a week for three weeks.

Orthotopic PC-3 tumor model: PC-3-VEGF human prostate cancer orthotopic Metastasis model was conducted by And Cancer Inc. PC-3-GE tumor fragments were surgically implanted into the ventral lobe of the prostate and closed by suture. Treatment was started three days after surgery (40 mg/kg). VEGF-C and VEGFR-2 inhibition were analyzed at week 6.

References