Revolutionary changes are on cards with immuno modulatory approaches for various tumours with solid understanding of molecular cancer biology. Such agents may be synergistic or additive to the standard cancer chemotherapy, radiotherapy or with surgery as adjuvant or as neoadjuvant chemotherapy. One such agent in this category is bevacizumab, a humanized monoclonal antibody targeted against circulatory proangiogenic vascular endothelial growth factor (VEGF). It stops tumours from making new blood vessels, an obligatory step specially for survival and growth of various solid tumours.

**Mechanism of action:** Tumour growth beyond a few cubic millimeters cannot occur without the nutritional support of induced new blood vessels called angiogenesis. Angiogenesis promotes this support essentially in solid tumour growth and metastasis. This process as such is tightly regulated depending upon the complex interplay of inhibitory and stimulatory angiogenic factors. VEGF is one of the best characterized proangiogenic growth factor the effect of which are mediated by VEGF-1 and VEGF-2 receptors expressed on vascular endothelium. VEGF binds with VEGF receptors and promotes endothelial cell migration and proliferation, the two foremost essential steps in the development of new blood vessels. VEGF also increases vascular permeability whereby contributing further angiogenesis and tumour growth. It is expressed substantially in tumour cells and the expression is correlated with chemotherapeutic resistance and poor prognosis in cancers. Thus bevacizumab acts by binding to VEGF thereby prevents triggering of blood vessel growth with subsequent inhibition of tumour growth and metastasis.

**Therapeutic uses:** Clinical phase II trials of bevacizumab as part of adjuvant therapy showed positive results in median progression free survival in untreated and metastasized colorectal cancer and renal cell carcinoma; the cancers in which chemotherapy is not of much significance. It is also being evaluated for other tumours i.e. metastatic breast cancer using variety of tumour treatment plans in terms of the dose, length of infusion, frequency of infusion and number of such treatments. It is also being evaluated in phase I/II clinical trials for other solid tumours i.e. previously treated metastatic breast carcinoma and others.

Phase II trials that are being conducted include carcinoma prostate, carcinoma cervix, carcinoma ovaries, pancreatic and lung carcinoma for its potential use in these cancers. It is also being studied for gastrointestinal stromal cell tumours, malignant mesotheliomas, AML, and myelodysplastic syndromes. Potential non-cancerous uses may be possible where angiogenesis is of disadvantage i.e. age related macular degeneration and others.

**Dose:** Bevacizumab is being studied using varied treatment plans in the dose range of 3-20 mg/kg, i.v. with varied length of infusions frequency of infusions and number of treatment cycles. Escalating doses of bevacizumab ranging from 3 -20 mg/kg, body weight every other week have been used in different types of tumours.10 mg/kg, body weight administered as an i.v. bolus injection every other week seemed to be the optimal dose with acceptable levels of tolerability.

**Side effects:** The limited experience with various clinical trials until now found that it is well tolerated by most patients. Serious life threatening adverse events such as thromboembolic episodes and bleeding have also been observed and few patients have experienced other adverse effects of concern i.e. hypertension, proteinuria, epistaxis, fever, headache, rash and chills. Perforation of the wall of the colon has also been observed in one patient.

**Conclusion:** While the evidence of antitumour activity over a broad spectrum of experimental tumours is clear the proper selection, dose, timing and sequence of antiVEGF treatment in human cancers is not all obvious. Bevacizumab might prove to be a valuable addition to the existing armamentarium of drugs against cancer; incorporation of which in cytotoxic regimens may increase overall response rates. It may also prove to be effective in other conditions characterized by pathological angiogenesis.

**Sources:**


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