Lung Cancer in the United States

Lung cancer (both small cell and non-small cell) is the second most common cancer in both men and women. About 14% of all new cancers are lung cancers. The American Cancer Society’s estimates for lung cancer in the United States for 2017 are:

- About 222,500 new cases of lung cancer (116,990 in men and 105,510 in women)
- About 155,870 deaths from lung cancer (84,590 in men and 71,280 in women)

Lung cancer is by far the leading cause of cancer death among both men and women; about 1 out of 4 cancer deaths are from lung cancer. Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined.

Non-small Cell Lung Cancer (NSCLC) is the most common type of lung cancer, accounting for 80% to 85% of all lung cancer diagnoses, which is what Bevacizumab treats.

Why is NSCLC so deadly?

A certain protein called Vascular Endothelial Growth Factor-A (VEGF-A) plays a big role in NSCLC’s deadly ways. VEGF-A is a signal protein produced by cells that stimulates vasculogenesis and angiogenesis. VEGF-A is a protein that is in humans is encoded by the VEGFA gene. It has been shown to stimulate endothelial cell mitogenesis and cell migration. VEGF-A is also a vasodilator and increases microvascular permeability and was originally referred to as vascular permeability factor.

The malignancy and progression-free survival (PFS) prognosis of NSCLC are significantly linked to VEGF A serum levels in the patients. The higher the VEGF A concentration, the shorter PFS time one has. Because of this, if VEGF A could be eliminated or have its effect masked then the prognosis would improve. This was the impetus behind developing monoclonal antibodies (MABs) for VEGF A (like bevacizumab) and MABs for the various VEGF receptors themselves.

Avastin (Bevacizumab)

- Bevacizumab is an anti-angiogenic monoclonal antibody and is used in combination with other chemotherapeutic drugs as a first line defense against unresectable, locally advanced, recurrent or metastatic non-small cell lung cancer (NSCLC).
- Contains antigen binding regions of a humanized murine antibody that binds to Vascular Endothelial Growth Factor A (VEGF-A).
- It’s produced by recombinant DNA technology in a Chinese hamster ovary mammalian cell expression system in a nutrient medium.

Bevacizumab binds to VEGF-A and prevents the interaction of VEGF-A to its receptor VEGF1 and VEGF2 on the surface of endothelial cells. Activation of VEGF1 alone is necessary and sufficient to affect the angiogenesis, and vascular VEGF-induced processes of mitogenesis. Interruption of this process results in disrupting tumor growth and retarding metastasis.

Mechanism of Action

- At the tumor site, Bevacizumab reduces growth factor signaling by inhibiting the interaction of VEGF-A with its receptor. This, in turn, disrupts the formation and function of new blood vessels (angiogenesis), which is crucial for tumor growth and metastasis.
- Bevacizumab also has a direct antiproliferative effect on tumor cells, leading to tumor growth inhibition and cell death.
- By blocking VEGF-A, Bevacizumab reduces the recruitment of new blood vessels (vasculogenesis) and the interaction of these vessels with tumor cells.

References

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