

HEPATECTOMY-INDUCED
METASTASIS

Darbepoetin-alpha, an agent for improving liver regeneration after hepatectomy, has been reported to cause a substantial increase in hepatectomy-induced stimulation of colorectal liver metastatic growth. Data from a mouse study suggest that erythropoiesis-stimulating agents are not suitable for patients in whom hepatectomy is performed for malignant tumor resection.

Liver resection is the gold standard treatment of colorectal liver metastases; however, liver insufficiency is a serious complication after major hepatectomy. Erythropoietin and its analog darbepoetin-alpha are suitable agents to improve liver function after resection, owing to their cytoprotective, antiapoptotic and anti-inflammatory effects. Despite this promise, reports on the effect of erythropoietin on overall survival in cancer patients vary and the agent may promote tumor progression.

Rupertus and colleagues evaluated the effect of darbepoetin-alpha on hepatic tumor growth in a mouse model of colorectal cancer. The growth of liver metastases was notably greater in mice that underwent 50% hepatectomy in comparison with unresected mice. Furthermore, hepatectomized mice treated with darbepoetin-alpha displayed dramatically enhanced hepatectomy-induced stimulation of colorectal liver metastatic growth. Treatment with darbepoetin-alpha alone had only a slight effect on metastatic growth.

The researchers associated this enhanced growth with increased neovascularization—a mechanism observed in the mice treated with hepatectomy alone but augmented by the addition of darbepoetin-alpha—reduction of tumor cell apoptosis and inhibition of leukocyte adhesion. In conclusion, erythropoietin-stimulating agents might be best avoided in patients undergoing hepatectomy.

Lisa Richards

Original article Rupertus, K. *et al.* Darbepoetin-alpha enhances hepatectomy-associated stimulation of colorectal liver metastatic growth. *Ann. Surg.* **252**, 131–141 (2010)