Azacitidine

Azacitidine (INN; trade name Vidaza) is a chemical analog of cytidine, a nucleoside in DNA and RNA. Azacitidine and its deoxy derivative, decitabine (also known as 5-aza-2′-deoxycytidine), are used in the treatment of myelodysplastic syndrome. Both drugs were first synthesized in Czechoslovakia as potential chemotherapeutic agents for cancer.

The epigenetically active ribonucleoside analog 5-azacitidine is a new therapy option that changes tumor cell chromatin, which is frequently modified by methylation and deacetylation in malignant gliomas.

METHODS: In vitro, we analyzed cell viability, cell apoptosis, and migration of human GBM cells. In vivo, we established subcutaneous and intracerebral GBM mouse models originating from U87MG, U373MG, and primary GBM cells as well as one patient-derived xenograft. Xenografts were treated with 5-azacitidine as well as valproic acid, bevacizumab, temozolomide, and phosphate buffered saline. The tumor sizes and Ki67 proliferation indices were determined. Glioma angiogenesis was examined immunohistochemically by expression analysis of endothelial cells (CD31) and pericytes (PDGFRβ).

RESULTS: In vitro, 5-azacitidine treatment significantly reduced human glioblastoma cell viability, increased cellular apoptosis, and reduced cellular migration. In vivo, 5-azacitidine significantly reduced growth in two intracerebral GBM models. Notably, this was also shown for a xenograft established from a patient surgery sample; whereas, epigenetically acting valproic acid did not show any growth reduction. Highly vascularized tumors responded to treatment, whereas low-vascularized xenografts showed no response. Furthermore, intracerebral glioblastomas treated with 5-azacitidine showed a clearly visible reduction of tumor angiogenesis and lower numbers of endothelial cells and tumor vessel pericytes.

CONCLUSIONS: Our data show significant growth inhibition as well as antiangiogenic effects in intracerebral as well as patient-derived GBM xenografts. This encourages to investigate in detail the multifactorial effects of 5-azacitidine on glioblastomas [1)].

1)
Kratzsch T, Kuhn SA, Joedicke A, Hanisch UK, Vajkoczy P, Hoffmann J, Fichtner I. Treatment with 5-azacitidine delay growth of glioblastoma xenografts: a potential new treatment approach for glioblastomas. J Cancer Res Clin Oncol. 2018 Feb 9. doi: 10.1007/s00432-018-2600-1. [Epub ahead of print] PubMed PMID: 29427211.