



A service of the [U.S. National Library of Medicine](#)
and the [National Institutes of Health](#)

Select 19221171

1: [Neuro Oncol.](#) 2009 Feb 16. [Epub ahead of print]



Cilengitide modulates attachment and viability of human glioma cells, but not sensitivity to irradiation or temozolomide in vitro.

[Maurer GD](#), [Tritschler I](#), [Adams B](#), [Tabatabai G](#), [Wick W](#), [Stupp R](#), [Weller M](#).

Department of Neurology, University Hospital of Tübingen, Hertie Institute for Clinical Brain Research, Tübingen, Germany; Department of Neurooncology, University of Frankfurt, Frankfurt, Germany.

Cilengitide is a cyclic peptide antagonist of integrins $\alpha v\beta 3$ and $\alpha v\beta 5$ which is currently evaluated as a novel therapeutic agent for recurrent and newly diagnosed glioblastoma. Its mode of action is thought to be mainly antiangiogenic, but may include direct effects on tumor cells, notably on attachment, migration, invasion and viability. Here we show that, at clinically relevant concentrations, cilengitide (1-100 μM) induces detachment in some, albeit not all glioma cell lines, while the effect on cell viability is modest. Detachment induced by 2 cilengitide could not be predicted by the level of expression of the cilengitide target molecules, $\alpha v\beta 3$ and $\alpha v\beta 5$, at the cell surface. Glioma cell death induced by cilengitide was associated with the generation of caspase activity, but caspase activity was dispensable for cell death since ectopic expression of cytokine response modifier (crm)-A or coexposure to the broad spectrum caspase inhibitor, zVAD-fmk, were not protective. Moreover, forced expression of Bcl-XL or altering the p53 status did not modulate cilengitide-induced cell death. No consistent effects of cilengitide on glioma cell migration or invasiveness were observed in vitro. Preliminary clinical results indicate a preferential benefit from cilengitide added to temozolomide-based radiochemotherapy in patients with O(6)-methyltransferase (MGMT) gene promoter methylation. Accordingly, we also examined whether the MGMT status determines glioma cell responses to cilengitide alone or in combination with temozolomide. Neither ectopic expression of MGMT in MGMT-negative cells nor silencing the MGMT gene in MGMT-positive cells altered their response to cilengitide alone or cilengitide in combination with temozolomide. These data suggest that the beneficial clinical effects derived from cilengitide in vivo may arise from altered perfusion which promotes temozolomide delivery to glioma cells.

PMID: 19221171 [PubMed - as supplied by publisher]
