

Trabectedin

Preusser et al., investigated the in vitro effects of trabectedin alone and in combination with hydroxyurea, cisplatin, and doxorubicin in primary cell cultures of benign (n = 9), atypical (n = 6), and anaplastic (n = 4) meningiomas using chemosensitivity assays (3-[4,5dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide [MTT]), Western blot analysis, cell cycle analysis, and immunofluorescent staining.

RESULTS: Strong antimeningioma activity of trabectedin was observed and was characterized by distinct cell cycle arrest, down-regulation of multiple cyclins, deregulated expression of cell death-regulatory genes, and massive apoptosis induction. Cytotoxic activity was especially intense in higher grade meningiomas with a half-maximal inhibitory concentration <10 nM. Combination with trabectedin synergistically enhanced the antimeningioma activity of hydroxyurea but also enhanced the activity of doxorubicin and cisplatin. On the basis of these findings, trabectedin was given to 1 patient who had heavily pretreated, anaplastic meningioma, and a favorable response was observed with radiologic disease stabilization, marked reductions in brain edema and requirement for corticosteroids, and improvement of clinical symptoms. However, treatment had to be discontinued after 5 cycles because of adverse drug effects.

CONCLUSIONS: The current results indicated that trabectedin may represent a promising new therapeutic option for patients with aggressive meningioma and should be evaluated in prospective clinical studies ¹⁾.

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Preusser M, Spiegl-Kreinecker S, Lötsch D, Wöhrer A, Schmook M, Dieckmann K, Saringer W, Marosi C, Berger W. Trabectedin has promising antineoplastic activity in high-grade meningioma. *Cancer*. 2012 Oct 15;118(20):5038-49. doi: 10.1002/cncr.27460. Epub 2012 Mar 5. PubMed PMID: 22392434.

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