Trabectedin has promising antineoplastic activity in high-grade meningioma.


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Abstract

BACKGROUND: Meningiomas are common intracranial tumors arising from the meninges and usually are benign. However, a few meningiomas have aggressive behavior and, for such patients, effective treatment options are needed. Trabectedin is a novel, marine-derived, antineoplastic agent that has been approved and is used routinely as therapy for advanced soft tissue sarcoma and ovarian cancer.

METHODS: The authors 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-[4,5-dimethylthiazol-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. Cancer 2012; © 2012 American Cancer Society.

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