Alpha therapy with 213Bi-DOTA-substance P in recurrent glioblastoma multiforme

Abstract:
Objectives: Glioblastoma multiforme (GBM) is the most common and malignant primary brain tumor, and has one of the worst prognoses among the various carcinomas, with a 5-year survival rate of ~10%. The median survival time is 14.6 months from time of diagnosis, in spite of aggressive surgery, radiation therapy and chemotherapy. Complete surgical resection beyond tumor margins cannot be achieved in GBM because of infiltrative nature. From previous studies it is known, that GBM has been demonstrated NK-1 receptor system and substance P can be used as a ligand for targeted therapy. Alpha emitter, like 213Bi offers the new potential for selective irradiation of tumors, with minimizing damage to adjacent tissue. Methods: 18 patients with glia tumor IV after standard therapy were included in the study during two years. Following intracavitary or intratumoral insertion of 1-2 catheter systems, patients were treated with 1-6 doses of 2 GBq 213Bi-DOTA-Substance P(213Bi-SP) in intervals of 2 months. 68Ga-DOTA-Substance P(68Ga-SP) was co-injected with the therapeutic doses to assess biodistribution using PET/CT. Therapeutic response was monitored with MRI. Study was approved by the ethical committee of the Medical University of Warsaw. Results: Treatment with activity up to 13 GBq 213Bi-SP was tolerated well with only mild transient adverse reactions: in 1 patient transient increase of focal neurological symptoms and in 3 patients episodes of epileptic seizures several days after treatment. PET/CT imaging showed high retention of the radiolabeled peptide at the tumor site. The data for statistical analysis was available for 11 patients. Median progression free survival was 3.7 months. The median overall survival from the first diagnosis was 22 months, and from the start of 213Bi-SP was 8.9 months. Conclusions: Treatment of recurrent GBM with 213Bi-SP is safe and well tolerated. Targeted alpha therapy with 213Bi-SP may evolve as a promising novel option for treatment of recurrent GBM.

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