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Titel des Beitrags: Enhanced efficacy of combined 213Bi-DTPA-F3 and paclitaxel therapy of peritoneal carcinomatosis is mediated by enhanced induction of apoptosis and G2/M phase arrest.

Abstract: Targeted therapy with ?-particle emitting radionuclides is a promising new option in cancer therapy. Stable conjugates of the vascular tumour-homing peptide F3 with the ?-emitter (213)Bi specifically target tumour cells. The aim of our study was to determine efficacy of combined (213)Bi-diethylenetriaminepentaacetic acid (DTPA)-F3 and paclitaxel treatment compared to treatment with either (213)Bi-DTPA-F3 or paclitaxel both in vitro and in vivo. Cytotoxicity of treatment with (213)Bi-DTPA-F3 and paclitaxel, alone or in combination, was assayed towards OVCAR-3 cells using the alamarBlue assay, the clonogenic assay and flow cytometric analyses of the mode of cell death and cell cycle arrest. Therapeutic efficacy of the different treatment options was assayed after repeated treatment of mice bearing intraperitoneal OVCAR-3 xenograft tumours. Therapy monitoring was performed by bioluminescence imaging and histopathologic analysis. Treatment of OVCAR-3 cells in vitro with combined (213)Bi-DTPA-F3 and paclitaxel resulted in enhanced cytotoxicity, induction of apoptosis and G2/M phase arrest compared to treatment with either (213)Bi-DTPA-F3 or paclitaxel. Accordingly, i.p. xenograft OVCAR-3 tumours showed the best
response following repeated (six times) combined therapy with (213)Bi-DTPA-F3 (1.85 MBq) and paclitaxel (120 µg) as demonstrated by bioluminescence imaging and histopathologic investigation of tumour spread on the mesentery of the small and large intestine. Moreover, mean survival of xenograft mice that received combined therapy with (213)Bi-DTPA-F3 and paclitaxel was significantly superior to mice treated with either (213)Bi-DTPA-F3 or paclitaxel alone. Combined treatment with (213)Bi-DTPA-F3 and paclitaxel significantly increased mean survival of mice with peritoneal carcinomatosis of ovarian origin, thus favouring future therapeutic application.