Fractionated intravesical radioimmunotherapy with (213)Bi-anti-EGFR-MAb is effective without toxic side-effects in a nude mouse model of advanced human bladder carcinoma.

Abstract:

Gold standard in therapy of superficial, non-muscle invasive urothelial tumors is transurethral resection followed by intravesical instillation therapies. However, relapse is commonly observed and therefore new therapeutic approaches are needed. Application of (213)Bi-immunoconjugates targeting EGFR had shown promising results in early tumor stages. The aim of this study was the evaluation of fractionated application of (213)Bi-anti-EGFR-MAb in advanced tumor stages in a nude mouse model. Luciferase-transfected EJ28 human bladder carcinoma cells were instilled intravesically into nude mice following electrocautery. Tumor development was monitored via bioluminescence imaging. One day after tumor detection mice were treated intravesically either 2 times with 0.93 MBq or 3 times with 0.46 MBq of (213)Bi-anti-EGFR-MAb. Therapeutic efficacy was evaluated via overall survival and toxicity toward normal urothelium by histopathological analysis. Mice without treatment and those treated with the native anti-EGFR-MAb showed mean survivals of 65.4 and 57.6 d, respectively. After fractionated treatment with 0.93 MBq of
Bi-anti-EGFR-MAb animals reached a mean survival of 141.5 d and 33% of the animals survived at least 268 d. Fractionated treatment with 0.46 MBq (213)Bi-anti-EGFR-MAb resulted in a mean survival of 131.8 d and 30% of the animals survived longer than 300 d. Significant differences were only observed between the control groups and the group treated twice with 0.93 MBq of (213)Bi-anti-EGFR-Mab. No toxic side-effects on the normal urothelium were observed even after treatment with 3.7 MBq of (213)Bi-anti-EGFR-Mab. The study demonstrates that the fractionated intravesical radioimmunotherapy with (213)Bi-anti-EGFR-MAb is a promising approach in advanced bladder carcinoma.

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