Pharmacokinetics and dosimetry in intraperitoneal radioimmunotherapy with ^{211}At

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I. Andersson H et al.
Intraperitoneal α-particle radioimmunotherapy of ovarian cancer patients: pharmacokinetics and dosimetry of ^{211}At-MX35 F(ab')$_2$ – A phase I study
J Nucl Med 2009;50(7):1153-1160

II. Cederkrantz E et al.
Evaluation of effects on the peritoneum after intraperitoneal α-radioimmunotherapy with ^{211}At
Cancer Biother Radiopharm 2012;27(6):353-364

III. Cederkrantz E et al.
Effective dose of intraperitoneal α-radioimmunotherapy with ^{211}At for ovarian cancer patients
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Pharmacokinetics and dosimetry in intraperitoneal radioimmunotherapy with ^{211}At

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Abstract

The prognosis for patients diagnosed with disseminated cancer is often poor. Radioimmunotherapy (RIT) is a new approach to treat disseminated disease. The aim is to target tumor cells with monoclonal antibodies (mAbs) labeled with radionuclides which release cytotoxic particle radiation upon decay. The radionuclide ^{211}At, with half-life 7.21h, is an interesting candidate for RIT. It emits an α-particle which leaves a short, dense ionization track along its path. The range of the α-particle (<100 μm) corresponds to a few cell diameters. Thus, with ^{211}At in combination with a tumor-specific mAb, a high level of irradiation may be achieved in very small tumors, while, at the same time, the surrounding tissue is spared.

In this thesis, the pharmacokinetics of intraperitoneal (IP) ^{211}At-MX35 F(ab')2 for ovarian cancer was investigated in 12 patients partaking in a phase I study. The *in vivo* distribution was monitored by sampling of bodily fluids and gamma camera imaging. Absorbed doses to normal organs and tissues were estimated. The peritoneum was subjected to the highest absorbed dose of all investigated tissues after the amendment of a thyroid blocking agent. The radiation tolerance of the peritoneum was unknown and was therefore studied in an animal model. The absorbed doses associated with therapeutic activity levels were found to be well tolerated in a short term perspective.

Exposure to α-particles is however associated with a high risk for cancer induction. The ICRP recommends a radiation weighting factor 20 for α-particles. The effective dose provides a tool for estimating the risk associated with a procedure involving irradiation. It was estimated to < 2 Sv for a general patient undergoing IP ^{211}At-RIT with 300 MBq in 1.5 L icodextrin.

Keywords: astatine-211, radioimmunotherapy, alpha-emitter, ovarian cancer, MX35, pharmacokinetics, dosimetry, effective dose

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