Contribution ID: **81** Type: **not specified**

Intraperitoneal alpha-emitting radio immunotherapy with Astatine-211 in relapsed ovarian cancer; long-term follow-up with individual absorbed dose estimations

Eliminating microscopic residual disease with α-particle radiation is theoretically appealing. Following extensive preclinical work with α-particle emitting astatine-211 (211At), we performed a phase I trial in epithelial ovarian cancer (EOC). This was a first-in-class intraperitoneal (i.p.) α-particle therapy and the first in human study using the conjugate 211At-MX35, a murine monoclonal F(ab')2 antibody. We now present clinical outcome data and toxicity in a long-term follow-up with individual absorbed dose estimations.

Methods: Twelve patients with relapsed EOC, achieving a second complete or near complete response with chemotherapy received i.p. treatment with escalating (20 to 215 MBq/L) activity concentrations of 211At-MX35 F(ab')2.

Results: The activity concentration was escalated to 215 MBq/L without any dose limiting toxicities. Most toxicities were low-grade and likely related to the treatment procedure, not clearly linked to the α-particle irradiation with no observed hematological toxicity. One grade 3 fatigue, and one grade 4 intestinal perforation during catheter implantation was observed. Four patients had a survival >6 years, one of whom did not relapse. At progression chemotherapy was given without signs of reduced tolerability. Overall median survival was 35 months with a 1-, 2-, 5-, and 10-year survival of 100%, 83%, 50% and 25%.

Calculations of the absorbed doses showed that a lower specific activity is associated with a lower single cell dose, whereas a high specific activity may result in a lower central dose in microtumors. Individual differences in absorbed dose to possible micro-tumors were due to variations in administered activity and the specific activity.

Conclusion: No apparent signs of radiation-induced toxicity, or decreased tolerance to relapse therapy were observed. The dosimetric calculations show that further optimization is advisable to increase the efficacy and reduce possible long-term toxicity.

Funding Agency

Swedish Research Council; the Swedish Cancer Society; the King Gustav V Clinic Research Foundation

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Presentation Type

Contributed Oral

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