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Targeting ovarian cancer with anti-MISR2 radiolabelled antibodies

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Ovarian cancer is the most lethal gynecologic malignancy and it has high rate of recurrence justifying the development of new therapeutic tools. Our project aims at developing new radiopharmaceuticals and innovative route of administration to target the small volume residual disease after complete cytoreductive surgery of peritoneal carcinomatosis on preclinical models. We use internalising murine monoclonal antibody (16F12) specific of the anti-müllerian hormone type 2 receptor (AMHR2/MISR2), overexpressed in ovarian cancer and gynaecologic malignancies. Antibodies are radiolabelled with Lutecium-177, a beta minus emitter, and Bismuth-213, an alpha emitter, to perform radioimmunotherapy. Radiolabelled antibodies are injected intraperitoneally but also after Brief IntraPeritoneal RadioImmunoTherapy (BIP-RIT), a technique delivering high activities in the peritoneal cavity for a short time before washing, like Hyperthermic IntraPEritoneal Chemotherapy (HIPEC). We studied biodistribution, dosimetry, toxicity and therapeutic efficacy on various models and combinaison of radionuclides and route of administration. BIP-RIT appears to be always favourable in term of biodistribution and dosimetry (especially for the tumour-over-blood ratio) whatever the radionuclide used. Bismuth-213 is particularly adapted for radioimmunotherapy of small residual tumours, showing therapeutic efficacy with no toxicity. PET/CT imaging of radiolabelled antibodies with Zirconium-89 was performed and may be used as a theranostic tool for (radio)immunotherapy with anti-AMHR2 antibodies. This work may lead to realistic theranostic options in ovarian cancer in clinic.

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