

Novel radiopharmaceutical for intraperitoneal treatment of peritoneal metastasis from colorectal and ovarian cancer after complete surgical resection



after complete surgical resection

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Background

- Radspherin is a novel radiopharmaceutical based on calcium carbonate (CaCO₃) microparticles radiolabelled with the alpha particle emitter radium-224 (²²⁴Ra).
- Radspherin is developed for treatment of peritoneal micrometastases after complete cytoreductive surgery (CRS).
- While surgical resection of visible metastases plays an important role in the treatment of peritoneal metastases, remaining micrometastases in the peritoneal lining as well as free-floating cancer cells frequently colonize and develop into new metastases, eventually resulting in relapse of the disease.
- The potential of Radspherin to eliminate those residual micrometastases may increase the prospect of a complete response.

Treatment concept

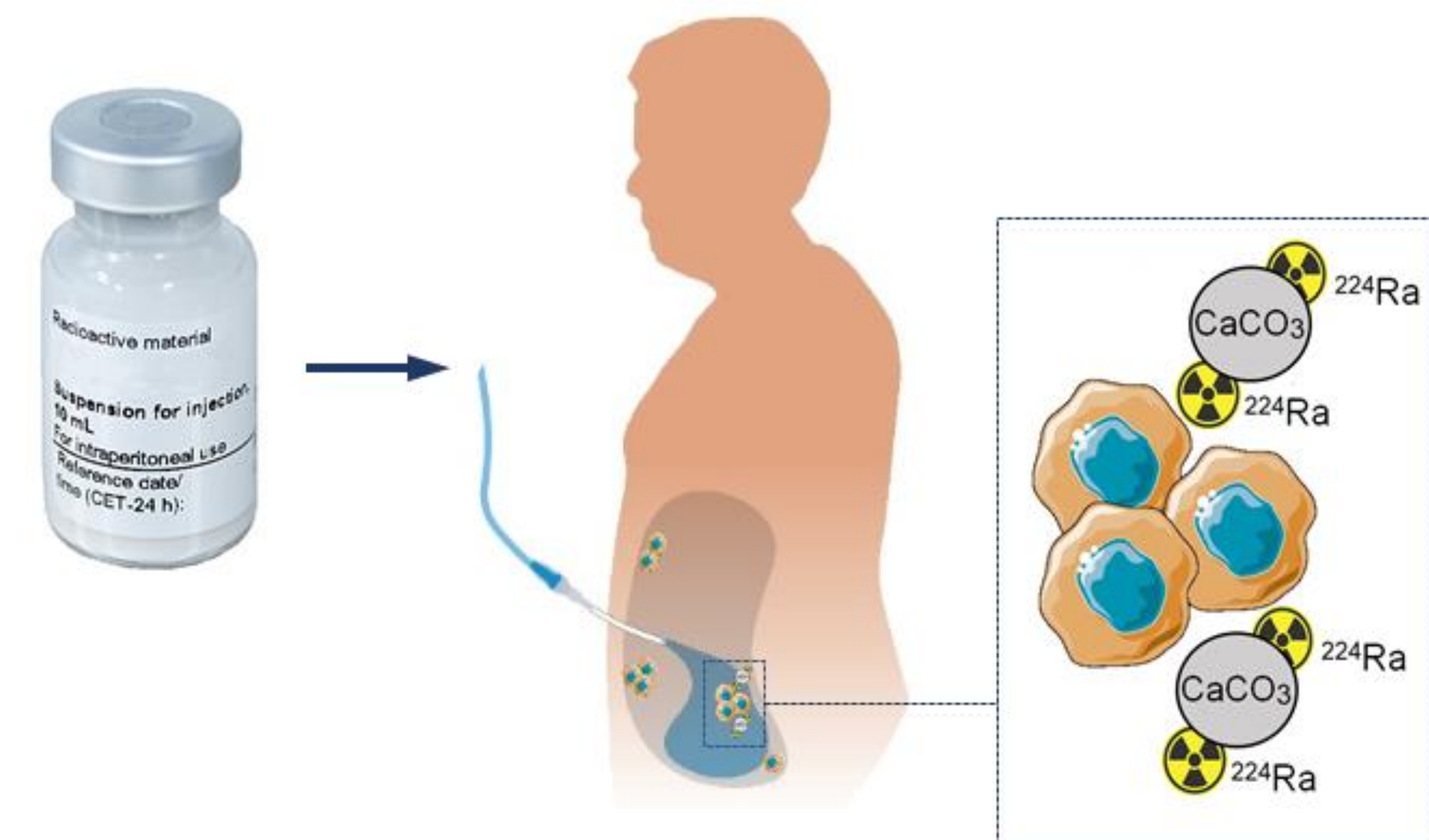


Figure 1. Conceptual scheme of Radspherin against peritoneal metastasis.

- Radspherin is administered postoperatively, one to two days after CRS, via an intraperitoneal catheter (Fig. 1).
- The mode of action is the delivery of alpha radiation to tumour cells and the induction of clustered DNA double strand breaks which are difficult to repair (Fig. 2).
- There are no known cellular resistance mechanisms to alpha radiation, which may be effective against dormant and chemoresistant cancer cells.

- The range of alpha particles in tissue is less than 0.1 mm (3-10 cell diameters) which limits penetration of the radiation into normal tissue (Fig. 2).

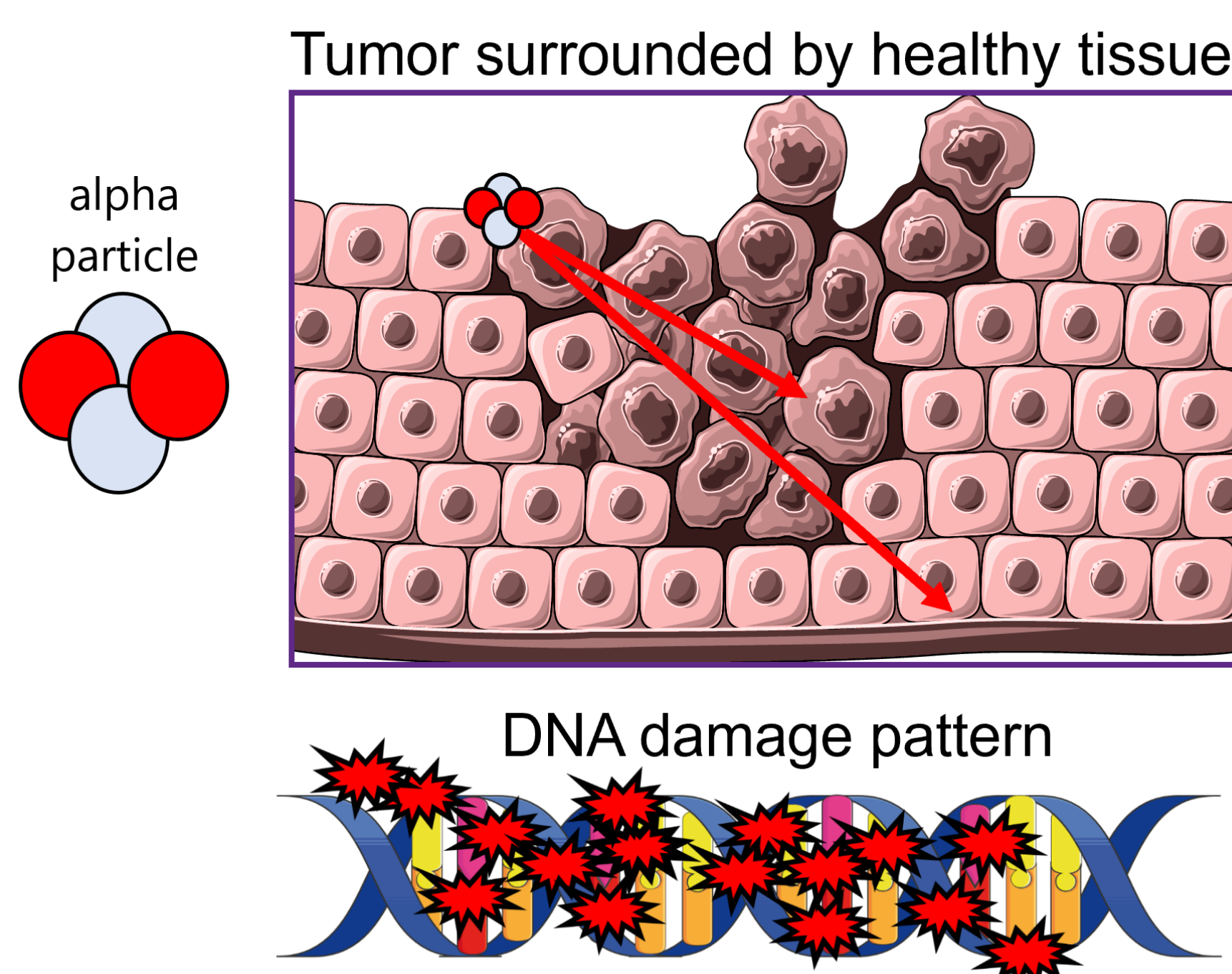


Figure 2. Tissue range and associated DNA damage caused by alpha particles.

- The CaCO₃ microparticles retain and distribute the radioactivity in the peritoneal volume.
- Radspherin may be effective on peritoneal micrometastases regardless of the origin of the primary malignancy.

Nonclinical and clinical data

- In vivo pharmacology studies indicate that Radspherin possesses substantial antitumour activity in different rodent models of disseminated peritoneal disease.
- In the ongoing phase 1/2a studies in patients with peritoneal metastasis from ovarian (NCT03732768) and colorectal cancer (NCT03732781), all administered doses of Radspherin were well tolerated.
- No dose-limiting toxicities, deaths, or discontinuations due to adverse events were reported.
- The highest dose tested has been selected as the recommended dose for future studies.
- In colorectal cancer patients, Radspherin has been studied in combination with hyperthermic intraperitoneal chemotherapy.
- 75-85% of the injected radioactivity was retained in the peritoneal cavity² and patient images showed that the radioactivity was evenly distributed in the peritoneal cavity (Fig. 3).

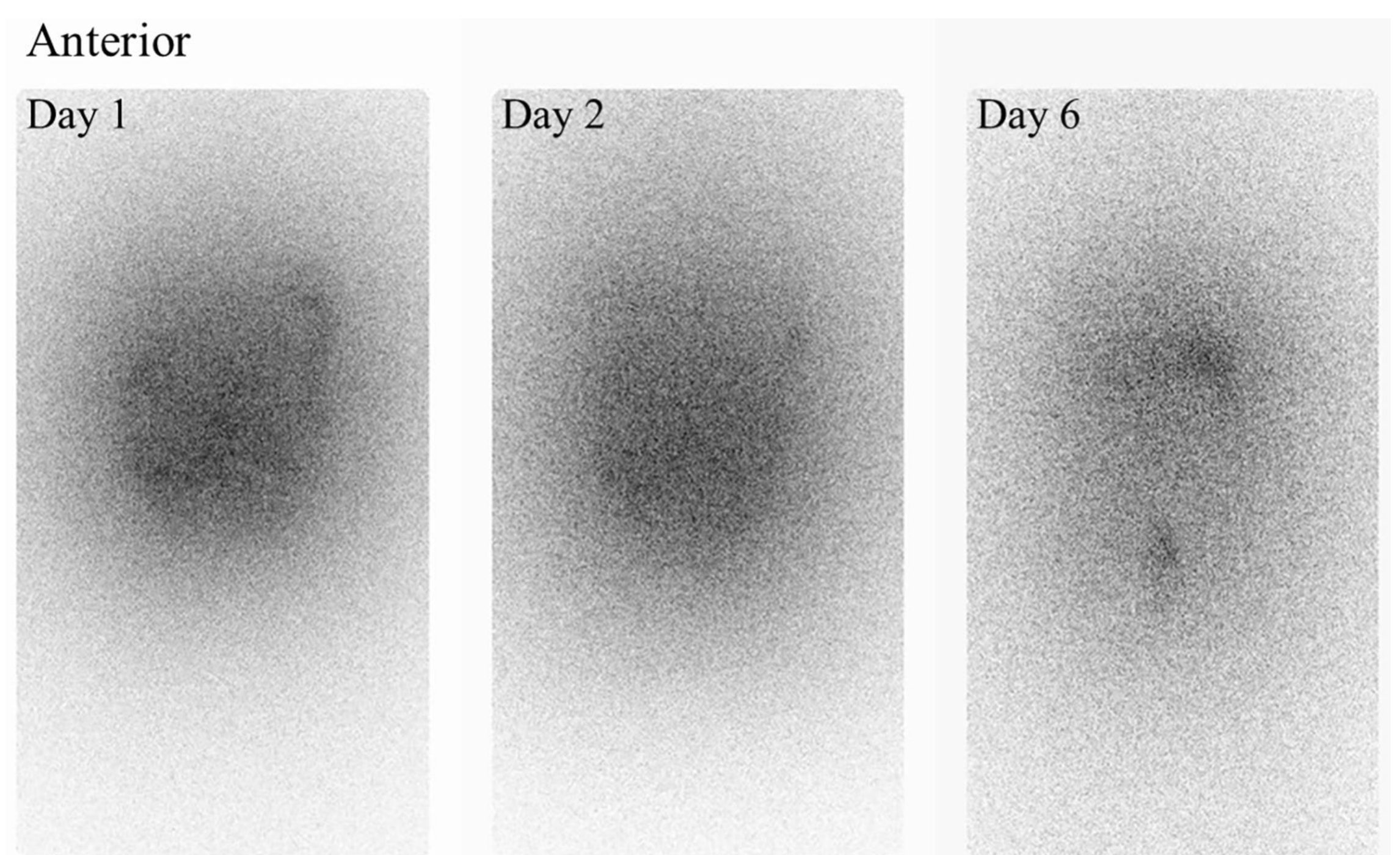


Figure 3. Anterior whole-body planar gamma camera images¹.

- No restrictions on physical contact after Radspherin administration are necessary for the patient¹.
- Encouraging preliminary efficacy data were presented this year at ASCO³.

Conclusion

Radspherin is a novel treatment concept with the prospect of being a valuable addition to the limited therapeutic landscape for patients with peritoneal metastasis.

ACKNOWLEDGEMENTS

Figure 1 and 2 were created with graphics from Servier Medical Art.

REFERENCES

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DISCLOSURES

All authors are employed in Oncoinvent AS. Westrøm and Bønsdorff hold ownership interest in Oncoinvent AS.