Oncoinvent

Transforming cancer care through direct alpha therapy

TRP Summit Europe – 12 November 2025

Expanding the Scope of Targeted Radiopharmaceuticals

Topic	A practical example of direct radiotherapy in peritoneal carcinomatosis
Content	○ ^{224}Ra labelled microparticles - Radspherin® - to target cancer in body cavities ○ Latest clinical data and development plans for Radspherin® - currently in Phase 2 in ovarian cancer
Presenter	Oystein Soug
Company	**Oncoinvent ASA** ○ Clinical stage biotech, 40 employees ○ Listed on Euronext Oslo

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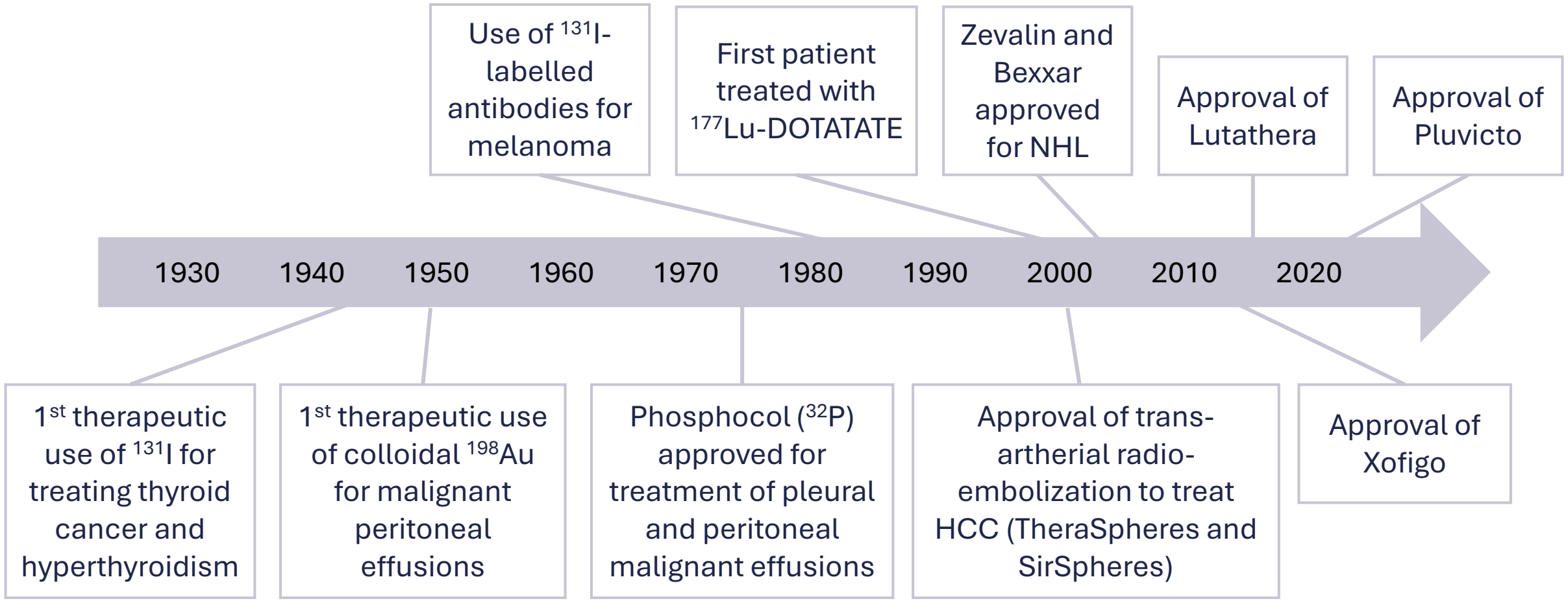
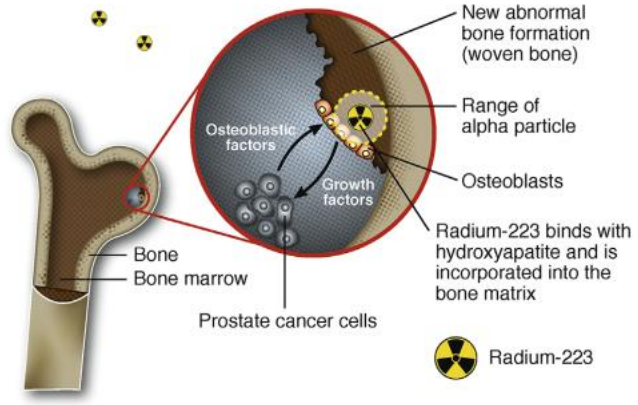
The history of targeted therapeutic radiopharmaceuticals



Primac, I. et al. The molecular blueprint of targeted radionuclide therapy. Nat Rev Clin Oncol 22, 869–894 (2025)

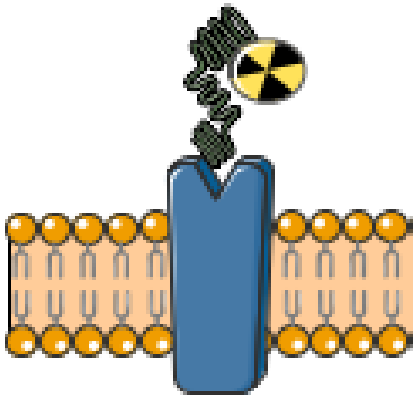
Ways to target cancer with radiopharmaceuticals

Natural homing



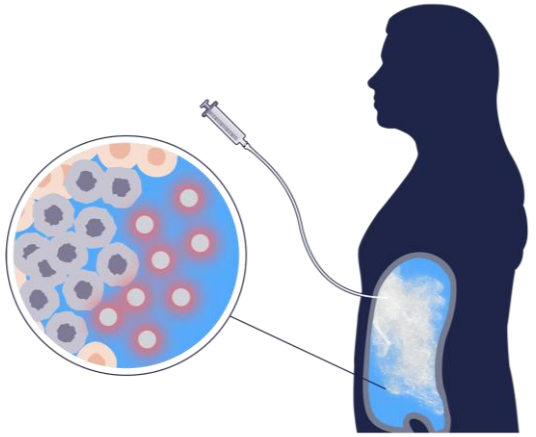
- Some radionuclides naturally targets certain organs. ^{223}Ra **Xofigo** goes to bone, ^{131}I goes to the thyroid
- Simple, proven in routine clinical practice, selective for tissues
- Limited to diseases with natural avidity, less adaptable

Molecular targeting



- Radioligands: Biological targeting agent linked to a radioactive payload e.g. Lutathera, **Pluvicto**
- Large potential
- Complex, risk of off-target effects

Direct radiotherapy



- Physically trapping radioactivity in an organ: e.g. **Radspherin®**, TheraSphere (Boston Scientific), REYOBIC (Plus)
- Non-systemic delivery: High local concentration, minimal systemic toxicity
- Requires direct access to site, not suitable for systemic disease

Targeting by proximity – brilliant in its simplicity

Bypasses
the need of biological targeting and systemic distribution of the radioactive payload

Retains
the radioactive payload in the target area

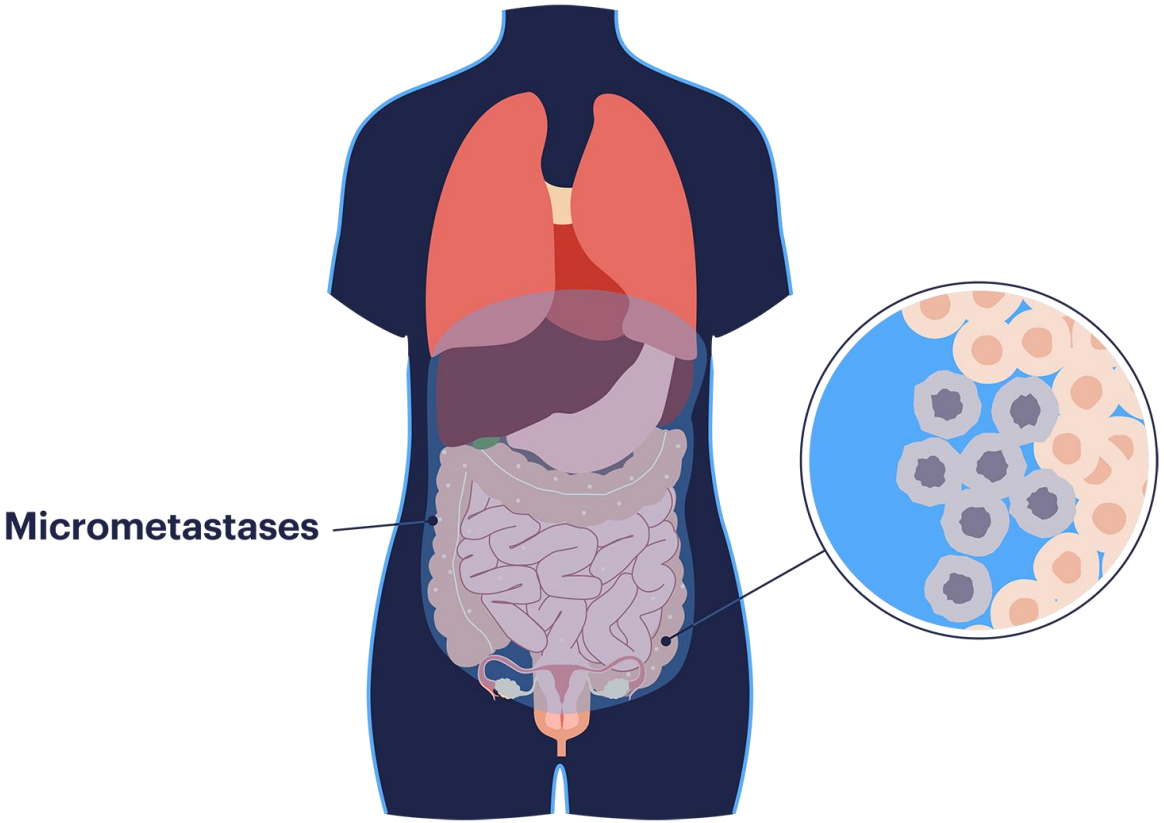
Increases
the radionuclide exposure at the tumor target sites

Reduces
the radionuclide exposure to radiation sensitive organs

Oncoinvent – directly targeted alpha therapy

1. Oncoinvent uses a targeted, non-biological, **receptor independent** mode of action with the alpha emitter ^{224}Ra
2. **Harnessing** the advantages of radiopharmaceuticals with **lower complexity** and risk
3. **Signals of efficacy**: potential game changer in ovarian and colorectal cancers
4. **In Phase 2** in ovarian cancer
5. **High unmet need** and limited competition
6. Developed by radiopharma pioneers and serial-entrepreneurs - seasoned management with **experience** bringing radiopharmaceuticals to the market

Peritoneal metastases - urgent need for novel treatments



- Peritoneal metastases arise from many **different primary cancers**
- The only treatment option with curative intent is **surgery**, effect of systemic therapy limited
- Surgery leaves behind **micro-metastases** giving rise to new metastases and disease progression
- Peritoneal metastases are confined to the peritoneum creating a '**closed compartment**'

The main cause of death in ovarian cancer

70% of all ovarian cancer patients have peritoneal metastasis at diagnosis

Up to 85% relapse after surgical resection

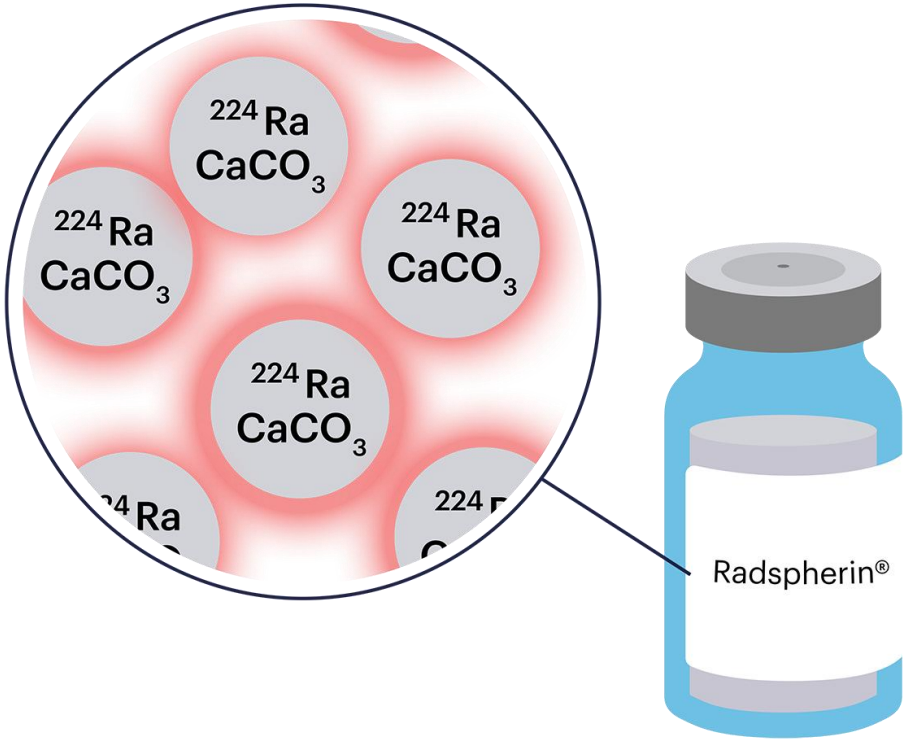
- The majority of patients experience disease recurrence
- Recurrences are almost exclusively **confined to the peritoneum**
- Large clinical need for **local control** of cancer in the peritoneum is key to improving life expectancy
- FDA Fast Track

Lengyel Am J Pathol. 2010 Sep; 177(3): 1053–1064.
González-Martín N Engl J Med 2019;381:2391-402
Jansen et al. Ann Med Surg (Lond). 2023 May; 85(5): 1539–1545.

Radspherin® - alpha therapy targeted to and retained in the peritoneum

Radspherin®

- Combining **alpha-emitting ^{224}Ra** with **$CaCO_3$ microparticles**
- Half-life 3.6 days
- **Therapy with depot effect** - 75% of radiation dose delivered the first week
- Shelf life 8 days allowing for **centralized manufacturing**
- Good **raw material availability** and simple manufacturing



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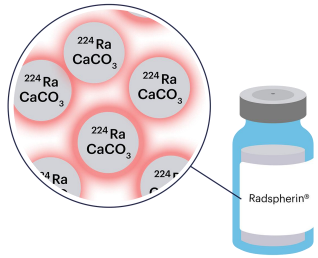
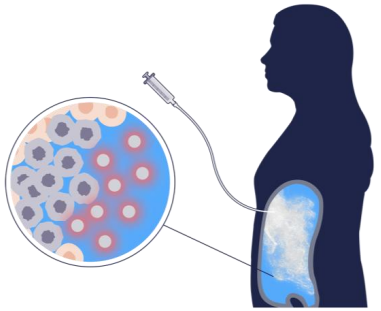


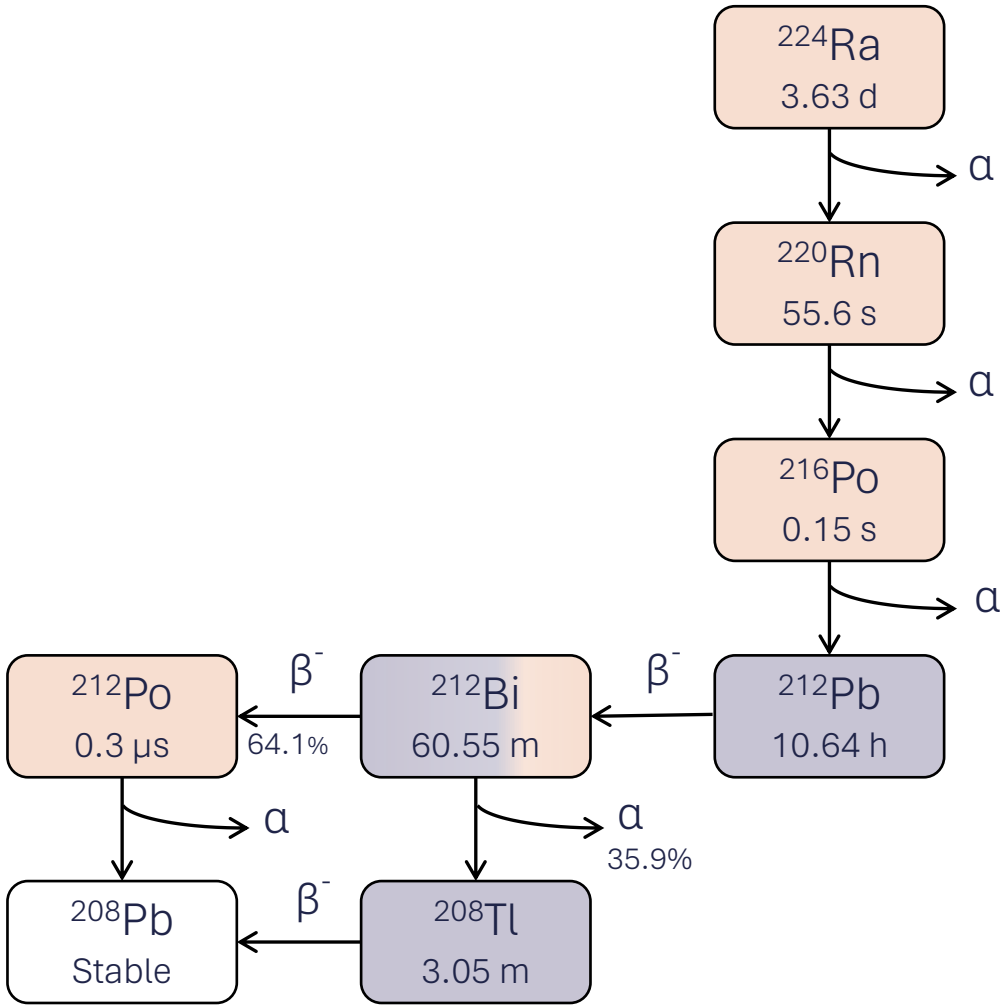
How does it work?

- Delivery directly to the peritoneum through an in-dwelling catheter
- Administration **1-3 days post-surgery**
- High energy and short radiation range enables effective killing of the targeted metastases **while sparing the surrounding normal tissue**

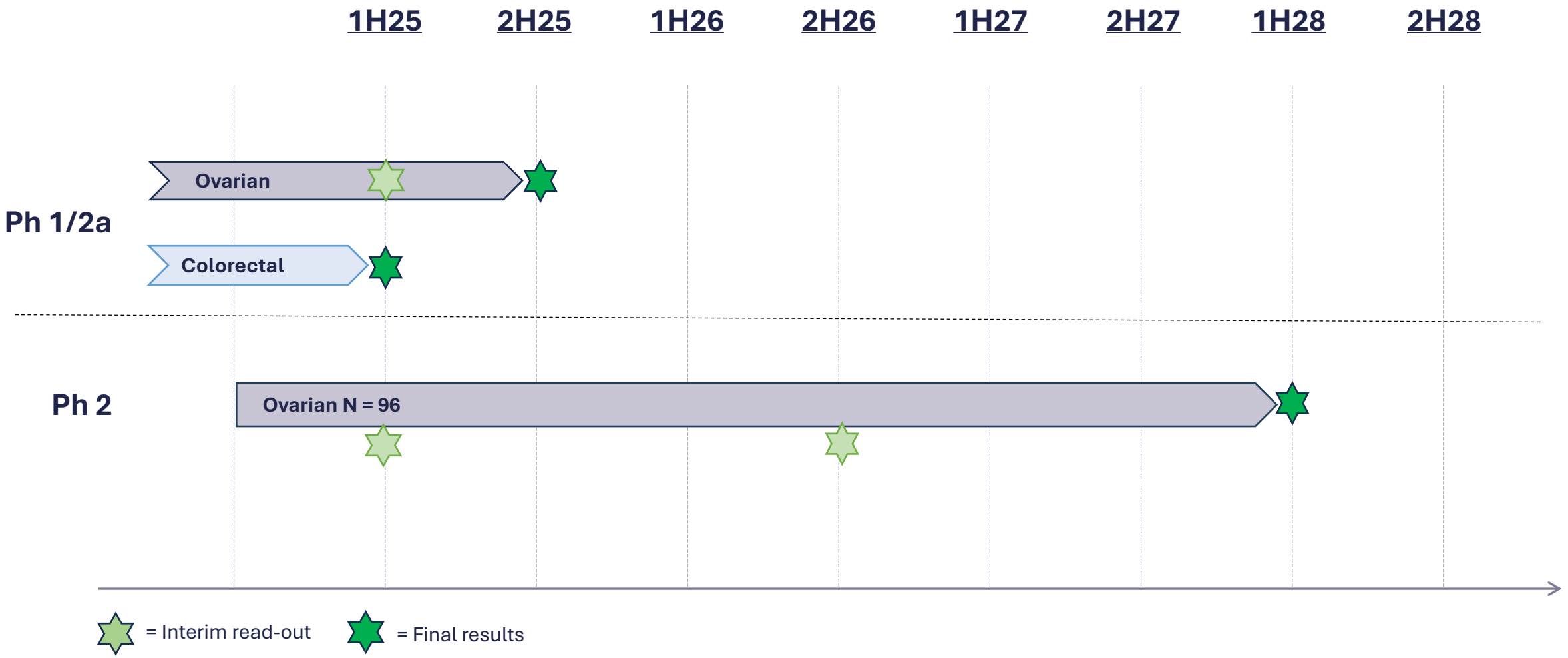


Properties of the radionuclide radium-224

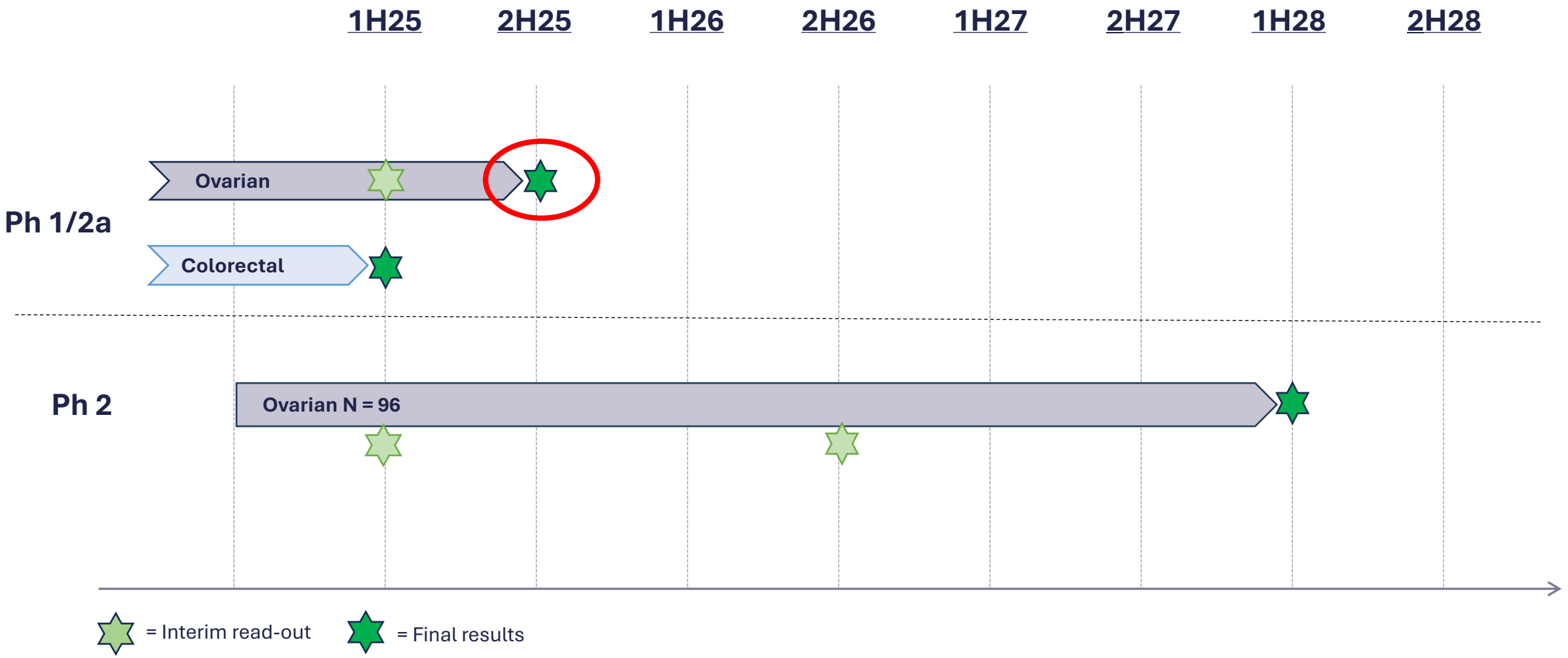
- Half life 3.6 days
- Decay of radium-224 to stable lead-208 via shorter-lived daughters
- 4 alpha particles released
- **93%** of the total decay energy emitted as alpha particles
- The amount of lead resulting from a dose of Radspherin® is **well below** toxic levels



Ongoing clinical development



Ongoing clinical development



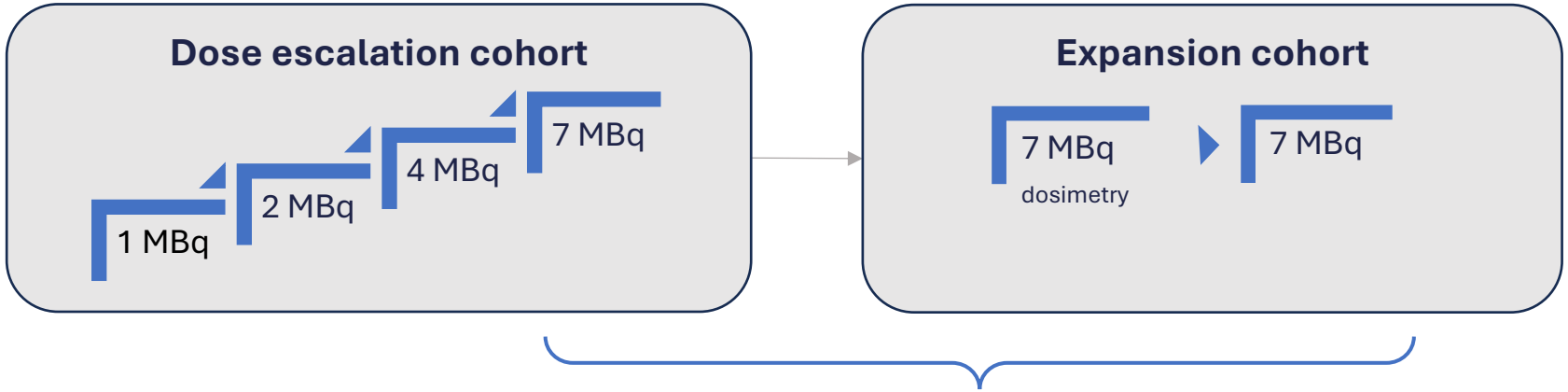
Radspherin® - phase 1 study in ovarian cancer

RAD-18-001: in patients after secondary debulking surgery of platinum-sensitive recurrent ovarian cancer

- single-arm open label study
- 3 + 3 dose-escalation (1, 2, 4, 7 MBq)
- 24 months follow-up

4 clinical sites:

- Oslo, Norway (PI: Yun Wang)
- Leuven, Belgium (PI: Els van Nieuwenhuysen)
- Madrid, Spain (PI: Luis Chiva)
- Pamplona, Spain (PI: Luis Chiva)



Total number of patients recommended dose 7MBq, **n=10**

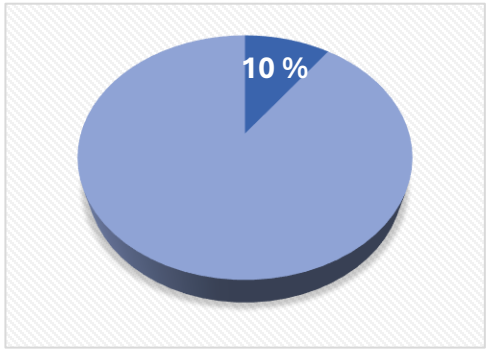
Ovarian cancer: Preventing disease progression

24 months data from 10 patients receiving 7 MBq dose vs historical recurrence rates

"These final results are **truly encouraging**, suggesting that Radspherin® could help **delay disease progression and offer patients hope for longer, healthier lives**. It is particularly promising to see that the new recurrences were limited to lymph nodes, which are typically associated with **longer survival** compared to peritoneal relapses.

Dr Luis Chiva, Principal Investigator and Director of Department of Obstetrics and Gynecology Clinica Universidad de Navarra

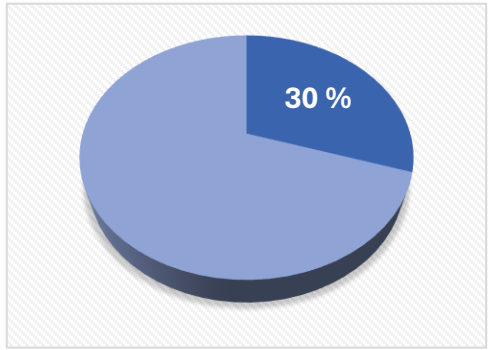
Recurrence rates RAD-18-001



10%

Peritoneal recurrence rate

One patient with recurrence

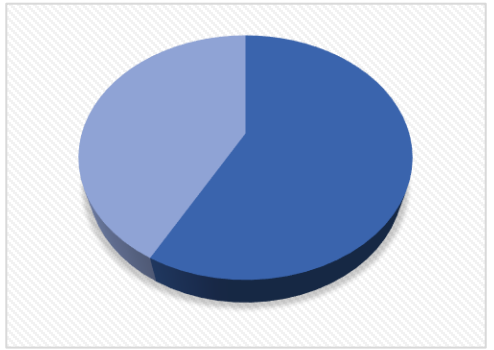


30%

Overall recurrence rate

Additionally, two lymph node recurrences

Recurrence rates historical controls



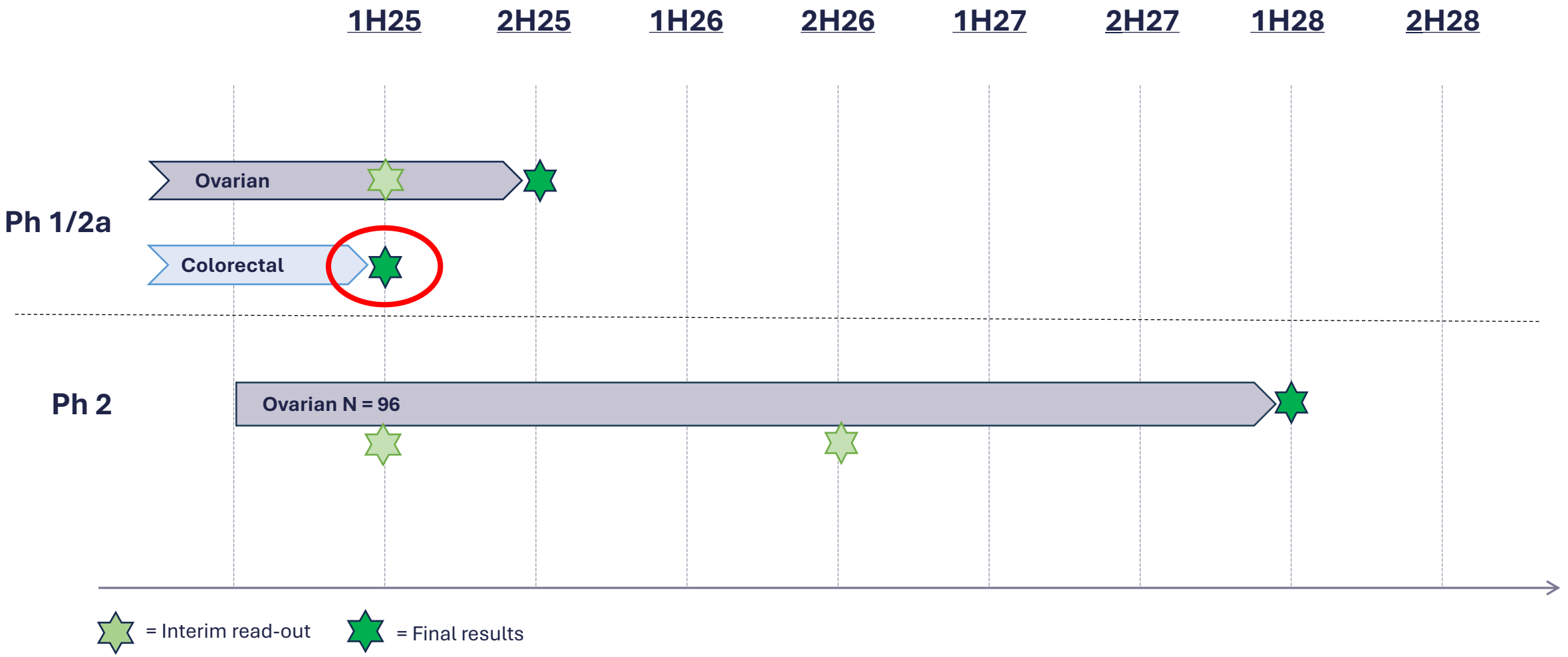
~55-60%

Overall recurrence rate*

Peritoneal recurrence rates or distribution of recurrences not available in historical control

Coleman et al. N Engl J Med. 2019 Nov 14;381(20):1929-1939
Harter et al. N Engl J Med. 2021 Dec 2;385(23):2123-2131
Shi et al. Lancet Oncol. 2021 Apr;22(4):439-449

Ongoing clinical development



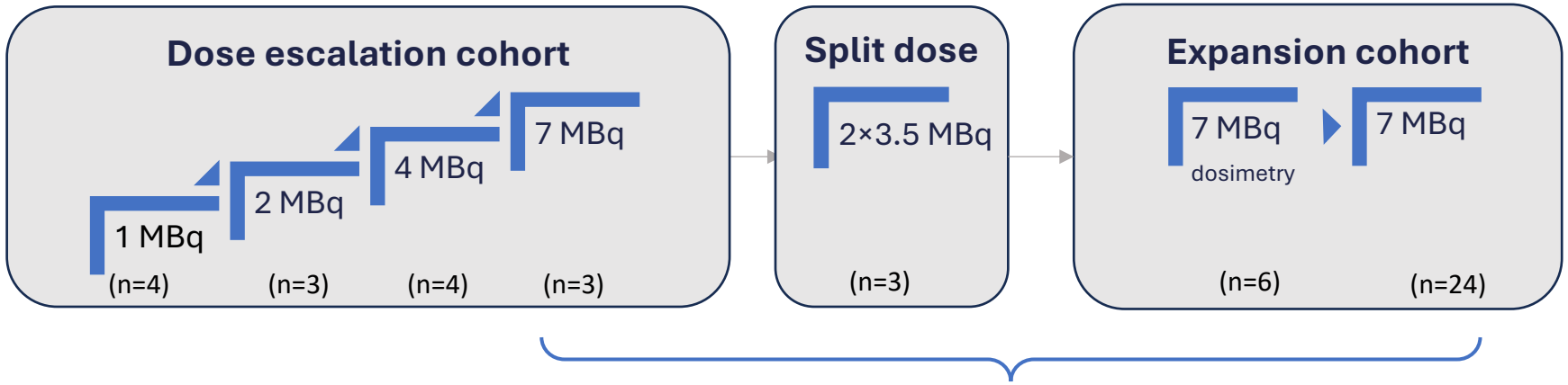
Design: Phase 1/2a in colorectal cancer

The trial: (RAD-18-002) Radspherin after cytoreductive surgery and HIPEC in patients with peritoneal metastasis from colorectal cancer

- Single-arm open label study
- 3 + 3 dose-escalation (1, 2, 4, 7 MBq)
- 18 months follow-up

Two clinical sites:

- Oslo, Norway (PI: Stein Larsen)
- Uppsala, Sweden (PI: Wilhelm Graf)



Total number of patients recommended dose 7MBq, **n=36**

Colorectal cancer: final phase 1/2a data confirm peritoneal control

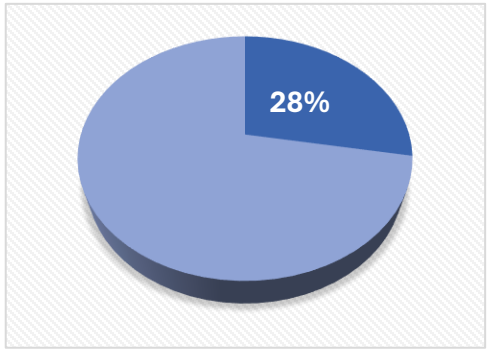
Topline 18-months data of 36 patients receiving 7 MBq dose vs historical recurrence rates

"It's highly encouraging to see patients treated with Radspherin achieving **outcomes that exceed expectations** for this challenging population. As a clinician, I'm hopeful that this promising therapy will become an option I can **offer to future patients** in need."

Dr. Stein Gunnar Larsen
Principal Investigator at the Oslo University Hospital, Norway

Peritoneal recurrence rate

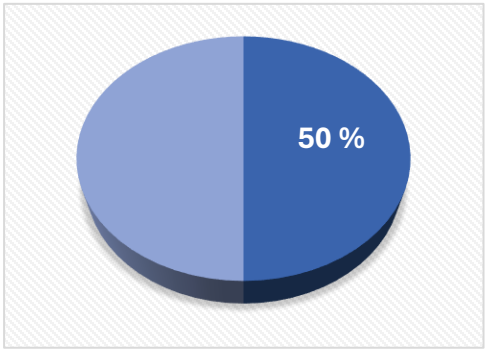
Radspherin®



28%

Peritoneal recurrence rate

Historical control

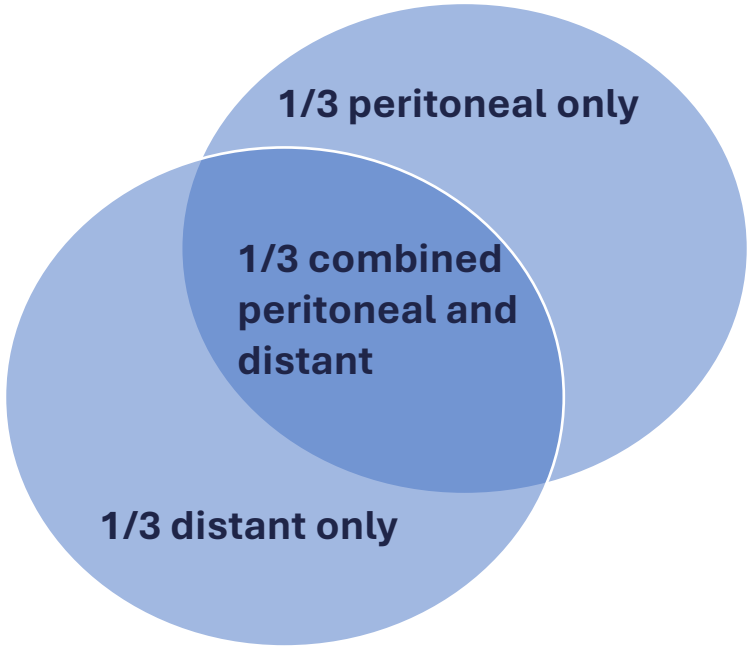


~50%

Peritoneal recurrence rate

Controlling peritoneal disease may significantly improve survival in colorectal cancer

First disease recurrence after treatment [1]



Impact of site of first site of recurrence [1]

Median overall survival - from the time of recurrence:

- After distant metastasis only: 44 months
- After peritoneal metastasis: 22 months

5-year overall survival – from the time of treatment

- Distant metastasis only: 53 %
- Peritoneal metastasis: 19 %

Frøysnes et al. J Surg Oncol. 2016 Aug;114(2):222-7

[1]Treatment with standard of care for resectable peritoneal metastases from colorectal cancer, i.e. cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

Baseline characteristics

RAD-18-002 Colorectal cancer (n=36)	
Age, median (min, max)	64 (28, 78)
Gender, n (%)	Males 16 (44%) Females 20 (56%)
PCI, median (min, max)	7.5 (2, 19)
Stage at diagnosis, n(%)	Stage II 8 (22%) Stage III 10 (28%) Stage IV 18 (50%)
Synchronous disease **Metachronous disease**	50% 50%
Days since diagnosis of peritoneal metastases, median (min, max)	66 (15, 268)

RAD-18-001 Ovarian cancer (N=21)	
Age, median (min, max)	65 (55, 79)
Gender, n (%)	Females 21 (100%)
PCI, median (min, max)	7 (3, 16)

Safety profile validated in two phase 1/2a studies treating 68 patients

Well tolerated and safe to use	• No dose limiting toxicity • Two SAEs possibly related to Radspherin*
No evidence of systemic radiation toxicity	• Radiation dose retained in the peritoneal cavity • Absorbed doses to other organs well below toxicity levels
Low exposure for hospital staff	• Low radioactivity dose in blood and urine • No precautions related to external exposure required

Strong safety profile demonstrated in the completed phase 1/2a studies ovarian and colorectal cancer

- *Per cut-off date of annual DSUR March 2025
- - one event of small bowel perforation, 72 days after Radspherin administration
  - one event of procedural complication during Radspherin administration (disconnection syringe-catheter)

Near-term significant milestone

Phase 2
ovarian cancer

- Interim data
- Following complete recruitment
- **2H26**

Phase 1
ovarian cancer

- Final 24 months data
- 10 patients 7 MBq
- October 2025

Phase 1/2a
colorectal cancer

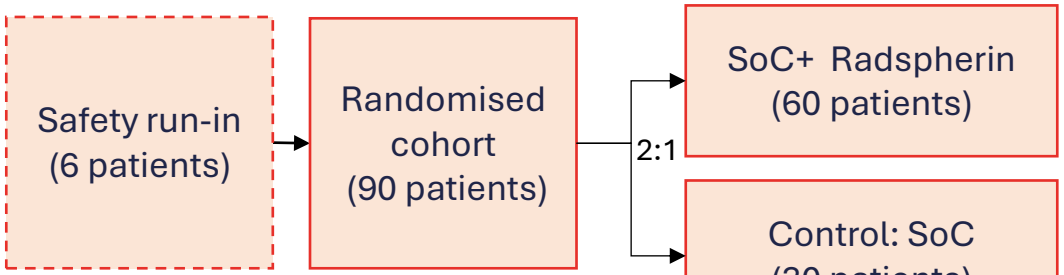
- Final 18 months data
- 36 patients 7 MBq
- June 2025

Ovarian cancer

Phase 2 study in ovarian cancer – enrollment on track

All 6 centers active

Patients
- with peritoneal metastases
- after neoadjuvant chemotherapy
- eligible for complete resection (R0)
- with HRD negative ovarian cancer



Assessment every 3 months up to 24 months, including CT/MRI

Long-term follow- up for up to 5 years according to standard of care

PFS
pPFS
OS
TFST
TSST

Safety
AESI
QoL
Biomarkers

6 study sites actively enrolling:
NO, BE, ES (2), UK, US

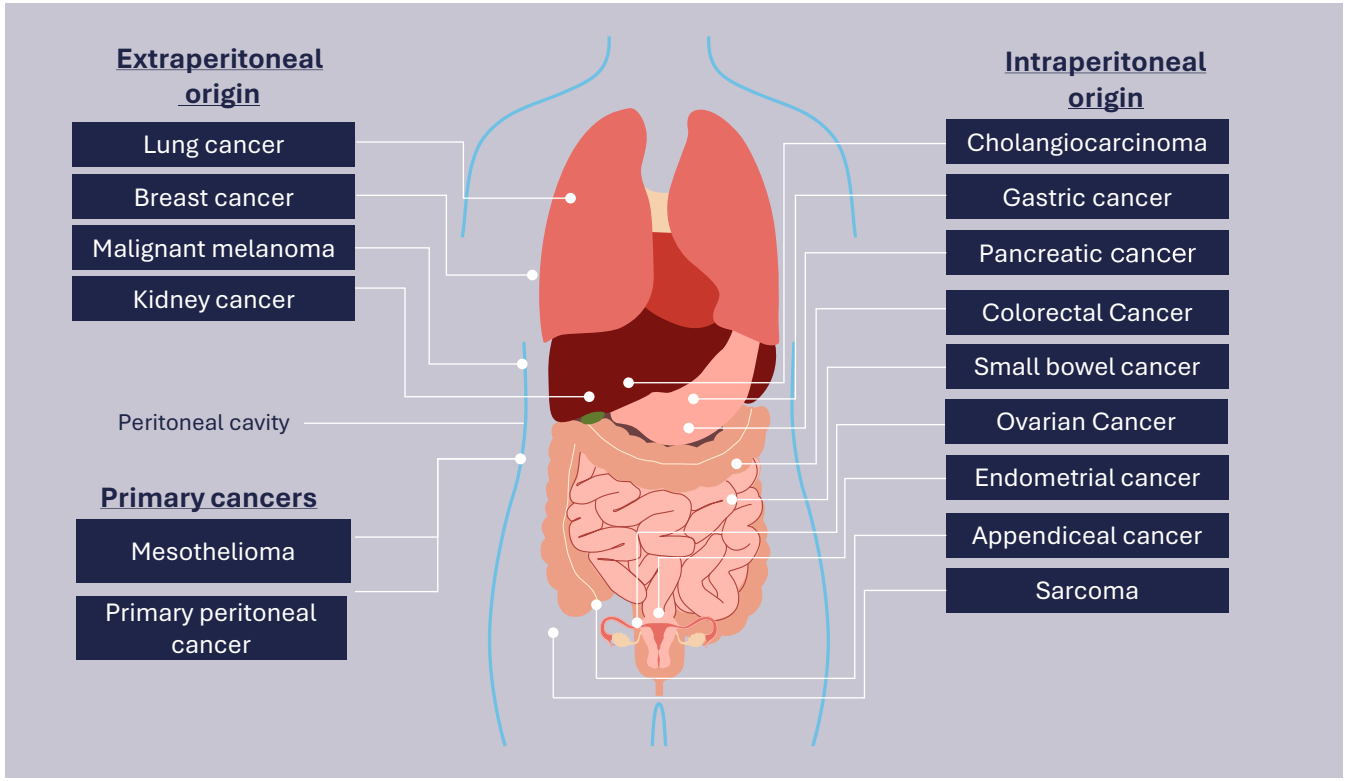
PFS: Progression Free Survival
pPFS: peritoneal Progression Free Survival
OS: Overall Survival

AESI: Adverse Event of Specialized interest
TFST: time to first subsequent anticancer therapy or death
TSST: time to second subsequent anticancer therapy or death

HRD: Homologous Recombination Deficiency
IDS: Interval Debulking Surgery

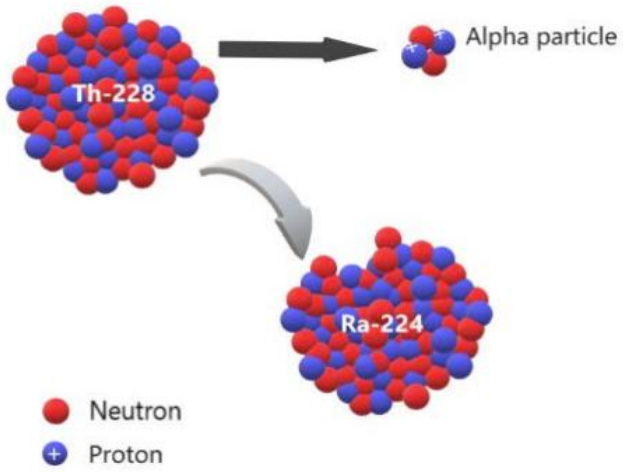
Pipeline in one product - broad clinical application

- Peritoneal metastases arise from many different cancers
- Radspherin® is a **receptor-independent** treatment: effective regardless of the origin of the primary malignancy

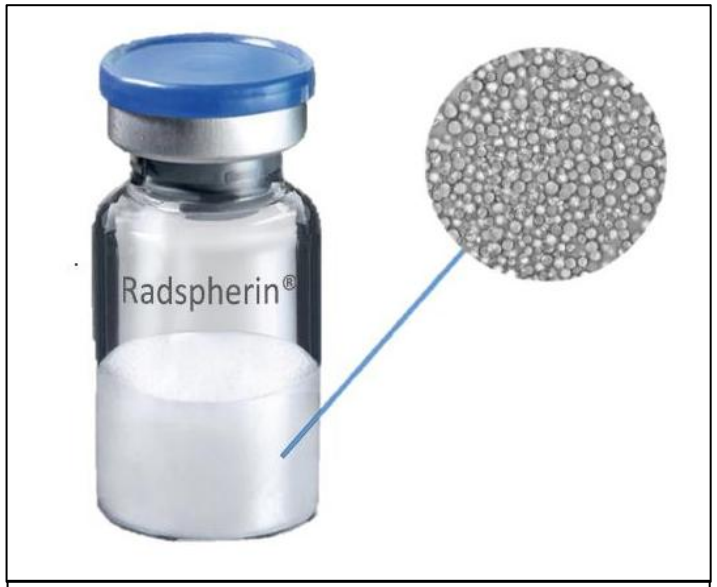


In-house GMP pilot plant

Oncoinvent has in-house GMP production capability



^{224}Ra produced from ^{228}Th, which has multiple sources



Microparticles and finished goods produced in-house

Capacity of ~200 doses Radspherin annually, outsourcing and scale-up required for phase 3
On selective basis offer GMP laboratory services to similar non-competing companies

GMP: Good manufacturing practice

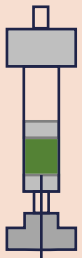
Radspherin® production process

Overview of the Radspherin® production process

Raw material input

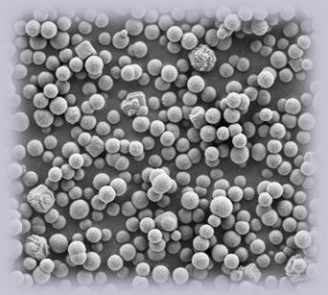
Elution of the alpha-emitter radium-224

Thorium-228 generator column



Radium-224

Pre-made calcium carbonate microparticles produced by precipitation



Combination

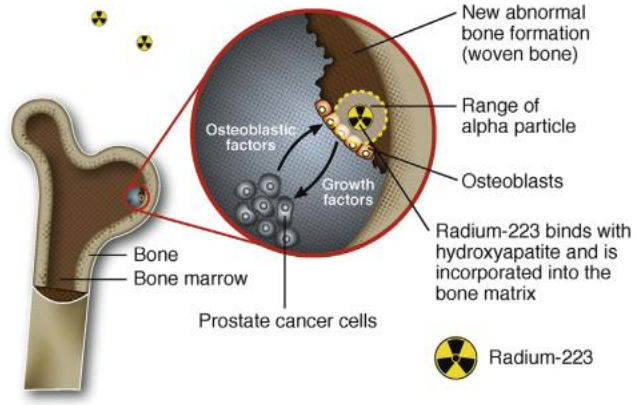
Labeling of radium-224 to microparticles

Final product

Ready-to-use Radspherin®

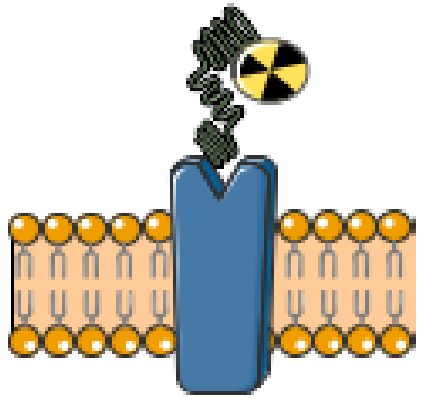
Ways to target cancer with radiopharmaceuticals

Natural homing



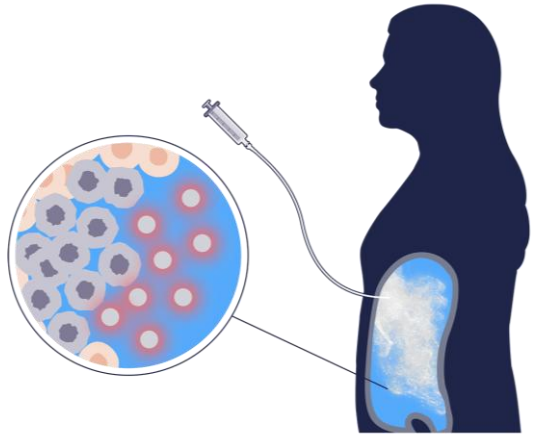
- Some radionuclides naturally targets certain organs. ^{223}Ra **Xofigo** goes to bone, ^{131}I goes to the thyroid
- Simple, proven in routine clinical practice, selective for tissues
- Limited to diseases with natural avidity, less adaptable

Molecular targeting



- Radioligands: Biological targeting agent linked to a radioactive payload e.g. Lutathera, **Pluvicto**
- Large potential
- Complex, risk of off-target effects

Direct radiotherapy



- Physically trapping radioactivity in an organ: e.g. **Radspherin®**, TheraSphere (Boston Scientific), REYOBIC (Plus)
- Non-systemic delivery: High local concentration, minimal systemic toxicity
- Requires direct access to site, not suitable for systemic disease

Summary

1. Peritoneal carcinomatosis is an area with **high unmet need**
2. Targeted, non-biological, **receptor independent** mode of action with alpha emitter
3. **Compatible** with established treatment regimes - adds well to existing patient flow
4. **Signals of efficacy**: potential game changer in ovarian and colorectal cancers
5. The **physical mode of action** of direct alpha therapy harnesses the advantages of radiopharmaceuticals with reduced **risk and complexity**