

Overview of Emerging Th-227 Radiotherapy

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Disclosures

Consultant for:

Bayer HealthCare Pharmaceuticals

Sirtex Medical

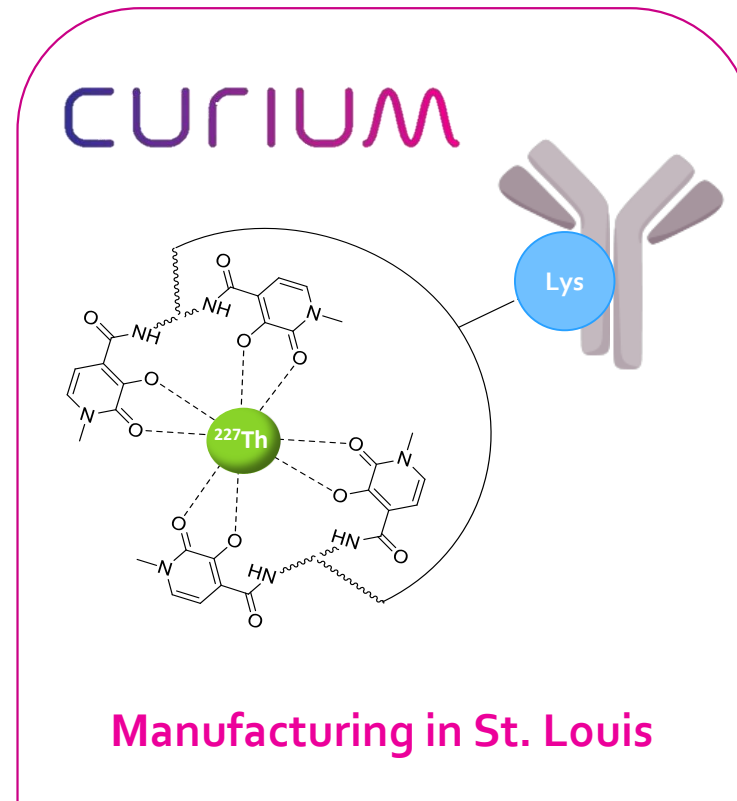
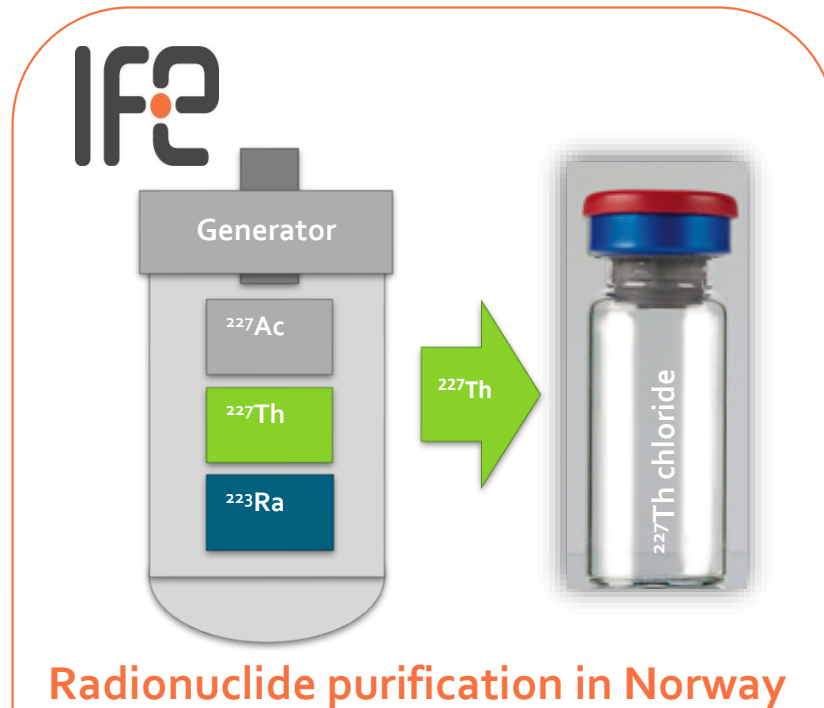
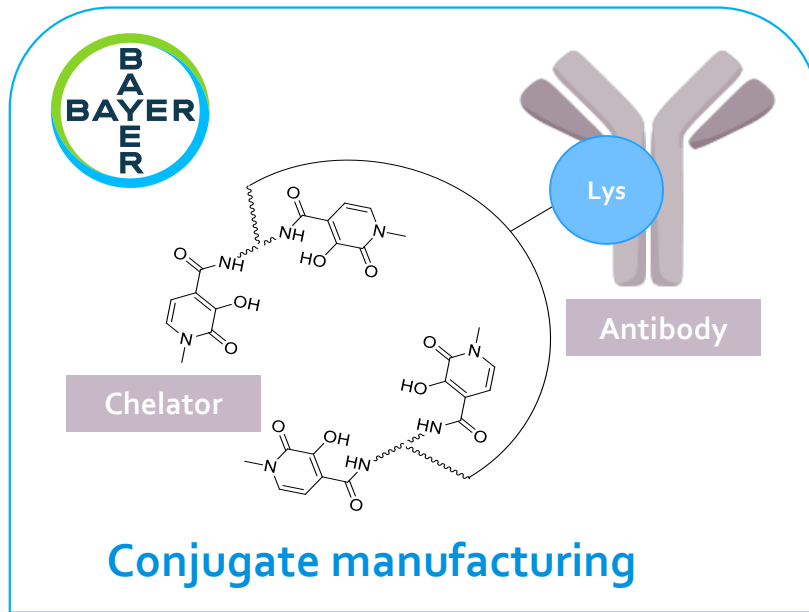
Overview

- What are targeted thorium conjugates
- Is there a clinical need
- Why alpha emitters

Regulatory Review

- How to detect contamination
- How to measure activity
- How to administer
- When to release patients
- How to dispose of waste

Targeted Thorium Conjugates Process



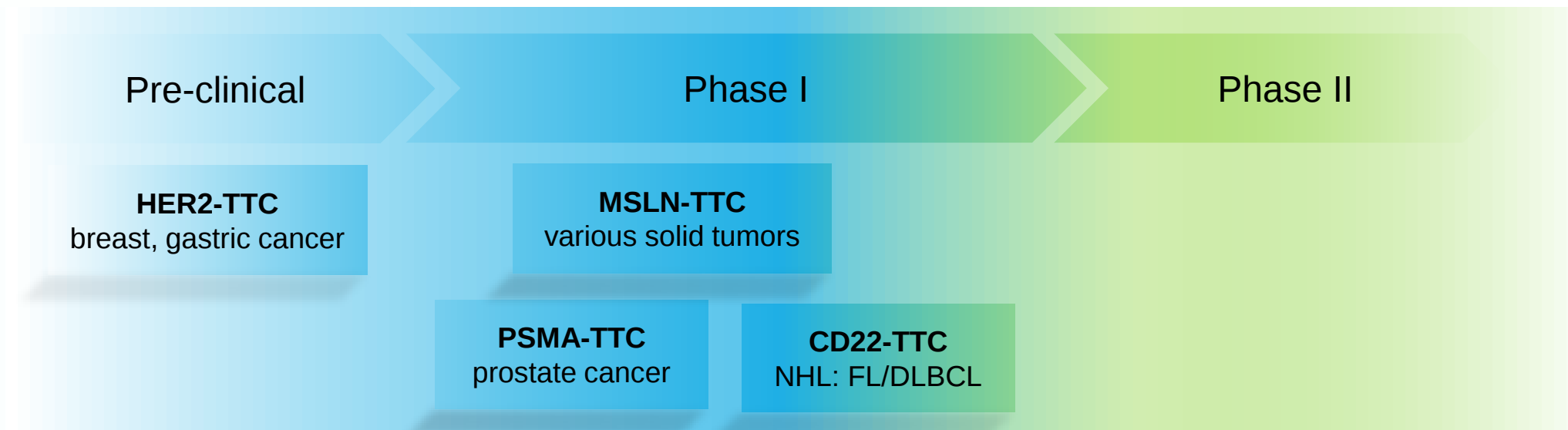
Patient dose



End user



Pipeline of Products



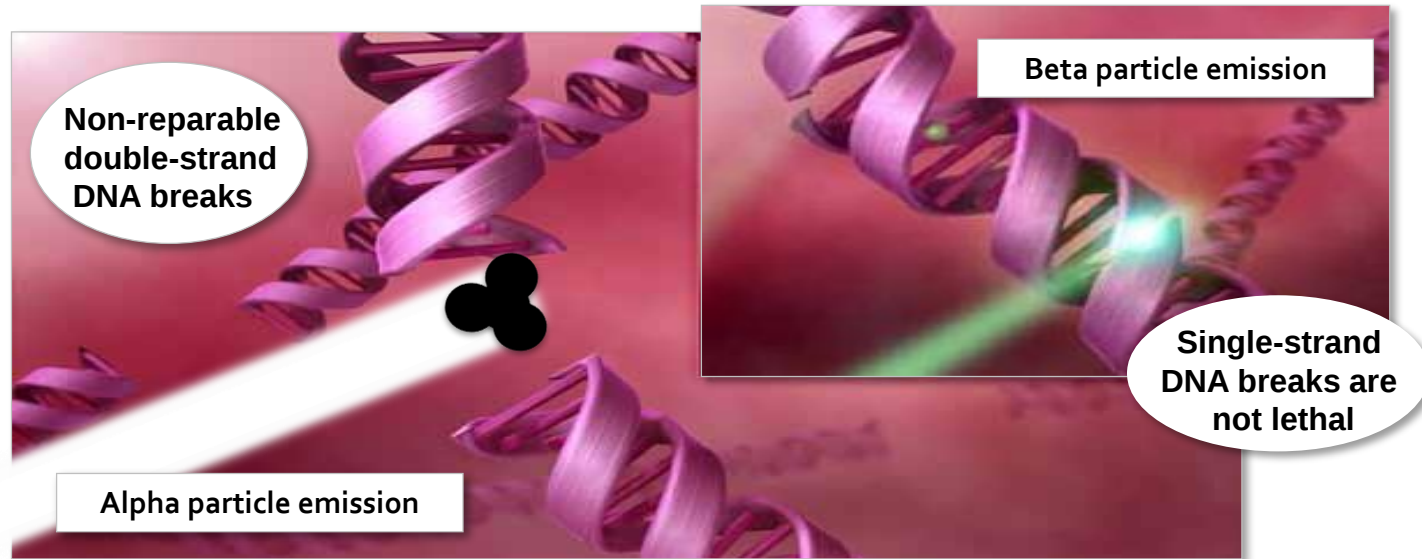
PSMA-TTC - prostate cancer

MSLN-TTC - mesothelioma, ovarian cancer, pancreatic cancer

CD22-TTC - non-Hodgkin lymphoma with focus on follicular lymphoma and diffuse large B cell lymphoma

HER2-TTC; HER2-positive breast cancer, gastric cancer

Mechanism of Action



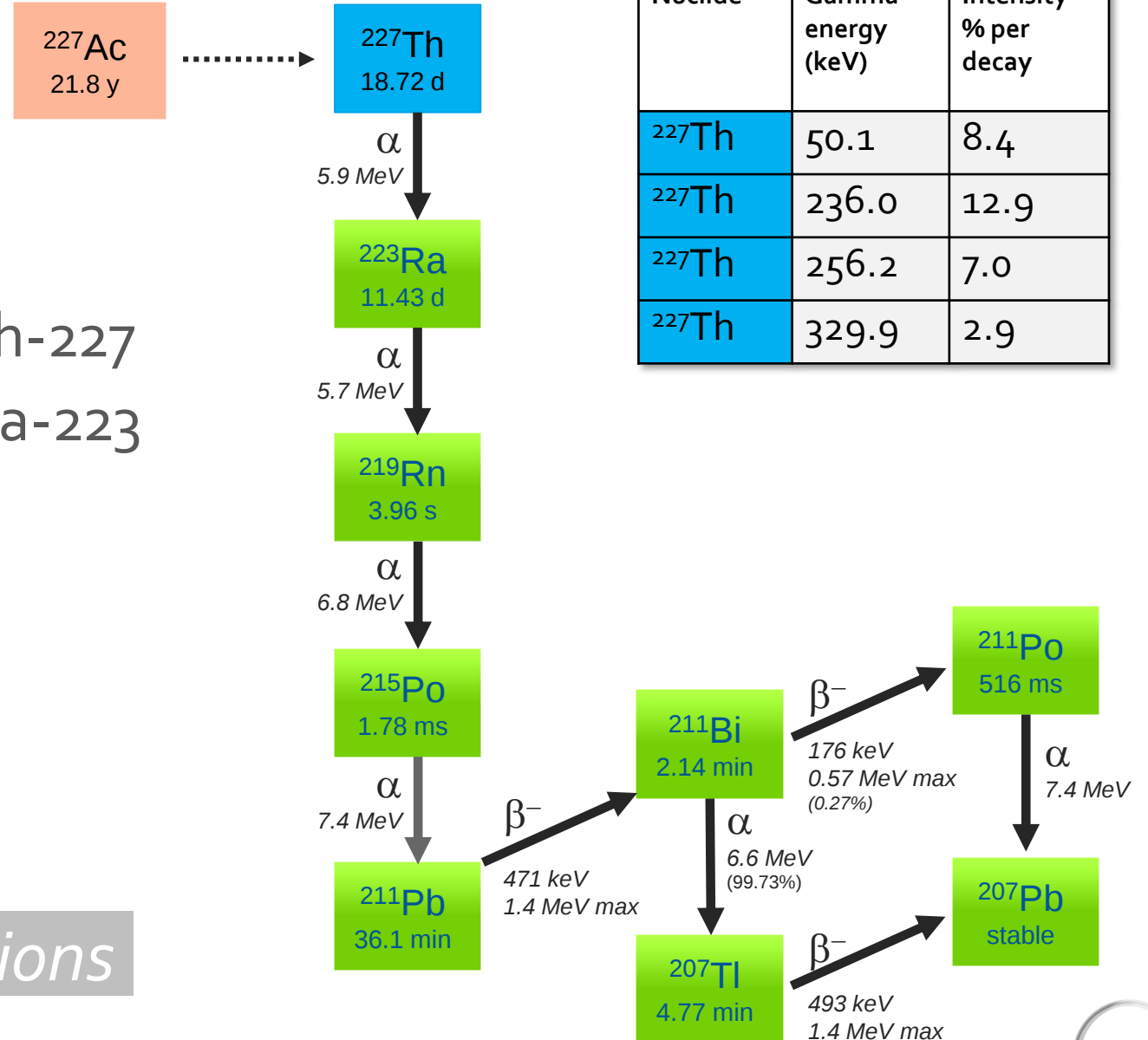
	α -particle	β -particle
Linear energy transfer	High 50–230 keV/ μ m	Low 0.2 keV/ μ m
Cellular DNA damage	Frequent double-stranded breaks	Base damage or single-stranded breaks
Difficulty repairing DNA damage	High	Low
Hits required to kill cell	Very few (1–20 hits)	Many (~2000 hits)

Th-227 Decay Chain

- $T_{1/2} = 18.7$ days
- Ac-227 parent radionuclide of Th-227
- Th-227 parent radionuclide of Ra-223
- Total decay energy
 - 95.7% emitted as α particles
 - 3.1% emitted as β particles
 - 1.2% emitted as γ or x-rays

Predominantly alpha emissions

Source material



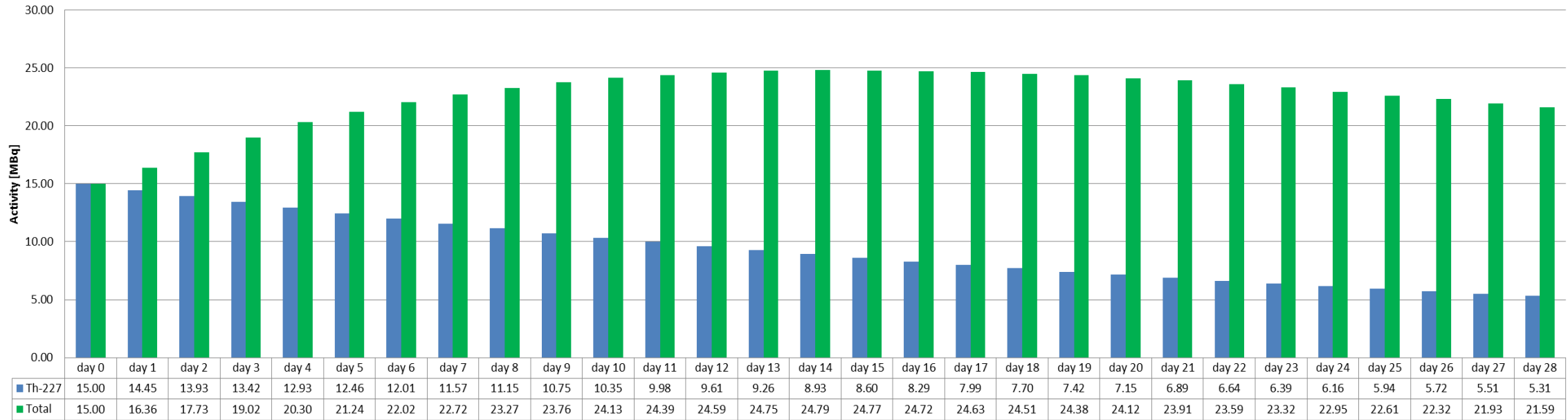
Regulatory Considerations

- Activity Measurement
- Exposure Risks
 - Internal & External
- Contamination Detection
- Disposal of Waste

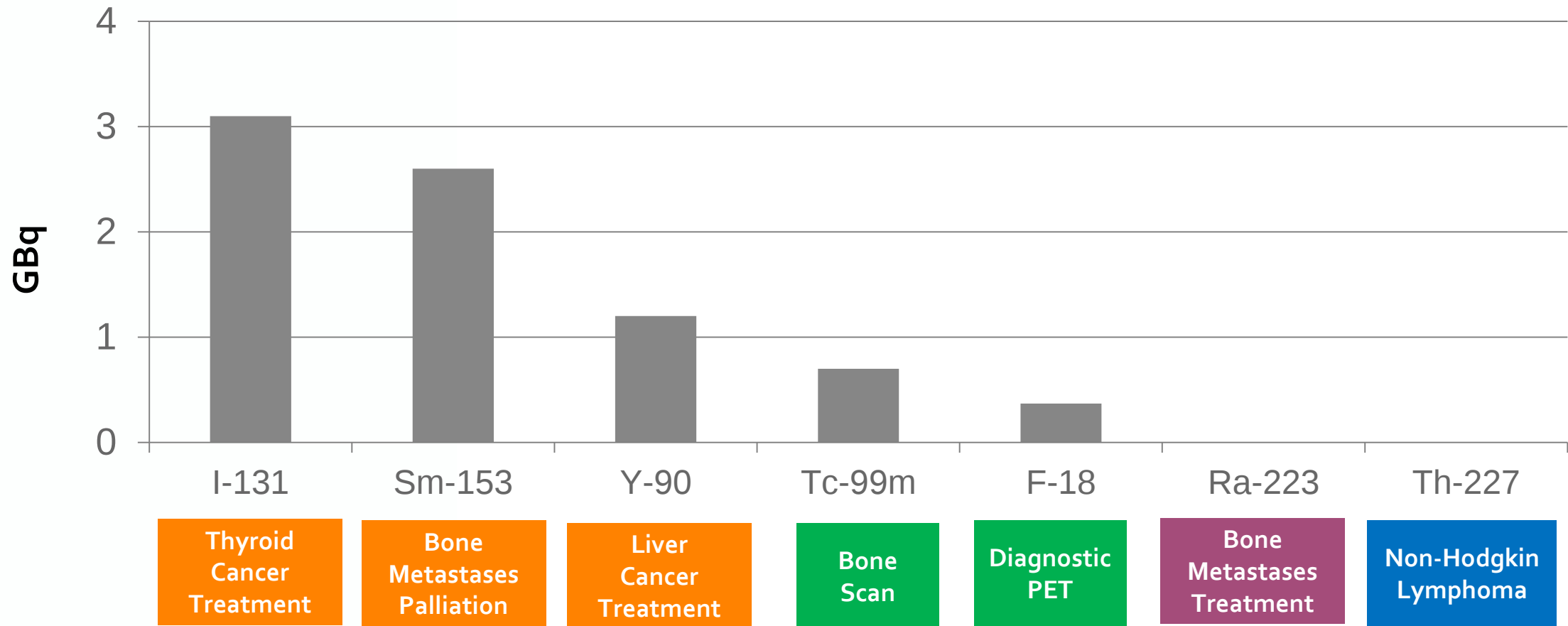
Activity Measurement

- Use standard dose calibrator
- Apply correction factor for Ra-223 in-growth

Read-out **Activity over shelf-life of technical sample (thorium-227 chloride)**



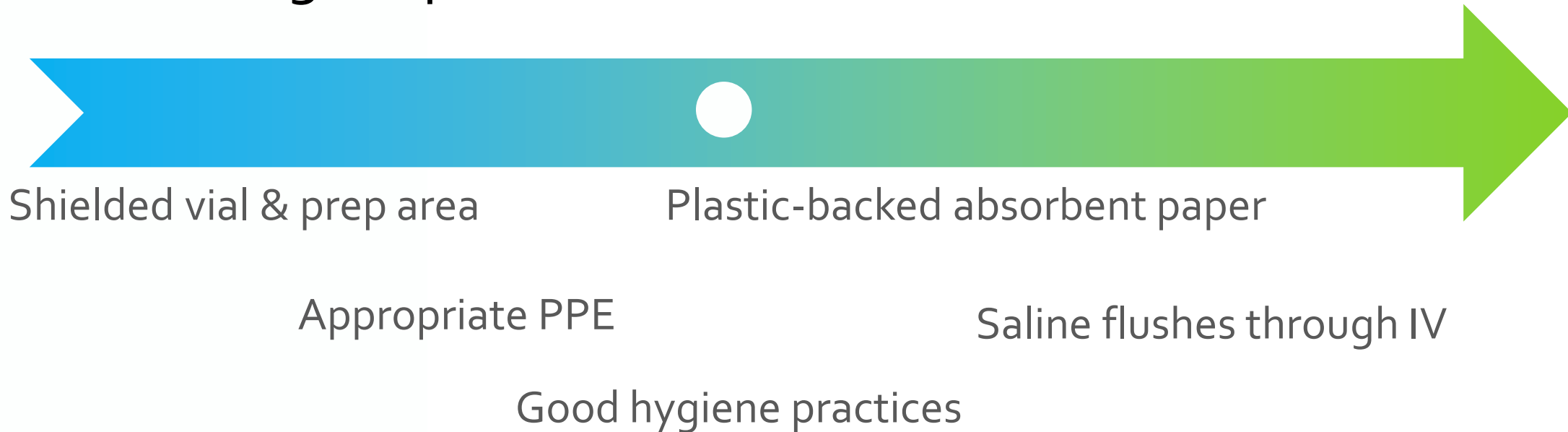
Activity Comparisons



*Alpha pharmaceuticals are prescribed on a one-digit **MBq** scale*

Exposure Risks

During Preparation & Administration



Internal and external exposure risks are low

Patient Release



Tc-99m	Ra-223	Ra-223	Th-227	Th-227
1110 MBq	4 MBq	4 MBq	4 MBq	4 MBq

Dose rate ($\mu\text{Sv/h}$)

22.2

0.2*

0.2

< 0.2*

TBD

*derived from exposure rate constants

Exposure to others negligible; TTC patients immediately releasable

Waste Considerations

Patients at Home

- // Urine and feces may be radioactive for up to 10 days post-administration
 - Use good hygiene practices (e.g. thoroughly wash hands)
 - Flush disposable items used for clean-up
 - Launder items contaminated with bodily fluids

Items at Facility

- // Radioactive waste should be sealed in plastic bags and stored in a secure area
 - Equipment used for administration (e.g. syringes, infusion lines, ports)
 - Remaining drug solution, technical samples used for calibration dial setting
 - Contaminated PPE
- // No measurable long-lived impurities
- // Up to 12 months decay-in-storage recommended (e.g. 7 MBq → 10 Bq)

Summary

- TTCs may provide new, effective cancer treatment options using alpha emitters
- Gamma emissions allow for routine detection and measurement
- Radium-223 in-growth addressed through limited shelf life and a correction factor
- External radiation exposure is very low; easy to shield
- Outpatient treatment; patient is immediately releasable
- Unintended internal exposure unlikely and avoidable following general hygiene rules
- Excretion to be addressed by providing patients with simple precautions
- Decay waste in storage