Overview of Emerging Th-227 Radiotherapy

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Disclosures

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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

Conjugate manufacturing

Radionuclide purification in Norway

Manufacturing in St. Louis

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

<table>
<thead>
<tr>
<th></th>
<th>α-particle</th>
<th>β-particle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear energy transfer</td>
<td><strong>High</strong> 50–230 keV/μm</td>
<td><strong>Low</strong> 0.2 keV/μm</td>
</tr>
<tr>
<td>Cellular DNA damage</td>
<td>Frequent double-stranded breaks</td>
<td>Base damage or single-stranded breaks</td>
</tr>
<tr>
<td>Difficulty repairing DNA damage</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Hits required to kill cell</td>
<td>Very few (1–20 hits)</td>
<td>Many (~2000 hits)</td>
</tr>
</tbody>
</table>
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 $\alpha$ particles
  - 3.1% emitted as $\beta$ particles
  - 1.2% emitted as $\gamma$ or x-rays

**Predominantly alpha emissions**
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
Alpha pharmaceuticals are prescribed on a one-digit MBq scale.

Activity Comparisons

- **I-131**: Thyroid Cancer Treatment
- **Sm-153**: Bone Metastases Palliation
- **Y-90**: Liver Cancer Treatment
- **Tc-99m**: Bone Scan
- **F-18**: Diagnostic PET
- **Ra-223**: Bone Metastases Treatment
- **Th-227**: Non-Hodgkin Lymphoma

**Non-Hodgkin Lymphoma**
Exposure Risks

During Preparation & Administration

- Shielded vial & prep area
- Plastic-backed absorbent paper
- Appropriate PPE
- Saline flushes through IV
- Good hygiene practices

*Internal and external exposure risks are low*
## Patient Release

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Activity (MBq)</th>
<th>Dose rate (µSv/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tc-99m</td>
<td>1110</td>
<td>22.2</td>
</tr>
<tr>
<td>Ra-223</td>
<td>4</td>
<td>0.2*</td>
</tr>
<tr>
<td>Ra-223</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>Th-227</td>
<td>4</td>
<td>&lt; 0.2*</td>
</tr>
<tr>
<td>Th-227</td>
<td>4</td>
<td>TBD</td>
</tr>
</tbody>
</table>

*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