XOFIGO® IS INDICATED

for the treatment of patients with castration-resistant prostate cancer (CRPC), symptomatic bone metastases and no known visceral metastatic disease.[1]

BAYER

Prolong life. Treat bone metastases.

Not an actual patient. Models used for illustrative purposes only.

The first agent to extend overall survival by exerting an antitumor effect on bone metastases in CRPC[1,2]

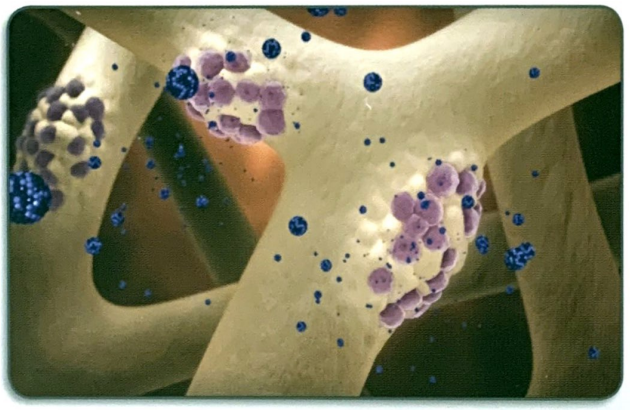
- **Exploratory updated analysis[a]: 3.6-month increase in median overall survival** vs placebo (hazard ratio [HR]=0.695; 95% confidence interval [CI]: 0.581-0.832)[1]
  —14.9 months for Xofigo (95% CI: 13.9-16.1) vs 11.3 months for placebo (95% CI: 10.4-12.8)[1]
- **Prespecified interim analysis: 2.8-month increase in median overall survival** vs placebo, *P*=0.00185 (HR=0.695; 95% CI: 0.552-0.875)[1]
  —14.0 months for Xofigo (95% CI: 12.1-15.8) vs 11.2 months for placebo (95% CI: 9.0-13.2)[1]

[a]An exploratory updated overall survival analysis was performed before patient crossover, incorporating an additional 214 events, resulting in findings consistent with the interim analysis.

Please see Important Safety Information throughout this brochure. Please see accompanying full Prescribing Information.

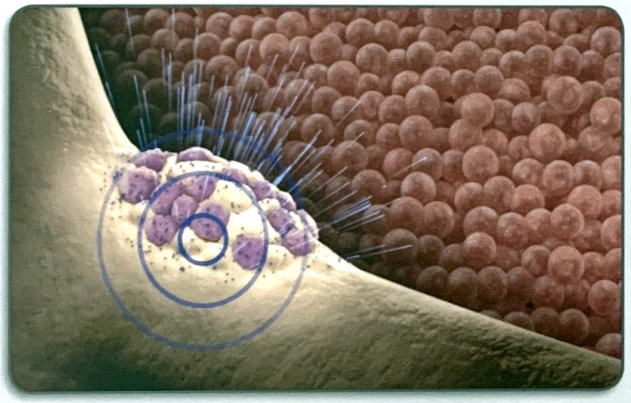
Xofigo®
radium Ra 223 dichloride
INJECTION

Xofigo® is an alpha particle-emitting pharmaceutical that exerts an antitumor effect on bone metastases in CRPC patients[1,2]



MIMICS CALCIUM

Xofigo **mimics calcium**, forming complexes with the bone mineral hydroxyapatite at areas of increased bone turnover such as bone metastases.[1]



SHORT RANGE

The **short range** of alpha particles emitted by Xofigo (<10 cell diameters) **limits damage to surrounding normal tissue**.[1]

HIGH LINEAR-ENERGY

Xofigo emits **alpha particles** that predominantly cause double-strand DNA breaks in adjacent cells, resulting in an **antitumor effect on bone metastases**.[1]

Xofigo can be absorbed by organs other than bone, primarily the bone marrow and gastrointestinal system, which can result in side effects in those healthy tissues

Important Safety Information[1]

- **Contraindications:** Xofigo is contraindicated in women who are or may become pregnant. Xofigo can cause fetal harm when administered to a pregnant woman

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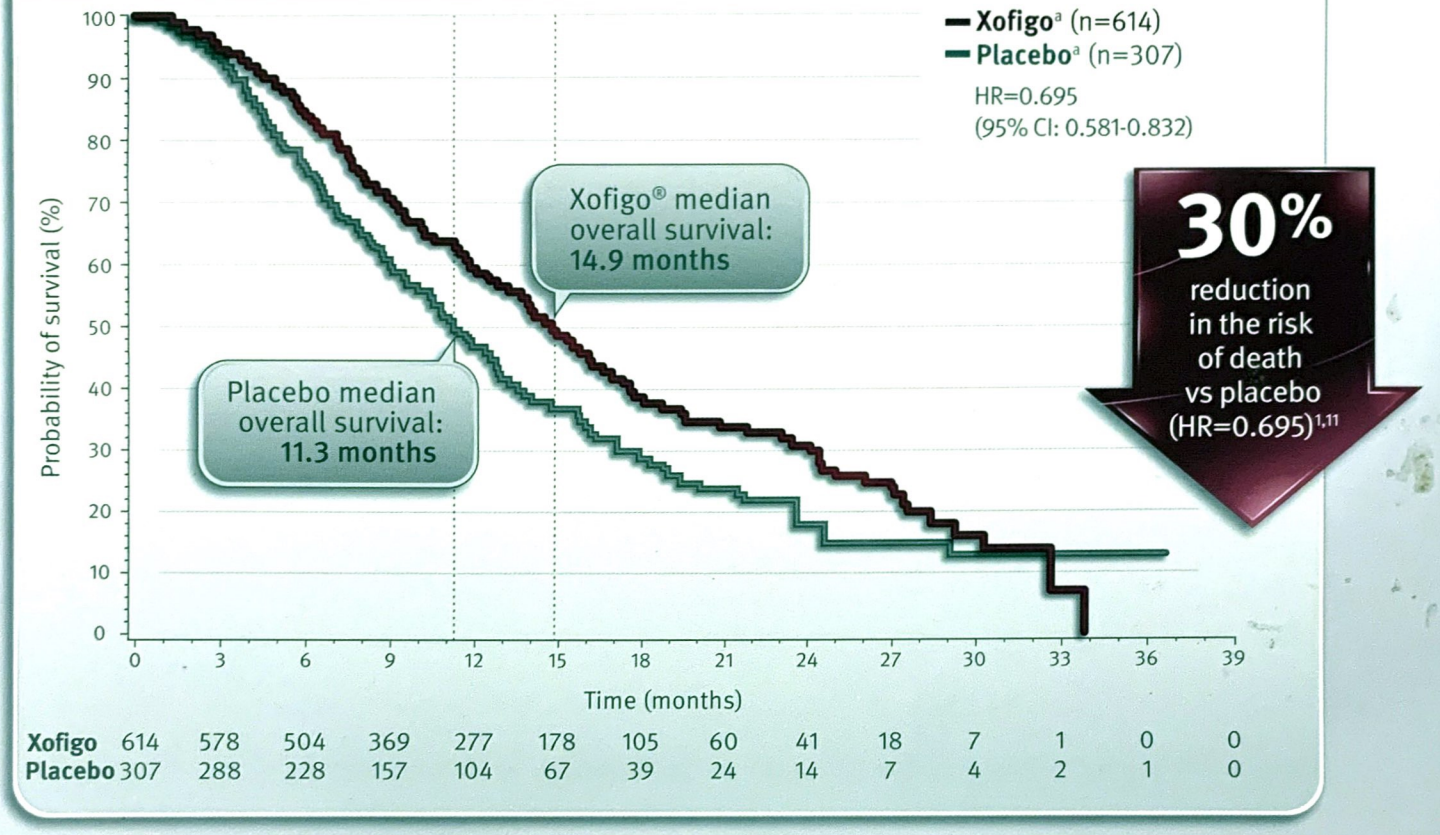
INJECTION

The first agent to extend overall survival by treating bone metastases[1,2]

Median Overall Survival Was Extended by 3.6 Months vs Placebo[1]



[a]Plus best standard of care.[1]

- **Exploratory updated analysis[b]: 3.6-month increase in median overall survival** vs placebo (HR=0.695; 95% CI: 0.581-0.832)[1]
  —14.9 months for Xofigo (95% CI: 13.9-16.1) vs 11.3 months for placebo (95% CI: 10.4-12.8)[1]
- **Prespecified interim analysis: 2.8-month increase in median overall survival** vs placebo, *P*=0.00185 (HR=0.695; 95% CI: 0.552-0.875)[1]
  —14.0 months for Xofigo (95% CI: 12.1-15.8) vs 11.2 months for placebo (95% CI: 9.0-13.2)[1]

[b]An exploratory updated overall survival analysis was performed before patient crossover, incorporating an additional 214 events, resulting in findings consistent with the interim analysis.[1]

Important Safety Information[1]

- **Adverse Reactions:** The most common adverse reactions (≥10%) in the Xofigo arm vs the placebo arm, respectively, were nausea (36% vs 35%), diarrhea (25% vs 15%), vomiting (19% vs 14%), and peripheral edema (13% vs 10%). Grade 3 and 4 adverse events were reported in 57% of Xofigo-treated patients and 63% of placebo-treated patients.
  The most common hematologic laboratory abnormalities in the Xofigo arm (≥10%) vs the placebo arm, respectively, were anemia (93% vs 88%), lymphocytopenia (72% vs 53%), leukopenia (35% vs 10%), thrombocytopenia (31% vs 22%), and neutropenia (18% vs 5%)

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INJECTION

Simple dosing: 1 injection at 4-week intervals for 6 injections[1]

A radiopharmaceutical license is required to administer Xofigo®. Administration of Xofigo is performed in a designated clinical setting, including an outpatient setting[1]

Slow intravenous injection over 1 minute of a patient-ready dose[1a]

There are no restrictions regarding contact with other people after receiving Xofigo.[1] Patients may return home after the injection[11,12]

Standard blood work required prior to every dose[1]

[a]A patient-ready dose with the requested activity will be provided in a syringe by Cardinal Health central radiopharmacy. The volume to be administered to a given patient is calculated using

- Patient's body weight (kg)[1]
- Dosage level 50 kBq/kg body weight[1]
- Radioactivity concentration of the product (1000 kBq/mL) at the reference date[1]
- Decay correction factor for the physical decay of radium 223[1]

Important Safety Information[1]

- **Subsequent Treatment With Cytotoxic Chemotherapy:** In the randomized clinical trial, 16% patients in the Xofigo group and 18% patients in the placebo group received cytotoxic chemotherapy after completion of study treatments. Adequate safety monitoring and laboratory testing was not performed to assess how patients treated with Xofigo will tolerate subsequent cytotoxic chemotherapy

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Routine monitoring requirements

Perform standard hematological evaluations before and during treatment with Xofigo[1]

Before first administration of Xofigo[1]

CONFIRM

- Absolute neutrophil count is ≥1.5 x 10^9/L
- Platelet count is ≥100 x 10^9/L
- Hemoglobin is ≥10 g/dL

Before subsequent administration of Xofigo[1]

CONFIRM

- Absolute neutrophil count is ≥1 x 10^9/L
- Platelet count is ≥50 x 10^9/L

If there is no recovery to these hematological values within 6 to 8 weeks after last administration of Xofigo despite receiving supportive care, further treatment with Xofigo should be discontinued[1]

Follow appropriate drug handling[1]

- Xofigo should be received, used, and administered only by authorized persons in designated clinical settings. The receipt, storage, use, transfer, and disposal of Xofigo are subject to the regulations and/or appropriate licenses of the competent official organization[1]
- Follow normal working procedures for the handling of radiopharmaceuticals and use universal precautions for handling and administration, such as gloves and barrier gowns, when handling blood and bodily fluids, to avoid contamination[1]
- In case of contact with skin or eyes, flush immediately with water[1]
- If spillage occurs, contact the local radiation safety officer immediately, to initiate necessary measurements and required procedures to decontaminate[1]
  - 0.01 M EDTA solution is recommended to remove contamination[1]

EDTA=ethylene-diamine-tetraacetic acid.

Xofigo® radium Ra 223 dichloride INJECTION

Patient instructions

Tell patients to be compliant with blood cell count monitoring appointments while receiving Xofigo®. Explain the importance of routine blood cell counts. Instruct patients to report signs of bleeding or infections[1]

Xofigo is administered only by authorized persons in a designated clinical setting, including an outpatient setting. Patients may return home after the injection[1,11,12]

There are no restrictions regarding contact with other people after receiving Xofigo[1]

Patients should be advised to maintain good hygiene practices while receiving Xofigo and for at least 1 week after the last injection; radioactivity will be present in excreted bodily waste[1]

—Whenever possible, patients should use a toilet and the toilet should be flushed several times after each use[1]

—Caregivers should use universal precautions for patient care such as gloves and barrier gowns when handling bodily fluids, to avoid contamination. When handling bodily fluids, wearing gloves and hand washing will protect caregivers[1]

—Clothing soiled with patient fecal matter or urine should be washed promptly and separately from other clothing[1]

Patients who are sexually active should use a condom, and their female partners of reproductive potential should use a highly effective method of birth control during treatment and for 6 months following completion of Xofigo treatment[1]

Patients should stay well hydrated and monitor oral intake, fluid status, and urine output while being treated with Xofigo. Instruct patients to report signs of dehydration, hypovolemia, urinary retention, or renal failure/insufficiency[1]

Important Safety Information[1]

- **Contraindications:** Xofigo is contraindicated in women who are or may become pregnant. Xofigo can cause fetal harm when administered to a pregnant woman

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Comprehensive support for providers and patients is available

Xofigo Access Services provides a variety of programs to support patients

- Processes all product orders
- Offers full scope of reimbursement information and patient assistance programs
- Provides treatment site location information
- Confirms patient scheduling

Xofigo Access Services℠

To access these services call

1-855-6XOFIGO (1-855-696-3446)

Or visit www.xofigo-us.com.

Xofigo Access Services Access Counselors are available from 9:00 AM to 8:00 PM ET, Monday through Friday.

Xofigo®
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For those who administer Xofigo®

Elimination, half-life, and radioactivity[1]

- After intravenous injection, Xofigo is rapidly cleared from the blood and is taken up primarily into bone or excreted into the intestine. Fecal excretion is the major route of elimination from the body

<1% of Xofigo Remains in Blood at 24 Hours

Time post injection	Distribution
At 10 minutes	• Radioactivity was observed in bone and in intestine
After 15 minutes	• About 20% of the injected radioactivity remained in blood
At 4 hours	• About 4% of the injected radioactivity remained in blood • The percentage of the radioactive dose present in bone and intestine was approximately 61% and 49% respectively
At 24 hours	• Less than 1% of the injected radioactivity remained in blood

No significant uptake was seen in other organs such as heart, liver, kidneys, urinary bladder, and spleen at 4 hours post injection.

- Xofigo has a physical half-life of 11.4 days and may be stored at room temperature. It should be stored in the original container or with equivalent radiation shielding
- Xofigo is predominantly an alpha emitter (95.3%); however, beta (3.6%) and gamma (1.1%) particles are also emitted during decay. The gamma radiation allows for measurement of radioactivity with standard instruments such as a dose calibrator

Important Safety Information[1]

- **Fluid Status:** Dehydration occurred in 3% of patients on Xofigo and 1% of patients on placebo. Xofigo increases adverse reactions such as diarrhea, nausea, and vomiting, which may result in dehydration. Monitor patients' oral intake and fluid status carefully and promptly treat patients who display signs or symptoms of dehydration or hypovolemia

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Dose delivery of Xofigo

Patient-ready-dose syringe[1,11]

- The patient dose is 1.35 microcurie (50 kBq) per kg body weight[1]
- A patient-ready dose with the requested activity will be provided in a syringe by Cardinal Health central radiopharmacy. The volume to be administered to a given patient is calculated as follows[1]

$$\text{Volume to be administered (mL)} = \frac{\text{Body weight in kg x 50 kBq/kg body weight}}{\text{Decay factor x 1000 kBq/mL}} \text{ or } \frac{\text{Body weight in kg x 1.35 microcurie/kg body weight}}{\text{Decay factor x 27 microcurie/mL}}$$

- The shelf-life of Xofigo in the patient-ready syringe is 96 hours[11]
- Xofigo is a ready-to-use solution and should not be diluted or mixed with any other solutions[1]

Administration[1]

- Administer Xofigo by slow intravenous injection over 1 minute
- Flush the intravenous access line or cannula with isotonic saline before and after injection of Xofigo
- Immediately before and after administration, the net patient dose of administered Xofigo should be determined by measurement in an appropriate radioisotope dose calibrator
- Xofigo should be received, used, and administered only by authorized persons in designated clinical settings. The receipt, storage, use, transfer, and disposal of Xofigo are subject to the regulations and/or appropriate licenses of the competent official organization
- Follow normal working procedures for the handling of radiopharmaceuticals and use universal precautions for handling and administration, such as gloves and barrier gowns, when handling blood and bodily fluids, to avoid contamination
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