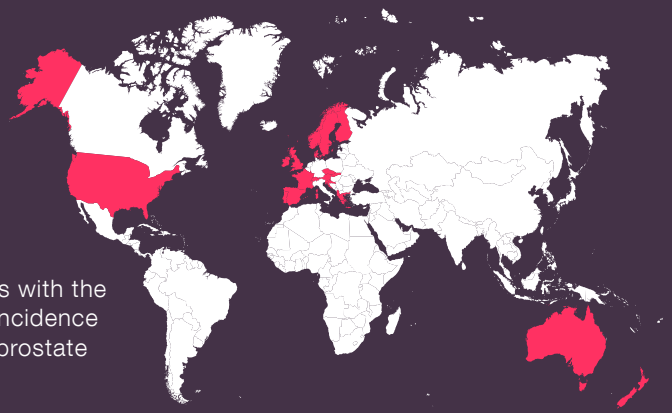
Radium-223 in Advanced Prostate Cancer

Prostate cancer *is…*

The *2nd* most common cancer in men[1]

The *5th* leading cause of cancer-related death in men worldwide[2]

The highest incidence rates are in North America, Northern and Western Europe, Australia and New Zealand[3]



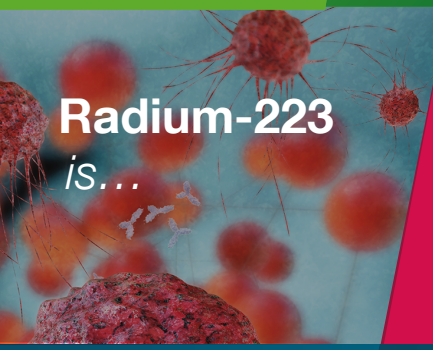
Countries with the highest incidence rates of prostate cancer[3]

The role of the bone in advanced prostate cancer:

In advanced prostate cancer, the disease has moved beyond the prostate gland and, in 80-90% of men, resides primarily in the bone. This is called bone metastasis.[4-6]

Bone metastases, which can be painful, are associated with a poor prognosis and decreased survival in men with metastatic castration-resistant prostate cancer (mCRPC).[4-6]

Certain treatments that target the bone can improve outcomes and extend life in advanced prostate cancer patients with bone metastases.



Radium-223 *is…*

// A treatment (alone or in combination with lutenising releasing hormone (LHRH) analogue) for adult patients with mCRPC, symptomatic bone metastases and no known visceral metastases in progression after at least two prior lines of systemic therapy for mCRPC (other than LHRH analogues), or ineligible for any available systemic mCRPC treatment.[7*]

// The first and only targeted alpha therapy that has been shown to **extend life and preserve quality of life** in mCRPC patients with bone metastases.[8,9^]

// Approved in **50+ countries worldwide.**

Radium-223 *works by…*

Preferentially targeting areas of **rapid bone growth**, including **bone metastases, osteoblasts** (cells that make bone), and **osteoclasts** (cells that break down bone tissue), giving off **radiation that kills cancer cells.**[7*]

Emitting **alpha particles** that cause cell death through double-strand DNA breaks, resulting in a **dual mode of action.** This directly **kills cancer cells** and helps **break the cycle of bone metastases** caused by cell signaling that stimulates tumor growth. Alpha particles from Xofigo® also have a **short range**, so they cause limited damage to surrounding healthy tissue.[10]

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ALSYMPCA[11]

***AL**pharadin in the treatment of patients with **SYMP**tomatic hormone refractory prostate **CA**ncer with skeletal metastases*

Patient Population:

921 patients with CRPC with symptomatic bone metastases but no known visceral metastases.

Primary Endpoint:

Overall survival (OS).

Trial Design:

Patients randomized 2:1 to receive **6 intravenous administrations of radium-223** plus best standard of care (BSC) or placebo plus BSC every **4 weeks**.

Secondary Endpoints:

Safety, time to occurrence of specific disease events, changes and time to progression in prostate-specific antigen (PSA), changes and time to progression in total alkaline phosphatase (ALP).

***ALSYMPCA:** Trial design and key results*

Patients with CRPC with symptomatic bone metastases but no known visceral metastases

n=921

Randomized 2:1

6 intravenous administrations of radium-223 + BSC

Placebo + BSC

Results from the pivotal Phase III ALSYMPCA trial show that for men with mCRPC, radium-223 extends life by 30% compared to placebo while significantly improving quality of life and minimizing treatment side effects with a comparable safety profile to placebo.[12]

Footnote:

* Use of Radium-223 is not recommended in patients with a low level of osteoblastic bone metastases.

References:

1. GLOBOCAN 2018: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2018. Population Fact Sheets Worldwide. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed January 2021. **2.** Bray F, Ferlay J, et.al. Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2018 Nov;68(6):394-424. doi: 10.3322/caac.21492. Epub 2018 Sep 1. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30207593. Last Accessed. January 2021. **3.** GLOBOCAN 2018: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2018. Prostate Cancer Factsheet. Available at: https://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact-sheet.pdf. Accessed January 2021. **4.** World Cancer Research Fund International. Prostate Cancer Report 2018. Available at: https://www.wcrf.org/dietandcancer/prostate-cancer. Accessed January 2021. **5.** Park JC, Eisenberger MA. Advances in the treatment of metastatic prostate cancer. Mayo Clin Proc. 2015;90(12):1719-1733: **6.** Jin JK, Dayyani F, Gallick GE. Steps in prostate cancer progression that lead to bone metastasis. Int J Cancer. 2011;128(11):2545-2561. **7.** Xofigo® (radium Ra-223 dichloride) solution for injection Summary of Product Characteristics (SmPC), Bayer Pharma AG, 51368 Leverkusen, Germany, 2018. **8.** Parker C, Heidenreich A, Nilsson S, Shore N. Current approaches to incorporation of radium-223 in clinical practice. Prostate Cancer Prostatic Dis. 2018;21(1):37-47. **9.** Nilsson S, Cislo P, Sartor O, et al. Patient-reported quality-of-life analysis of radium-223 dichloride from the phase III ALSYMPCA study. Ann Oncol. 2016;27(5):868-874. **10.** Suominen MI et al. Radium-223 Inhibits Osseous Prostate Cancer Growth by Dual Targeting of Cancer Cells and Bone Microenvironment in Mouse Models. ClinCancer Res. 2017; 23(15):4335-4346. **11.** A Phase III Study of Radium-223 Dichloride in Patients With Symptomatic Hormone Refractory Prostate Cancer With Skeletal Metastases (ALSYMPCA). ClinicalTrials.gov: U.S. National Institutes of Health; April 2016. Available at: https://clinicaltrials.gov/ct2/show/record/ NCT00699751. Accessed January 2021. **12.** Parker, C, Nilsson, S, Heinrich, D et al. N Engl J Med 2013; 369:213-223.

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