Xofigo® (radium 223) pocket treatment guide

Xofigo®
radium Ra 223 dichloride
SOLUTION FOR INJECTION

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This pocket treatment guide has been written for, and is intended for use by, healthcare practitioners.

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A patient-centric approach to CRPC

Before starting any therapy, at any stage, in a patient with castration-resistant prostate cancer (CRPC), it is important to take a full history, and consider the needs of each individual patient.[1,2]

Factors to consider before making any treatment decisions may include:

Patient-specific factors

- Age[1]
- Current health status/general well-being[2]
- Any comorbidities[1,2]
- Bone health[1,2]

Treatment-specific factors[1]

- Prior treatments received
- How the patient managed on earlier treatment(s)
- Any challenging adverse events from previous therapies

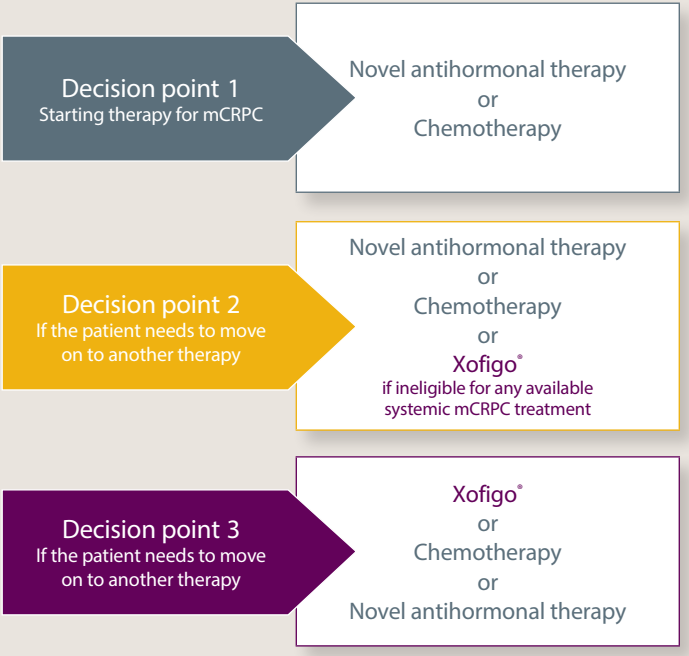
Taking all these factors into consideration, what does the patient think?

It is important to share relevant information and make the treatment decisions with your patient, to ensure they are engaged and involved in their treatment journey[3,4]

Where does Xofigo® fit in?

Xofigo® is a treatment option for adult patients with metastatic CRPC (mCRPC), symptomatic bone metastases and no visceral metastases, progressing after ≥2 lines of systemic therapy, or ineligible for systemic treatment for mCRPC.[5]

The treatment paradigm for patients with mCRPC can be defined by key decision points:[5]



The principles that guide the treatment of CRPC in general should be applied when making treatment choices for metastatic disease.

For the key decision points in mCRPC, you may wish to consider the following:

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- What is your centre's treatment of choice/preferred paradigm?
- Are there any patient-specific reasons to choose a particular therapy? For example:
  - How is your patient's general health/well-being?
  - How well did they do on previous therapies (in terms of efficacy and adverse events)?
  - Do you consider that your patient is ineligible for chemotherapy or a novel antihormonal treatment?
- How do you ensure your patients receive as many life-prolonging therapies as possible? For example:
  - Can you plan a few steps ahead for the treatment sequence in your patient?
  - Can you optimize follow-up for patients on active treatment to detect progression?
  - Evidence suggests back-to-back antihormonal therapies could have limited efficacy.[6–11] Should this be avoided for this patient?

Defining symptomatic bone metastases

Early identification of bone metastases will allow you to plan optimally for treatment with Xofigo®.

Symptomatic bone metastases
☐ Hypercalcaemia[12]
☐ Pathological fracture[12]
☐ Fatigue/generalized weakness[13]
☐ Impaired mobility[13]
☐ Anaemia, neutropenia, or thrombocytopenia[13]
☐ Loss of bladder and bowel function[13]
☐ Dyspnoea[13]
☐ General weakness/weakness in legs[13]
☐ Mild sensory loss, numbness[13]
☐ Pain and discomfort[13,14]
☐ Interference with daily activities[14]
☐ Sleep disturbance[14]
☐ Neurological impairment[15]
☐ Back ache[16]
☐ Loss of appetite and vomiting[16]

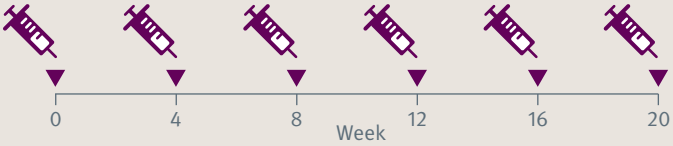
Key questions to ask your patients

?

- Are you experiencing any difficulties with day-to-day activities?
- How are you sleeping?
- Have you noticed any stiffness or numbness?
- How frequently are you taking painkillers?
- Are you having any difficulties urinating or are you constipated?
- Have you experienced loss of appetite?

Before giving Xofigo®

The Xofigo® dose is 55 kBq/kg, given at 4-week intervals for six intravenous injections.[5]



BEFORE INITIAL INJECTION (CYCLE 1)		
Requirements		☐
Imaging[17,18]	Confirmed presence of bone metastases by ^{99m}Tc-phosphonate bone scan or ^{18}F-NaF PET/CT, or MRI	
	Visceral metastases excluded by abdominal/pelvic CT or MRI	
Haematological evaluation[5]	Absolute neutrophil count ≥1.5 x 10^9/L	
	Platelet count ≥100 x 10^9/L	
	Haemoglobin ≥10.0 g/dL	
Overall health[19]	ECOG PS 0–1 preferred (0–2 allowed)	
	Life expectancy ≥6 months	

CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; F, fludeoxyglucose; MRI, magnetic resonance imaging; NaF, sodium fluoride; PET, positron emission tomography; Tc, technetium.

BEFORE SUBSEQUENT INJECTIONS (CYCLES 2–6)[5]		
Requirements		☐
Haematological evaluation	Absolute neutrophil count ≥1.0 x 10^9/L	
	Platelet count ≥50 x 10^9/L	

Additional considerations before starting or resuming treatment with Xofigo®[5]

Xofigo® is contraindicated in combination with abiraterone acetate and prednisone/prednisolone.

Spinal cord compression and bone fractures should be treated with standard of care, as clinically indicated. For existing bone fractures, orthopaedic stabilization of fractures should be performed.

Benefit–risk assessment should be completed for patients with:

- Advanced diffuse infiltration of bone (superscan)
- Ulcerative colitis
- Crohn's disease
- High baseline risk of fracture

Monitoring treatment with Xofigo®

Suggested regimen for monitoring treatment based on a European consensus.[17]

Treatment cycle

		Baseline	1	2	3
Biomarkers	Total ALP	✔	(✔)	(✔)	✔
	PSA[a]	✔	–	–	(✔)
	LDH	✔	✔	✔	✔
Imaging	Bone scintigraphy[b,c]	✔	–	–	–
	CT[c]	✔	–	–	(✔)
	Axial MRI[c,d]	✔	–	–	(✔)
Other assessments	Clinical symptoms	✔	✔	✔	✔
	Haematological parameters	✔	✔	✔	✔

✔ Indicates recommended; (✔) indicates 'if clinically indicated';
– indicates 'not routinely recommended'.

[a]PSA levels do not correlate with survival in patients receiving Xofigo®.[20]
[b]Progression of bone metastases is uncommon during Xofigo® treatment. Bone flare (pain and/or radiological) may be noted during the first 3 months of treatment and should not be confused with progression.[21]
[c]Bone scintigraphy and CT scans can be replaced with MRI if available.

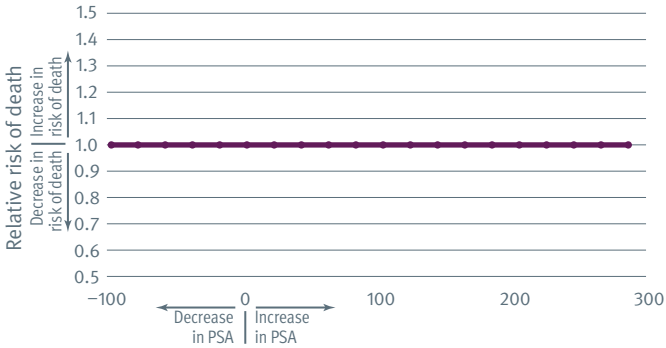
4	5	6	Follow-up
(✔)	(✔)	✔	✔
–	–	✔	✔
✔	✔	✔	✔
–	–	✔	–
–	–	✔	✔
–	–	(✔)	(✔)
✔	✔	✔	✔
✔	✔	✔	✔

[d]Next-generation imaging techniques (e.g. MRI and PET/CT) may have better accuracy than bone scintigraphy when monitoring treatment response in bone.[22]
ALP, alkaline phosphatase; CT, computed tomography; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; PET, positron emission tomography; PSA, prostate-specific antigen.

Biomarker changes with Xofigo® at 12 weeks

Treatment decisions about continuing Xofigo® **should not be made on the basis of biomarker changes**, particularly rising prostate-specific antigen (PSA) levels, as a large fraction of patients who may benefit would be denied effective treatment.[20]

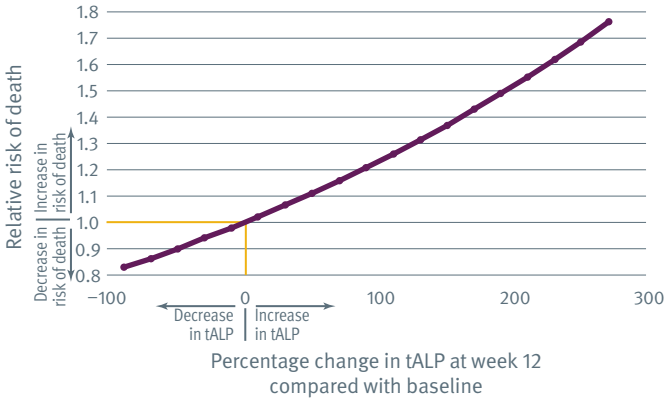
PSA LEVELS DO NOT CORRELATE WITH SURVIVAL IN PATIENTS RECEIVING XOFIGO®[20]



PSA, prostate-specific antigen.

PSA level is not a useful surrogate for monitoring response to Xofigo®, but changes in total alkaline phosphatase (tALP) may prove to be useful.[17]

CHANGES IN tALP LEVELS MAY BE USEFUL FOR MONITORING RESPONSE TO XOFIGO®[20]



tALP, total alkaline phosphatase.

When to consider stopping Xofigo®

The Advanced Prostate Cancer Consensus Conference Panel recommends that at least two of three criteria should be fulfilled to stop treatment:[23]

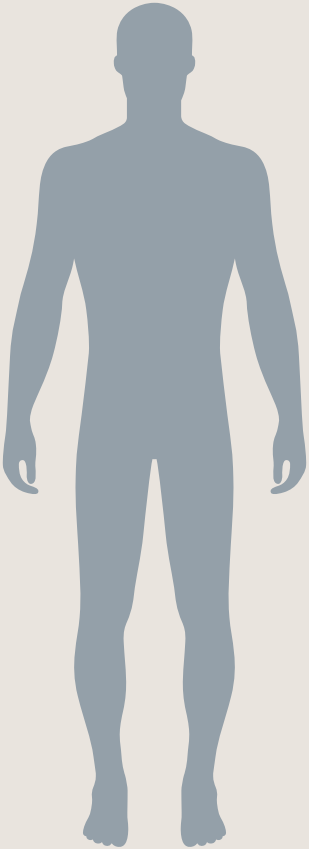
- PSA progression
- Radiographic progression
- Clinical deterioration

Special considerations for Xofigo®[17]

During the first course of Xofigo®, some patients may experience a 'flare phenomenon', which can present as pain, a PSA rise, or a radiological flare; all of these are unrelated to disease progression.

As such, only radiological visceral progression on a CT scan (or suspected spinal cord compression) should be a clear indication for Xofigo® treatment discontinuation.

Optimizing the patient experience



Stay on schedule[5,24]

The full course of Xofigo® treatment is six injections. To get the most benefit from Xofigo®, patients should receive all six cycles

Be proactive regarding adverse events

Have a discussion with your patient about the types of adverse events that they may experience so they are prepared,[24] and encourage them to report any adverse events to their healthcare team

Be clear on monitoring[24]

Patients should understand that PSA levels do not correlate with the effectiveness of Xofigo®, so will not be used to monitor the impact of treatment

Engage with the individual patient[3,4]

Collaboration and the sharing of information between patients and healthcare professionals can help to ensure patient perspectives are considered, and the patient is at the heart of decision making

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Essential Information

Xofigo® (radium Ra-223-diklorid) 1 100 kBq/ml injektionsvätska, lösning. För intravenös användning. Rx, EF, V10XX03.
Indikation: Xofigo i monoterapi eller i kombination med gonadotropinfrisättande hormon (GnRH)-analog, är avsett för behandling av vuxna patienter med metastaserande kastrationsresistent prostatacancer, (mCRPC), med symtomatiska skelettmetastaser och ingå känd visceral a metastaser, med progress efter minst två tidigare behandlingar med systemisk terapi mot mCRPC (andra än GnRH-analoger), eller då behandling med tillgänglig systemisk mCRPC-behandling är olämplig.
Farmakoterapeutisk grupp: V10XX03, radiofarmaceutiska terapeutika, diverse.

Varning och försiktighet: Diarré, illamående och kräkningar.

En ökad incidens av frakturer och dödsfall har observerats hos patienter som behandlats med Xofigo i kombination med abirateronacetat och prednison/prednisolon.

Säkerhet och effekt av Xofigo i kombination med cancerterapier andra än GnRH-analoger har inte fastställts; en ökad risk för mortalitet och frakturer är möjlig. Radium-223 i kombination med andra systemiska cancerterapier än GnRH-analoger rekommenderas därför inte.
Behandlingsnyttan med Xofigo hos vuxna med kastrationsresistent prostatacancer och endast asymtomatiska skelettmetastaser har inte fastställts. Användning av Xofigo rekommenderas därför inte för behandling av vuxna med kastrationsresistent prostatacancer och endast asymtomatiska skelettmetastaser. Hos vuxna med kastrationsresistent prostatacancer och lindrigt symtomatiska skelettmetastaser ska nyttan med behandlingen vägas noga mot riskerna med hänsyn till att hög osteoblastisk aktivitet sannolikt krävs för att uppnå behandlingsnytta.

Radium-223 rekommenderas inte till patienter med en låg nivå av osteoblastiska skelettmetastaser.

Essential Information

Innan behandling med Radium-223 inleds ska skelettstatus och frakturrisk noggrant bedömas och följas minst 24 månader.
Xofigo kan leda till benmärgssuppression med trombocytopeni och neutropeni var för blodstatus måste kontrolleras före behandling. Radiofarmaka ska endast tas emot, användas och administreras av behörig personal i ändamålsenliga lokaler. Administrering av radiofarmaka kan utgöra en risk för andra personer på grund av extern strålning eller kontamination från spill av urin, feces, uppkastningar. Med tanke på de potentiella effekter på spermatogenesen som är förknippade med strålning, bör män rådas att använda effektiva preventivmetoder under och upp till 6 månader efter behandling med Xofigo.
Kontraindikationer: Xofigo är kontraindicerat i kombination med abirateronacetat och prednison/prednisolon.
Kontaktuppgifter: Bayer AB, Box 606, 169 26 Solna, tel: 08-580 223 00.
Datum för senaste översyn av SPC: April 2020. För mer information, samt före förskrivning, vänligen läs produktresumé på fass.se
▼ Detta läkemedel är föremål för utökad övervakning. Hälso- och sjukvårdspersonal uppmanas att rapportera varje misstänkt biverkning till Läkemedelsverket.

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Notes

Bayer AB
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