Summary of the Risk Management Plan for XOFIGO®

Active substance: Radium-223 dichloride

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Based on the EU-RMP v5.1 dated 13-Jun-2023 for XOFIGO®

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of XOFIGO® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of XOFIGO® in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Bayer (Schweiz) AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of XOFIGO®.

Summary of risk management plan for Xofigo® (Radium-223 dichloride)

This is a summary of the risk management plan (RMP) for Xofigo®. The RMP details important risks of Xofigo®, how these risks can be minimised, and how more information will be obtained about Xofigo®'s risks and uncertainties (missing information).

Xofigo®'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Xofigo® should be used.

This summary of the RMP for Xofigo® should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Xofigo®'s RMP.

I. The medicine and what it is used for

Xofigo®, as monotherapy or in combination with luteinising hormone releasing hormone (LHRH) analogue, is authorised for the treatment of adult patients with metastatic castration-resistant prostate cancer (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 (see SmPC for the full indication). It contains Radium-223 dichloride as the active substance and it is administered by intravenous injection.

Further information about the evaluation of Xofigo®'s benefits can be found in Xofigo®'s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage found on the following link: https://www.ema.europa.eu/en/medicines/human/EPAR/xofigo.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Xofigo®, together with measures to minimise such risks and the proposed studies for learning more about Xofigo®'s risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PBRER/PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Xofigo® is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Xofigo® are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Xofigo®. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

Table Part VI.1: Summary of safety concerns

List of important risks and missing information	
Important identified risks	• Bone fractures • Bone marrow toxicity leading to reduced formed elements in blood
Important potential risks	• Late bone marrow toxicity • Myelodysplastic syndrome/ Acute myeloid leukaemia (MDS/AML) • Bone sarcoma • Secondary malignancies (other than MDS/AML and bone sarcoma) • Osteonecrosis of the jaw • Off-label use in women or children • Off-label administration of repeated courses of treatment, or other administration of doses in excess of those recommended in the product information

Table Part VI.1: Summary of safety concerns

List of important risks and missing information	
Missing information	• Safety in patients with insufficient wash-out period • Safety of Radium-223 with other cancer therapy apart from therapy for maintenance of castration-level • Reproductive toxicity in men with metastatic CRPC (mCRPC) • Reproductive toxicity due to off-label use in women • Developmental toxicity due to off-label use in children • Clinical safety in patients with inflammatory bowel disease • Clinical safety in non-white ethnic groups • Clinical safety in patients receiving chemotherapy • Clinical safety in patients receiving calcium supplementation, phosphates or vitamin D • Clinical safety in patients receiving external beam radiation therapy (EBRT) to bone or prostate

II.B Summary of Important Risks

Important identified risk: Bone fractures	
Evidence for linking the risk to the medicine	Data from Bayer Global Pharmacovigilance database and clinical studies with Xofigo®.
Risk factors and risk groups	Patients receiving Xofigo® in combination with abiraterone plus prednisone/ prednisolone. Patients with a medical history of osteoporosis and <6 metastases.

Important identified risk: Bone fractures	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.1 (Therapeutic indication) Section 4.3 (Contraindications) Section 4.4 (Special warnings and precautions for use) Section 4.8 (Undesirable effects) Section 5.1 (Pharmacodynamic properties) Section 5.3 (Preclinical safety data) PLs: Section 2 ("Xofigo® must not be given"; Warnings and precautions, Other medicines and Xofigo®) Section 4 (Possible side effects) SmPC sections 4.3, 4.4 and PL section 2: Xofigo® is contraindicated in combination with abiraterone and predniso(lo)ne. The combination of Xofigo® with other systemic cancer therapies other than LHRH analogues is not recommended. Physicians are advised to carefully assess bone status and baseline risk of fractures in patients prior to initiating the therapy. Patients should be closely monitored for at least 24 months. Administration of bone protective agents is recommended as a preventive measure before starting or resuming treatment with Xofigo®. In patients with a high baseline risk of fracture, the benefit of treatment should be carefully assessed to outweigh the risk. Sufficient treatment wash-out period is recommended before and/or after treatment with Xofigo® and other cancer therapies. In patients with bone fractures, orthopaedic stabilisation of fractures should be performed before starting or resuming treatment with Xofigo®. Patients are instructed to inform their healthcare practitioner if they have osteoporosis or a known increased risk for fractures. Patients are instructed to inform their healthcare practitioner if they taking any systemic cancer therapies and/or second generation androgen receptors antagonists. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** A DHPC to communicate the final recommendation has been circulated following the conclusion of the article 20 procedure (EMEA/H/A-20/1459/C/002653/0028).

Important identified risk: Bone fractures	
Additional pharmacovigilance activities	20510 – RADIANT – Phase IV randomised open-label multicentre study (ongoing) 20511 – Phase I biodistribution study (ongoing) 17739 – PEACE-3 – EORTC-sponsored Phase III study (ongoing) 19263 – DoRA – PCCTC-sponsored Phase III study (ongoing) 20702 – Drug utilisation study to investigate the risk of off-label use (ongoing) 16913 – REASSURE – Long-term safety study (ongoing) See section II.C of this summary for an overview of the post-authorisation development plan

Important identified risk: Bone marrow toxicity leading to reduced formed elements in blood	
Evidence for linking the risk to the medicine	Pooled data from clinical studies with Xofigo® Re-treatment safety study 16506
Risk factors and risk groups	Patients with reduced bone marrow capacity e.g., following prior cytotoxic and/or radiation treatment
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.4 (Special warnings and precautions for use) Section 4.5 (Interaction with other medicinal products and other forms of interaction) Section 4.8 (Undesirable effects) Section 5.3 (Preclinical safety data) PLs: Section 2 (Warnings and precautions) Section 4 (Possible side effects) SmPC section 4.4 and PL section 2: Instructions on monitoring haematological parameters. Patients with evidence of compromised bone marrow reserve or prostate cancer patients with advanced diffuse infiltration of the bone should be treated with caution. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Important potential risk: Late bone marrow toxicity	
Evidence for linking the risk to the medicine	Data from clinical studies with Xofigo® Re-treatment safety study 16506
Risk factors and risk groups	Prior exposure to systemic radionuclide therapy, and/or chemotherapy
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.4 (Special warnings and precautions for use) Section 4.8 (Undesirable effect) PLs: Section 2 (Warnings and precautions) Section 4 (Possible side effects) SmPC section 4.4 and PL section 2: Instructions on monitoring haematological parameters. Patients with evidence of compromised bone marrow reserve or prostate cancer patients with advanced diffuse infiltration of the bone should be treated with caution. Prescription-only medicine Trained physicians **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	16913 – REASSURE – Long-term safety study See section II.C of this summary for an overview of the post-authorisation development plan

Important potential risk: Myelodysplastic syndrome/ Acute myeloid leukaemia (MDS/AML)	
Evidence for linking the risk to the medicine	No cases have been reported in interventional clinical trials of Radium-223 dichloride. Information obtained from literature regarding risks from radiation.
Risk factors and risk groups	Patients who survive cancer treatment with alkylating agents, with or without radiotherapy, have a high risk of developing MDS or secondary acute leukaemia.

Important potential risk: Myelodysplastic syndrome/ Acute myeloid leukaemia (MDS/AML)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.4 (Special warnings and precautions for use) Section 4.8 (Undesirable effects) Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	16913 – REASSURE – Long-term safety study See section II.C of this summary for an overview of the post-authorisation development plan

Important potential risk: Bone sarcoma	
Evidence for linking the risk to the medicine	No cases have been reported in clinical studies of Xofigo®. Information obtained from literature regarding risks from radiation.
Risk factors and risk groups	Prior external radiation therapy to bone and /or systemic bone seeking radionuclide therapy. Young age (growing skeleton) at the time of exposure.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.4 (Special warnings and precautions for use) Section 4.8 (Undesirable effects) Section 5.3 (preclinical safety data) Prescription-only medicine Trained physicians **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	16913 – REASSURE – Long-term safety study See section II.C of this summary for an overview of the post-authorisation development plan

Important potential risk: Secondary malignancies (other than MDS/AML and bone sarcoma)	
Evidence for linking the risk to the medicine	Data from clinical studies with Xofigo® Re-treatment safety study 16506.
Risk factors and risk groups	No defined risk group in target population

Important potential risk: Secondary malignancies (other than MDS/AML and bone sarcoma)	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.8 (Undesirable effects) Prescription-only medicine Trained physicians **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	16913 – REASSURE – Long-term safety study See section II.C of this summary for an overview of the post-authorisation development plan

Important potential risk: Osteonecrosis of the jaw	
Evidence for linking the risk to the medicine	Data from clinical studies with Xofigo®.
Risk factors and risk groups	Bisphosphonate and/or denosumab use is a known risk factor for developing osteonecrosis of the jaw. Risk groups or risk factors for Xofigo® treatment are unknown.
Risk minimisation measures	**Routine risk minimisation measures:** PLs: Section 4 (Possible side effects) SmPC section 4.4 and PL section 2 where instructions are given for patients who take or have taken bisphosphonates or have received chemotherapy prior to treatment with Xofigo® to inform their healthcare practitioner. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	16913 – REASSURE – Long-term safety study See section II.C of this summary for an overview of the post-authorisation development plan

Important potential risk: Off-label use in women and children	
Evidence for linking the risk to the medicine	PASS 17399
Risk factors and risk groups	Breast cancer with bone metastases and children with osteosarcoma

Important potential risk: Off-label use in women and children	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.1 (Therapeutic indications) Section 4.2 (Posology and method of administration) Section 4.6 (Fertility, pregnancy and lactation) PLs: Section 2 (Children and adolescents) Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Important potential risk: Off-label administration of repeated courses of treatment, or other administration of doses in excess of those recommended in the product information	
Evidence for linking the risk to the medicine	PASS 17399
Risk factors and risk groups	Unknown
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.2 (Posology and method of administration) Posology SmPC Section 4.9 (Overdose) and PL Section 3 (How Xofigo is used) Instructions that in the event of an inadvertent overdose, general supportive measures, including monitoring for potential haematological and gastrointestinal toxicity should be undertaken. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Safety in patients with insufficient wash-out period	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.4 (Special warnings and precautions for use) PLs: Section 2 (Warnings and precautions) Sufficient treatment wash-out period is recommended before and/or after treatment with Xofigo® and other cancer therapies. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Safety of Radium-223 with other cancer therapy apart from therapy for maintenance of castration-level	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.1 (Therapeutic indication) Section 4.5 (Interaction with other medicinal products and other forms of interaction) Section 5.1 (Pharmacodynamic properties) Package leaflets (PLs): Section 4 (Possible side effects) SmPC sections 4.3, 4.4 and PL section 2: Xofigo® is contraindicated in combination with abiraterone and predniso(lo)ne. The combination of Xofigo® with other systemic cancer therapies other than LHRH analogues is not recommended. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Reproductive toxicity in men with metastatic CRPC	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.6 (Fertility, pregnancy and lactation) Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Reproductive toxicity due to off-label use in women / **Missing information: Reproductive toxicity in men with metastatic CRPC**	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.6 (Fertility, pregnancy and lactation) PLs: Section 2 (Pregnancy and breast feeding; Contraception in males and females; Fertility) Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Developmental toxicity due to off-label use in children	
Risk minimisation measures	Routine risk minimisation measures: SmPC: Section 4.2 (Posology and method of administration) PLs: Section 2 (Children and adolescents) Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Clinical safety in patients with inflammatory bowel disease / **Missing information: Developmental toxicity due to off label use in children**	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section 4.4 and PL section 2 where instructions are given for careful case-by-case assessment of the benefit risk in patients with inflammatory bowel disease by healthcare practitioners. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Clinical safety in patients receiving chemotherapy	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.4 (Special warnings and precautions for use) Section 4.5 (Interaction with other medicinal products and other forms of interaction) PLs: Section 2 (Warnings and precautions) Respective patients should be treated with caution. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmaco-vigilance activities	None

Missing information: Clinical safety in patients receiving calcium supplementation, phosphates or vitamin D	
Risk minimisation measures	**Routine risk minimisation measures:** SmPCs: Section 4.5 (Interaction with other medicinal products and other forms of interaction) PLs: Section 2 (Other medicines and Xofigo®) Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

Missing information: Clinical safety in patients receiving external beam radiation therapy (EBRT) to bone or prostate	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.4 (Special warnings and precautions for use) PL: Section 2 (Warnings and precautions) Instructions that the respective patient population should be treated with caution. Prescription-only medicine. Trained physicians. **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

The following studies are conditions of the marketing authorisation (refer to Table Part VI.2 for a tabulated summary):

20510 – RADIANT - Phase IV randomised open-label multicentre study

Study short name and title:

Phase IV randomised open-label multicentre study.

Purpose of the study:

The MAH was required to conduct and submit the results of a phase IV randomised open-labelmulticentre study according to an agreed protocol in order to further characterise the efficacy and safety, in particular the risk of fractures with Radium-223 dichloride in the authorised indication.

The protocol should foresee a stratified randomisation of patients according to total ALP levels.

This study will specifically address the important identified risk of bone fractures. The study also includes bone biomarker assessments (markers of bone formation and bone resorption) in the control arm.

20511 – Phase I biodistribution study

Study short name and title:

Phase I biodistribution study.

Purpose of the study:

The MAH was required to conduct and submit the results of a phase I biodistribution study according to an agreed protocol in order to further characterise correlation between the extent of the disease, the dose and the distribution of Radium-223 dichloride in bone metastases versus sites of impaired bone health (e.g., osteoporosis) versus normal bone structure.

The study will specifically address the important identified risk of bone fractures.

Table Part VI.2: Summary of studies which are Conditions of the Marketing Authorisation

Study Status	Summary of objectives	Safety concerns/ efficacy issue addressed	Milestones	Due dates
Category 1 – Imposed mandatory additional pharmacovigilance activities which are conditions of the marketing authorisation				
20510 – RADIANT Phase IV randomised open-label multicentre study Ongoing	The MAH was required to conduct and submit the results of a phase IV randomised open-label multicentre study according to an agreed protocol in order to further characterise the efficacy and safety, in particular the risk of fractures, with Radium-223 dichloride in the authorised indication. The protocol should foresee a stratified randomisation of patients according to total ALP levels. The study also includes bone biomarker assessments (markers of bone formation and bone resorption) in the control arm.	Important identified risk: Bone fractures	Protocol submission to PRAC Final CSR submission	Within 6 months of the EC decision Q3 2025
20511 Phase I biodistribution study Ongoing	The MAH was required to conduct and submit the results of a phase I biodistribution study according to an agreed protocol in order to further characterise correlation between the extent of the disease, the dose and the distribution of Radium-223 dichloride in bone metastases versus sites of impaired bone health (e.g., osteoporosis) versus normal bone structure.	Important identified risk: Bone fractures	Protocol submission to PRAC FPFV Final CSR submission	6 months after EC decision AUG 2020 Q1 2026

II.C.2 Other studies in post-authorisation development plan

The following studies are required additional pharmacovigilance activities (refer to Table Part VI.3 for a tabulated summary):

16913 – REASSURE – Long-term safety study

Study short name and title:

Radium-223 alpha Emitter Agent in non-intervention Safety Study in metastatic castration-resistant prostate cancer (mCRPC) popUlation for long-teRm Evaluation (REASSURE).

Purpose of the study:

The REASSURE study is to evaluate the short and long-term safety profile of Radium-223 dichloride and will assess the safety and tolerability of Radium-223 dichloride and the risk of developing second primary cancers among castration resistant prostate cancer patients receiving Radium-223 dichloride in the routine clinical practice setting. In addition overall survival and pain-related data will be collected.

The study will specifically address the following important potential risks: bone fractures, late bone marrow toxicity, MDS/AML, bone sarcoma, second primary malignancies (other than MDS/AML and bone sarcoma), osteonecrosis of the jaw.

17739 – PEACE-3 – EORTC-sponsored Phase III study

Study short name and title:

A Randomised multicentre phase III trial comparing enzalutamide vs. a combination of Radium-223 dichloride and enzalutamide in asymptomatic or mildly symptomatic castration resistant prostate cancer patients metastatic to bone.

Purpose of the study:

The study sponsored by the European Organisation for Research and Treatment of Cancer (EORTC) is investigating the combination use with enzalutamide in asymptomatic and mildly symptomatic CRPC patients. The study will specifically address the important identified risk of bone fractures.

19263 – DoRa – PCCTC-sponsored Phase III study

Study short name and title:

Phase III Trial of Docetaxel vs. Docetaxel and Radium-223 dichloride for Metastatic Castration-Resistant Prostate Cancer.

Purpose of the study:

The study sponsored by the Prostate Cancer Clinical Trials Consortium (PCCTC) is investigating the combination use of Xofigo® with docetaxel in CRPC patients.

The study will specifically address the important identified risk of bone fractures.

20702 – Drug utilisation study to investigate the risk of off-label use

Study short name and title:

Drug utilisation study to investigate the risk of off-label use.

Purpose of the study:

The study will investigate the risk of off-label use. The study will specifically address the important identified risk of bone fractures.

Table Part VI.3: Summary of other studies in post-authorisation development plan

Study Status	Summary of objectives	Safety concerns addressed	Milestones	Due dates
Category 3 – Required additional pharmacovigilance activities				
16913 – REASSURE Long Term Safety of Radium-223 in Castrate Resistant Prostate Cancer (CRPC) patients with bones metastasis in Routine Clinical Practice Settings Ongoing	To assess the long-term safety profile and risks of developing second primary malignancies and their potential relationship to Radium-223 dichloride in the routine clinical practice setting	Important identified risk: Bone fractures Important potential risks: Late bone marrow toxicity MDS/AML Bone sarcoma Second primary malignancies (other than MDS/AML and bone sarcoma) Osteonecrosis of the jaw	Final draft protocol Submission to PRAC Study initiation Recruitment completion 1st Interim Report 2nd Interim Report Final report	OCT 2013 OCT 2013 Q1 2014 Q1 2017 Q4 2017 Q4 2019 Q2 2025
17739 – **PEACE-3** EORTC-sponsored Phase III study Ongoing	To investigate the combination use of Radium-223 dichloride with enzalutamide in asymptomatic and mildly symptomatic CRPC patients.	Important identified risk: Bone fractures	Study start date Interim status update Primary completion Final CSR submission	OCT 2015 APR 2020 MAR 2024 Q4 2024
19263 – DoRA PCCTC-sponsored Phase III study Ongoing	To investigate the combination use of Radium-223 dichloride with docetaxel in CRPC patients.	Important identified risk: Bone fractures	Study start date Interim status update Primary completion	20 JUN 2018 30 APR 2021 NOV 2025

Table Part VI.3: Summary of other studies in post-authorisation development plan

Study Status	Summary of objectives	Safety concerns addressed	Milestones	Due dates
Category 3 – Required additional pharmacovigilance activities				
			Final CSR submission to PRAC	Q3 2026
			DMC reports will be provided and discussed in PBRERs/PSURs	
20702 Drug utilisation study to investigate the risk of off-label use Ongoing	To investigate the risk of off-label use	<u>Important identified risk:</u> Bone fractures	Protocol submission	Within 4 months after EC decision
			FPFV	JUN 2020
			Start of data collection	Q2 2021
			Final CSR submission	Q2 2023

AML: Acute Myeloid Leukaemia, CRPC: Castration-resistant prostate cancer, CSR: Clinical study report, DMC: Data Monitoring Committee, EC: European Committee, FPFV: First patient first visit, LPLV: Last patient last visit, MDS: Myelodysplastic Syndrome, PBRER: Periodic Risk Evaluation Report, PRAC: Pharmacovigilance Risk Assessment Committee, PSUR: Periodic Safety Update Report, Q: Quarter.