Radium223Insight: Een onderzoek naar betere methodes voor het meten van het vroege behandeleffect en het effect van radium-223 op het afweersysteem bij patiënten met uitgezaaide prostaatkanker.

Gepubliceerd: 30-10-2018 Laatst bijgewerkt: 15-05-2024

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Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Voortplantingsorgaan- en urogenitale neoplasmata, geslacht niet-gespecificeerd NEG
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26890

Bron
NTR

Verkorte titel
Radium223Insight

Aandoening

- Voortplantingsorgaan- en urogenitale neoplasmata, geslacht niet-gespecificeerd NEG

Aandoening

Prostate cancer, castration resistant prostate cancer, mCRPC, radium-223, biomarker, immune response. Prostaatkanker, castratieresistente prostaatkanker, radium-223,

biomarker, immuunrespons.

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Bayer
Overige ondersteuning: Bayer

Onderzoeksproduct en/of interventie

- Overige

Toelichting

Uitkomstmaten

Primaire uitkomstmaten

1. Exploratory analysis of multiple biomarkers in relation to failure-free survival, defined as time to next line of treatment, best supportive care or death. Next line of treatment or best supportive care will be started upon clinical, biochemical and/or radiological signs of progression according to the PCWG3 criteria.

2. Exploratory analysis of the immune response during radium-223 treatment in relation to failure-free survival as defined above.

Toelichting onderzoek

Achtergrond van het onderzoek

Based on the survival results of a randomized phase 3 trial, the European Medicines Agency (EMA) and Committee for the Assessment of Oncological Medicines (‘Commissie BOM’) have approved radium-223 for the treatment of metastatic castration resistant prostate cancer (mCRPC) with bone metastases only. As traditional parameters, including PSA, fail in (early) response evaluation, other parameters are needed to guide treatment planning in mCRPC patients. As the efficacy of immunotherapy is limited in mCRPC and radium-223 may initiate an immune response by activation of CD8 T lymphocytes, further understanding is required for the rational development of combination strategies, including those with radium-223.

Doel van het onderzoek

In the current study, biomarkers for tumor and immune response during radium-223 are evaluated, thereby potentially contributing to a better understanding of immune responses during radium-223 and the rational design of future treatment strategies combining radium-233 with immunotherapy.

We hypothesize that:

1) Multidimensional biomarker collection enhances our understanding of tumor responses during radium-223, thereby potentially identifying biomarkers for early response.

2) Radium-223 induces DNA damage, resulting in immunogenic cell death and activation of the immune system, thereby making tumors more prone to immunotherapy.

Onderzoeksopzet

- Baseline: week -1

- During treatment: week 3, 7, 11, 15, 19

- End of treatment: week 24

- During follow-up: every 12 weeks

- At progression of disease

Onderzoeksproduct en/of interventie

Patients will be treated with radium-223 according to standard of care. Prior and during treatment, multi-parametric biomarkers will be collected. These biomarkers are obtained from blood samples, imaging and tissue.

Blood samples:

- Conventional markers (PSA, ALP, LDH)

- Circulating tumor cells

- Circulating tumor derived DNA

- Immune cells and markers

Imaging:

- Conventional imaging (CT and bone scintigraphy)

- [68Ga]PSMA PET-CT

- [89Zr]atezolizumab PET-CT

Tissue (bone biopsy):

- Whole genome sequencing, focusing on mutational and immune profiling data.

- In situ multiplex immune fluorescence of FFPE using automated quantitative pathology imaging.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
Volwassenen (18-64 jaar)
65 jaar en ouder
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• Age ≥ 18 years

• Histologically confirmed, progressive prostate cancer during ADT. Castration-resistant disease is defined as a serum testosterone level of 50 ng per deciliter or lower (≤1.7 nmol per liter) after bilateral orchiectomy or during maintenance treatment consisting of androgen-ablation therapy with a luteinizing hormone–releasing hormone agonist.

• Baseline PSA level of ≥ 2 ng per milliliter with evidence of progressively increasing PSA values (two consecutive increases over the previous reference value) • Prior treatment with at least two other approved agents for metastatic prostate cancer, unless the patient is not able and/or willing to receive other treatments.

• Eastern Cooperative Oncology Group (ECOG) performance-status score of 0 or 1 (on a scale of 0 to 5, with 0 indicating no symptoms and full activity and higher scores indicating greater functional compromise)

• Life expectancy of 6 months or longer

• Adequate hematologic, renal, and liver function, including trombocytes >100x109/L, granulocytes >1.5x109/L, Hb >6.2 mmol/L.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• Prior chemotherapy, other than docetaxel.

• Previous hemibody external radiotherapy or systemic radiotherapy with radioisotopes within the previous 24 weeks.

• A blood transfusion or use of erythropoietin-stimulating agents within the previous 4 weeks

• Pathological lymphadenopathy > 1.5 cm in the short-axis diameter on CT or MRI. [68Ga]-PSMA positive lymph nodes at baseline are allowed.

• A history of presence of visceral metastases on CT or MRI. Patients with [68Ga]-PSMA positive lesions that are highly suspected for visceral metastases and are retrospectively visible on CT or MRI should be excluded as well.

• Imminent or established spinal cord compression on CT or MRI.

• A second active malignancy.

Onderzoeksopzet

Opzet

Fase onderzoek:	N.V.T.
Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Enkelvoudig
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend
Doel:	Anders

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-01-2019
Aantal proefpersonen:	28
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Goedgekeurd WMO

Datum:	18-01-2019
Soort:	Eerste indiening
Toetsingscommissie:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55470
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7380
NTR-old	NTR7588
CCMO	NL66323.078.18
OMON	NL-OMON55470

Resultaten

Datum resultaten gemeld: 22-09-2023

Samenvatting resultaten
CT and bone scintigraphy are not useful for response evaluation of bone metastases to 223Ra treatment in metastatic castration-resistant prostate cancer (mCRPC). PET using 68Ga prostate-specific membrane antigen 11 (68Ga-PSMA) is a promising tool for response evaluation of mCRPC. The aim of this study was to determine the utility of 68Ga-PSMA PET/CT for response evaluation of 223Ra treatment in patients with mCRPC. Methods: Within this prospective, multicenter, imaging discovery study, 28 patients with mCRPC, eligible for 223Ra treatment, were included between 2019 and 2022. Patients received 223Ra according to the standard of care. Study procedures included CT, bone scintigraphy, and 68Ga-PSMA PET/CT at baseline, after 3 and 6 cycles of 223Ra treatment, and on treatment failure. Response to 223Ra treatment was visually assessed on all 3 imaging modalities. Total tumor volume within bone (TTVbone) was determined on 68Ga-PSMA PET/CT. Intrapatient heterogeneity in response was studied using a newly developed image-registration tool for sequential images of PET/CT. Results were compared with failure-free survival (good responders vs. poor responders; cutoff, 24 wk) and alkaline phosphatase (ALP) response after 3 cycles. Results: Visual response assessment criteria could not distinguish good responders from poor responders on 68Ga-PSMA PET/CT and bone scintigraphy. For 68Ga-PSMA PET/CT, TTVbone at baseline was lower in good responders than in poor responders, whereas TTVbone increased in both groups during treatment. TTVbone was higher in patients with new extraosseous metastases during 223Ra treatment. Although TTVbone and ALP correlated at baseline, changes in TTVbone and ALP on treatment did not. 68Ga-PSMA response of

TTVbone showed intrapatient heterogeneity in most patients. Conclusion: mCRPC patients with lower TTVbone on 68Ga-PSMA PET/CT have the best clinical outcome after 223Ra treatment. Response is highly heterogeneous in most patients. A decrease in ALP, which occurred in most patients, was not correlated with a decrease in TTVbone, which might make one question the value of ALP for disease monitoring during 223Ra treatment in clinical practice.

Datum eerste publicatie onderzoek
03-08-2023