Trattamento delle metastasi ossee nel paziente con tumore della prostata resistente alla castrazione (mCRPC) — Valutazione della Risposta

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DICHIARAZIONE

Relatore: Sergio Baldari

Le nuove regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, richiede la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Consulenza ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazione ad Advisory Board (Bayer)
- Sottorità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
Characteristics of Ra-223

- A radioactive isotope of the alkaline earth metal radium, therefore a calcium mimetic
- Incorporates into bone mineral hydroxyapatite
- Preferential uptake in areas of new bone formation
- Has a half-life of 11.4 days
- Primarily an alpha-particle emitter
  - ~94% emitted as alpha-particles
  - ~4% emitted as beta-particles
  - ~2% emitted as gamma rays
α-Particles cause lethal double-strand DNA breaks

**β-emitters**

- Low-LET β-radiation → single-strand DNA breaks
- Single-strand breaks: easily repaired using the opposite strand as a template
- Single-strand breaks → less likely to induce cell death

**α-emitters**

- High-LET α-particles → double-strand DNA breaks
- Double-strand breaks: difficult to repair
- Failure to repair → to apoptosis
- Misrepaired double-strand breaks → chromosomal aberrations → mitotic cell death
Biodistribution

- Radium-223 dichloride goes to the target immediately after IV administration
- More than 75% of the activity had left the blood and plasma at 15 minutes after injection
- Only 4 ± 1% (range 2–6%) of the activity remained in the blood at 4 hours post injection, decreasing to less than 1% at 72 hours

Radium 223 selectively targeted bone tissue and was localized in areas of increased bone formation in bone metastases

The remainder was rapidly eliminated, predominantly via the GI tract

No specific renal, urinary bladder, cardiac, gallbladder, or splenic uptake was visible on scintillation camera images

- ~ 60% of activity injected is taken up in bone by 4 hours
- ~ 75% excreted within 1 week
- < 5% excreted through urine (low renal and bladder adsorbed doses)
Radium 223 Is a Bone-Seeking Radionuclide

Radium 223 has preferential uptake in areas of new bone formation

Normal spongious bone

Osteoblastic zone

Microautoradiography from a dog injected with radium 223
Distribution of α-particle tracks in normal spongious bone and an osteoblastic zone

Short range of alpha-emitters reduces bone marrow exposure

<table>
<thead>
<tr>
<th></th>
<th>Beta</th>
<th>Alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range in tissue (μm)</td>
<td>50–12 000</td>
<td>40–100</td>
</tr>
<tr>
<td>Relative particle mass</td>
<td>1</td>
<td>7000</td>
</tr>
<tr>
<td>DNA hits for cell kill</td>
<td>&gt;1000</td>
<td>1–4</td>
</tr>
</tbody>
</table>

Range of alpha particle (2–10 cell diameters$^2$)

Range of beta particle (10–1000 cell diameters$^2$)


Radium 223

Beta emitter
Table 3 - Number of treatment-related adverse events and total number of hematology events reported up to week 24 by dose group and Common Toxicity Criteria safety grade (safety population)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ra 223 dose group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25 kBq/kg, n = 41</td>
</tr>
<tr>
<td></td>
<td>1  2  3  4</td>
</tr>
<tr>
<td>CTC safety grade</td>
<td></td>
</tr>
<tr>
<td>Treatment-related AEs by system organ class</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>16  2 - -</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>5  2 - -</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>1  3 - -</td>
</tr>
<tr>
<td>Investigations</td>
<td>- - 2 -</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>- - - 2</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>- - - -</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>- - - -</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>- - - -</td>
</tr>
<tr>
<td>Total treatment-related AEs</td>
<td>23  7 2 0</td>
</tr>
<tr>
<td>Total hematology events</td>
<td></td>
</tr>
<tr>
<td>White blood cell count</td>
<td>7  2 0 0</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>16  0 0 0</td>
</tr>
<tr>
<td>Platelets</td>
<td>5  1 1 0</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>18 12 1 1</td>
</tr>
</tbody>
</table>

AE = adverse event; CTC = Common Toxicity Criteria.

* One case of grade 3 constipation was reported in the 80-kBq/kg group.

b All reported grade 3 or 4 AEs were classified as anemia.

c One case each of grade 3 decreased hemoglobin or platelet counts occurred in the 25-kBq/kg group; decreased hemoglobin (grade 3) and decreased platelet counts (grade 4) occurred in the 50-kBq/kg group.

d All reported grade 3 AEs were classified as bone pain.
### Treatment-Related Adverse Events (AEs) Reported during the Designated ALSYMPCA Follow-up

<table>
<thead>
<tr>
<th>ALSYMPCA Follow-up, n (%)</th>
<th>Radium-223 (n = 404*†)</th>
<th>Placebo (n = 167*†)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades</td>
<td>Grades 3/4</td>
</tr>
<tr>
<td><strong>Hematologic AEs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>11 (3)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>2 (&lt;1)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>2 (&lt;1)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4 (1)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Nonhematologic AEs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiopulmonary failure</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>General physical health deterioration</td>
<td>1 (&lt;1)†</td>
<td>0</td>
</tr>
<tr>
<td>Multorgan failure</td>
<td>1 (&lt;1)†</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (&lt;1)†</td>
<td>0</td>
</tr>
<tr>
<td>Weight decrease</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Pathologic fracture</td>
<td>2 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Primary Cancers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph node metastasis not originating from prostate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma rectosigmoid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin cancer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\*Safety population
†Grade 5
Alpha Radin e Valutazione della Risposta

Clinica - Personalizzata
Non è Standardizzata
Non è Temporizzata
Non esistono indicatori certi
Non è chiaro il ruolo dell'imaging
Esistono tuttavia alcune evidenze.......
CARATTERISTICHE CLINICHE

Severe pain
Daily opioid use

Moderate pain
Occasional opioid use

Mild pain
Non-opioid analgesics
EBRT

Paracetamolo
Medicazione Genetica
Compresse

Opioid-Based Drugs

Fentanyl Transdermal System
75 mcg/hr

Pain in the context of the disease can vary in severity. It is important to distinguish between different pain levels: mild, moderate, and severe. Mild pain can be managed with non-opioid analgesics such as paracetamol (Paracetamolo). Moderate pain may require occasional opioid use, while severe pain necessitates daily opioid use, often starting with a transdermal fentanyl system (Fentanyl Transdermal System).

In the context of this presentation, we emphasize the importance of accurately assessing pain levels to select the appropriate treatment method. Proper management can significantly improve the quality of life for patients experiencing pain.
CARATTERISTICHE CLINICHE

Patients can be considered for Radium-223 as soon as the symptoms of bone metastases appear.

43% of patients had mild pain and no opioid use in ALSYMPCA.

Severe pain
Daily opioid use

Moderate pain
Occasional opioid use

Mild pain
Non-opioid analgesics
EBRT
Slice Patients have ≥ 2 bone metastases detectable by 99mTc-phosphonate bone scan.

Radium-223 is indicated for patients with mCRPC and symptomatic bone metastases without visceral metastases.

Patient 1: No Metastasis
Patient 2: > 2 Metastasis
Patient 3: > 20 Metastasis
Patient 4: <SuperScan>
The Scan Index as a prognostic imaging marker during androgen deprivation therapy

Reza¹*, Anders Bjartell², Mattias Ohlsson³, Reza Kaboteh⁴, Per Wollmer¹, Lars Edenbrandt¹, Trägårdh¹

Reza et al. EJNMMI Research 2014, 4:58
http://www.ejnmмир.es/content/4/1/58

Figure 3 At follow-up, Kaplan-Meier curves showing patient survival probability stratified by BSI changes categories. BSI changes from baseline to follow-up were evaluated among the 146 patients studied. In accordance with their BSI change values at follow-up, these patients were classified into two BSI changes categories: High BSI change (BSI increase n = 67) and low BSI change (stable BSI or BSI decrease, n = 79). These two groups demonstrated significantly different 5-year survival rates of 41% and 75%, respectively (p = 0.0004).
Quality of life (QOL), updated survival, and safety of radium-223 dichloride in patients with castration-resistant prostate cancer (CRPC) with bone metastases from the phase 3 double-blind, randomized, multinational study (ALSYMPCA)

C. Parker,1 R.E. Coleman,2 S. Nilsson,1 N. Vogelzang,4 A. Lloyd,3 K. Staudacher,6 P. Cislo,7 R. Van Gool,6 O. Sartor8

1The Royal Marsden NHS Foundation Trust, Sutton, UK; 2Weston Park Hospital, Sheffield, UK; 3Karolinska University Hospital, Stockholm, Sweden; 4Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA; 5Oxford Outcomes, Oxford, UK; 6Algeta ASA, Oslo, Norway; 7Bayer Healthcare, Montville, NJ, USA; 8Bayer Healthcare, Berlin, Germany; 9Tulane Cancer Center, New Orleans, LA, USA

QOL FINDINGS

The percentage of patients with a baseline QOL measurement and a QOL measurement at specified post-baseline visits shows that more patients in the radium-223 group than in the placebo group completed the QOL assessments (Figure 1).

Figure 1. Percentage of Patients Who Have a Baseline QOL Measurement and a QOL Measurement at the Specified Post-baseline Visits

There was a trend toward improvement in all subscales of the FACT-P, with $P < 0.05$ for the PCS and EWB subscales (Figure 2B).

Figure 2. ALSYMPCA QOL Responder Analysis Based on Improvement (Minimally Important Difference; MID) in FACT-P Summary Scores (A) and Subscale Scores (B) at Week 16 and/or Week 24

(b) Responder Analysis Based on Changes in FACT-P Subscale Scores

- Patients with improvement from baseline: 1.0 MID

* $P < 0.05$
** $P < 0.01$
 *** $P < 0.001$

For each subscale, MID = 3

*FACT-P MID = 16 points; TOI MID = 9 points
Bone Metastases in Patients with Prostate Cancer

Underlying mechanisms

Factors are released by tumor cells that stimulate both osteoclast and osteoblast activity\(^1,2\)

Excessive new bone formation occurs around tumor cell deposits, resulting in low bone strength and potential vertebral collapse\(^3\)

Osteoclastic and osteoblastic activity releases growth factors that stimulate tumor cell growth, perpetuating the cycle of bone resorption and abnormal bone growth\(^4\)

Bone biomarkers outlined are elevated

\(^1\) Goltzman D. Cancer. 1997;80:1581-1587
\(^2\) Adami S. Cancer. 1997;80:1674-1679
\(^3\) Mundy GR. Cancer. 1997;80:1546-1556
\(^4\) Boyce BF, Yoneda T, Guise TA. Endocr Relat Cancer. 1999;6:333-347
Randomized, dose-response, multicenter phase II study of radium-223 chloride for the palliation of painful bone metastases in patients with castration-resistant prostate cancer


Abstract

**Purpose:** To investigate the dose–response relationship and pain-relieving effect of radium-223, a highly bone-targeted alpha-pharmaceutical.

**Methods:** One hundred patients with bone metastases were randomized to receive radium-223. The primary end point was pain assessed by a numerical rating scale (0–10). The primary endpoint was to evaluate the pain relief over time.

**Results:** A significant improvement in the pain was observed in the patients who received radium-223. The pain decreased by a median of 20% at 2 weeks, 25% at 4 weeks, and 30% at 8 weeks, compared to baseline, with a further decrease to 35% at 16 weeks. The pain relief was consistent across all treatment groups.

**Conclusion:** Pain relief was observed in patients with bone metastases following radium-223 treatment. The treatment was well tolerated, and no significant adverse events were reported.

Fig. 3. Bone-alkaline phosphatase (ALP): median percentage change from baseline (safety set).
All main secondary efficacy endpoints demonstrate the benefit of radium 223 (+ BSoC) over placebo. The table below shows the main secondary efficacy endpoints in the intention-to-treat population:

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Radium-223 (N=614)</th>
<th>Placebo (N=307)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first symptomatic skeletal event — mo</td>
<td>15.6</td>
<td>9.8</td>
<td>0.66 (0.52–0.83)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to increase in total alkaline phosphatase — mo</td>
<td>7.4</td>
<td>3.8</td>
<td>0.17 (0.13–0.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to increase in PSA level — mo</td>
<td>3.6</td>
<td>3.4</td>
<td>0.64 (0.54–0.77)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Patients who had elevated total alkaline phosphatase levels at baseline are included.

Appendix, respectively. In addition, a significantly higher proportion of patients in the radium-223 group than in the placebo group had a response according to the total alkaline phosphatase level (≥30% reduction, P<0.001) and normalization of this level (P<0.001). A 30% or greater reduction in PSA blood levels at week 12 was achieved in 16% of patients in the radium-223 group and in 6% of patients in the placebo group (P<0.001). This reduction was sustained 4 weeks after the last injection in 14% of patients in the radium-223 group and in 4% of patients in the placebo group (P<0.001).
Changes in prostate-specific antigen, markers of bone metabolism, and bone scans after treatment with radium-223

Abstract

Objective. The aim of this study was to assess treatment-related changes in prostate-specific antigen (PSA), total and bone alkaline phosphatase (total ALP, bone ALP), and changes on conventional bone scans in patients with metastatic castration-resistant prostate cancer (mCRPC) with bone metastases who received six cycles of radium-223 (Ra-223). Materials and methods. Changes in PSA, total ALP and bone ALP (≥30% increase or decrease), and changes on bone scans were assessed before and after six monthly cycles of Ra-223 therapy (50 kBq/kg body weight). 14 patients with mCRPC with bone metastases and four patients on placebo. Results. Post-treatment PSA increased by at least 30% in 11 out of 14 patients and remained stable in three. ALP and bone ALP decreased in six and nine patients, respectively. In 10 out of 12 evaluable patients the uptake on post-treatment bone scan was reduced in lesions with high pretreatment uptake, in 11 patients accompanied by the development of new or expanded bone lesions. FACBC position emission tomography/computed tomography scans confirmed the growth of new or expanded bone metastases in two patients. Conclusions. These observations support the notion that Ra-223 kills tumour cells in metastases surrounded by highly proliferating osteoblasts, consistent with the reported survival benefit. The radiation effect in small tumour deposits not surrounded by increased osteoblast activity seems, however, insufficient, thus allowing continuous tumour growth. Long-lasting PSA reductions are the exception rather than the rule during Ra-223 treatment, whereas alkaline phosphatases decrease more frequently. To improve the overall anticancer effect, Ra-223 might be a valuable component of combination treatment.
Figure 2: Radionuclide bone scan trend and response to radium-223. A. June 2008, metastatic prostate cancer diagnosis. B. May 2010, disease progression on combined androgen blockade. C. May 2011, disease progression following sipuleucel-T immunotherapy. D. December 2011, disease progression just prior to docetaxel chemotherapy. E. June 2013, widespread disease progression associated with severe diffuse bone pain on enzalutamide ("pre-radium-223"). F. February 2014, dramatic bone scan response two months after completing six treatments of radium-223 ("post-radium-223").
B.E. 69 Anni
Gleason 9 (4+5)
Terapia Antalgica: Targin, Tachipirina
No Evidenza di Malattia Viscerale
Maggior dolore presente al tratto L-S
In terapia con 223Ra-Cl dal Luglio 2015 (1 ciclo ogni 4 settimane circa)

**PSA History**
Luglio 2015: 13.86 ng/ml (0-4) (I Ciclo)
Agosto 2015: 11.36 ng/ml (0-4) (II Ciclo)
Settembre 2015: 5.44 ng/ml (0-4) (III Ciclo)
Ottobre 2015: 5 ng/ml (0-4) (IV Ciclo)

**ALP History**
Luglio 2015: 119 U/L (I Ciclo)
Agosto 2015: 58 U/L (II Ciclo)
Settembre 2015: 50 U/L (III Ciclo)
Ottobre 2015: 37 U/L (IV Ciclo)
Instructions (adopted from McCaffery, Beebe et al. 1989):
Indicate the intensity of current, best, and worst pain levels over 24 hours on a scale of 0 (no pain) to 10 (worst pain imaginable).”

NRS History
Luglio 2015 1 (I Ciclo)
Luglio 2015 1 (I Ciclo)
Agosto 2015 1 (II Ciclo)
Agosto 2015 1 (II Ciclo)
Settembre 2015 4 (III Ciclo)
Settembre 2015 4 (III Ciclo)
Ottobre 2015 3 (IV Ciclo)
Ottobre 2015 2 (IV Ciclo)
B.E. 69 Anni
Gleason 9 (4+5)
Terapia Antalgica: Targin, Tachipirina
No Evidenza di Malattia Viscerale
Maggior dolore presente al tratto L-S
In terapia con 223Ra-Cl dal Luglio 2015 (1 ciclo circa 4 settimane)
B.S. 69 Anni
Gleason: 9 (4+5)
Da Giugno ad Settembre 2014: 7 cicli Docetaxel
No Evidenza Malattia Viscerale
Terapia Antalgica: 2014 EBTR su art. coxofemorale sin.
In terapia con 223Ra-Cl dall'Ottobre 2014 al Marzo 2015 (ciclo ogni 4 settimane circa)

**PSA History**
- Ottobre 2014: 145.88 ng/ml (0-4) (I Ciclo)
- Novembre 2014: 85.13 ng/ml (0-4) (II Ciclo)
- Dicembre 2014: 60.38 ng/ml (0-4) (III Ciclo)
- Gennaio 2015: 55.87 ng/ml (0-4) (IV Ciclo)
- Febbraio 2015: 50.13 ng/ml (0-4) (V Ciclo)
- Marzo 2015: 51.20 ng/ml (0-4) (VI Ciclo)

**ALP History**
- Ottobre 2014: 142 U/L (I Ciclo)
- Novembre 2014: 79 U/L (II Ciclo)
- Dicembre 2014: 71 U/L (III Ciclo)
- Gennaio 2015: 72 U/L (IV Ciclo)
- Febbraio 2015: 69 U/L (V Ciclo)
- Marzo 2015: 70 U/L (VI Ciclo)
Patient Instructions (adopted from McCaffery, Beebe et al. 1989):

"Please indicate the intensity of current, best, and worst pain level in the past 24 hours on a scale of 0 (no pain) to 10 (worst pain imaginable)."

Reference:

NRS History
Ottobre 2014 3 (I Ciclo)
Ottobre 2014 4 (I Ciclo)
Novembre 2014 1 (II Ciclo)
Novembre 2014 2 (II Ciclo)
Dicembre 2014 6 (III Ciclo)
Dicembre 2014 4 (III Ciclo)
Gennaio 2015 3 (IV Ciclo)
Gennaio 2015 3 (IV Ciclo)
Febbraio 2015 0 (V Ciclo)
Febbraio 2015 2 (V Ciclo)
Marzo 2015 4 (VI Ciclo)
Marzo 2015 4 (VI Ciclo)
69 Anni
Diagnosis: 9 (4+5)
Giugno ad Settembre 2014: 7 cicli
Docetaxel
Evidenza Malattia Viscerale
Terapia Antalgica: 2014 EBTR su art. coxofemorale sin.
Terapia con 223Ra-Cl dall’Ottobre 2014 al Marzo 2014 (1 ciclo ogni 4 settimane circa)
A.M. 75 Anni
Gleason 4+5
No Evidenza Malattia Viscerale
Terapia Antalgica ASA, Durogesic
Maggior Espressione del dolore al Femore Dx
In terapia con 223Ra-Cl da Dicembre 2014 a Marzo 2015 (1 ciclo ogni 4 settimane circa)

**PSA History**
- Dicembre 2014: 163.03 ng/ml (0-4) (I Ciclo)
- Gennaio 2015: 804 ng/ml (0-4) (II Ciclo)
- Febbraio 2015: 364 ng/ml (0-4) (III Ciclo)
- Marzo 2015: 472 ng/ml (0-4) (IV Ciclo)

**ALP History**
- Dicembre 2014: 123 U/L (I Ciclo)
- Gennaio 2015: 148 U/L (II Ciclo)
- Febbraio 2015: 86 U/L (III Ciclo)
- Marzo 2015: 108 U/L (IV Ciclo)
Instructions (adopted from McCaffery, Beebe et al. 1989): 

*The NRS pain scale indicates the intensity of current, best, and worst pain levels over the last 24 hours on a scale of 0 (no pain) to 10 (worst pain imaginable)*

<table>
<thead>
<tr>
<th>NRS PAIN SCALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
</tr>
</tbody>
</table>

**Reference:**

**History**
- Dicembre 2014 3 (I Ciclo)
- Gennaio 2015 5 (II Ciclo)
- Febbraio 2015 2 (III Ciclo)
- Marzo 2015 6 (IV Ciclo)
- Dicembre 2014 3 (I Ciclo)
- Gennaio 2015 6 (II Ciclo)
- Febbraio 2015 2 (III Ciclo)
- Marzo 2015 7 (IV Ciclo)
A.M. 75 Anni
Gleason 4+5
No Evidenza Malattia Viscerale
Terapia Antalgica ASA, Durogesic
Maggior Espressione del dolore al Femore
In terapia con 223Ra-Cl da Dicembre 2014 a Marzo 2015 (1 ciclo ogni 4 settimane circa)
**Table 1** Disease extent, measured metastatic sites and changes in mean SUVmax, PSA and ALP at 6 and 12 weeks after first administration of $^{223}$Ra

<table>
<thead>
<tr>
<th>Subject (disease extent)</th>
<th>Measured sites</th>
<th>Mean SUVmax (range)</th>
<th>Baseline PSA (ng/ml)</th>
<th>Baseline ALP (U/L)</th>
<th>6 weeks</th>
<th>12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (6-20 metastases)</td>
<td>C6, T6, L Sacrum, R Ilium, L femur</td>
<td>46.4 (33.1-75.3)</td>
<td>370</td>
<td>118</td>
<td>31.3</td>
<td>(26.5-40.5) [67.5%]</td>
</tr>
<tr>
<td>B (superscan)</td>
<td>C3, L1, L5, L femur, R tibia</td>
<td>15.0 (13.2-17.2)</td>
<td>508</td>
<td>761</td>
<td>16.0</td>
<td>(11.9-21.1) [106.7%]</td>
</tr>
<tr>
<td>C (6-20 metastases)</td>
<td>L1, L3, L5, sternum, R ischium</td>
<td>74.6 (54.7-98)</td>
<td>78</td>
<td>129</td>
<td>66.7</td>
<td>(51.3-76.7) [89.4%]</td>
</tr>
<tr>
<td>D (&gt;20 metastases)</td>
<td>Skull, L scapula, T11, L3, L Ilium</td>
<td>27.5 (20.3-35.4)</td>
<td>551</td>
<td>89</td>
<td>25.3</td>
<td>(20.6-29.5) [92%]</td>
</tr>
<tr>
<td>E (superscan)</td>
<td>Skull, T12, L3, R ilium, R femur</td>
<td>22.3 (11.4-28.6)</td>
<td>254</td>
<td>393</td>
<td>20.3</td>
<td>(11-25) [91%]</td>
</tr>
</tbody>
</table>
Monitoraggio del Trattamento con 223Radiocloruro nel Paziente mCRPC Sintomatico Stato Dell’Arte

- Diminuzione dolore:
  - presente, indicatore clinico affidabile

- PSA:
  - dubbia valenza

- ALP:
  - potenziale marker

- Scintigrafia Scheletrica:
  - necessaria attenta valutazione, a fine trattamento, salvo chiari segni di progressione.

Il trattamento va protratto fino all’insorgenza di eventuali gravi effetti collaterali o deterioramento clinico
- Prendere in considerazione tutti i segni e sintomi clinici disponibili
- Valutare il paziente nella sua globalità

- Ruolo dell’Imaging:
  - assenza di criteri standardizzati

- Se presente, indicatore clinico affidabile