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ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

Policlinico S. Orsola-Malpighi
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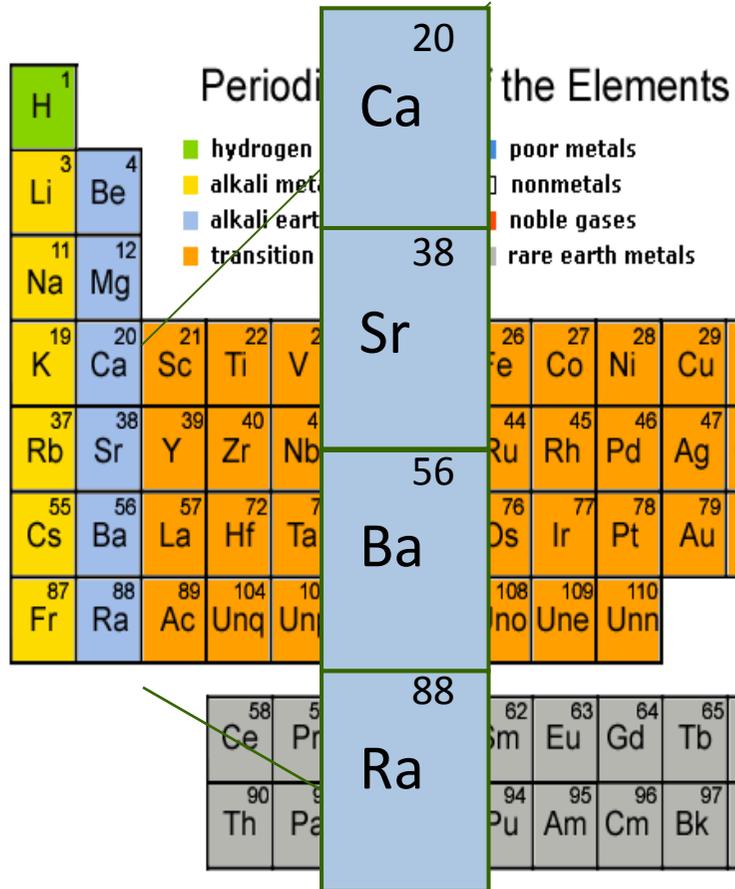


**TERAPIA CON RADIUM 223 NELLE METASTASI OSSEE DA CRPC:
ESPERIENZA PRELIMINARE MONOCENTRICA DEL POLICLINICO
S. ORSOLA MALPIGHI DI BOLOGNA**

**AIRO – Comunicazione orale
Rimini, 8 Novembre 2015**

Dott. Giuseppe Zanirato Rambaldi

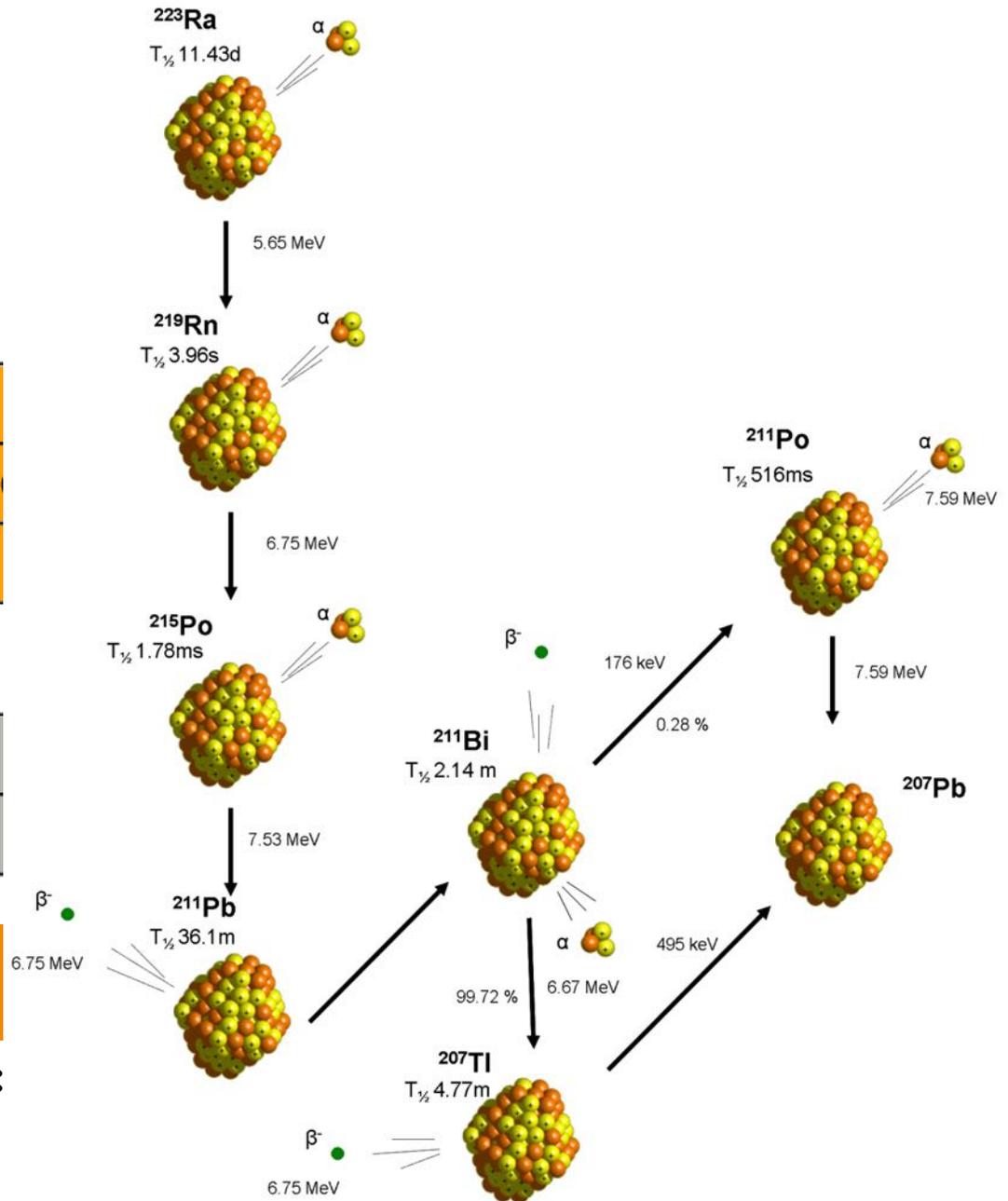
Radiation Oncology Center, Dept. of Experimental, Diagnostic and Specialty Medicine –
DIMES, University of Bologna, S.Orsola-Malpighi Hospital, Bologna, Italy



Caratteristiche ²²³Ra

Energia totale emessa all'equilibrio:

- 95.3% all'emissione di particelle α
- 3.6% a emissioni β^-
- 1.1% a raggi X e γ .



Captazione preferenziale nelle aree di neoformazione ossea

Spongiosa ossea normale



Zona osteoblastica



Il Radio-223 si accumula rapidamente e in modo selettivo nelle diverse aree di neoformazione ossea, nelle metastasi ed intorno ad esse, e di conseguenza agisce in modo molto localizzato e mirato

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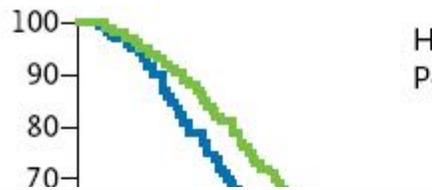
VOL. 369 NO. 3

Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer

C. Parker, S. Nilsson, D. Heinrich, S.I. Helle, J.M. O'Sullivan, S.D. Fosså, A. Chodacki, P. Wiechno, J. Logue, M. Seke, A. Widmark, D.C. Johannessen, P. Hoskin, D. Bottomley, N.D. James, A. Solberg, I. Syndikus, J. Kliment, S. Wedel, S. Boehmer, M. Dall'Oglio, L. Franzén, R. Coleman, N.J. Vogelzang, C.G. O'Bryan-Tear, K. Staudacher, J. Garcia-Vargas, M. Shan, Ø.S. Bruland, and O. Sartor, for the ALSYMPCA Investigators*

- Più del 90% dei pazienti con cancro della prostata castration-resistant (CRPC) hanno evidenza radiologica di metastasi ossee.
- Queste possono causare dolore, anche severo, e costituiscono una importante causa di morte, disabilità, riduzione della qualità della vita (QoL), fratture patologiche e aumento dei costi di trattamento in pazienti con CRPC.
- Nello studio ALSYMCA 3 l'utilizzo del Radium 223 di cloruro EV ha dimostrato di prolungare l'Overall Survival, il tempo per un evento scheletrico sintomatico e la QoL.

A Overall Survival



B Time to First Symptomatic Skeletal Event

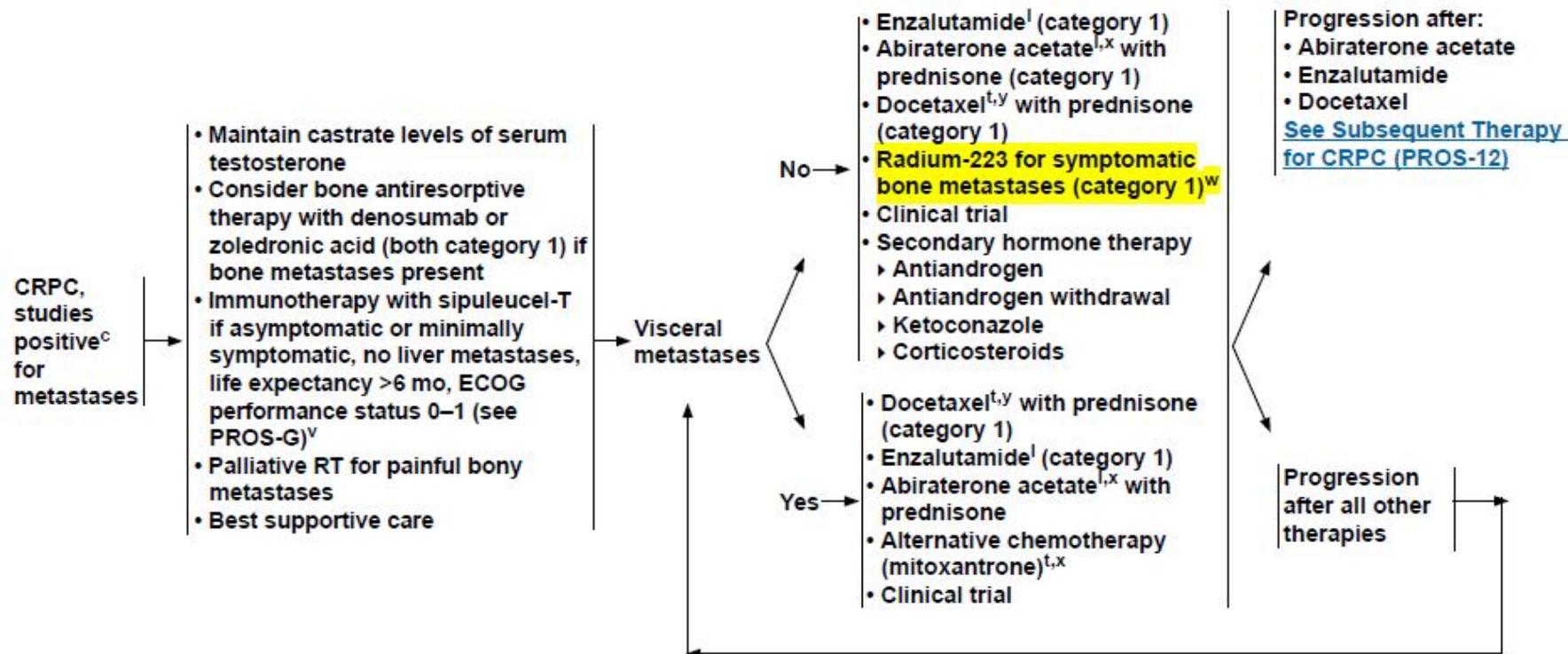


Subgroup	Radium-223 no. of patients	Placebo no. of patients	Radium-223 median overall survival (mo)	Placebo median overall survival (mo)	Hazard Ratio (95% CI)
All patients	614	307	14.9	11.3	0.70 (0.58-0.83)
Total ALP level at baseline					
<220 U/liter	348	169	17.0	15.8	0.82 (0.64-1.07)
≥220 U/liter	266	138	11.4	8.1	0.62 (0.49-0.79)
Current bisphosphonate use					
Yes	250	124	15.3	11.5	0.70 (0.52-0.93)
No	364	183	14.5	11.0	0.74 (0.59-0.92)
Previous docetaxel use					
Yes	352	174	14.4	11.3	0.71 (0.56-0.89)
No	262	133	16.1	11.5	0.74 (0.56-0.99)
Baseline ECOG performance-status score					
0 or 1	536	265	15.4	11.9	0.68 (0.56-0.82)
≥2	77	41	10.0	8.4	0.82 (0.50-1.35)
Extent of disease					
<6 metastases	100	38	27.0	NE	0.95 (0.46-1.95)
6-20 metastases	262	147	13.7	11.6	0.71 (0.54-0.92)
>20 metastases	195	91	12.5	9.1	0.64 (0.47-0.88)
Superscan	54	30	11.3	7.1	0.71 (0.40-1.27)
Opioid use					
Yes	345	168	13.9	10.4	0.68 (0.54-0.86)
No	269	139	16.4	12.8	0.70 (0.52-0.93)

Figure 2. Subgroup Analysis of Hazard Ratios for Death in the Two Study Groups.



ADVANCED DISEASE: FIRST-LINE SYSTEMIC THERAPY FOR CRPC



^cSee Principles of Imaging (PROS-B).

^lSee Principles of Androgen Deprivation Therapy (PROS-F).

^vSee Principles of Immunotherapy and Chemotherapy (PROS-G).

^wSipuleucel-T has not been studied in patients with visceral metastases.

^xRadium-223 is not approved for use in combination with docetaxel or any other chemotherapy. See Principles of Radiation Therapy (PROS-D, page 2 of 2).

^tFor patients who are not candidates for docetaxel-based regimens.

^yAlthough most patients without symptoms are not treated with chemotherapy, the survival benefit reported for docetaxel applies to those with or without symptoms. Docetaxel may be considered for patients with signs of rapid progression or visceral metastases despite lack of symptoms.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Policlinico S. Orsola Malpighi - Bologna



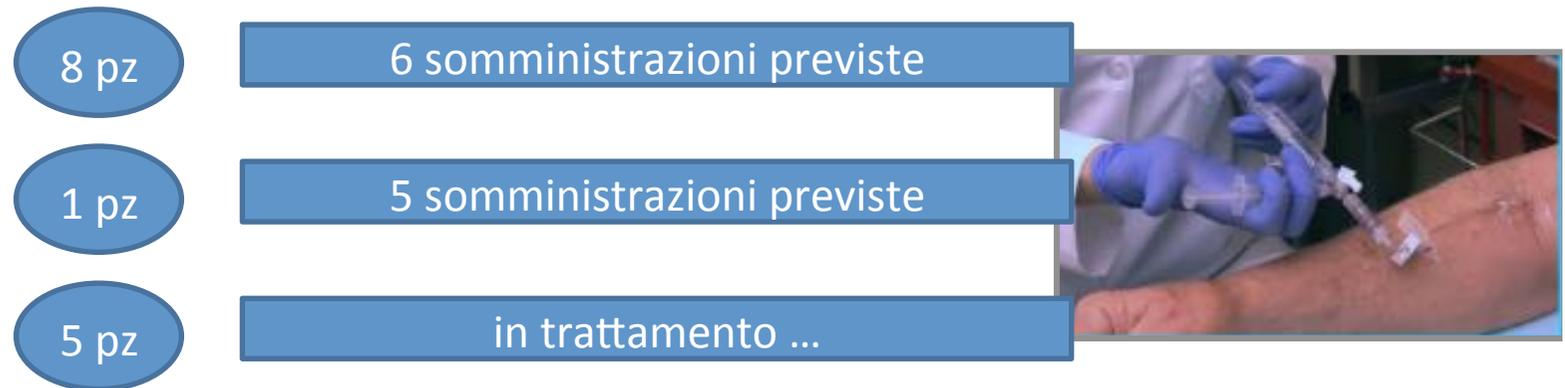
Da Novembre 2014 abbiamo iniziato il trattamento delle metastasi ossee sintomatiche da CRPC con Radium-223 dicloruro (50 kBq/kg, ogni 4 settimane, per 6 somministrazioni totali).

Prima e dopo ogni somministrazione sono stati registrati: i valori di PSA e fosfatasi alcalina (FA), la valutazione del dolore (NRS), performance status (ECOG scale), l'uso di terapie antalgiche e gli eventuali effetti avversi (CTCAE v. 4 classification).

È stato inoltre valutato l'imaging:
scintigrafia con Radio 223 dopo ogni somministrazione;
scintigrafia ossea total body prima e un mese dopo il trattamento;
PET colina prima e dopo tre mesi dal trattamento.



sono stati trattati 20 pazienti, per un totale di 70 somministrazioni.



Eventi scheletrici avversi: 1 frattura patologica di femore.

Eventi avversi minori: molti pazienti hanno mostrato tossicità di grado G1: anemia (15 pz), astenia (3 pz), diarrea (1 pz), nausea (1 pz), e “flare-phenomenon” (6 pz). Da notare che tutti i pazienti che hanno presentato anemia G1 la presentavano già in partenza.

Eventi avversi maggiori: 1 anemia G3, 2 severi sanguinamenti (rettoragia , epistassi) in assenza trombocitopenia.

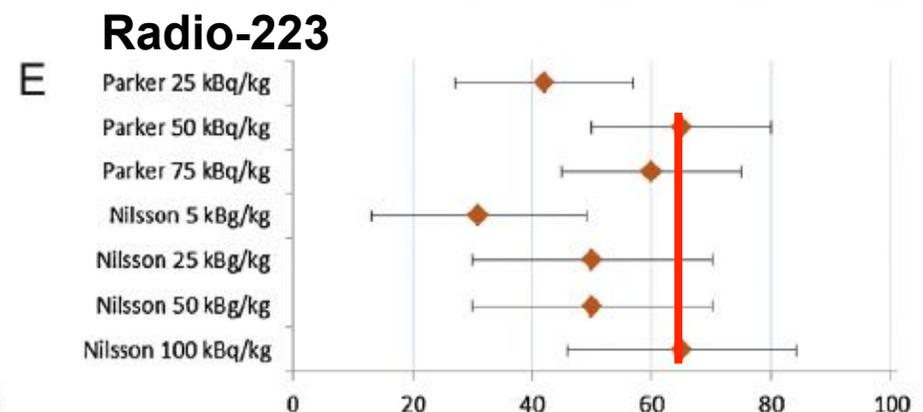
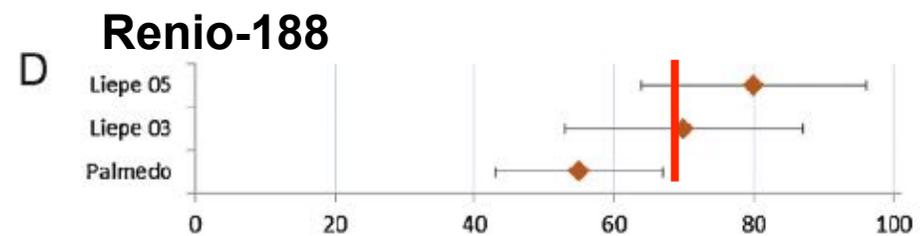
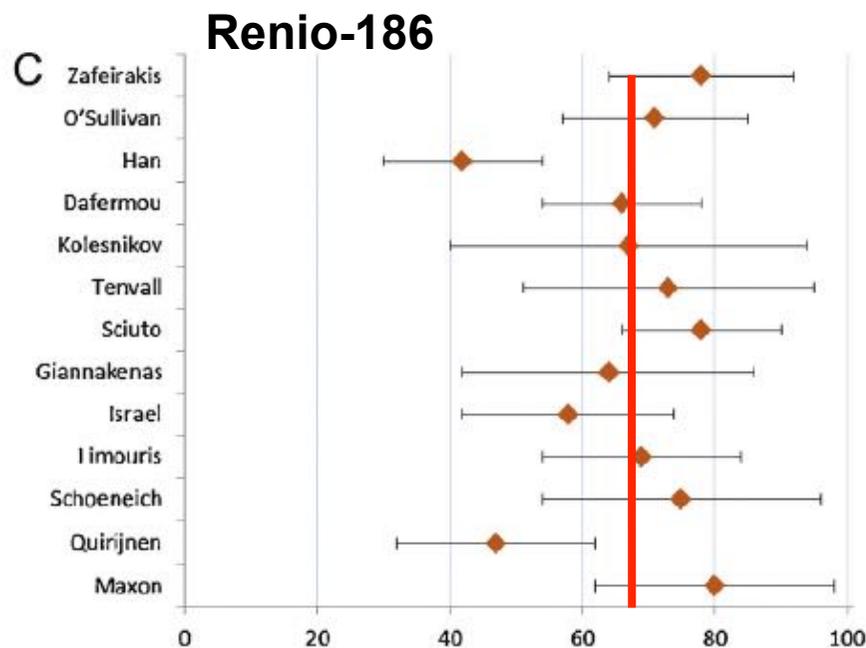
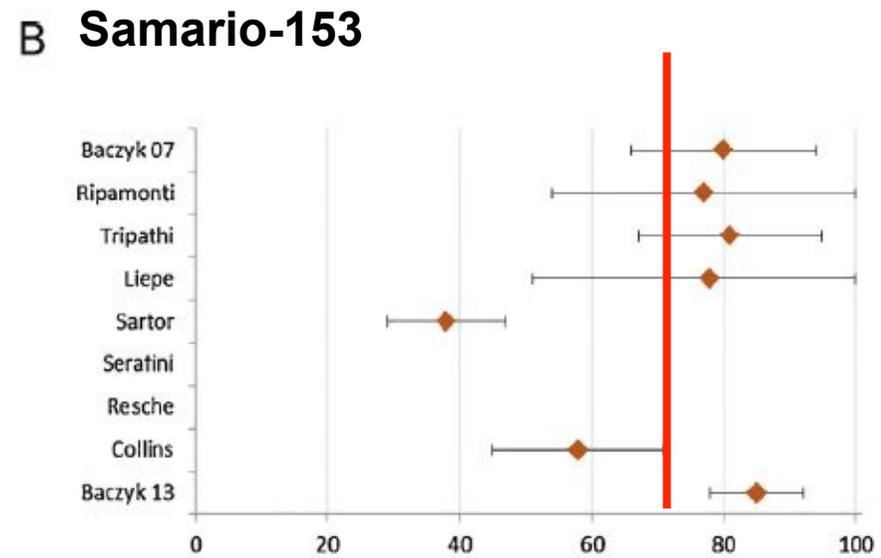
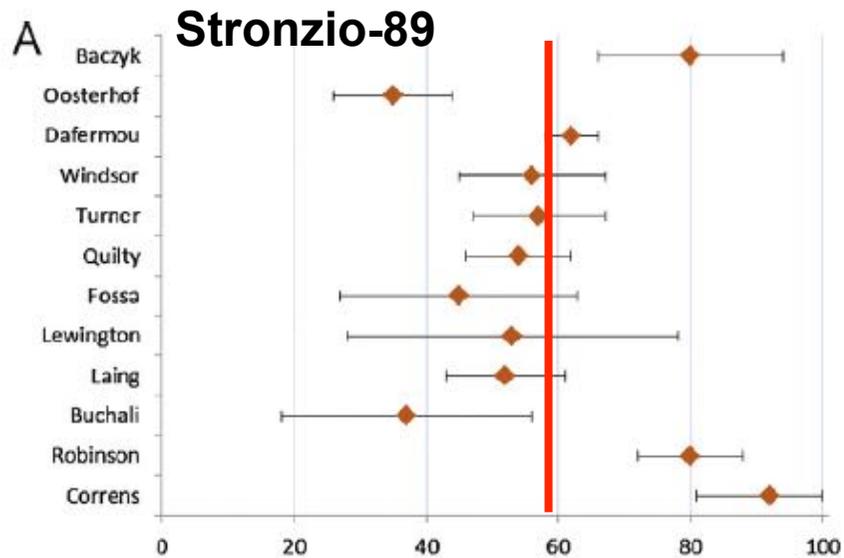
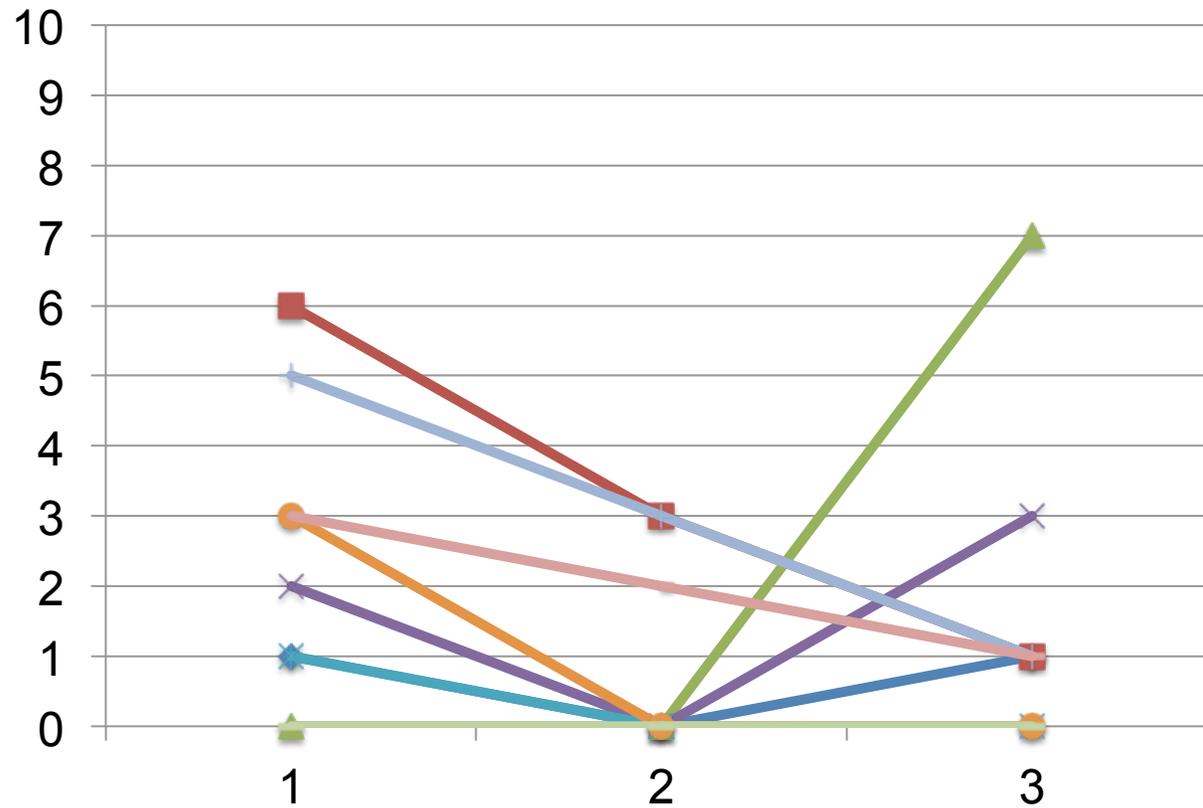


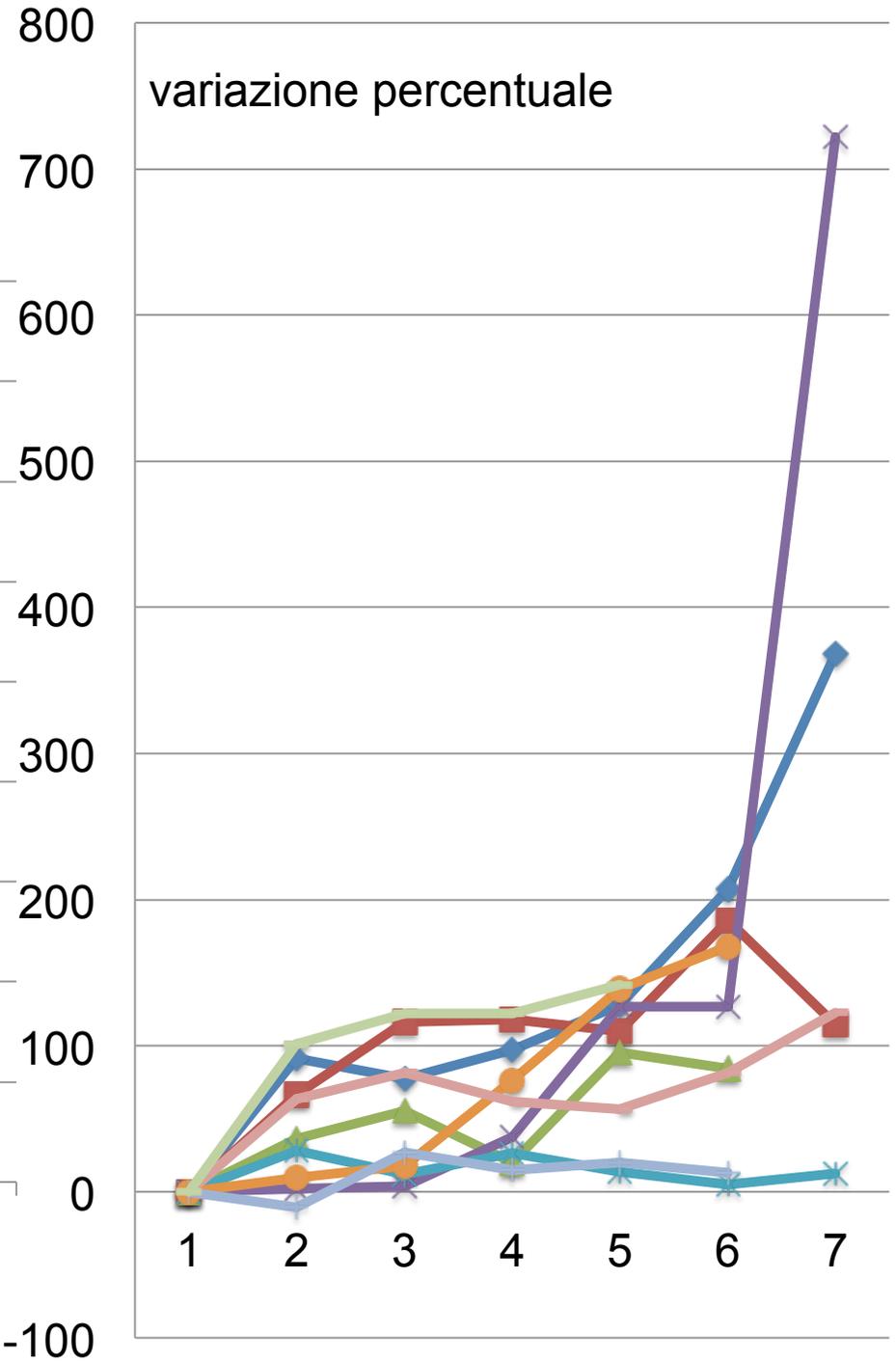
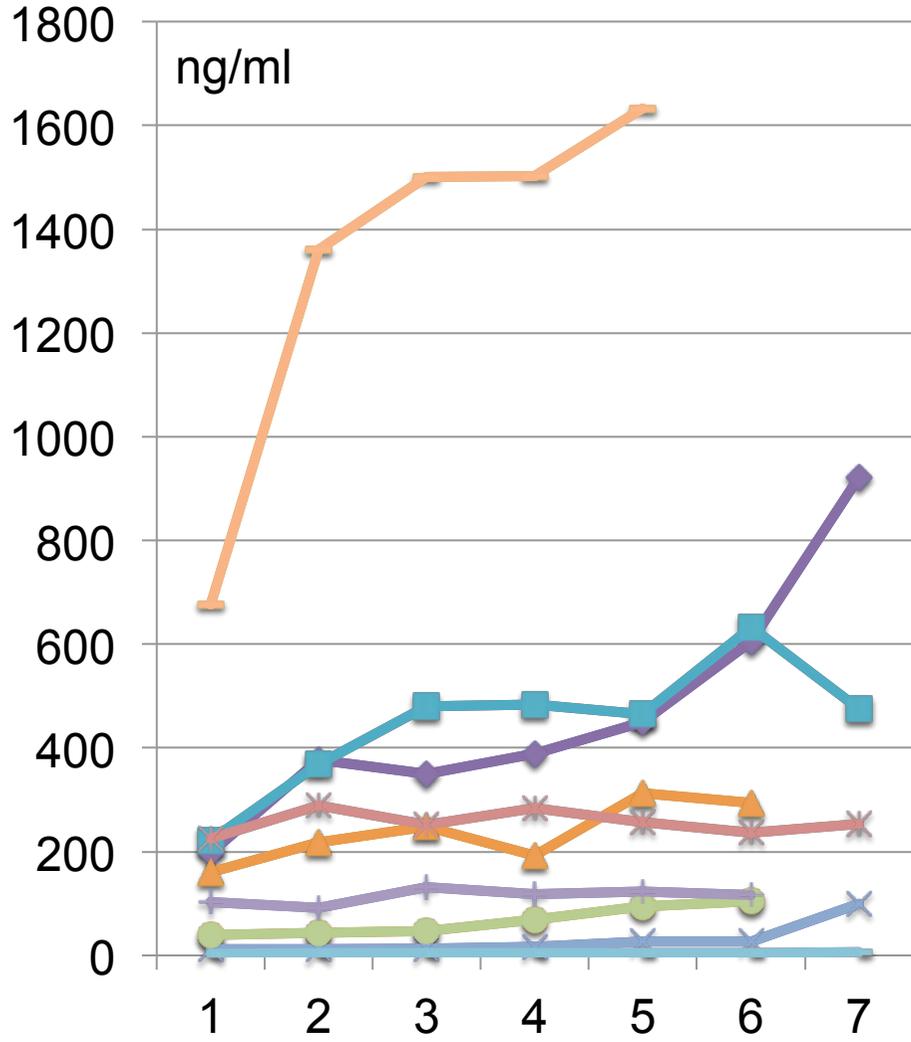
Fig. 3 – Efficacy results presented as percentage pain response with 95% confidence interval (intention-to-treat). (A) Strontium-89-chloride. (B) Samarium-153-EDTMP. (C) Rhenium-186-HEDP. (D) Rhenium-188-HEDP. (E) Radium-223-chloride.

NRS

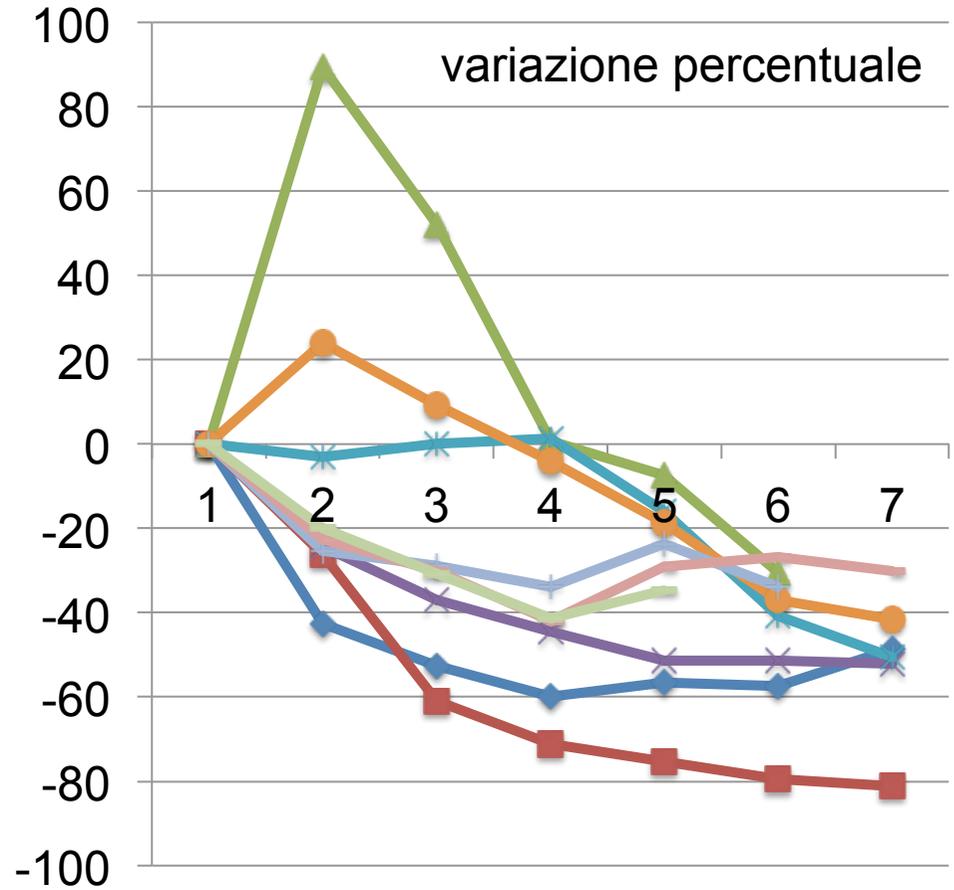
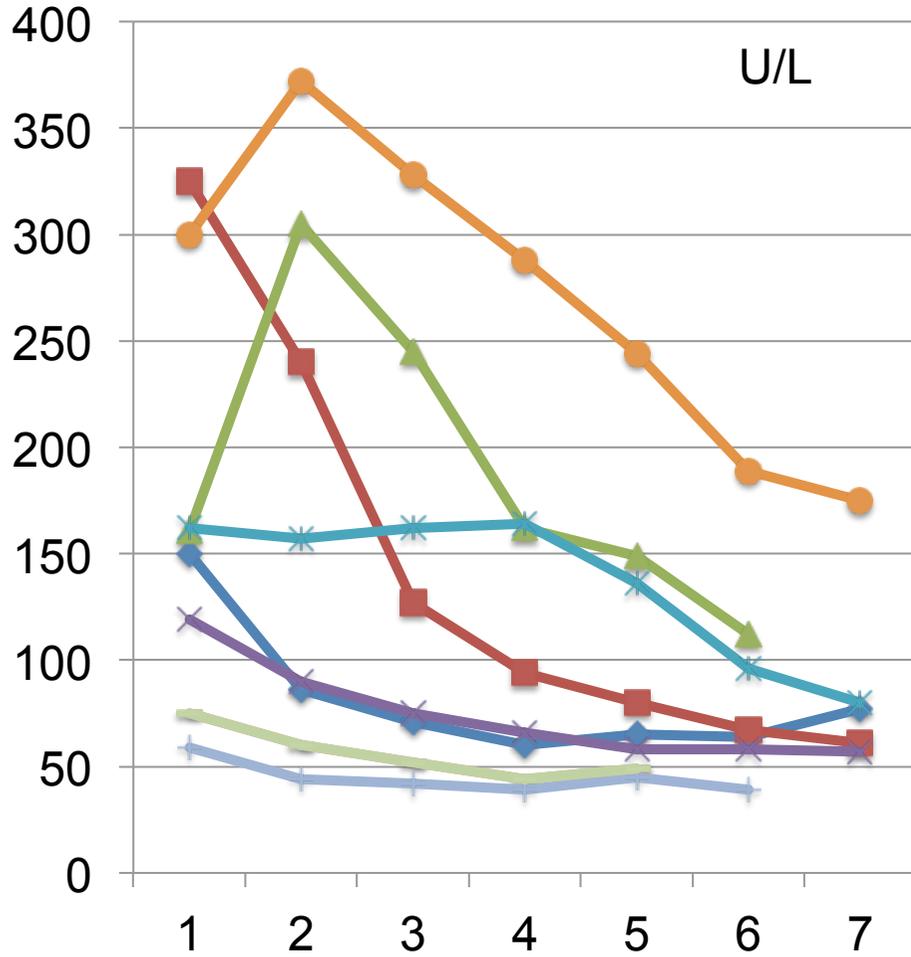


Si è assistito inoltre ad un miglioramento dell'**ECOG** score in tutti i pazienti, ed a una riduzione della assunzione di **terapie antalgiche**.

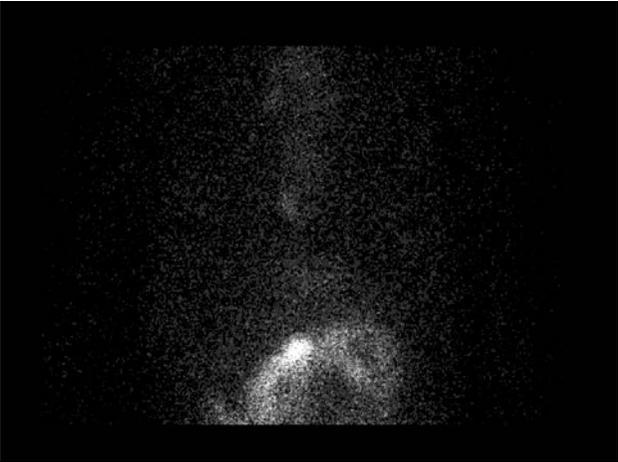
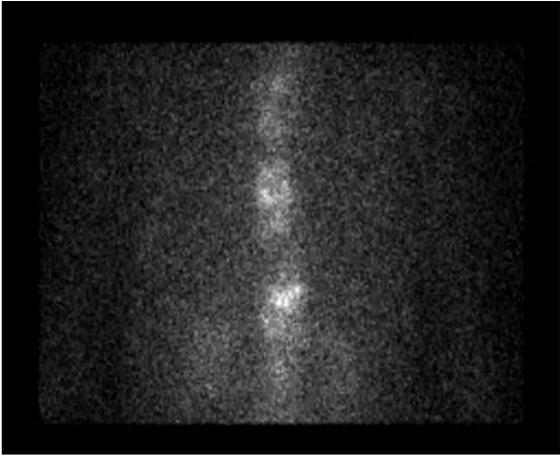
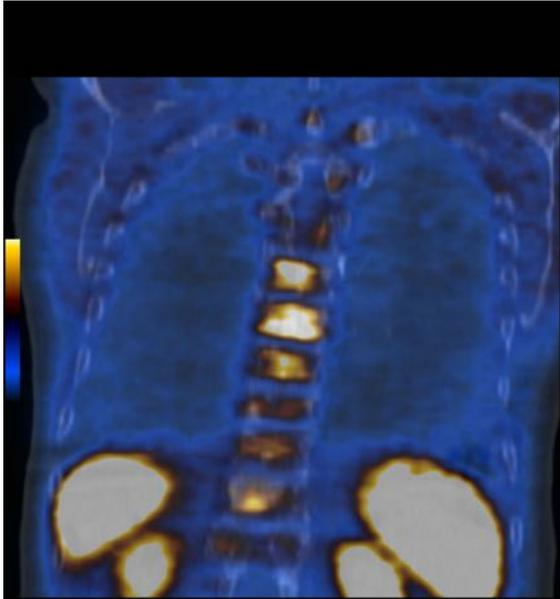
VARIAZIONE PSA



VARIAZIONE FA

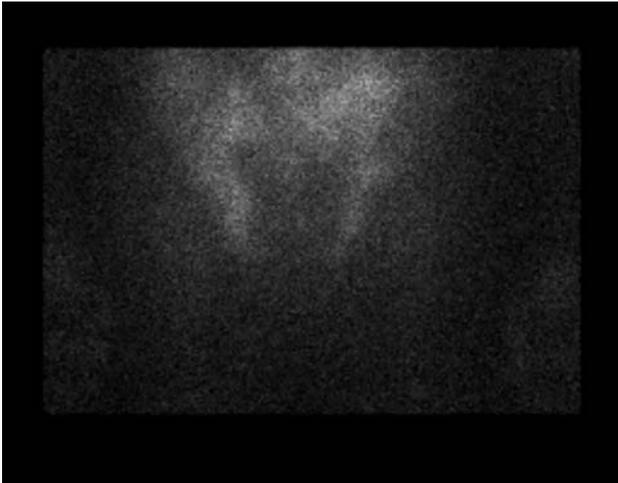
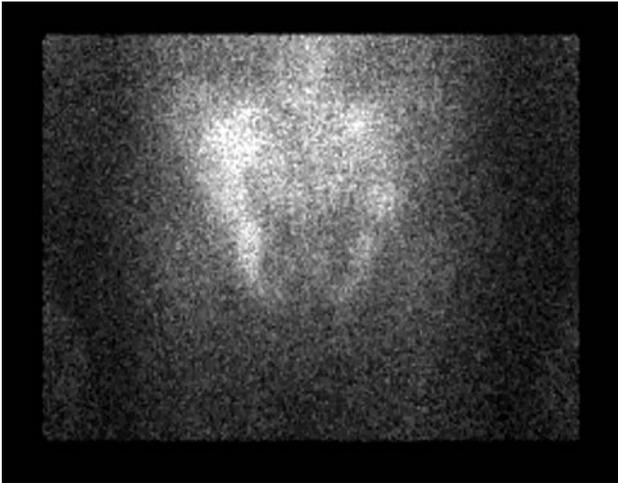
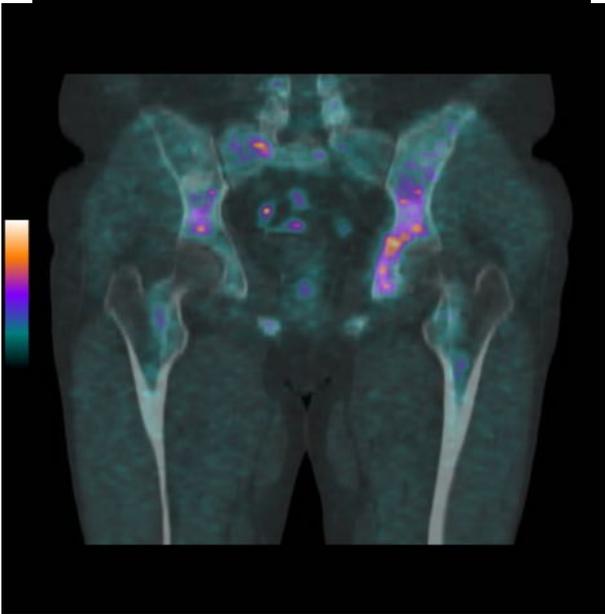


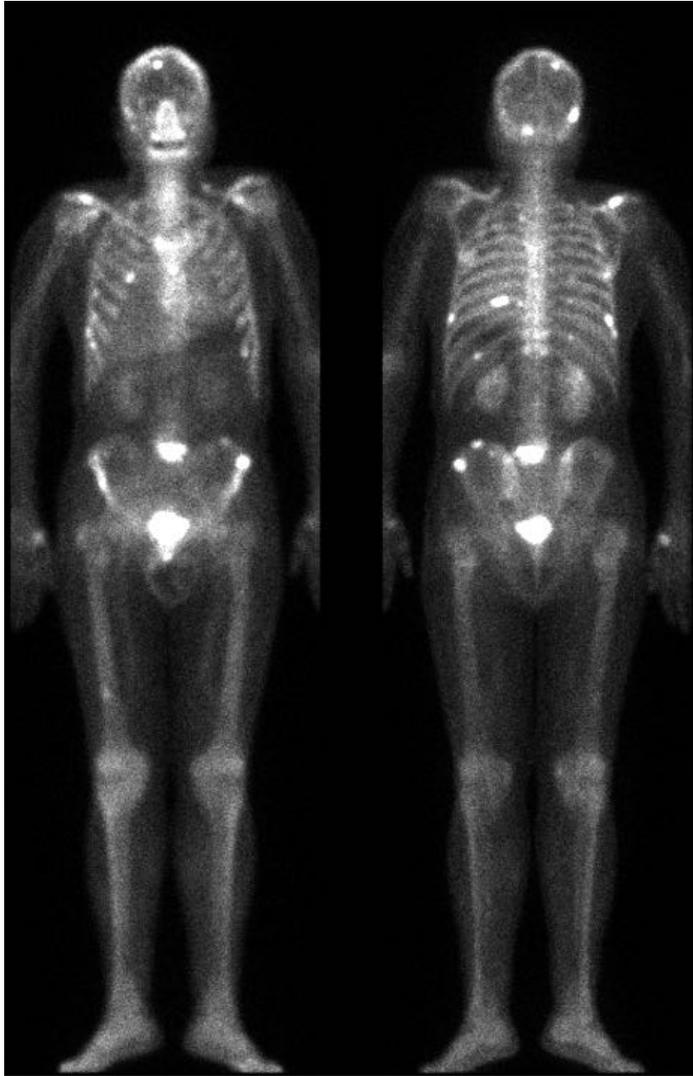
Scintigrafia con Radio 223 post trattamento



I somministrazione

VI somministrazione





Scinti Pre-terapia

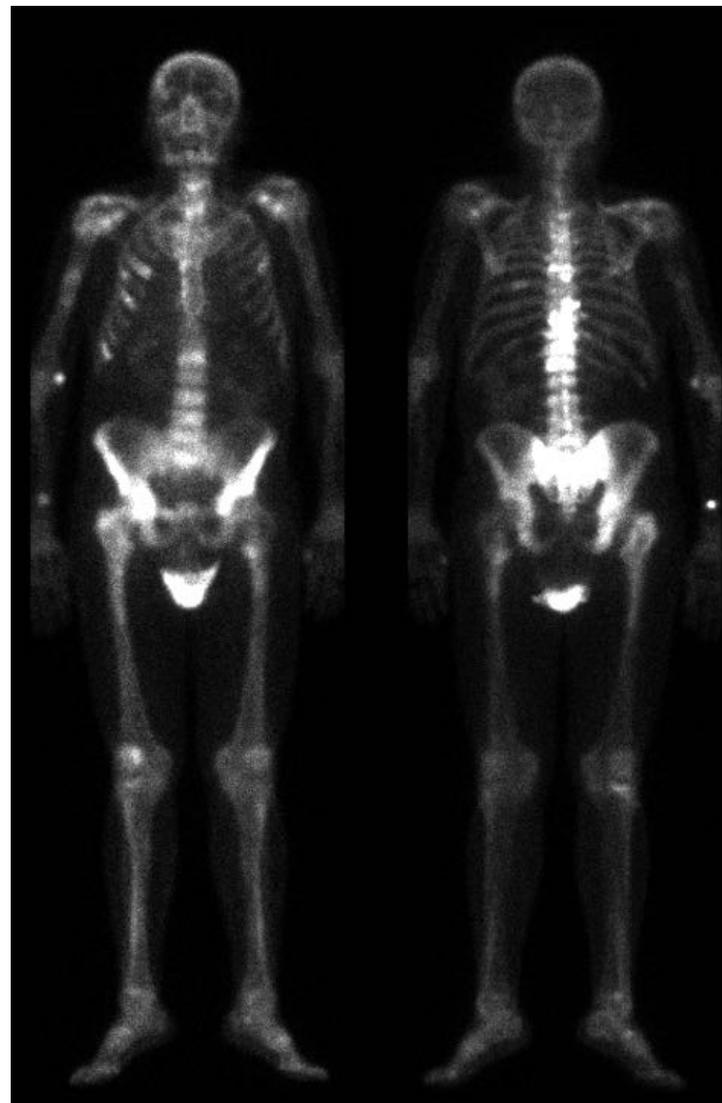


Scinti Post-Terapia

Caso di Buona
Risposta

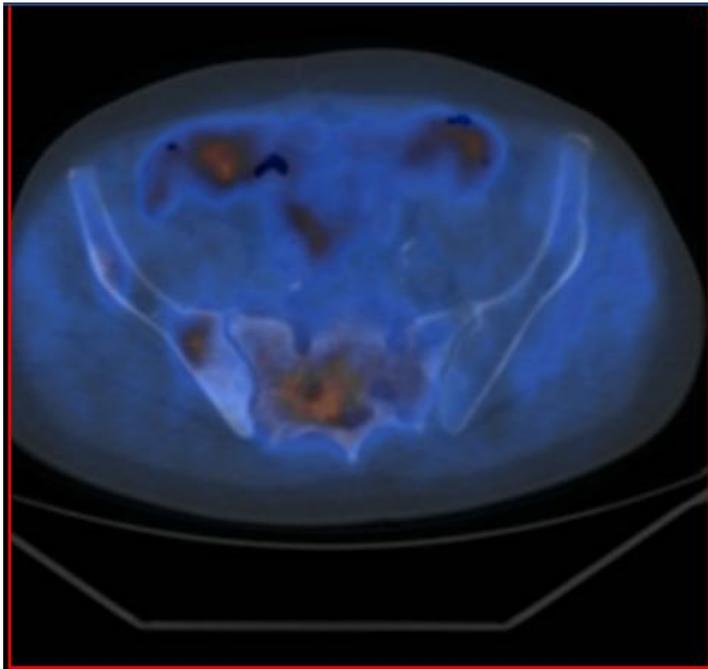


Scinti Pre-terapia

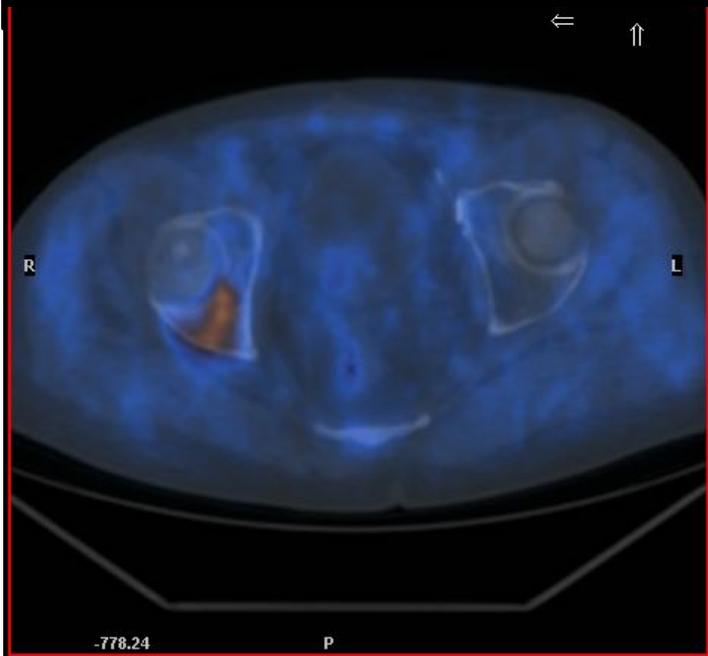


Scinti Post-Terapia

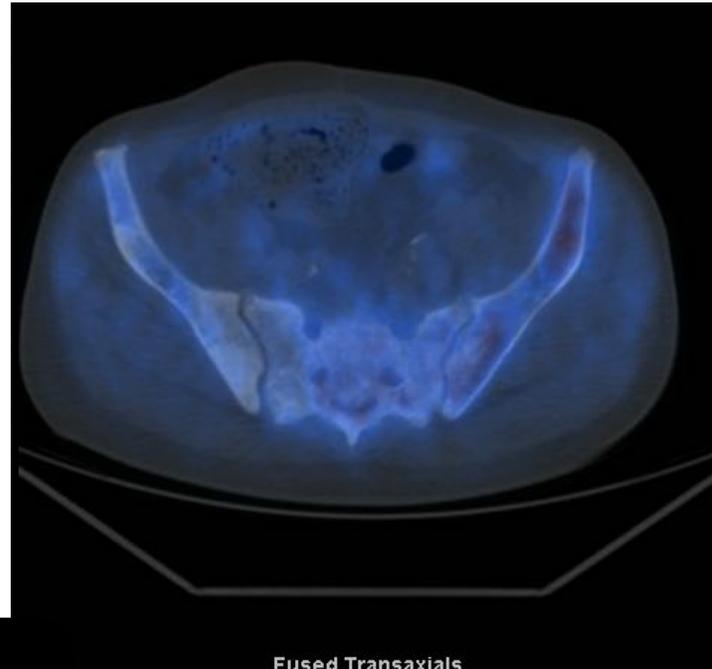
Caso di Risposta
Mista



PRE

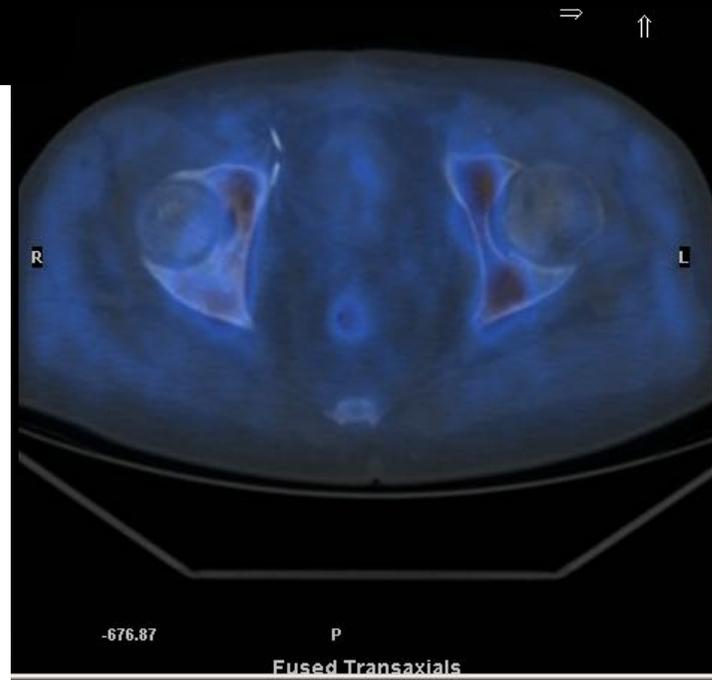


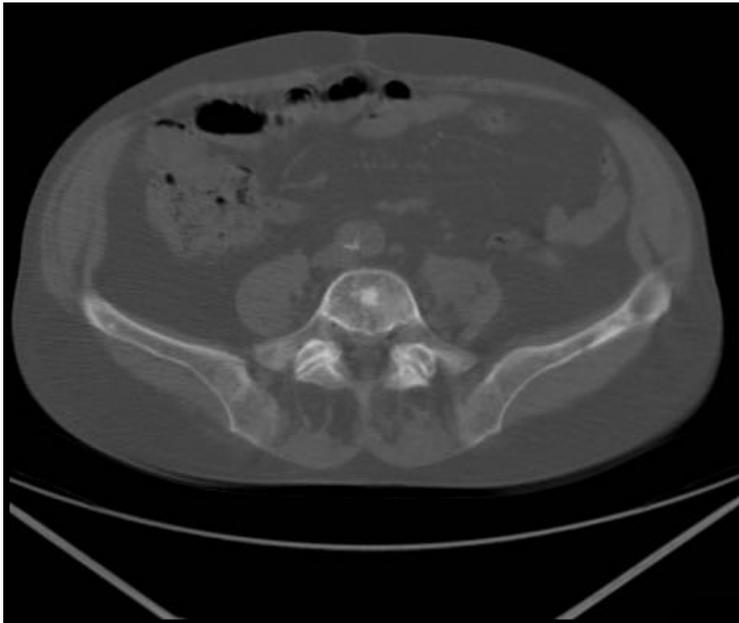
PET Colina



Fused Transaxials

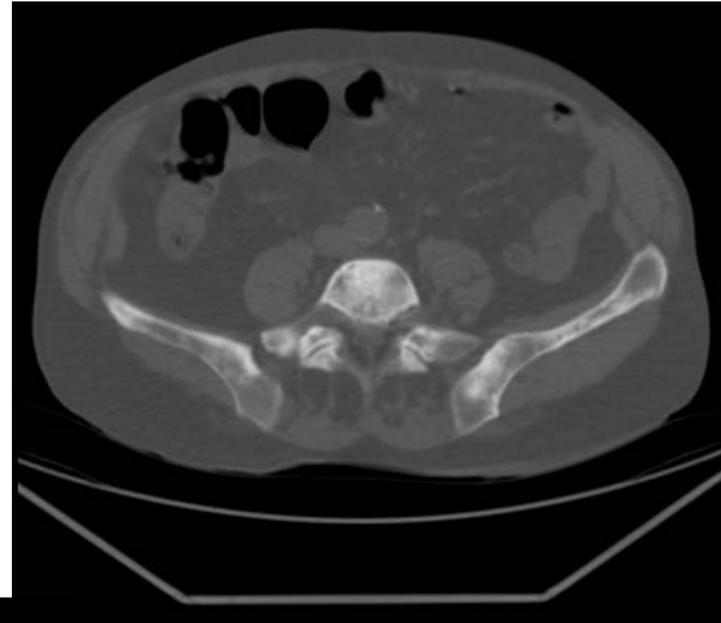
POST





CT Transaxials

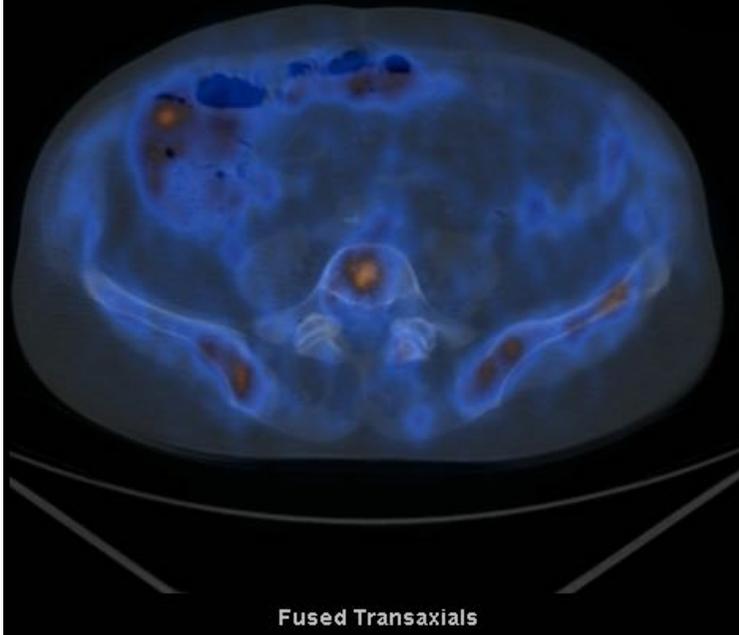
PRE



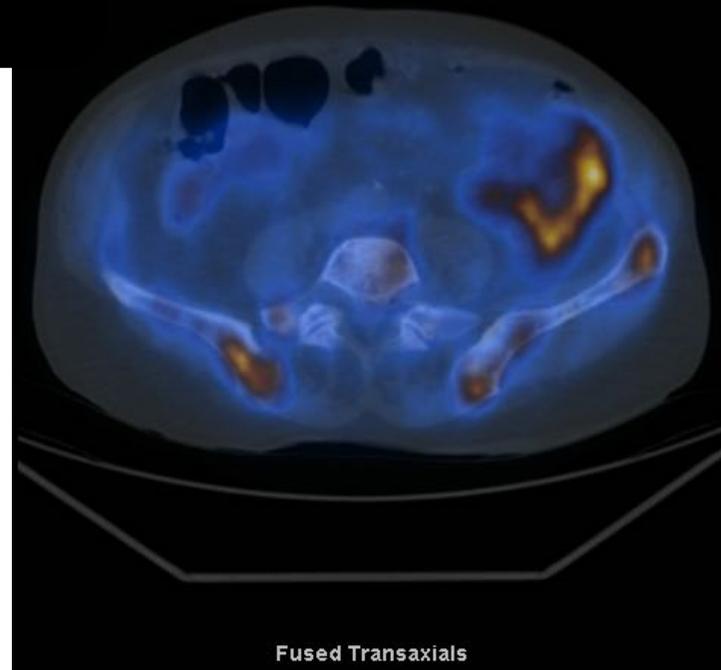
CT Transaxials

POST

PET Colina



Fused Transaxials



Fused Transaxials

Conclusioni di una esperienza preliminare

- **Ottimo controllo del dolore ; miglioramento QoL;**
- **Tossicità accettabile.**

- **PSA: pseudo-progressione biochimica**
- **FA : buon indicatore della risposta; predittore di sopravvivenza?**

- **Scintigrafia con Radio 223: tempo acquisizione lungo, imaging selettivo.**
- **Scintigrafia ossea : buon esame di controllo**
- **PET colina: da studiare..**