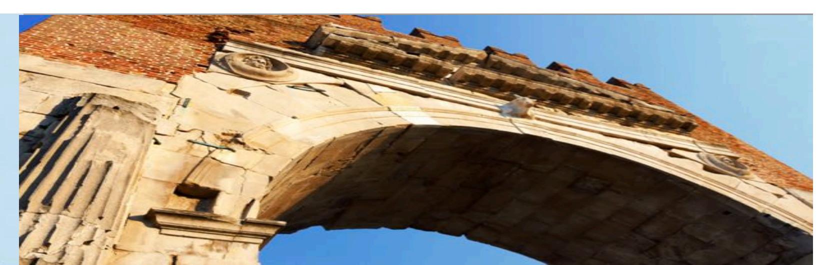
XXV CONGRESSO NAZIONALE
AIRO 2015
PALACONGRESSI - Rimini, 7-10 novembre



# DICHIARAZIONE

## Relatore: STEFANO PERGOLIZZI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta 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 **(NIENTE DA DICHIARARE)**
- Titolarietà 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)**
- Altro **(NIENTE DA DICHIARARE)**

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

# Scelta terapeutica multidisciplinare

Stefano Pergolizzi

Rimini, 7-10 Novembre 2015

## Scelta terapeutica multidisciplinare

# Perché è necessaria?

# Current PCa Treatment Paradigm Is Evolving

| M0 Local disease | M0 Untreated Rising PSA | M0 Treated Biochemical relapse Rising PSA | mCNPC Newly diagnosed metastases | mCRPC Asymptomatic disease (failed ADT) | mCRPC Symptomatic disease | mCRPC Post-docetaxel |
|---|---|---|---|---|---|---|
| | | | mCNPC Rapid progressors | Docetaxel | Docetaxel | Cabazitaxel |
| Surgery / EBRT (AS) | LHRH | LHRH | LHRH | Sipuleucel-T | Enzalutamide | Abiraterone |
| | | | Docetaxel + LHRH | Abiraterone | | Enzalutamide |
| | | | | Enzalutamide | Radium 223 | |
| | | | | + supportive care (eg, denosumab, bisphosphonates, or IVRP) | | |

Positive phase 3 data
Ongoing phase 3 study
Approved for use

# Practical aspects of metastatic castration-resistant prostate cancer management: patient case studies

Amit Bahl*, Joaquim Bellmunt† and Stéphane Oudard‡

***Incremento delle scelte terapeutiche***

**Selezione dei pazienti**

**Combinazione dei vari trattamenti**

**Sequenza delle terapie**

**Studi clinici**

***"…..a structured patient-focused multidisciplinary setting"***

## ADVANCED DISEASE: SUBSEQUENT SYSTEMIC THERAPY FOR CRPC

**No visceral metastases** →

**Prior therapy enzalutamide/abiraterone:**
- Docetaxel with prednisone (category 1)[t]
- Abiraterone acetate[l] or enzalutamide
- Radium-223 (category 1) if bone-predominant disease
- Sipuleucel-T if asymptomatic or minimally symptomatic, no liver metastases, life expectancy >6 mo, ECOG 0–1
- Clinical trial
- Other secondary hormone therapy
  - Antiandrogen
  - Antiandrogen withdrawal
  - Ketoconazole
  - Corticosteroids
  - DES or other estrogen
- Best supportive care

**Prior therapy docetaxel:**
- Enzalutamide (category 1)
- Abiraterone acetate[l] with prednisone (category 1)
- Radium-223 (category 1) if bone-predominant disease
- Cabazitaxel with prednisone (category 1)[t]
- Sipuleucel-T if asymptomatic or minimally symptomatic, no liver metastases, life expectancy >6 mo, ECOG 0–1
- Clinical trial
- Docetaxel rechallenge[t]
- Alternative chemotherapy (mitoxantrone)[t]
- Other secondary hormone therapy
  - Antiandrogen
  - Antiandrogen withdrawal
  - Ketoconazole
  - Corticosteroids
  - DES or other estrogen
- Best supportive care

**Visceral metastases** →

**Prior therapy enzalutamide/abiraterone:**
- Docetaxel with prednisone (category 1)[t]
- Clinical trial
- Abiraterone acetate[l] or enzalutamide
- Other secondary hormone therapy
  - Antiandrogen
  - Antiandrogen withdrawal
  - Ketoconazole
  - Corticosteroids
  - DES or other estrogen
- Best supportive care

**Prior therapy docetaxel:**
- Enzalutamide (category 1)
- Abiraterone acetate[l] with prednisone (category 1)
- Cabazitaxel with prednisone (category 1)[t]
- Clinical trial
- Docetaxel rechallenge[t]
- Alternative chemotherapy (mitoxantrone)[t]
- Other secondary hormone therapy
  - Antiandrogen
  - Antiandrogen withdrawal
  - Ketoconazole
  - Corticosteroids
  - DES or other estrogen
- Best supportive care

Linee guida

CARCINOMA DELLA PROSTATA

American Urological Association (AUA) Guideline

**CASTRATION-RESISTANT PROSTATE CANCER: AUA GUIDELINE**

**Michael S. Cookson, Bruce J. Roth, Philipp Dahm, Christine Engstrom, Stephen J. Freedland, Maha Hussain, Daniel W. Lin, William T. Lowrance, Mohammad Hassan Murad, William K. Oh, David F. Penson and Adam S. Kibel**

VOLUME 32 · NUMBER 30 · OCTOBER 20 2014

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Systemic Therapy in Men With Metastatic Castration-Resistant Prostate Cancer: American Society of Clinical Oncology and Cancer Care Ontario Clinical Practice Guideline

*Ethan Basch, D. Andrew Loblaw, Thomas K. Oliver, Michael Carducci, Ronald C. Chen, James N. Frame, Kristina Garrels, Sebastien Hotte, Michael W. Kattan, Derek Raghavan, Fred Saad, Mary-Ellen Taplin, Cindy Walker-Dilks, James Williams, Eric Winquist, Charles L. Bennett, Ted Wootton, R. Bryan Rumble, Stacie B. Dusetzina, and Katherine S. Virgo*

Guidelines on

**Prostate Cancer**

N. Mottet (Chair), J. Bellmunt, E. Briers (Patient Representative), R.C.N. van den Bergh (Guidelines Associate), M. Bolla, N.J. van Casteren (Guidelines Associate), P. Cornford, S. Culine, S. Joniau, T. Lam, M.D. Mason, V. Matveev, H. van der Poel, T.H. van der Kwast, O. Rouvière, T. Wiegel

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eau European Association of Urology

GRUPPO di STUDIO AIRO PROSTATA

Coordinatore: Riccardo Santoni

EUROPEAN UROLOGY 65 (2014) 467–479

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

Guidelines

**EAU Guidelines on Prostate Cancer. Part II: Treatment of Advanced, Relapsing, and Castration-Resistant Prostate Cancer**

*Axel Heidenreich [a,*,†], Patrick J. Bastian [b], Joaquim Bellmunt [c], Michel Bolla [d], Steven Joniau [e], Theodor van der Kwast [f], Malcolm Mason [g], Vsevolod Matveev [h], Thomas Wiegel [i], Filiberto Zattoni [j], Nicolas Mottet [k,‡]*

# Il carcinoma della prostata resistente alla castrazione, metastatico, è (generalmente) inguaribile

Rimini, 7-10 Novembre 2015

**Le terapie disponibili sono destinate alla**

**palliazione e/o prolungare la sopravvivenza.**

EUROPEAN UROLOGY 65 (2014) 467–479

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

Guidelines

**EAU Guidelines on Prostate Cancer. Part II: Treatment of Advanced, Relapsing, and Castration-Resistant Prostate Cancer**

*Axel Heidenreich[a,*,†], Patrick J. Bastian[b], Joaquim Bellmunt[c], Michel Bolla[d], Steven Joniau[e], Theodor van der Kwast[f], Malcolm Mason[g], Vsevolod Matveev[h], Thomas Wiegel[i], Filiberto Zattoni[j], Nicolas Mottet[k,‡]*

Ad oggi, **non esiste una evidenza sulla migliore sequenza dei trattamenti**.

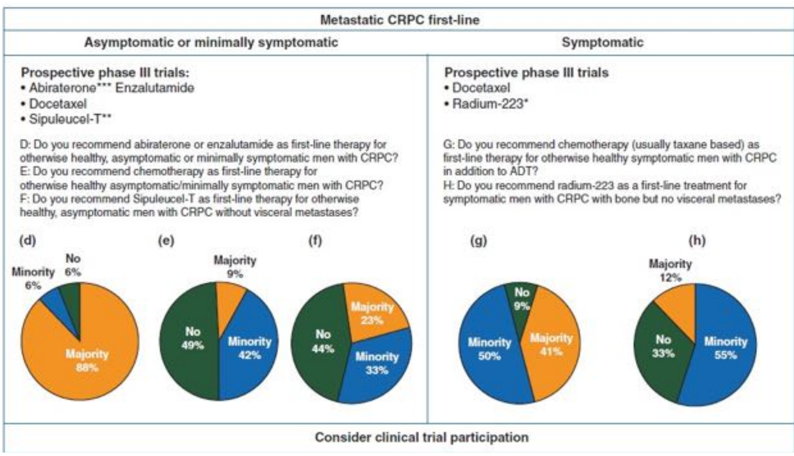
…..i clinici dovrebbero **aderire ai criteri di inclusione dei vari trials quando trattano pazienti CRPC nella pratica clinica quotidiana**

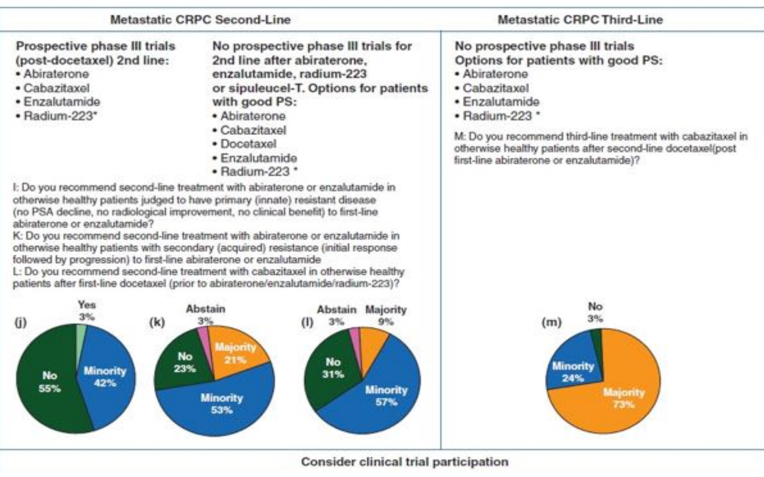
Le linee guida **suggeriscono di includere i pazienti con CRPC in studi clinici**

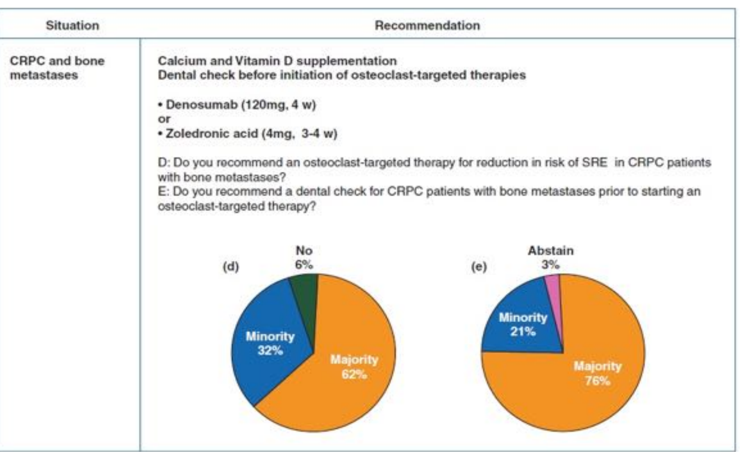
*Annals of Oncology* 26: 1589–1604, 2015
doi:10.1093/annonc/mdv257
Published online 3 June 2015

## Management of patients with advanced prostate cancer: recommendations of the St Gallen Advanced Prostate Cancer Consensus Conference (APCCC) 2015

S. Gillessen[1,†,*], A. Omlin[1,†], G. Attard[2], J. S. de Bono[2], E. Efstathiou[3,4,5], K. Fizazi[6], S. Halabi[7], P. S. Nelson[8], O. Sartor[9], M. R. Smith[10], H. R. Soule[11], H. Akaza[12], T. M. Beer[13], H. Beltran[14], A. M. Chinnaiyan[15,16,17], G. Daugaard[18], I. D. Davis[19], M. De Santis[20,21], C. G. Drake[22], R. A. Eeles[23], S. Fanti[24], M. E. Gleave[25], A. Heidenreich[26], M. Hussain[27], N. D. James[20,28], F. E. Lecouvet[29], C. J. Logothetis[3,4], K. Mastris[30], S. Nilsson[31], W. K. Oh[32], D. Olmos[33,34,35], A. R. Padhani[36], C. Parker[37], M. A. Rubin[38], J. A. Schalken[39], H. I. Scher[14,40], A. Sella[41], N. D. Shore[42], E. J. Small[43], C. N. Sternberg[44], H. Suzuki[45], C. J. Sweeney[46], I. F. Tannock[47,‡] & B. Tombal[48,‡]



Rimini, 7-10 Novembre 2015

# Oligometastasi ossee

1. **Lesione ossea oligometastatica non complicata asintomatica**
2. **Lesione ossea oligometastatica non complicata sintomatica**
3. **Lesione ossea oligometastatica complicata**

# Metastasi ossee

1. Lesioni ossee multiple asintomatiche
2. Lesioni ossee multiple non complicate sintomatiche
3. Lesioni ossee multiple sintomatiche
4. Lesioni ossee e viscerali
5. ………………………………

Nella malattia prostatica in progressione ossea

la radioterapia ha ruolo in **TUTTI** i quadri clinici

## ADVANCED DISEASE: FIRST-LINE SYSTEMIC THERAPY FOR CRPC

**CRPC, studies positive[c] for metastases** →

- Maintain castrate levels of serum testosterone
- Consider bone antiresorptive therapy with denosumab or zoledronic acid (both category 1) if bone metastases present
- Immunotherapy with sipuleucel-T if asymptomatic or minimally symptomatic, no liver metastases, life expectancy >6 mo, ECOG performance status 0–1 (category 1) (see PROS-G)[v]
- Palliative RT for painful bony metastases
- Best supportive care

→ **Visceral metastases**

**No** →

- Enzalutamide[l] (category 1)
- Abiraterone acetate[l,x] with prednisone (category 1)
- Docetaxel[t,y] with prednisone (category 1)
- Radium-223 for symptomatic bone metastases (category 1)[w]
- Clinical trial
- Secondary hormone therapy
  - Antiandrogen
  - Antiandrogen withdrawal
  - Ketoconazole
  - Corticosteroids

**Yes** →

- Docetaxel[t,y] with prednisone (category 1)
- Enzalutamide[l] (category 1)
- Abiraterone acetate[l,x] with prednisone
- Alternative chemotherapy (mitoxantrone)[t,x]
- Clinical trial

Progression after:
- Abiraterone acetate
- Enzalutamide
- Docetaxel

See Subsequent Therapy for CRPC (PROS-12)

Progression after all other therapies → (return to Visceral metastases)

Radiotherapy and Oncology 112 (2014) 125–127

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Bone metastases

# Overall response rates to radiation therapy for patients with painful uncomplicated bone metastases undergoing initial treatment and retreatment

**Revisione sistematica di 25 studi randomizzati 8Gy vs altro e di uno studio randomizzato (*Lancet Oncology 2014*) 8Gy vs 20Gy come retreatment**

Radiotherapy and Oncology 112 (2014) 125–127

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Bone metastases

Overall response rates to radiation therapy for patients with painful uncomplicated bone metastases undergoing initial treatment and retreatment

## CONCLUSION:

**……..It is therefore recommended that patients with uncomplicated painful bone metastases be treated with a single 8 Gy fraction of radiation at both the initial treatment and retreatment.**

## Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial

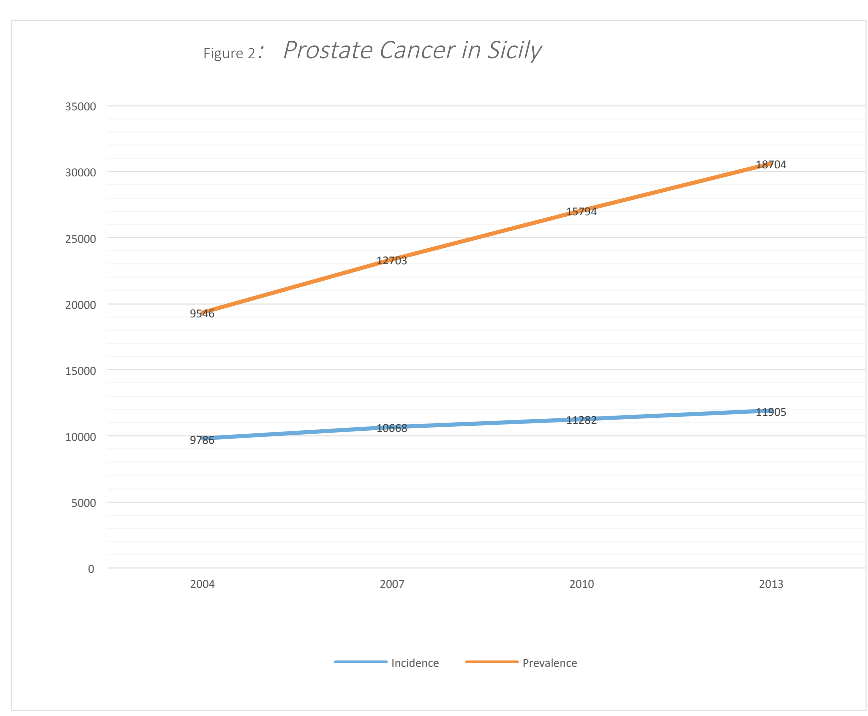
Edward Chow, Yvette M van der Linden, Daniel Roos, William F Hartsell, Peter Hoskin, Jackson S Y Wu, Michael D Brundage, Abdenour Nabid, Caroline J A Tissing-Tan, Bing Oei, Scott Babington, William F Demas, Carolyn F Wilson, Ralph M Meyer, Bingshu E Chen, Rebecca K S Wong

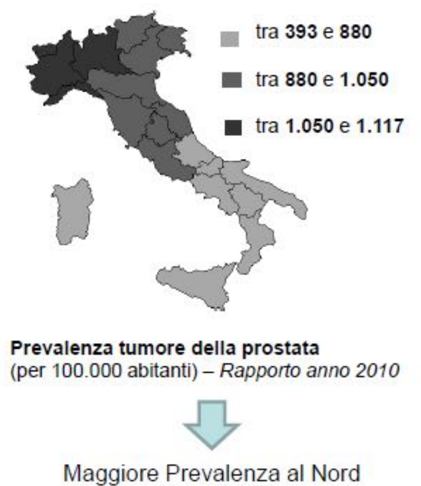
Lancet Oncol 2014; 15: 164–71

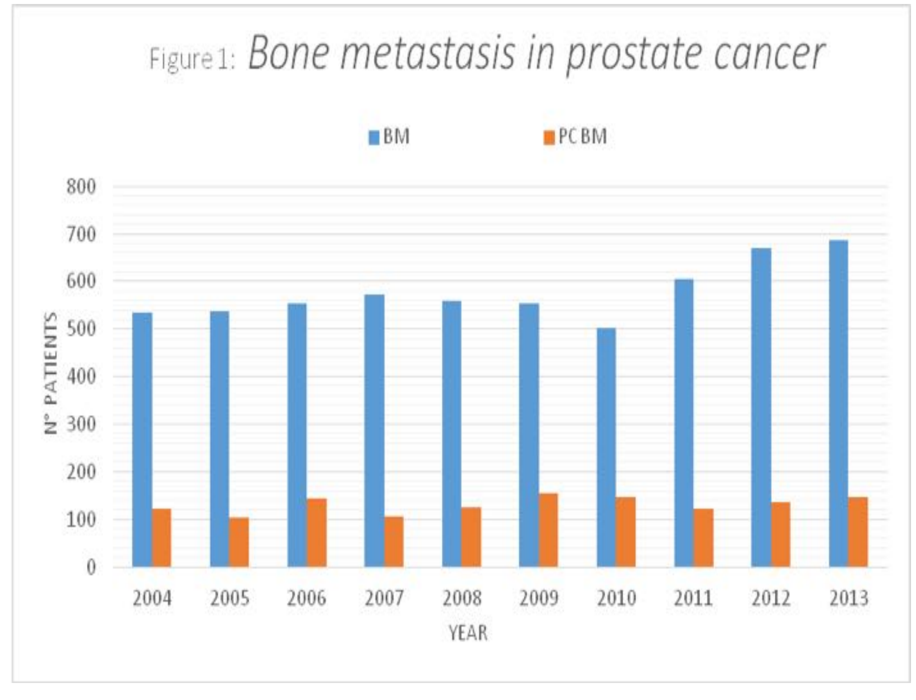
Summary
Background Although repeat radiation treatment has been shown to palliate pain in patients with bone metastases

### 425 pz -> Già RT -> Necessità Retreatment su sede già irradiata

| | 8Gy | vs | 20Gy |
|---|---|---|---|
| Risposta dolore | 45% | p=0.17 | 51% |
| Comparsa fratture | 7% | p=0.03 | 5% |
| CME | 2% | p=0.094 | <1% |
| Diarrea | 23% | p=0.018 | 31% |
| Inappetenza | 56% | p=0.011 | 66% |



Rimini, 7-10 Novembre 2015

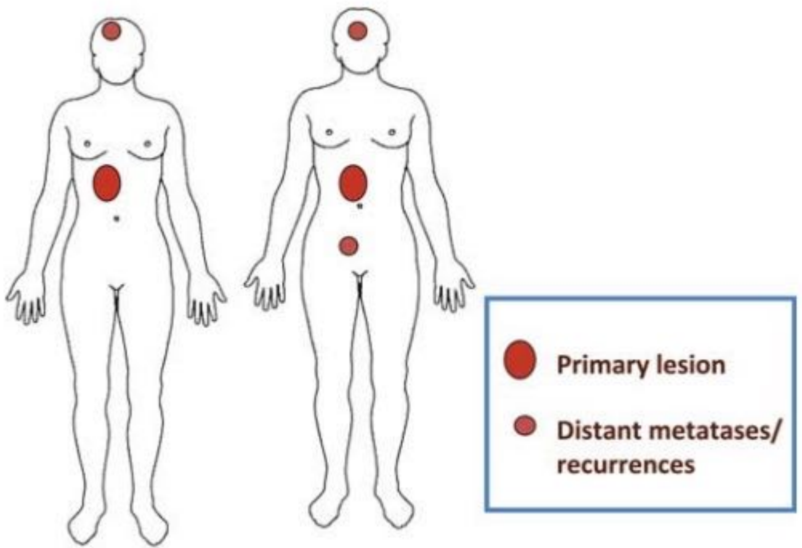
**Table 1.** Baseline Characteristics of the Patients.*

| Characteristic | Radium-223 (N=614) | Placebo (N=307) |
|---|---|---|
| <6 sedi* | 100 (16) | 38 (12) |
| 6-20 | 262 (43) | 147 (48) |
| >20^ | 192 (32) | 91 (30) |
| Superscan^ | 54 (9) | 30 (10) |

* Anche pazienti oligometastatici

Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer

^Pazienti eleggibili per half-body irradiation



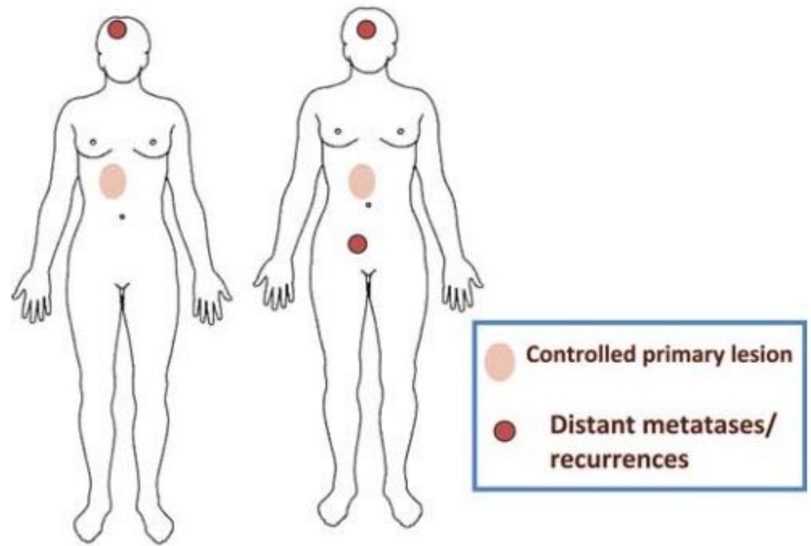




**Table 1.** Oligometastases and oligo-recurrence

| | Oligometastases | Oligo-recurrence |
|---|---|---|
| Reference | Hellman and Weichselbaum (1) | Niibe et al. (2,3,4) |
| Primary lesion | Uncontrolled/controlled | Controlled |
| No. of distant/metastases/ recurrences | One to several | One to several (one is better) |

Yuzuru Niibe* and Kazushige Hayakawa

Jpn J Clin Oncol 2010;40:107– 1110

## Comments

**Targeted local therapy in oligometastatic prostate cancer: a promising potential opportunity after failed primary treatment**

Fairleigh Reeves*, Declan Murphy*†‡, Christopher Evans§, Patrick Bowden† and Anthony Costello*†

*Department of Urology and Surgery, The Royal Melbourne Hospital, University of Melbourne, Melbourne, Australia, ‡Peter MacCallum Cancer Centre, Melbourne, Australia, †Australian Prostate Cancer Research Centre, Epworth Healthcare, Richmond, Vic., Australia, and §Department of Urologic Surgical Oncology, University of California Davis School of Medicine, Sacramento, CA, USA

**ClinicalTrials.gov identifier**

**Current ongoing trials for prostate cancer oligometastases (www.clinicaltrials.gov)**

NCT01859221

NCT02206334

NCT01558427

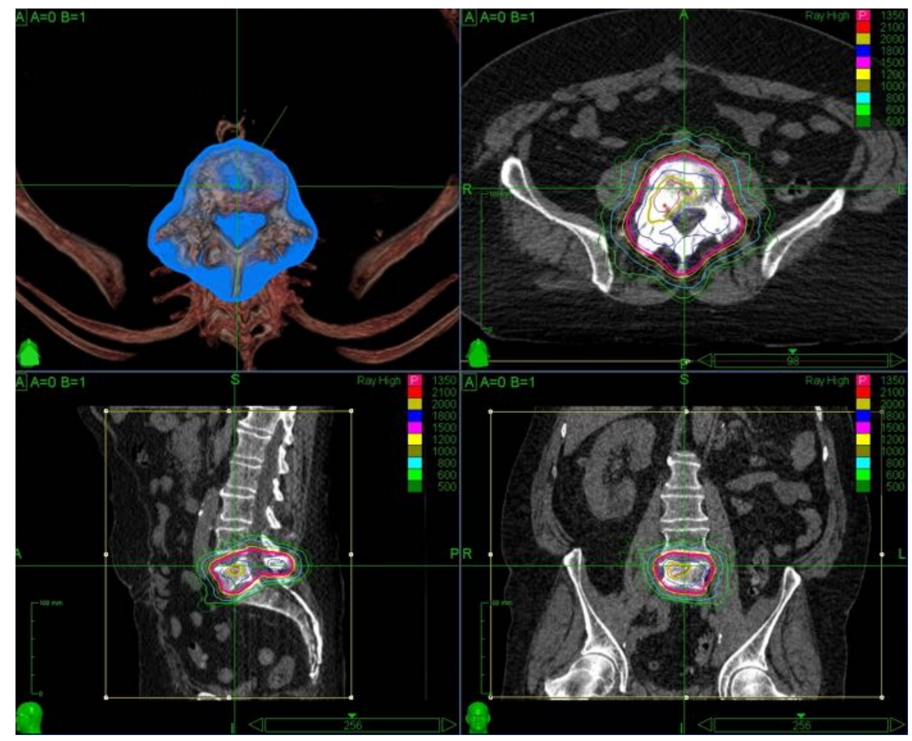
NCT02192788

Moreno *et al. Radiation Oncology* 2014, **9**:258
http://www.ro-journal.com/content/9/1/258

**REVIEW** Open Access

Oligometastases in prostate cancer: restaging stage IV cancers and new radiotherapy options

Antonio José Conde Moreno*, Carlos Ferrer Albiach, Rodrigo Muelas Soria, Verónica González Vidal, Raquel García Gómez and María Albert Antequera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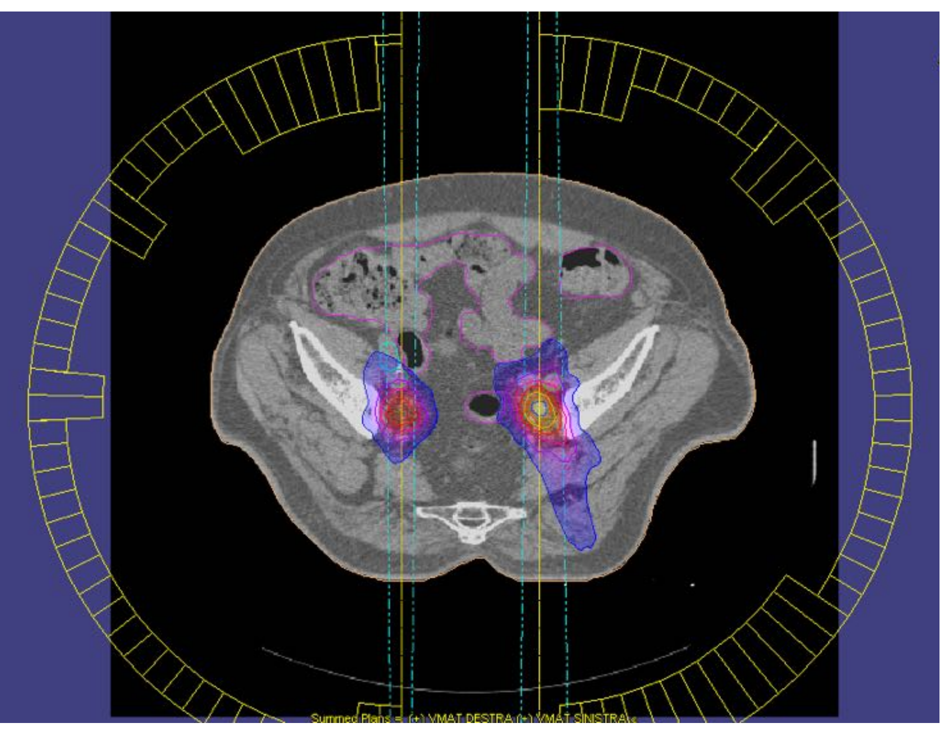
Summed Plans = (+) VMAT DESTRA (+) VMAT SINISTRA

XXV CONGRESSO NAZIONALE
AIRO2015

THE CUTTING EDGE OF RADIOTHERAPEUTICS Original Article

## Hemi body irradiation: An economical way of palliation of pain in bone metastasis in advanced cancer

Santanu Pal, Samrat Dutta[1], Shyam Sundar Adhikary, Biswamit Bhattacharya, Balaram Ghosh[2], Niladri B. Patra

International Journal of Radiation Oncology biology • physics

Official Journal of the American Society for Radiation Oncology ASTRO

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< Previous Article July 1, 2001 Volume 50, Issue 3, Pages 765–775 Next Article >

To read this article in full, please review your options for gaining access at the bottom of the page.

Fractionated half–body irradiation (HBI) for the rapid palliation of widespread, symptomatic, metastatic bone disease: a randomized Phase III trial of the International Atomic Energy Agency (IAEA)☆

*Acta Oncologica*, 2009; 48: 556–561

ORIGINAL ARTICLE

### Half body irradiation of patients with multiple bone metastases: A phase II trial

RANDI S. BERG[1], METTE K. YILMAZ[1], MORTEN HØYER[2], NINA KELDSEN[3], OLE S. NIELSEN[2] & MARIANNE EWERTZ[4]

[1]*Department of Oncology, Aalborg Hospital, Aarhus University, Aalborg, Denmark,* [2]*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark,* [3]*Department of Oncology, Herning Hospital, Herning, Denmark and* [4]*Department of Oncology, Odense University Hospital, Odense, Denmark*

**Remissione del dolore 91% (45 RC 46 RP)**

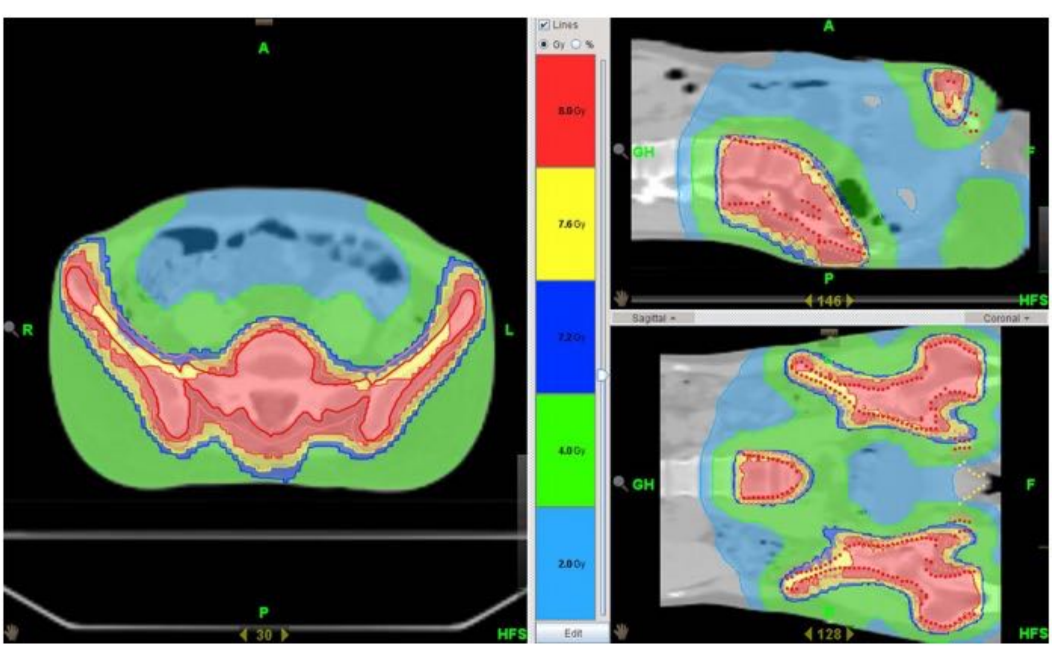
**Sopravvivenza mediana 150gg**

174 Journal of Pain and Symptom Management Vol. 47 No. 1 January 2014

*Brief Report*

# Half-Body Irradiation With Tomotherapy for Pain Palliation in Metastatic Breast Cancer

Carlo Furlan, MD, Marco Trovo, MD, Annalisa Drigo, ScD, MPh,
Elvira Capra, ScD, MPh, and Mauro Gaetano Trovo, MD
*Department of Radiation Oncology (C.F., M.T., M.G.T.) and Department of Medical Physics (A.D., E.C.), Centro di Riferimento Oncologico (CRO), National Cancer Institute, Aviano, Italy*



Rimini, 7-10 Novembre 2015

Acido Zoledronico e Denosumab sono utilizzati per ridurre il rischio di “skeletal-related events” (SREs) Resultati da studi di fase III in CRPC metastatici.

L’utilizzo ottimale di queste terapie “osteoclast-targeted” Sequenza, Inizio, Frequenza e Durata del trattamento ad oggi non è standardizzato.

Il loro ruolo e la loro efficacia nell’era delle nuove opzioni terapeutiche (molte delle quali riducono il rischio di SREs) non è stato valutato

Gillessen S Ann Oncol 2015

# Effect of radium-223 dichloride on symptomatic skeletal events in patients with castration-resistant prostate cancer and bone metastases: results from a phase 3, double-blind, randomised trial

Oliver Sartor, Robert Coleman, Sten Nilsson, Daniel Heinrich, Svein I Helle, Joe M O'Sullivan, Sophie D Fosså, Aleš Chodacki, Paweł Wiechno, John Logue, Anders Widmark, Dag Clement Johannessen, Peter Hoskin, Nicholas D James, Arne Solberg, Isabel Syndikus, Nicholas J Vogelzang, C Gillies O'Bryan-Tear, Minghua Shan, Øyvind S Bruland, Christopher Parker

Lancet Oncol 2014; 15: 738–46

**Summary**

**Background** Bone metastases frequently cause skeletal events in patients with metastatic castration-resistant prostate

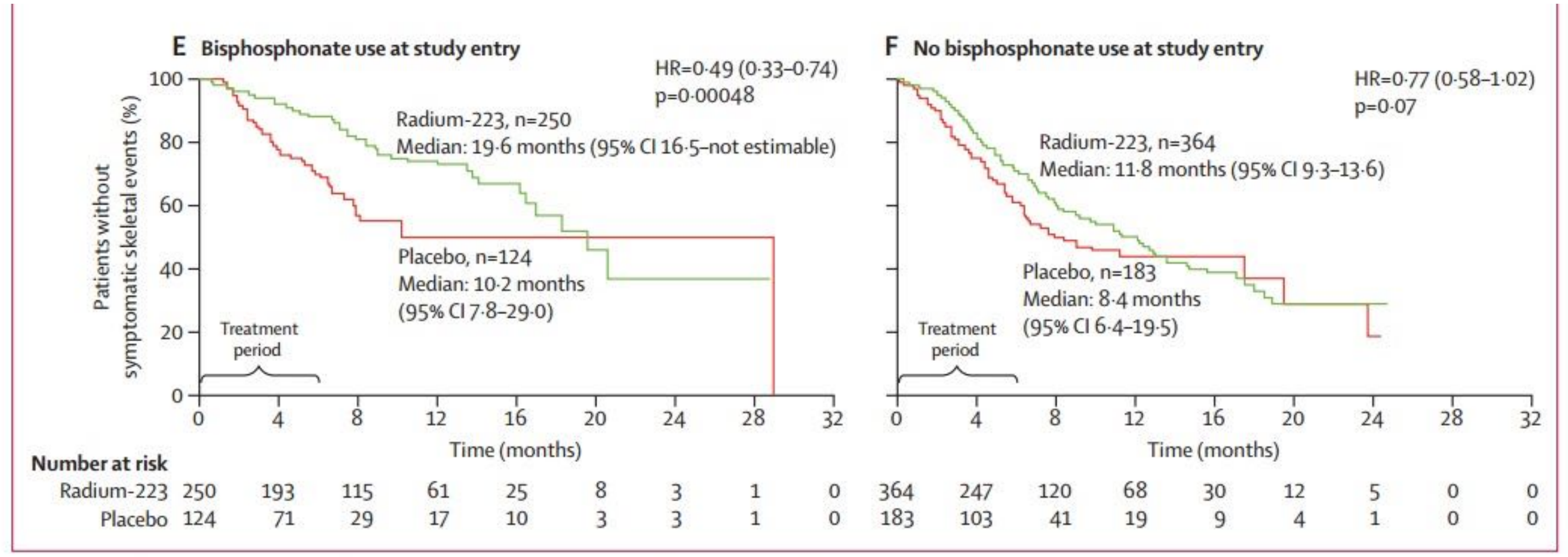



*Figure 2*: **Kaplan–Meier estimates of time to first symptomatic skeletal event, by baseline stratification factors**
ALP=total alkaline phosphatase. HR=hazard ratio. SSE=symptomatic skeletal event. p values are for descriptive purpose only and not adjusted for multiplicity.

Radium-223 in an international early access program (EAP): Effects of concomitant medication on overall survival in metastatic castration-resistant prostate cancer (mCRCP) patients.

Fred Saad MD

| Characteristic | Pts, n | Median OS, mos (95% CI) | Log-rank p-value |
|---|---|---|---|
| Concomitant denosumab | | | |
| Yes | 138 | NA (15–NE) | 0.00940 |
| No | 558 | 13 (12–NE) | |
| Concomitant abiraterone | | | |
| Yes | 156 | NA (16–NE) | < 0.0001 |
| No | 540 | 14 (12–16) | |

Annals of Oncology

special articles

*Annals of Oncology* 26: 1589–1604, 2015
doi:10.1093/annonc/mdv257
Published online 3 June 2015

## Management of patients with advanced prostate cancer: recommendations of the St Gallen Advanced Prostate Cancer Consensus Conference (APCCC) 2015

S. Gillessen[1,†*], A. Omlin[1,†], G. Attard[2], J. S. de Bono[2], E. Efstathiou[3,4,5], K. Fizazi[6], S. Halabi[7], P. S. Nelson[8], O. Sartor[9], M. R. Smith[10], H. R. Soule[11], H. Akaza[12], T. M. Beer[13], H. Beltran[14], A. M. Chinnaiyan[15,16,17], G. Daugaard[18], I. D. Davis[19], M. De Santis[20,21], C. G. Drake[22], R. A. Eeles[23], S. Fanti[24], M. E. Gleave[25], A. Heidenreich[26], M. Hussain[27], N. D. James[20,28], F. E. Lecouvet[29], C. J. Logothetis[3,4], K. Mastris[30], S. Nilsson[31], W. K. Oh[32], D. Olmos[33,34,35], A. R. Padhani[36], C. Parker[37], M. A. Rubin[38], J. A. Schalken[39], H. I. Scher[14,40], A. Sella[41], N. D. Shore[42], E. J. Small[43], C. N. Sternberg[44], H. Suzuki[45], C. J. Sweeney[46], I. F. Tannock[47,‡] & B. Tombal[48,‡]

**In the absence of level one evidence or in areas where there are conflicting data or conflicting interpretation of existing data,**

***weighted expert recommendations are helpful for making treatment decisions in daily clinical practice***

Rimini, 7-10 Novembre 2015

## Il Team multi-disciplinare (TMD)

*Gruppo coordinato di tutte le professioni mediche e sanitarie che si occupano di una specifica malattia tumorale,*

*Decisioni cliniche condivise basate sull'evidenza*

*Coordinare l'esecuzione delle cure in ogni momento del processo terapeutico*

*Il paziente dovrebbe essere "parte attiva"*

**European Partnership for Action Against Cancer-EPAAC**

# La legislazione

Legge finanziaria del 1996, art. 1 comma 28

PDTA concepito come strumento di coordinamento tra i professionisti in grado, tra l'altro, di contribuire all'ottimizzazione dell'impiego delle risorse.

PSN 1998-2000 D.lgs. 229/99:

le linee guida e i PDTA vengono riconosciuti come strumento di garanzia dei Lea e mezzo di revisione e valutazione della pratica clinica.

PSN 2006/2008 DPR 7/4/2006

**Art 3 c.d. "Legge Balduzzi"**

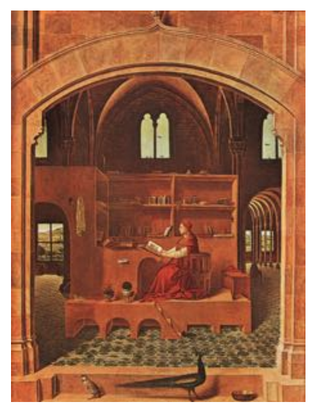
*L'esercente la professione sanitaria che nello svolgimento della propria attività si attiene a linee guida e buone pratiche accreditate dalla comunità scientifica non risponde penalmente per colpa lieve*

PDTA: Percorso Diagnostico e Terapeutico Assistenziale

# Progetto
# Team Multidisciplinare Uro-Oncologico
# Una Sfida Comune

Consensus Conference Milano 16-17 Dicembre 2015

Rimini, 7-10 Novembre 2015



Rimini, 7-10 Novembre 2015