



Associazione
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Società Italiana di Radiobiologia



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Farmaci innovativi e ipofrazionamento

PALACONGRESSI DI RIMINI
30 settembre, 1-2 ottobre 2016

XXVI CONGRESSO NAZIONALE AIRO
Presidente: Elvio G. Russi

XXX CONGRESSO NAZIONALE AIRB
Presidente: Renzo Corvò

IX CONGRESSO NAZIONALE AIRO GIOVANI
Coordinatore: Daniela Greto

Valutazione della sicurezza e del controllo del PSA a lungo termine dell'associazione tra Abiraterone Acetato e Radioterapia nei pazienti CRPC oligometastatici: uno studio di coorte retrospettivo multicentrico osservazionale

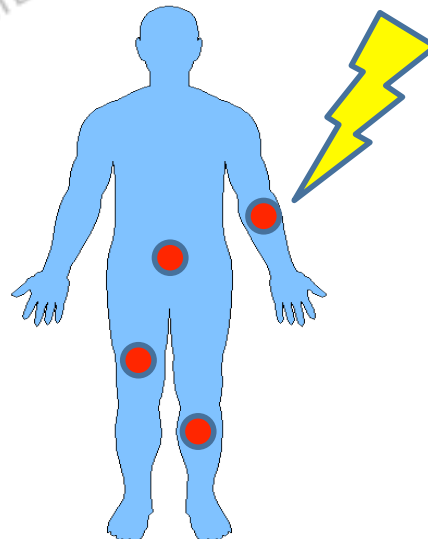
E. Olmetto, M. Loi, I. Giacomelli, J. Topulli, L. Trombetta, A. Turkaj, B. Detti, V. Baldazzi, R. M. D'Angelillo, L. E. Trodella, A. Sicilia, G. Ingrosso, R. Santoni, S. Borghesi, L. Lastrucci, A. Rampini, P. G. Gennari, S. Bertocci, P. Bastiani, S. Fondelli, R. Barca, P. Alpi, T. Carfagno, G. Battaglia, V. Nardone, M. Stefanacci, R. Santini, A. Bruni, F. Lohr, L. Triggiani, S. M. Magrini, L. Livi.

Firenze AOU Careggi, Roma Campus Bio-Medico, Roma Tor Vergata, Arezzo, Firenze OSMA, Siena, Pistoia, Modena, Brescia.



Introduction

- ✓ Oligometastatic patients with mCRPC : a new clinical «entity» which can benefit of Hypofractionated Radiotherapy
- ✓ Abiraterone Acetate, a selective inhibitor of androgen biosynthesis that irreversibly blocks CYP17, has proven to be effective both in the Pre and Post Chemotherapy settings.





Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study

Karim Fizazi, Howard I Scher, Arturo Molina, Christopher J Logothetis, Kim N Chi, Robert J Jones, John N Staffurth, Scott North, Nicholas J Vogelzang, Fred Saad, Paul Mainwaring, Stephen Harland, Oscar B Goodman Jr, Coira N Sternberg, Jin Hui Li, Thian Kheoh, Christopher M Haqq, Johann S de Bono, for the COU-AA-301 Investigators*

Lancet Oncol 2012; 13:983-92

OS: 15,8 m VS 11,2 m; HR: 0,74, 95% CI 0,64-0,86 p<0,0001

Median Time to PSA Progression: 8,5 m VS 6,6 m; HR: 0,66, 95% CI 0,58-0,76; p<0,001

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Abiraterone in Metastatic Prostate Cancer without Previous Chemotherapy

Charles J. Ryan, M.D., Matthew R. Smith, M.D., Ph.D., Johann S. de Bono, M.B., Ch.B., Ph.D., Arturo Molina, M.D., Christopher J. Logothetis, M.D., Paul de Souza, M.B., Ph.D., Karim Fizazi, M.D., Ph.D., Paul Mainwaring, M.D., Josep M. Piulats, M.D., Ph.D., Siobhan Ng, M.D., Joan Carles, M.D., Peter F.A. Mulders, M.D., Ph.D., Ethan Basch, M.D., Eric J. Small, M.D., Fred Saad, M.D., Dirk Schrijvers, M.D., Ph.D., Hendrik Van Poppel, M.D., Ph.D., Som D. Mukherjee, M.D., Henrik Suttman, M.D., Winald R. Gerritsen, M.D., Ph.D., Thomas W. Flaig, M.D., Daniel J. George, M.D., Evan Y. Yu, M.D., Eleni Efstathiou, M.D., Ph.D., Allan Pantuck, M.D., Eric Winquist, M.D., Celestia S. Higano, M.D., Mary-Ellen Taplin, M.D., Youn Park, Ph.D., Thian Kheoh, Ph.D., Thomas Griffin, M.D., Howard I. Scher, M.D., and Dana E. Rathkopf, M.D., for the COU-AA-302 Investigators*

**Median Radiographic PFS:
16,5 m VS 8,3 m; HR: 0,53, 95% CI
0,45-0,62, p = 0,01**

Abiraterone-prednisone showed superiority with respect to time to initiation of cytotoxic chemotherapy

N Eng J Med 2013; 368:138-48



Aims

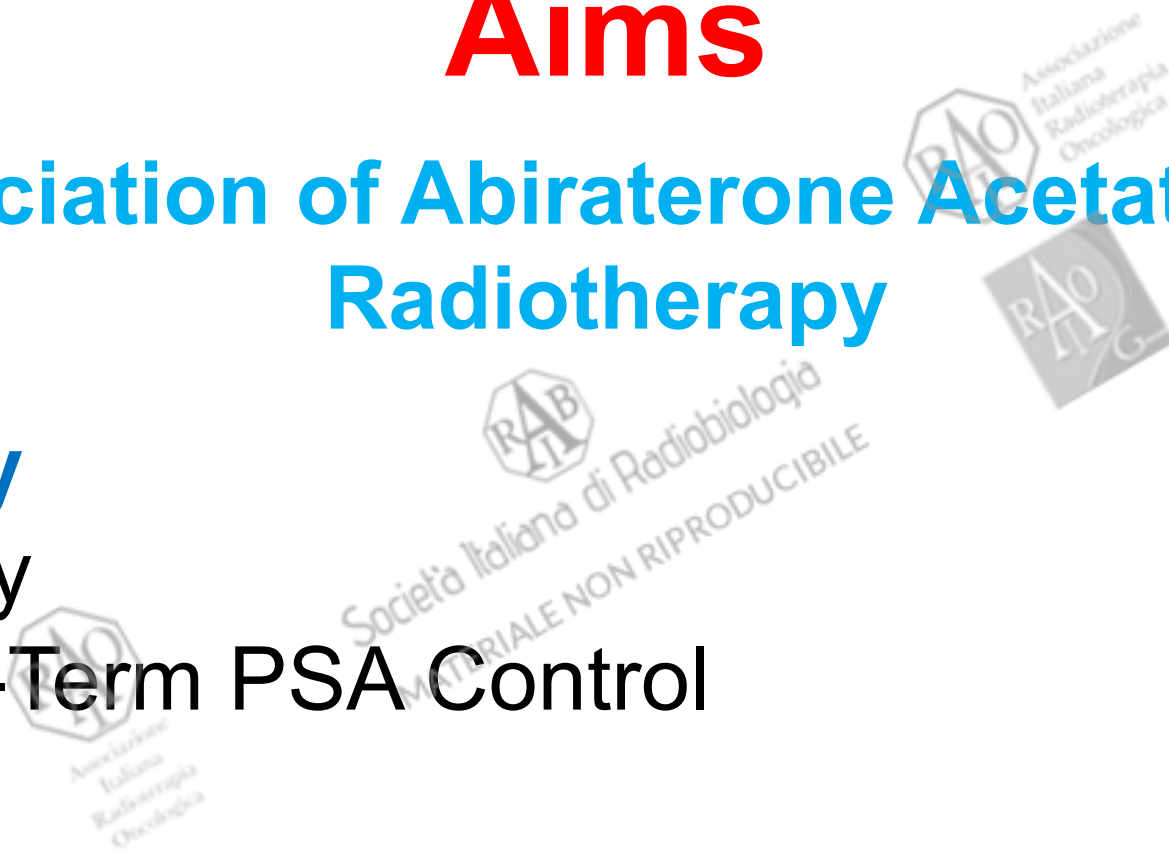
Association of Abiraterone Acetate and Radiotherapy

Primary

- Safety
- Long-Term PSA Control

Secondary

- PFS
- OS





Materials and Methods

Partecipating Centers

- Firenze AOU Careggi
- Firenze OSMA
- Roma Campus Bio-Medico
- Roma Tor Vergata
- Siena
- Arezzo
- Pistoia
- Brescia
- Modena

January 2010
July 2016

✓ N= 64



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Details at diagnosis	N. Patients :64
Age	
< 60 years	8 (14%)
61-70 years	31 (48%)
>70 years	24 (38%)
PSA ng/dl	
Median (range)	21 (4,33-48)
< 10	15 (23%)
10-20	15 (23%)
> 20	34 (53%)
Gleason Score	
Median (range)	7 (5-9)
5	1 (2%)
6	6 (10%)
7	25 (39%)
8	15 (23%)
9	17 (26%)



Treatments	N. Patients: 64
CHT Treatment	
- CHT	29 (45%)
+ CHT	35 (55%)
Response to CHT	
CR	0 (0%)
PR	1 (3%)
SD	14 (40%)
PD	20 (57%)
Clinical Benefit Rate (CR + PR + SD)	15 (43%)

Details at the initiation of AA	N Patients : 64
Age	
Median (range)	75 (55-86)
< 60	4 (5%)
61-70	16 (25%)
> 70	44 (70%)
Concomitant Treatment	
Agonist LH RH	46 (72%)
Antagonist LH RH	18 (28%)
Metastatic Site	
Lymph node	14 (22%)
Bone	25 (39%)
Limph Node + Bone	25 (39%)
PSA ng/dl	
Median (range)	33,16 (0,41-118)
<10	17 (28%)
10-20	7 (11%)
> 20	37 (61%)

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 RAO
 RAB
 MATERIALE NON PUBLICEBILI



Irradiated Site (Single site of Progression or Symptomatic)

- Bone: 49 (77%)
- Lymph Node: 13 (20%)
- Prostatic Recurrence 2 (3%)

Abiraterone 1000 mg/die

+

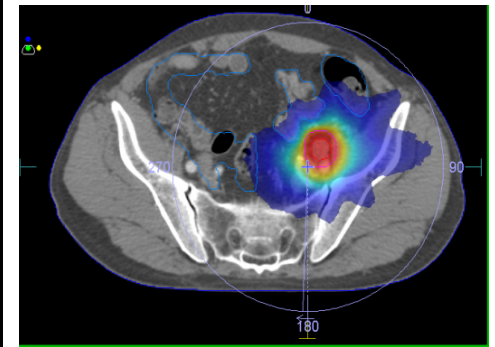
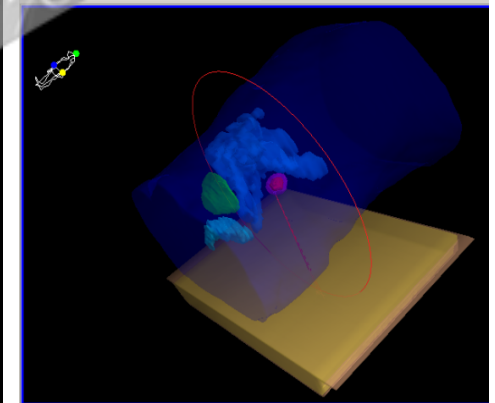
Prednisone 10 mg/die

Radiotherapy Technique

- RT 3D: 49 (77%)
- Stereo with LINAC: 9 (14%)
- Stereo with Cyber Knife: 5 (7%)
- Stereo with Tomotherapy: 1 (2%)

Schedules of Radiotherapy

- 30 Gy in 10 fractions of 3 Gy (47%)
- 20 Gy in 5 fractions of 4 Gy (26%)
- 8 Gy in single fraction (12%)
- 45 Gy in 15 fractions of 3 Gy (6%)
- 36 Gy in 12 fractions of 3 Gy (3%)
- 18 Gy in single fraction (1,5 %)
- 12 Gy in 2 fractions of 6 Gy (1,5%)
- 30 Gy in 3 fractions of 10 Gy (1,5%)
- 30 Gy in 4 fractions of 7,5 Gy (1,5%)



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Results

Safety



Adverse Events	N. Patients:64
None	62 (97%)
Cardiovascular Event	1 (1,5%)
Intestinal Subocclusion	1 (1,5%)

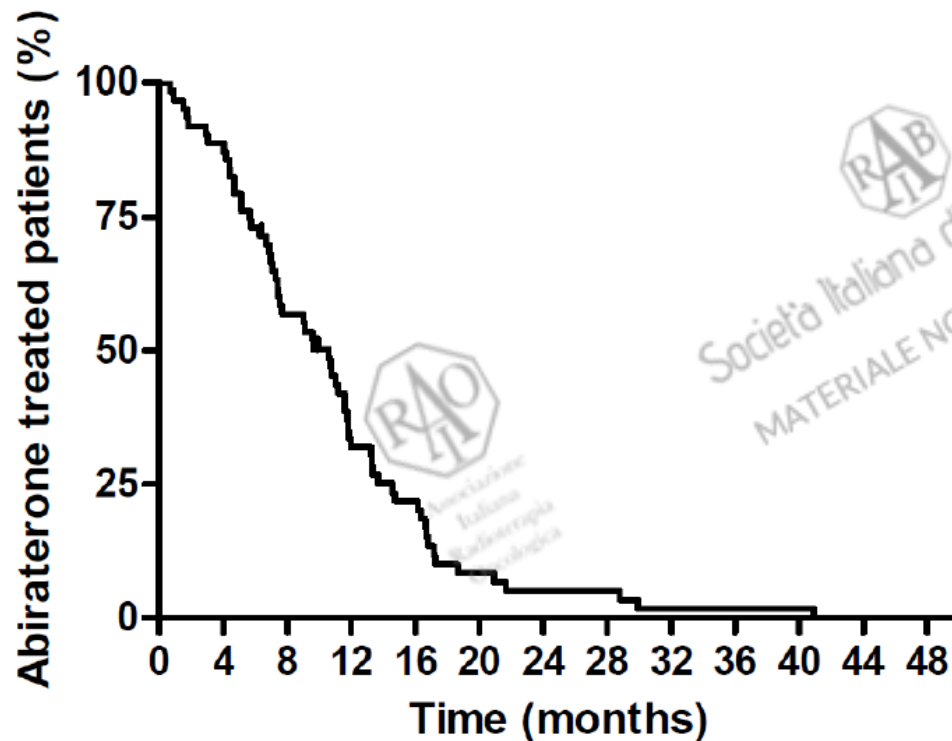
The Cardiovascular Event caused suspension of Abiraterone

The Intestinal Subocclusion event caused the discontinuation of Abiraterone

Cardiovascular Comorbidity	N. Patients:64
None	46 (72%)
>1	18 (28%)

Results

Long Term PSA Control



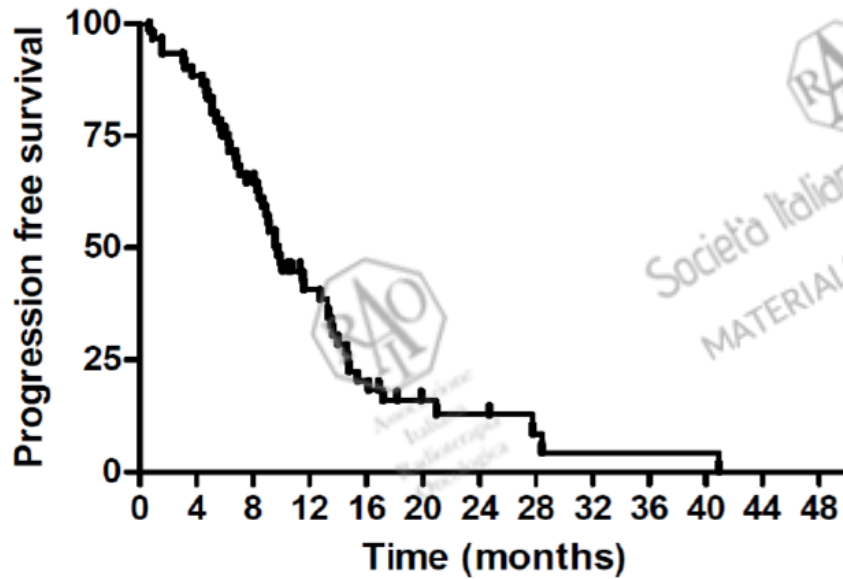
Treatment Duration:
 Mean Time 10,8 m (CI 95% 9,01-12,72)

PSA Reduction	N Patients
> 50%	30 (47%)
<50%	27 (42%)
Biochemical Progression	7 (11%)



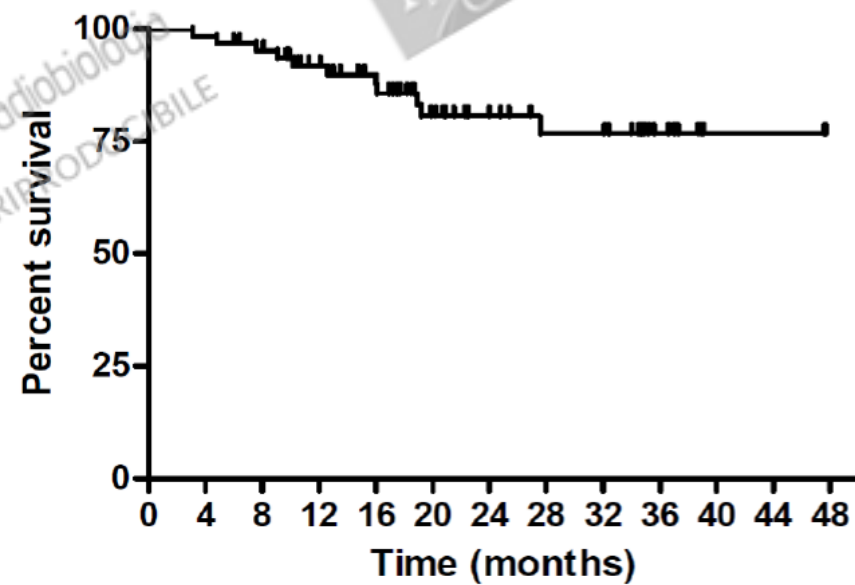
Results

PFS



PFS Mean 12,34 months
(CI 95% 9,74-14,93)

OS

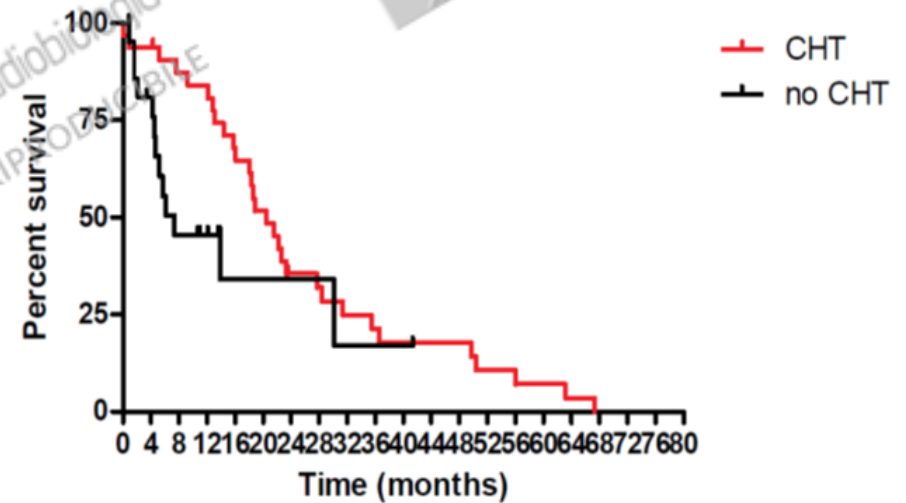
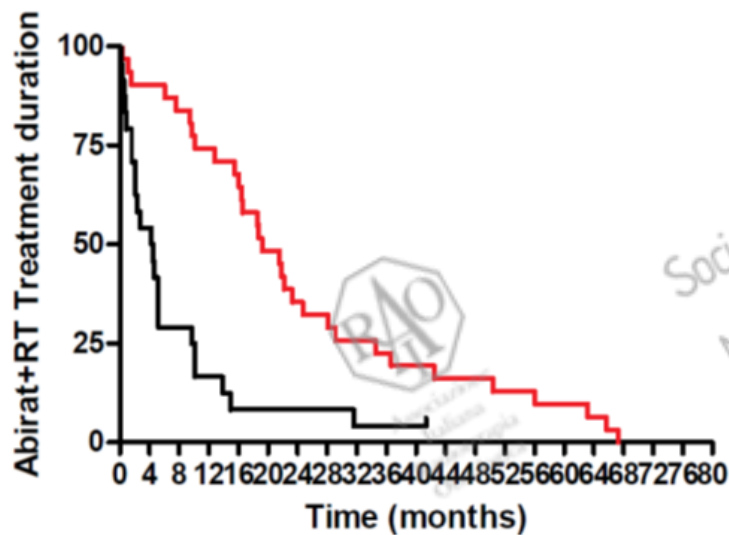


OS Mean 40,15 months
(CI 95% 35,96-44,34)



Results

Sub Groups Analysis CHT VS NO CHT



CHT: Mean 24,7 m (CI95% 18,08-31,4)
NO CHT: Mean 7,34 m (CI 95% 3,33-11,34)
P<0,001

CHT: Mean 26 m (CI95% 19,57-32,42)
NO CHT: Mean 14,2 m (CI 95% 6,97-21,46)
P=0,013



Conclusions

- **The association between Radiotherapy and Abiraterone Acetate is safe and doesn't add toxicity**
- **Good efficacy of the combination**
- **Prospective data needed for a better selection of patients**



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**Grazie
per l'attenzione**