Post docetaxel Abiraterone in patients with metastatic castration-resistant prostate cancer: survival and prognostic factors.

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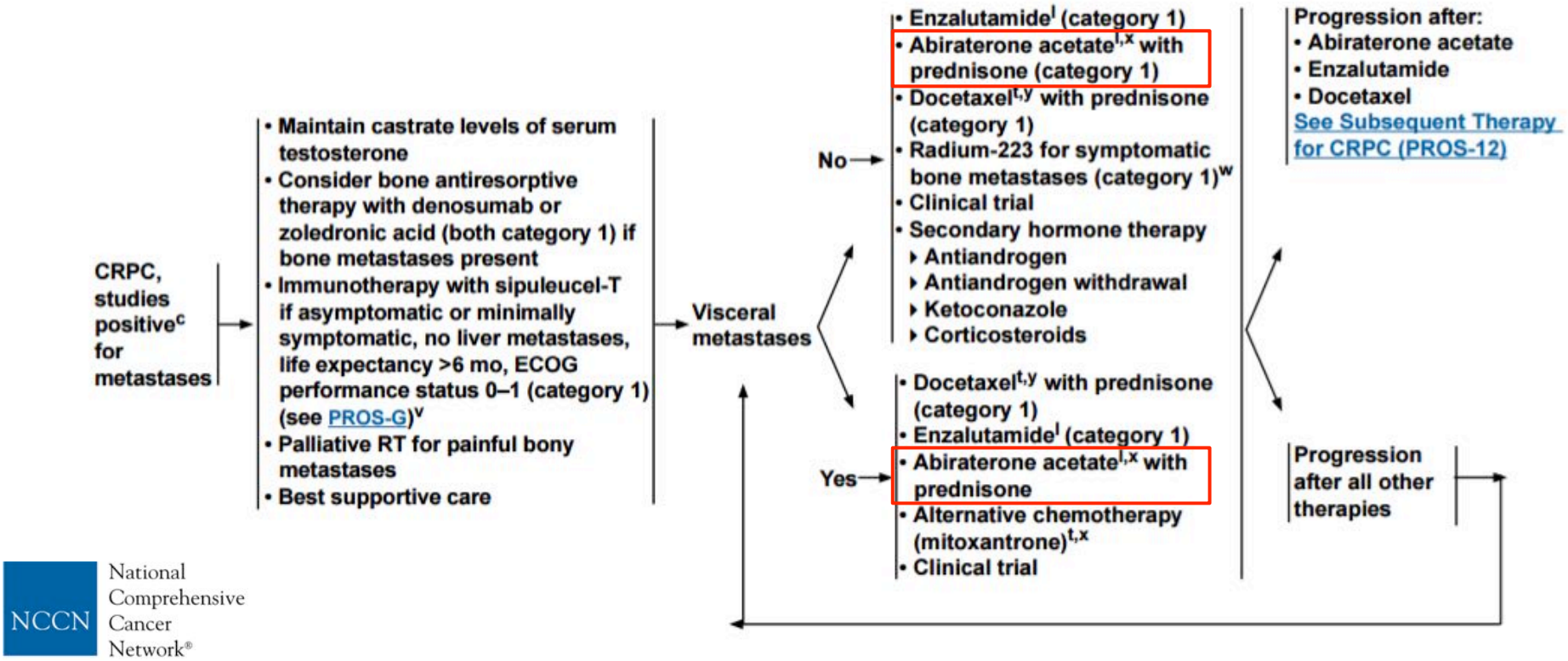
BACKGROUND

ADVANCED DISEASE: FIRST-LINE SYSTEMIC THERAPY FOR CRPC



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BACKGROUND

ADVANCED DISEASE: SUBSEQUENT SYSTEMIC THERAPY FOR CRPC

No visceral metastases →

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

Visceral metastases →

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

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PATIENTS

- **PSA progression:** sequence of rising values at a minimum of 1-week intervals, 2.0 ng/mL minimum starting value (PCWG2 Criteria)
- Serum testosterone less than 50 ng/dL (< 1.7 nmol/L)

- **Radiologic progression** with or without PSA increase

Sher et al, JCO, 2008

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TREATMENT

Total number: 40 Patients with mCRPC previous treated with docetaxel

Treatment schedule: Abiraterone 1000 mg+ Prednisone 10 mg+LH RH analogue (agonist or antagonist)

Median Follow Up: 12 months (range 4-29.5)

Median time of duration of AA therapy: Therapy was 8.33 months (range 1-20)

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POPULATION FEATURES

Metastases	n (%)
LN	11 (27.5)
Only visceral	2 (5)
LN + visceral	1 (2.5)
Bones	15(37,5)
LN+bones	10 (25)
LN+visceral+bones	1 (2.5)

Variable	n (%)
Response to docetaxel*	
CR	-
PR	2 (5)
SD	19 (47.5)
PD	19 (47.5)
PSA at start abirat.	
<10	16 (40)
10-20	3 (7.5)
>20	21 (52.5)
HB at start abirat.	
<10	4 (10)
>10	36 (90)
Concomit. HT	
LHRH agonist	15 (37.5)
LHRH antagonist	25 (62.5)

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EVALUATIONS/CONCOMITANT TREATMENTS

- Complete blood test and PSA were collected at baseline and then monthly.
- Radiological evaluations were performed at baseline and then every three months.
- Performance status was evaluated according to ECOG score at baseline and then monthly.
- Best supportive care therapy was allowed during the treatment, including palliative EBRT, Bisphosphonates or Denosumab and opioid use.

15% of patients had concomitant palliative radiotherapy during AA treatment, without increase of toxicity

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RESULTS

Variable	PD	%PFS	p
Docetaxel response*			
CR	-	-	
PR	1	0	
SD	11	0	
PD	9	16.1	**0.031**
PSA at start abirat.			
<10	6	18.2	
10-20	0	100	
>20	16	0	**0.014**
HB at start abirat.			
<10	3	0	
>10	19	9.1	**0.008**
PSA reduction			
>50%	11	10.2	
<50%	11	8.8	**0.012**
Concomit. HT			
LHRH agonist	5	35.0	
LHRH antagonist	17	0	**0.17**

- **AE causing discontinuation/ interruption:12.5%**
- **CV AE: 5%**
- **No G2-G3 hypokalaemia/ fluid retention**
- **Median baseline PSA:**

  104.3 ng/ml

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RESULTS

UNIVARIATE **MULTIVARIATE**

variable	HR	(95%CI)	p		HR	(95%CI)	p
HB at start abirat. <10 >10	1 0.20	(0.05-0.74)	**0.016**		1 0.23	(0.06-0.92)	**0.038**
PSA reduction >50% <50%	1 2.88	(1.21-6.87)	**0.017**		1 5.13	(1.80-14.64)	**0.002**

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RESULTS

Metastases	%PFS	p
LN	0	0.90
Only visceral	0	
LN + visceral	100	
Bones	14.1	
LN+bones	14.6	
LN+visceral +bones	0	

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DISCUSSION

	n patients	PSA reduction >50%	BiochemicalTTP (months)	RadiologicalTTP (months)
Florence	**40**	**55%**	**9.81**	**9.47**
Fizazi, Lancet 2012	**797**	**29.5%**	**8.5**	**5.6**
Clayton, can Urol Assoc, 2014	**187**	**36%**	**3.5**	**na**
Danila, JCO, 2010	**58**	**36%**	**5.6**	**na**
Reid, JCO, 2010	**47**	**51%**	**5.6**	**na**

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DISCUSSION

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, Cora 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

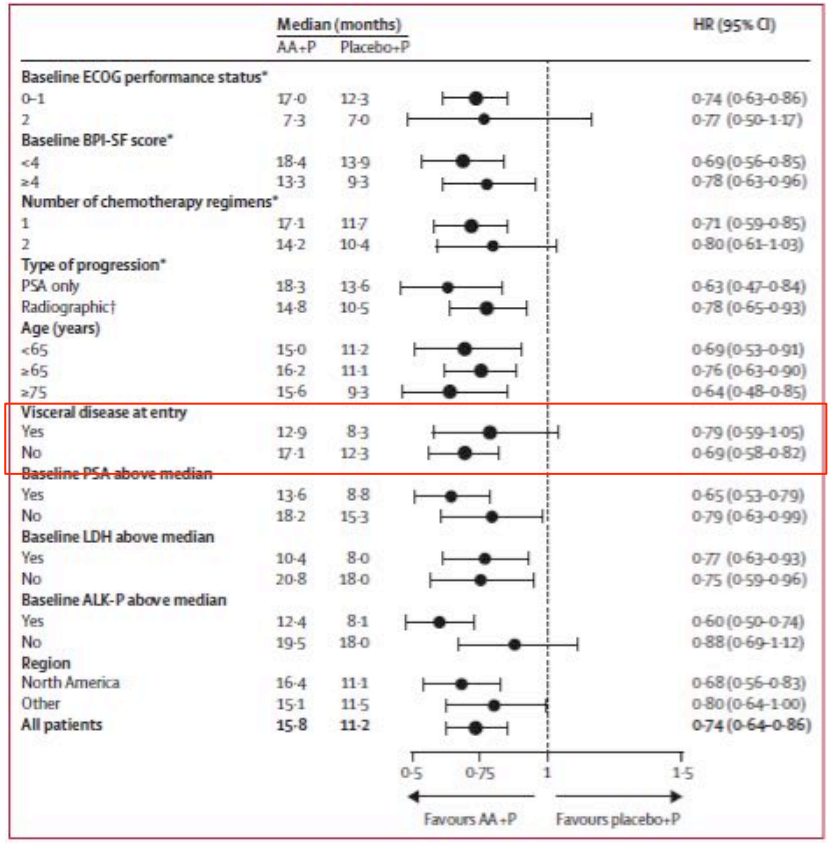

Figure 3: Overall survival by subgroup analyses

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Conclusion

- No correlation between metastatic sites (bone, lymph nodes, viscera) and patients outcome.
- Abiraterone should be administered to low baseline PSA patients
- Association between Abiraterone and LH RH antagonists could be an interesting issue on order to reduce cardiovascular morbidity
- Association between RT and Abiraterone is safe

GRAZIE
PER L'ATTENZIONE