

Fourth session: mCRPC further lines

Clinical case and evidences from literature



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Clinical case:

May 2003 Radical Prostatectomy

Mar 2013 Diagnosis of mHSPC → **ADT**

20 Jan 2015 Starting **Docetaxel** 75 mg/m² + **Zoledronic Acid** 4 mg, PSA=7,5

04 Apr 2015 PSA=2,7, ECOG=1, NRS=0,

15 Jun 2015 PSA=0.81 (8th cycle of docetaxel)

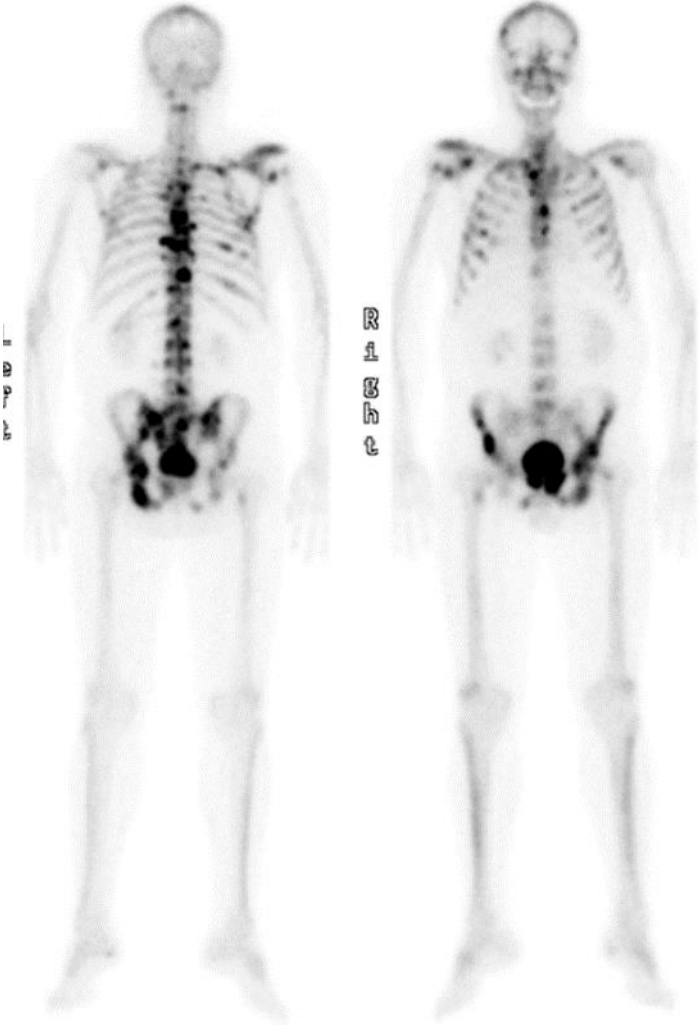
Side effects from CT: *asthenia G1, alopecia G2, onychopathy G1, anemia G1, neutropenia G2*

Clinical case:

Post

Ant

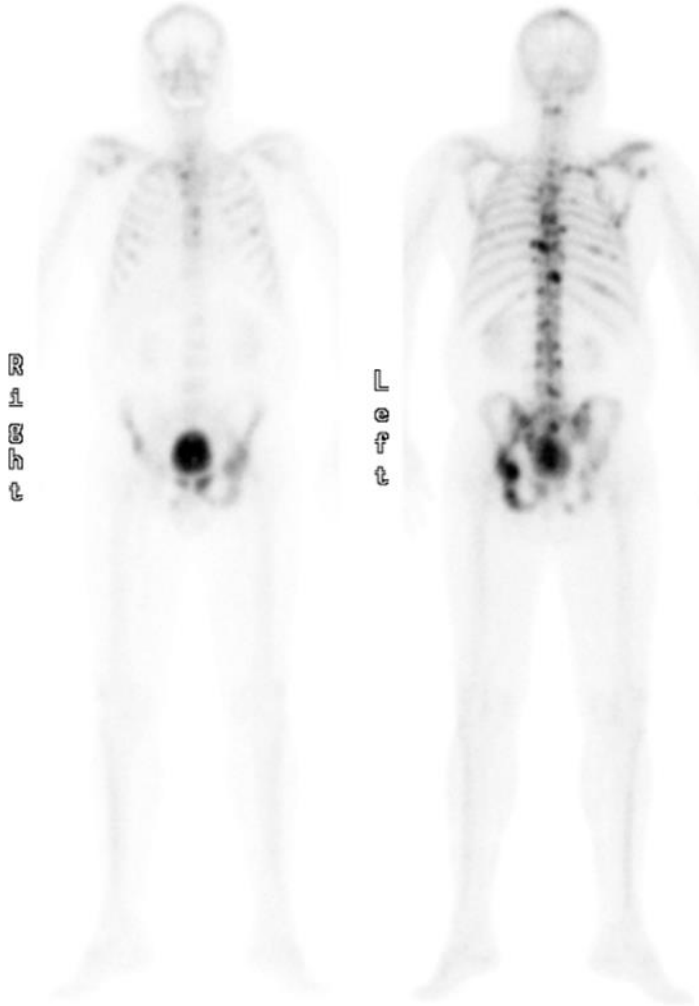
Jan 2015



Ant

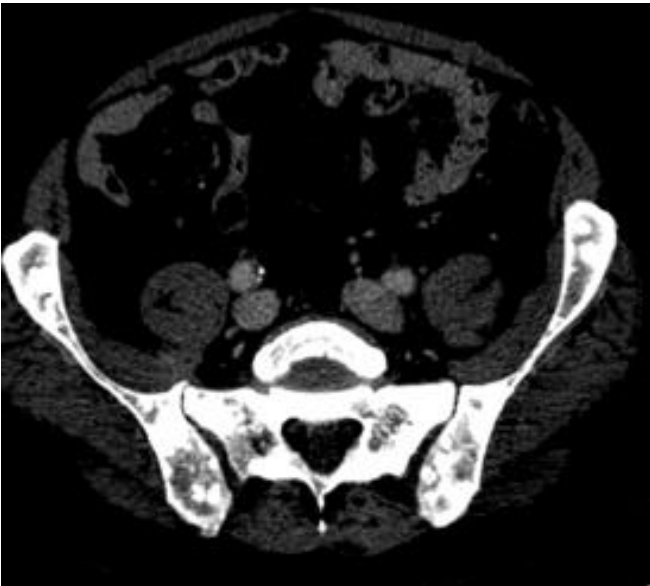
Post

Jun 2015

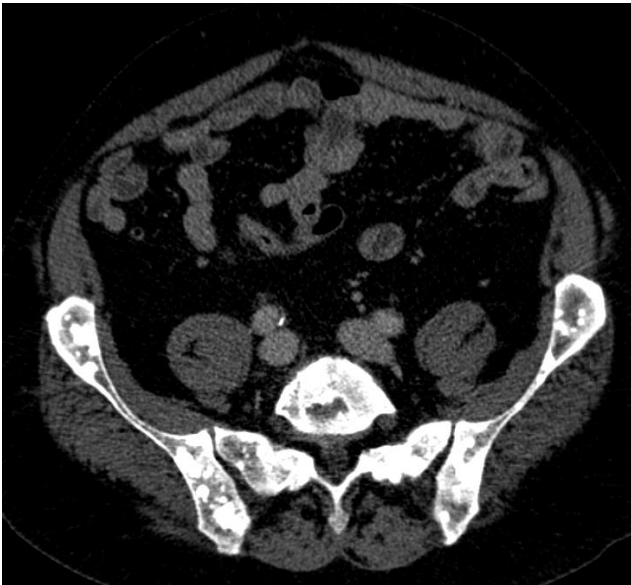
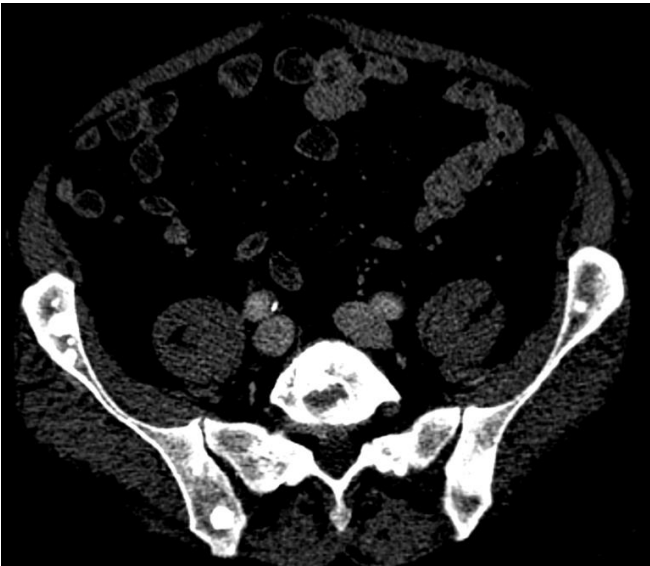


Clinical case:

Jan 2015



Jun 2015



Clinical case:

20 Jan 2015 Starting **Docetaxel** x 8 cycles + **Zoledronic Acid** 4 mg, PSA=7,5

15 Jun 2015 PSA=0.81 (end of docetaxel)

15 Oct 2015 PSA=0.77

18 Dec 2015 PSA=1,1

05 Apr 2016 PSA=5,7; ECOG=1, NRS=7/10 on right pelvis despite Paracetamole 1 g x 3.

13 Apr 2016 end of RT (20 Gy) on the left pelvis,

20 Apr 2016 Patient status: 74 yo, ECOG=1, NRS=2/10 (Codeine+Paracetamole x 3), W 71 Kg.

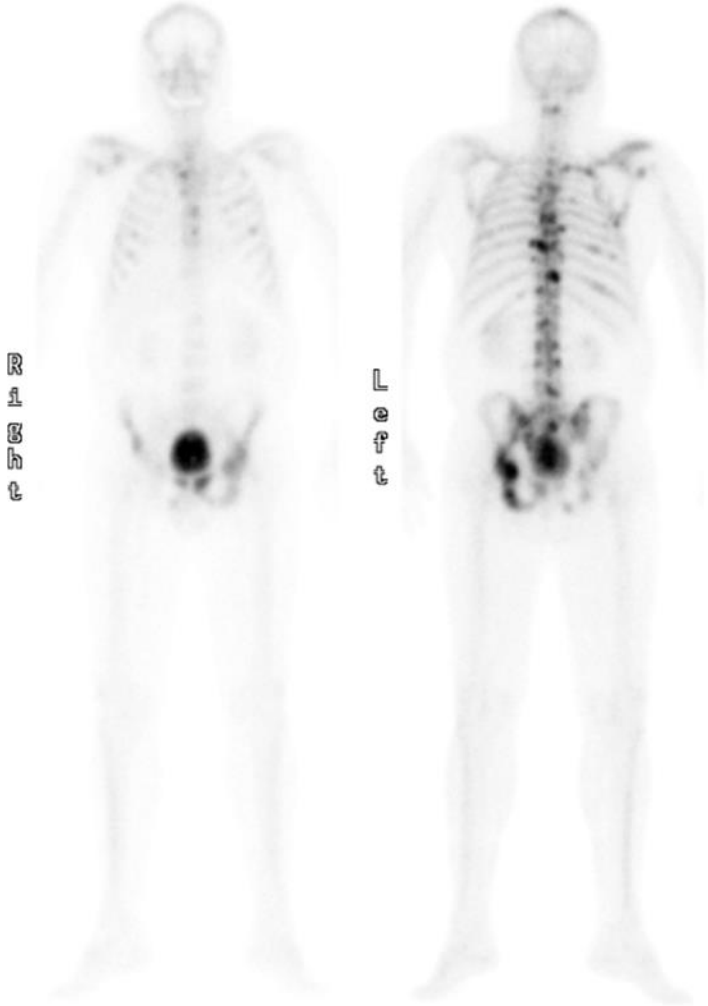
Blood Test	Value	Normal rage
Hemoglobin	11.8	13.5 – 17.5
PLT	294	150 - 400
Ca	8.9	8.4 – 10.4
ALP	321	50 - 130
PSA	5.7	

Clinical case:

Ant

Post

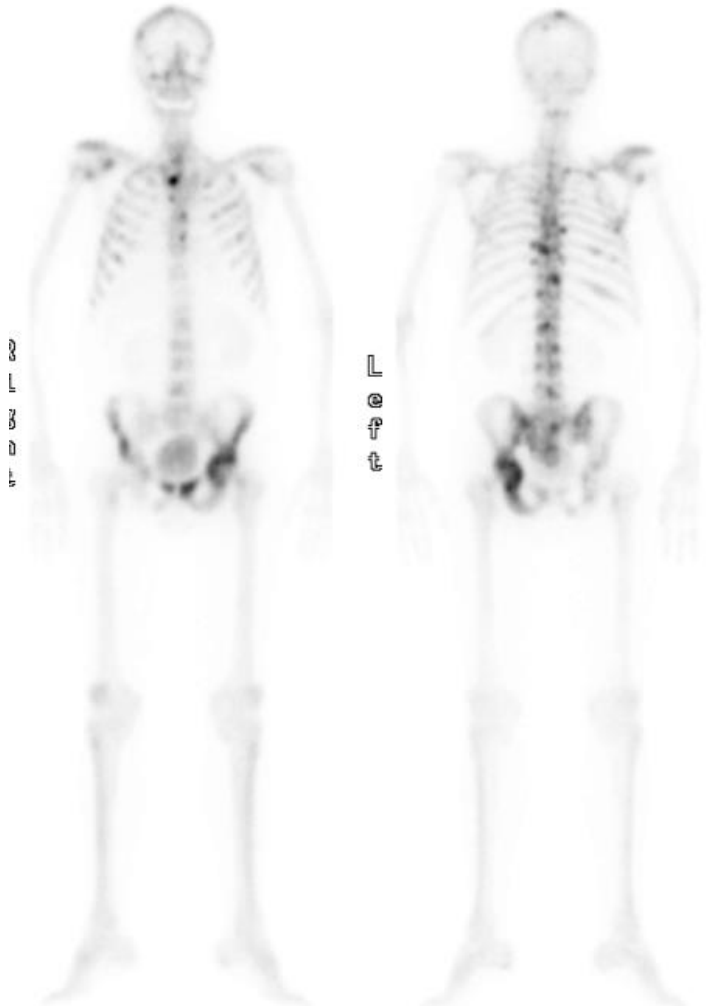
Jun 2015



Ant

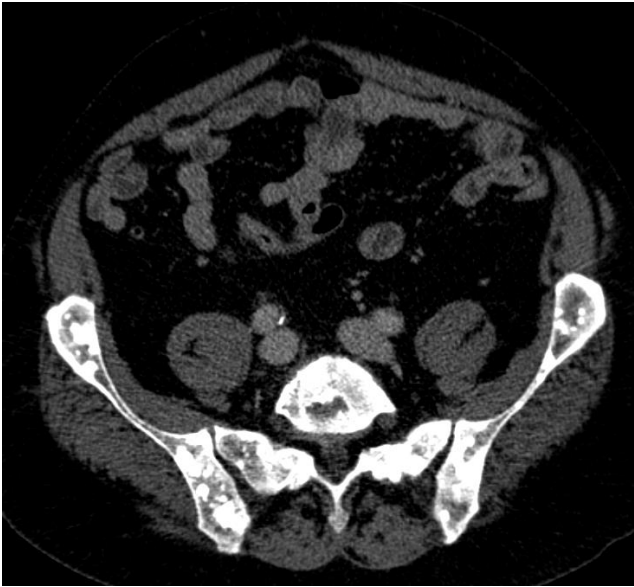
Post

Apr 2016

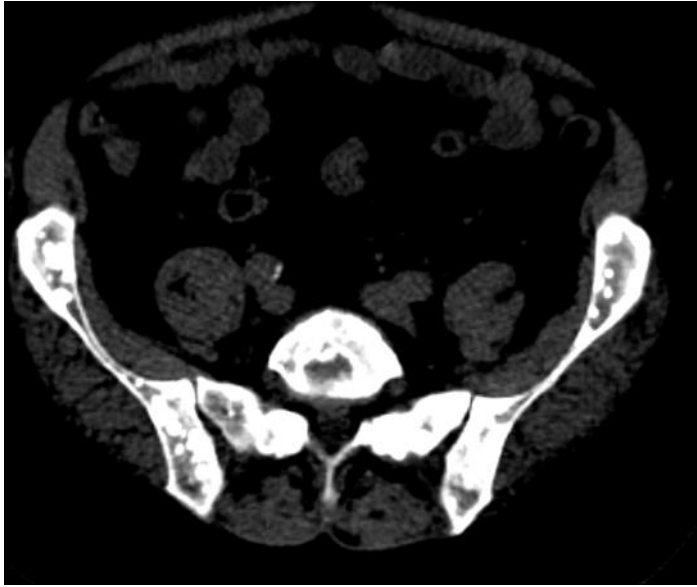
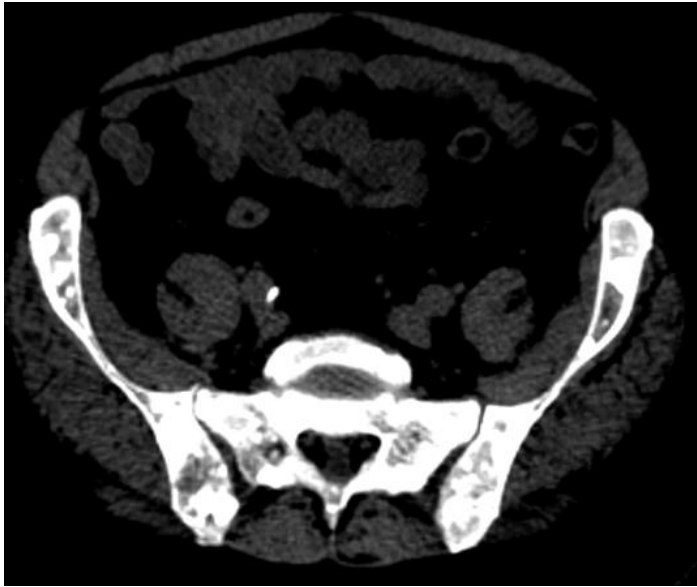


Clinical case:

Jun 2015



Apr 2016



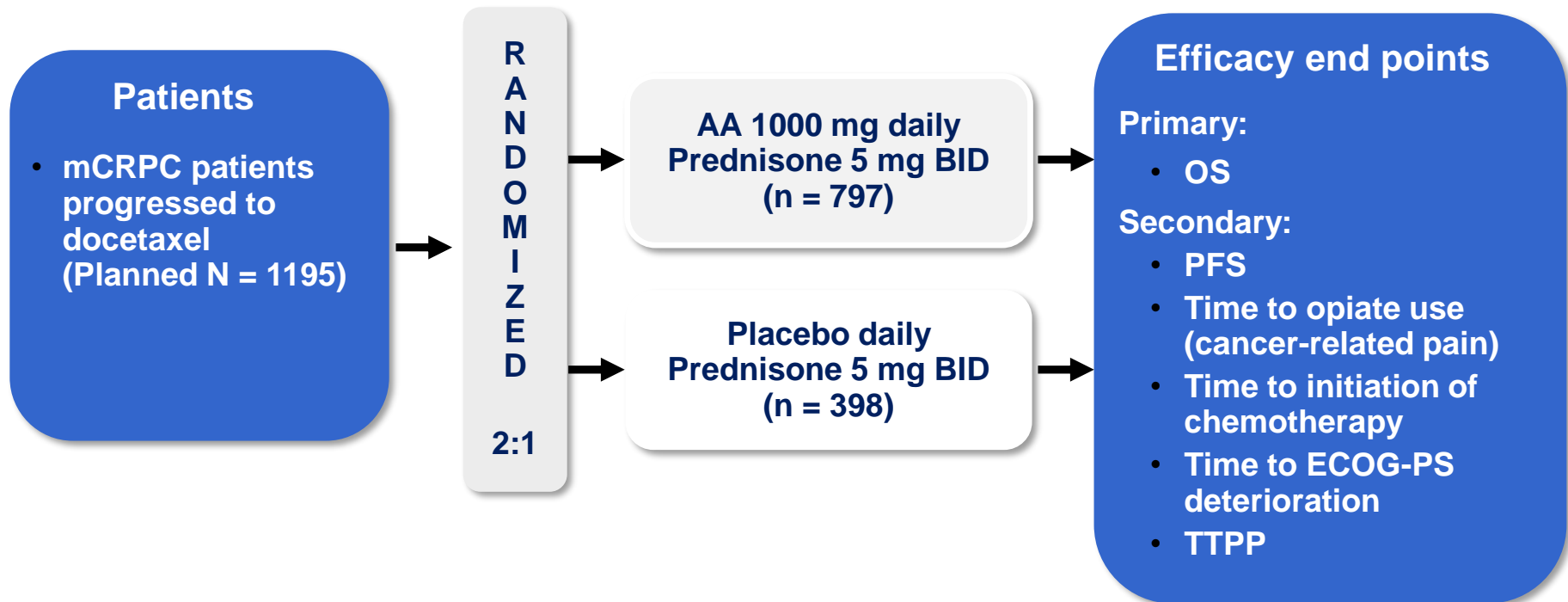
Clinical case:

What is the best treatment for this patients?

- Abiraterone
- Cabazitaxel 25 or 20 mg/m², 3 weekly
- Docetaxel 75 mg/m², 3 weekly (rechallenge)
- Enzalutamide
- Radium 223

Further-line mCRPC, *Evidences from the literature: Abiraterone*

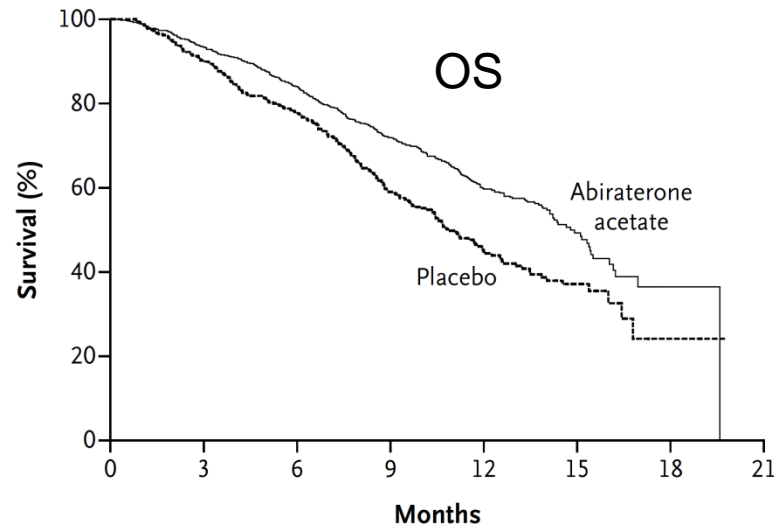
The COU-301 Trial: Study design



Further-line mCRPC, *Evidences from the literature: Abiraterone*

The COU-301 Trial: Results

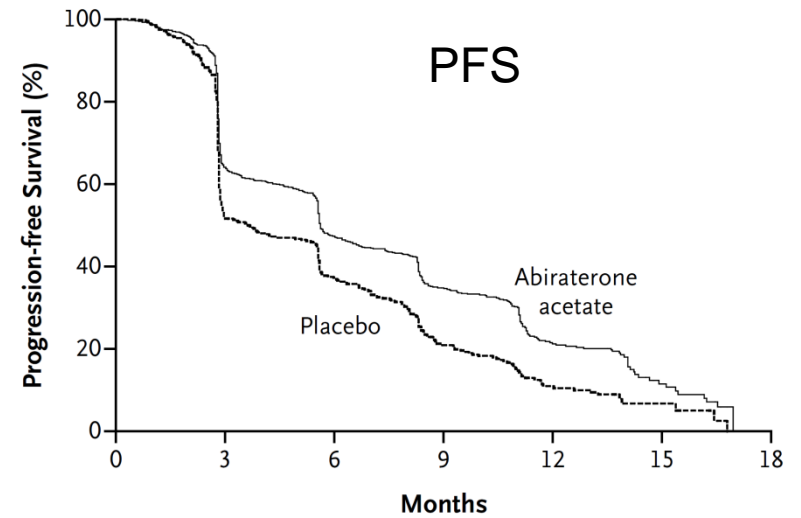
A Overall Survival



No. at Risk

	0	3	6	9	12	15	18	21
Abiraterone acetate	797	736	657	520	282	68	2	0
Placebo	398	355	306	210	105	30	3	0

C Progression-free Survival



No. at Risk

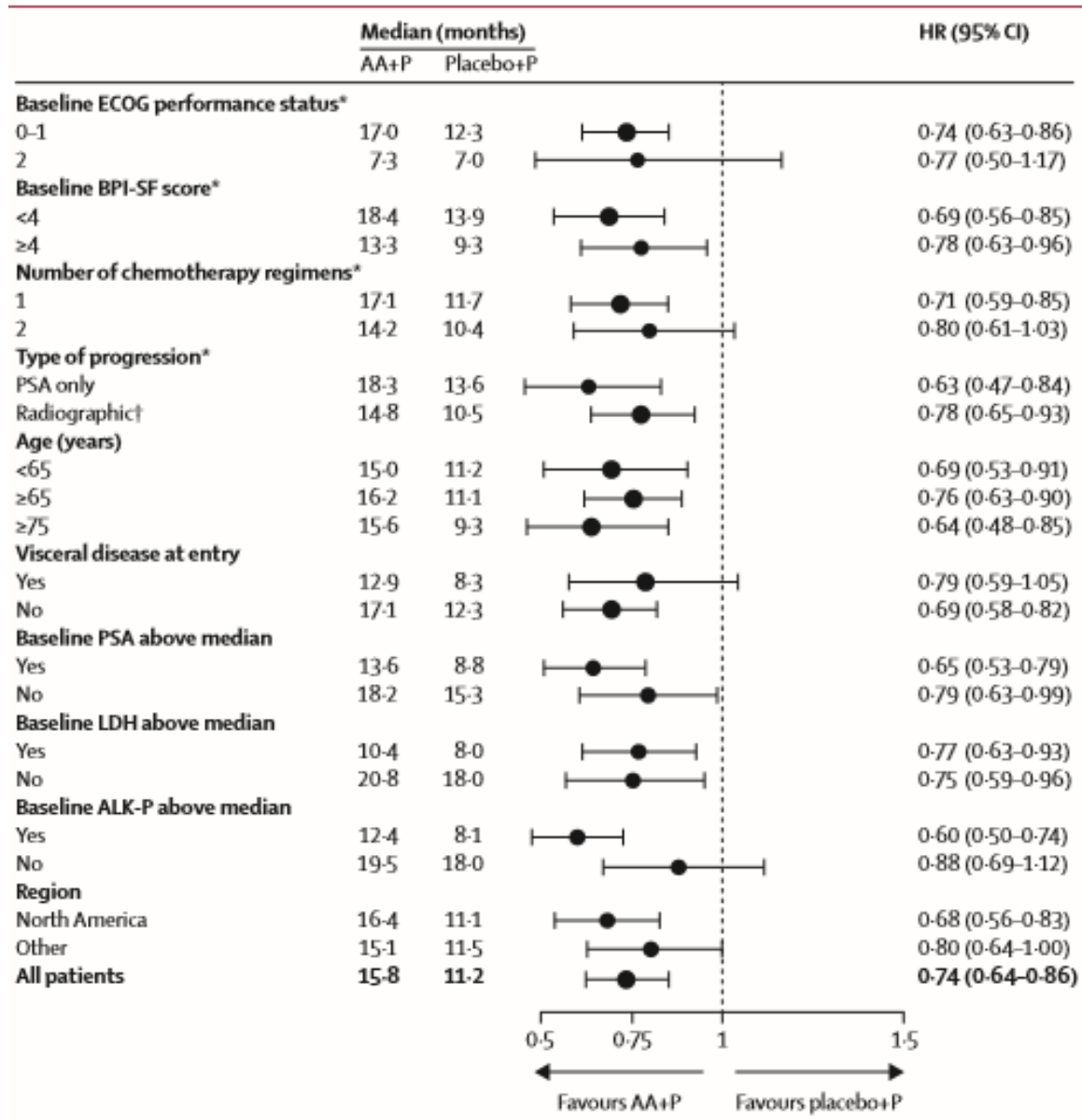
	0	3	6	9	12	15	18
Abiraterone acetate	797	490	352	202	76	14	0
Placebo	398	193	129	64	22	4	0

	Pbo	ABI
Median OS, mos	10.9	14.8
HR	0.65	
95% CI	0.54-0.77	
P value	< .0001	

	Pbo	ABI
Median PFS, mos	3.6	5.6
HR	0.58	
95% CI	0.46-0.73	
P value	< .0001	

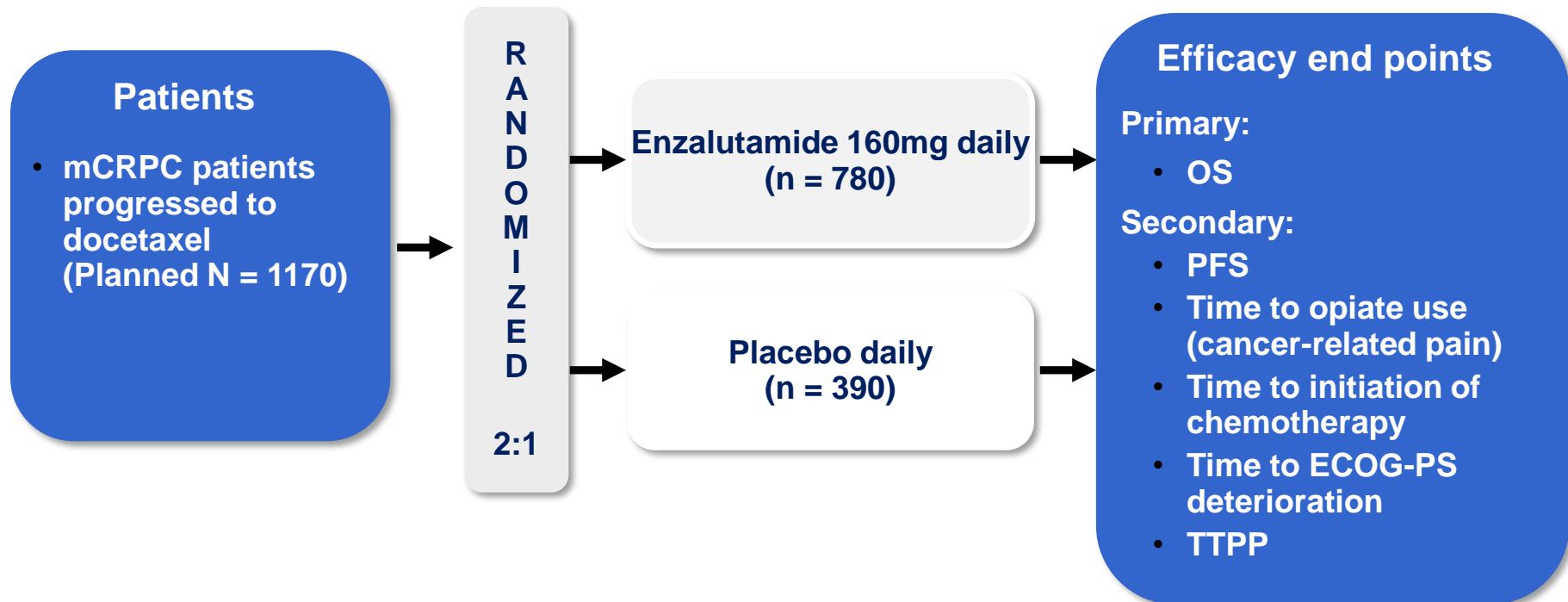
Further-line mCRPC, *Evidences from the literature: Abiraterone*

The COU-301 Trial: Population



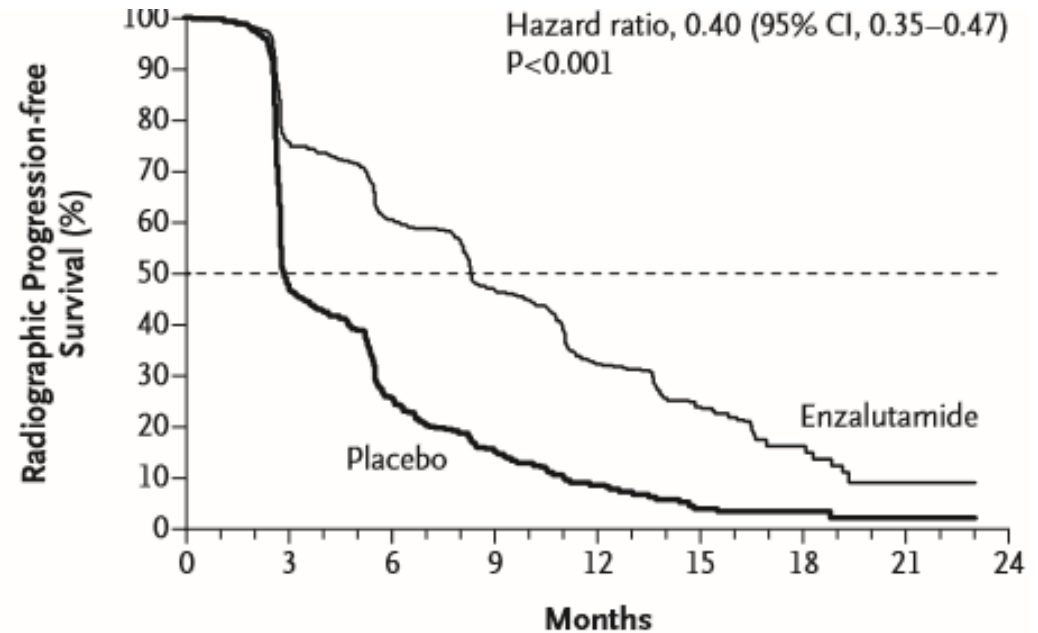
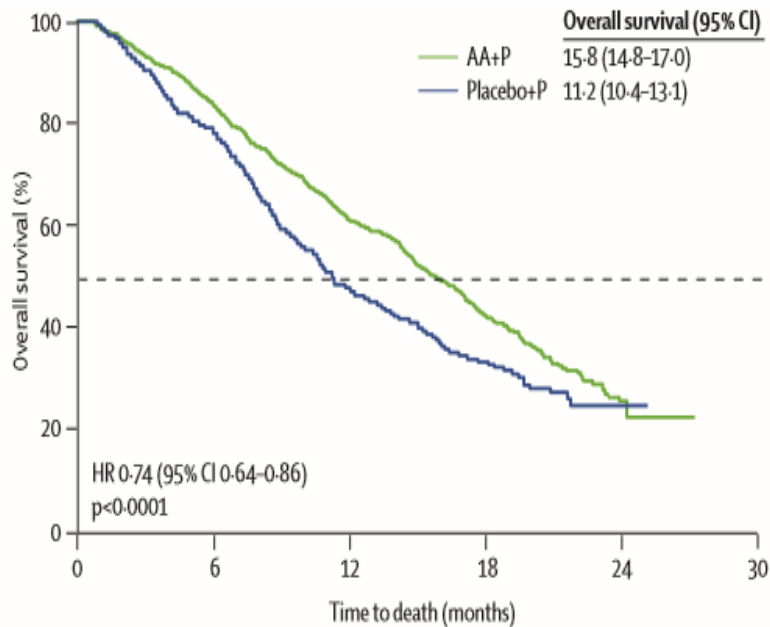
Further-line mCRPC, *Evidences from the literature*: Enzalutamide

The AFFIRM Trial: Study design



Further-line mCRPC, *Evidences from the literature: Enzalutamide*

The AFFIRM Trial: Results

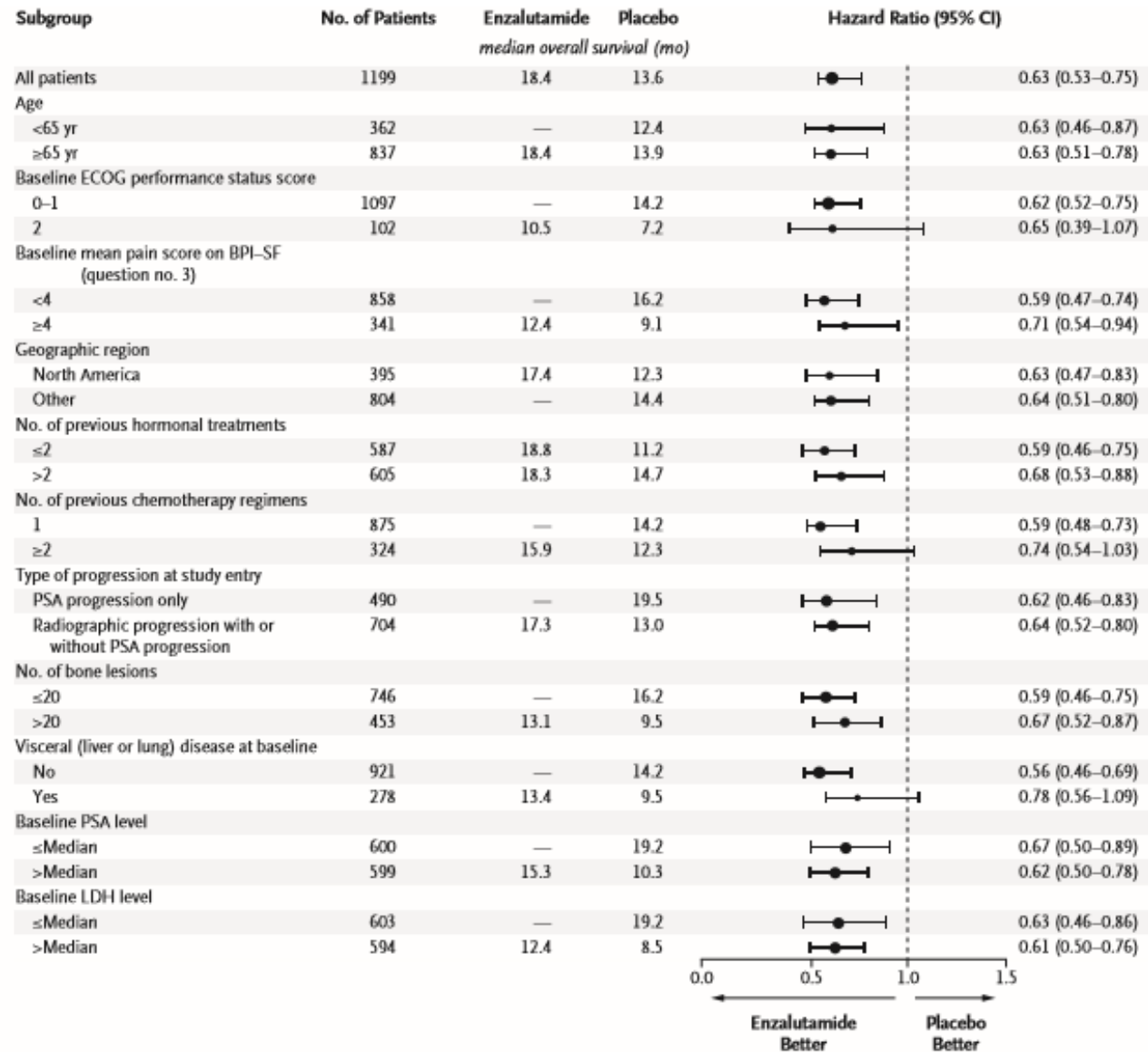


	Pbo	ENZ
Median OS, mos	13.6	18.4
HR	0.63	
95% CI	0.53-0.75	
P value	< .0001	

	Pbo	ENZ
Median PFS, mos	2.9	8.3
HR	0.40	
95% CI	0.35-0.47	
P value	< .0001	

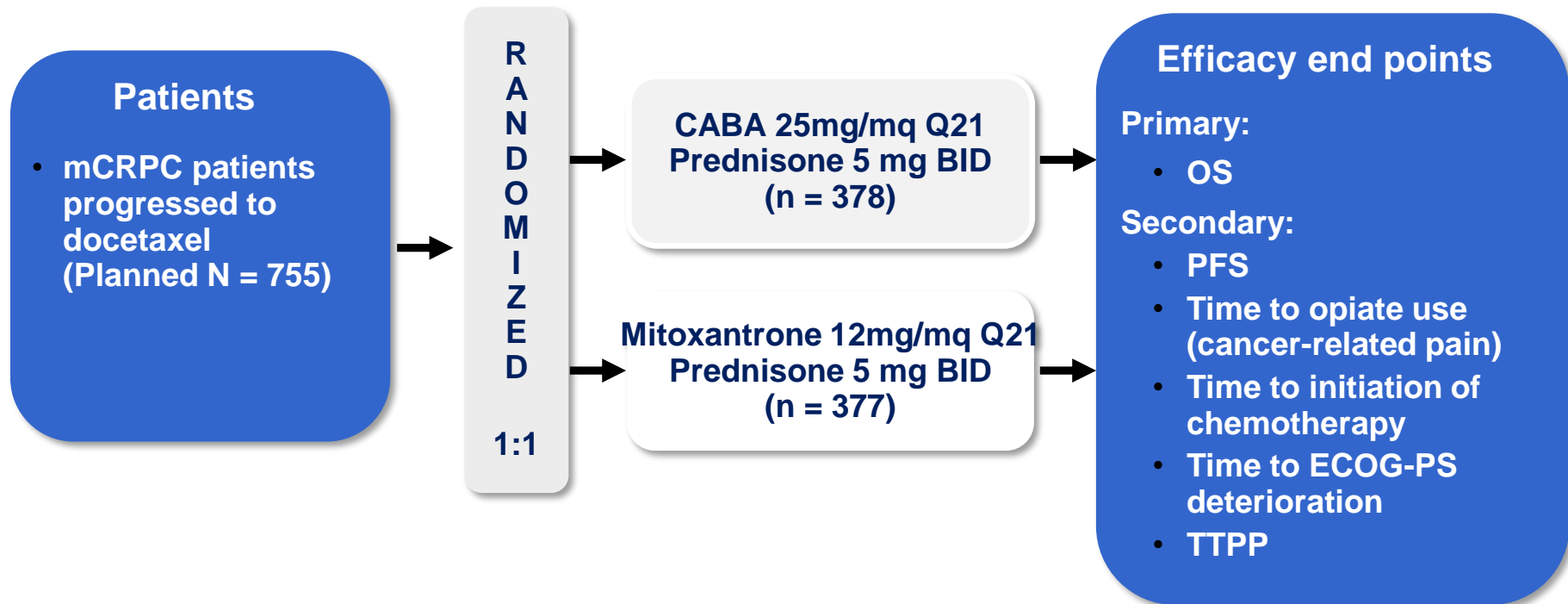
Further-line mCRPC, *Evidences from the literature: Enzalutamide*

The AFFIRM Trial: Population



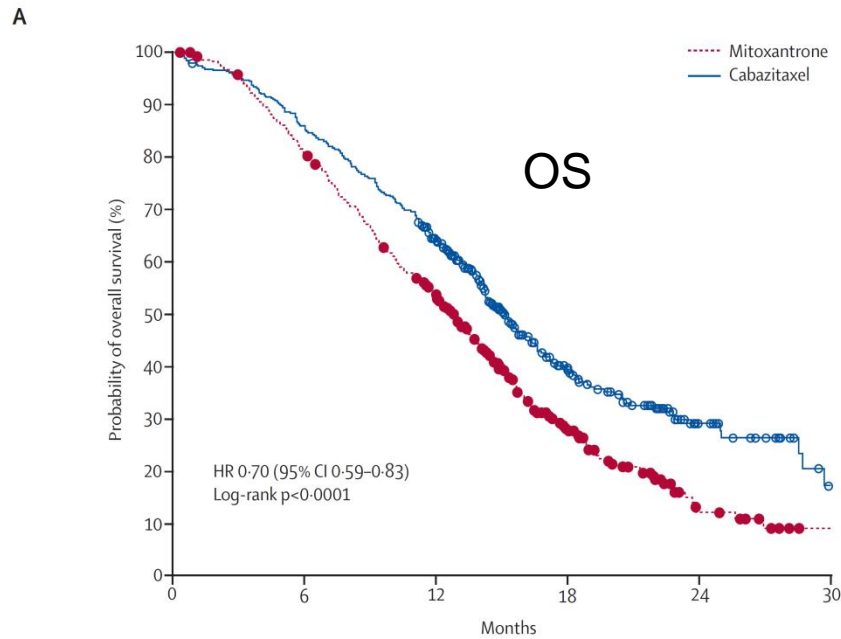
Further-line mCRPC, *Evidences from the literature: Cabazitaxel*

The TROPIC Trial: Study design

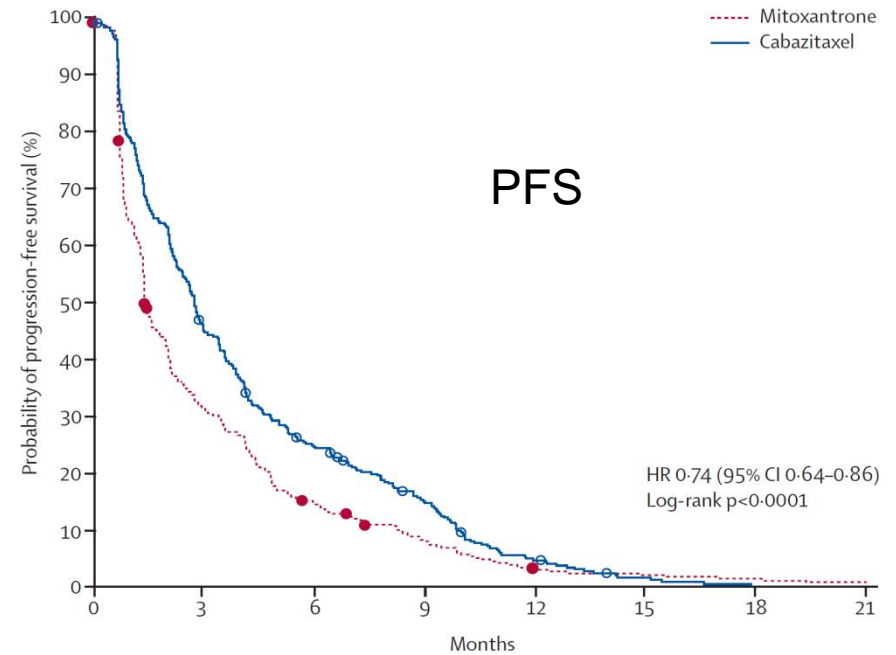


Further-line mCRPC, Evidences from the literature: Cabazitaxel

The TROPIC Trial: Results



Number at risk		0	6	12	18	24	30
Mitoxantrone	377	300	188	67	11	1	
Cabazitaxel	378	321	231	90	28	4	



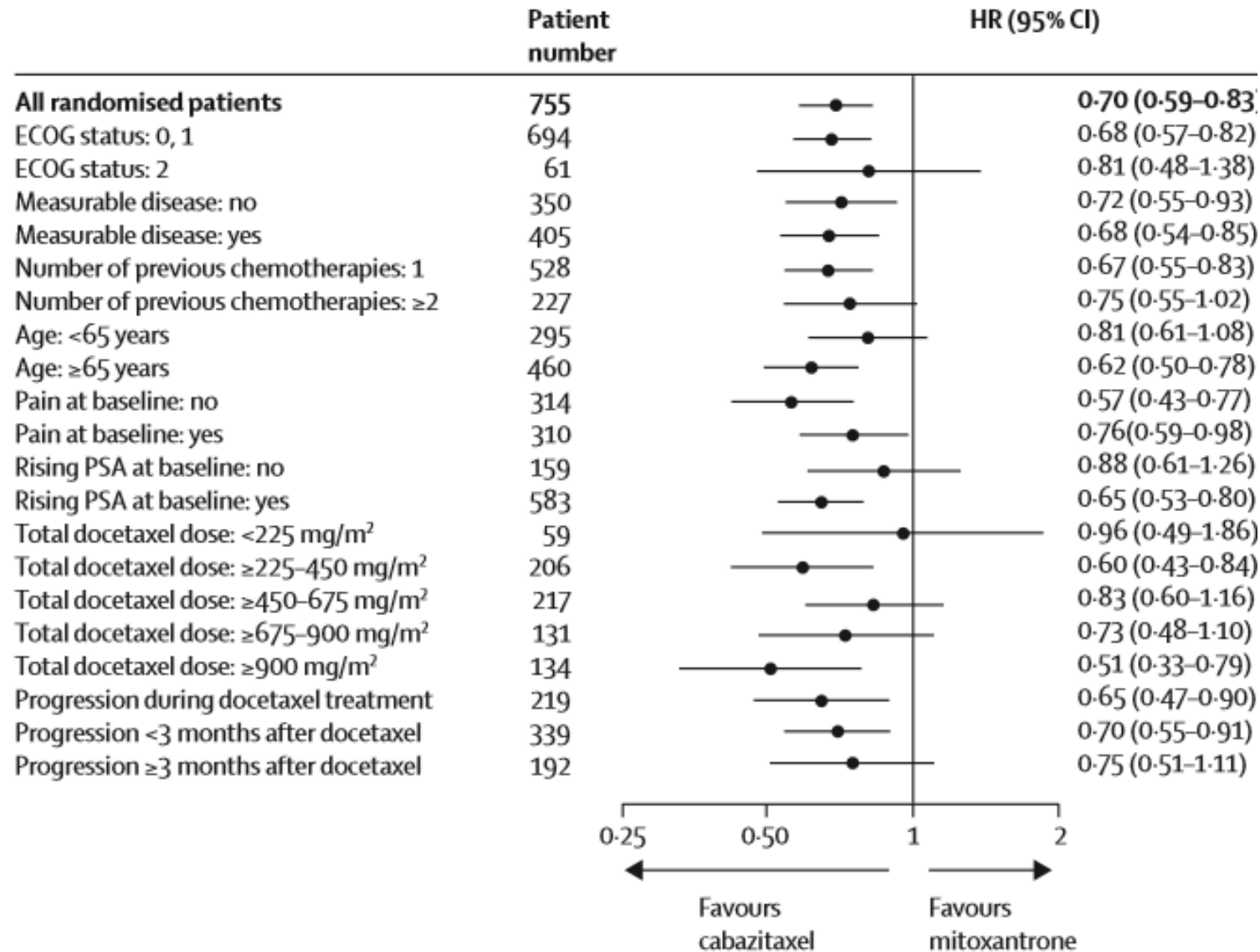
Number at risk		0	3	6	9	12	15	18	21
Mitoxantrone	377	115	52	27	9	6	4	2	
Cabazitaxel	378	168	90	52	15	4	0	0	

	Mitx	Caba
Median OS, mos	12.7	15.1
HR	0.72	
95% CI	0.61-0.84	
P value	< .0001	

	Mitx	Caba
Median PFS, mos	1.4	2.8
HR	0.74	
95% CI	0.64-0.86	
P value	< .0001	

Further-line mCRPC, *Evidences from the literature: Cabazitaxel*

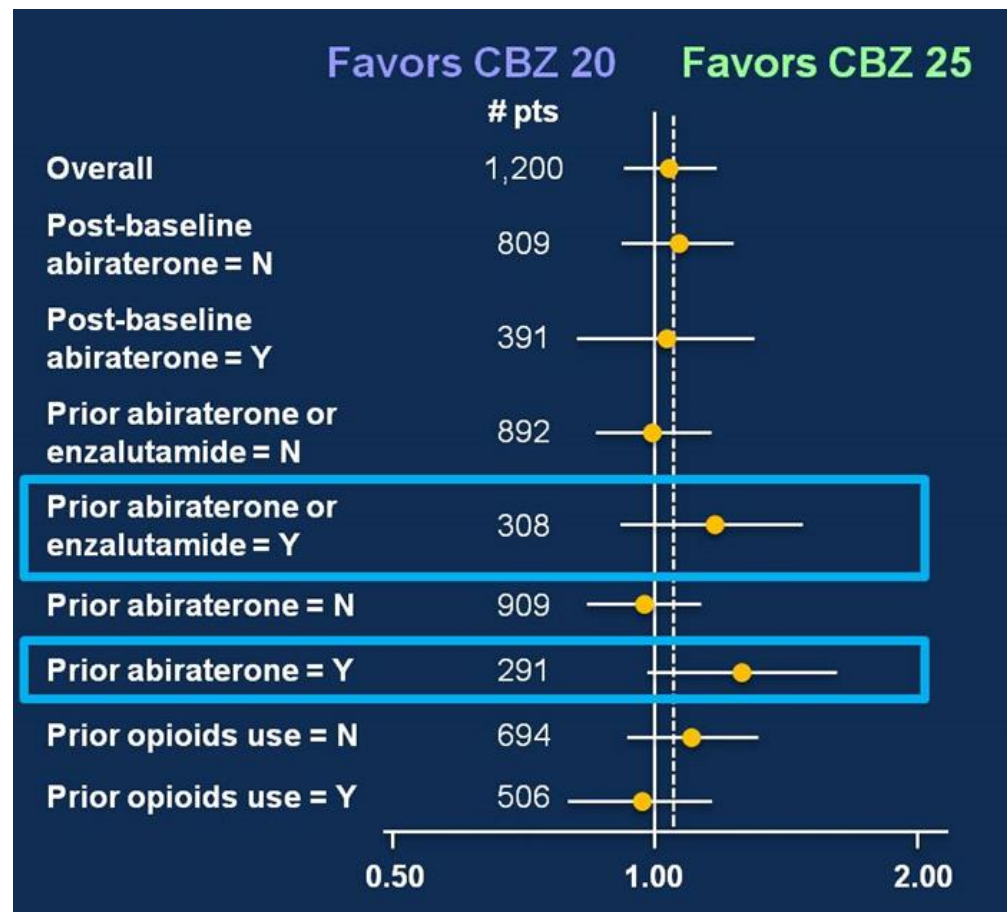
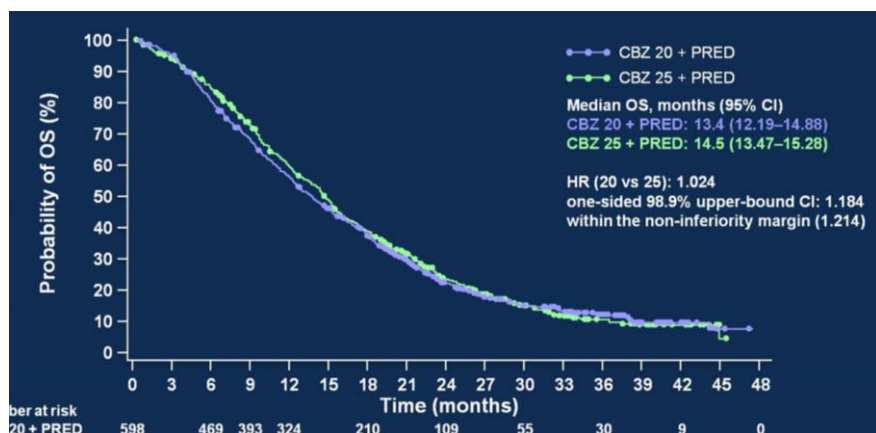
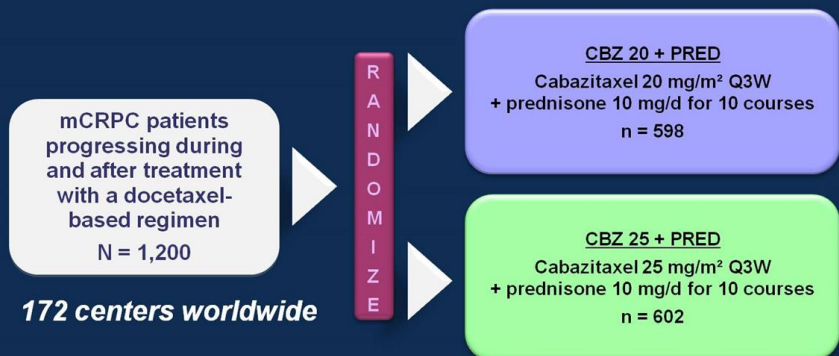
The TROPIC Trial: Population



Further-line mCRPC, *Evidences from the literature: Cabazitaxel*

What about cabazitaxel after ABI/ENZA?

PROSELICA: Study Design



Clinical case:

20 Apr 2016 PSA=6.3, **Starting abiraterone + prednisone**

27 Oct 2016 PSA=0,45

27 Oct 2016 Bone scan: SD

12 Apr 2017 PSA=0,78

04 Jul 2017 PSA=1,23

20 Jul 2017 Bone scan: SD

02 Aug 2017 CT scan: SD

02 Aug 2017 PSA=1.58, testosterone 45.8 ng/dl

Triptoreline 11.5 Q 12 wks → Leuprorelina 7,5 mg Q 4 wks

21 Sep 2017 PSA=1.39, testosterone 22.0 ng/dl

14 Nov 2017 PSA=1.99

11 Dec 2017 PSA=2.56, testosterone 27.0 ng/dl

07 Dec 2017 Bone scan: progression of disease

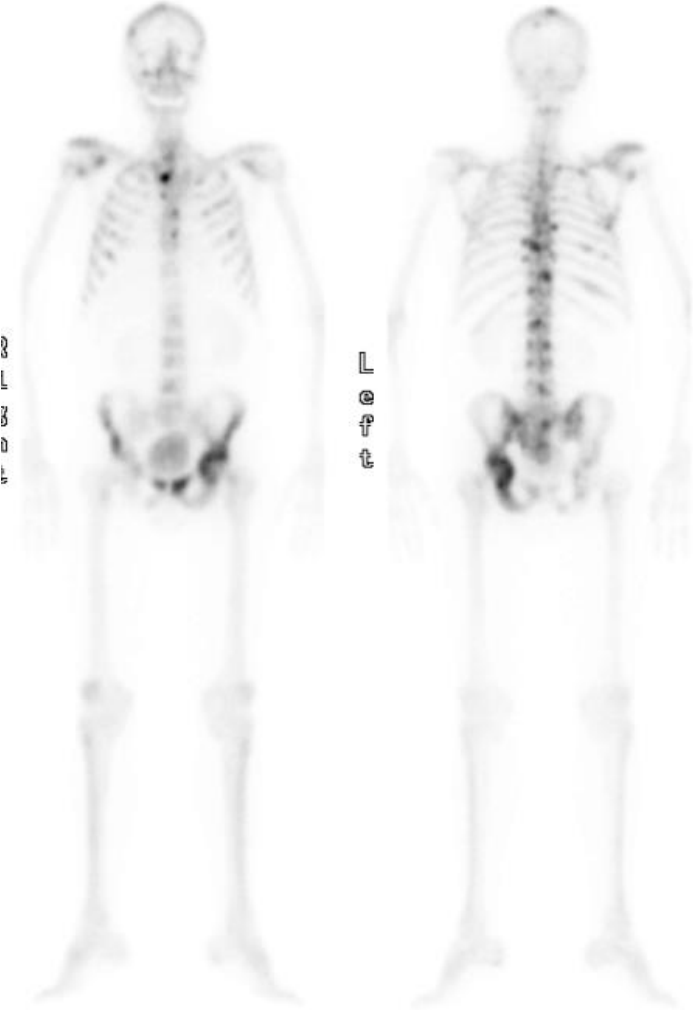
28 Dec 2017 CT scan: progression of the bone disease. Stable the lymph nodes (< 20 mm short axis) and the lung nodule.

Clinical case:

Ant

Post

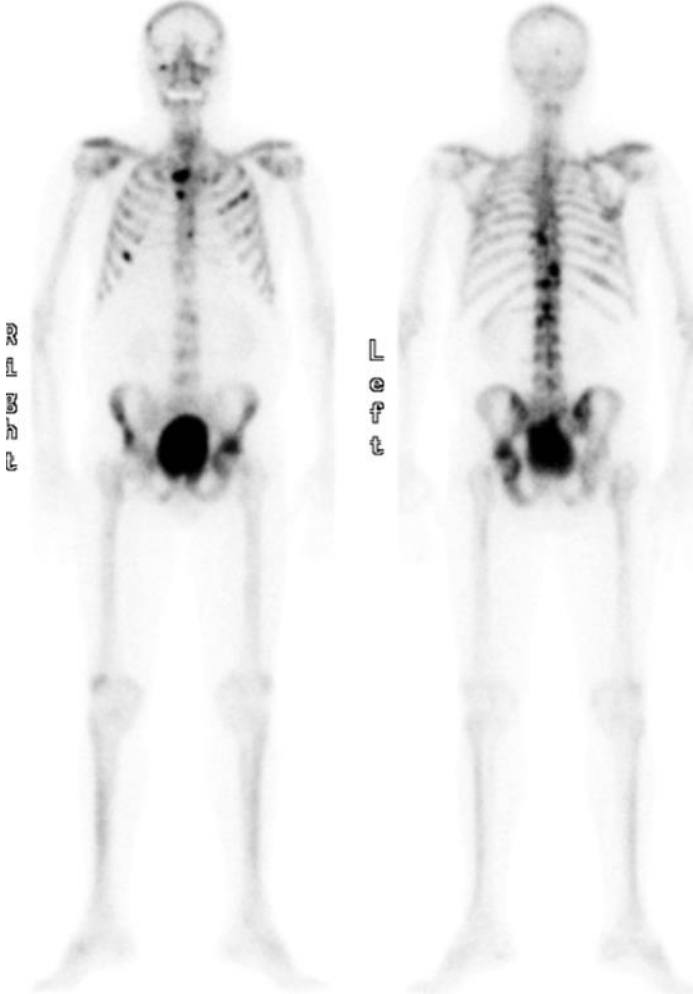
Apr 2016



Ant

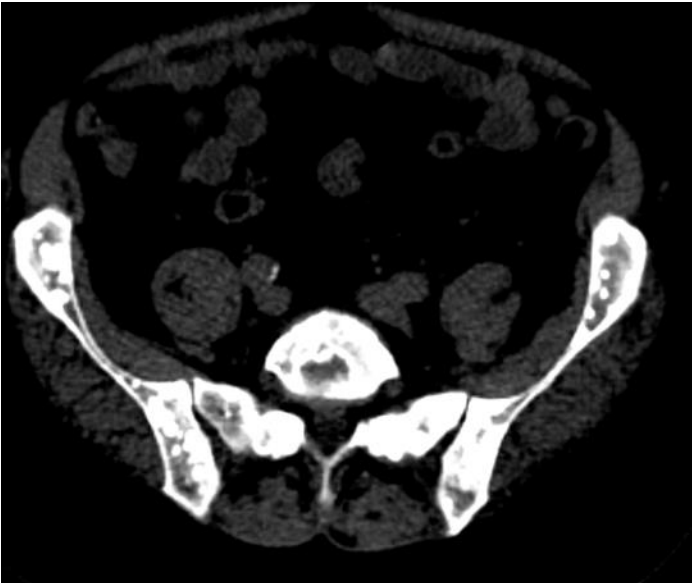
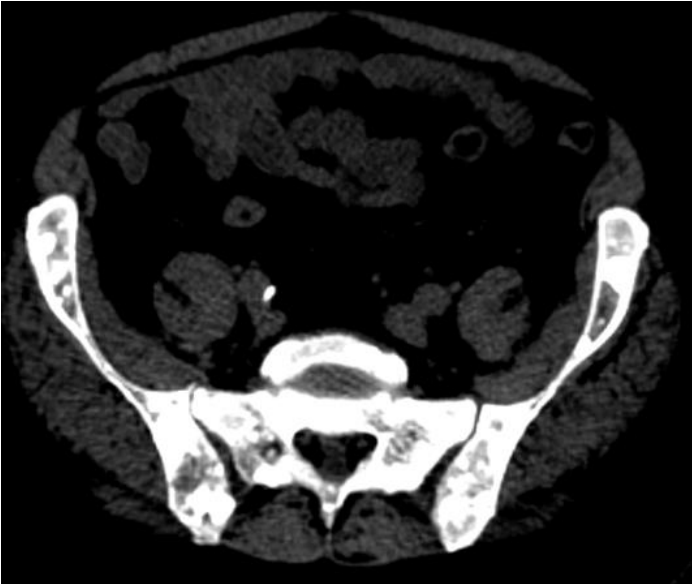
Post

Dec 2017



Clinical case:

Apr 2016



Dec 2017



Clinical case:

May 2003 Radical Prostatectomy

Mar 2013 Diagnosis of mHSPC → **ADT**

Jan 2015 Diagnosis of mCRPC → **Docetaxel** x 8 (end Jun 2015) (*TTP 15 months*)

Apr 2016 Progression of disease → **Abiraterone** until Dec 2017 (*TTP 20 months*)

10 Jan 2017 Patient status: 75 yo, ECOG=1, NRS=3/10, W 72 Kg.

Blood test	Value	Normal rage
Hemoglobin	11.5	13.5 – 17.5
PLT	305	150 - 400
Ca	8.7	8.4 – 10.4
ALP	265	50 - 130
PSA	5.7	

Clinical case:

What is the best treatment for this patients?

- Cabazitaxel 25 or 20 mg/m, 3 weekly
- Docetaxel 75 mg/m², 3 weekly (rechallenge)
- Enzalutamide
- Radium 223
- DNA repair defects screening (BRCA2, ATM)

Further-line mCRPC, *Evidences from the literature:*

Treatments sequence:

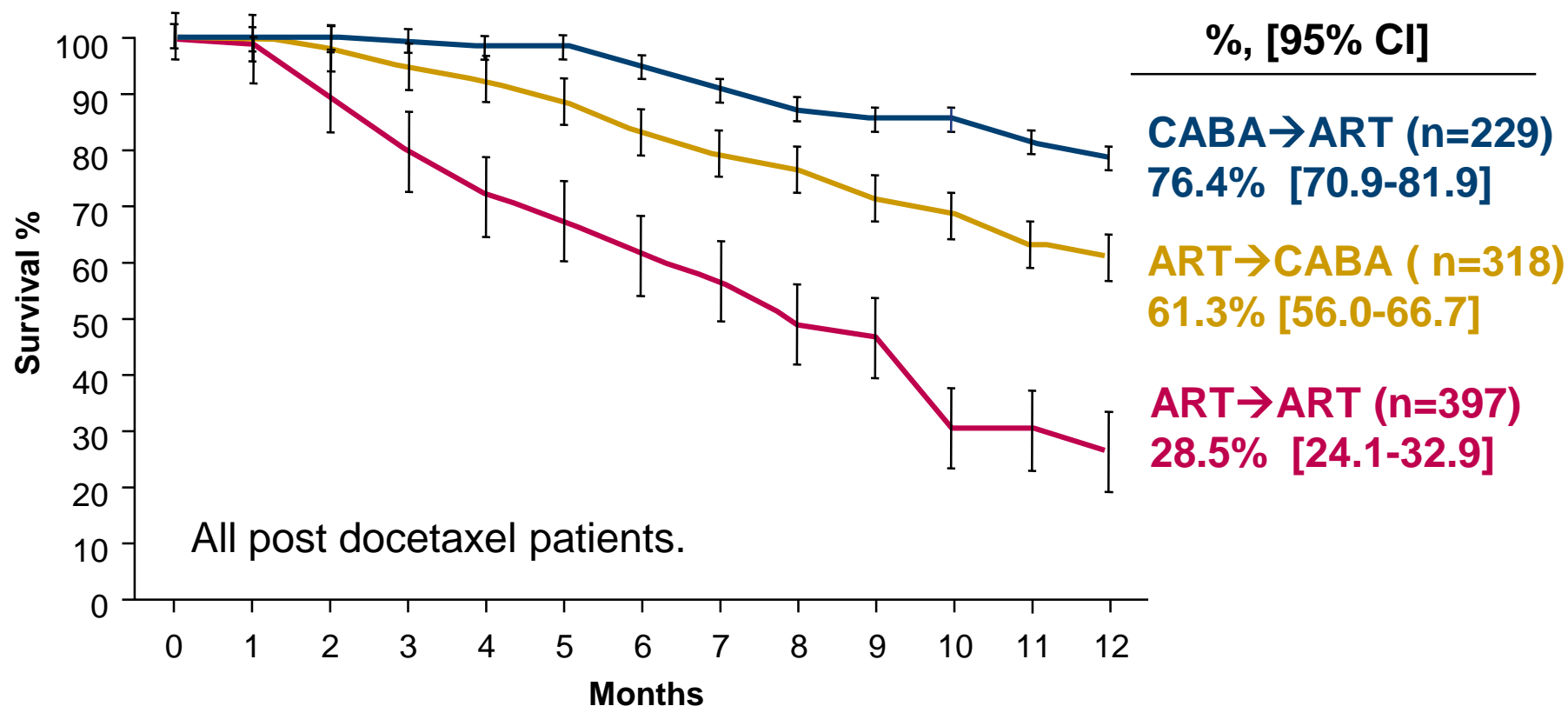
Table 3. Completed retrospective studies of sequencing abiraterone acetate and enzalutamide (Enza) in patients with metastatic castration-resistant prostate cancer in the post-chemotherapy setting.

Authors	Year published	Number of patients	Duration of second treatment	≥ 50% decline in PSA	Median PFS
Enzalutamide → Abiraterone Acetate					
Loriot <i>et al.</i>	2013	38	3 months	3%	2.7 months
Noonan <i>et al.</i>	2013	30	13 weeks	3%	3.8 months
Abiraterone Acetate → Enzalutamide					
Schrader <i>et al.</i>	2013	35	4.9 months	29%	
Badrising <i>et al.</i>	2014	61	3 months	21%	
Bianchini <i>et al.</i>	2014	39	2.9 months	23%	
Schmid <i>et al.</i>	2014	35	2.8 months	10%	
Brasso <i>et al.</i>	2014	137	3.2 months	18%	

AA: Abiraterone acetate; PFS: Progression-free survival; PSA: Prostate-specific antigen.

Further-line mCRPC, *Evidences from the literature:*

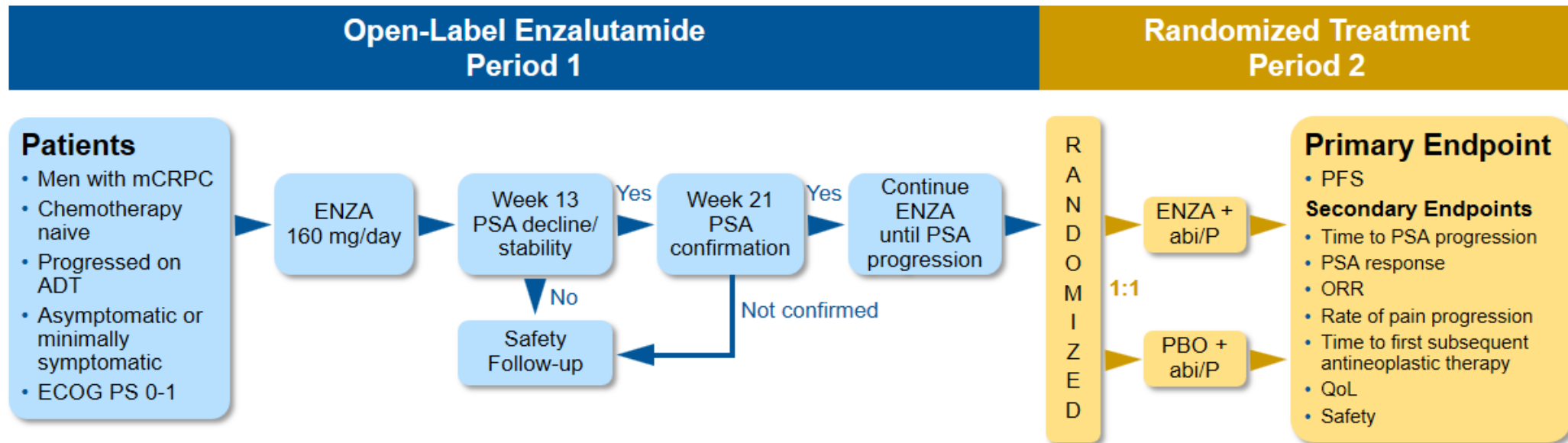
Treatments sequence: Systematic review of 13 published retrospective studies in mCRPC (n=1016) 12-month cumulative OS rate by sequence



ART: androgen receptor therapy; CABA: cabazitaxel.

Further-line mCRPC, *Evidences from the literature:*

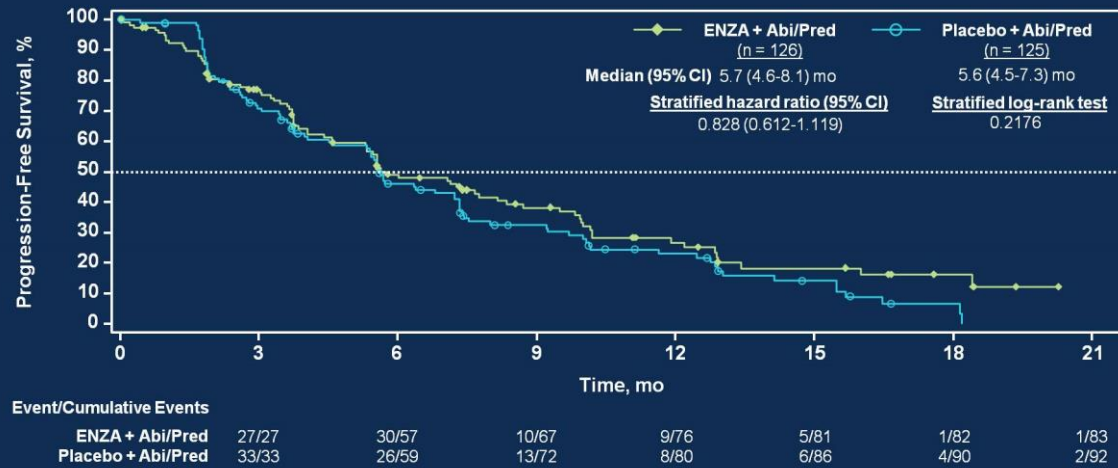
Treatments sequence: The PLATO Double-Blind, Placebo-Controlled, Two-Period Randomized Phase IV Trial (n=509)



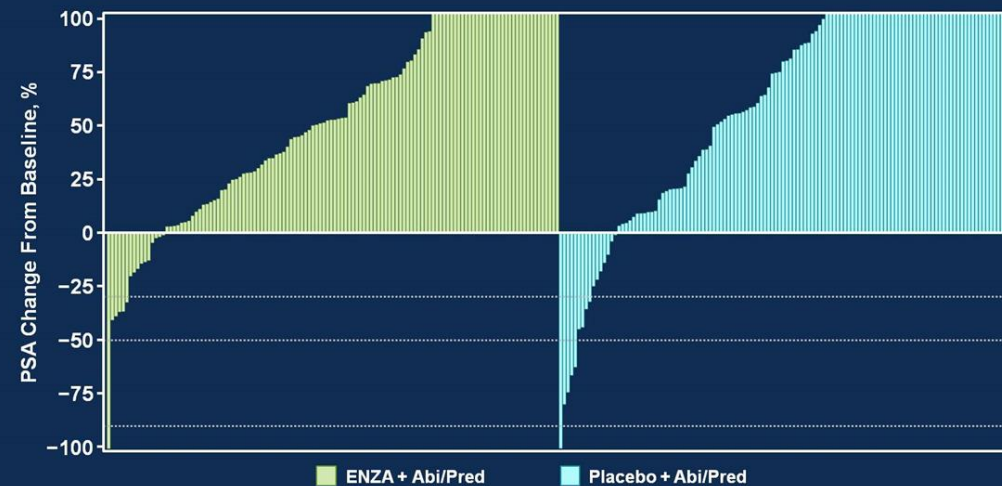
Further-line mCRPC, *Evidences from the literature:*

Treatments sequence: The PLATO Double-Blind, Placebo-Controlled, Two-Period Randomized Phase IV Trial (n=509)

Primary Endpoint: PFS



Best PSA Change From Baseline: Period 2

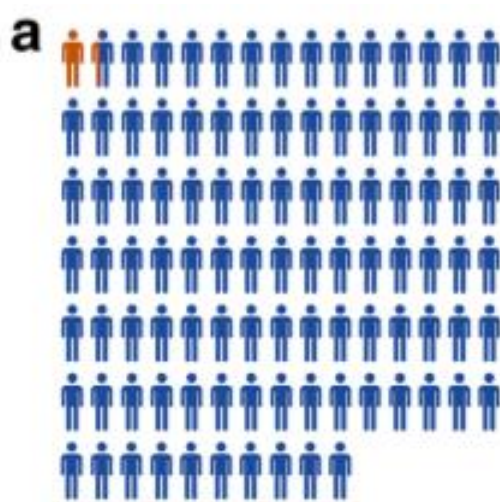


Attard G et al. *J Clin Oncol.* 2017;35 (suppl; abstr 5004).

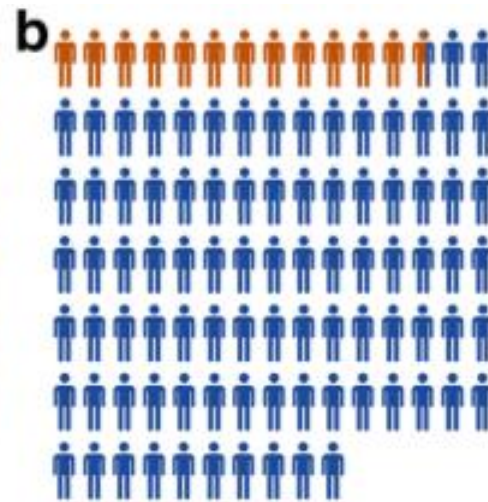
Further-line mCRPC, *Evidences from the literature:*

DNA repair defects

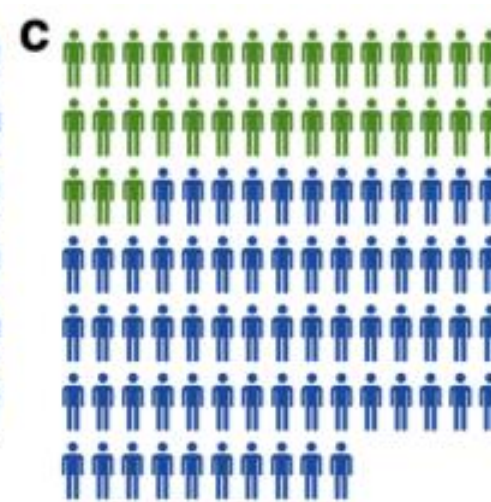
Incidence of BRCA Mutations:



1.2% in men with prostate cancer diagnosis before 65 years



12.7% in men with metastatic castration-resistant prostate cancer (mCRPC).



33% of DNA-repair defects was found in mCRPC if, in addition to BRCA2, other mutations were included, such as BRCA1, FANCA, ATM, CHEK2, PALB2, HDAC2, MLH3, ERCC3, MRE11 and NBN.



Thank you

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