II CURSO DE RESIDENTES DE SAOM

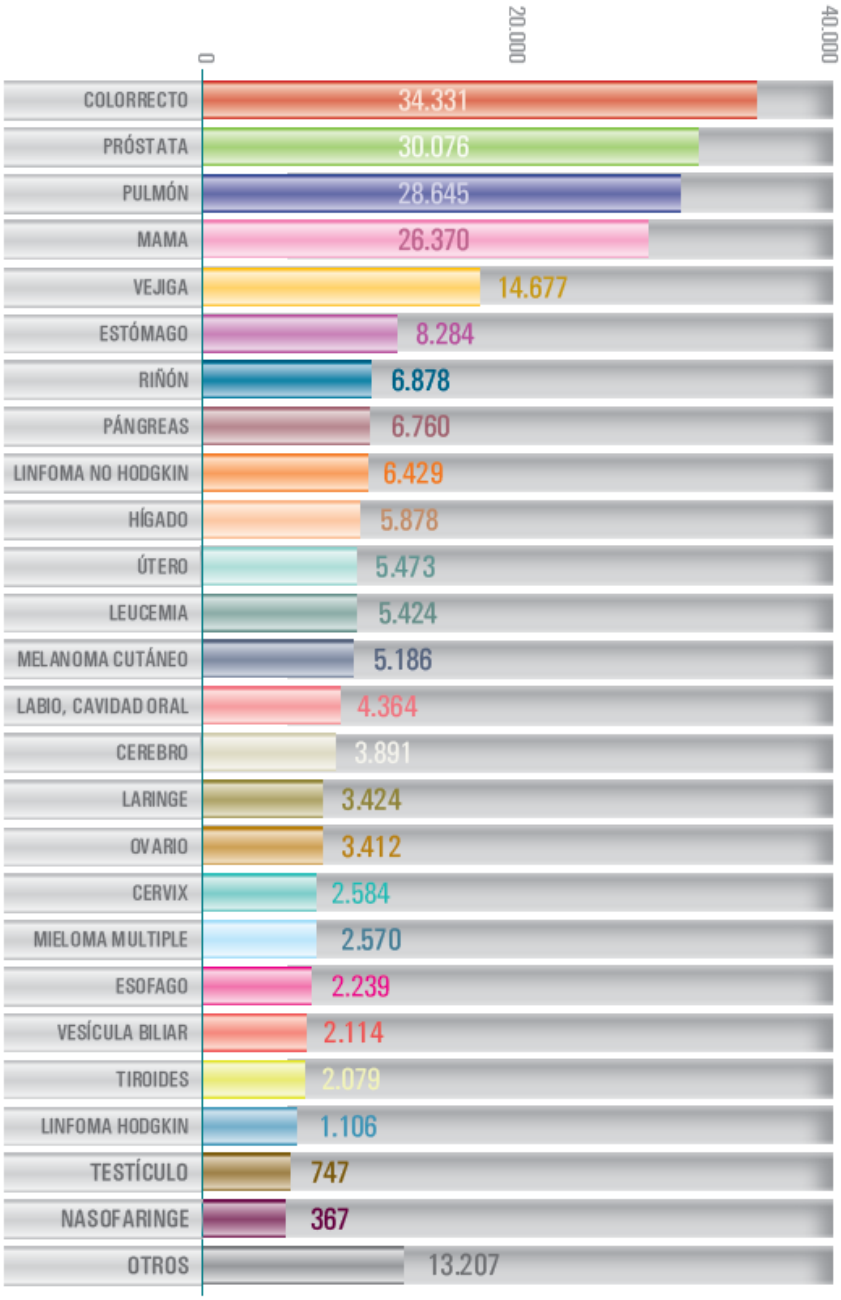
13 y 14 DE ABRIL 2018
GRANADA

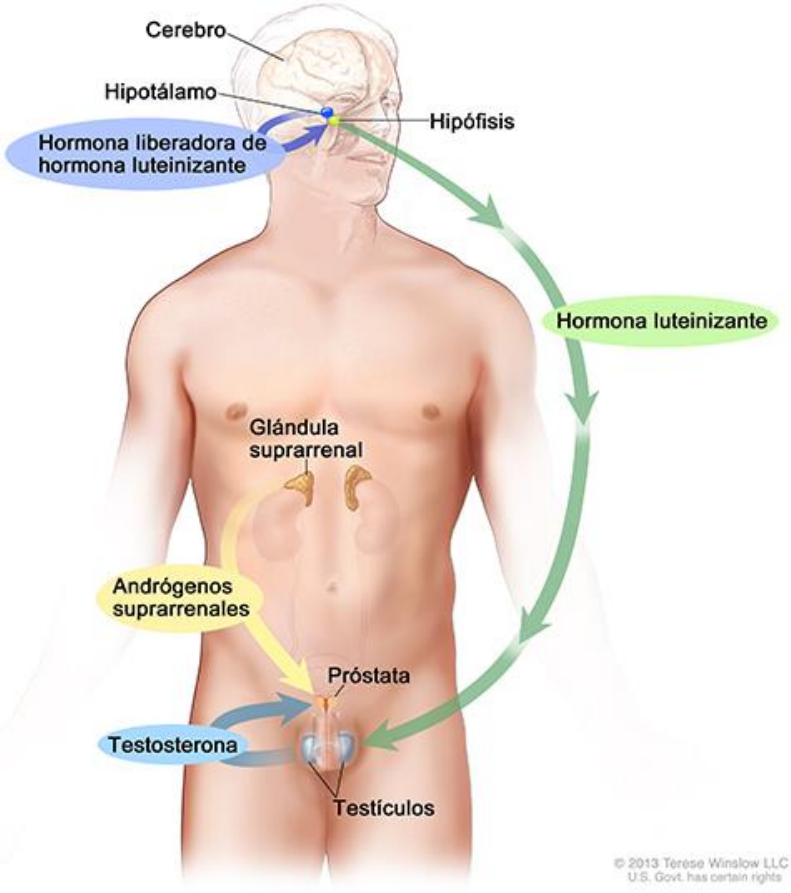
Organizado por:

SAOM
Sociedad Andaluza de Oncología Medica

TRATAMIENTO DEL CÁNCER DE PRÓSTATA RESISTENTE A CASTRACIÓN METASTÁSICO

CARMEN GARCÍA DURÁN
H.REINA SOFIA CÓRDOBA


0
20.000
40.000
COLORRECTO 34.331
PRÓSTATA 30.076
PULMÓN 28.645
MAMA 26.370
VEJIGA 14.677
ESTÓMAGO 8.284
RIÑÓN 6.878
PÁNGREAS 6.760
LINFOMA NO HODGKIN 6.429
HÍGADO 5.878
ÚTERO 5.473
LEUCEMIA 5.424
MELANOMA CUTÁNEO 5.186
LABIO, CAVIDAD ORAL 4.364
CEREBRO 3.891
LARINGE 3.424
OVARIO 3.412
CERVIX 2.584
MIELOMA MULTIPLE 2.570
ESOFAGO 2.239
VESÍCULA BILIAR 2.114
TIROIDES 2.079
LINFOMA HODGKIN 1.106
TESTÍCULO 747
NASOFARINGE 367
OTROS 13.207



Terapia de deprivación androgénica

CPRC: DEFINICIÓN

- Entidad clínica y biológica heterogénea.

- Progresión tumoral pese a mantener niveles de castración de andrógenos (testosterona <50ng/dl). La progresión puede ser:
  - Elevación de PSA
  - Presencia de metástasis.

CPRC: M0

Pacientes que tras elevación de PSA, no se evidencian nuevas lesiones de su enfermedad tumoral.

¿Qué se recomienda hacer?

CRPC: M0

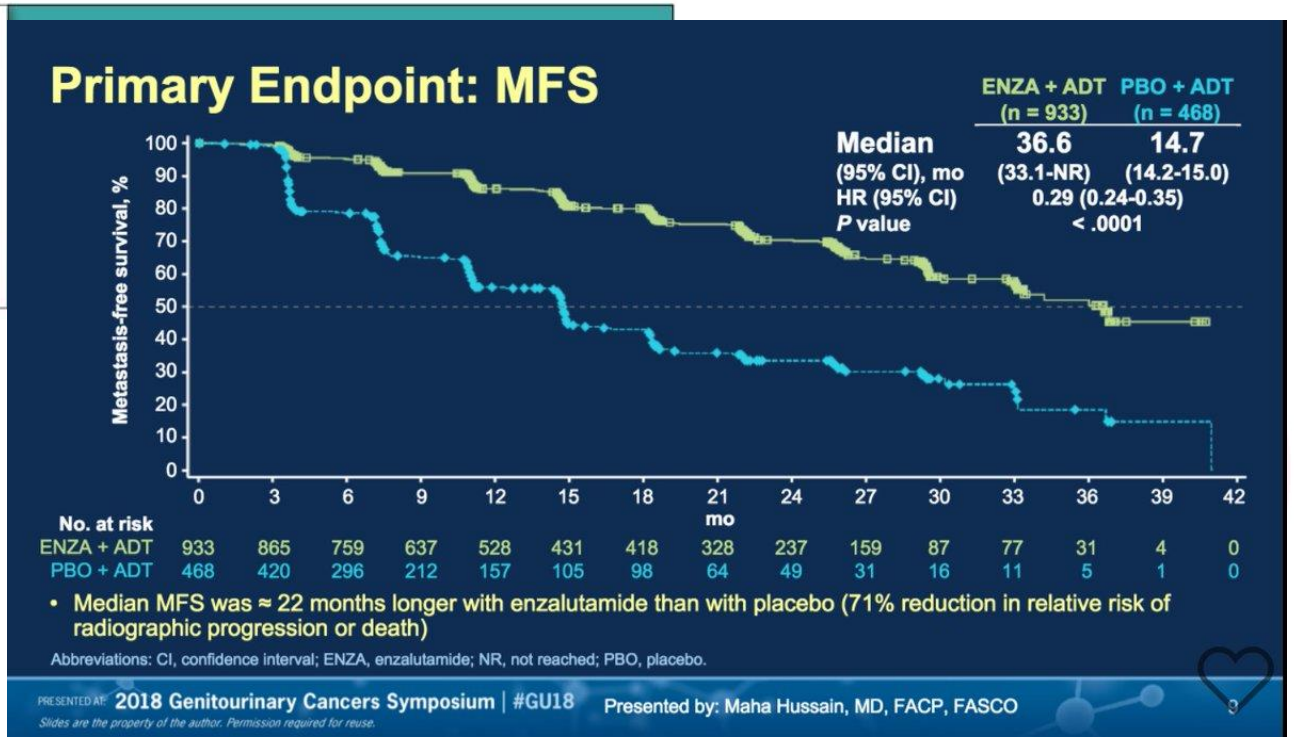
- Mantener tratamiento con ADT.
- Valorar el tiempo de doblaje del PSA:
  - Si más de 10 meses, observación y si se vuelve a elevar el PSA ➡ prueba de imagen
  - Si menos de 10 meses ➡ enzalutamida, apalutamida. Si se vuelve a elevar el PSA ➡ prueba de imagen

CRPC: M0

– Si menos de 10 meses ➡ enzalutamida apalutamida.
Si se vuelve a elevar el PSA ➡ prueba de imagen

PROSPER

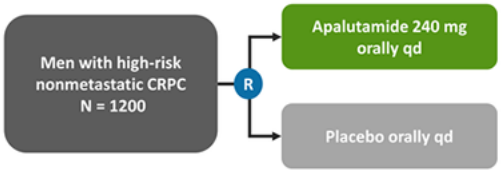
- ~1,560 non-metastatic CRPC patients
- Primary endpoint: MFS*
- 2 arm study: enzalutamide + continued ADT vs placebo + continued ADT



CPRC: M0

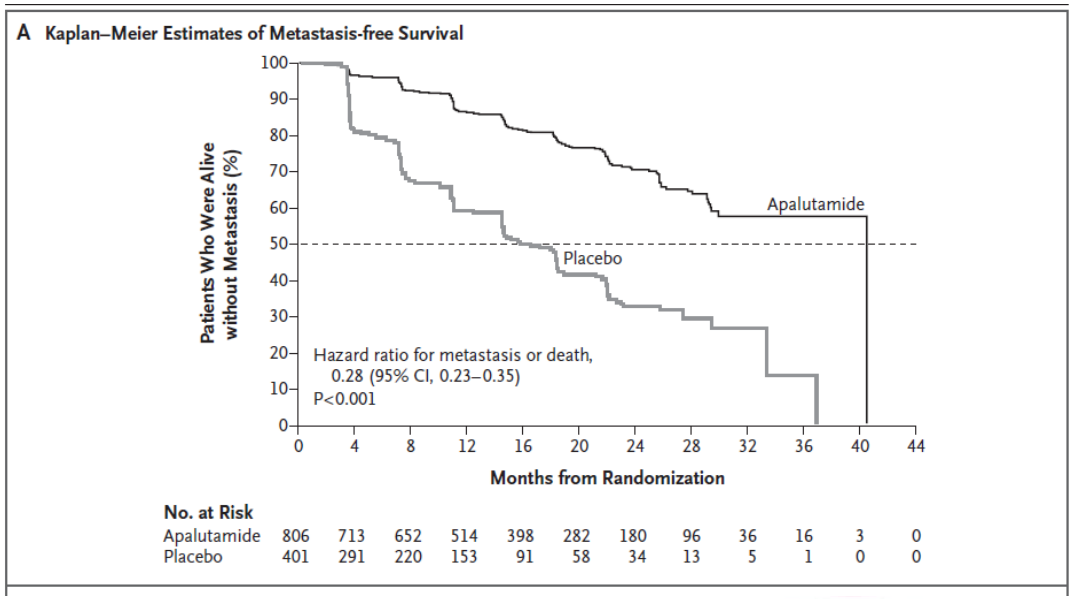
– Si menos de 10 meses ➡ enzalutamida apalutamida.
Si se vuelve a elevar el PSA ➡ prueba de imagen

SPARTAN
Randomized, Double-Blind, Phase 3 Trial of Apalutamide in Nonmetastatic CRPC



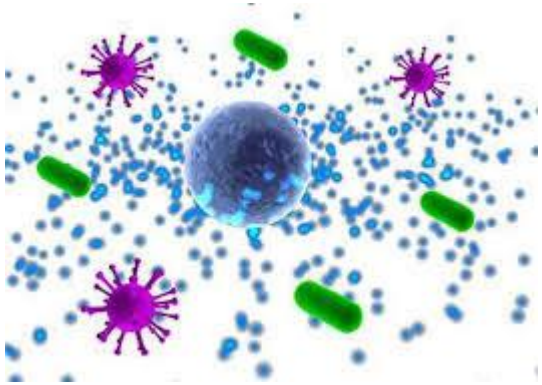
- **Primary endpoint**: metastasis-free survival
- **Secondary endpoints**: OS, time to symptomatic progression, time to first cytotoxic chemotherapy, PFS, time to metastasis, change in FACT-P and EQ-5D scores, AEs, pharmacokinetics

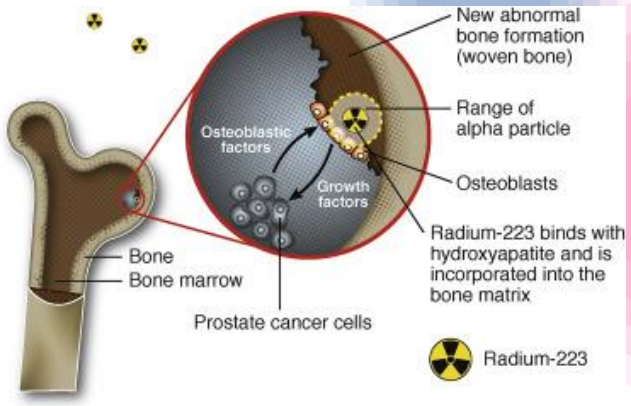
ClinicalTrials.gov. NCT01946204.



CPRC: M1


CYTOXAN
ADRIAMYCIN
DTIC-




New abnormal bone formation (woven bone)
Range of alpha particle
Osteoblastic factors
Growth factors
Osteoblasts
Radium-223 binds with hydroxyapatite and is incorporated into the bone matrix
Bone
Bone marrow
Prostate cancer cells
Radium-223

CPRC M1: DOCETAXEL

TAX-327 Study: Design

Stratification:

Pain level
PPI ≥2 or AS ≥10
vs.
PPI <2 or AS <10

KPS
≤70 vs. ≥80

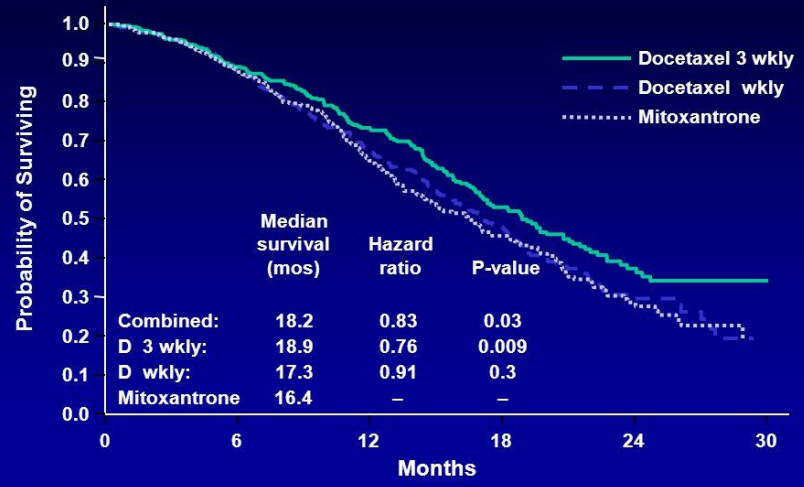
RANDOMIZATION

- Docetaxel 75 mg/m² q3 wkly + Prednisone 5 mg bid
- Docetaxel 30 mg/m² wkly 5 of 6 wks + Prednisone 5 mg bid
- Mitoxantrone 12 mg/m² q3 wkly + Prednisone 5 mg bid

Treatment duration in all 3 arms = 30 wks
n=1,006 patients

Tannock IF. N Engl J Med 2004;351:1502-1512.

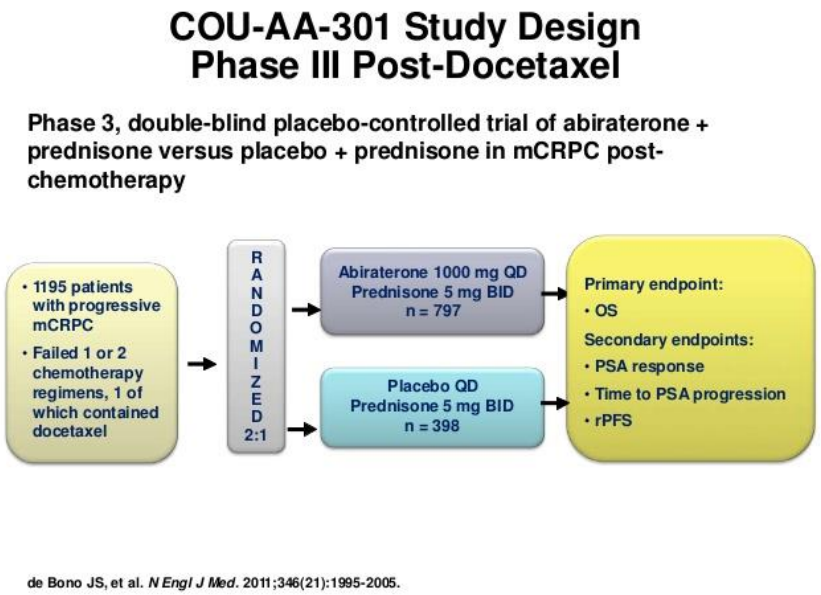
Docetaxel – CRPC
Overall Survival—TAX 327



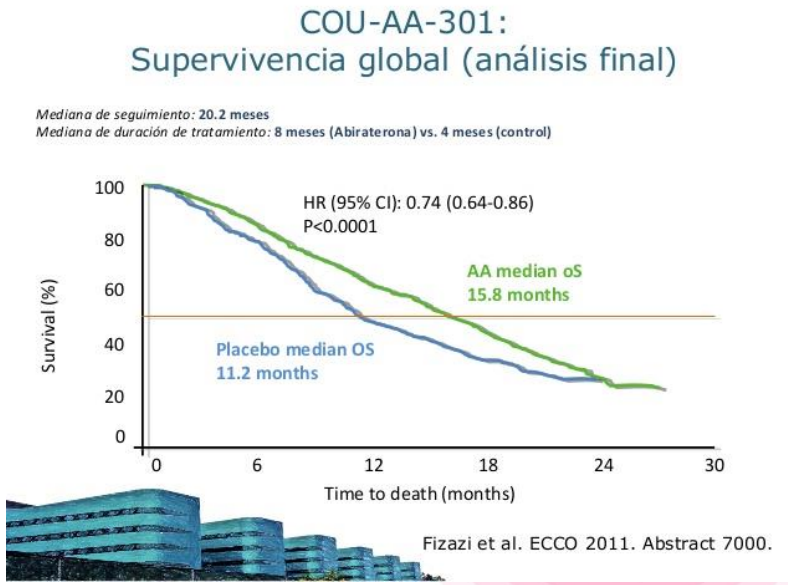
Eisenberger M, et al. ASCO Annual Meeting Proceedings. June 2004. Abstract 4.

CPRC M1: ACETATO DE ABIRATERONA

Inhibidor de la biosíntesis de andrógenos.

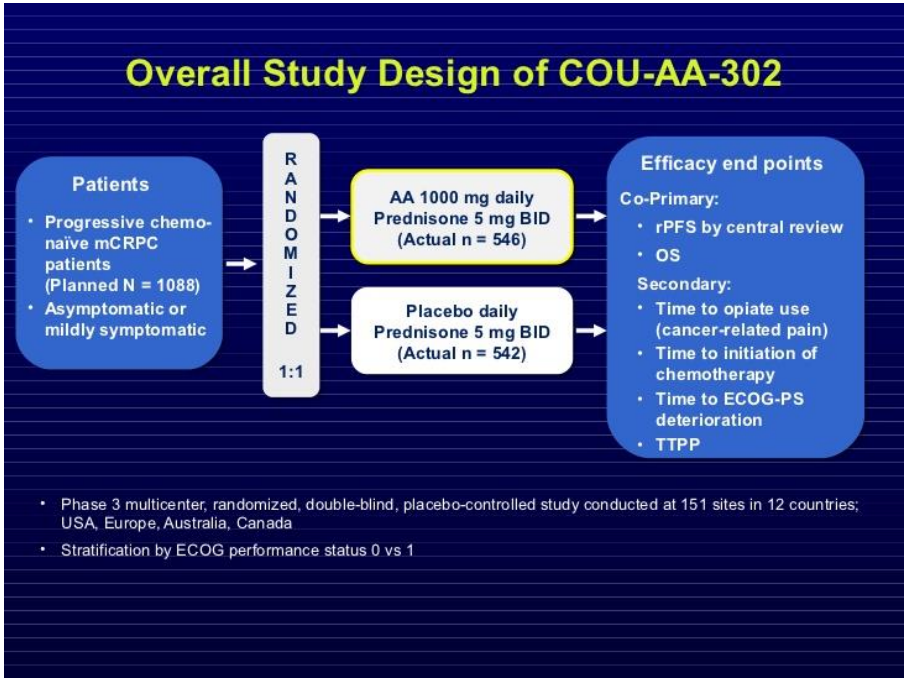


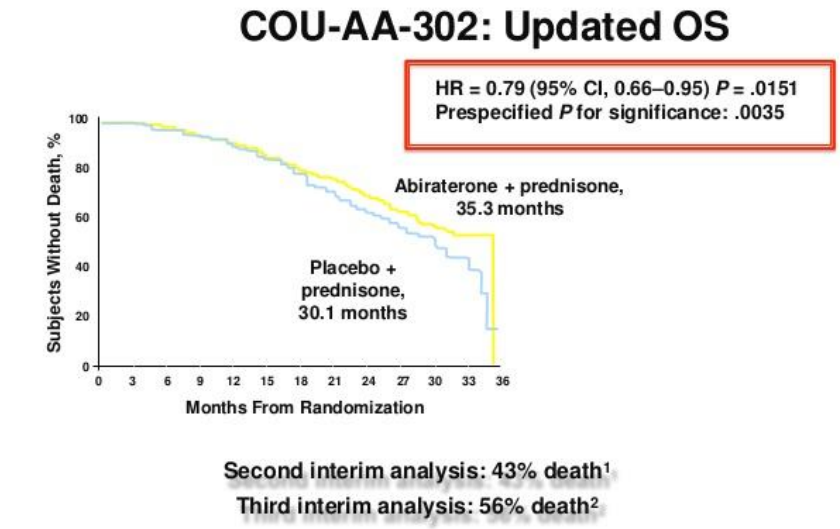
de Bono JS, et al. *N Engl J Med*. 2011;346(21):1995-2005.



Fizazi et al. ECCO 2011. Abstract 7000.

CPRC M1: ACETATO DE ABIRATERONA

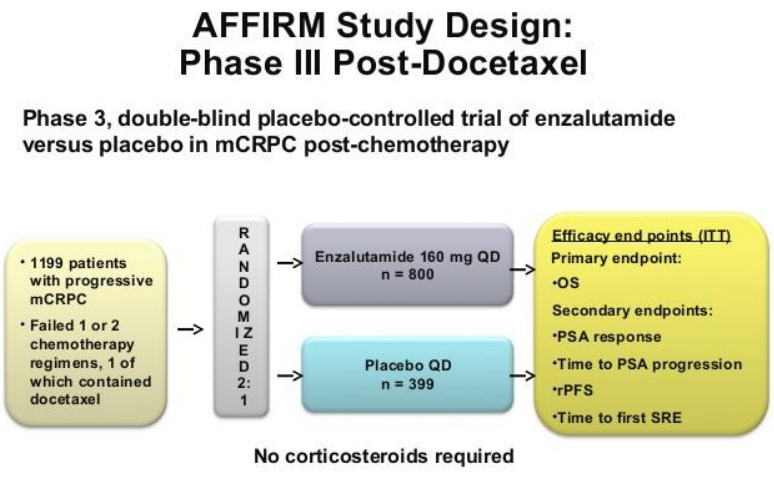




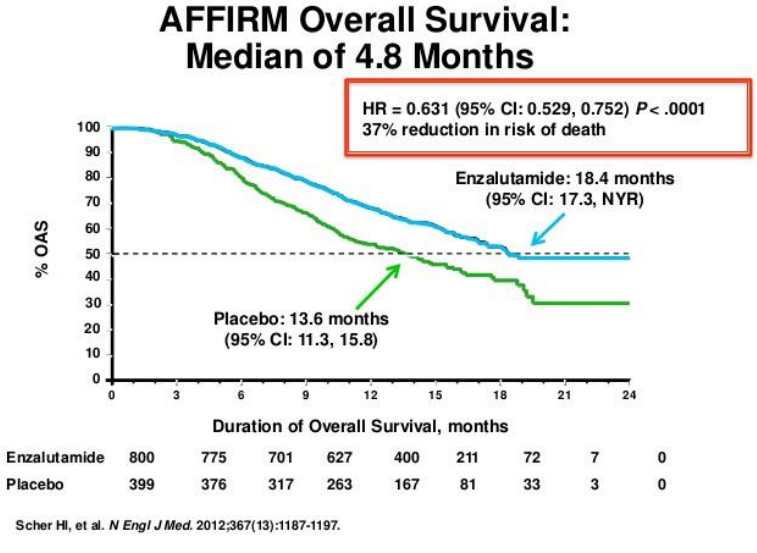
1. Ryan CJ, et al. *N Engl J Med*. 2013;368(2):138-148. 2. Rathkopf DE, et al. *J Clin Oncol*. 2013;31(Suppl 6): Abstract 5.

CPRC M1: ENZALUTAMIDA

Antagonista no-esteroideo de los receptores de andrógenos de segunda generación.



Scher HI, et al. *N Engl J Med.* 2012;367(13):1187-1197



Scher HI, et al. *N Engl J Med.* 2012;367(13):1187-1197.

CPRC M1: ENZALUTAMIDA

2014 Genitourinary Cancers Symposium
clinicaloptions.com/oncology
CLINICAL CARE OPTIONS ONCOLOGY

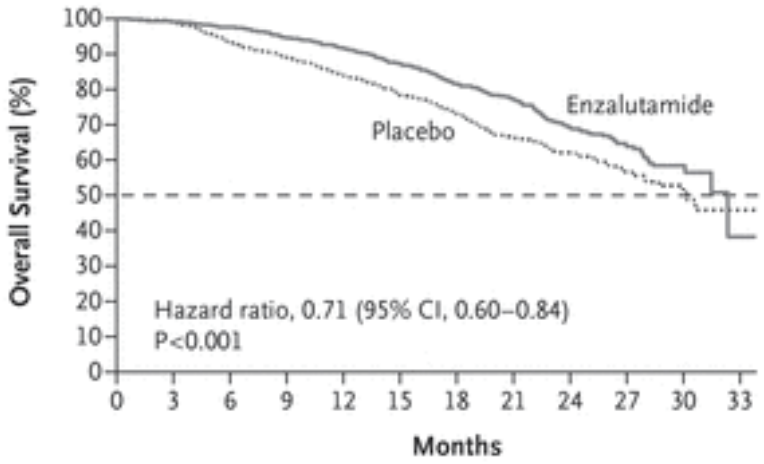
PREVAIL Phase III Trial: Enzalutamide After Progression in mCRPC

Patients with progressive mCRPC, asymptomatic/mildly symptomatic, chemotherapy naive, steroids allowed (N = 1717)

- Enzalutamide 160 mg/day (n = 872)
- Placebo (n = 845)

- Primary endpoints: OS, radiographic PFS

Beer T, et al. ASCO GU 2014. Abstract 1. ClinicalTrials.gov. NCT01212991.



No. at Risk												
Enzalutamide	872	863	850	824	797	745	566	395	244	128	33	2
Placebo	845	835	781	744	701	644	484	328	213	102	27	2

CPRC M1: CABIZATEXEL

Institut de cancérologie GUSTAVE ROUSSY VILLEJUIF - www.igr.fr

Cabazitaxel in Second-line CRPC TROPIC Study

mHRPC Progression after TXT

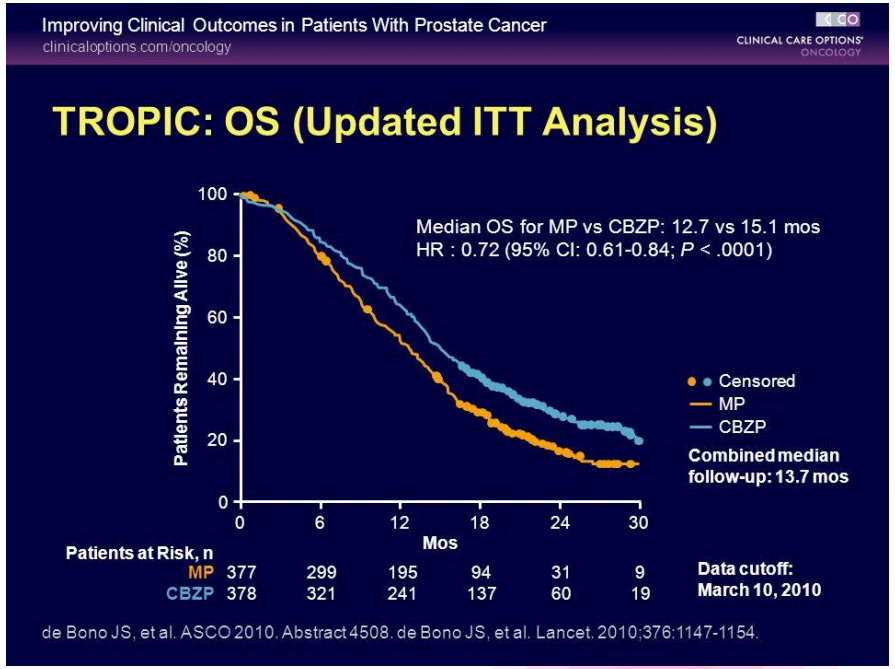
RANDOMIZE

360 pts
Cabazitaxel 25mg/m2 q3w
Prednisone 10mg qd

Mitoxantrone 12mg/m2 q3w
Prednisone 10mg qd
360 pts

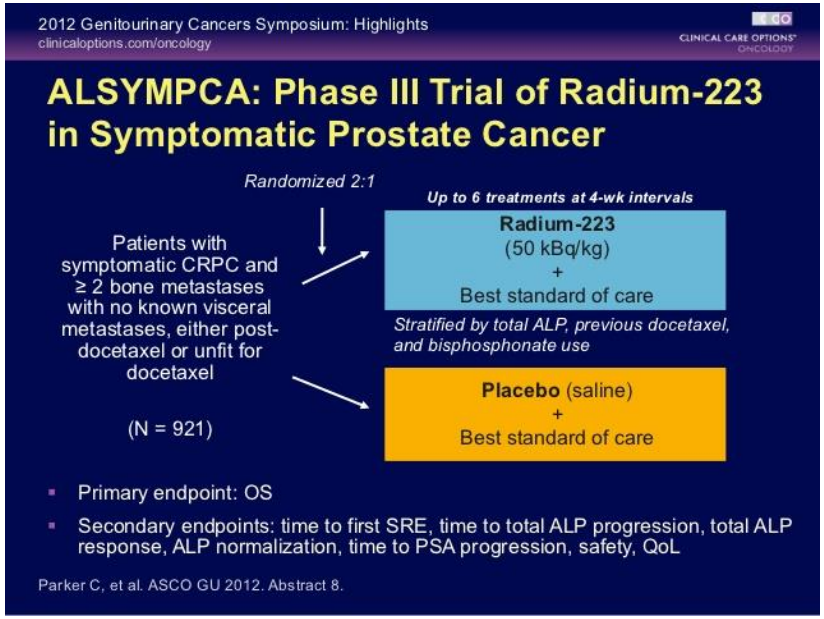
- *Stratification factor :*
  - ECOG PS (0,1 vs 2)
  - Mesurable/non_mesurable
- *Primary Endpoint:*
  - Overall survival
- *Secondary Endpoint:*
  - PSA response, PSA progression, PFS, RR, Pain progression, Safety, PK of cabazitaxel

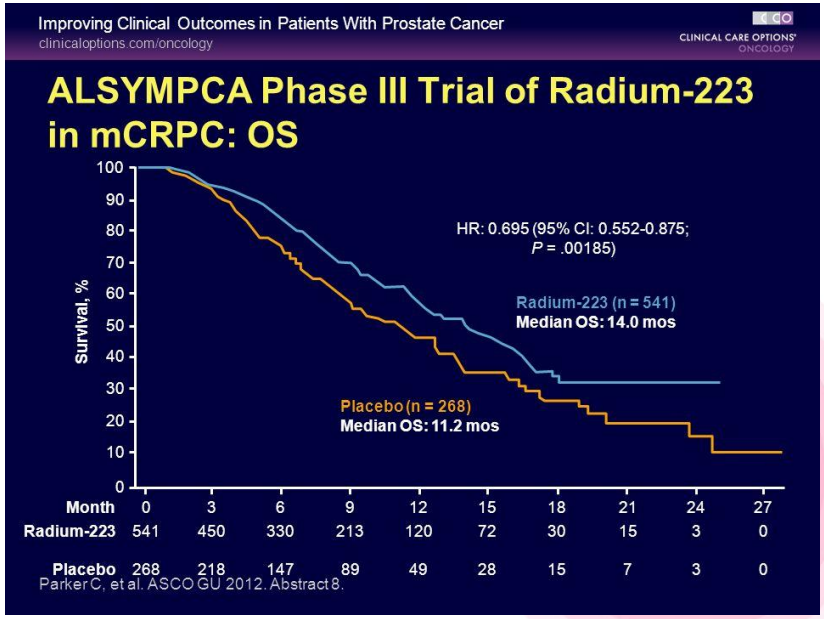
Enrollment closed: 745/720 pts
Hypothesis: Reduction of 25% in the risk of death or median OS=10.67 months for cabazitaxel vs 8 months
511 events, duration 36 months



CPRC M1: RADIUM 223

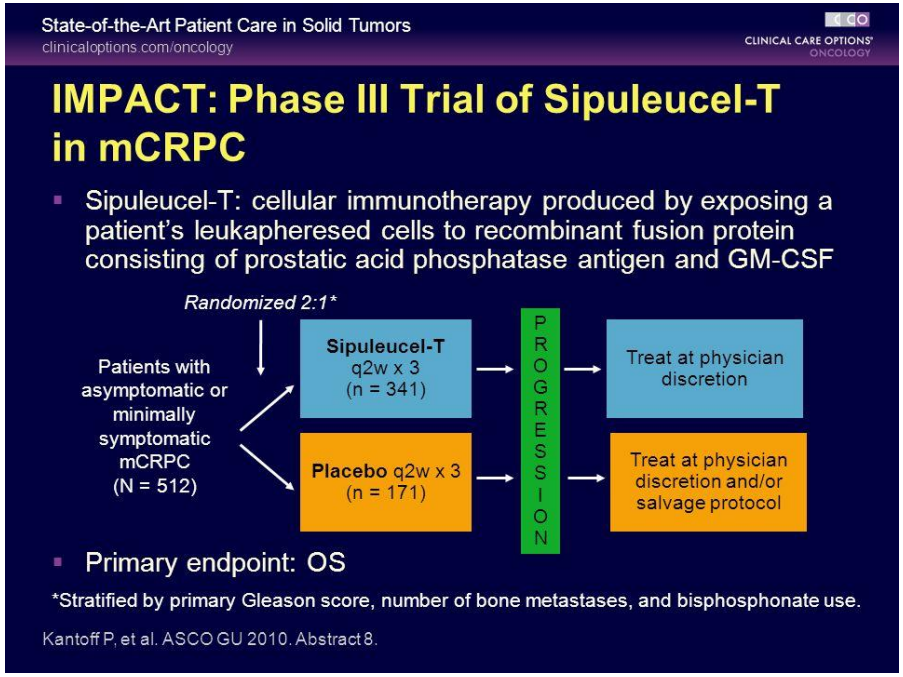
Es un agente terapéutico emisor de partículas alfas.

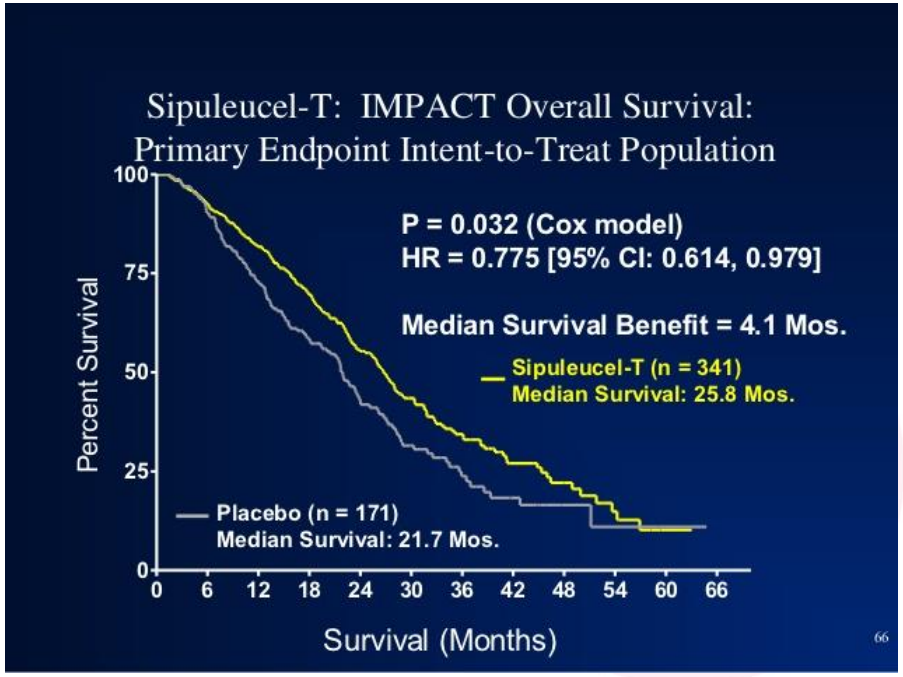




CPRC M1: SIPULEUCEL-T

Células mononucleares autólogas de sangre periférica activadas con FAP-GM-CSF

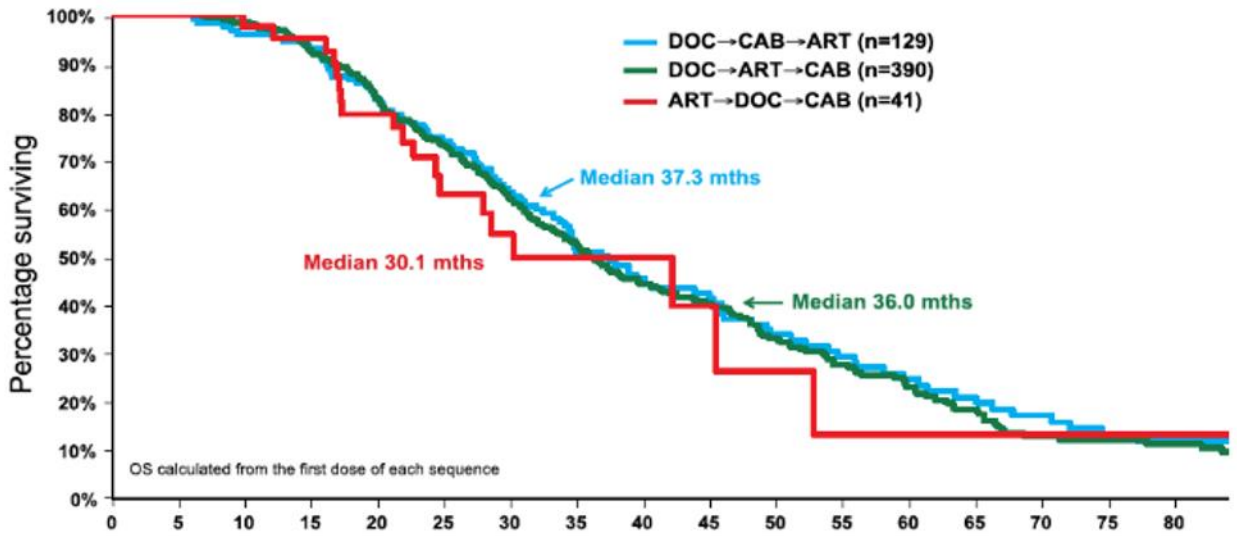




ESTUDIO	COU-AA-301	COU-AA-302	AFFIRM	PREVAIL	TAX-327	TROPIC	ALSYMPCA
Fármaco	Abiratero-na	Abiratero-na	Enzalutami-da	Enzalutami-da	Docetaxel	Cabizataxel	Radium-223
Estado sintomáti-co	Sintomáti-co	Mínima-mente sintomáti-co	Sintomát-ico	Mínima-mente sintomáti-co	Sintomáti-cos	Sintomáti-cos	Mínima-mente sintomáti-co
Enferme-dad visceral	Permitada	Excluida	Permitada	Permitida	Permitida	Permitada	Excluida
OS	14,8m vs 10,9m	35,3m vs 30,1m	18,4m vs 13,6m	32,4m vs 30m	18,9m vs 16,4m	15,1m vs 12,7m	14m vs 11,2m
Hazard ratio	0,74	0,79	0,63	0,71	0,76	0,72	0,69

NO EXISTE UNA SECUENCIA ÓPTIMA DE TRATAMIENTO.

CATS study: retrospective, multinational study of sequences



Angelergues A, et al. ESMO 2016

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
Enza → AA					
Loriot *et al.* [51]	2013	38	3 months	3%	2.7 months
Noonan *et al.* [52]	2013	30	13 weeks	3%	3.8 months
AA → Enza					
Schrader *et al.* [53]	2013	35	4.9 months	29%	
Badrising *et al.* [54]	2014	61	3 months	21%	
Bianchini *et al.* [55]	2014	39	2.9 months	23%	
Schmid *et al.* [56]	2014	35	2.8 months	10%	
Brasso *et al.* [57]	2014	137	3.2 months	18%	

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

Retrospective trials based on a small number of patients

Zhang T et al. *Expert Opin Pharmacother.* 2014;16:1–9.

- **Mezynski**[2]: ABI→DOC (N=35); 2nd line therapy in pts with visceral mets:
  - PSA decline ≥50%= 26%
  - Median OS 12.5 mo
- **Schweizer**[3]: ABI→DOC (N=24); 2nd line therapy in pts with visceral mets:
  - PSA decline ≥50%= 38%
- **Azad**[4] : ABI→DOC (N=86); 2nd line therapy in pts with visceral mets:
  - PSA decline ≥50%= 35%
  - Median OS 11.7 mo
- **de Bono**[5]: ABI→DOC (N=100) 2nd line therapy in pts without visceral mets:
  - PSA decline ≥50%= 27%

**Retrospective studies in small number of patients.*

- No existe una clara secuencia de tratamiento.
- No hay estudios randomizados y prospectivos que comparen docetaxel, abiraterona ni enzalutamida.
- Hay que individualizar en cada paciente de acuerdo a su ECOG, carga tumoral, síntomas…

recommendations

- Abiraterone or enzalutamide are recommended for asymptomatic/mildly symptomatic men with chemotherapy-naïve metastatic CRPC [I, A].
- Radium-223 is recommended for men with bone-predominant, symptomatic metastatic CRPC without visceral metastases [I, A].
- Docetaxel is recommended for men with metastatic CRPC [I, A].
- Sipuleucel-T is an option in asymptomatic/mildly symptomatic patients with chemotherapy-naïve metastatic CRPC [II, B].

II CURSO DE RESIDENTES DE SAOM
GRANADA, 13 y 14 DE ABRIL 2018
Organizado por:
SAOM
Sociedad Andaluza de Oncología Médica

¿Qué papel juegan estos fármacos en el CPHS?

ESTUDIO CHARTEED

CHAARTED:
diseño del estudio de TDA más docetaxel

Cáncer de próstata ECOG 0-1-2; enfermedad metastásica (790 pacientes)

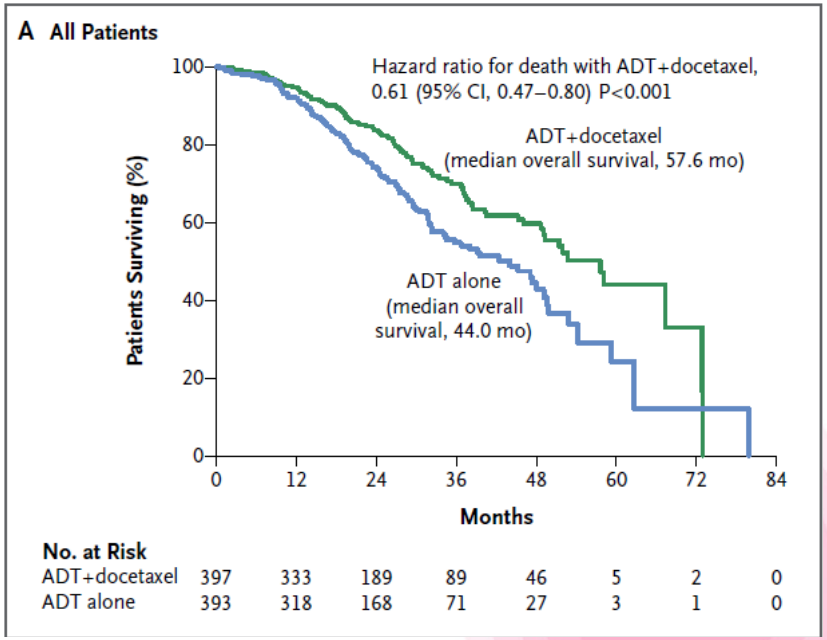
- **GRUPO A:** bloqueo androgénico + docetaxel, 75mg/m2 cada 21 días, máx. 6 ciclos
- **GRUPO B:** bloqueo androgénico

Alta carga tumoral: enfermedad visceral, > 4 lesiones metastásicas y 1 lesión fuera del esqueleto apendicular

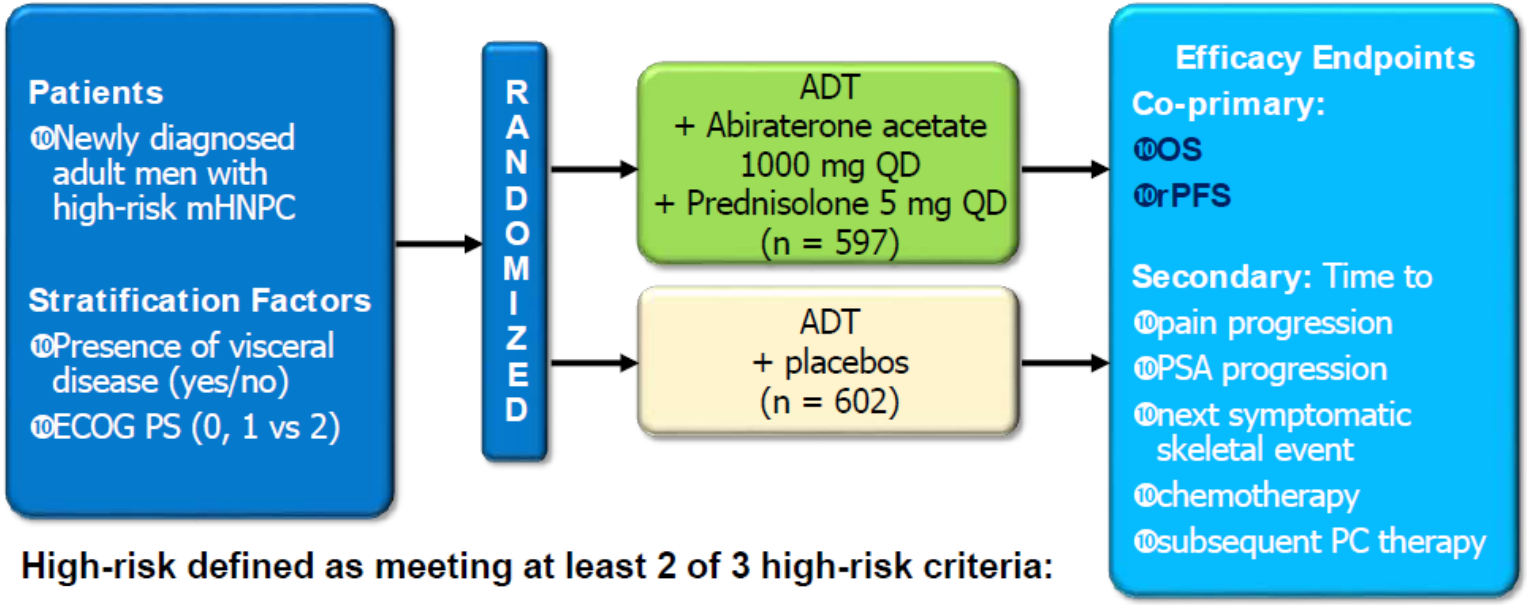
El 65 % de los pacientes tenía un alto volumen de metástasis

Seguimiento de 28,9 meses

Sweeney, C. J. *et al.: N Engl J Med.* 2015;373:737-746.



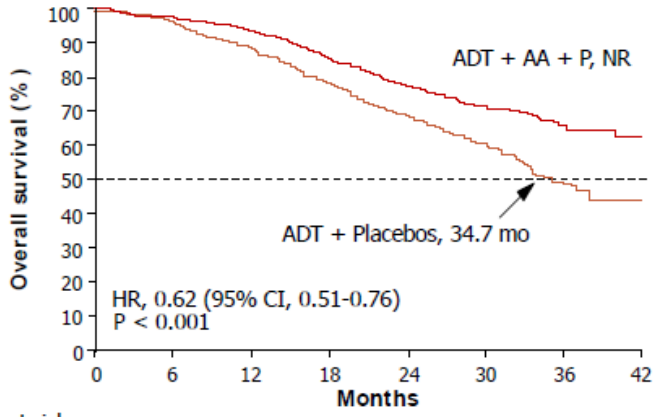
LATITUDE: Phase III Trial of Abiraterone in patients with newly diagnosed metastatic prostate cancer (n=1,199)



High-risk defined as meeting at least 2 of 3 high-risk criteria:

LATITUDE: Co-primary End Points

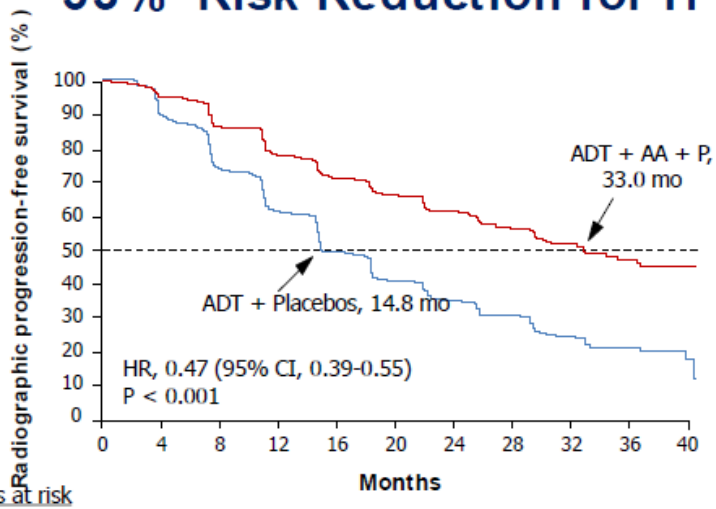
38% Risk Reduction for Death



Patients at risk

ADT + AA + P	597	565	529	479	388	233	93	9
ADT + Placebos	602	564	504	432	332	172	57	2

53% Risk Reduction for rPFS



Patients at risk

ADT + AA + P	597	533	464	400	353	316	251	177	102	51	21
ADT + Placebos	602	488	367	289	214	168	127	81	41	17	7

Fizazi K, et al. N Engl J Med. 2017;377:352-360. CI, confidence interval; HR, hazard ratio; NR, not reached.

CONCLUSIONES

- Se debe mantener con ADT.
- No existe una secuenciación clara de tratamiento, hay que individualizar a cada paciente.
- En pacientes CPCR M0, con tiempo de doblaje de PSA <10 meses, se valorará el uso de enzalutamida/apalutamida.
- Actualmente existen 4 opciones en 1ª línea: docetaxel, enzalutamida, abiraterona o Radium-223.
- CPRC M1 sintomático, valorar el uso de docetaxel.