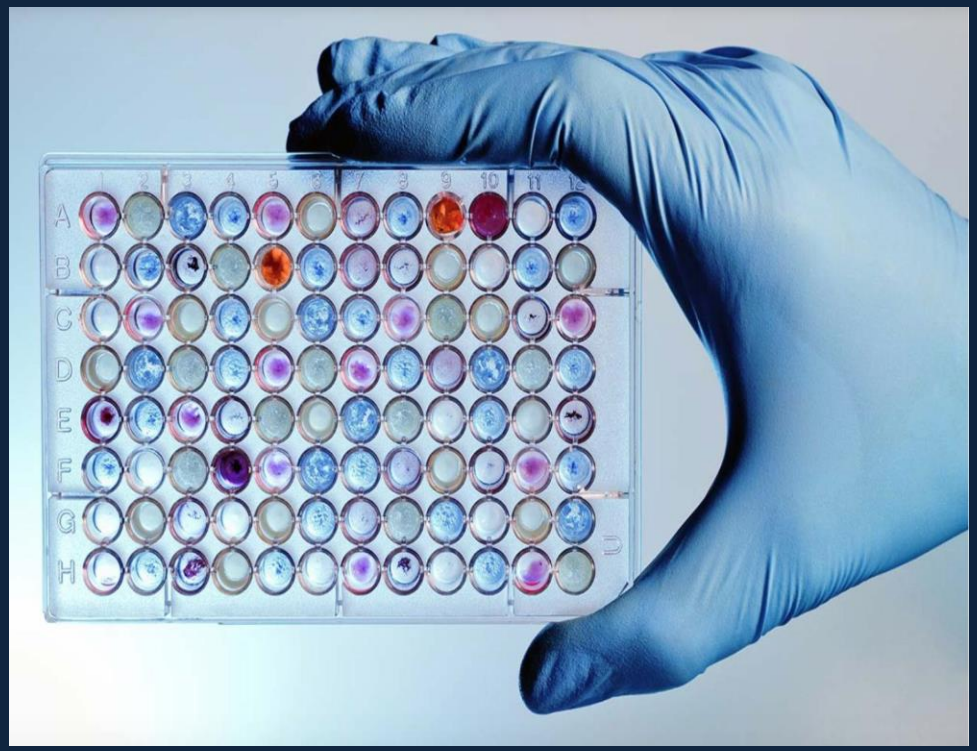
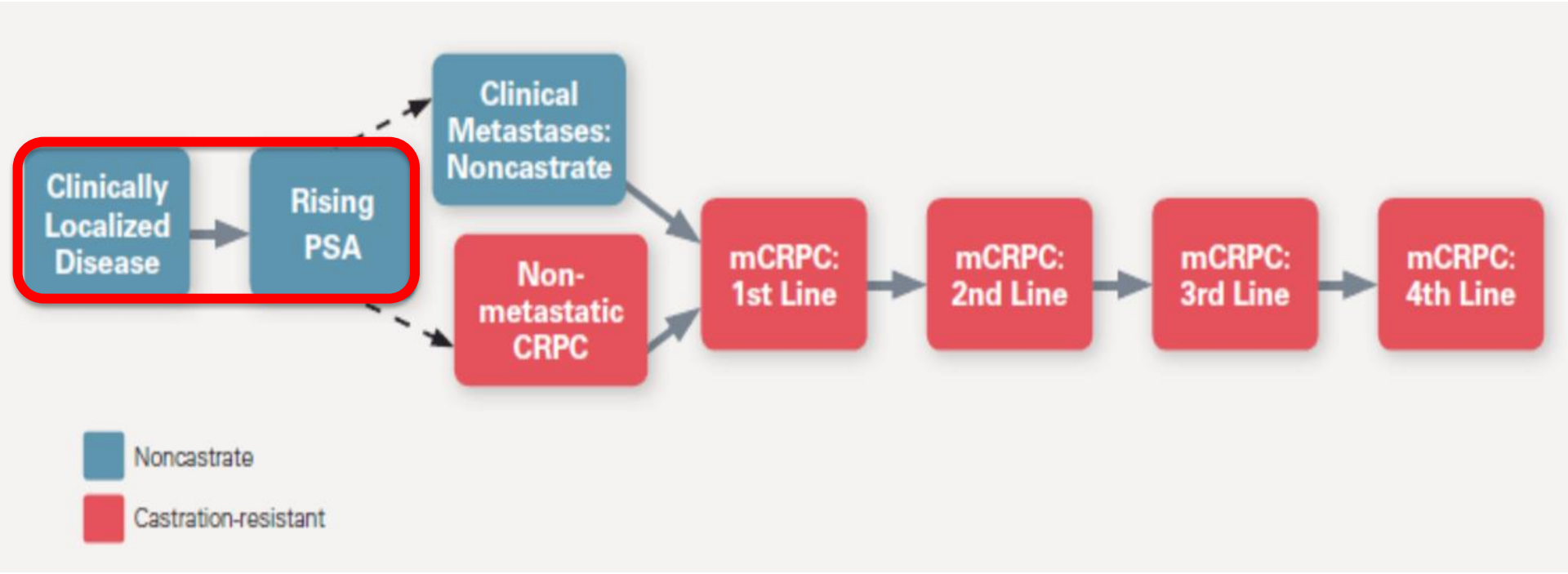
HOW TO MANAGE PROSTATE CANCER IN 2023

Ana Plata Bello
Médico Adjunto CHUC



PROSTATE CANCER IN 2023

1. New developments in High Risk localised PC & BCR setting



ADT have been the gold standard treatment in **ADVANCED NON METASTATIC RECURRENT PC**

1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING

Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

Gerhardt Attard, Laura Murphy, Noel W Clarke, William Cross, Robert J Jones, Christopher C Parker, Silke Gillessen, Adrian Cook, Chris Brawley, Claire L Amos, Nafisah Atako, Cheryl Pugh, Michelle Buckner, Simon Chowdhury, Zafar Malik, J Martin Russell, Clare Gilson, Hannah Rush, Jo Bowen, Anna Lydon, Ian Pedley, Joe M O'Sullivan, Alison Birtle, Joanna Gale, Narayanan Srihari, Carys Thomas, Jacob Tanguay, John Wagstaff, Prantik Das, Emma Gray, Mymoona Alzoueb, Omi Parikh, Angus Robinson, Isabel Syndikus, James Wylie, Anjali Zarkar, George Thalmann, Johann S de Bono, David P Dearnaley*, Malcolm D Mason*, Duncan Gilbert, Ruth E Langley, Robin Millman, David Matheson, Matthew R Sydes†, Louise C Brown†, Mahesh K B Parmar†, Nicholas D James†, on behalf of the Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators‡

Pre-specified subgroup analysis for High-risk M0 from 2 STAMPEDE trials

ABI+ADT VS ADT

High-risk M0 defined on **CONVENTIONAL IMAGING:**

- **Synchronous**
  - N0: at least 2/3 criteria of T3-T4, GG4-5, PSA≥40 ng/dl
  - N1
- **Metachronous**
  - PSA≥4 ng/dl with a doubling time <6 months or PSA≥20 ng/dl (ADT interval ≥12 months and total treatment ≤12 months)

Attard G. Et al. The lancet 2022

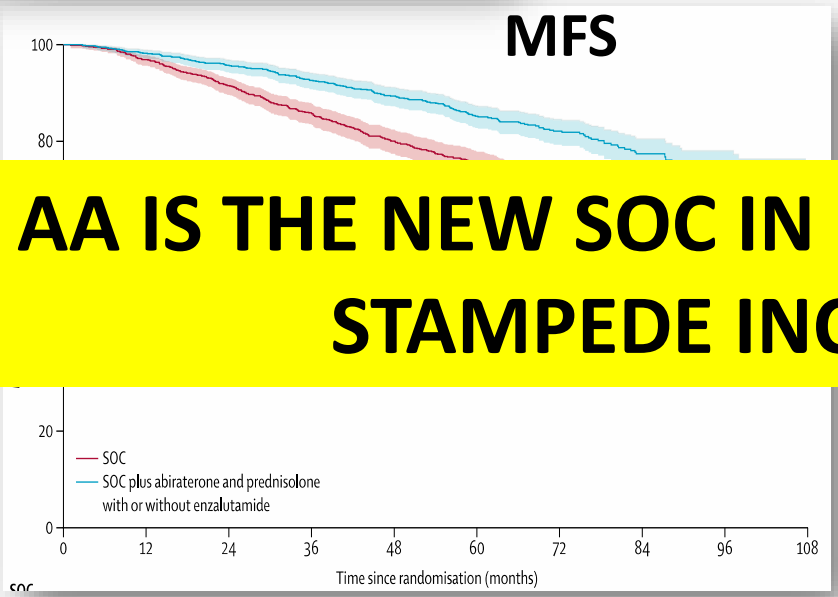
1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING

Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol

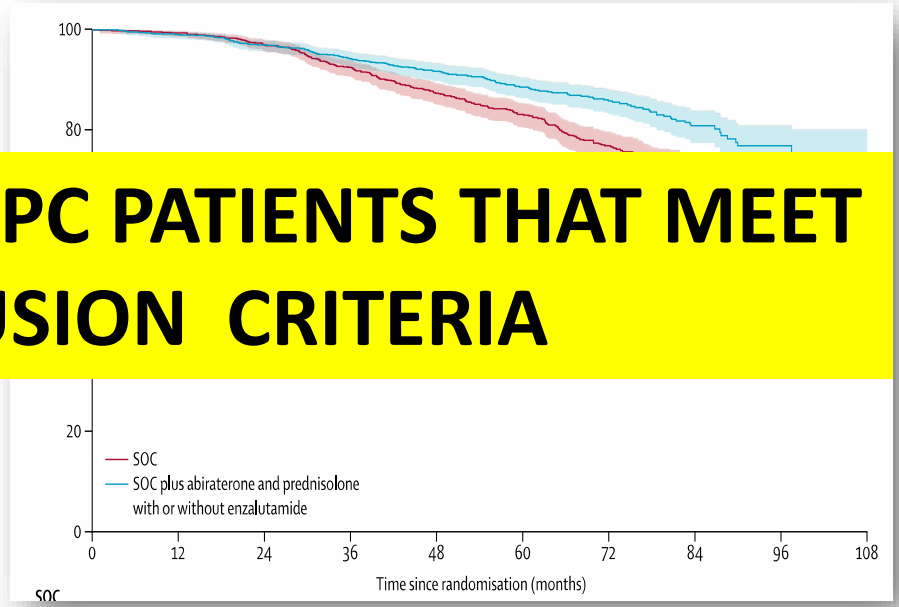
Gerhardt Attard, Laura Murphy, Noel W Clarke, William Cross, Robert J Jones, Christopher C Parker, Silke Gillessen, Adrian Cook, Chris Brawley, Claire L Amos, Nafisah Atako, Cheryl Pugh, Michelle Buckner, Simon Chowdhury, Zafar Malik, J Martin Russell, Clare Gilson, Hannah Rush, Jo Bowen, Anna Lydon, Ian Pedley, Joe M O'Sullivan, Alison Birtle, Joanna Gale, Narayanan Srihari, Carys Thomas, Jacob Tanguay, John Wagstaff, Prantik Das, Emma Gray, Mymoona Alzoueb, Omi Parikh, Angus Robinson, Isabel Syndikus, James Wylie, Anjali Zarkar, George Thalmann, Johann S de Bono, David P Dearnaley*, Malcolm D Mason*, Duncan Gilbert, Ruth E Langley, Robin Millman, David Matheson, Matthew R Sydes†, Louise C Brown†, Mahesh K B Parmar†, Nicholas D James†, on behalf of the Systemic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators‡

ABI+ADT vs ADT

MFS

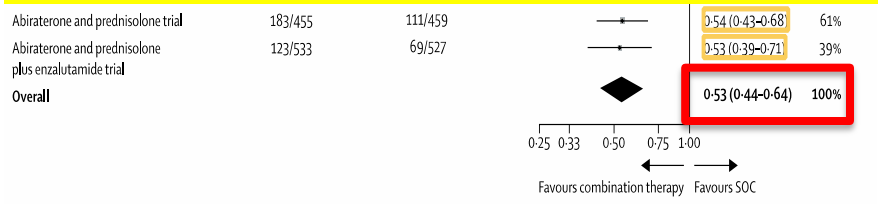


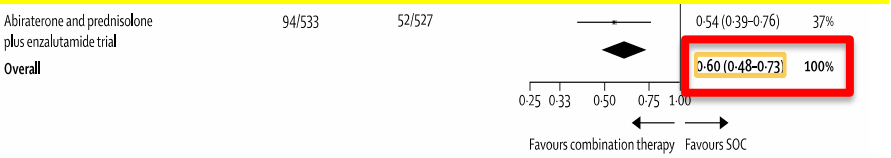
OS



AA IS THE NEW SOC IN HRPC PATIENTS THAT MEET STAMPEDE INCLUSION CRITERIA

RELAPSED PATIENTS UNDER-REPRESENTED





Attard G. Et al. The lancet 2022

1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING

AUA 2023

CHICAGO ★ APR 28-MAY 1

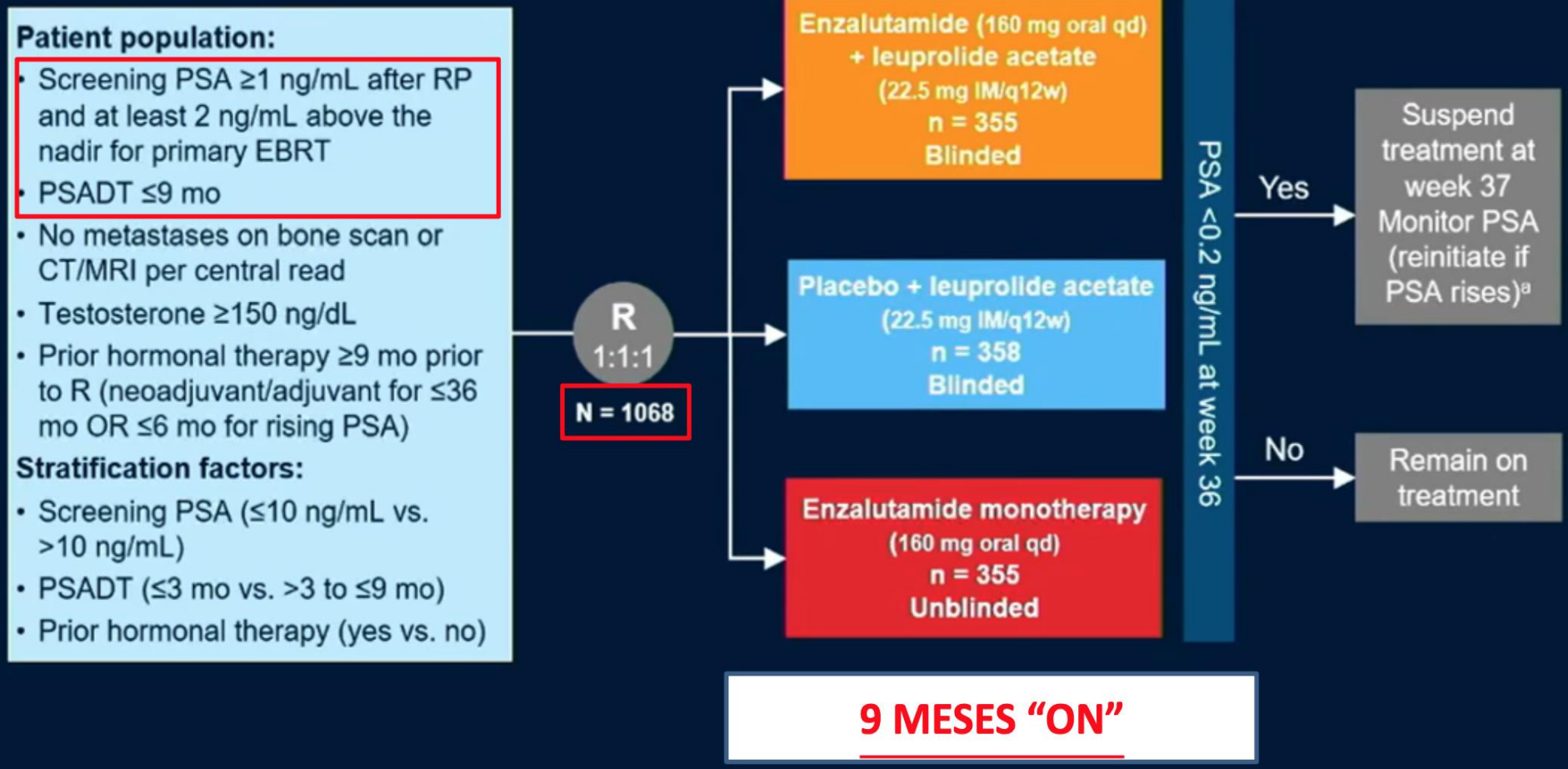
EMBARK: A Phase 3 Randomized Study of Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in High-Risk Biochemically Recurrent Prostate Cancer

Neal D. Shore,[1] Murilo de Almeida Luz,[2] Ugo De Giorgi,[3] Martin Gleave,[4] Geoffrey T. Gotto,[5] Gabriel P. Haas,[6] Miguel Ramirez-Backhaus,[7] Antti Rannikko,[8] Jamal Tarazi,[9] Swetha Sridharan,[10] Jennifer Sugg,[6] Yiyun Tang,[11] Ronald F. Tutrone, Jr.,[12] Balaji Venugopal,[13] Arnauld Villers,[14] Henry H. Woo,[15] Fabian Zohren,[16] Stephen J. Freedland[17]

[1]Carolina Urologic Research Center/GenesisCare US, Myrtle Beach, SC, USA; [2]Erasto Gaertner Hospital, Curitiba, Brazil; [3]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola, Italy; [4]University of British Columbia, Vancouver, BC, Canada; [5]University of Calgary, Calgary, AB, Canada; [6]Astellas Pharma Inc., Northbrook, IL, USA; [7]Servicio de Urología, Fundación Instituto Valenciano de Oncología, Valencia, Spain; [8]University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [9]Pfizer Inc., Collegeville, PA, USA; [10]Calvary Mater Newcastle, NSW, Australia; [11]Pfizer Inc., San Francisco, CA, USA; [12]Chesapeake Urology Research Associates, Towson, MD, USA; [13]Beatson West of Scotland Cancer Centre, University of Glasgow, Glasgow, UK; [14]University of Lille, Department of Urology, Claude Huriez Hospital, CHU LILLE, Lille, France; [15]Sydney Adventist Hospital, Sydney, NSW, Australia; [16]Pfizer Inc., Cambridge, MA, USA; [17]Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

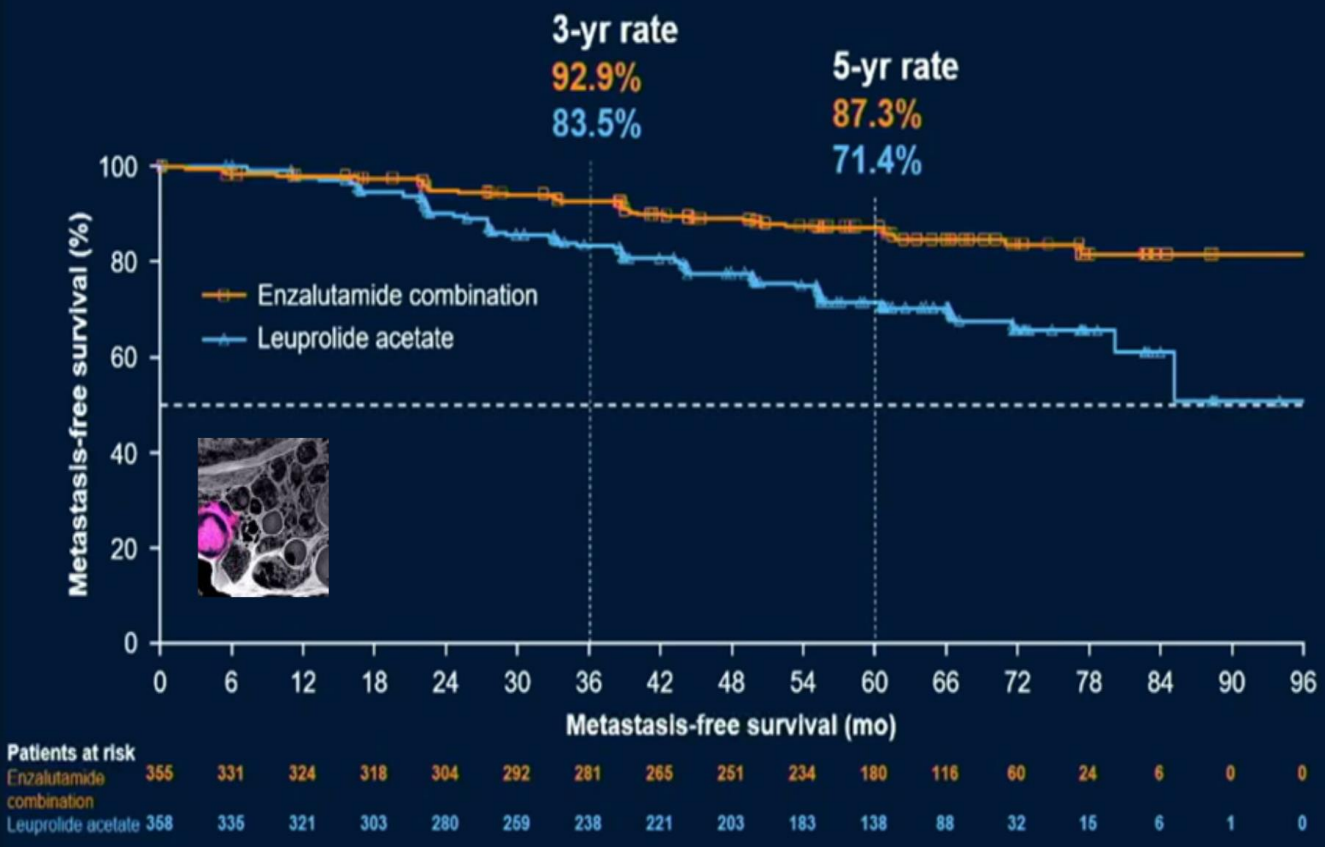
Enero 2015- Agosto 2019.
Análisis Enero 2023

1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING



[a]Study treatment was suspended once at week 37 if PSA was <0.2 ng/mL and restarted when PSA was ≥5.0 ng/mL (without prior RP) and ≥2 ng/mL (prior RP). [b]Intent-to-treat population. [c]Primary endp combination and enzalutamide monotherapy are alpha-protected. *P*-value to determine significance for OS of combination and monotherapy treatment comparisons was dependent on outcomes of prim population. BICR, blinded independent central review; CT, computed tomography; d, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnet prostate-specific antigen; PSADT, PSA doubling time; q, every; R, randomization; RP, radical prostatectomy; w, weeks.

1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING



	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Median follow-up, mo	60.7	60.6
Events, n (%)	45 (13)	92 (26)
Per BICR, median MFS (95% CI), mo	NR (NR)	NR (85.1–NR)

HR (95% CI): 0.42 (0.31–0.61); *P*<0.0001[a]

A consistent treatment effect was seen for investigator-assessed MFS: HR (95% CI): 0.47 (0.37–0.67); *P*<0.0001

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value was based on a stratified log-rank. CI, confidence interval; HR, hazard ratio; IWRS, interactive web response system; NR, not reached.

1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING

1/3 DE LOS EVENTOS PLANIFICADOS

	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	33 (9)	55 (15)
Median time to death (95% CI), mo	NR (NR)	NR (NR)

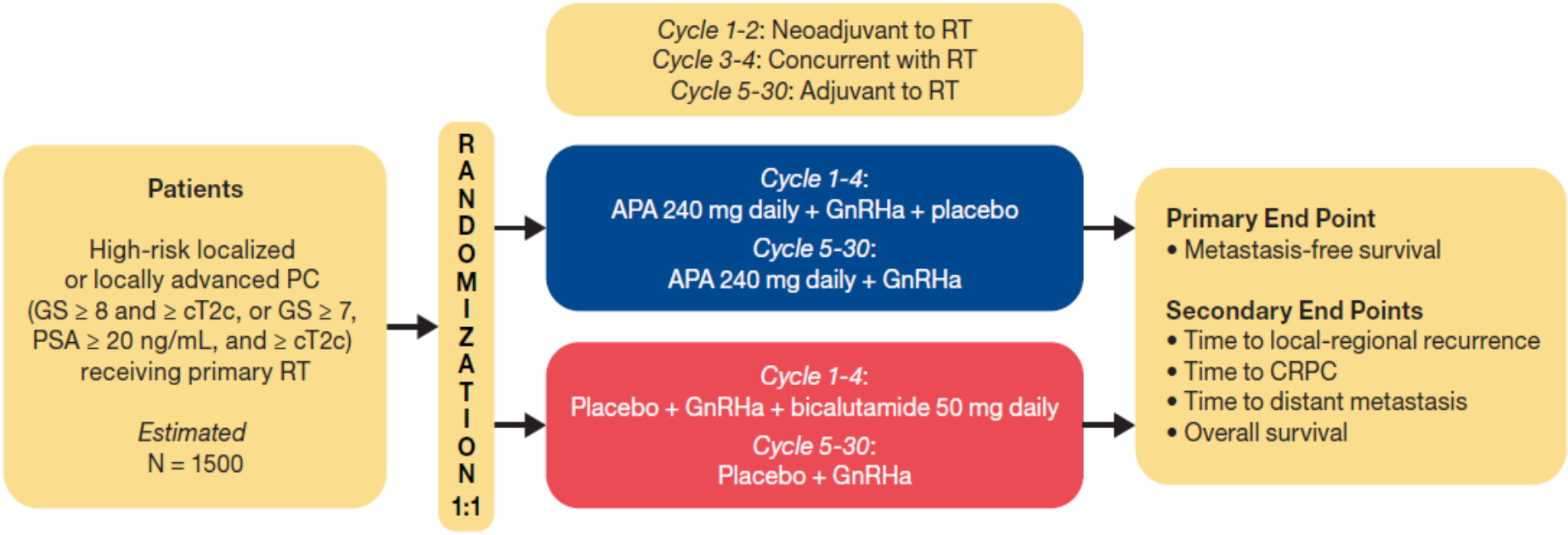
HR (95% CI): 0.59 (0.38–0.90) *P*=0.0142[a]

(Pre-specified efficacy boundary, *P*<0.0001)

Final analysis at 271 deaths across all treatment groups.

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

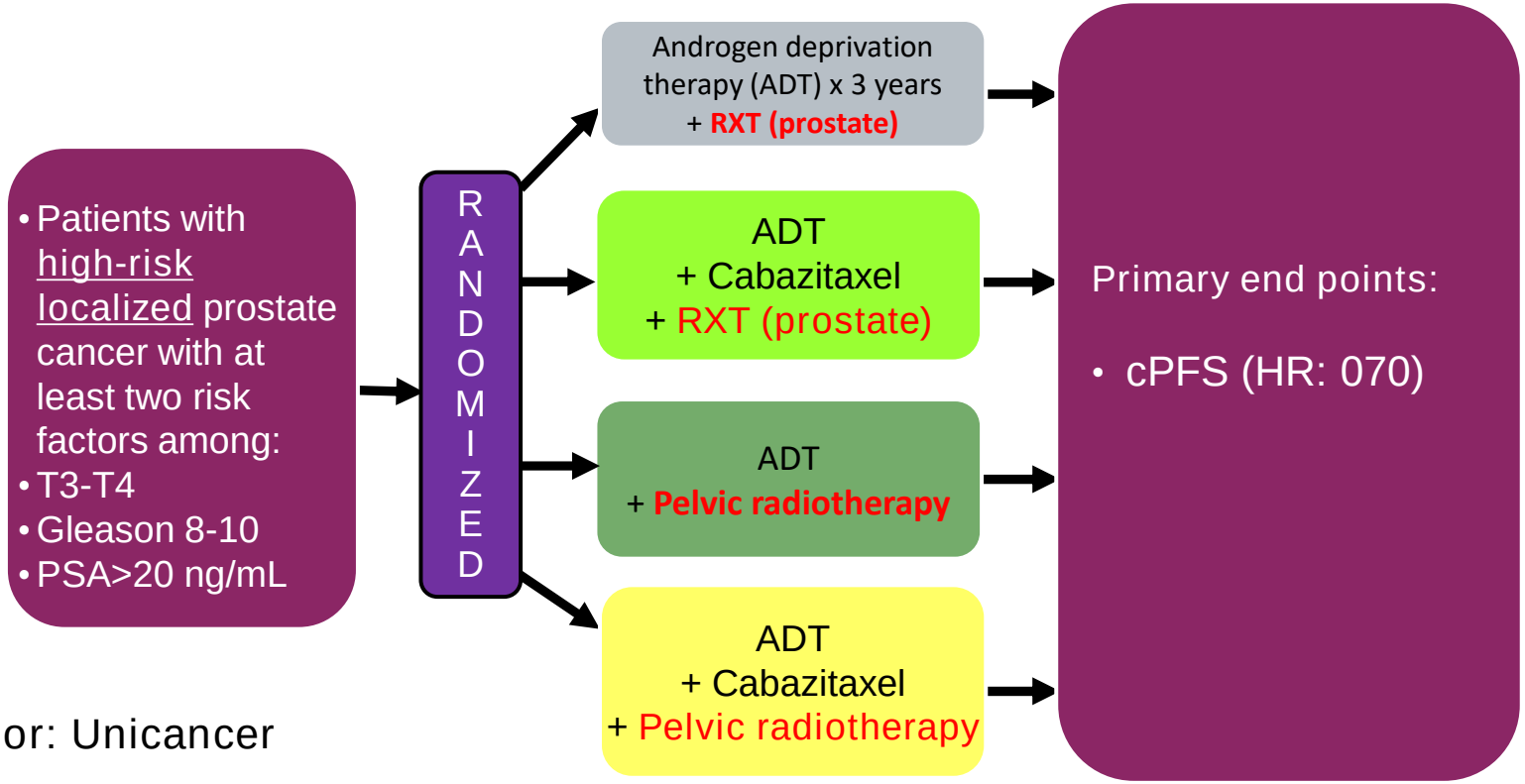
ATLAS: a Phase 3 Trial evaluating the efficacy of Apalutamide in pts with Localised or Locally Advanced CaP receiving primary RT



Similar trials with Enza, Daro,…

PA, apalutamide; PC, prostate cancer; GS, Gleason score; CRPC, castration-resistant PC.

PEACE-2: European Phase III Trial of Cabazitaxel and Pelvic Radiation in high-risk localised prostate cancer

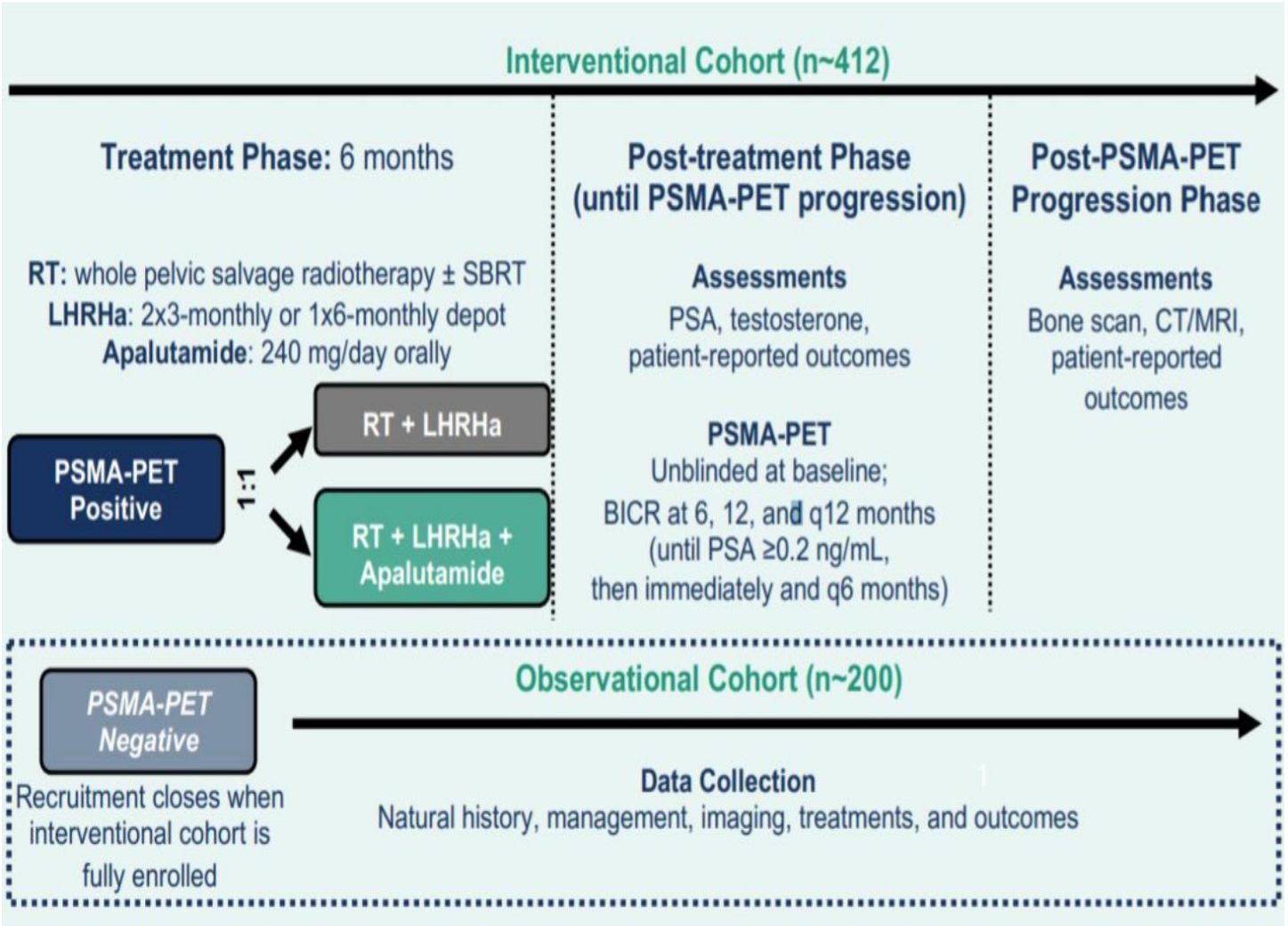


2x2 design
Study sponsor: Unicancer

PI K Fizazi – P Blanchard

1. INTENSIFYING TREATMENT IN High Risk localised PC & BCR SETTING

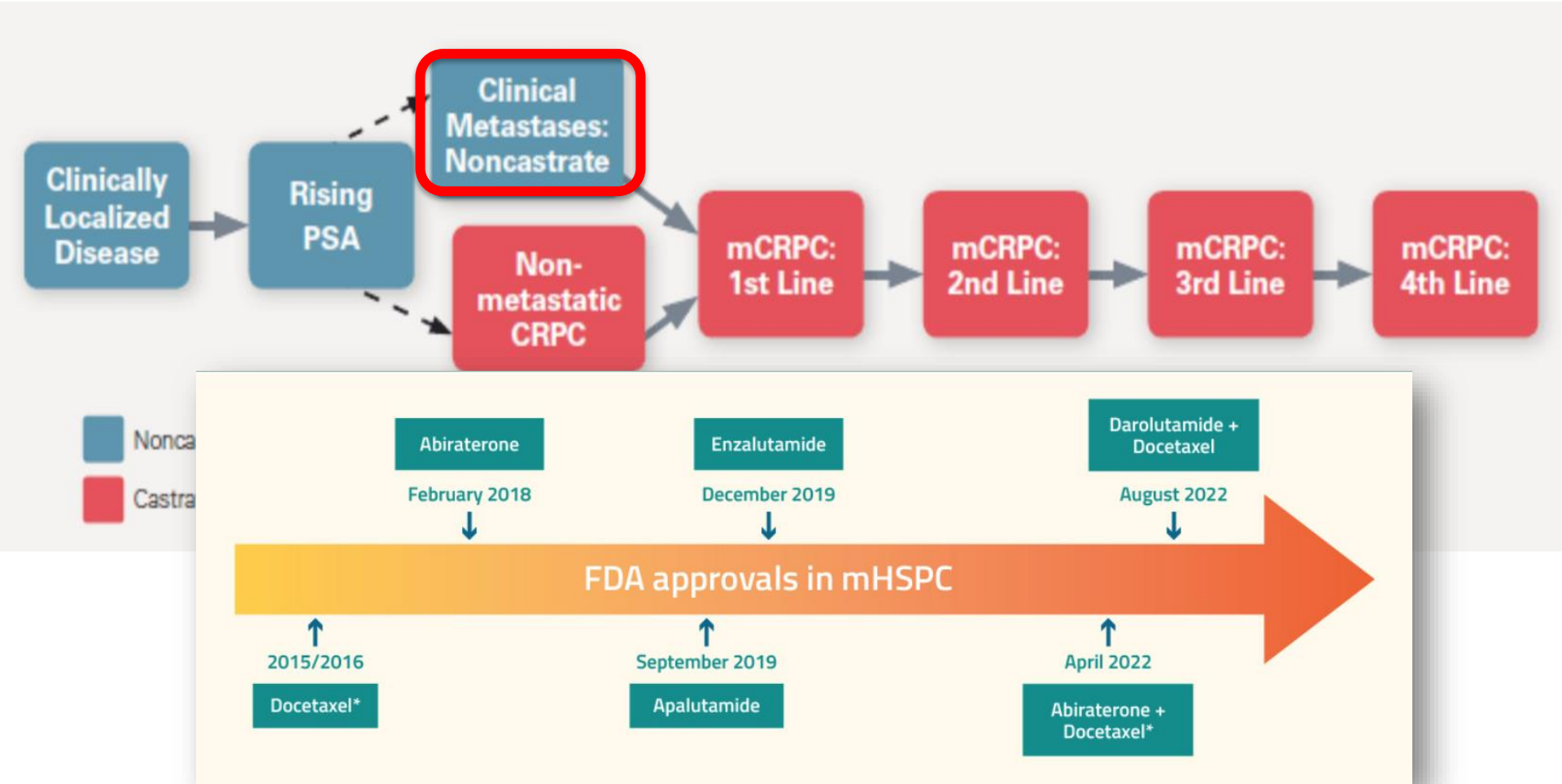
PET-PSMA



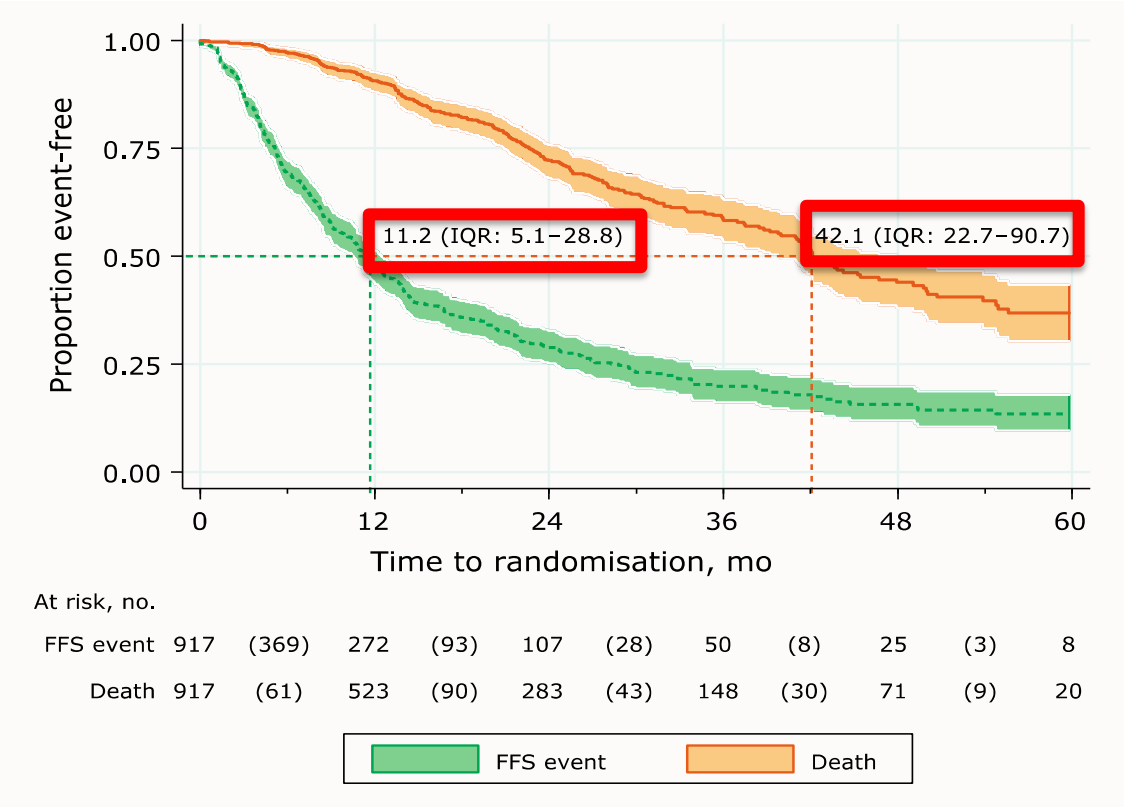
PRIMORDIUM TRIAL

PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease



2. ADT is mandatory in metastatic PC and must be continued throughout the disease



STAMPEDE trial: control group

(ADT +/- Bicalutamide +/-RT)

FFS (median)	11.2 m
OS (median)	42.1 m
2-yr OS	72%

BUT… ADT alone is SUBOPTIMAL and should be COMBINED with other agents

James ND. Eur Urol 2015

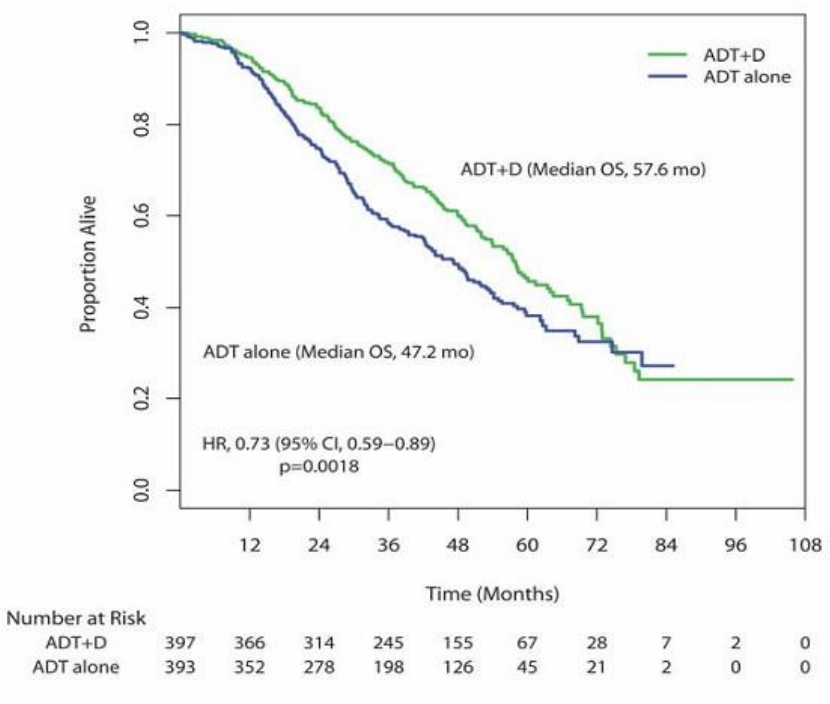
PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**

3. ADT alone in metastatic PC is INFERIOR TO ADT+DOCETAXEL

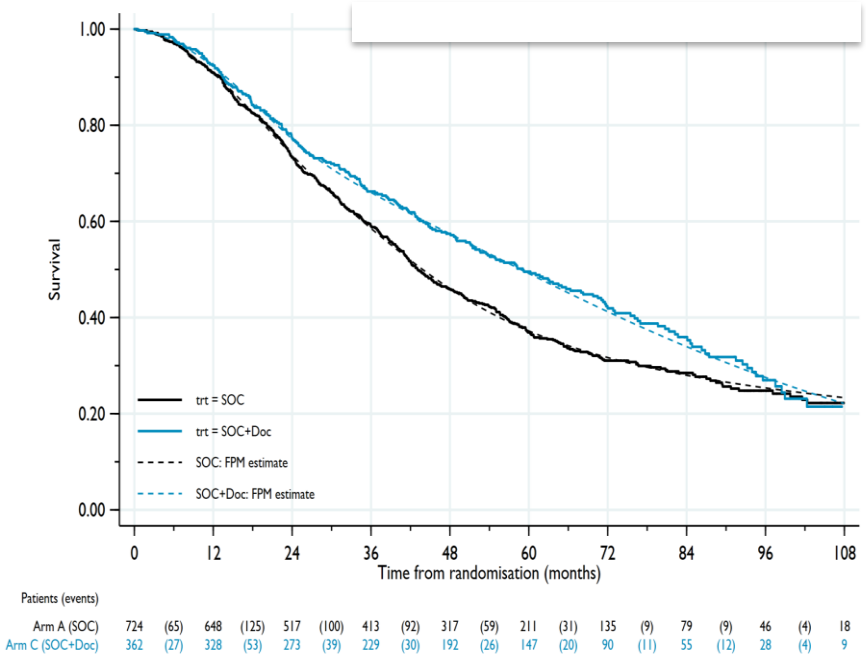
Phase III trials: ADT + Docetaxel vs ADT alone

CHAARTED trial



HR: 0.73 (95%CI 0.59-0.89)
P=0.0018

STAMPEDE trial



HR: 0.81 (95%CI 0.69-0.95)
P=0.016

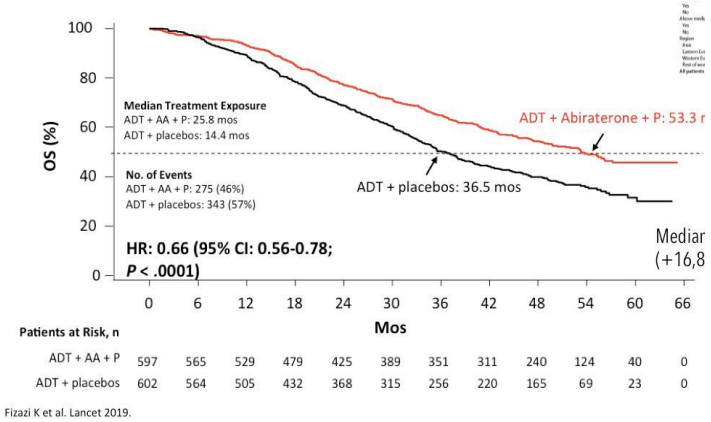
. Sweeney et al. NEJM. 2015, . James et al. Lancet. 2016 (updated ESMO 2019)

PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**

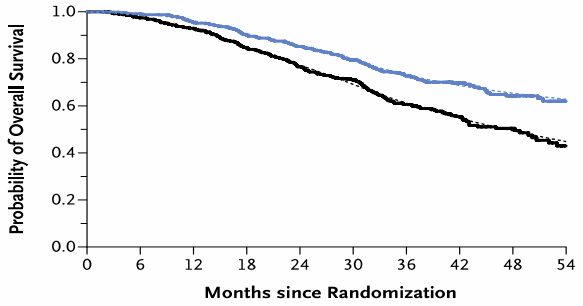
4. ADT alone in metastatic PC is INFERIOR TO ADT+NOVEL HORMONAL AGENTS

LATITUDE: ADT+ABI



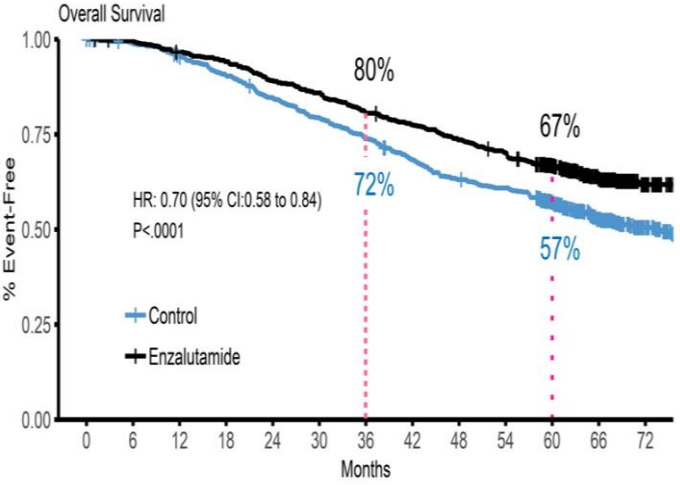
Fizazi K et al. Lancet 2019.

STAMPEDE: ADT+ABI

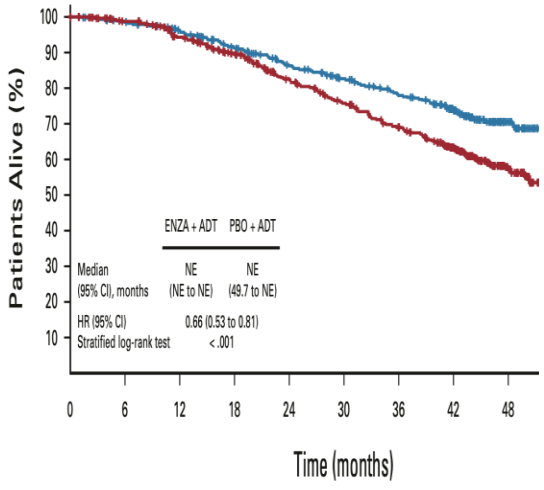


No. of Patients (no. of deaths)									
Combination therapy	500	(22)	469	(50)	415	(57)	256	(18)	81
ADT alone	502	(35)	460	(80)	371	(73)	215	(23)	60

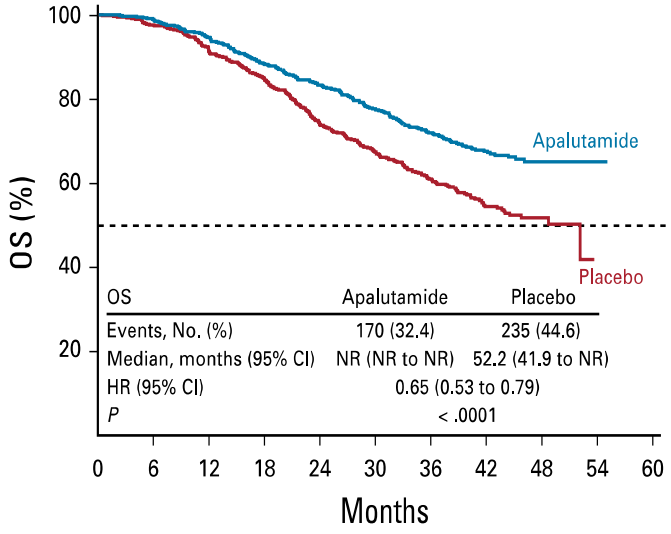
ENZAMET: ADT+ENZA



ARCHES: ADT+ENZA



TITAN: ADT+APA



Fizazi et al. NEJM. 2017, James et al. NEJM. 2017, Davis et al. NEJM 2019, Armstrong A. et al. JCO 2022;40, Kim. et al. JCO 2021.

PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**
5. **HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?**

5. HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?

No trials have compared ADT + Docetaxel vs a ADT + a novel hormonal agent (NHA)

	FUP	OS tto		OS control		HR (95%CI)	Δ 3yr OS	p-value
		Median	3-yr	Median	3-yr			
CHAARTED	53.7 m	57.6 m	~71%*	47.2 m	~58%*	0.72 (0.59-0.89)	~13%	p=0.0018
STAMPEDE (Docetaxel)	78.2 m	59.1 m	~66%*	43.1 m	~59%*	0.81 (0.69-0.95)	~7%	p=0.003
LATITUDE	51.8 m	53.3 m	~65%*	36.5 m	~51%**	0.66 (0.56-0.78)	~14%	p<0.001
STAMPEDE (Abiraterone)	73 m	79.2 m	~73%*	45.6	~60%*	0.60 (0.50-0.71)	~13%	p<0.001
ENZAMET	68 m	NR	80%	73.2 m	72%	0.67 (0.52-0.86)	8%	p=0.002
ARCHES	44.6 m	NR	78%	NR	69%	0.66 (0.53-0.81)	9%	p<0.001
TITAN	44 m	NR	-	52.2 m	-	0.67 (0.51-0.89)	-	p=0.005

Kyriakopoulos J Clin Oncol 2018; Fizazi et al. Lancet Oncol 2019; Clarke et al. Ann Oncol 2019; James et al. ESMO 2020. Abs 611O.

5. HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?

Heterogeneity in population included in trials

	CHAARTED	STAMPEDE		LATITUDE	ENZAMET	ARCHES	TITAN	CHART
		Docetaxel	Abiraterone					
Patients	mHSPC	mHSPC & high risk nmHSPC		High risk mHSPC	mHSPC	mHSPC	mHSPC	mHSPC
Primary endpoint	OS	OS		OS & rPFS	OS	rPFS	OS	OS & rPFS
Comparator arm	ADT	SOC	SOC	ADT	ADT +/- Doce	ADT + AA +/- Doce	ADT +/- Doce	ADT + AA
Follow-up	53.7 m	78.2 m	73 m	51.8 m	68 m	44.6 m	44 m	30.4 m
High volume	64.9%	56%	52%	-	52.3%	63.2%	62.8%	100%
Prior local therapy	27.2%	5%	7%	4%	-	12-26%	16.4%	~10%
Docetaxel for mHSPC	0	0	0	0	45%	15.5%	10.7%	0
ECOG PS 2	1.5%	NR	NR	?	0	0	0	0
Age	64 a	66 a	66 a	67 a	69 a	70 a	69 a	69 a
Gleason ≥ 8	60.7%	67.5%	77.3%	97.6%	58.3%	66%	67.4%	81.5%
Visceral metastases	15%	5%	6%	12-17%	11.5%	?	12.1%	20%

Sweeney et al. NEJM 2015. James et al. Lancet 2015. Fizazi et al N Eng J Med 2017. James et al. N Eng J Med 2017.

5. HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?

ADT+ novel hormonal agents have a better toxicity profile

DOCETAXEL

	Grade ≥ 3
Fatigue	0.3%
Allergic reaction	3.3%
Neuropathy	0.7%
Fatigue	1.7%
Anemia	0.3%
Thrombopenia	0.3%
Neutropenia	12.1%
Febrile neutropenia	6.1%

ABIRATERONE

	All Grades	G ≥ 3
Hypertension	37%	20%
Hypokalemia	20%	11%
AST/ALT increase	16%	6%
Hyperglycemia	13%	4%
Cardiac disorder	12%	4%
Fatigue	13%	2%

APALUTAMIDE

	All Grades	Grade ≥ 3
Rash	27.1%	6.3%
Fatigue	19.7%	1.5%
Fall	7.4%	0.8%
Hypothiroidism	6.5%	0
Fracture	6.3%	1.3%
Seizure	0.6%	0.2%

ENZALUTAMIDE

	All Grades	Grade ≥ 3
Seizures	0.3%	0.3%
Hypertension	8.6%	3.3%
Cognitive/memory	4.5%	0.7%
Fatigue	24.1%	1.7%
Fall	3.7%	0.3%
CV events	4%	1.5%

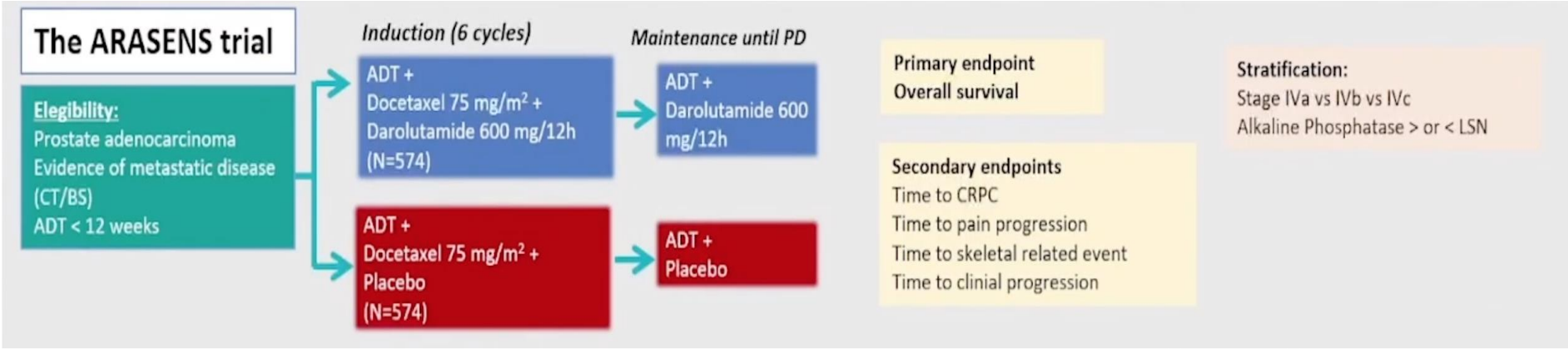
5. HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?

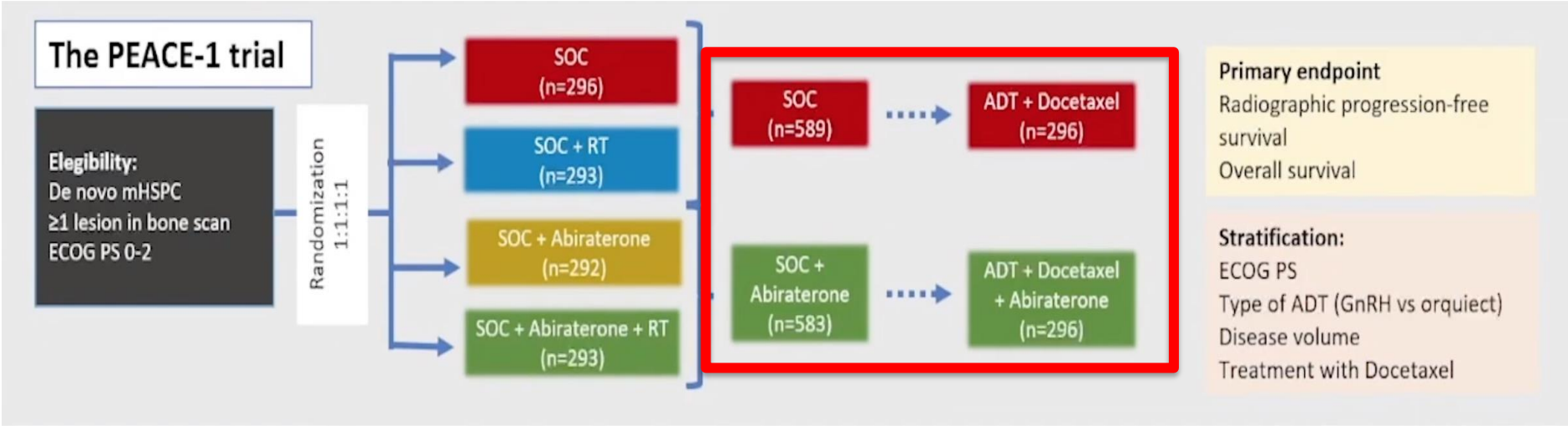
ADT+NHA are the prefered treatment option based on oral administration & a more favorable toxicity profile

PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**
5. **HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?**
6. **Is more better? TRIPLET THERAPY in mHSPC**

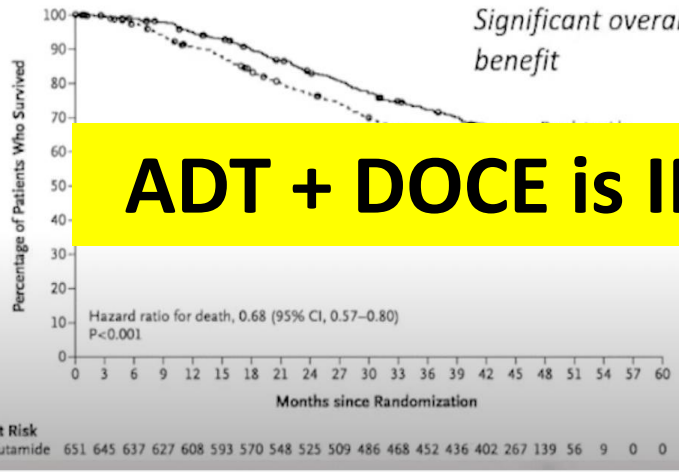
6. Is more better? TRIPLET THERAPY in mHSPC





6. Is more better? TRIPLET THERAPY in mHSPC

The ARASENS trial



Significant overall survival benefit

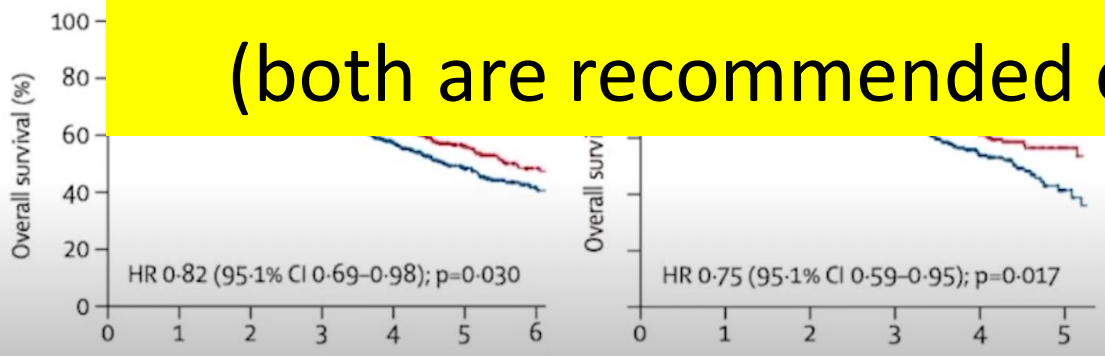
Results with a median follow-up of 43.7 months (overall survival)

	ADT+D+Daro	ADT+D	HR (IC95%);p-val
			001
TTCRPC	NA	19.1 m	0.36 (0.30-0.42); p<0.001
T to pain prog	NA	27.5 m	0.79 (0.66-0.95); p=0.01
SRE-PFS	51.2 m	39.7 m	0.61 (0.52-0.72); p <0.001

ADT + DOCE is INFERIOR to TRIPLET THERAPY

NO DATA OF TRIPLET THERAPY VS ADT+NOVEL HORMONAL AGENTS

(both are recommended option in mHSPC)



PCSM	NA	56.4 m	0.50 (0.34-0.71); p=0.006
rPFS	54 m	36 m	0.36 (0.30-0.42); p<0.001
TT mCRPC	45.6 m	18 m	0.38 (0.66-0.95); p=0.01

Fizazi et al. Lancet 2022

PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**
5. **HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?**
6. **Is more better? TRIPLET THERAPY in mHSPC**
7. **How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC**

7. How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC

Burden of metastatic disease & **timing of presentation** have a prognostic value

VOLUME/RISK

Overall survival in pts treated with ADT alone (control arm)

	Median		5 yr OS	
	Hi vol	Low vol	Hi vol	Low vol
CHAARTED	34,4m	NR	~27%*	~54%*
STAMPEDE (Docetaxel)	35,2m	76,7m	~23%*	~56%*
STAMPEDE (Abi)**	~34m*	NR	28%	55%

*Estimation based on the inspection of the Kaplan Meier curves

**Using LATITUDE high/low risk criteria

PRIOR THERAPY

Overall survival in pts treated with ADT alone (control arm)

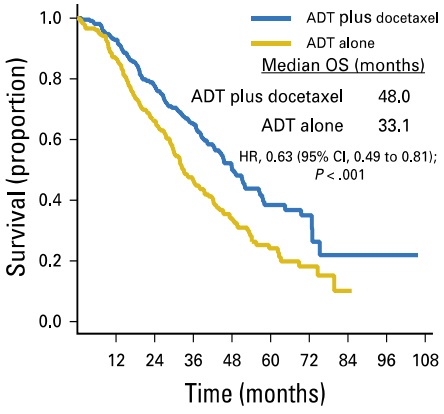
GETUG-AFU-16, STAMPEDE, CHAARTED trials

Overall survival		5-yr OS
High volume	Synchronous (n=1044)	26%
	Metachronic (n=132)	28%
Low volume	Synchronous (n=582)	52%
	Metachronic (n=229)	72%

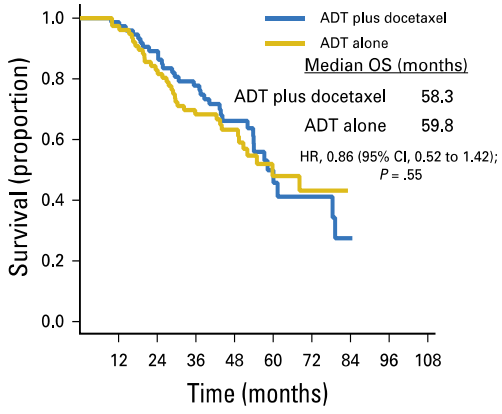
Sweeney et al. N Eng J Med 2015 . James et al. Lancet 2015. James et al. N Eng J Med 2017.

7. How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC

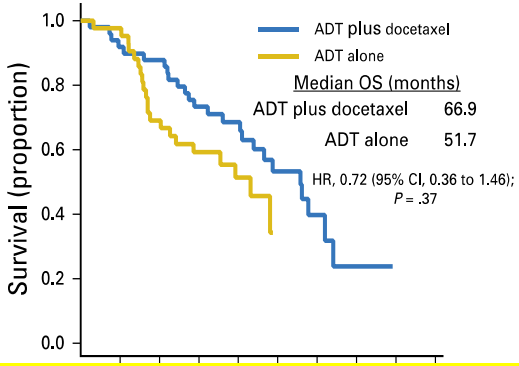
DE NOVO HV



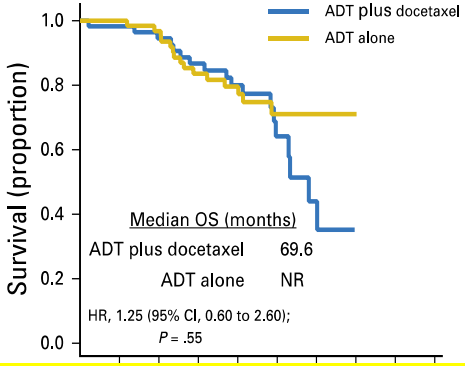
DE NOVO LV



RELAPSED HV



RELAPSED LV



DOCETAXEL (Chaarted)

Characteristics	HR
DE NOVO HV	**HR: 0.63**; 95% CI, 0.49 to 0.81; **P , .001**
DE NOVO LV	**HR 0.72;** 95% CI, 0.36 to 1.46; **P = .37;**
RELAPSED HV	**HR: 0.86**; 95% CI, 0.52 to 1.42; **P = .55;**
RELAPSED LV	**HR 1.25**; 95% CI, 0.60 to 2.60; **P = .55**

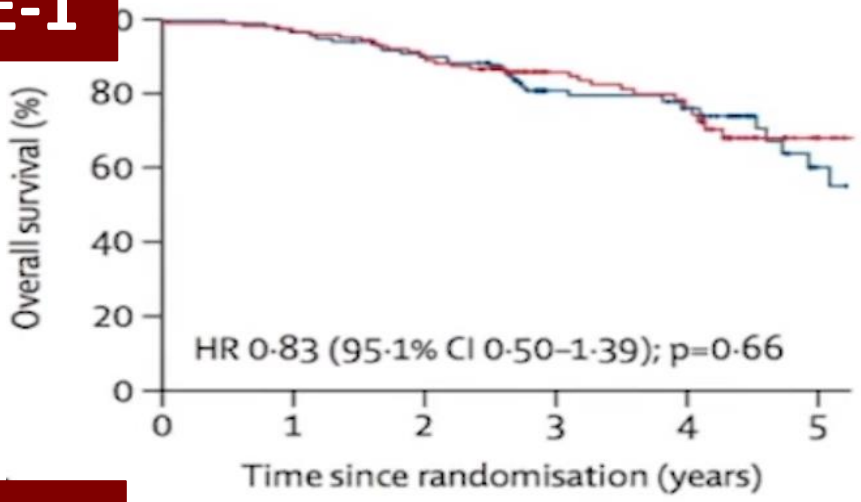
Only De Novo HV Benefit from Docetaxel+ADT

Kyriakopoulos et al. JCO 2018

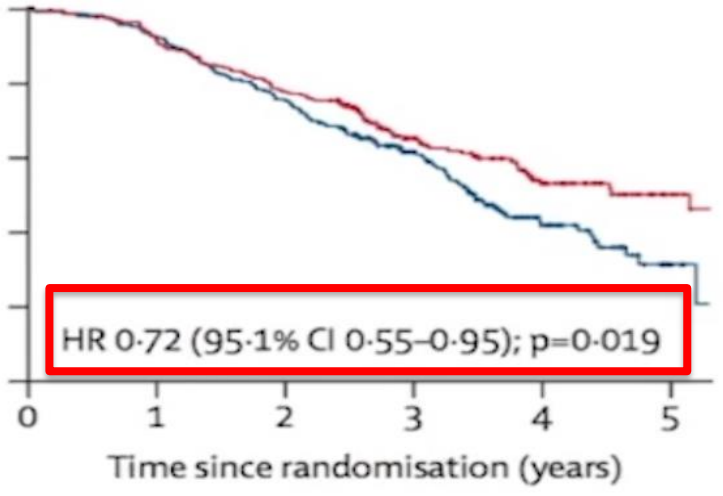
7. How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC

PEACE-1

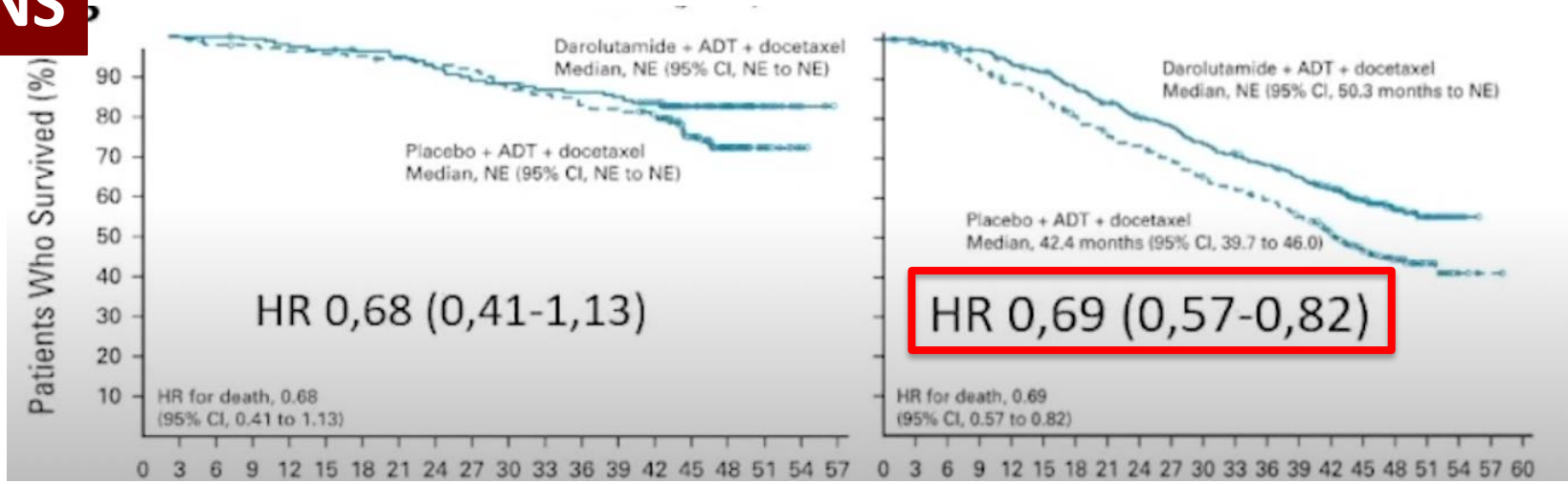
LOW-VOLUME disease



HIGH-VOLUME disease



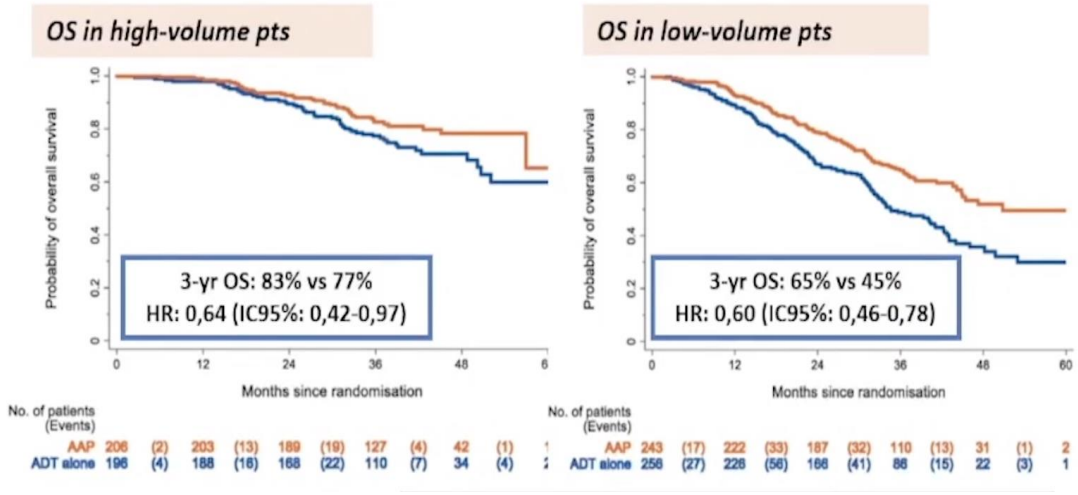
ARASENS



7. How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC

NOVEL HORMONAL THERAPIES BENEFIT INDEPENDENT OF DISEASE VOLUME

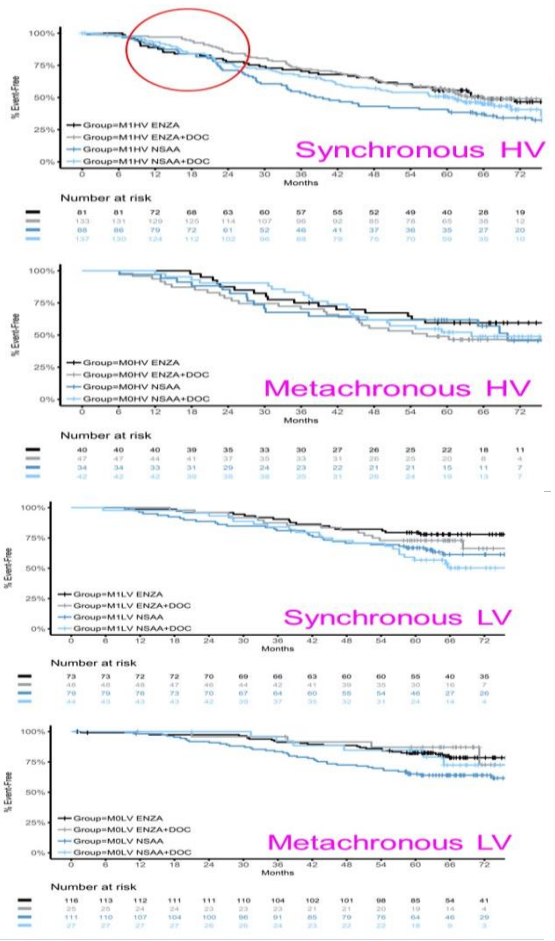
STAMPEDE (ABIRATERONE)



Trial	HR low volume	HR high volume
ENZAMET	0.43 (0.26-0.72)	0.80 (0.59-1.07)
ARCHES	0.66 (0.43-1.03)	0.66 (0.52-0.83)
TITAN	0.36 (0.22-0.57)	0.53 (0.41-0.67)

NOVEL HORMONAL THERAPIES BENEFIT INDEPENDENT OF TYPE

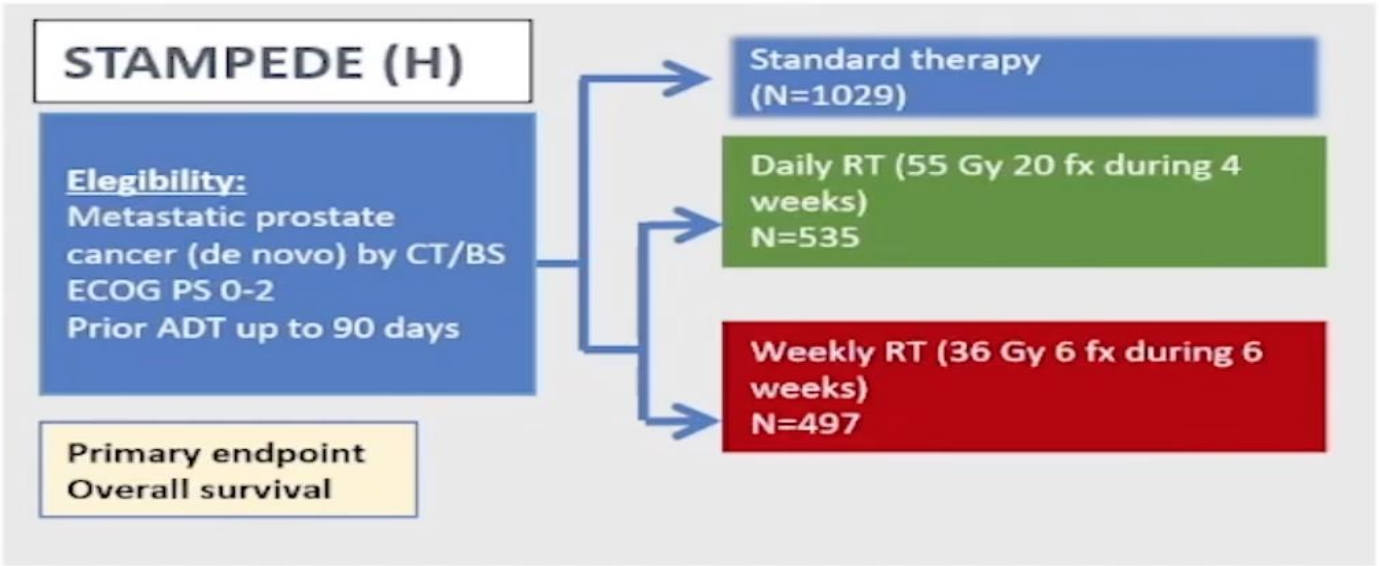
ENZAMET trial



PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**
5. **HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?**
6. **Is more better? TRIPLET THERAPY in mHSPC**
7. **How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC**
8. Role of local treatment- **RT to the primary** tumor in mHSPC

8. Role of local treatment- **RT to the primary** tumor in mHSPC



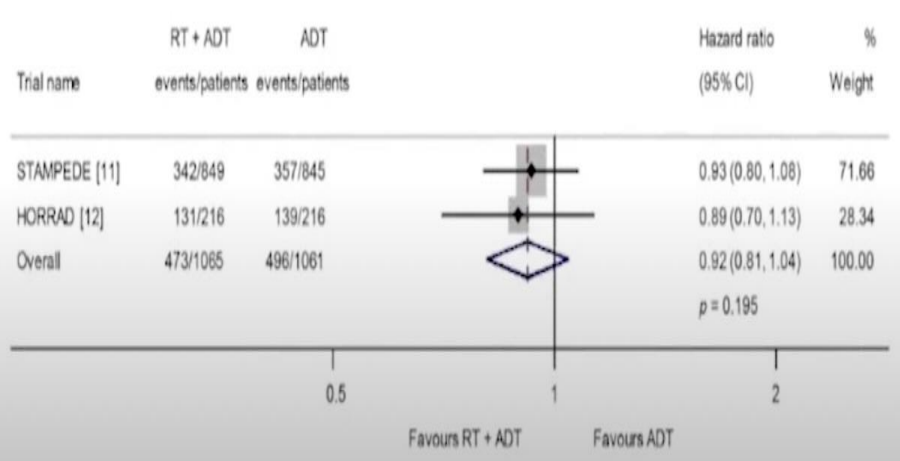
Global population: no difference in overall survival

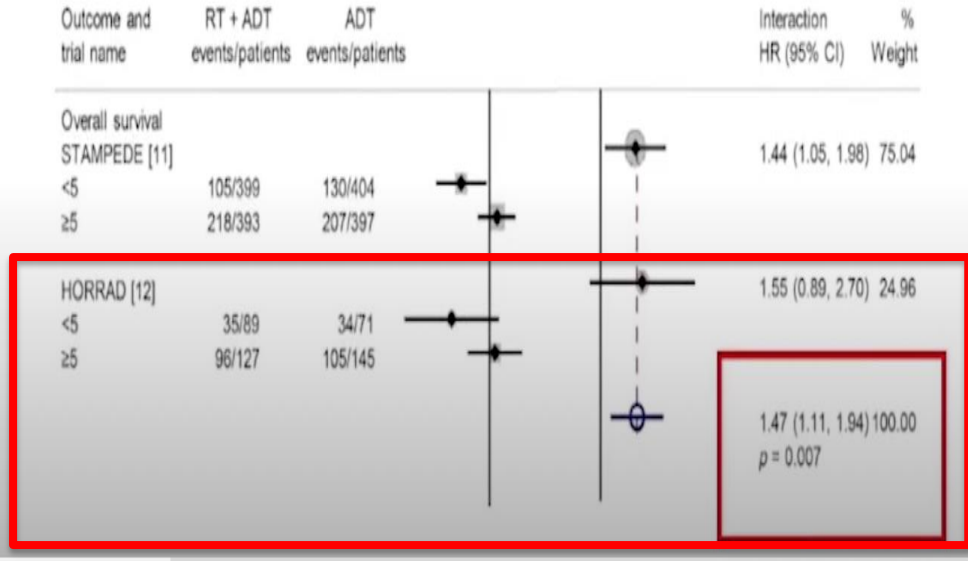
	SOC	SOC + RT
3-yr OS	62%	65%
HR	0.92 (0.8-1.06)	
p-avl	p=0.266	

Significant survival benefit in low-volume patients

8. Role of local treatment- **RT to the primary** tumor in mHSPC

STOPCAP Metaanalysis (STAMPEDE + HORRAD): significant interaction between volume and OS





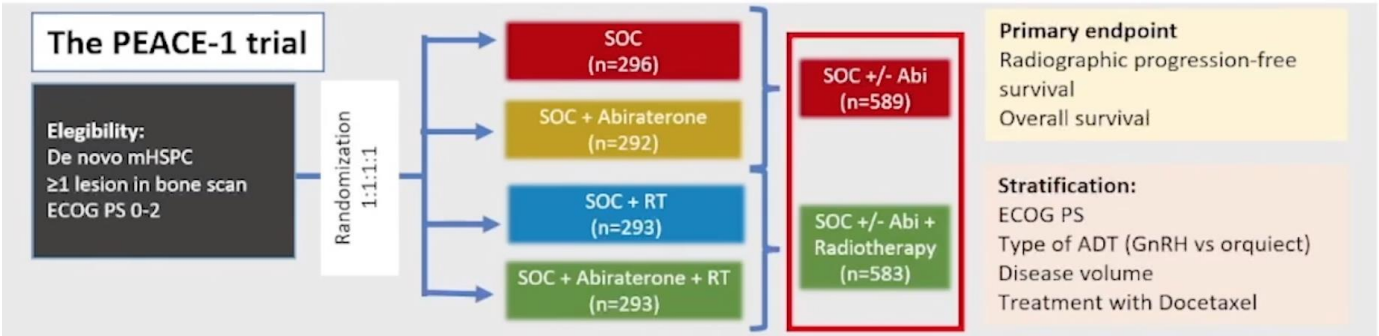
Parker et al. Lancet 2018;392:2353-2366. Boevé et al. Eur Urol 2019;75(3):410-18

PROSTATE CANCER IN 2023

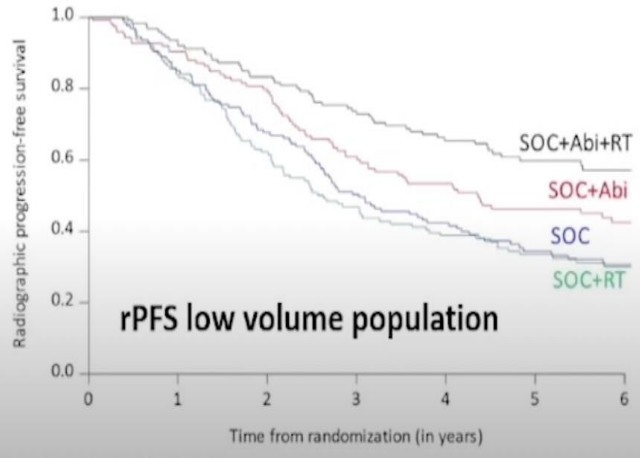
1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**
5. **HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?**
6. **Is more better? TRIPLET THERAPY in mHSPC**
7. **How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC**
8. Role of local treatment- **RT to the primary** tumor in mHSPC
9. Combination **Novel hormonal agents & RT to the primary** tumor in mHSP

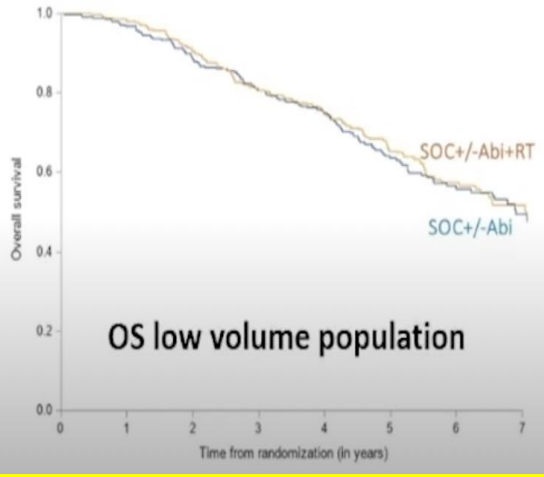
9. Combination **Novel hormonal agents & RT to the primary** tumor in mHSPC

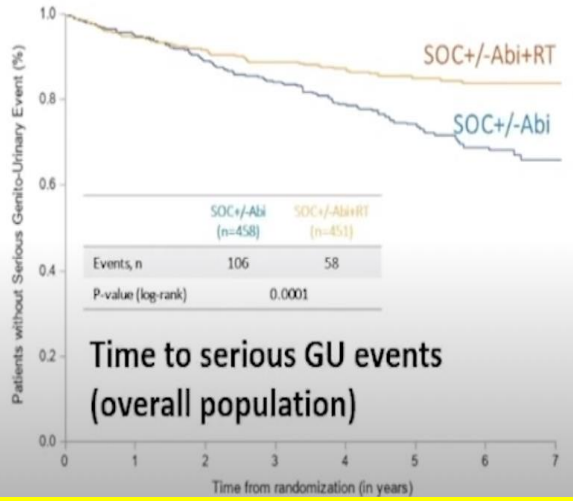
SOC+RT+ABI



	SOC +/- Abi	SOC +/- Abi + RT
Low Vol	253 (43%)	252 (43%)
High Vol	335 (57%)	332 (57%)







Rossi et al. ASCO 2022

ABI + RT to the primary tumor in **LOW-VOLUME mHSPC INCREASES rPFS & time to GU symptoms** but there is **not benefit in OS**

PROSTATE CANCER IN 2023

1. **New developments in High Risk localised PC & BCR setting**
2. **In mHSPC ADT is mandatory in metastatic PC** and must be continued throughout the disease
3. **ADT alone** in metastatic PC is **INFERIOR TO ADT+DOCETAXEL**
4. **ADT alone** in metastatic PC is **INFERIOR TO ADT+NOVEL HORMONAL AGENTS**
5. **HOW TO SELECT between ADT+ NOVEL HORMONAL AGENTS OR DOCE?**
6. **Is more better? TRIPLET THERAPY in mHSPC**
7. **How to SELECT between TRIPLET vs DOUBLET THERAPY in mHSPC**
8. Role of local treatment- **RT to the primary** tumor in mHSPC
9. Combination **Novel hormonal agents & RT to the primary** tumor in mHSCP
10. **Dilemmas in TREATMENT SELECTION IN mCRPC**

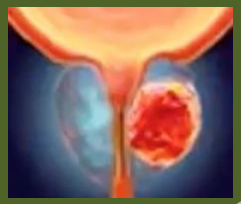
10. Dilemmas in TREATMENT SELECTION IN mCRPC

CLINICAL factors

- Symptoms
- Performance status
- Comorbidities
- Cocurrent medications

- Volume of disease
- Sites of metastases
- PSMA status
- Genomic features

DISEASE factors



TREATMENT mCRPC

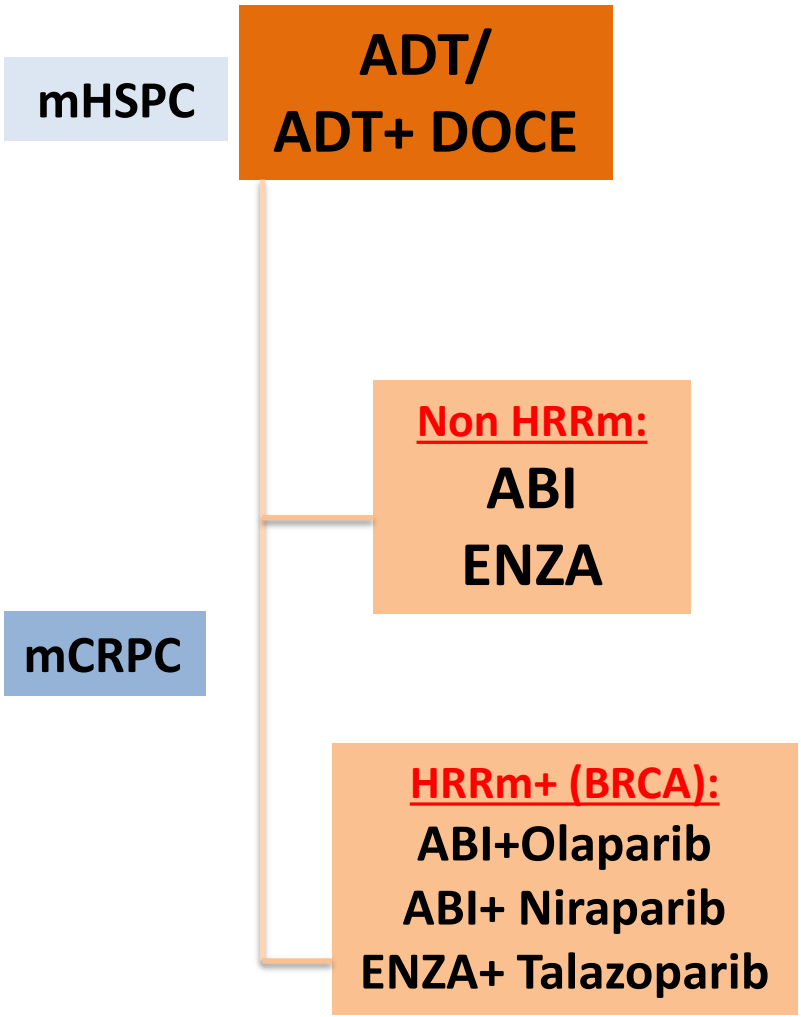
DRUG factors

PREVIOUS treatments

- Mechanisms of action
- Administration mode
- Toxicity
- Impact on QOL
- Cost

10. TREATMENT SELECTION IN mCPRC: 1st LINE

Treatment in mHSPC conditioned mCRPC sequence



10. TREATMENT SELECTION IN mCPRC: 1st LINE

COMBO iPARP+HORMONES IN 1st LINE mCPRC

PROPEL trial

ABIRATERONE + OLAPARIB

MAGNITUDE trial

ABIRATERONE + NIRAPARIB

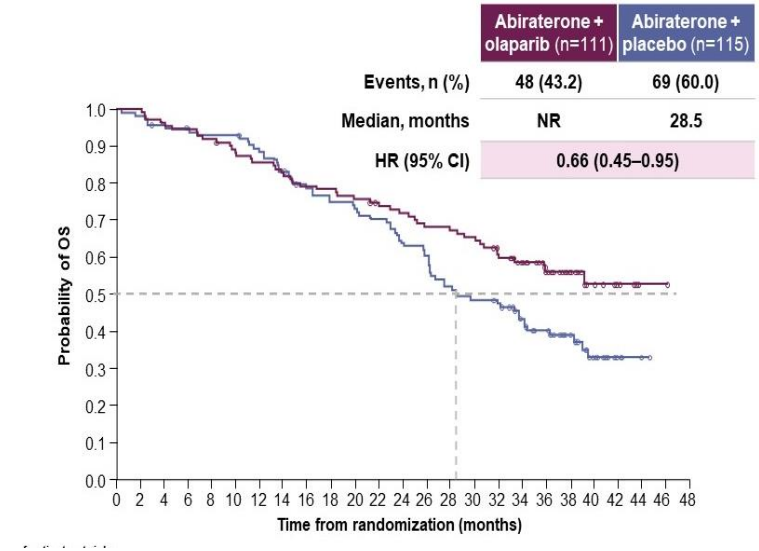
TALAPRO-2 trial

ENZA + TALAZOPARIB

10. TREATMENT SELECTION IN mCPRC: 1st LINE

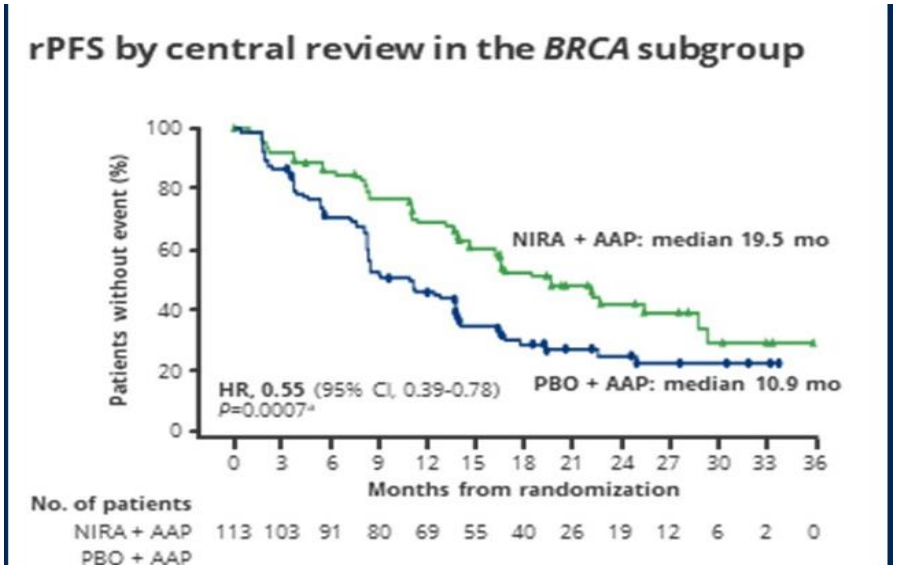
PROPEL trial

ABIRATERONE + OLAPARIB



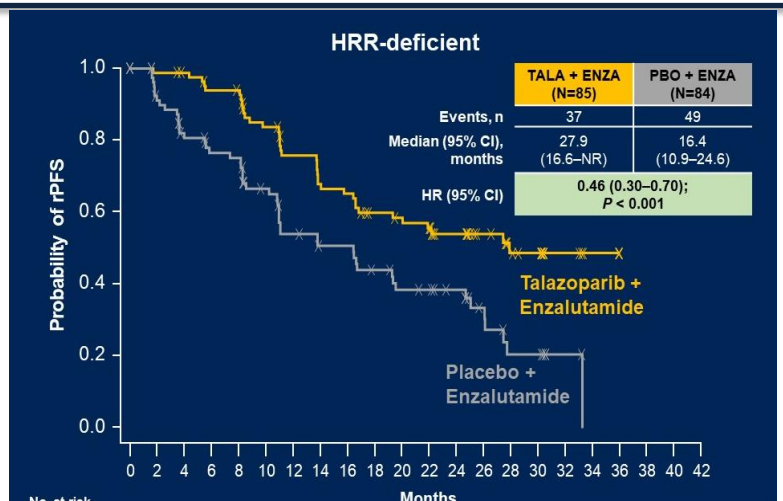
MAGNITUDE trial

ABI + NIRAPARIB



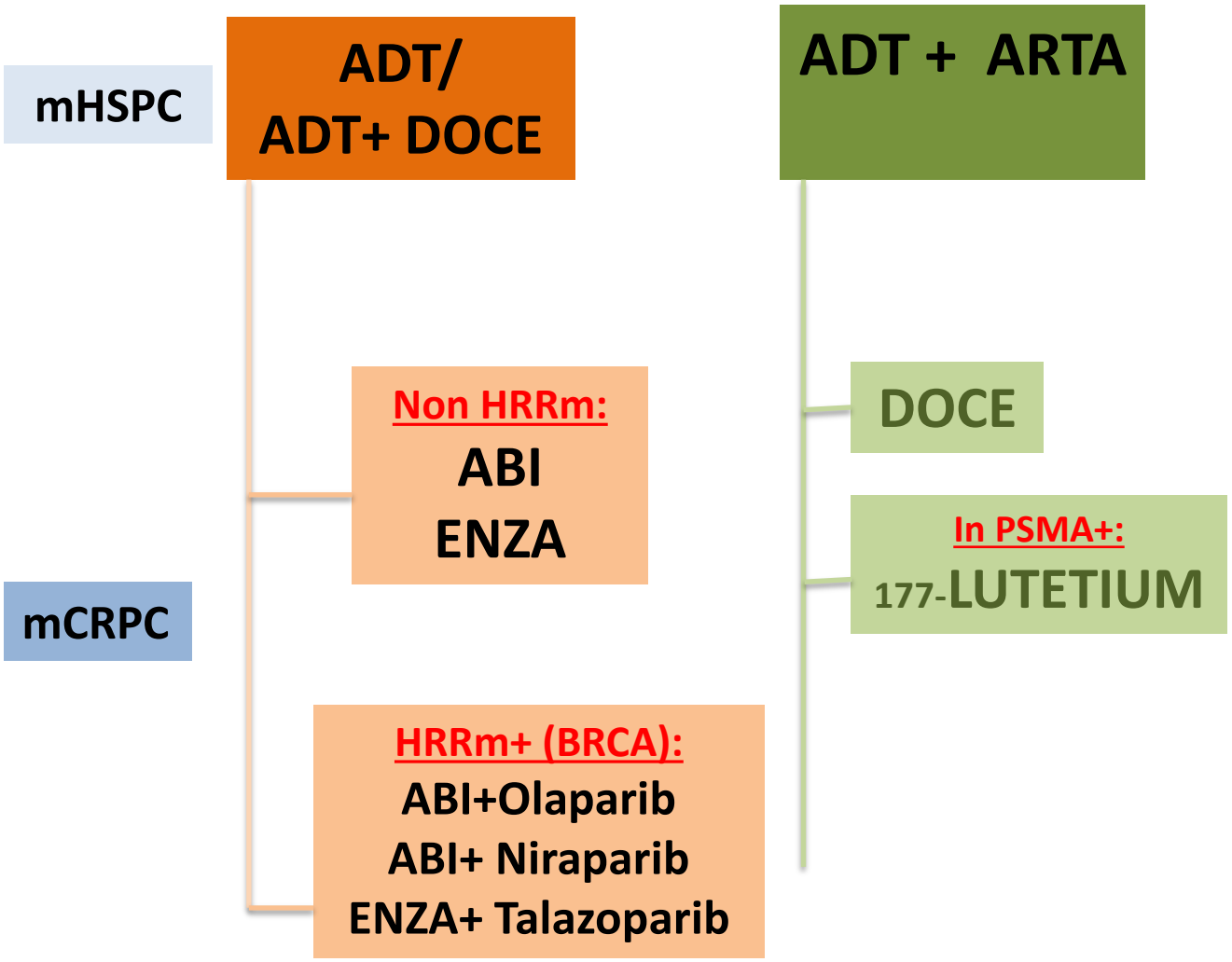
TALAPRO-2 trial

ENZA + TALAZOPARIB

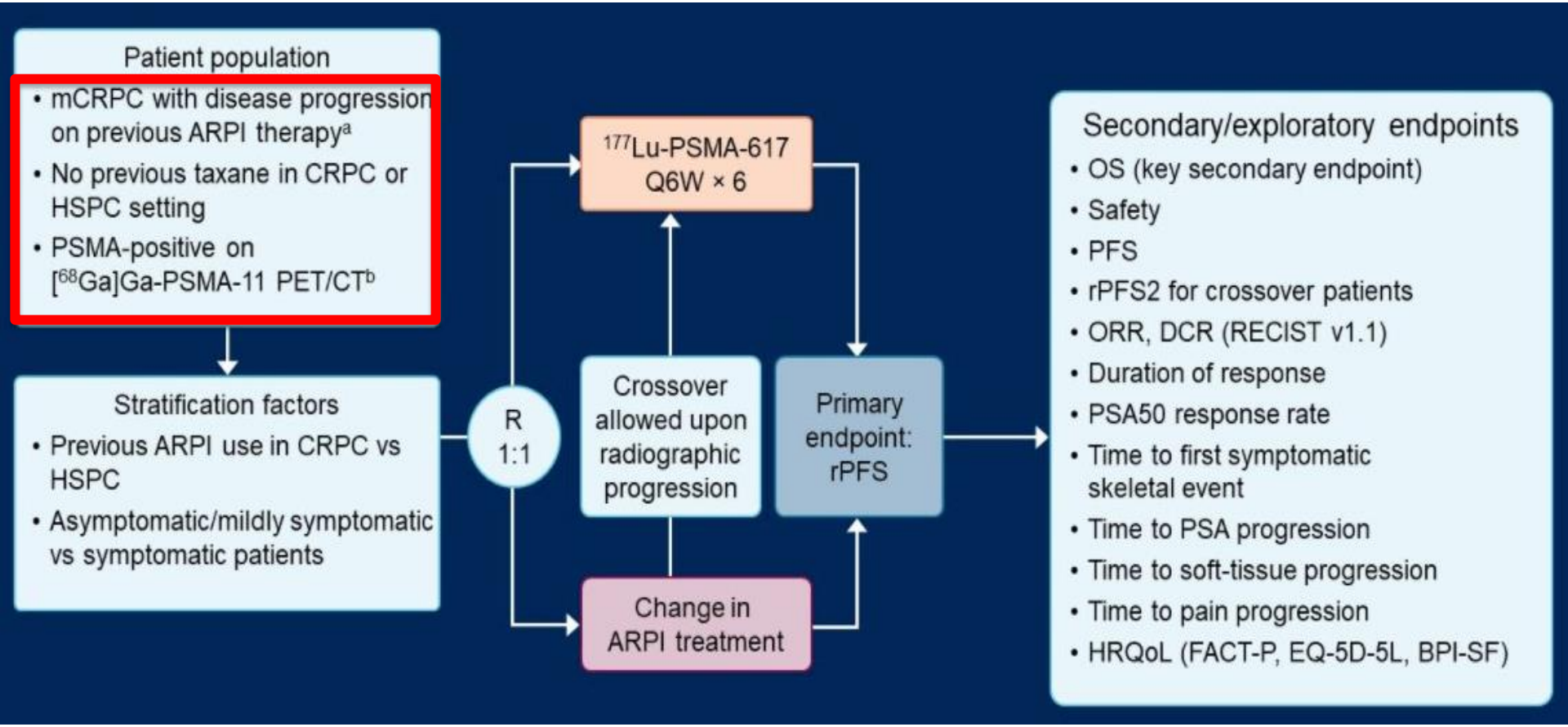


10. TREATMENT SELECTION IN mCPRC: 1st LINE

Treatment in mHSPC conditioned mCRPC sequence



PSMAFORE: ^{177}LuPSMA in 1L mCRPC treated with ARPI

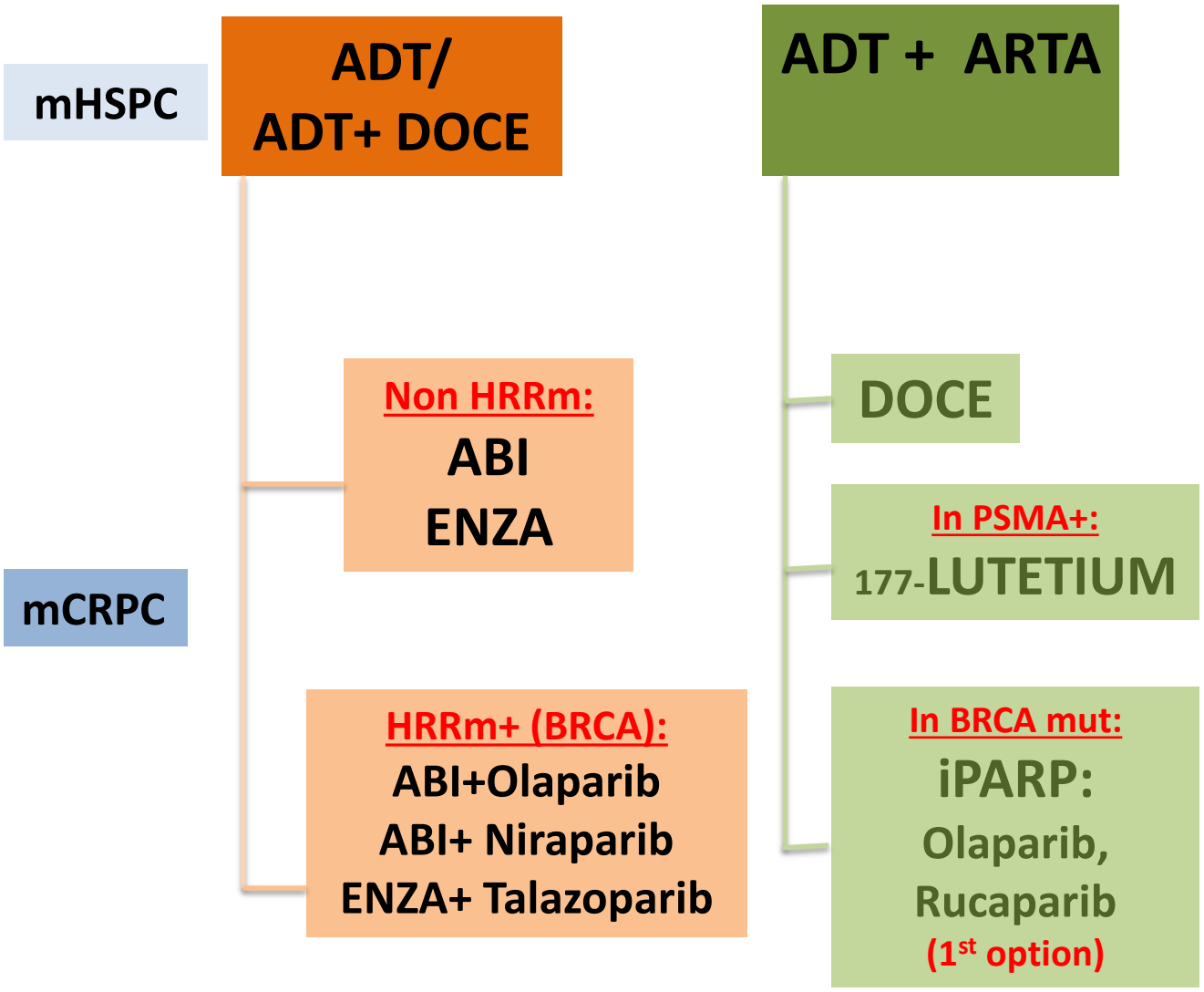


Novartis Pluvicto™* shows statistically significant and clinically meaningful radiographic progression-free survival benefit in patients with PSMA–positive metastatic castration-resistant prostate cancer

Dec 05, 2022

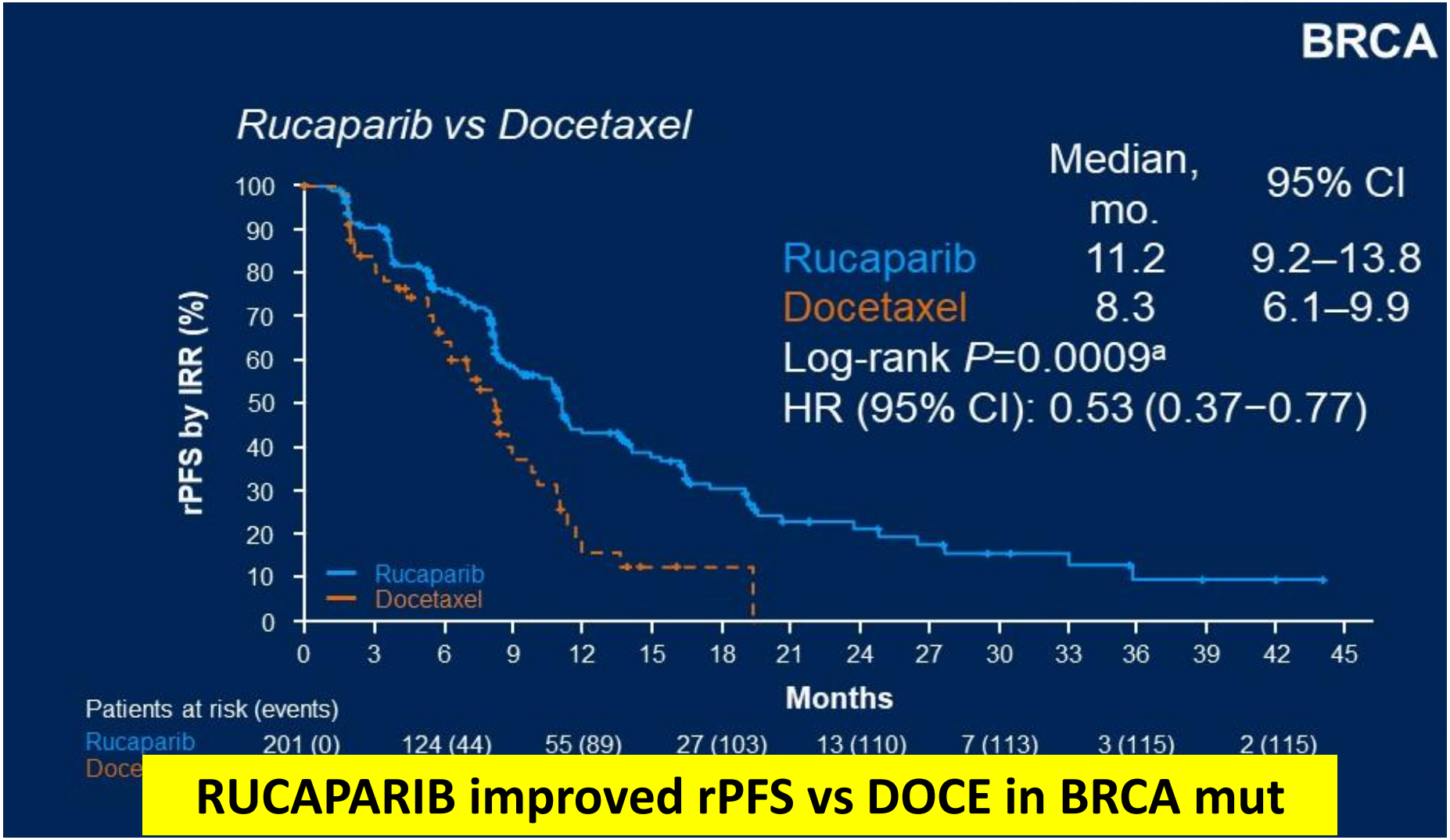
10. TREATMENT SELECTION IN mCPRC: 1st LINE

Treatment in mHSPC conditioned mCRPC sequence



New data at ASCO GU 2023: **TRITON-3**

Radiographic PFS-BRCA subgroup: Rucaparib vs DOCE

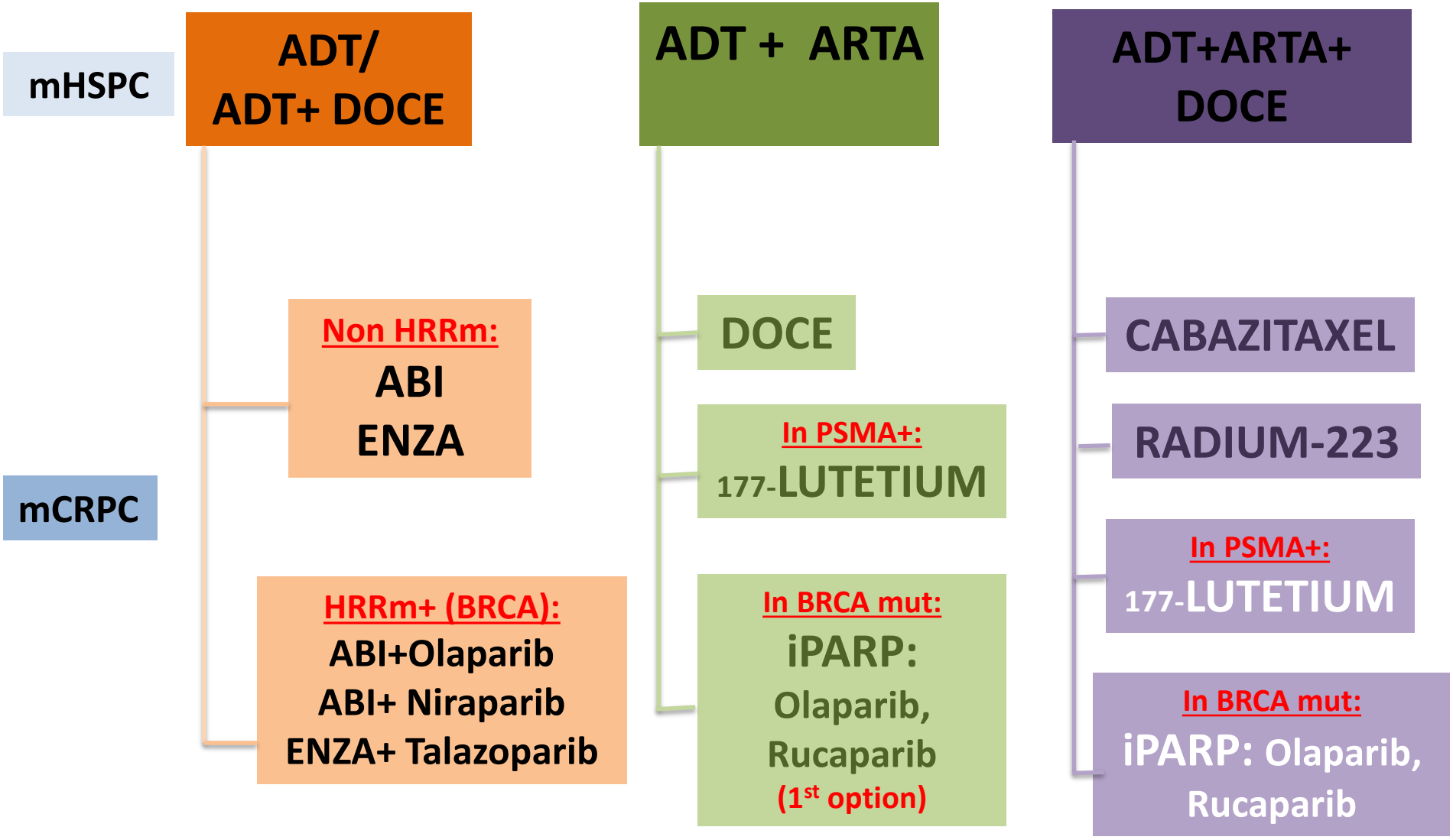


RUCAPARIB improved rPFS vs DOCE in BRCA mut

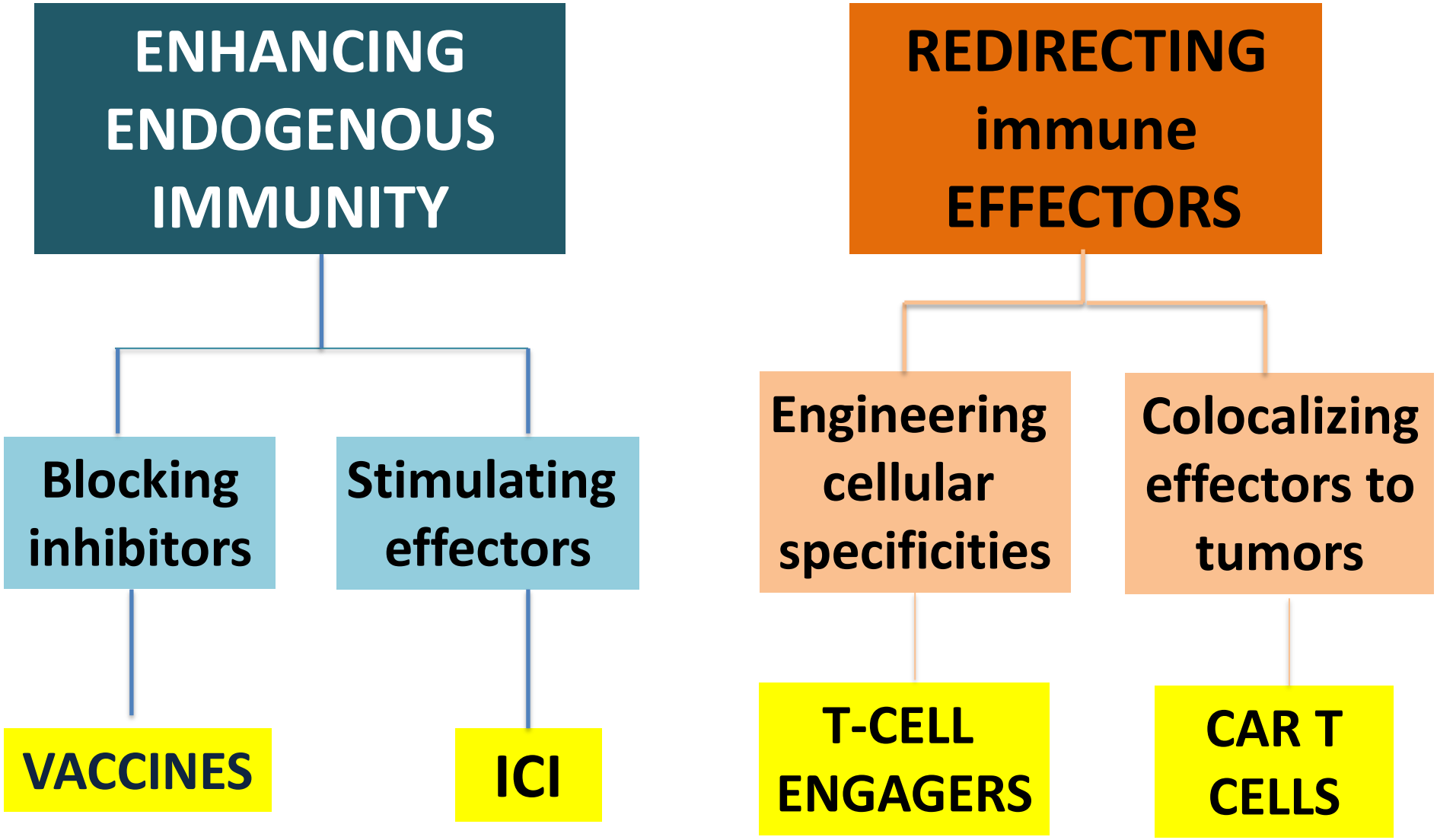
Presented by Alan H. Bryce at ASCO GU 2023

10. TREATMENT SELECTION IN mCPRC: 1st LINE

Treatment in mHSPC conditioned mCRPC sequence



CRPC FUTURE: IMMUNOTHERAPEUTIC APPROACHES




THANK YOU
anaplatabello@hotmail.com
@AnaPlatabello1
@GuardConsortium