Cancer de la prostate

6 décembre 2023

Niort

Dr PILLET Armelle

Rétrospectives et perspectives en cancérologie urologique

Liens d’intérêts

- Sanofi, ipsen, janssen

- **Cancer de la prostate métastasé hormonosensible**

Prostate irradiation in men with *de novo*, low-volume, metastatic castration-sensitive prostate cancer (mCSPC): Results of PEACE-1, a phase 3 randomized trial with a 2x2 design

Alberto BOSSI,
Institut Gustave Roussy, Amethyst RT Group, France

Stéphanie Foulon, Xavier Maldonado, Paul Sargos, Ray McDermott, Paul Kelly, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacso, Naji Salem, Fabio Calabro', Jean-François Berdah, Ali Hasbini, Marlon Silva, Jihane Boustani, Hélène Ribault, Karim Fizazi

Etude PEACE 1

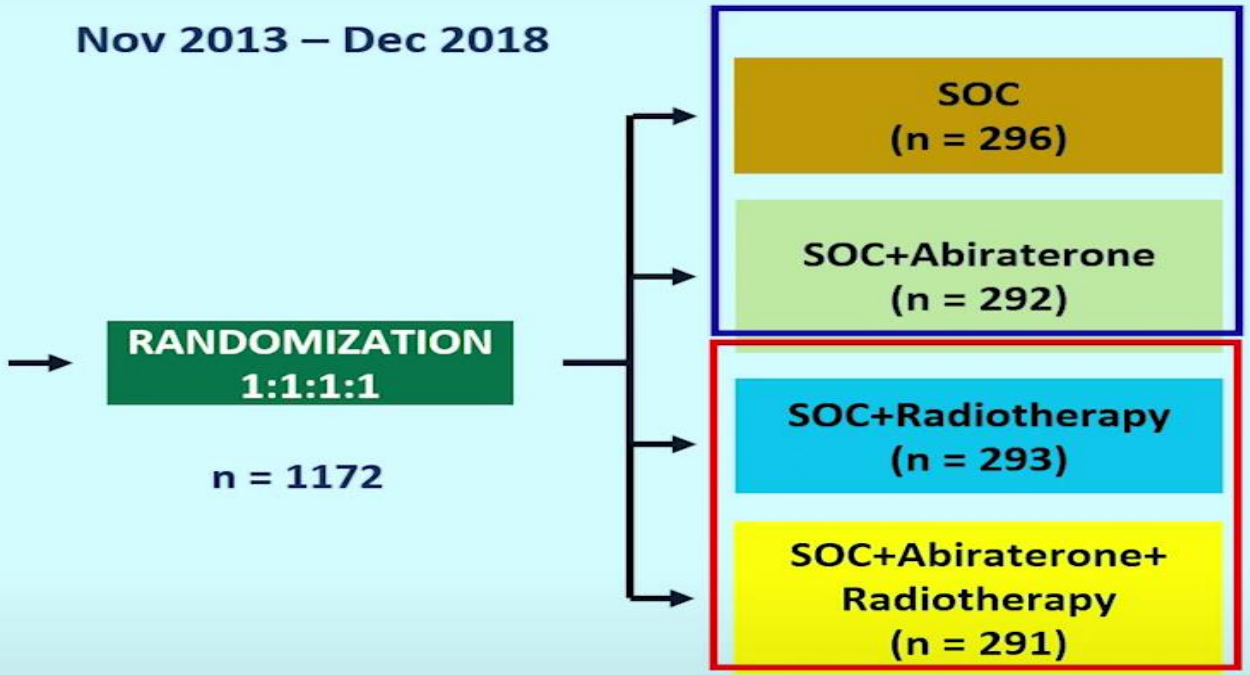
Design de l'étude

Key Eligibility Criteria
De novo mCSPC
Distant metastatic disease: ≥ 1 lesion on bone scan and/or CT scan
ECOG PS 0 -2

On-Study Requirement
Continuous ADT

Permitted
ADT ≤ 3 months

Stratification
ECOG PS (0 vs 1-2)
Metastatic sites (LN vs bone vs visceral)
Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)
Docetaxel (yes vs no)

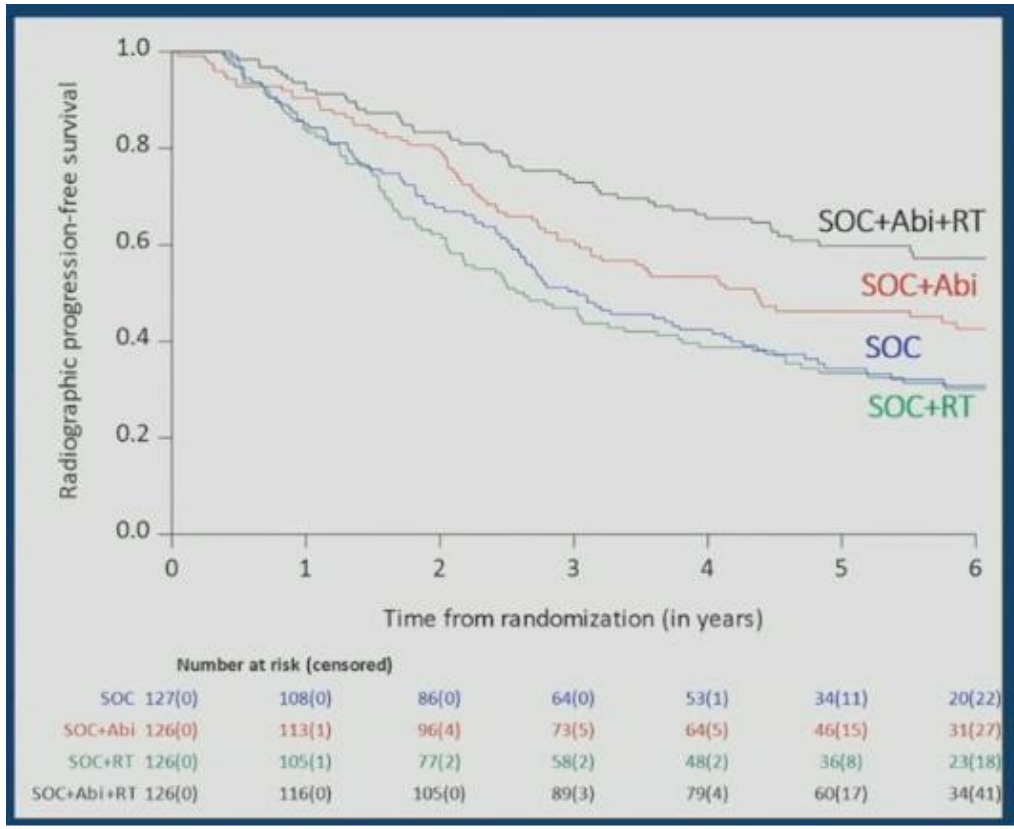


ECOG PS, Eastern Cooperative Oncology Group performance status

Etude PEACE 1

Critère de jugement principal

rPFS patient de faible volume

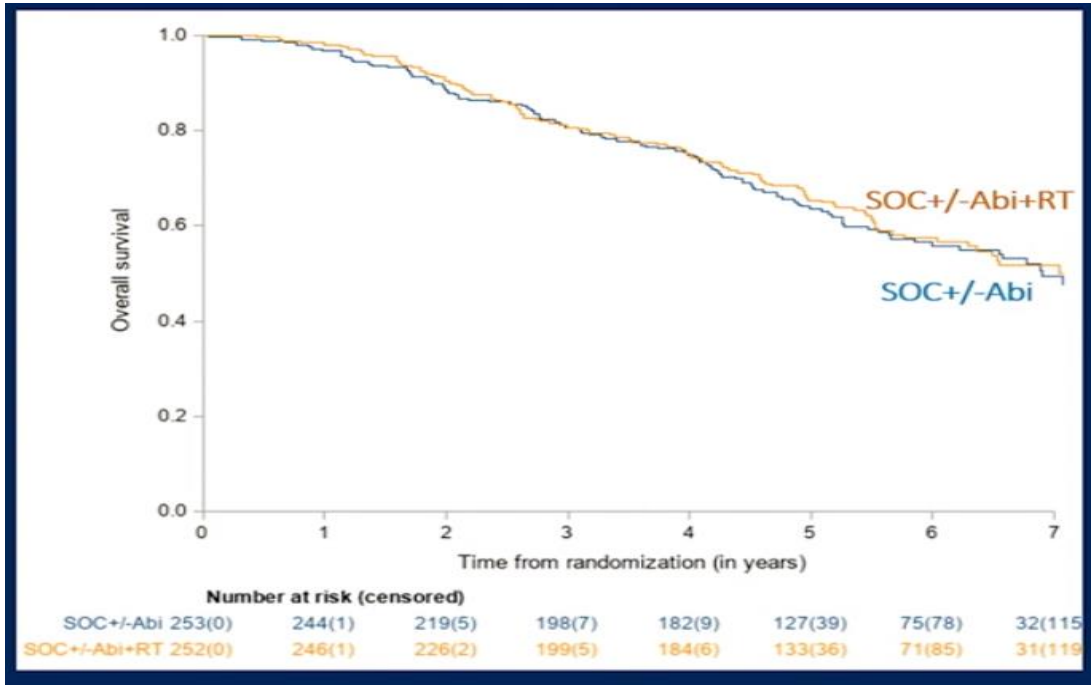


	SOC (n=127)	SOC+RT (n=126)	SOC+Abi (n=126)	SOC+Abi+RT (n=126)
Median, ys. (99.9% CI)	3.0 (2.3-4.8)	2.6 (1.7-4.6)	4.4 (2.5-7.3)	7.5 (4,0-NE)
Events, n.	87	89	74	55
HR (99.9%CI)*	Ref	1.11 (0.67-1.84)	0.76 (0.45-1,28)	0.50 (0.28-0.88)
Global p-value	<0.0001			
HR (99.9% CI)*	Ref	1.08 (0.65-1.80)	Ref	0.65 (0.36-1.19)
P-values arms w/wo Abi	0.61		0.02	

*Adjusted on stratification factors (PS, type of castration, docetaxel)

Etude PEACE 1

Survie globale



	SOC+/Abi (n=253)	SOC+/-Abi+RT (n=252)
Median, ys. (95.1% CI)	6.9 (5,9-7,5)	7,5 (6-NE)
Events, n	111	104
HR*	Ref	0,98 (0.74-1.28)
p-value	0.86	

*Adjusted on Abitraterone and stratification factors (PS, type of castration, docetaxel)

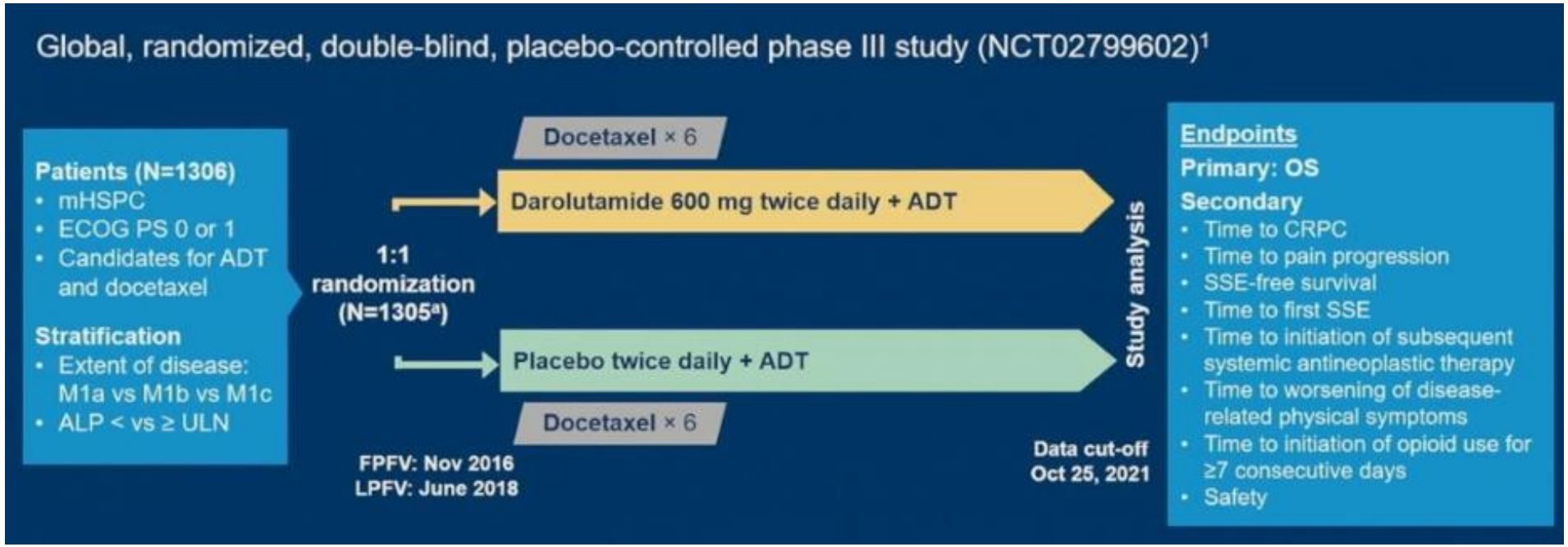
Etude PEACE 1

Evènements urologiques majeurs

Population globale

Etude ARASENS

Design de l'étude



A. Hussain, ASCO GU 2023

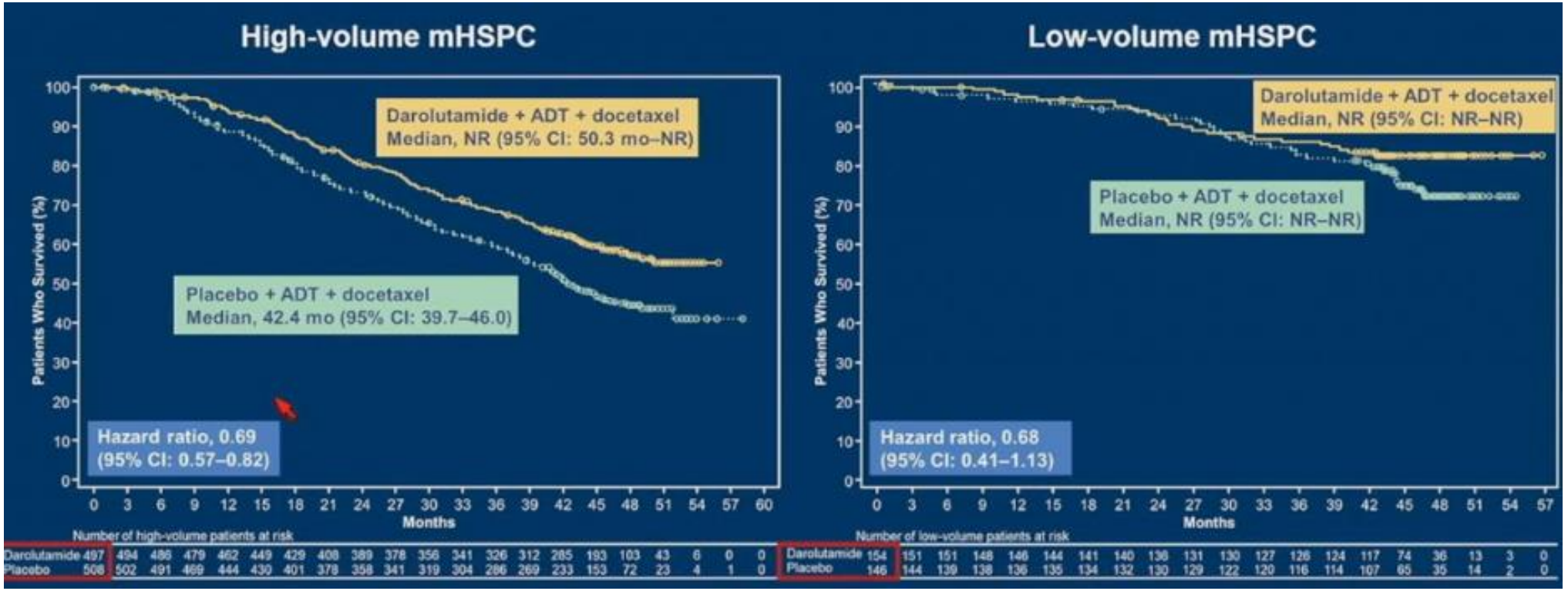
Etude ARASENS

Population de l'étude

Characteristic at Baseline	High Volume		Low Volume	
	Darolutamide (n=497)	Placebo (n=508)	Darolutamide (n=154)	Placebo (n=146)
Age, median (range), y	67.0 (41–89)	67.0 (44–86)	67.0 (41–84)	67.5 (42–81)
Gleason score at initial diagnosis ≥8, n (%)	381 (76.7)	403 (79.3)	124 (80.5)	113 (77.4)
Metastasis stage at initial diagnosis, n (%)[a]				
De novo	**432 (86.9)**	**445 (87.6)**	**126 (81.8)**	**121 (82.9)**
Recurrent	58 (11.7)	59 (11.6)	28 (18.2)	23 (15.8)
Metastasis stage at screening, n (%)				
M1a (nonregional LN only)	0	0	23 (14.9)	15 (10.3)
M1b (bone ± LN)	386 (77.7)	390 (76.8)[b]	131 (85.1)	131 (89.7)
M1c (visceral ± LN or bone)	111 (22.3)	118 (23.2)	0	0
Serum PSA, median (range), ng/mL[c]	38.7 (0–9219.0)	27.9 (0–11,947.0)	11.7 (0–3771.0)	14.5 (0–3372.9)

Etude ARASENS

Survie globale



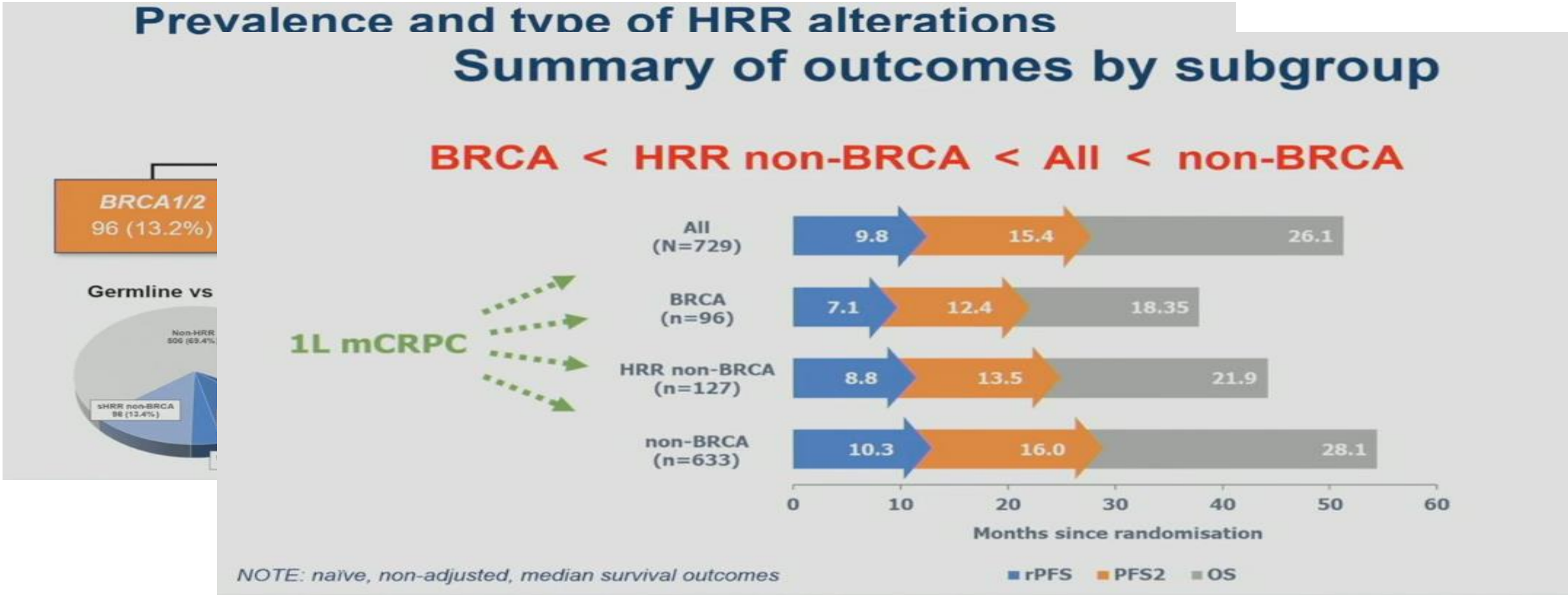
Etude ARASENS

Secondary endpoint	Patient subgroups	Number of events/ Number of patients		Median (95% CI), months		HR (95% CI)[a]
		DARO	PBO	DARO	PBO	
Time to pain progression	All patients[b]	222/651	248/654	NE (30.5–NE)	27.5 (22.0–36.1)	0.79 (0.66–0.95)
	High volume	161/497	192/508	NE (26.7–NE)	24.4 (16.8–33.3)	0.75 (0.61–0.93)
	Low volume	61/154	56/146	46.1 (25.0–NE)	39.5 (24.6–NE)	0.94 (0.66–1.36)
	High risk	155/452	173/460	35.4 (25.0–NE)	25.0 (18.2–35.9)	0.81 (0.65–1.01)
	Low risk	67/199	75/194	NE (39.2–NE)	28.8 (19.3–NE)	0.76 (0.55–1.06)
Time to first symptomatic skeletal event	All patients[b]	95/651	108/654	NE (NE–NE)	NE (NE–NE)	0.71 (0.54–0.94)
	High volume	82/497	96/508	NE (NE–NE)	NE (NE–NE)	0.71 (0.53–0.96)
	Low volume	13/154	12/146	NE (NE–NE)	NE (NE–NE)	0.89 (0.40–1.95)
	High risk	78/452	79/460	NE (NE–NE)	NE (NE–NE)	0.84 (0.61–1.15)
	Low risk	17/199	29/194	NE (51.2–NE)	NE (NE–NE)	0.46 (0.25–0.84)
Time to initiation of subsequent systemic antineoplastic therapy	All patients[b]	219/651	395/654	NE (NE–NE)	25.3 (23.1–28.8)	0.39 (0.33–0.46)
	High volume	187/497	324/508	NE (49.6–NE)	22.7 (19.6–25.1)	0.40 (0.34–0.49)
	Low volume	32/154	71/146	NE (NE–NE)	42.5 (34.0–NE)	0.34 (0.22–0.52)
	High risk	173/452	299/460	NE (49.6–NE)	21.3 (19.2–24.0)	0.40 (0.33–0.48)
	Low risk	46/199	96/194	NE (NE–NE)	39.0 (31.8–NE)	0.36 (0.26–0.52)

[a]Based on unstratified Cox regression model.
[b]Includes all randomized patients according to planned treatment.

- **Altérations HRR, place des inhibiteurs de PARP**

Etude CAPTURE



David Olmos et al
Presence of somatic/germline homologous recombination repair (HRR) mutations and outcomes in metastatic castration-resistant prostate cancer (mCRPC) patients (pts) receiving first-line (1L) treatment stratified by BRCA status.

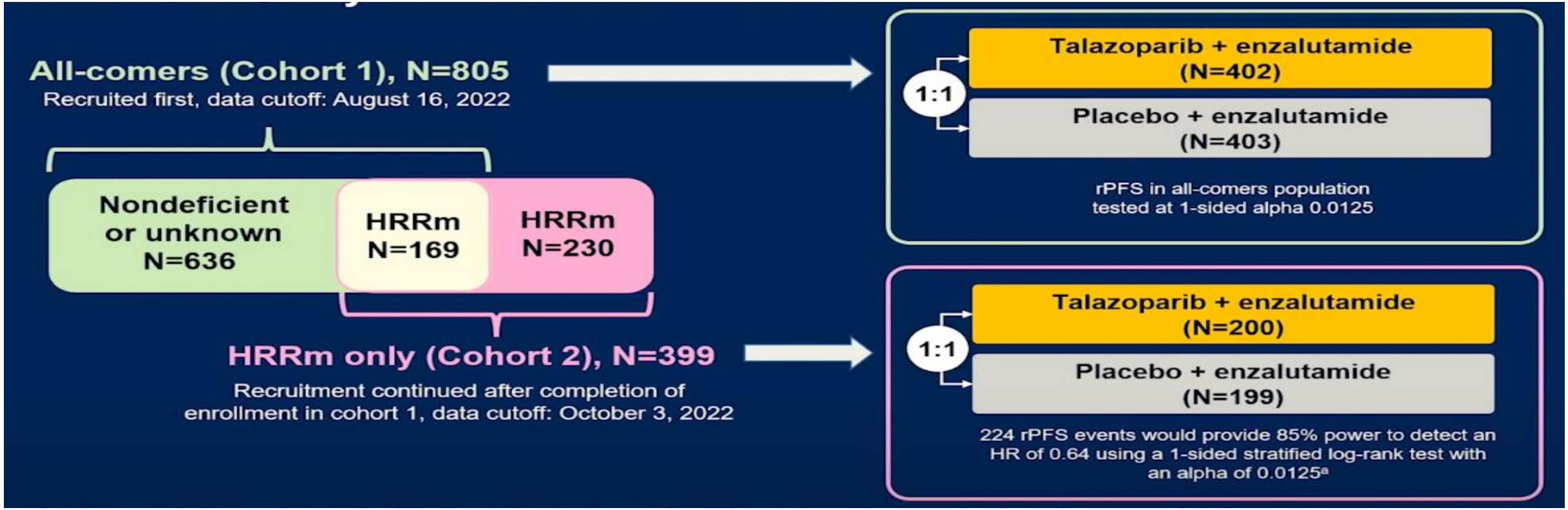
TALAPRO-2: Phase 3 study of talazoparib plus enzalutamide versus placebo plus enzalutamide as first-line treatment for patients with metastatic castration-resistant prostate cancer harboring homologous recombination repair gene alterations (HRR-deficient population)

Karim Fizazi,[1] Arun A. Azad,[2] Nobuaki Matsubara,[3] Joan Carles,[4] Andre P. Fay,[5] Ugo De Giorgi,[6] Jae Young Joung,[7] Peter C. C. Fong,[8] Eric Voog,[9] Robert J. Jones,[10] Neal D. Shore,[11] Curtis Dunshee,[12] Stefanie Zschäbitz,[13] Jan Oldenburg,[14] Xun Lin,[15] Cynthia G. Healy,[16] Nicola Di Santo,[17] Fabian Zohren,[18] Neeraj Agarwal[19]

Etude TALAPRO 2

Design de l'étude

Etude TALAPRO 2



Etude TALAPRO 2

Caractéristiques de la population HRR-deficient

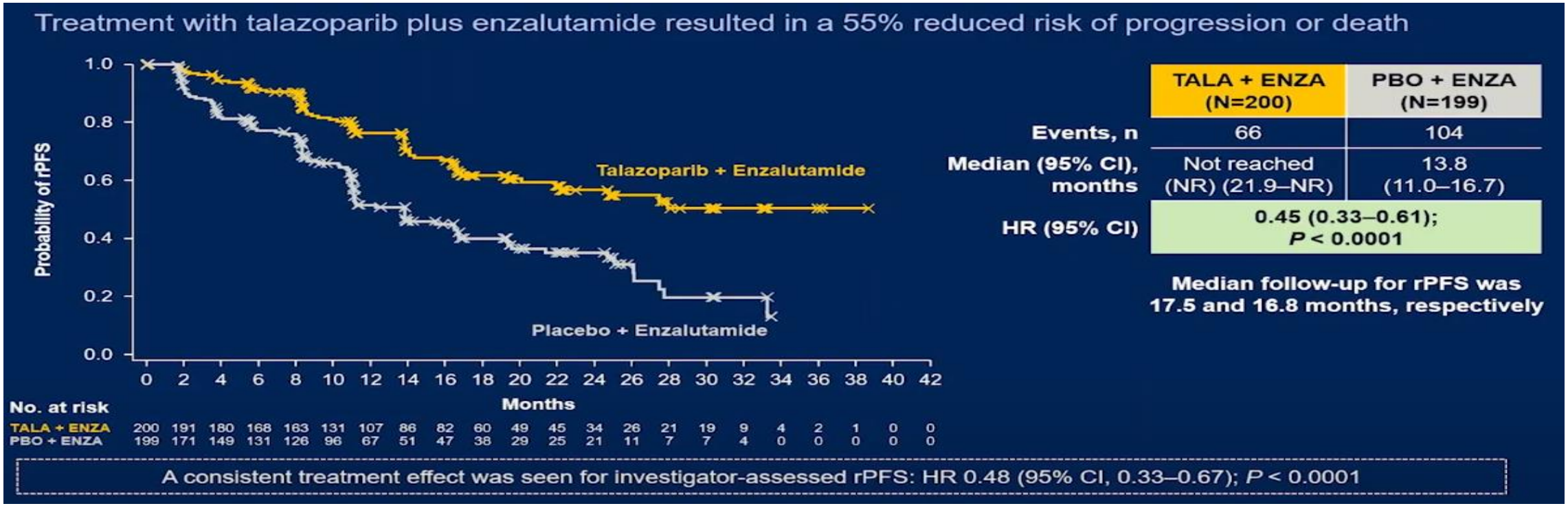
These were well-balanced between treatment arms

	Talazoparib + Enzalutamide (N=200)	Placebo + Enzalutamide (N=199)
Age, median (range), years	70 (41–90)	71 (44–90)
Prostate-specific antigen (PSA), median (range), ng/mL	19.6 (0.2–3412.0)	18.0 (0.0–1055.0)
Disease site, n (%)		
Bone	175 (87.5)	158 (79.4)
Lymph node	82 (41.0)	94 (47.2)
Visceral (lung/liver)	23 (11.5)/9 (4.5)	26 (13.1)/6 (3.0)
ECOG PS 0/1, n (%)	128 (64.0)/72 (36.0)	118 (59.3)/81 (40.7)
Prior abiraterone[a] or docetaxel, n (%)	75 (37.5)	74 (37.2)
Abiraterone	16 (8.0)	16 (8.0)
Docetaxel	57 (28.5)	60 (30.2)
Tissue source for prospective HRR gene alteration testing, n (%)		
Tumor tissue only	76 (38.0)	80 (40.2)
Tumor tissue and blood (circulating tumor DNA)	121 (60.5)	115 (57.8)
Blood (circulating tumor DNA) only	3 (1.5)	4 (2.0)

[a]One patient in each treatment arm received prior orteronel.

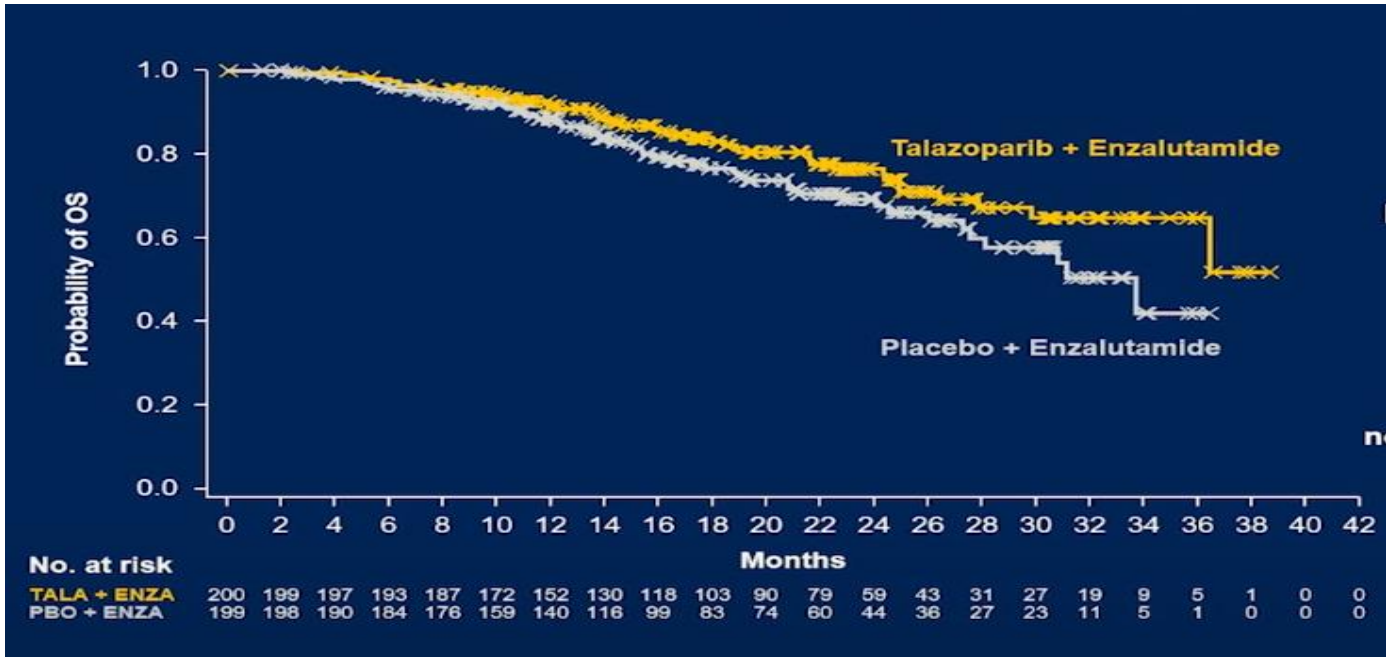
Etude TALAPRO 2

Critère principal : rPFS



Etude TALAPRO 2

Survie globale



	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	43	53
Median (95% CI), months	NR (36.4–NR)	33.7 (27.6–NR)
HR (95% CI)	HR 0.69 (95% CI, 0.46–1.03) *P* = 0.068	

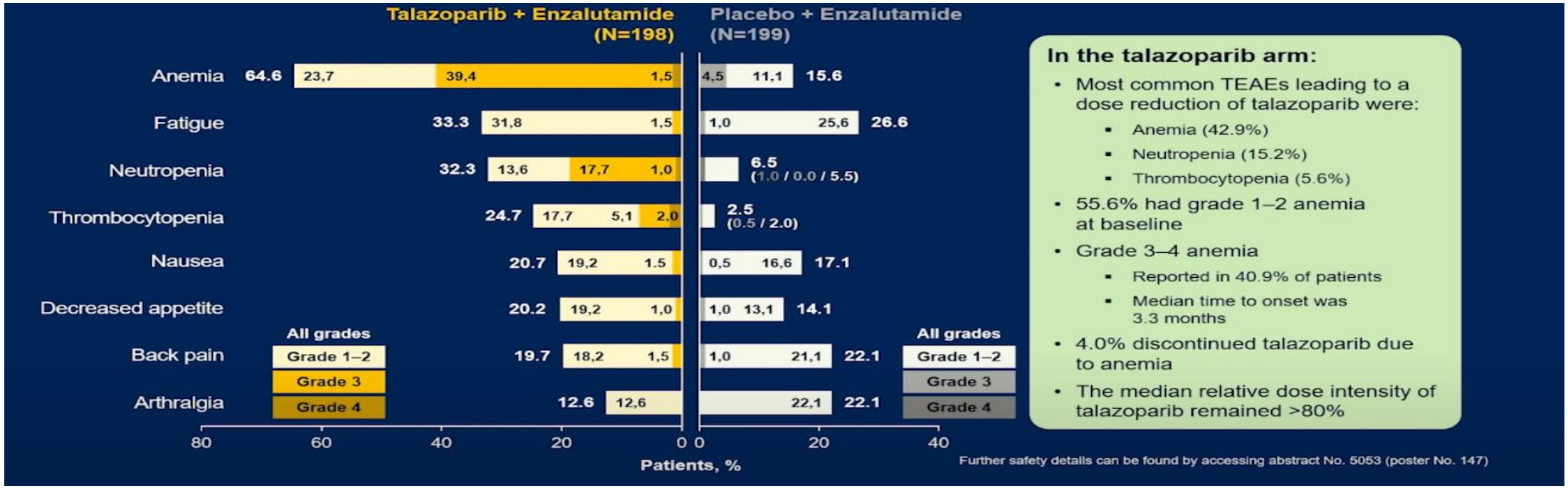
***BRCA* alterations: HR 0.61 (95% CI, 0.31–1.23; *P* = 0.16)**
non-*BRCA* alterations: HR 0.66 (95% CI, 0.40–1.10; *P* = 0.11)

18 patients in the control arm and 3 patients in the talazoparib arm subsequently received olaparib

Etude TALAPRO 2

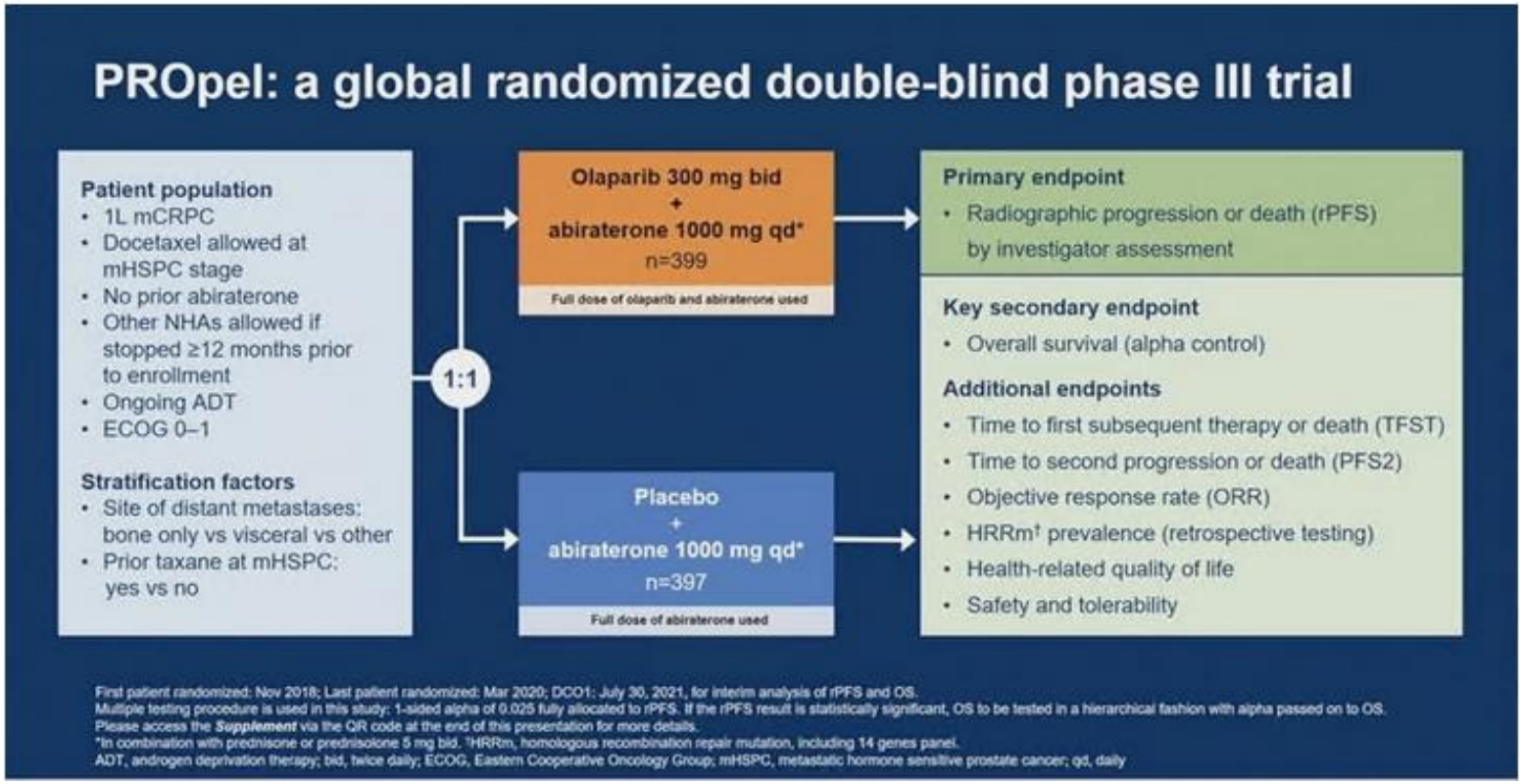
Tolérance

	TALA + ENZA (N=198)	PBO + ENZA (N=199)
Dose interruption of talazoparib or placebo due to AE	133 (67.2)	39 (19.6)
Dose reduction of talazoparib or placebo due to AE[a]	110 (55.6)	12 (6.0)
Discontinuation of talazoparib or placebo due to AE	20 (10.1)	14 (7.0)



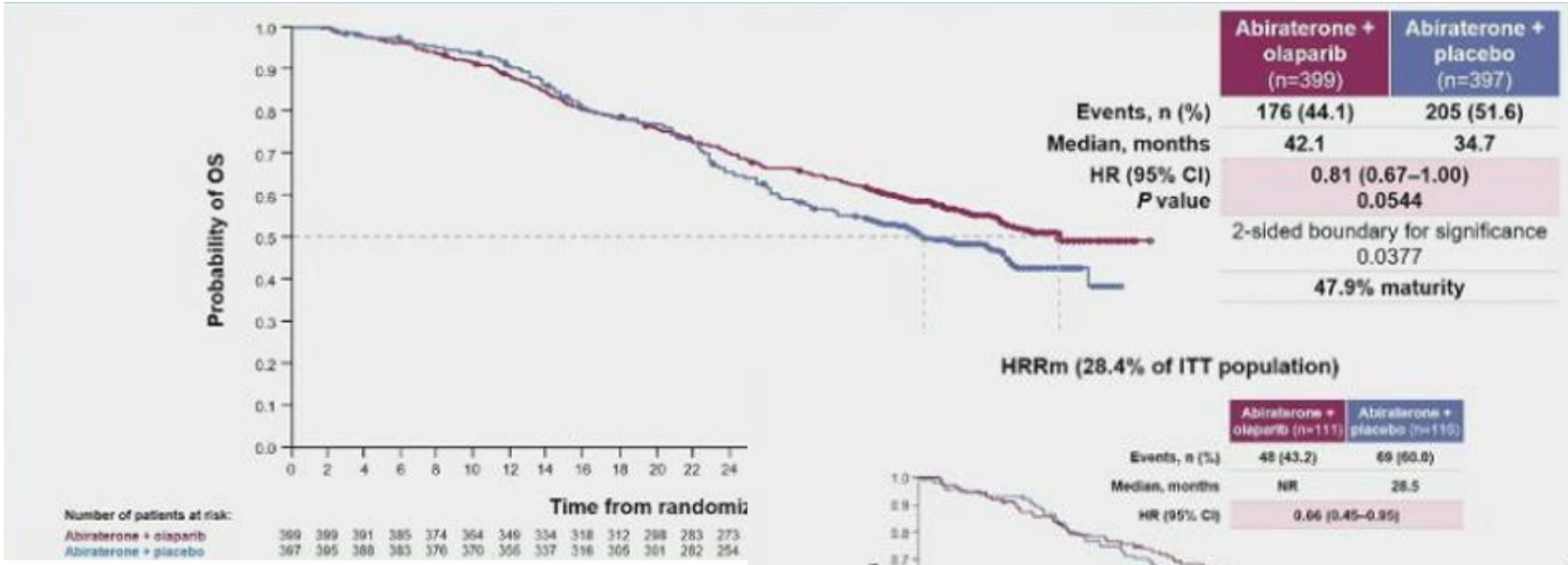
Etude PROPEL

Design étude

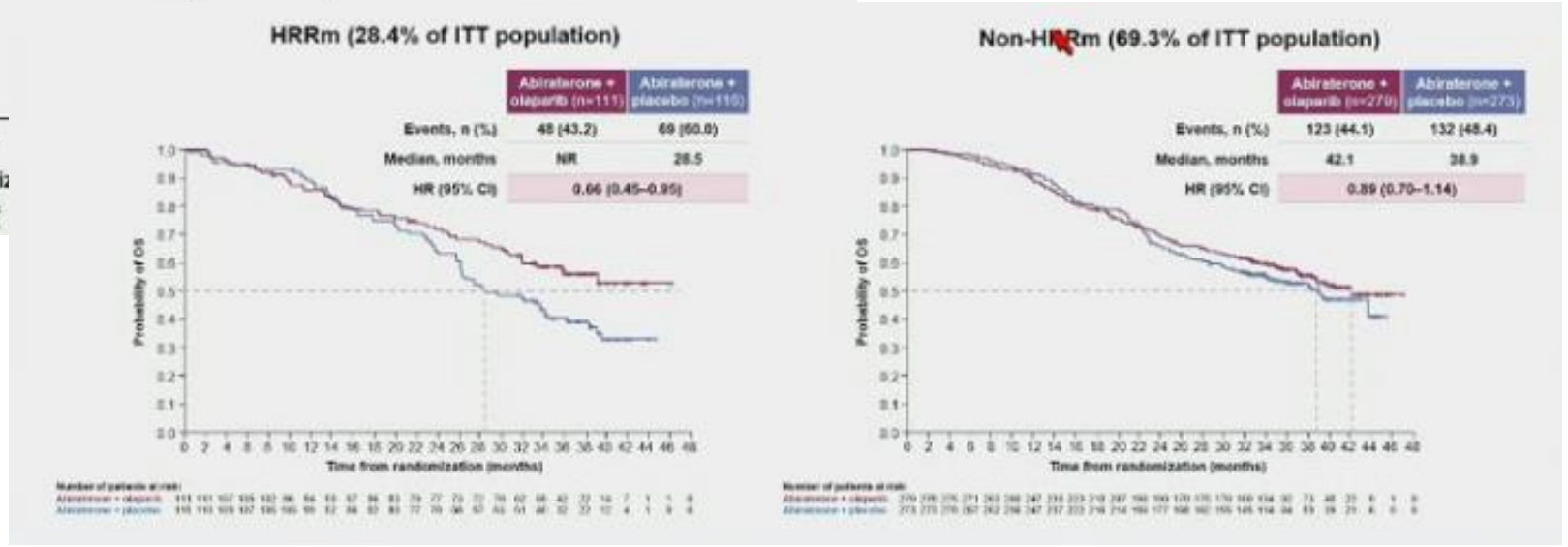


Etude PROPEL

Survie globale

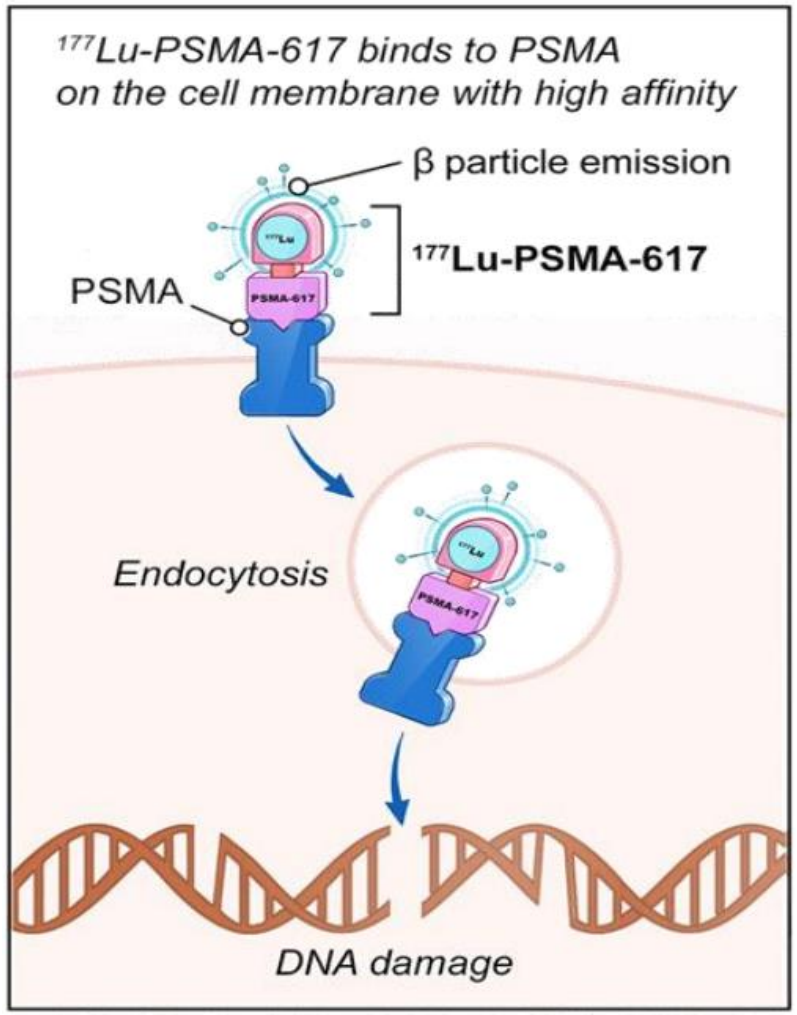


	Abiraterone + olaparib (n=399)	Abiraterone + placebo (n=397)
Events, n (%)	176 (44.1)	205 (51.6)
Median, months	42.1	34.7
HR (95% CI)	0.81 (0.67–1.00)	
P value	0.0544	
2-sided boundary for significance	0.0377	
	47.9% maturity	



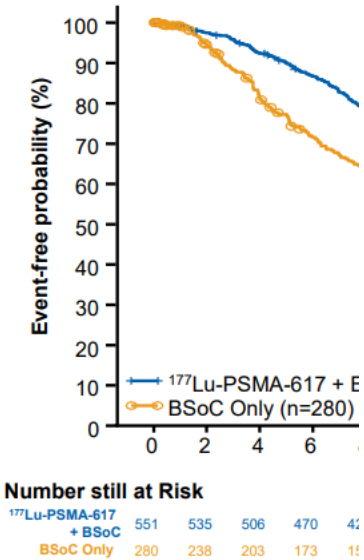
- **Lu – PSMA, radiothérapie interne vectorisée**

Place du Lu-PSMA



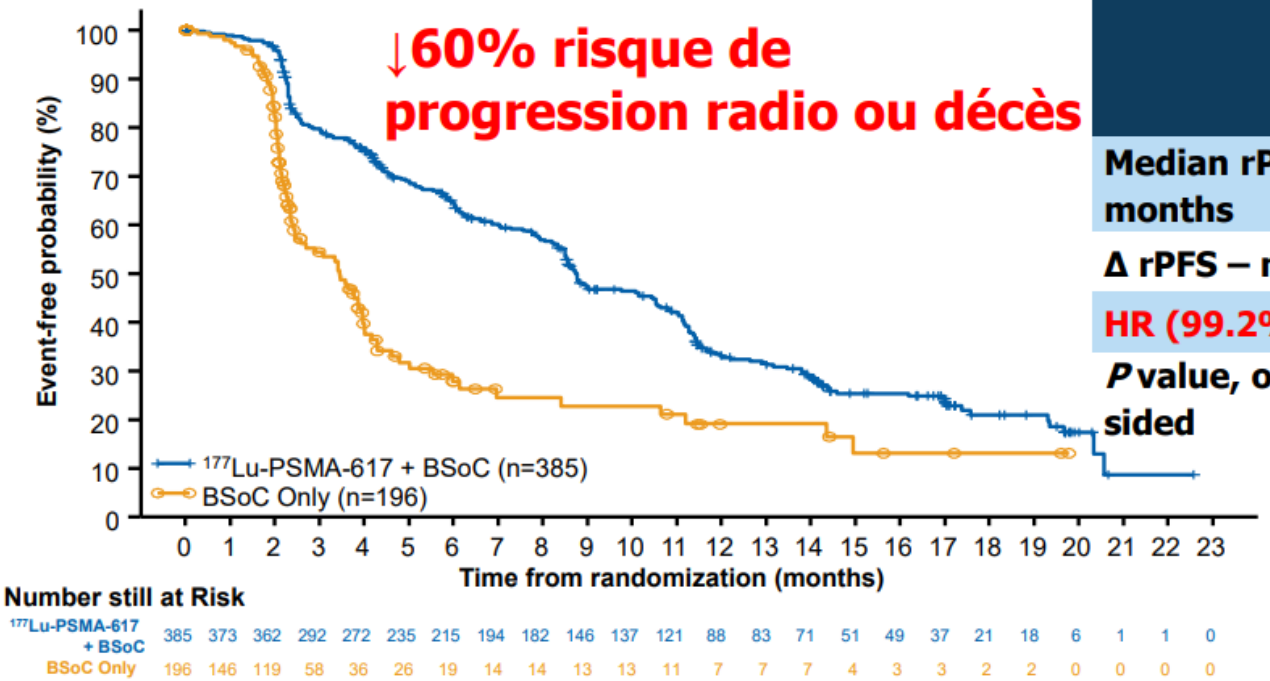
Etude VISION

Résultat -> survi



SG significativeme

Résultats -> survie sans progression radiologique



	177Lu-PSMA-617 + BSoC (n=385)	BSoC only (n=196)
Median rPFS – months	8.7	3.4
Δ rPFS – months	5.3	
HR (99.2% CI)	0.40 (0.29–0.57)	
P value, one-sided	<0.001	

SSPr significativement prolongée dans le bras 177Lu-PSMA-617 + meilleur traitement standard *versus* meilleur traitement standard seul

Etude PSMAfore

MADRID 2023 ESMO congress

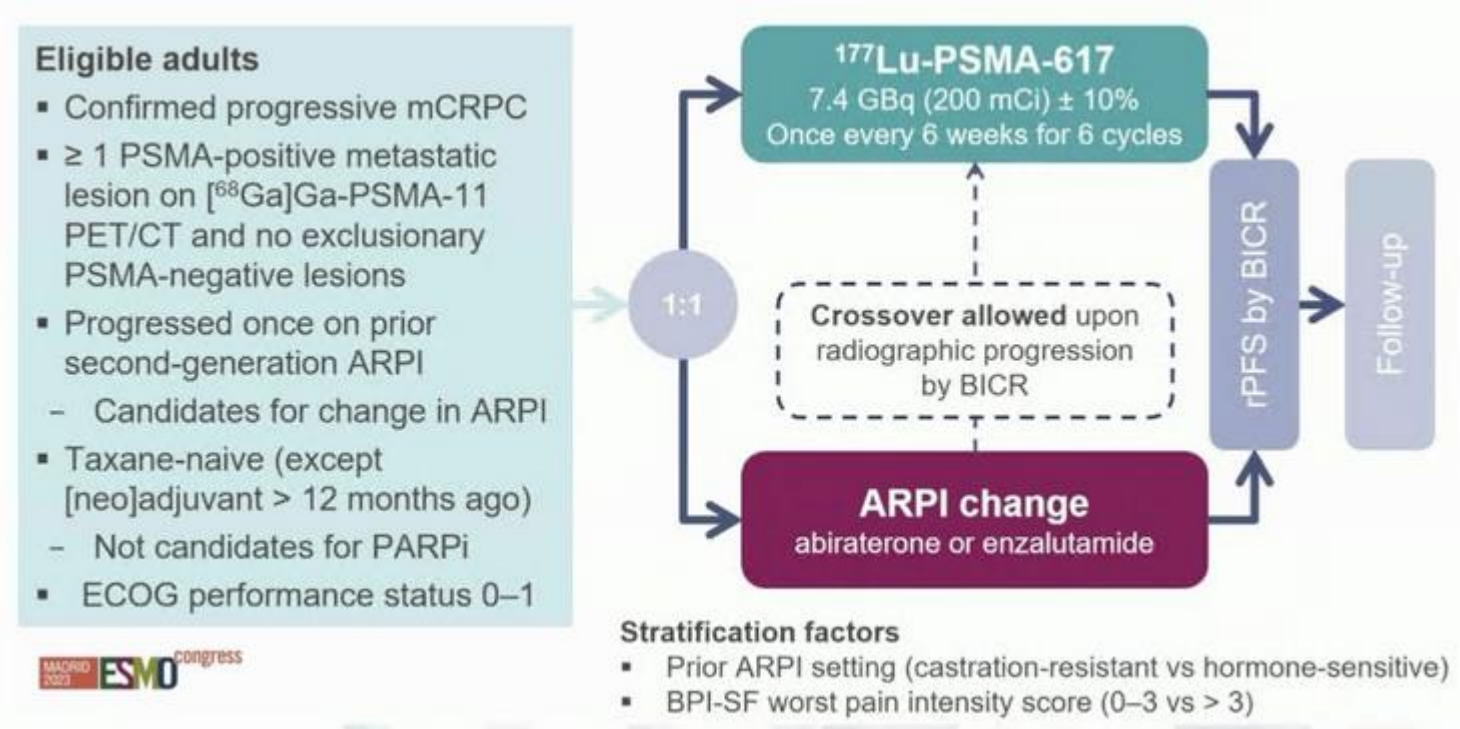
Phase 3 trial of [^{177}Lu]Lu-PSMA-617 in taxane-naive patients with metastatic castration-resistant prostate cancer (PSMAfore)

Presenter: Oliver Sartor,*
Mayo Clinic, Rochester, MN, USA

Co-authors: D Castellano, K Herrmann, J de Bono, ND Shore, KN Chi, M Crosby, JM Piulats, A Flechon, XX Wei, H Mahammedi, G Roubaud, H Studentova, S Ghebremariam, E Kpamegan, TN Kreisl, N Delgoshaie, K Lehnhoff, MJ Morris,* K Fizazi,*
on behalf of the PSMAfore investigators

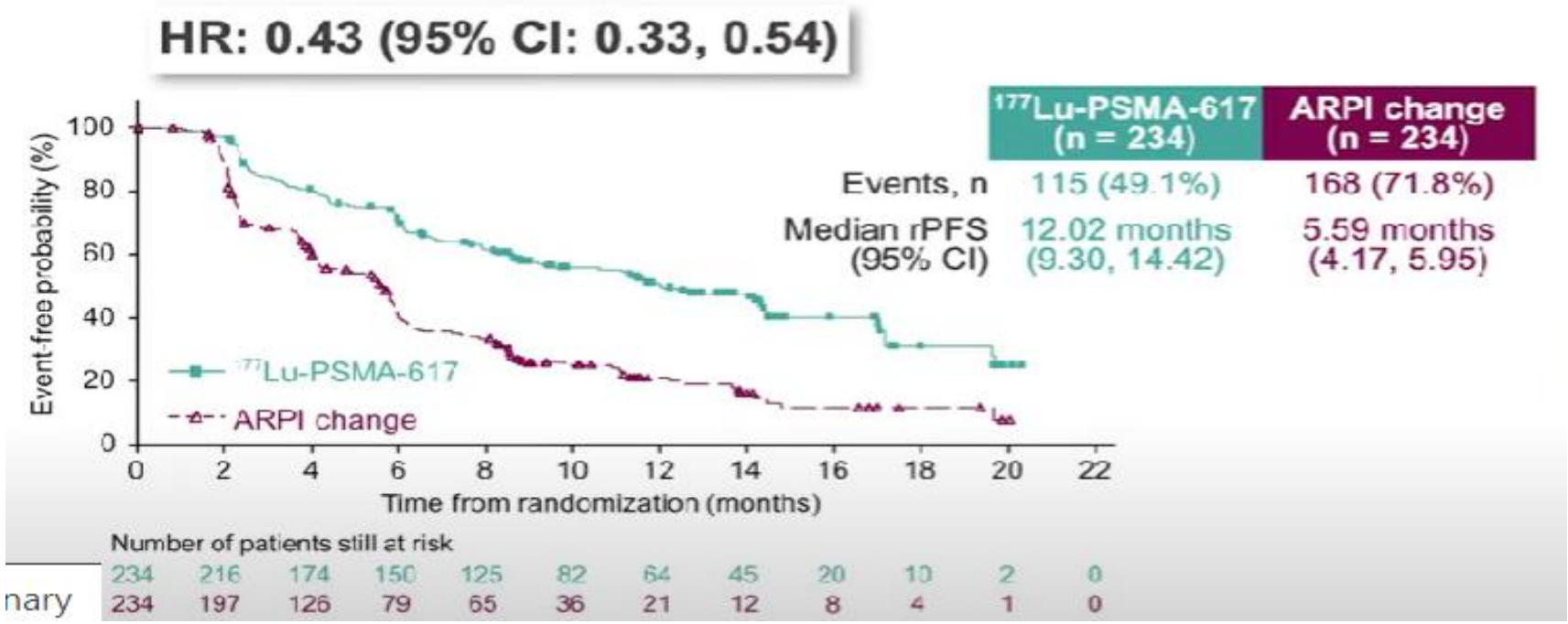
Etude PSMAfore

Design étude



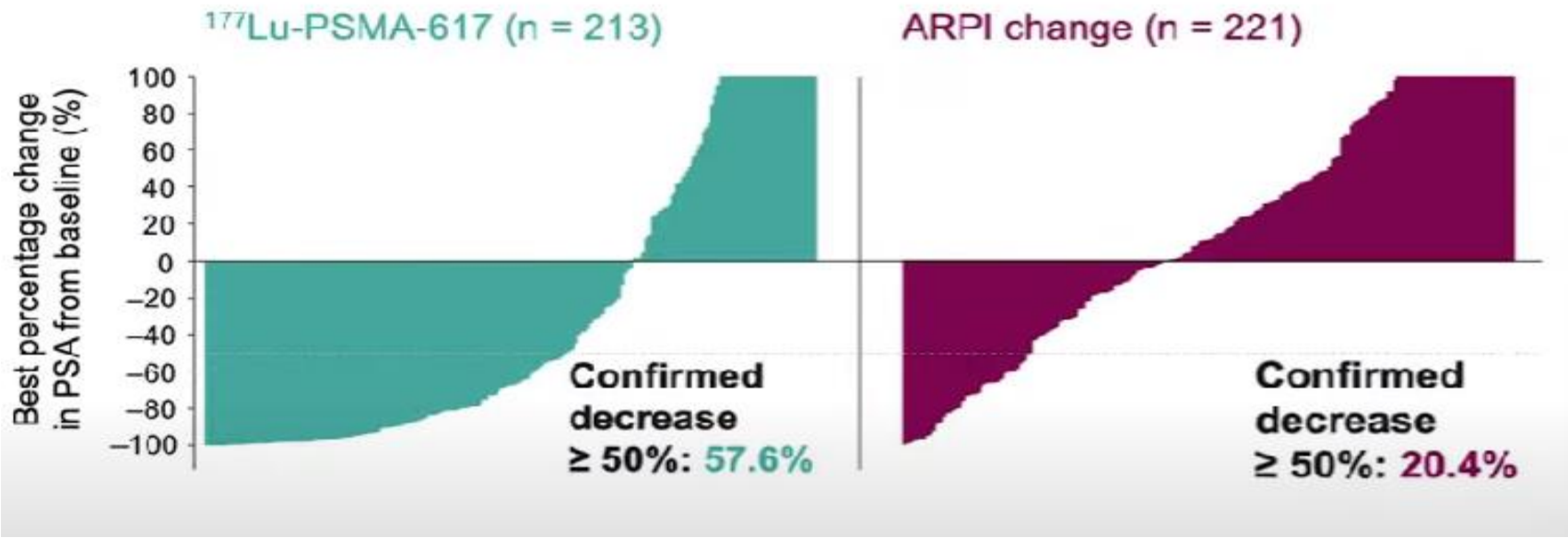
Etude PSMAfore

Primary endpoint : rPFS



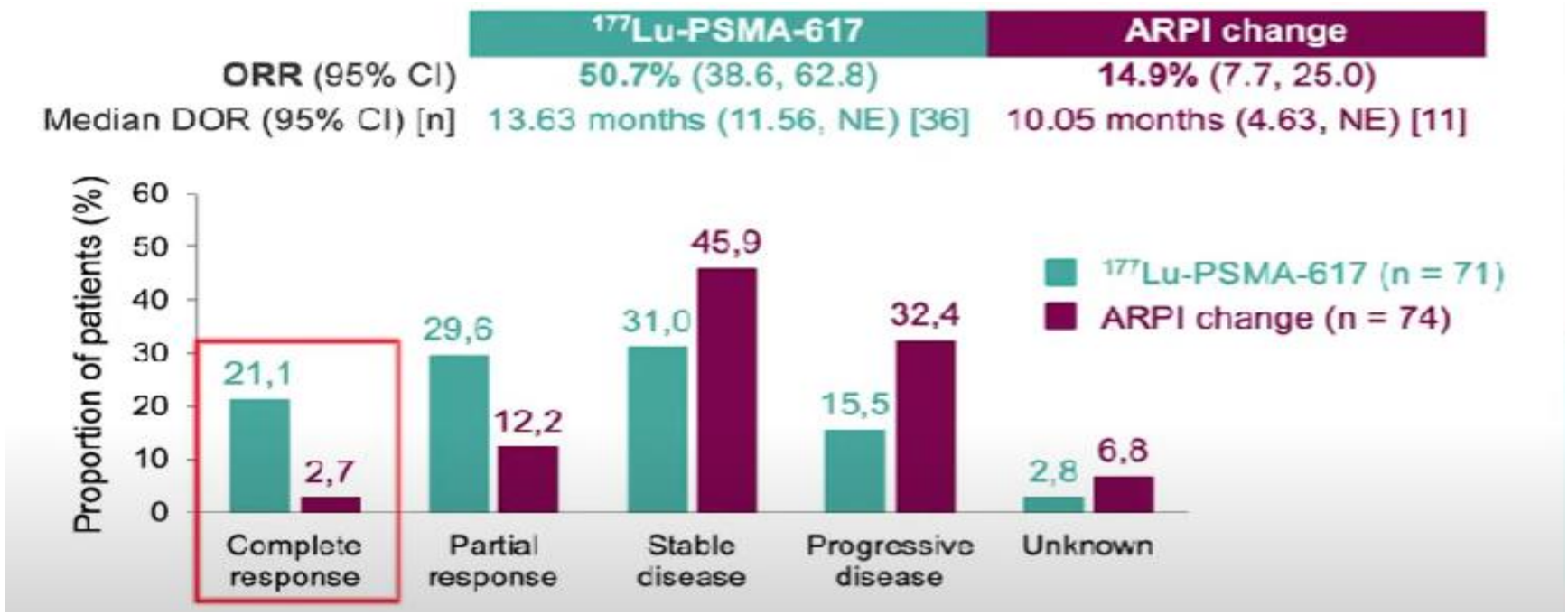
Etude PSMAfore

Critère secondaire : décroissance PSA



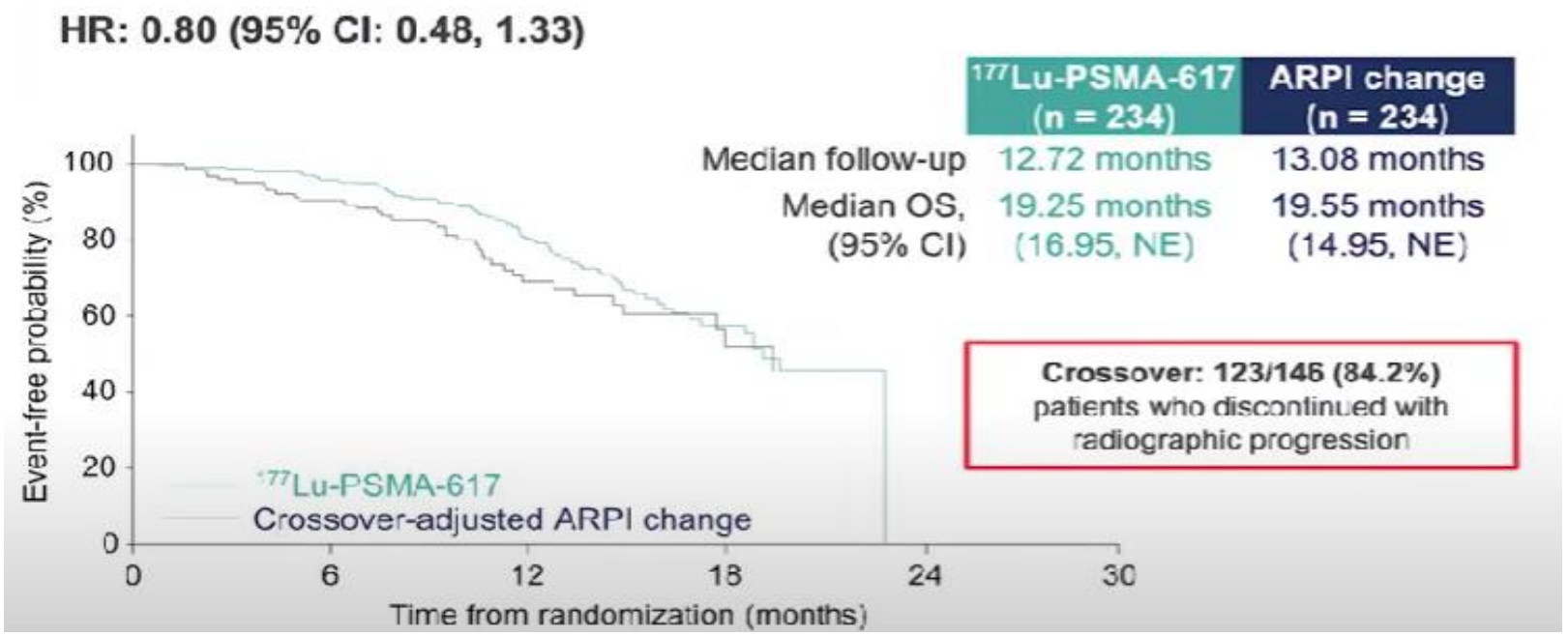
Etude PSMAfore

Critère secondaire : taux de réponse



Etude PSMAfore

Critère secondaire : survie globale

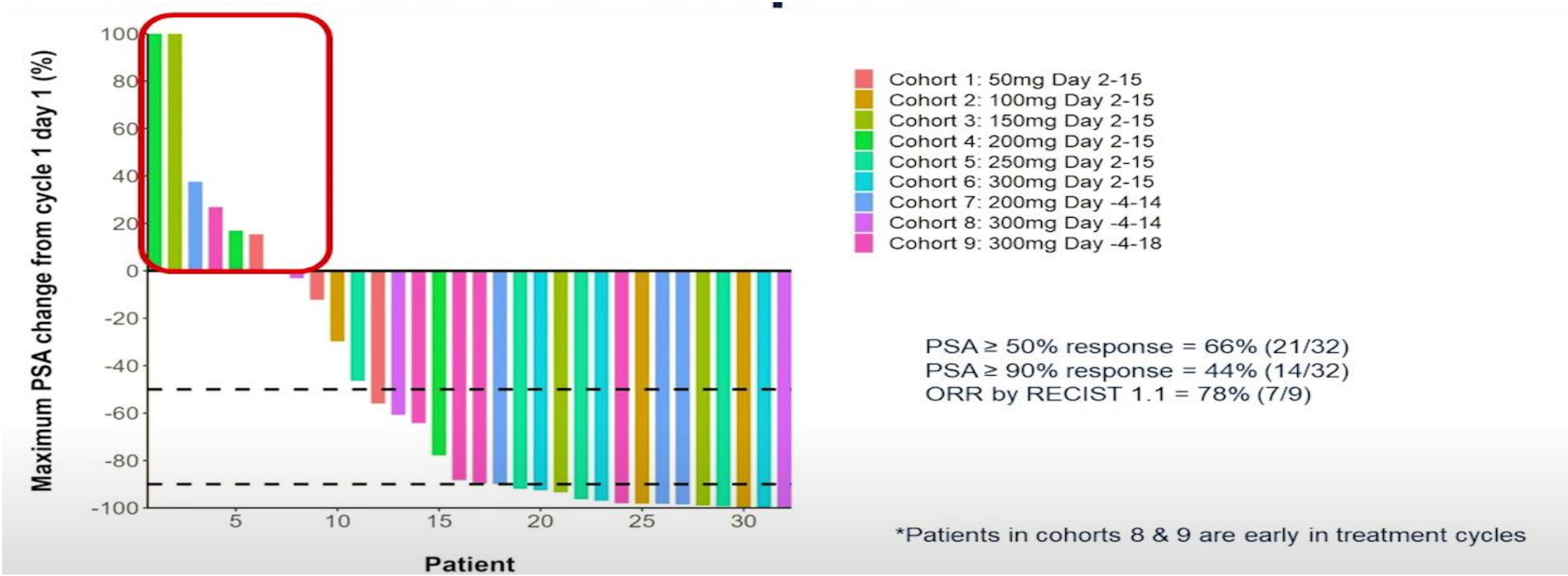


Etude PSMAfore

Tolérance

AEs, n (%)	All grades		Grades 3–5	
	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Dry mouth	130 (57.3)	5 (2.2)	3 (1.3)	0
Asthenia	72 (31.7)	67 (28.9)	1 (0.4)	8 (3.4)
Nausea	71 (31.3)	28 (12.1)	0	1 (0.4)
Anaemia	55 (24.2)	39 (16.8)	14 (6.2)	14 (6.0)
Fatigue	52 (22.9)	59 (25.4)	0	4 (1.7)
Constipation	50 (22.0)	31 (13.4)	1 (0.4)	0
Decreased appetite	48 (21.1)	42 (18.1)	0	1 (0.4)
Arthralgia	43 (18.9)	48 (20.7)	0	1 (0.4)
COVID-19	37 (16.3)	26 (11.2)	1 (0.4)	1 (0.4)
Diarrhoea	37 (16.3)	20 (8.6)	0	1 (0.4)
Back pain	28 (12.3)	38 (16.4)	2 (0.9)	5 (2.2)
Vomiting	26 (11.5)	11 (4.7)	0	0
Peripheral oedema	19 (8.4)	26 (11.2)	0	0
Weight loss	15 (6.6)	28 (12.1)	2 (0.9)	5 (2.2)

Avenir Lu PSMA



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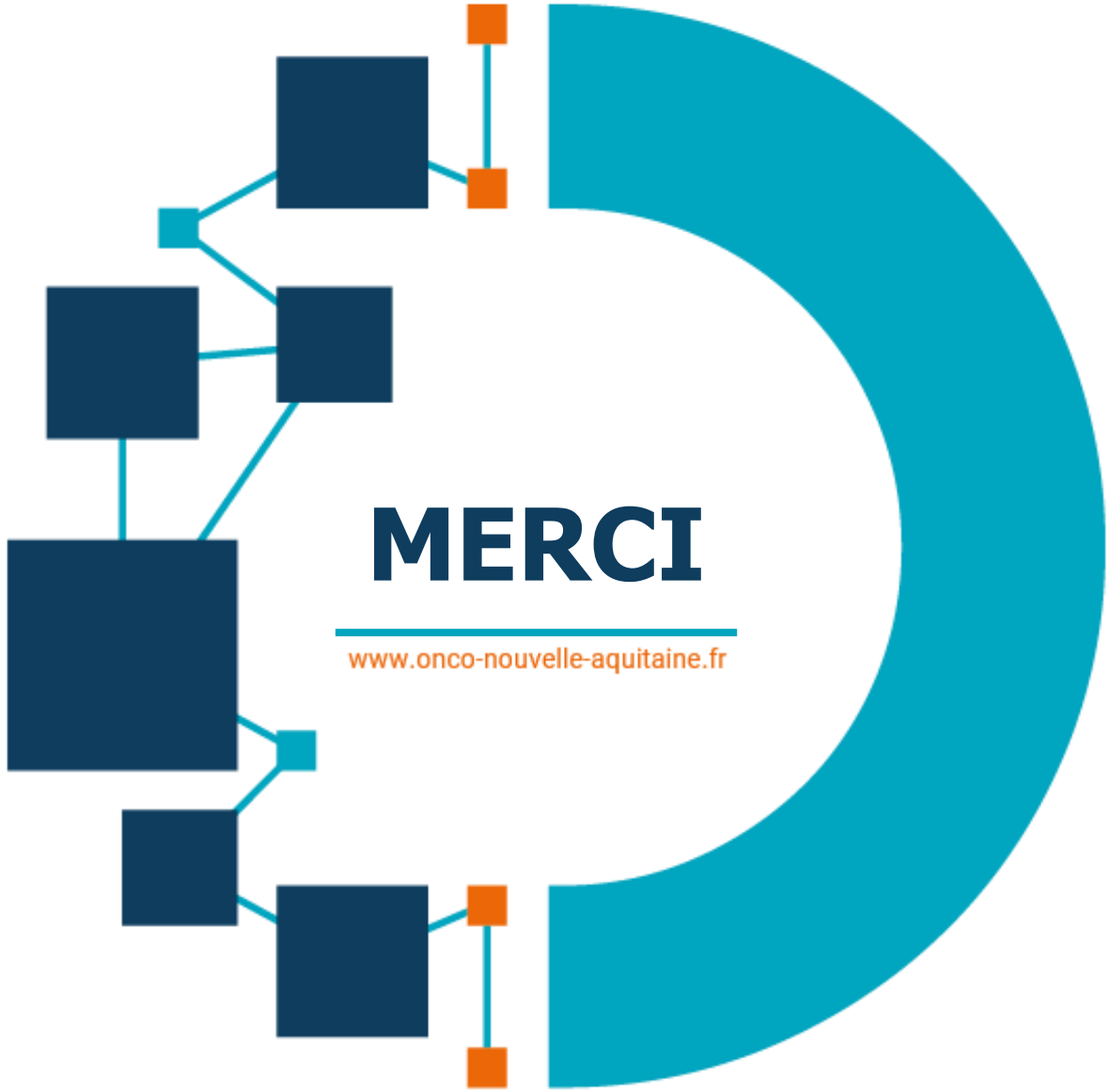
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