Les Scoops de l'uro-oncologie

Date de la réunion

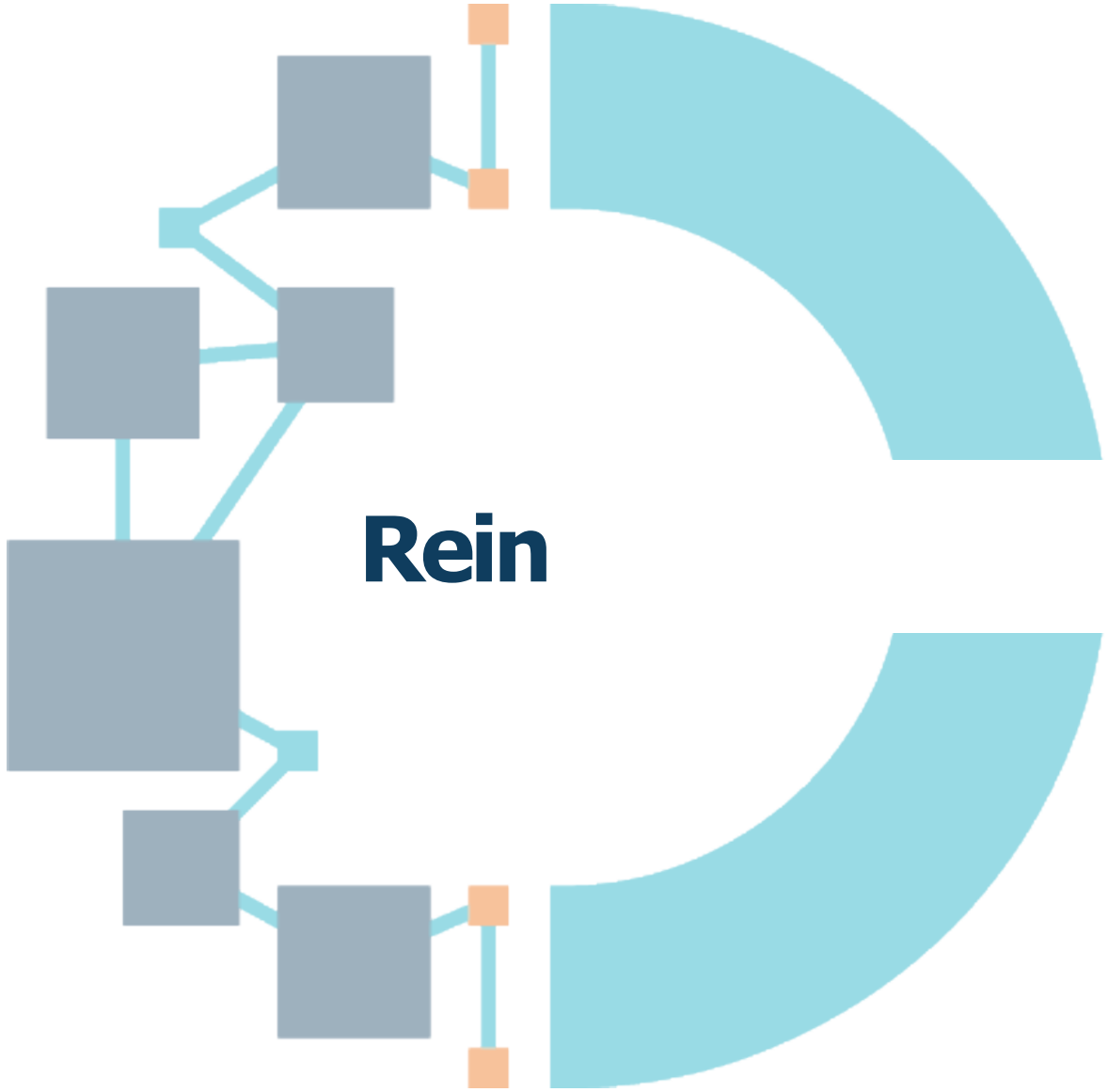
Sabrina Falkowski

Oncologue – Polyclinique de Limoges

3ème post-ASCO en Nouvelle-Aquitaine -20/06/2023

Liens d’intérêts

- Multiples : AAA, Astellas, Astra Zeneca, BMS, Ipsen, Janssen, Merk, MSD, Pfizer, Sanofi
- Invitée par Sanofi



Rein

ESSAI de phase III CONTACT-03

Intérêt de poursuivre IO en combo après une 1ère exposition?

Efficacy and safety of atezolizumab plus cabozantinib vs cabozantinib alone after progression with prior immune checkpoint inhibitor treatment in metastatic renal cell carcinoma: Phase III CONTACT-03 study

Toni K. Choueiri,[1] Laurence Albiges,[2] Piotr Tomczak,[3] Cristina Suárez,[4] Martin H. Voss,[5] Guillermo de Velasco,[6] Jad Chahoud,[7] Giuseppe Procopio,[8] Hakim Mahammedi,[9] Friedemann Zengerling,[10] Chan Kim,[11] Suyasha Gupta,[12] Guillaume Bergthold,[13] Bo Liu,[12] Melania Kalaitzidou,[14] Mahrukh Huseni,[12] Christian Scheffold,[15] Thomas Powles,[16] Sumanta Kumar Pal[17]

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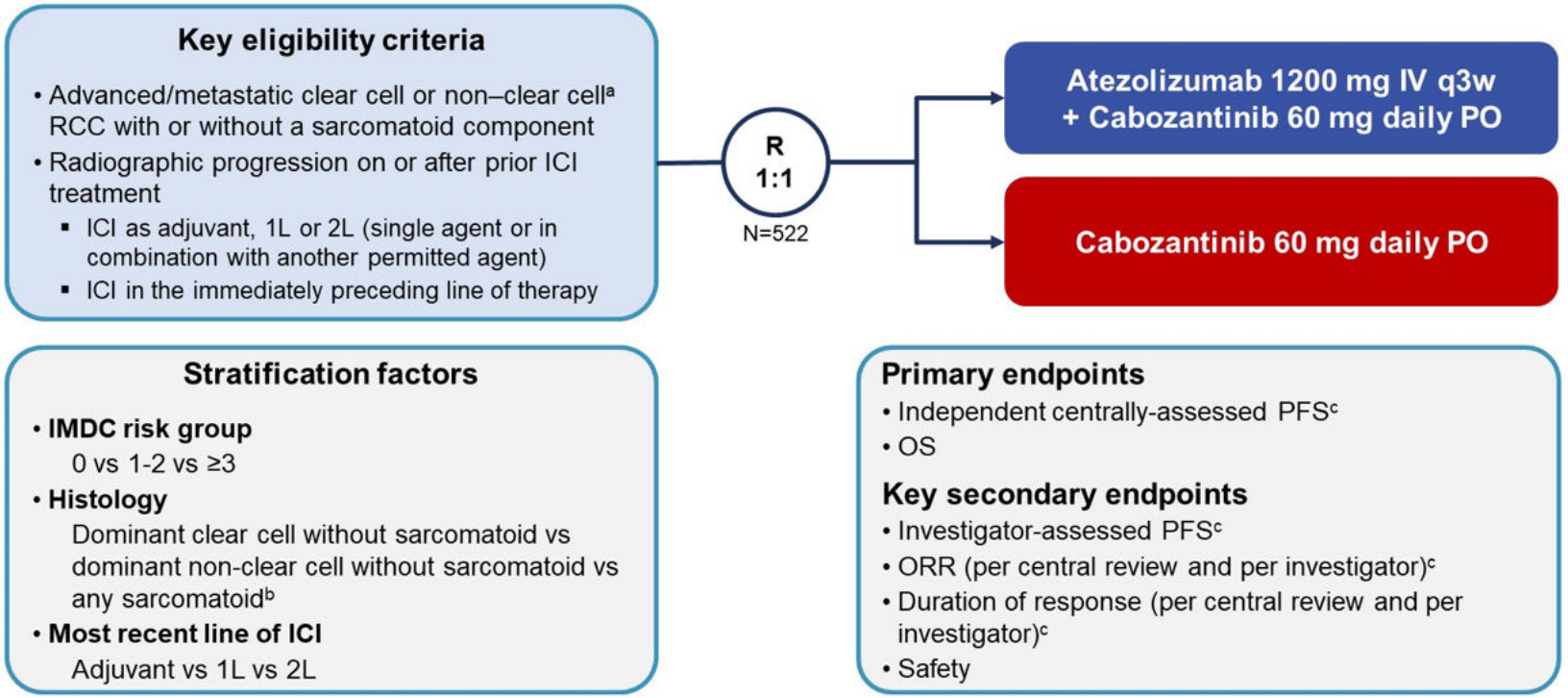
Design



linicalTrials.gov ID, NCT04338269. IMDC, International Metastatic RCC Database Consortium. Patients were enrolled between July 28, 2020 and December 27, 2021.
Papillary, chromophobe or unclassified (chromophobe requires sarcomatoid differentiation). [b] Clear cell or non-clear cell. [c] Assessed according to RECIST 1.1.

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Caractéristiques

Characteristic	Atezo + Cabo (n=263)	Cabo (n=259)
Age, median (range), y	62 (20-85)	63 (18-89)
Male sex, n (%)	204 (77.6)	197 (76.1)
Race, n (%)		
White	219 (83.3)	213 (82.2)
Asian	33 (12.5)	23 (8.9)
Other	11 (4.2)	23 (8.9)
Most recent line of immune checkpoint inhibitor therapy, n (%)[a]		
Adjuvant	1 (0.4)	1 (0.4)
Locally advanced or metastatic; first line	144 (54.8)	132 (51.0)
Locally advanced or metastatic; second line	118 (44.9)	124 (47.9)
Histology, n (%)[b]		
Dominant clear cell without sarcomatoid	207 (78.7)	200 (77.2)
Dominant non-clear cell without sarcomatoid	30 (11.4)	31 (12.0)
Any sarcomatoid	25 (9.5)	28 (10.8)
IMDC score, n (%)[c]		
0	49 (18.6)	69 (26.6)
1-2	172 (65.4)	153 (59.1)
≥3	41 (15.6)	36 (13.9)
Prior VEGFR-TKI use, n (%)		
0	93 (35.4)	95 (36.7)
1	166 (63.1)	159 (61.4)
2	4 (1.5)	5 (1.9)

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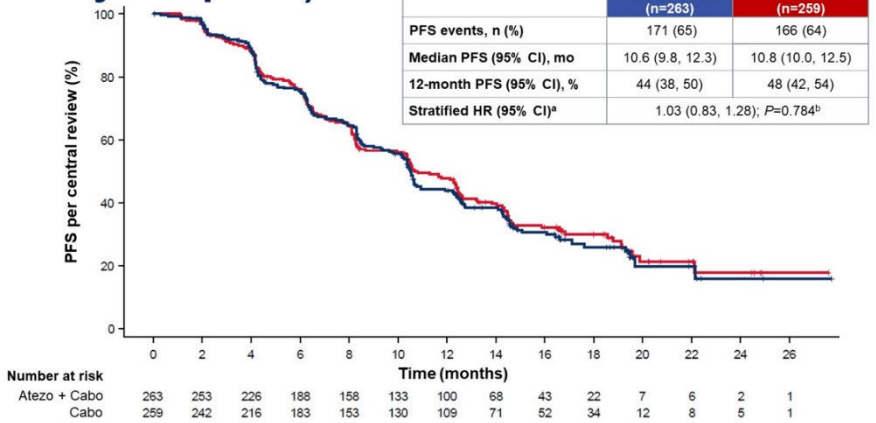
Traitements reçus antérieurement

	Atezo + Cabo (n=263)	Cabo (n=259)
First-line treatment, n (%)[a,b]	**262 (99.6)**	**258 (99.6)**
Ipilimumab + nivolumab	80 (30.5)	70 (27.1)
Sunitinib	77 (29.4)	72 (27.9)
Pazopanib	36 (13.7)	43 (16.6)
Axitinib + pembrolizumab	36 (13.7)	28 (10.9)
Nivolumab	6 (2.3)	10 (3.9)
Avelumab + axitinib	7 (2.7)	6 (2.3)
Bempegaldesleukin + nivolumab	3 (1.1)	9 (3.5)
Lenvatinib + pembrolizumab	6 (2.3)	3 (1.2)
Sorafenib	3 (1.1)	1 (0.4)
Second-line treatment, n (%)[a,b]	**119 (45.2)**	**125 (48.3)**
Nivolumab	104 (87.4)	116 (92.8)
Ipilimumab + nivolumab	4 (3.4)	3 (2.4)
Axitinib + pembrolizumab	2 (1.7)	3 (2.4)
Adjuvant treatment, n (%)[a,b]	**8 (3.0)**	**4 (1.5)**
Sunitinib	2 (25)	2 (50)

ESSAI de phase III CONTACT-03

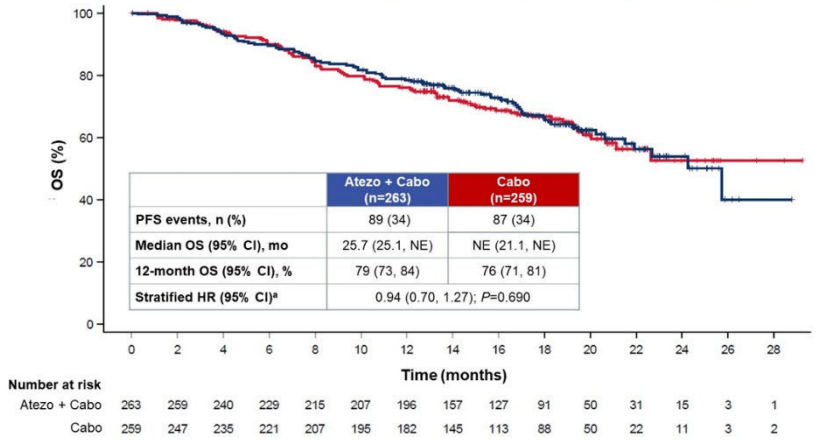
Etude négative

Primary analysis of centrally reviewed PFS (primary endpoint)



	Atezo + Cabo (n=263)	Cabo (n=259)
PFS events, n (%)	171 (65)	166 (64)
Median PFS (95% CI), mo	10.6 (9.8, 12.3)	10.8 (10.0, 12.5)
12-month PFS (95% CI), %	44 (38, 50)	48 (42, 54)
Stratified HR (95% CI)[a]	1.03 (0.83, 1.28); *P*=0.784[b]	

Interim analysis of OS (primary endpoint)



	Atezo + Cabo (n=263)	Cabo (n=259)
PFS events, n (%)	89 (34)	87 (34)
Median OS (95% CI), mo	25.7 (25.1, NE)	NE (21.1, NE)
12-month OS (95% CI), %	79 (73, 84)	76 (71, 81)
Stratified HR (95% CI)[a]	0.94 (0.70, 1.27); *P*=0.690	

The addition of atezolizumab to cabozantinib did not result in improved clinical outcomes in patients with mRCC who progressed on or after prior ICI treatment

- Subgroup analysis did not identify a subset of patients who may benefit from atezolizumab + cabozantinib

Increased toxicity was observed with the combination, although no specific safety signal was identified

En vrac

Actualisation des essais KN-426 et CLEAR

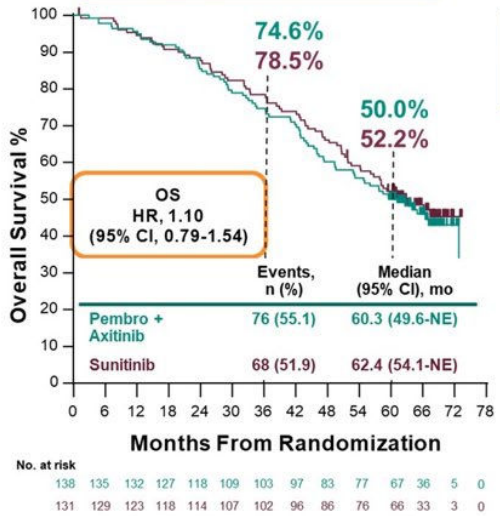
- Maintien du gain en OS = OUI
- Maintien de la durée de réponse = Peut-être
- Augmentation de l'OS pour IMDC favorable = NON

Median DOR: ~ 2 years

Lack of CTLA-4 blockade

Anti-PD-1 agent discontinued at 2 years

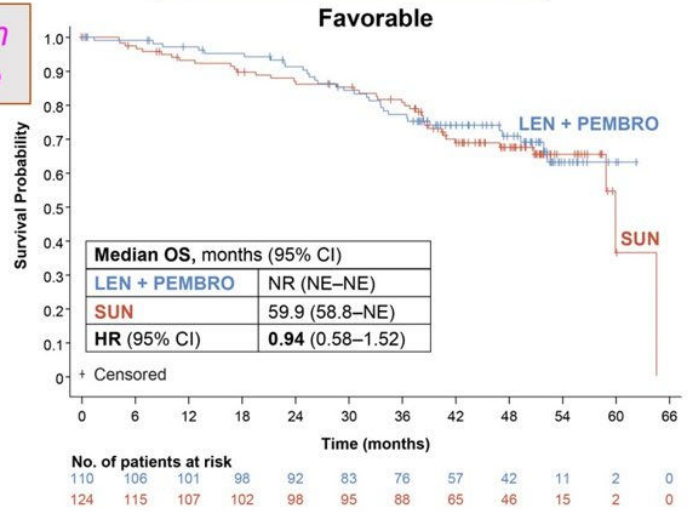
KN-426
(pembrolizumab+axitinib)



No OS benefit in IMDC favorable

CM-214

CLEAR
(pembrolizumab+lenvatinib)



Rini, ASCO 2023 ANNUAL; Rini, ASCO 2023, LBA4501; Motzer & Hutson, ASCO 2023, 4501.

2023 ASCO ANNUAL MEETING #ASCO23

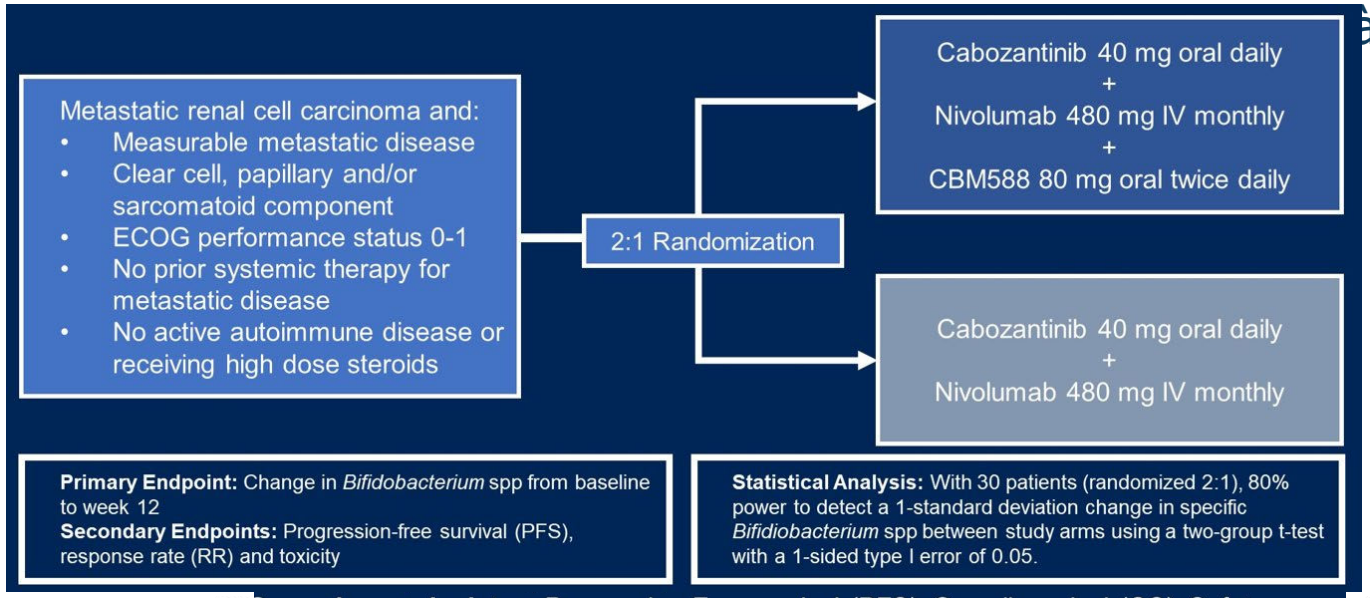
PRESENTED BY: David A. Braun, MD, PhD @BraunMDPhD

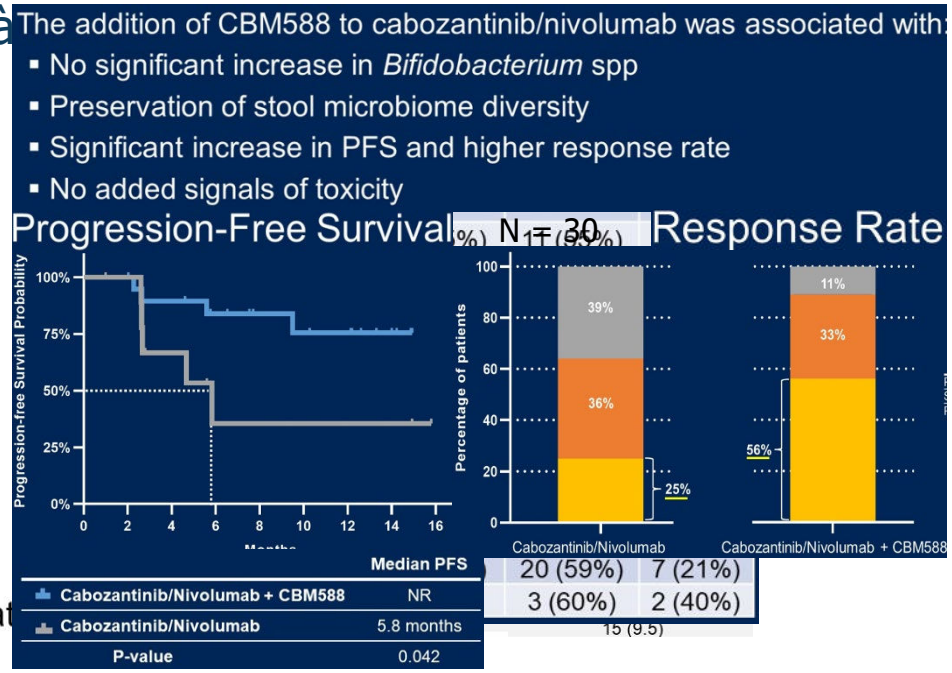
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

En vrac

Microbiome / carcinomes non à cellules claires

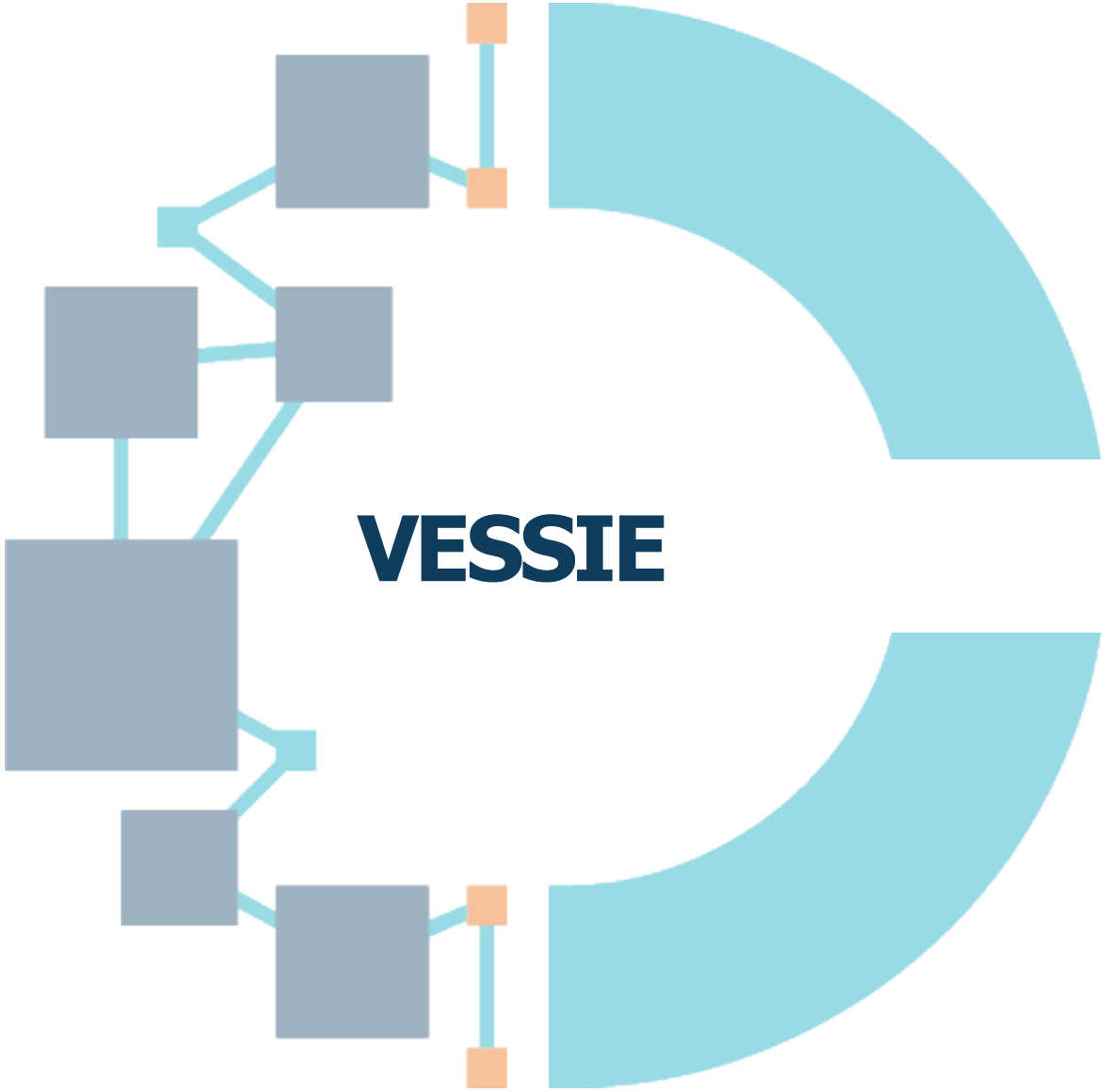
- Immunothérapie et microbiome: Le CBM588 = souche bactérienne qui peut restaurer des espèces de Bifidobacterium dans le microbiome





Fi**Secondary endpoints** – Progression Free survival (PFS), Overall survival (OS), Safety
advanced non–clear cell RCC, with a median 14.9 months of follow-up
- 49% of patients had a confirmed objective response
- Responses were durable, with 75% of responders remaining in response for ≥12 months
- At 12 months, the PFS rate was 63% and the OS rate was 82%
- Consistent efficacy was demonstrated across histologic subtypes

Suivi médian à 10,4 mois
A 12 mois, PFS à 51% et une OS à 79%

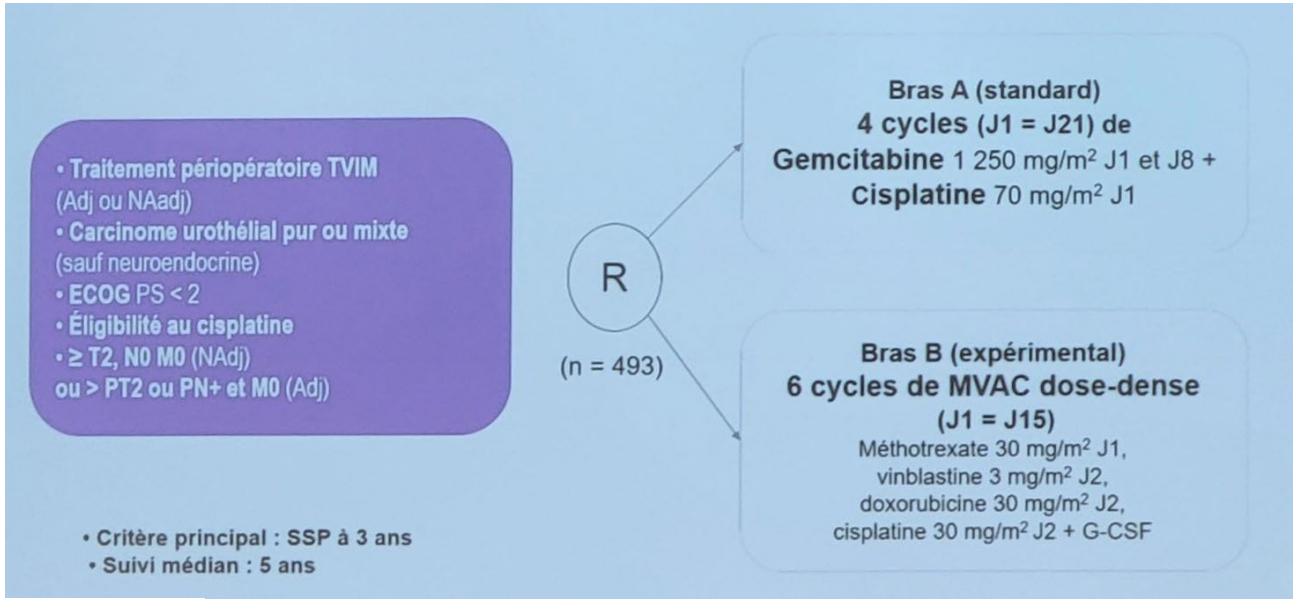


VESSIE

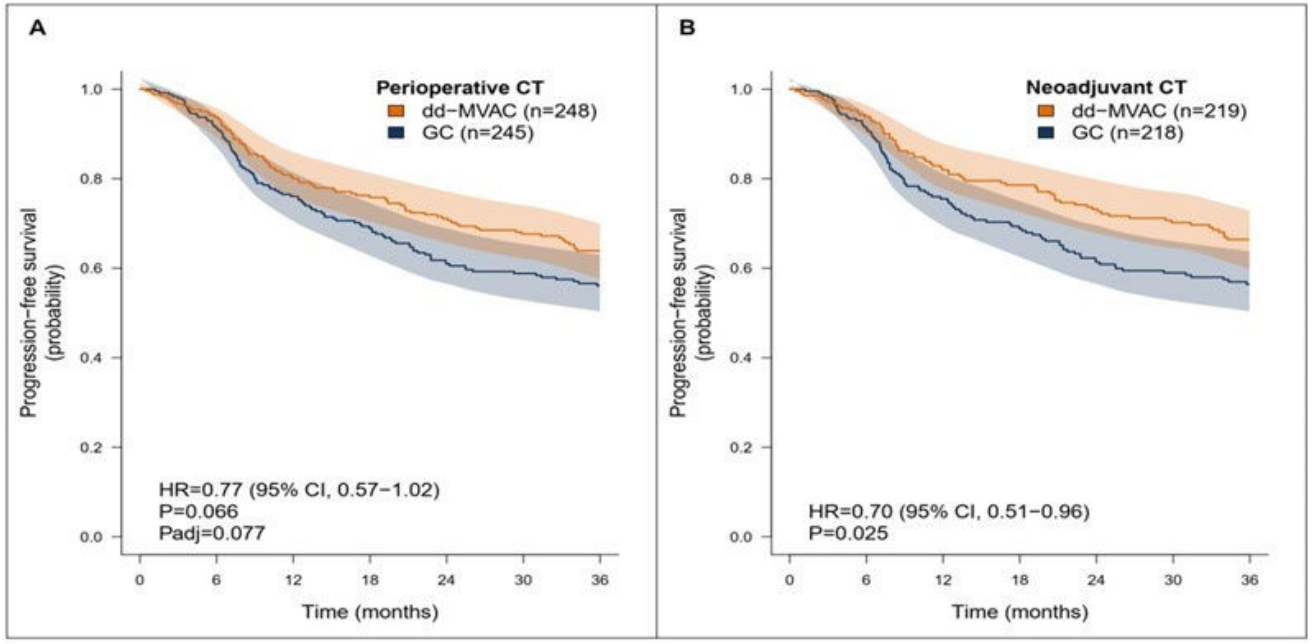
ONCO NOUVELLE-AQUITAINE
Dispositif spécifique régional du cancer

Essai VESPER

Données de survie à 5 ans



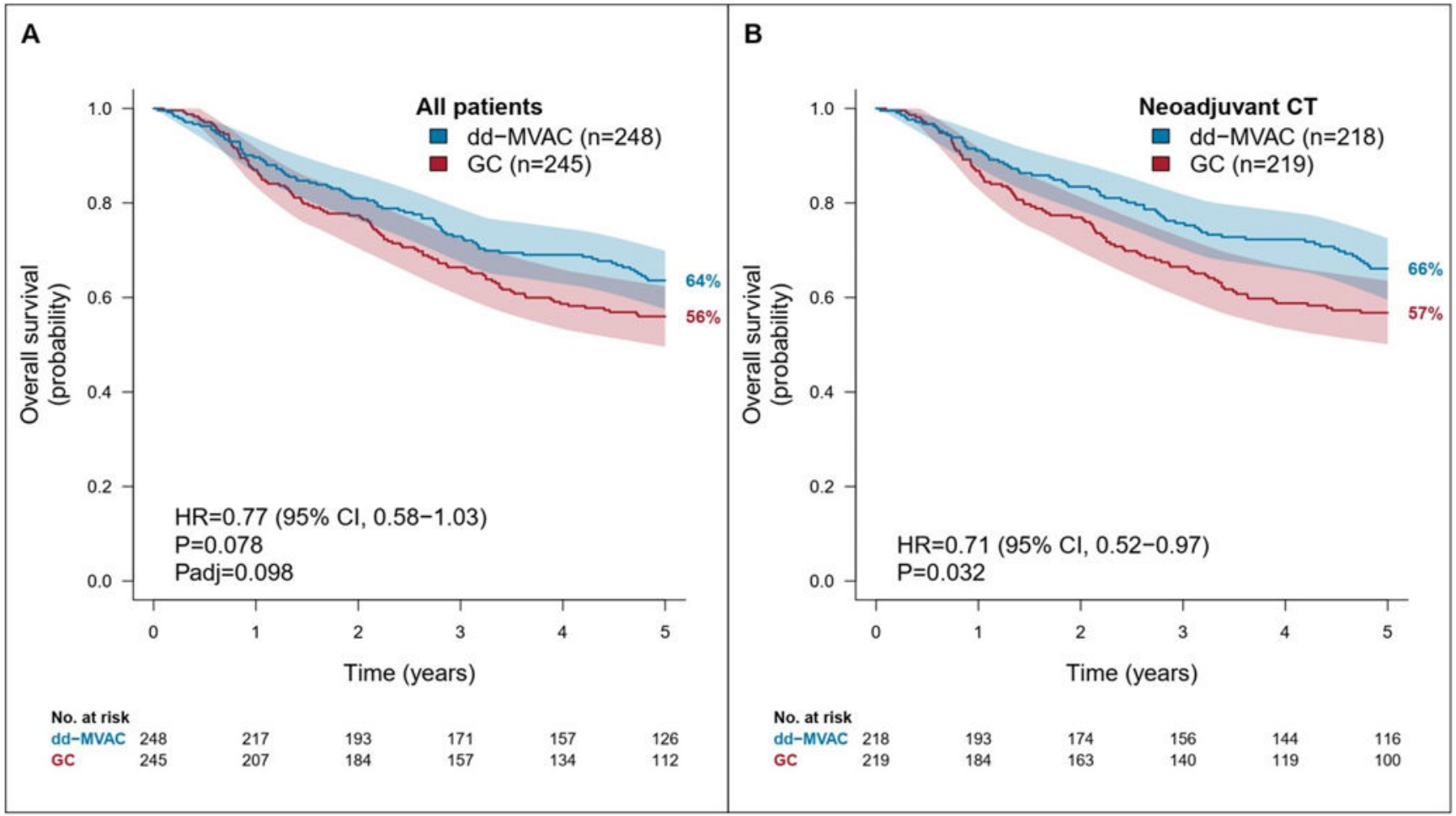
Pfister et al. J Clin Oncol 2022



PFS à 3 ans augmentée avec un meilleur contrôle local dans le groupe neoadjuvant

Essai VESPER

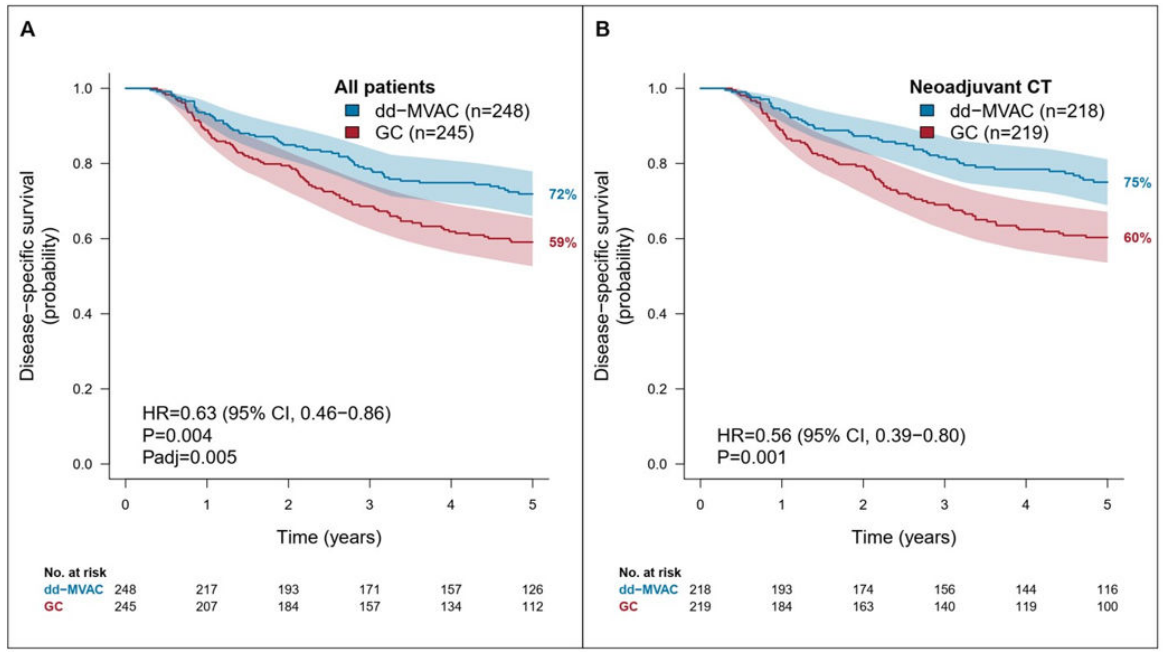
Données de survie à 5 ans



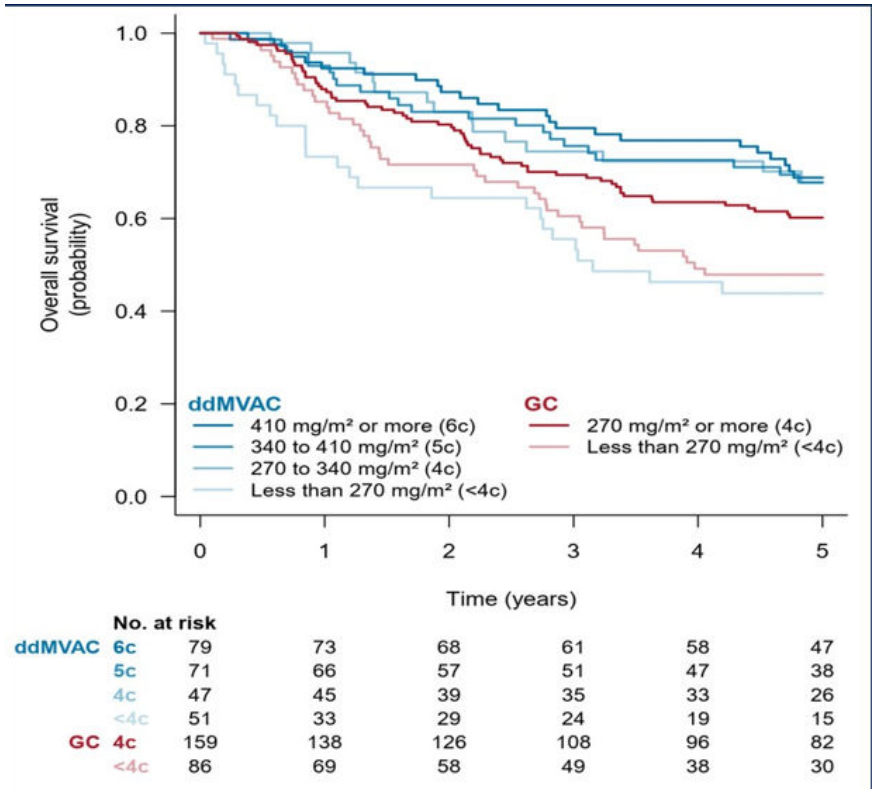
Essai VESPER

Autres enseignements

- Gain en Survie Spécifique



- Importance des doses cumulées cisplatine



ESSAI Phase III THOR

Mutations et altération de FGFR2/3

Phase 3 THOR Study: Results of Erdafitinib Versus Chemotherapy in Patients With Advanced or Metastatic Urothelial Cancer With Select Fibroblast Growth Factor Receptor Alterations

Yohann Loriot[1], Nobuaki Matsubara[2], Se Hoon Park[3] , Robert A. Huddart[4], Earle F. Burgess[5], Nadine Houede[6], Severine Banek[7], Brigitte Laguerre[8], Valentina Guadalupi[9], Ja Hyeon Ku[10], Spyros Triantos[11], Sydney Akapame[11], Kris Deprince[12], Sutapa Mukhopadhyay[13], Arlene O Siefker-Radtke[14]

[1]Department of Cancer Medicine, INSERM U981, Gustave Roussy, Université Paris-Saclay, Villejuif, France; [2]Department of Medical Oncology, National Cancer Center Hospital East, Chiba, Japan; [3]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Section of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, UK; [5]Medical Oncology Department, Levine Cancer Institute, Charlotte, NC; [6]Medical Oncology Department, Institut de Cancérologie du Gard - CHU Caremeau, Nîmes, France and Montpellier University, Montpellier, France; [7]Department of Urology, University Hospital Frankfurt, Goethe Universtity Frankfurt, Frankfurt am Main, Germany; [8]Department of Medical Oncology, Centre Eugene Marquis, Rennes, France; [9]Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy; [10]Seoul National University Hospital, Seoul, South Korea; [11]Janssen Research & Development, Spring House, PA; [12]Janssen Research & Development, Beerse, Belgium; [13]Janssen Research & Development, Lexington, MA; [14]Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

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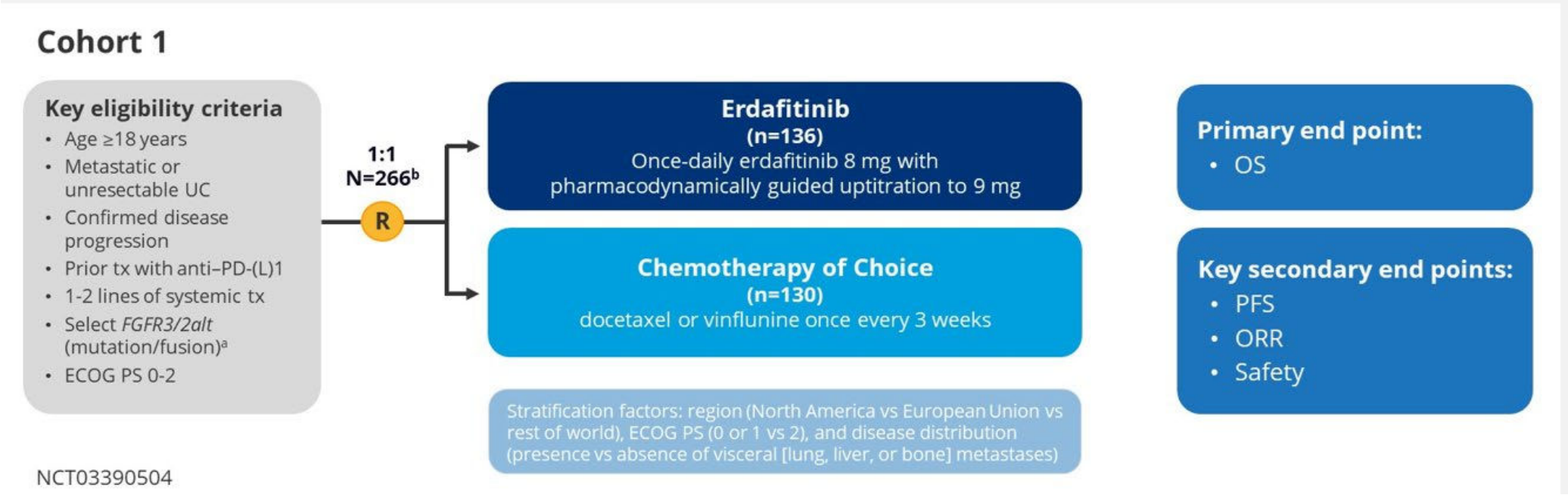
Environ 20% de mutations/fusion FGFR 2/3



The interim analysis was planned to assess both efficacy and futility with stopping thresholds derived based on the O'Brien-Fleming alpha-spending function

– At the data cutoff for this interim analysis (January 15, 2023), 155 deaths had occurred corresponding to ~75% information fraction

The significance level for stopping for efficacy was p-value=0.019, corresponding to a HR of 0.69

ESSAI Phase III THOR

Caractéristiques de la population

Characteristic	Erdafitinib (n=136)	Chemotherapy (n=130)
Age, median (range), years	66 (32-85)	69 (35-86)
Men, n (%)	96 (70.6)	94 (72.3)
Race, n (%)		
White	81 (59.6)	63 (48.5)
Asian	37 (27.2)	40 (30.8)
Black or African American	0	1 (0.8)
Multiple	0	1 (0.8)
Not reported	18 (13.2)	25 (19.2)
Presence of visceral metastases, n (%)	101 (74.3)	97 (74.6)
Liver	31 (22.8)	38 (29.2)

Characteristic	Erdafitinib (n=136)	Chemotherapy (n=130)
ECOG PS 0-1, n (%)	124 (91.2)	117 (90)
Primary tumor upper tract, n (%)	41 (30.1)	48 (36.9)
PD-L1 low (CPS <10), n (%)	89 (92.7)[a]	68 (86.1)[a]
FGFRalt, n (%)[b]	(n=135)	(n=129)
Mutations	108 (79.4)	107 (82.3)
Fusions	25 (18.4)	19 (14.6)
Mutations and fusions	2 (1.5)	3 (2.3)
Prior lines of systemic therapy[c]		
1 line	45 (33.1)	33 (25.4)
2 lines	90 (66.2)	97 (74.6)

- Patient baseline characteristics were generally balanced between treatment arms

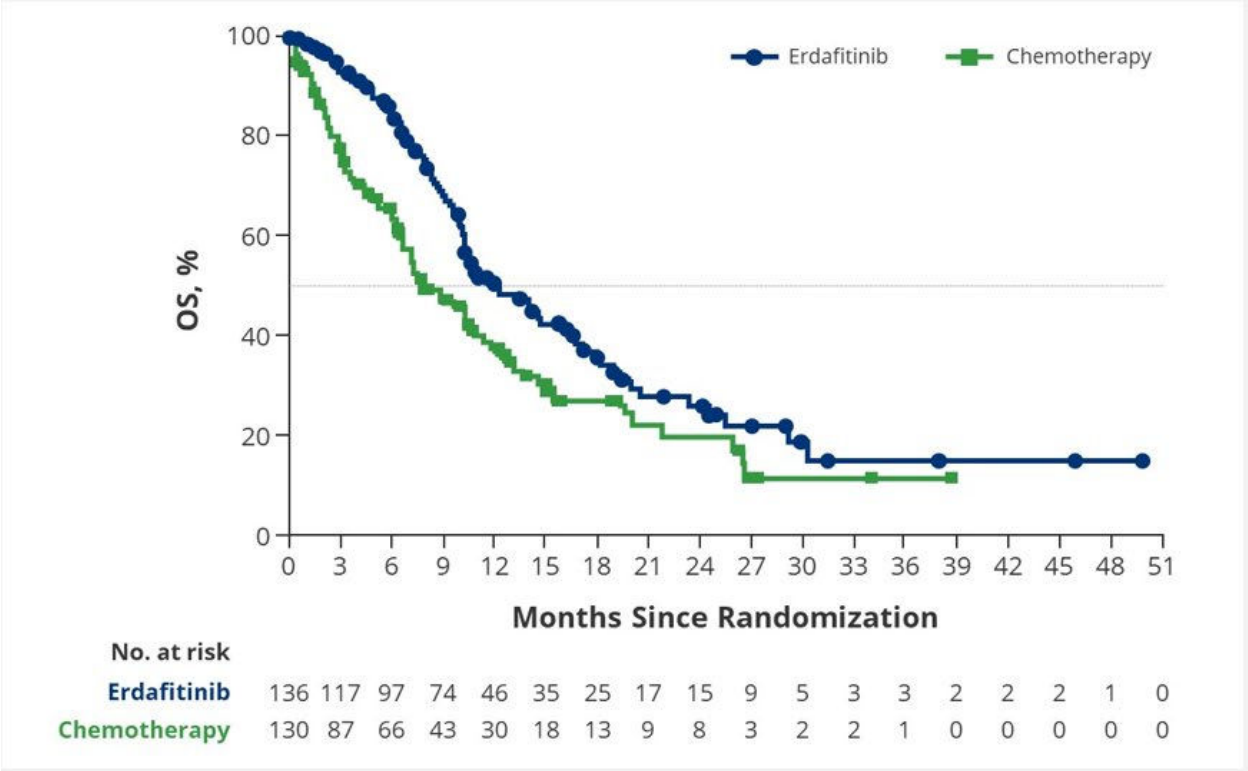
ESSAI Phase III THOR

Traitements reçus précédemment

Patients receiving prior therapy, n (%)	Erdafitinib (n=136)[a]	Chemotherapy (n=130)
1 line of prior systemic therapy	**45 (33.1)**	**33 (25.4)**
Chemotherapy + anti–PD-(L)1[b]	33 (24.3)	15 (11.5)
Anti–PD-(L)1[c]	11 (8.1)	16 (12.3)
Chemotherapy	1 (0.7)	2 (1.5)
2 lines of prior systemic therapy	**90 (66.2)**	**97 (74.6)**
First line of therapy		
Chemotherapy	77 (56.6)	76 (58.5)
Chemotherapy + anti–PD-(L)1	6 (4.4)	10 (7.7)
Other	7 (5.1)	11 (8.5)
Second line of therapy		
Anti–PD-(L)1	76 (55.9)	76 (58.5)
Chemotherapy	10 (7.4)	14 (10.8)
Other	4 (2.9)	7 (5.4)

ESSAI Phase III THOR

OS supérieure pour l'erdafitinib vs chimiothérapie ap CT et IO



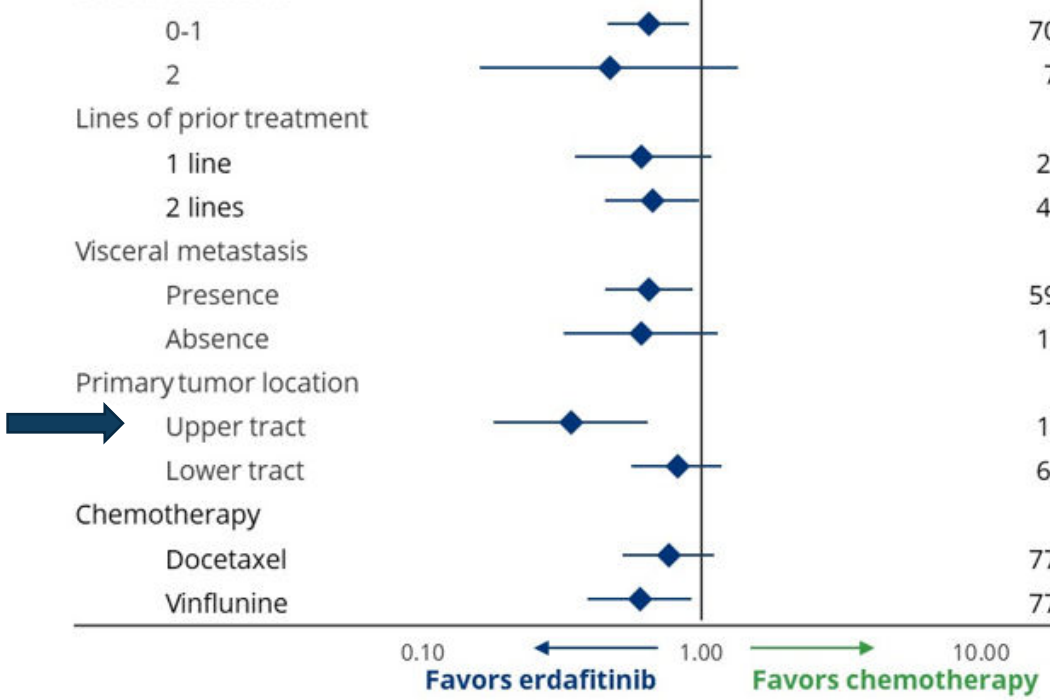
- Median follow-up was 15.9 months
- Median OS was 12.1 months for erdafitinib versus 7.8 months for chemotherapy
- Erdafitinib reduced the risk of death by 36% versus chemotherapy
  - HR, 0.64 (95% CI, 0.47-0.88; *P* = 0.005)[a]
- Based on these interim analysis results, the IDMC recommended to stop the study, unblind data, and cross over patients from chemotherapy to erdafitinib

CI, confidence interval; HR, hazard ratio; IDMC, independent data monitoring committee; OS, overall survival.
[a]The significance level for stopping for efficacy was p=0.019, corresponding to a HR of 0.69.

8

ESSAI Phase III THOR

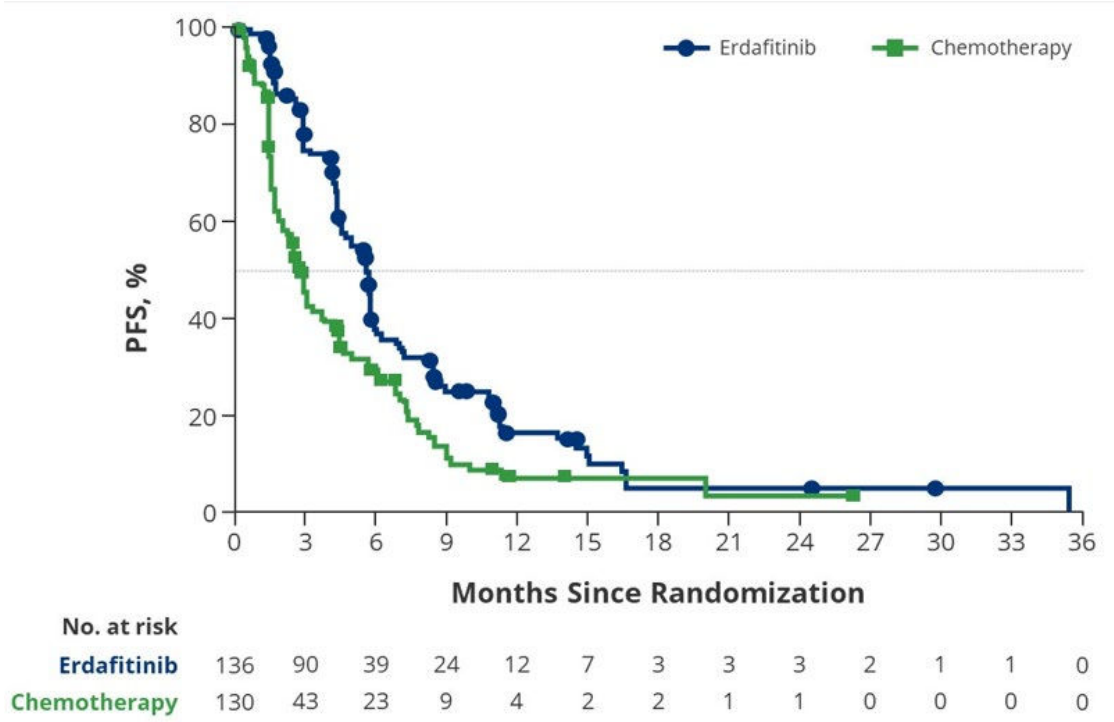
Analyse des sous-groupes

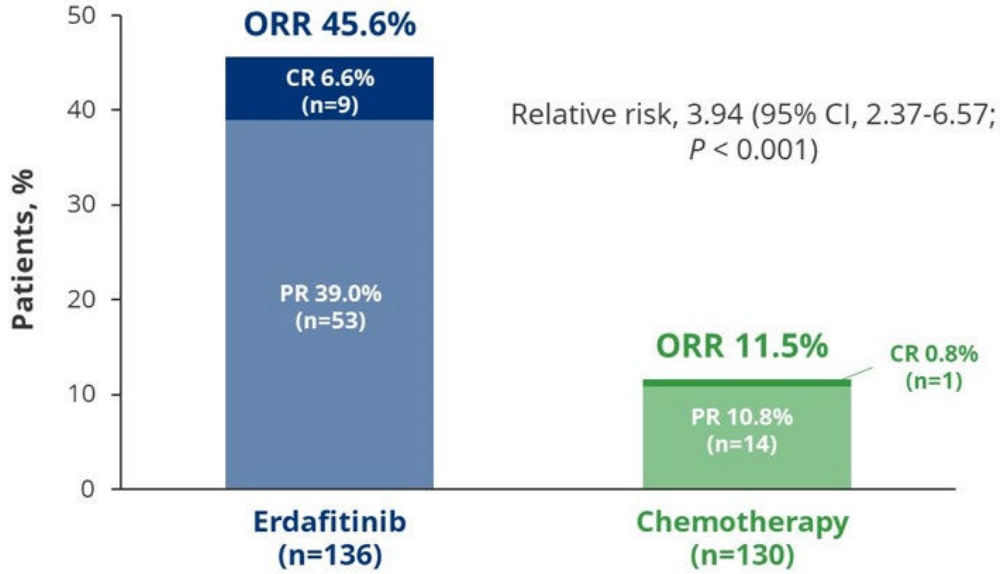


	Erdafitinib		Chemotherapy		
	n/N[a]	Median	n/N[a]	Median	HR and 95% CI
Overall	77/136	12.1	78/130	7.8	0.64 (0.47-0.88)
FGFR alteration type					
Translocation	13/25	16.4	15/19	8.0	0.49 (0.23-1.03)
Mutation	63/108	10.9	60/107	7.7	0.67 (0.47-0.95)
Baseline ECOG PS					
0-1	70/125	12.2	71/119	8.7	0.65 (0.46-0.90)
2	7/11	6.1	7/11	2.8	0.47 (0.16-1.35)
Lines of prior treatment					
1 line	27/45	14.0	21/33	7.8	0.61 (0.35-1.09)
2 lines	49/90	11.6	57/97	7.7	0.67 (0.45-0.98)
Visceral metastasis					
Presence	59/103	12.2	57/101	7.7	0.65 (0.45-0.93)
Absence	18/33	10.6	21/29	8.8	0.61 (0.32-1.14)
Primary tumor location					
Upper tract	16/41	23.3	27/48	7.2	0.34 (0.18-0.64)
Lower tract	61/95	10.5	51/82	9.6	0.82 (0.56-1.18)
Chemotherapy					
Docetaxel	77/136	12.1	40/69	10.6	0.76 (0.52-1.11)
Vinflunine	77/136	12.1	30/43	7.7	0.60 (0.39-0.92)

ESSAI Phase III THOR

Critères secondaires :PFS et ORR





PFS médiane de 5,6m vs 2,7m en faveur de l'erdafinitinib

Réduction du risque de progression ou de décès de 42% (HR 0,58 (IC95%, 0,44-0,78;p=0,0002))

ESSAI Phase III THOR

Critères secondaires :Toxicités

Patients with AEs of interest, n (%)	Erdafitinib (n=135)		Chemotherapy (n=112)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Nail disorders[a]	90 (66.7)	15 (11.1)	6 (5.4)	0
Skin disorders[b]	74 (54.8)	16 (11.9)	14 (12.5)	0
Eye disorders (excluding central serous retinopathy)[c]	57 (42.2)	3 (2.2)	6 (5.4)	0
Central serous retinopathy[d]	23 (17.0)	3 (2.2)	0	0

% d'effets secondaires grade 3-4: 13,3% pour l'erdafitinib vs 24,1% pour la chimio

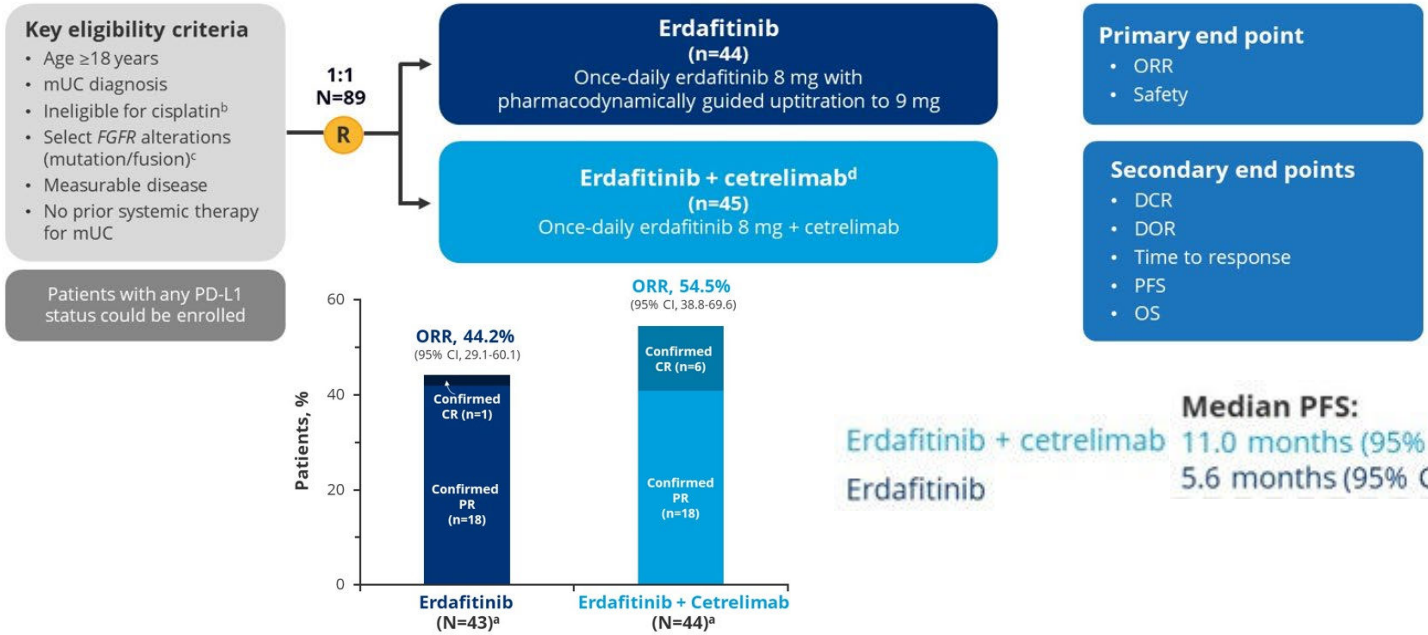
Arrêts pour toxicités: 8,1% pour l'erdafinitinib vs 13,4% pour la chimio

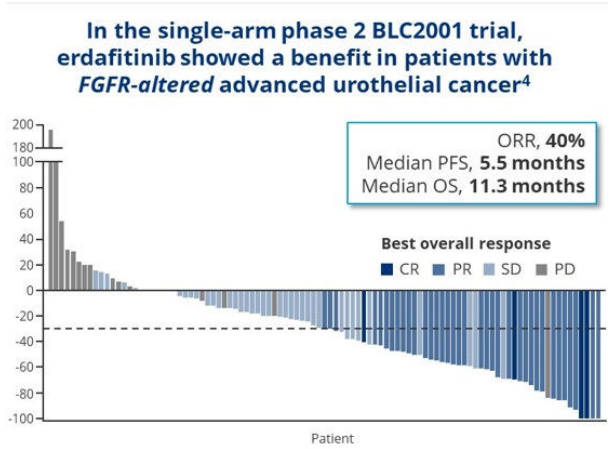
Patients with AEs, n (%)[a]	Erdafitinib (n=135)	
	Any grade	Grade 3-4
≥1 treatment-related AE	131 (97.0)	62 (45.9)
Hyperphosphatemia	106 (78.5)	7 (5.2)
Diarrhea	74 (54.8)	4 (3.0)
Stomatitis	62 (45.9)	11 (8.1)
Dry mouth	52 (38.5)	0
PPE syndrome	41 (30.4)	13 (9.6)
Onycholysis	31 (23.0)	8 (5.9)

ESSAI Phase III THOR

Take home message

- Erdafitinib : SOC ap CT et IO pour les patients porteurs d'une altération de FGFR2/3 (mutations, fusion)
  - Conforte les résultats et les toxicités de la phase II
  - Efficacité « similaire » à l'essai de phase II NORSE





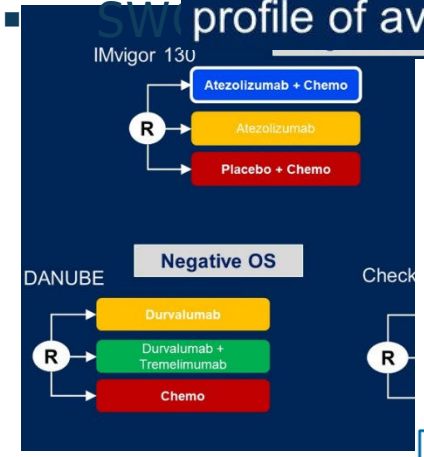
	Median PFS:	Median OS:
Erdafitinib + cetrelimab	11.0 months (95% CI, 5.5-13.6)	20.8 months (95% CI, 12.0-NE)
Erdafitinib	5.6 months (95% CI, 4.3-7.4)	16.2 months (95% CI, 8.3-NE)

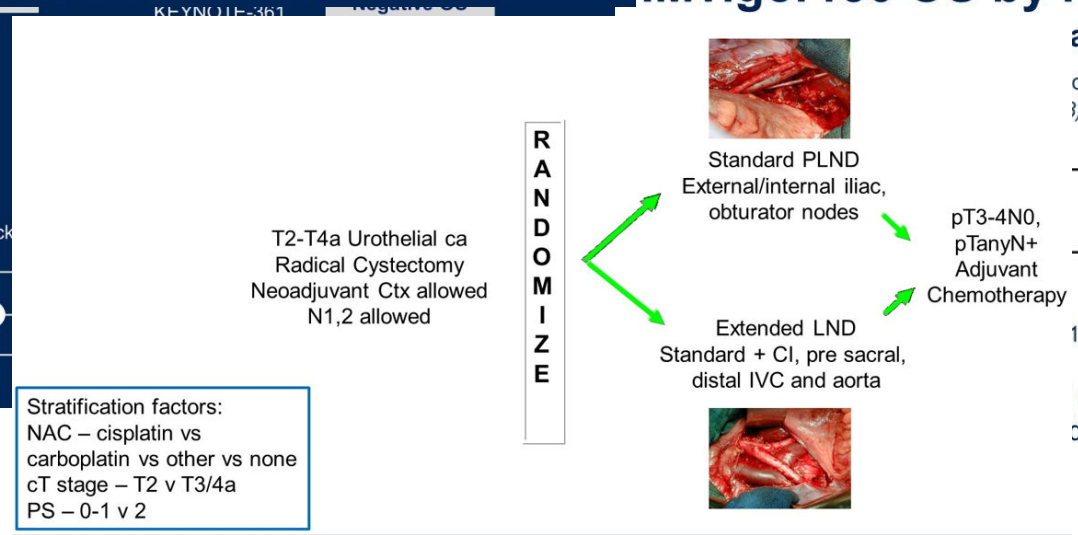
- **Testés tous les patients dès la phase M+ pour FGFR2/3. En accès précoce**

En vrac

- Confirmation de la place de l'avélumab en maintenance de 1L post platine chez les patients en SD/RP
- Pas de place pour l'association IO+CI en 1L
- SWOG

Post hoc analyses from the JAVELIN Bladder 100 trial after a minimum of 2 years of follow-up confirm the tolerable and manageable long-term safety profile of avelumab 1L maintenance





IMvigor130 OS by response analysis

alysis

out PD at/before Week 18):

Atezo

Placebo

Maintenance period

1 dose atezo/placebo monotherapy

on the IMvigor130 final analysis showed that initial did not seem to impact OS outcomes

Prostate

ESSAI de phase III PEACE I

Intérêt de la radiothérapie

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

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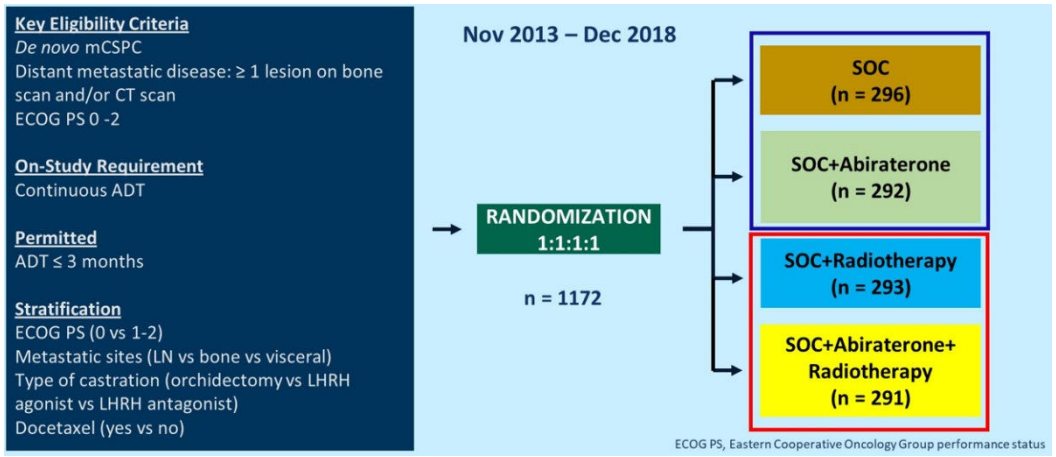


Radiotherapy (RXT) of the prostate 74 Gy in 37 fractions (after docetaxel is completed)

Co-primary

- Radiographic progression-free survival (rPFS):
  - PCWG2 criteria
  - Imaging at least q6m after PSA rise
- Overall survival (OS)

Secondary

- Castration resistance-free survival
- Serious genitourinary event-free survival
- Prostate cancer specific survival
- Time to next skeletal-related event
- PSA response rate
- PSA at 8 months after initiation of SOC
- Time to pain progression
- Time to chemotherapy for CRPC
- Quality of life
- Toxicity
- Changes in bone mineral density (BMD)
- Biomarkers
- Outcomes for pts with NE differentiation

ESSAI de phase III PEACE I

Caractéristiques de la population bas volume (43%)

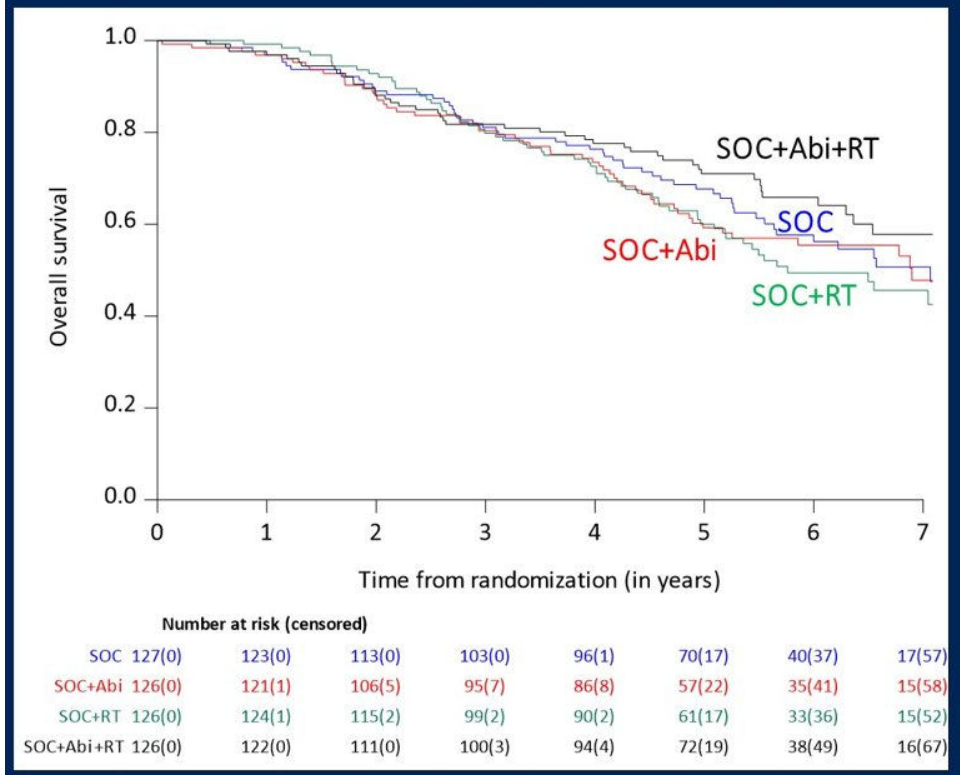
		SOC (+/- Abi) (n = 253)	SOC (+/- Abi) + Radiotherapy (n = 252)
Median age, year (Min-Max)		67 (43–86)	66 (46–84)
ECOG PS score, n (%)	0 1-2	180 (71) 73 (29)	194 (77) 58 (23)
Gleason score at diagnosis, n (%)	≤ 7 ≥ 8 Missing	71 (27) 173 (70) 9 (3)	66 (26) 184 (73) 2 (1)
Median time from diagnosis, month (IQR)		2.5 (1.8-3.4)	2.6 (1.7-3.5)
Metastatic sites, n (%)	Lymph nodes only Bone only	47 (19) 206 (81)	41 (16) 211 (84)
Median baseline PSA, ng/mL (IQR)		10.3 (3.3-31)	9 (2.3-39.1)
Docetaxel, n (%) →	Yes No	127 (50) 126 (50)	127 (50) 125 (50)

median follow-up : 73 months

ESSAI de phase III PEACE I

Co-primary endpoints

OS (low volume population)



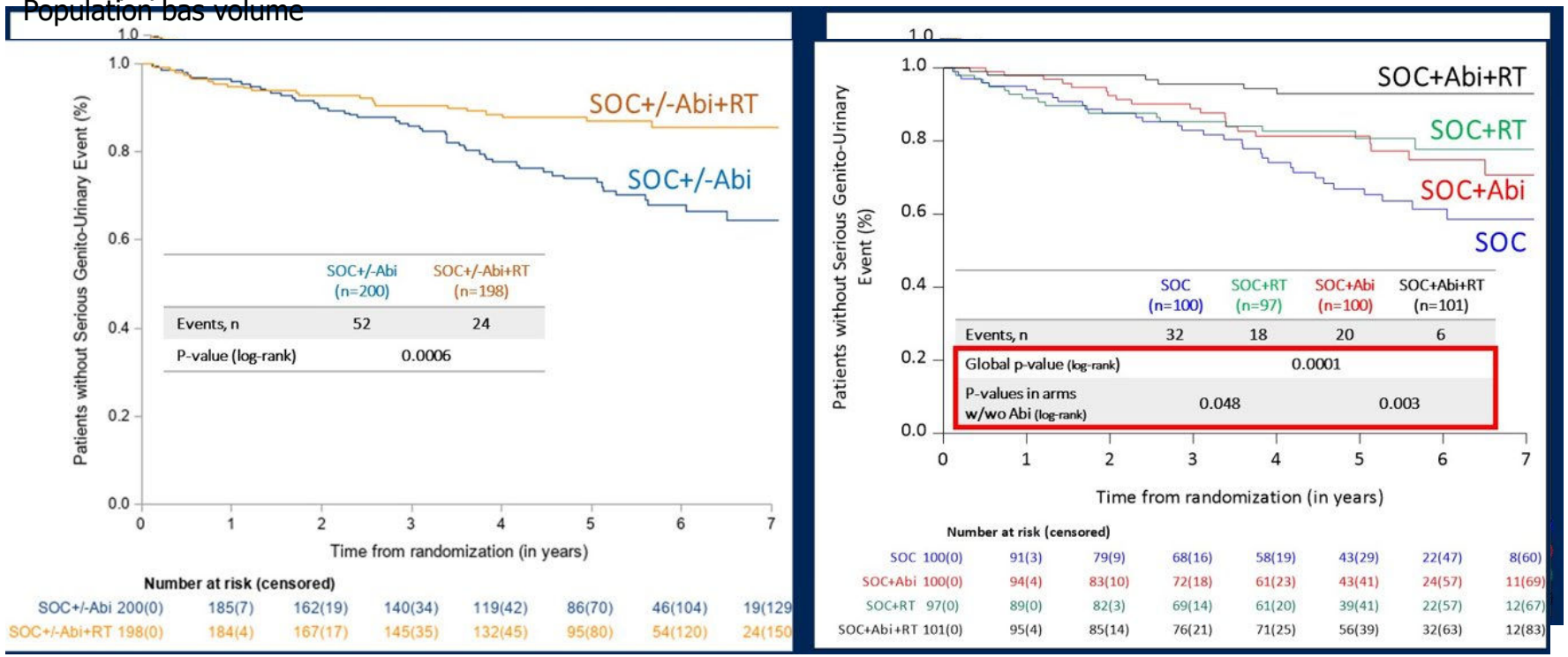
	SOC (n=127)	SOC+RT (n=126)	SOC+Abi (n=126)	SOC+Abi+RT (n=126)
Median, ys. (95.1% CI)	7.1 (5.6-NE)	5.8 (5.1-NE)	6.9 (5.0-NE)	NE (6.4-NE)
Events, n.	57	60	54	44
HR (95.1% CI)*	Ref	1.19 (0.82-1.72)	1.05 (0.72-1.54)	0.81 (0.55-1.21
Global p-value	0.29			
HR (95.1% CI)*	Ref	1.18 (0.81-1.71)	Ref	0.77 (0.51-1.16)
P-values arms w/wo Abi	0.39		0.21	

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

ESSAI de phase III PEACE I

Survie sans complications uro-génitales graves

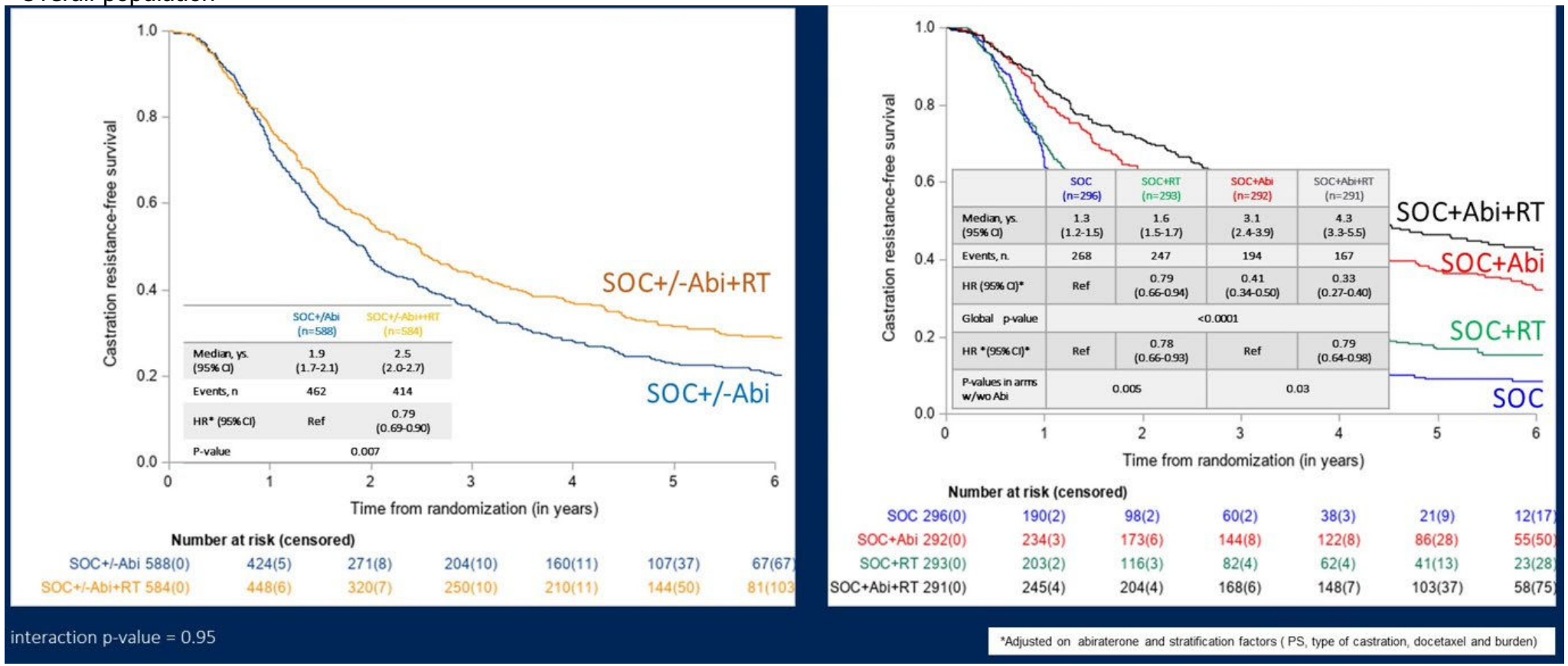
Overall population
Population bas volume



ESSAI de phase III PEACE I

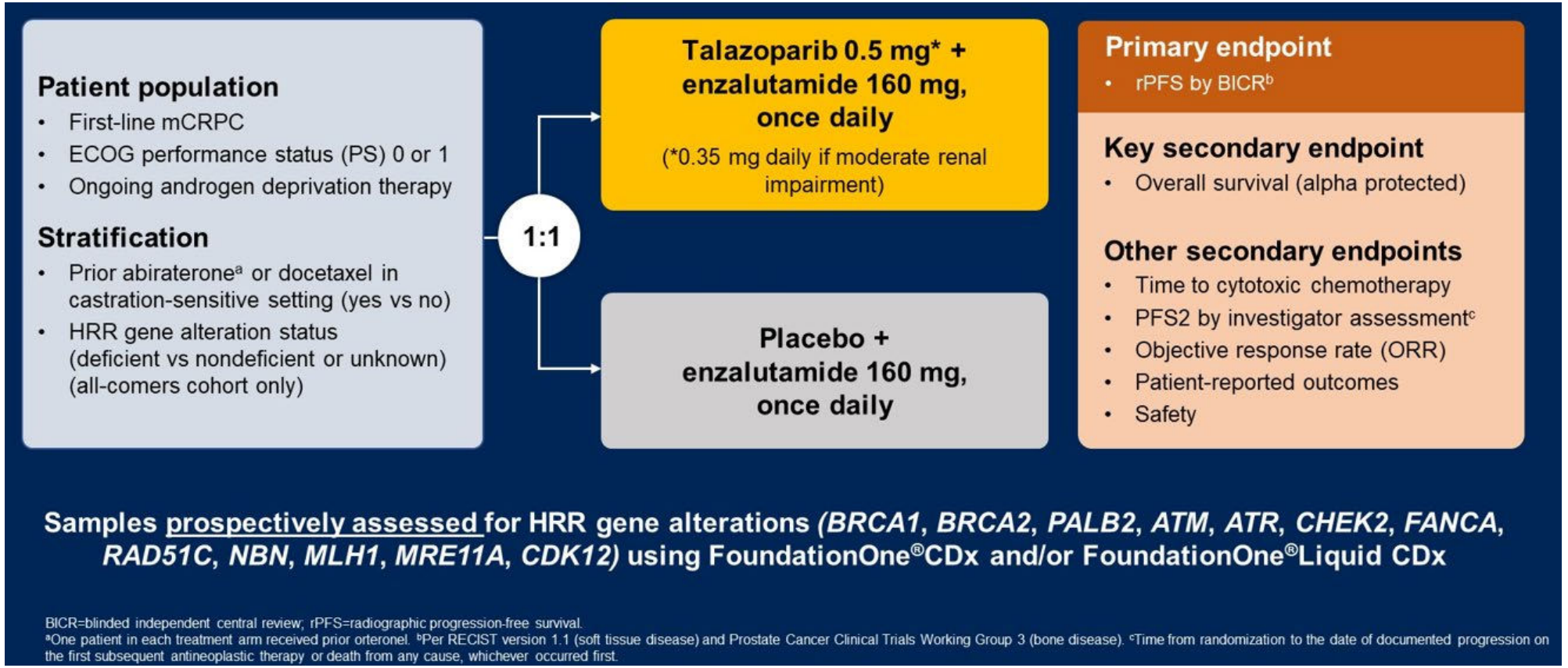
Survie sans résistance à la castration

Overall population



ESSAI phase III TALAPRO-2

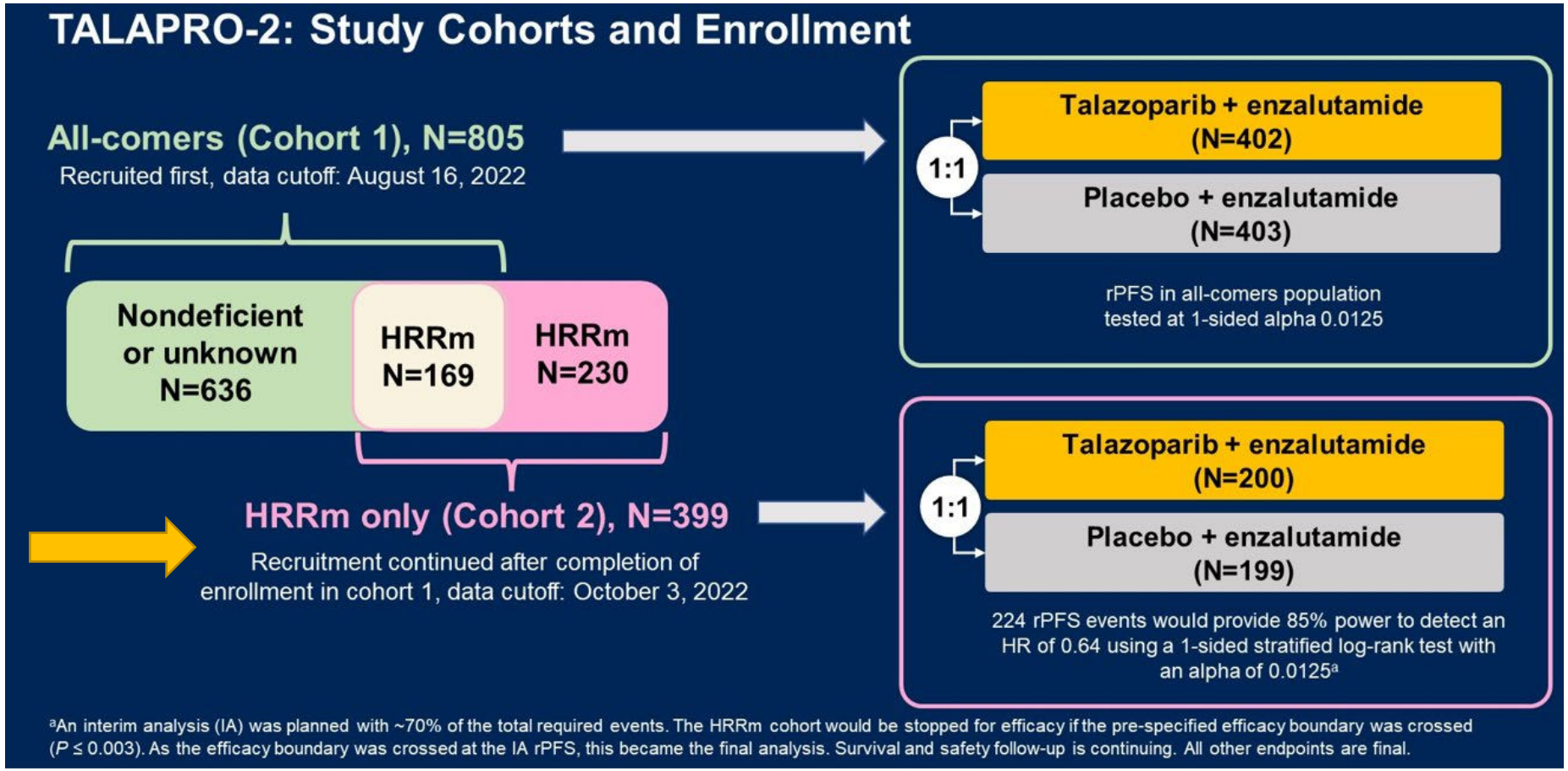
Design



BICR=blinded independent central review; rPFS=radiographic progression-free survival.
[a]One patient in each treatment arm received prior orteronel. [b]Per RECIST version 1.1 (soft tissue disease) and Prostate Cancer Clinical Trials Working Group 3 (bone disease). [c]Time from randomization to the date of documented progression on the first subsequent antineoplastic therapy or death from any cause, whichever occurred first.

ESSAI phase III TALAPRO-2

Design



ESSAI phase III TALAPRO-2

Caractéristiques de la population HRR-deficient

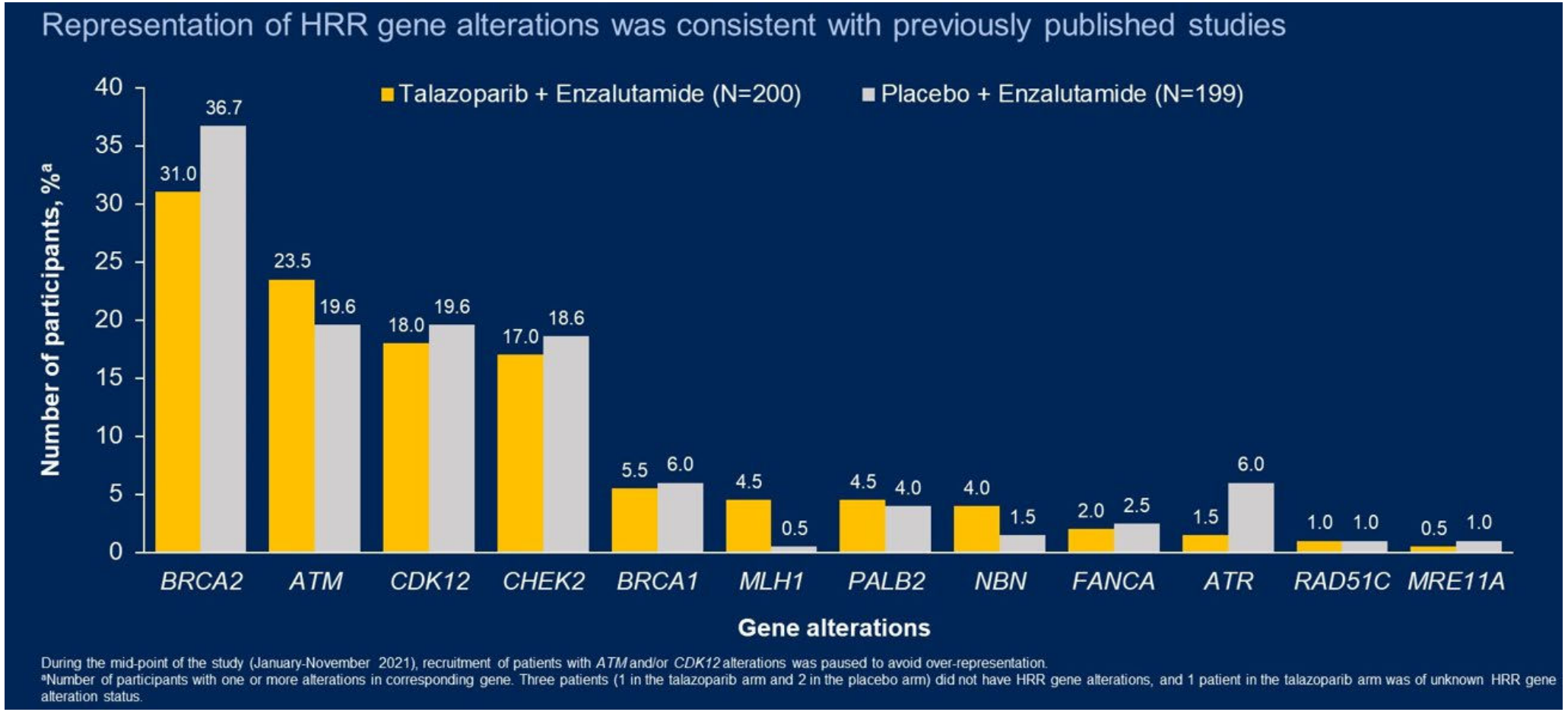
These were well-balanced between treatment arms

	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.

ESSAI phase III TALAPRO-2

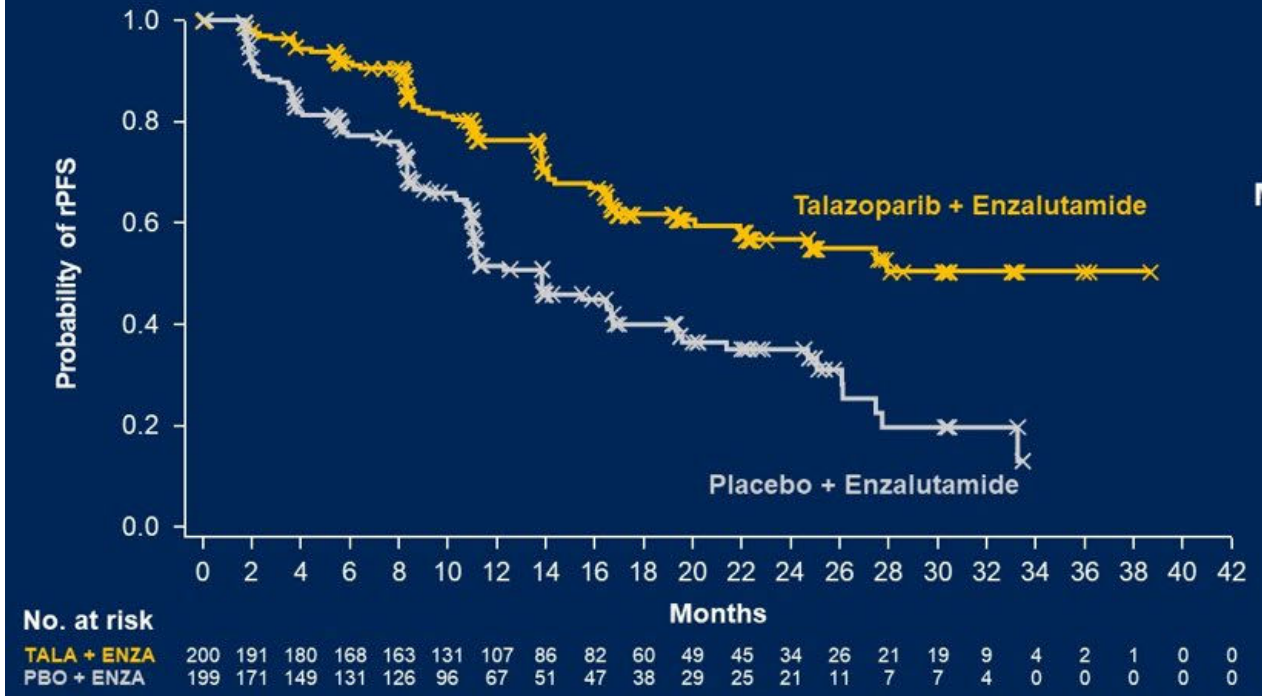
Profils de mutations



ESSAI phase III TALAPRO-2

Critère principal : rPFS en faveur de l'association

Treatment with talazoparib plus enzalutamide resulted in a 55% reduced risk of progression or death



	TALA + ENZA (N=200)	PBO + ENZA (N=199)
Events, n	66	104
Median (95% CI), months	Not reached (NR) (21.9–NR)	13.8 (11.0–16.7)
HR (95% CI)	0.45 (0.33–0.61); *P* < 0.0001	

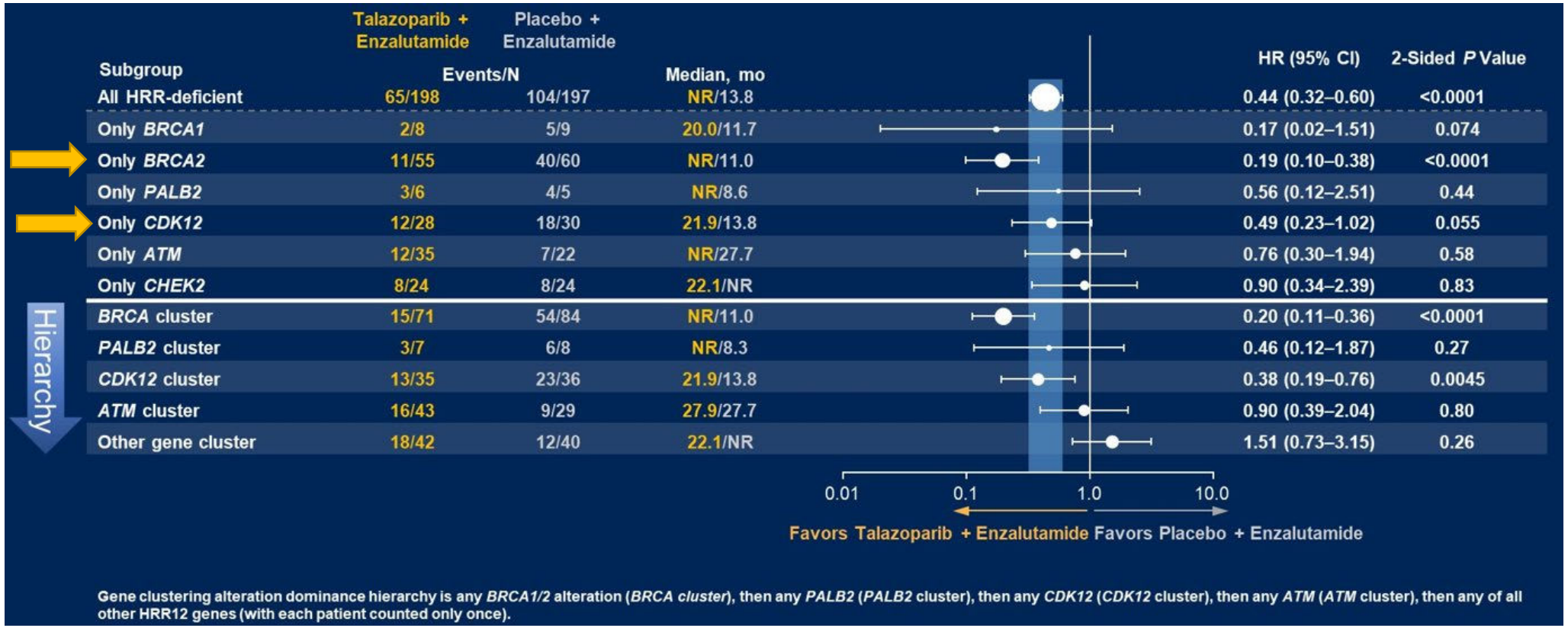
Median follow-up for rPFS was 17.5 and 16.8 months, respectively

A consistent treatment effect was seen for investigator-assessed rPFS: HR 0.48 (95% CI, 0.33–0.67); *P* < 0.0001

Stratified hazard ratios (HRs) and 2-sided *P* values are reported throughout this presentation unless otherwise stated.

ESSAI phase III TALAPRO-2

Critère principal : rPFS selon la mutation



Gene clustering alteration dominance hierarchy is any *BRCA1/2* alteration (*BRCA cluster*), then any *PALB2* (*PALB2* cluster), then any *CDK12* (*CDK12* cluster), then any *ATM* (*ATM* cluster), then any of all other HRR12 genes (with each patient counted only once).

ESSAI phase III TALAPRO-2

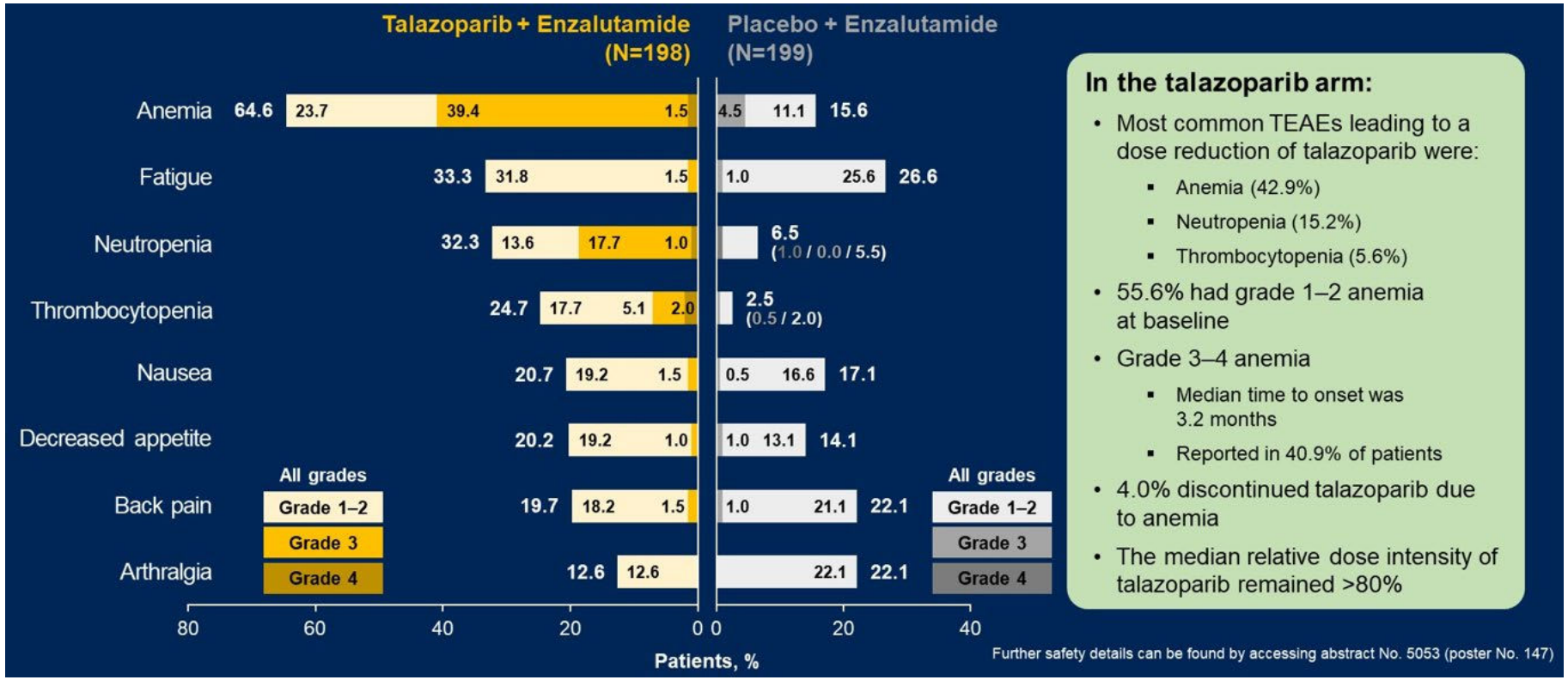
Critères secondaires en faveur de l'association

- OS immature mais un trend
- Temps avant progression du PSA: HR 0.41 (95% CI, 0.30–0.57) *P* < 0.0001
- Temps avant chimiothérapie: HR 0.46 (95% CI, 0.31–0.70) *P* = 0.0001
- PFS2 : HR 0.57 (95% CI, 0.39–0.85) *P* = 0.0045
- Taux de réponse objective: 67,1% vs 40% (p=0,0015)

ESSAI phase III TALAPRO-2

Toxicités

	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)



ESSAI phase III TALAPRO-2

Positionnement du talazoparib

1L mCRPC	Ph3 PROpel [2, 3]	Ph3 MAGNITUDE [4, 5]
Eligibility	Allowed: ✗ NO prior AAP • Other ARi, if >/=12 mos • Prior doce (mCSPC)	Allowed: • AAP </= 4mos for 1L mCRPC • Prior ARi (nmCRPC/mCSPC) • Prior taxane (mCSPC)
Biomarker considerations	Unselected (retrospective HRRm testing)	Prospective HRRm stratification (*BRCA1 and BRCA2*)
Treatment	Olap 300BID +AAP vs PBO +AAP	Nira 200qD +AAP vs PBO +AAP
rPFS AAP vs AAP+PARPi	16.6 mos (AAP +PBO) vs 24.8 mos (AAP +olap)	10.9 mos (AAP +PBO) vs 16.6 mos (AAP +nira)

Trial	Therapies	rPFS HRRm (CI)	rPFS BRCA1/2 (CI)	Prior ARPI	Subsequent PARPi
TALAPRO-2[1]	**Enzalutamide + Talazoparib**	**0.45 (0.33-0.61)**	**0.20 (0.11-0.36)**	**8%**	**17%**
PROpel[2]	Abiraterone + Olaparib	0.50 (0.34-0.73)	0.23 (0.12-0.43)	0.15%	2%
MAGNITUDE[3]	Abiraterone + Niraparib	0.73 (0.56-0.96)	0.53 (0.36-0.79)	3.1%	?

[1]Fizazi et al, ASCO GU, 2023
[2]Clarke et al, NEJM Evidence, 2022
[3]Chi et al, JCO, 2023

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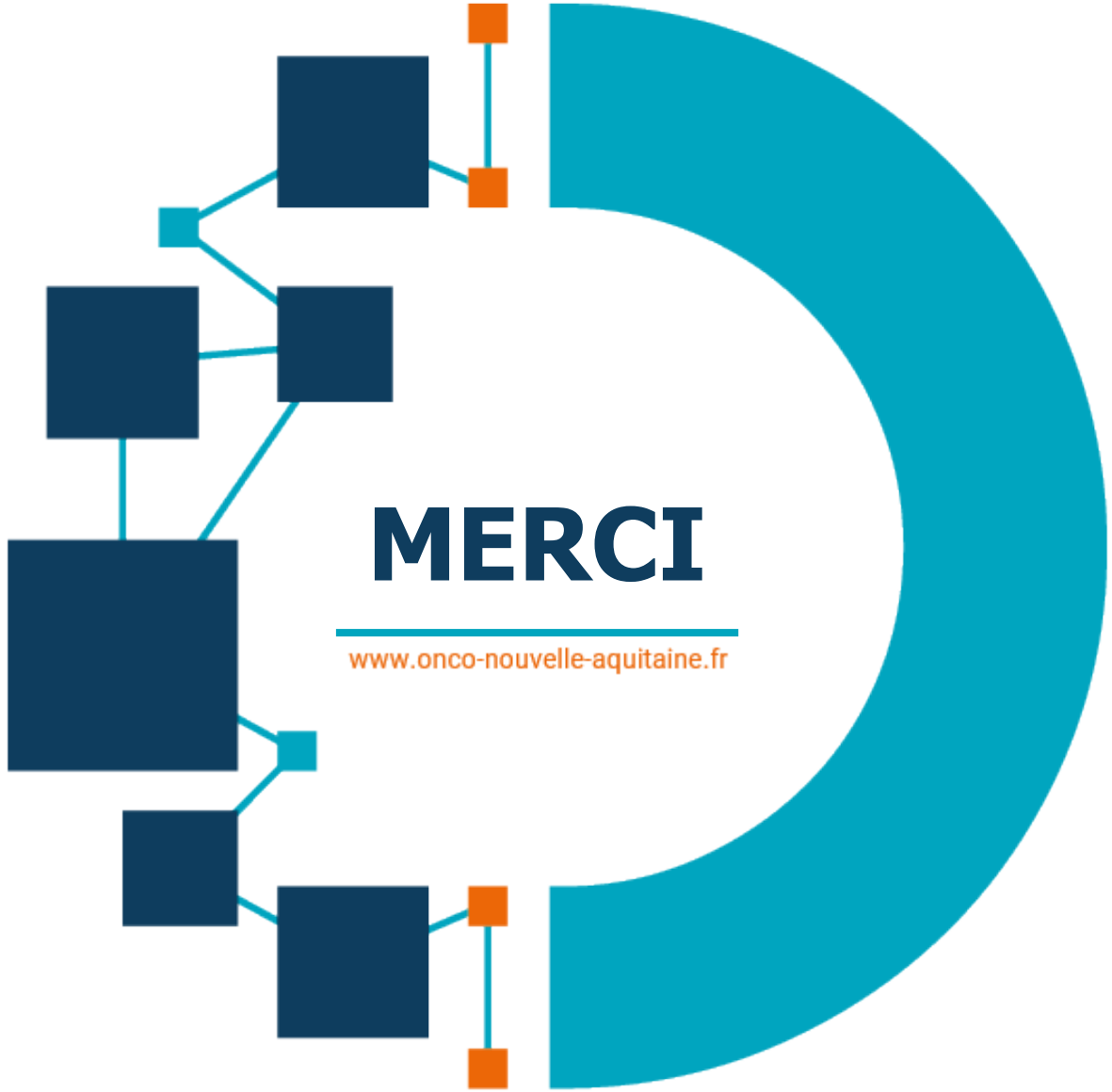
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