2022 ASCO ANNUAL MEETING

ONCO NOUVELLE-AQUITAINE Réseau Régional de Cancérologie

BRIO BORDEAUX | Recherche Intégrée Oncologie

Les « Scoops » en Oncologie Urologique

Prostate

Dr Sabrina FALKOWSKI

Oncologue médicale – Polyclinique de Limoges Chénieux

I.M.R.O. Imagerie Médicale, Radiothérapie et Oncologie

Liens d'intérêts

- Invitée par Jannsen
- Orateurs et/ou congrès : Astellas, AstraZeneca, BMS, Ipsen, Janssen, Merk, MSD, Pfizer, Sanofi

Quels sont les scoops ?

- Des changements de pratiques : OUI !!!

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Mais pour la PEC du cancer de prostate : pas de changement de pratique

Sujets abordés

- Le TEP-PSMA dans tous ses états
- Les mutations des gènes de réparation de l'ADN

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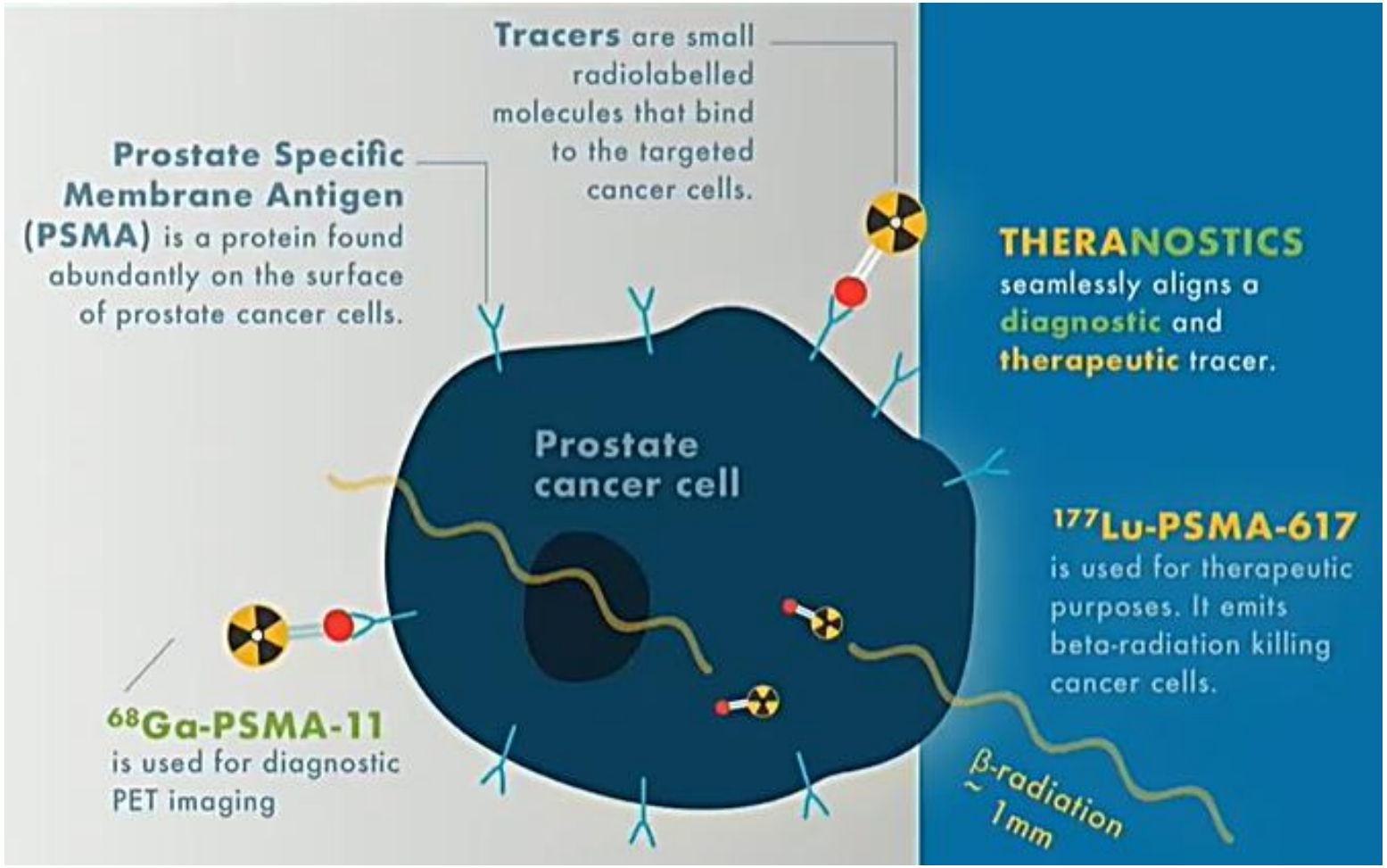
Le TEP PSMA


Tracers are small radiolabelled molecules that bind to the targeted cancer cells.
Prostate Specific Membrane Antigen (PSMA) is a protein found abundantly on the surface of prostate cancer cells.
THERANOSTICS seamlessly aligns a diagnostic and therapeutic tracer.
Prostate cancer cell
177Lu-PSMA-617 is used for therapeutic purposes. It emits beta-radiation killing cancer cells.
68Ga-PSMA-11 is used for diagnostic PET imaging
β-radiation ~ 1mm

Points des 2 essais phase III

TheraP

Vision

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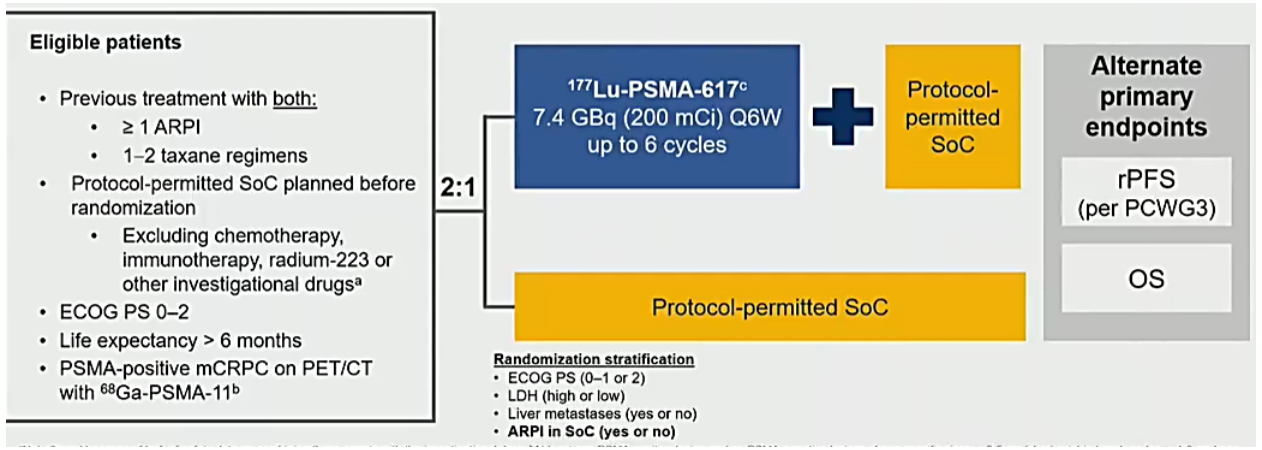

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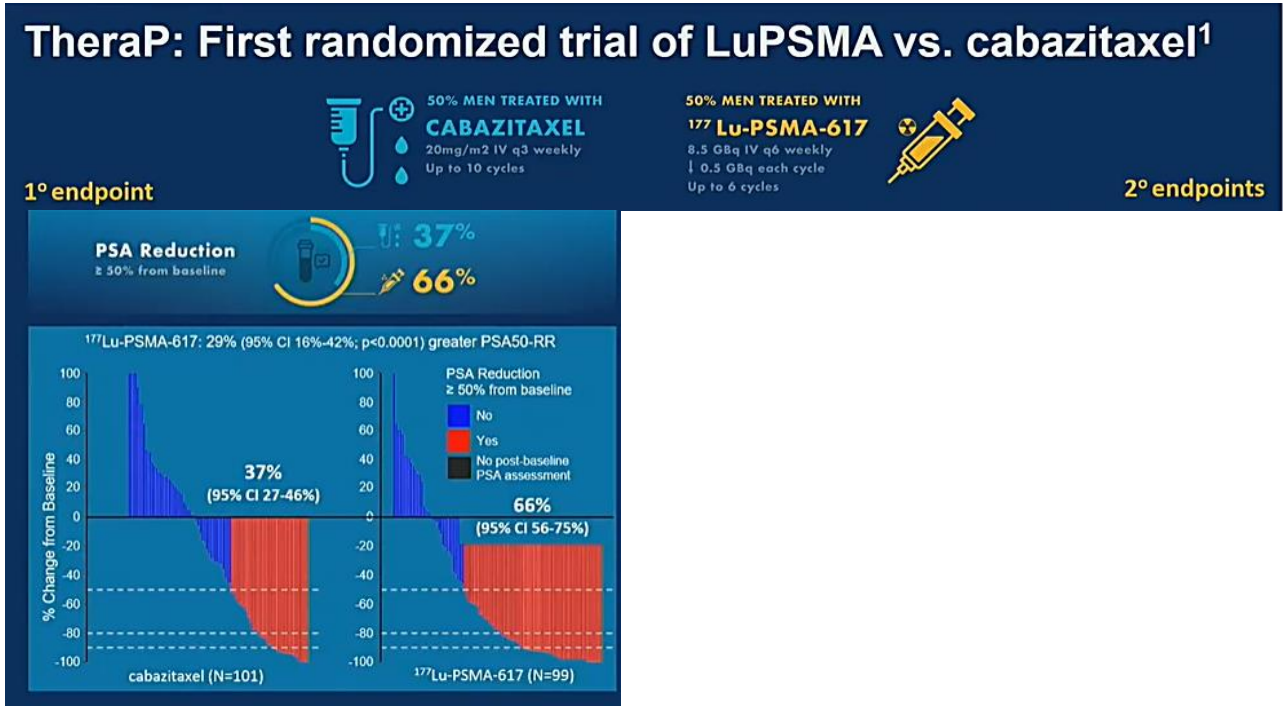

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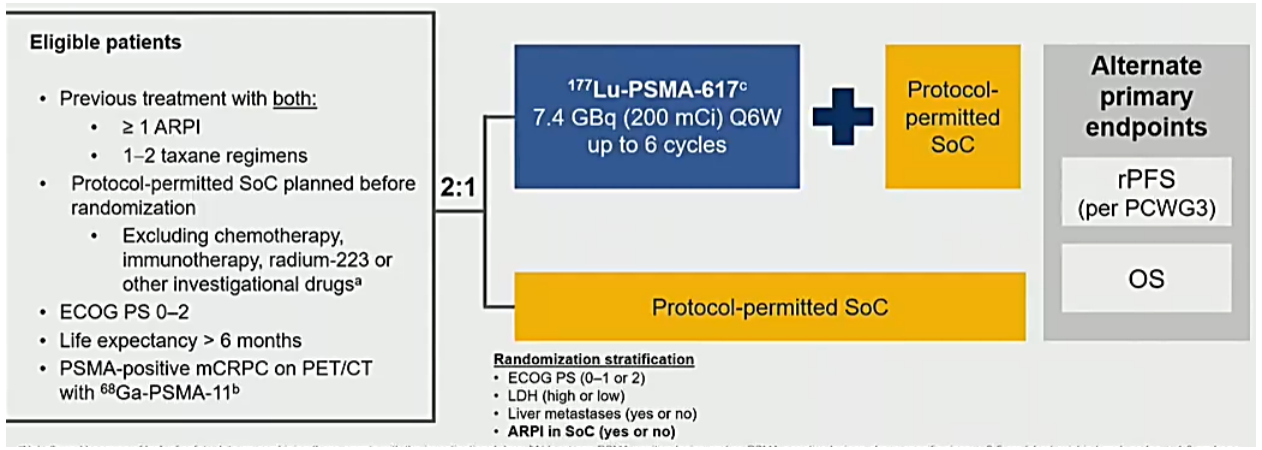

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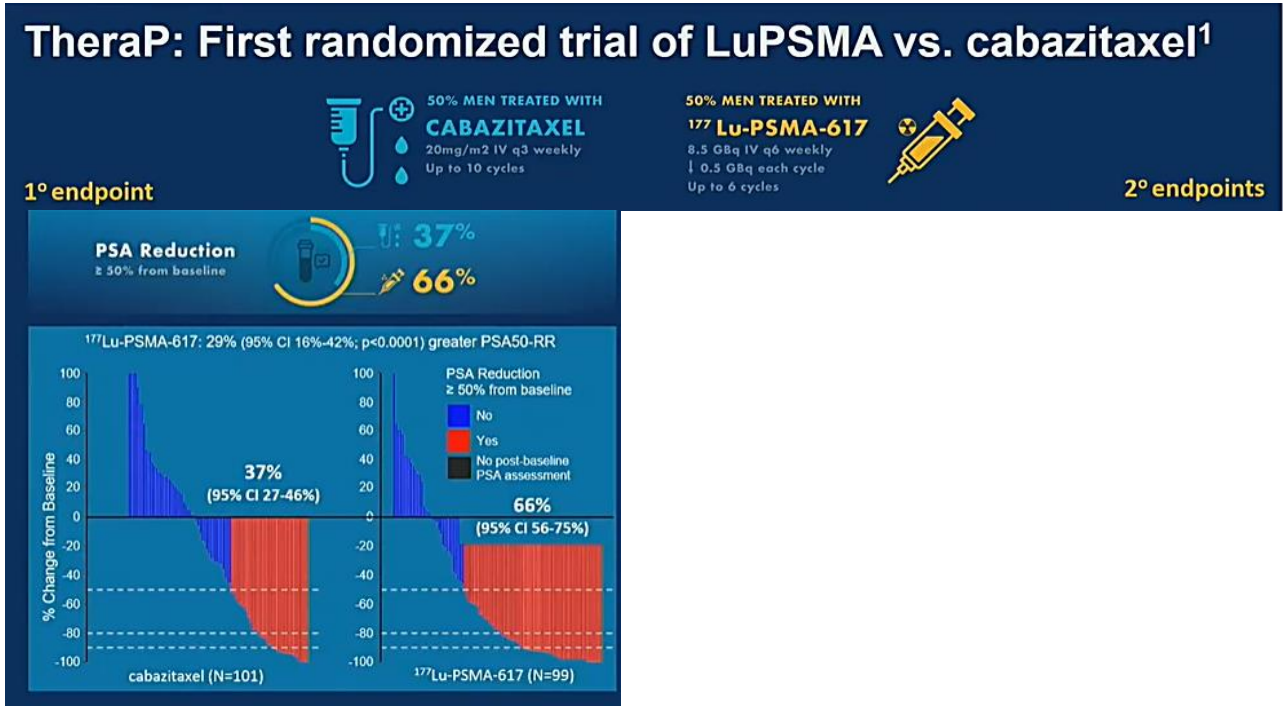

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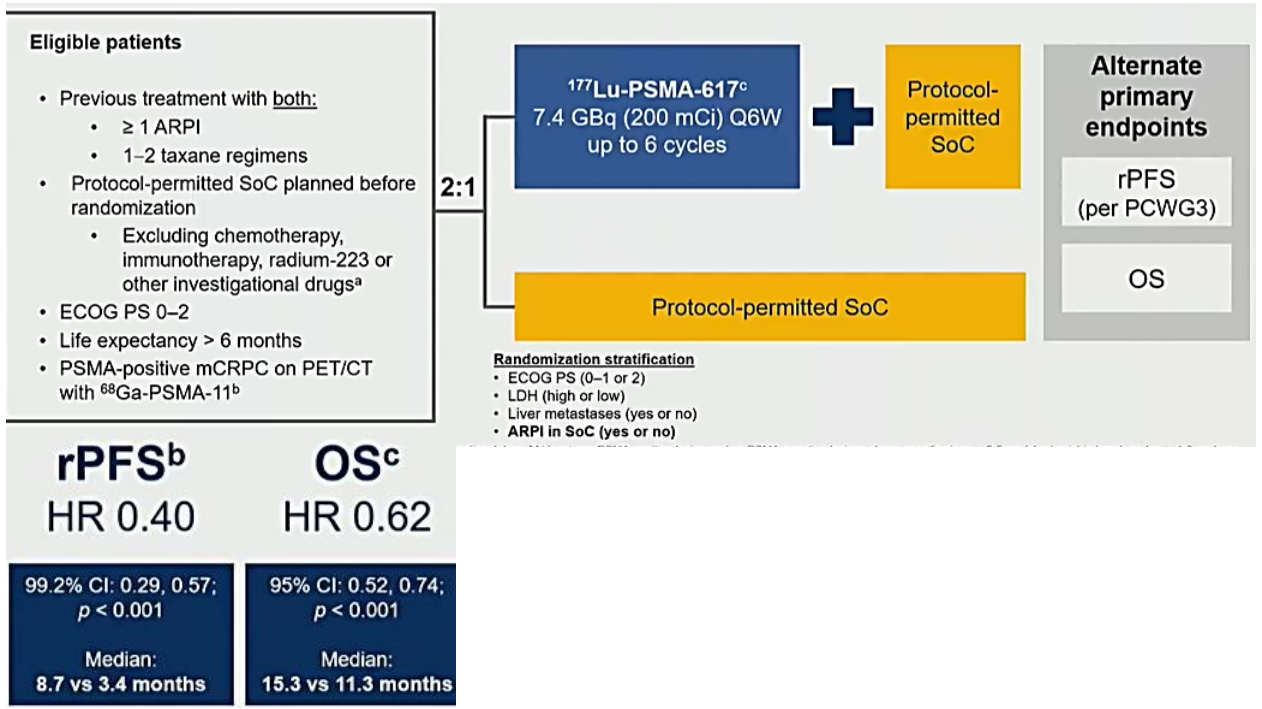

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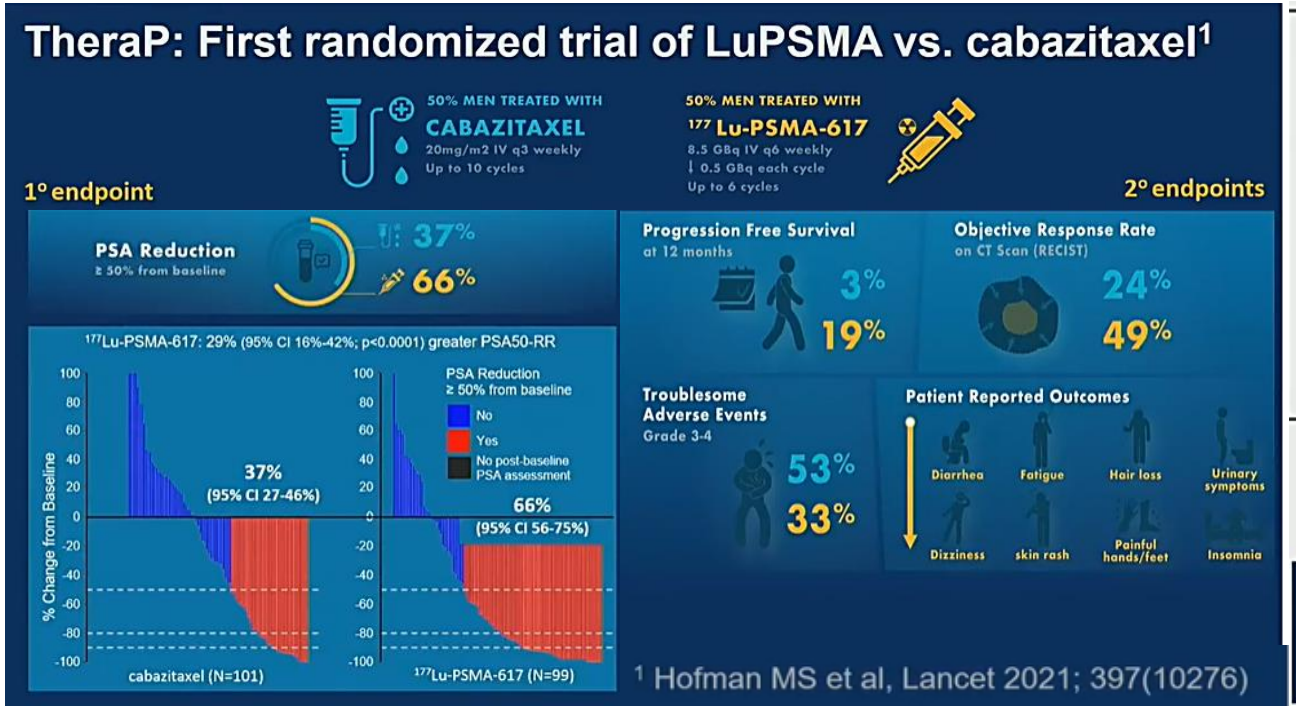

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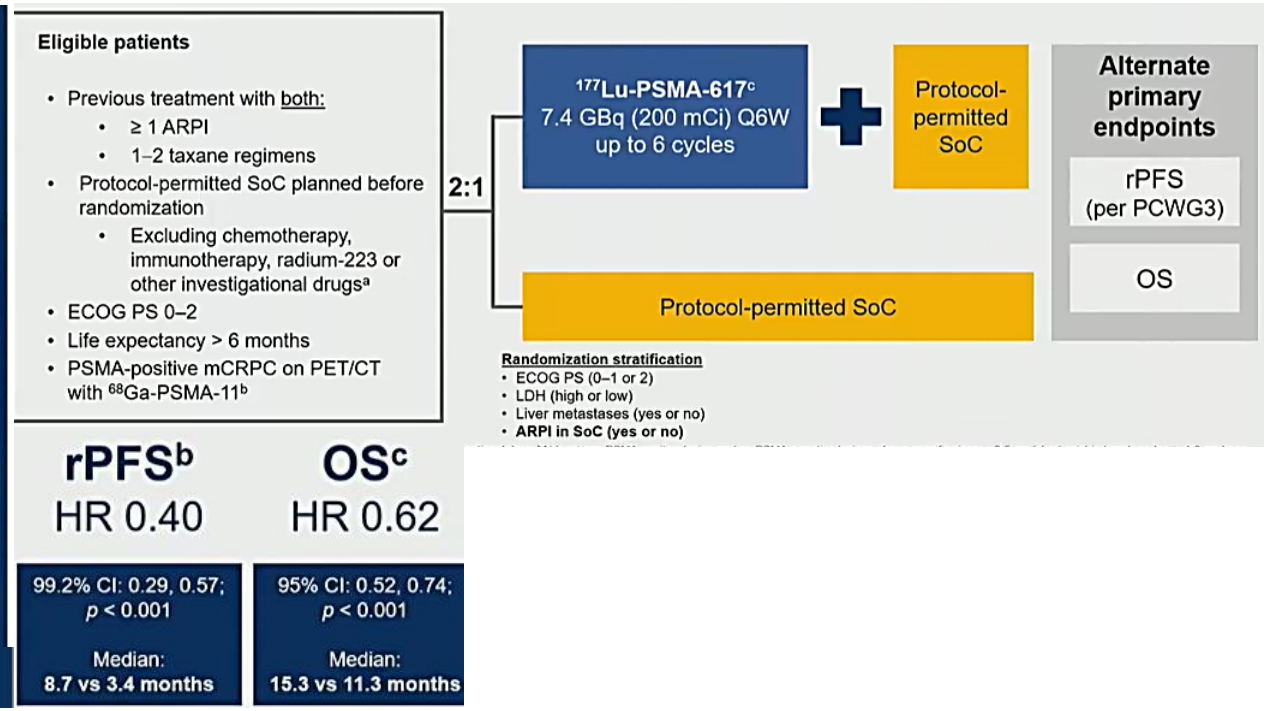

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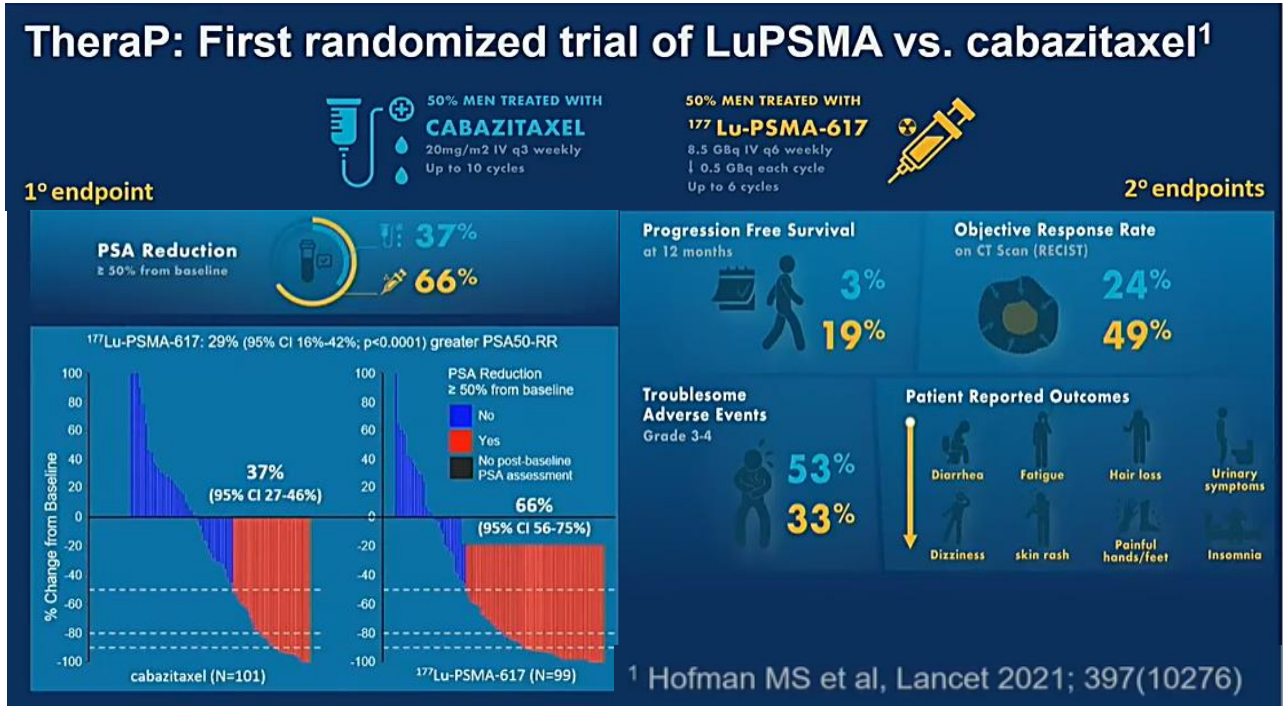

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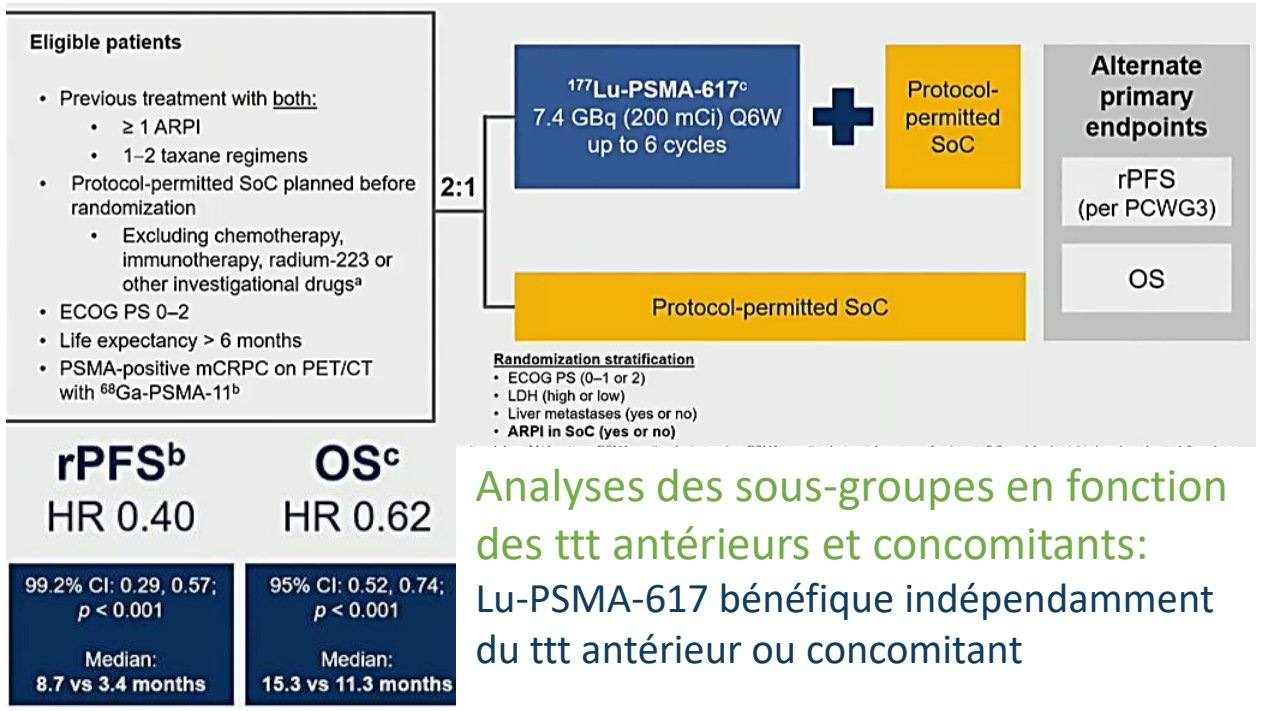

Analyses des sous-groupes en fonction des ttt antérieurs et concomitants:
Lu-PSMA-617 bénéfique indépendamment du ttt antérieur ou concomitant

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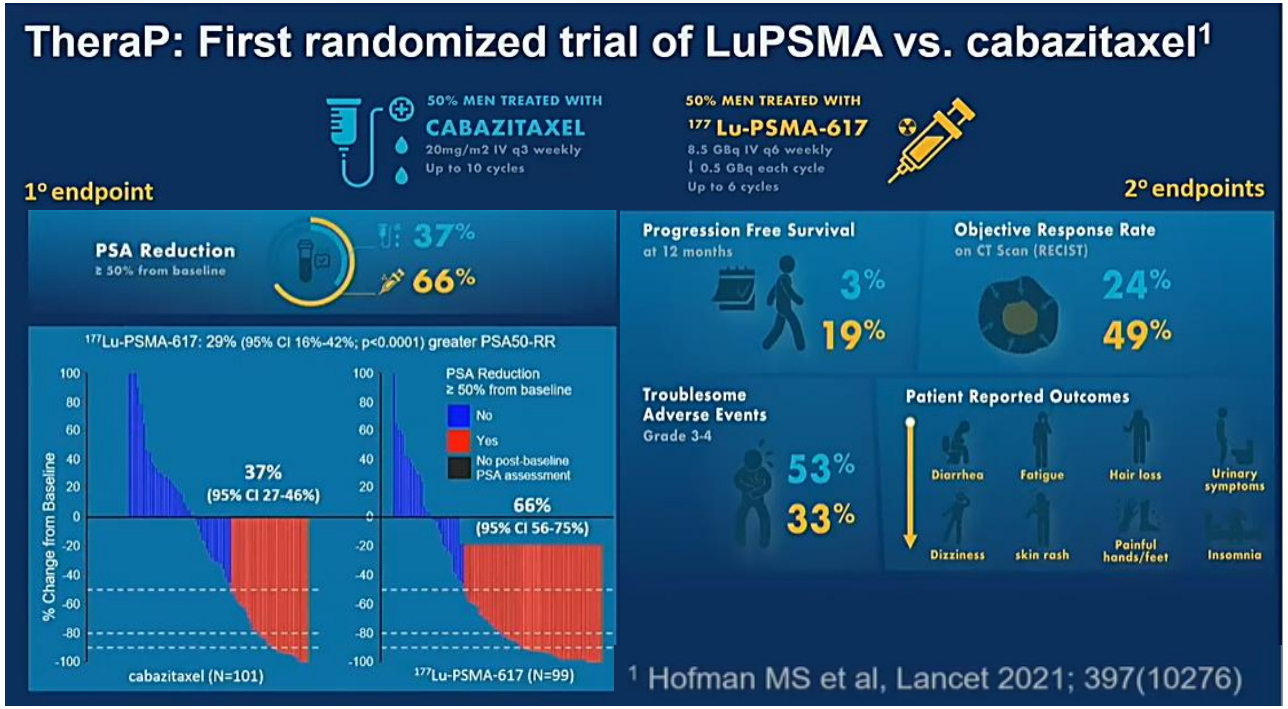
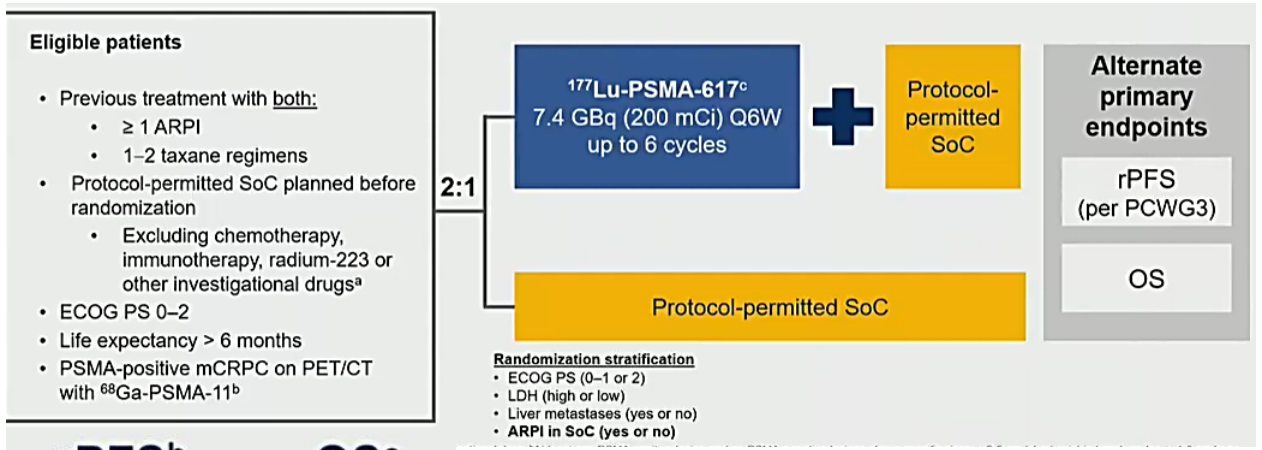


No difference in OS
HR 0.97 95%CI 0.70-1.4 P=0.99

La SGm 19,4m dans TheraP vs13,6m dans CAR
15% « caba » ont retiré leur consentement
20% « caba »ont reçu du Lu-PSMA

Vision



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Odds of PSA50-RR to LuPSMA *vs* cabazitaxel

	OR (95% CI)	
PSMA SUVmean < 10	2.2 (1.1 – 4.5)	P=0.03
PSMA SUVmean ≥ 10	12.2 (3.4 - 59)	

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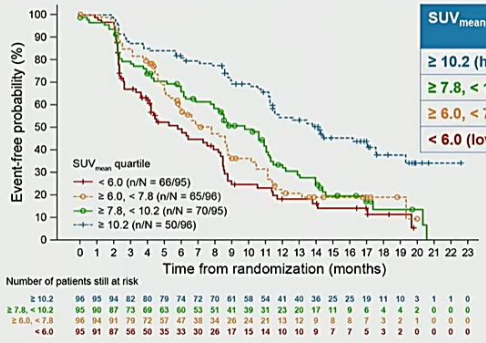
P=0.03

rPFS by whole-body SUV_{mean} quartiles (PFS-FAS)

- Higher whole-body SUV_{mean} was associated with prolonged rPFS

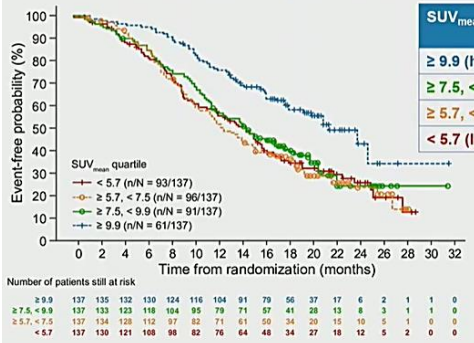


SUV_{mean} quartile	Median rPFS (months)
≥ 10.2 (highest)	14.1
≥ 7.8, < 10.2	9.8
≥ 6.0, < 7.8	7.8
< 6.0 (lowest)	5.8

SUV_{mean}	rPFS HR [95% CI], *p* value
Univariate analysis	**0.88** [0.84, 0.91], < 0.001
Multivariate analysis	**0.86** [0.82, 0.90], < 0.001

OS by whole-body SUV_{mean} quartiles (FAS)

- Higher whole-body SUV_{mean} was associated with improved OS



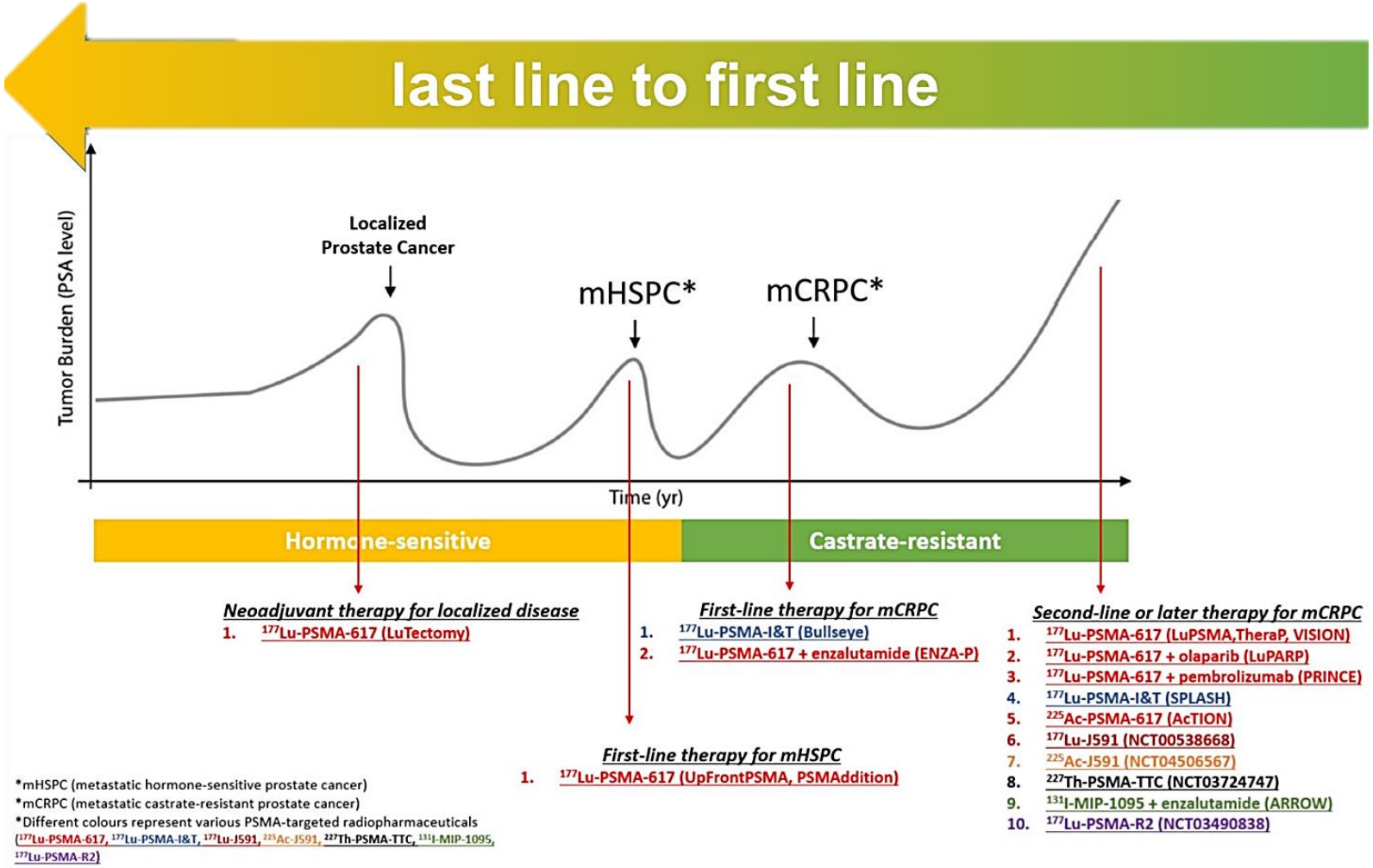
SUV_{mean} quartile	Median OS (months)
≥ 9.9 (highest)	21.4
≥ 7.5, < 9.9	14.6
≥ 5.7, < 7.5	12.6
< 5.7 (lowest)	14.5

SUV_{mean}	OS HR [95% CI], *p* value
Univariate analysis	**0.92** [0.89, 0.95], < 0.001
Multivariate analysis	**0.88** [0.84, 0.91], < 0.001

CI, confidence interval; HR, hazard ratio; FAS, full-analysis set; OS, overall survival; SUV, standardized uptake value

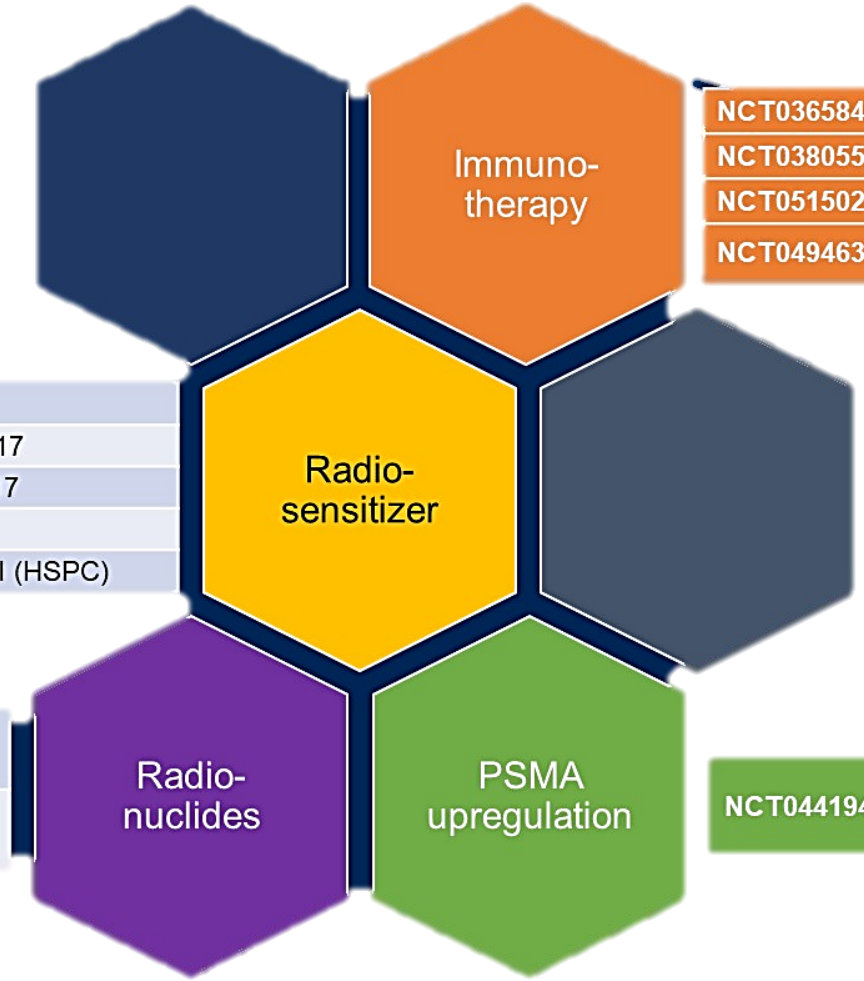
Absence de lésions PSMA+ sur os et foie: Facteur pronostique indépendant de SG et SSP

Les essais en cours avec le TEP PSMA



Zhang H et al, *Cancers* 2021

Les essais de combinaison



NCT03658447	^{177}LuPSMA-617 + Pembrolizumab
NCT03805594	^{177}LuPSMA-617 + Pembrolizumab
NCT05150236	^{177}Lu-PSMA-617 + Ipilimumab + Nivolumab
NCT04946370	^{225}Ac-J591 + Pembrolizumab + ARPI (eg. enzalutamide)

NCT03874884	Olaparib + ^{177}Lu-PSMA-617
NCT05113537	Abemaciclib + ^{177}Lu-PSMA-617
NCT05340374	Cabazitaxel + ^{177}Lu-PSMA-617
NCT00916123	Docetaxel + ^{177}Lu-J591
NCT04343885	^{177}Lu-PSMA-617 → docetaxel (HSPC)

NCT04886986	^{225}Ac-J591 + ^{177}Lu-PSMA-I&T
AlphaBet	^{233}Ra + ^{177}Lu-PSMA-I&T

NCT04419402	Enzalutamide + ^{177}Lu-PSMA-617

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Actualités PROpel, MAGNITUDE vs BRCAAway

#5018 **BRCAAway: A randomized Ph2 trial of abiraterone, olaparib, or abiraterone + olaparib** in patients with metastatic castration-resistant prostate cancer (mCRPC) with DNA repair defects. (M. Hussain, et al.)

#5019 **Tolerability of abiraterone combined with olaparib** in patients with metastatic castration-resistant prostate cancer: further results from the Phase III **PROpel trial** (A. Thiery-Vuillemin, et al.)

#5020 **Gene-by-gene analysis in the MAGNITUDE study of niraparib with abiraterone acetate** and prednisone in patients with mCRPC and homologous recombination repair gene alterations (S. Sandhu, et al.)

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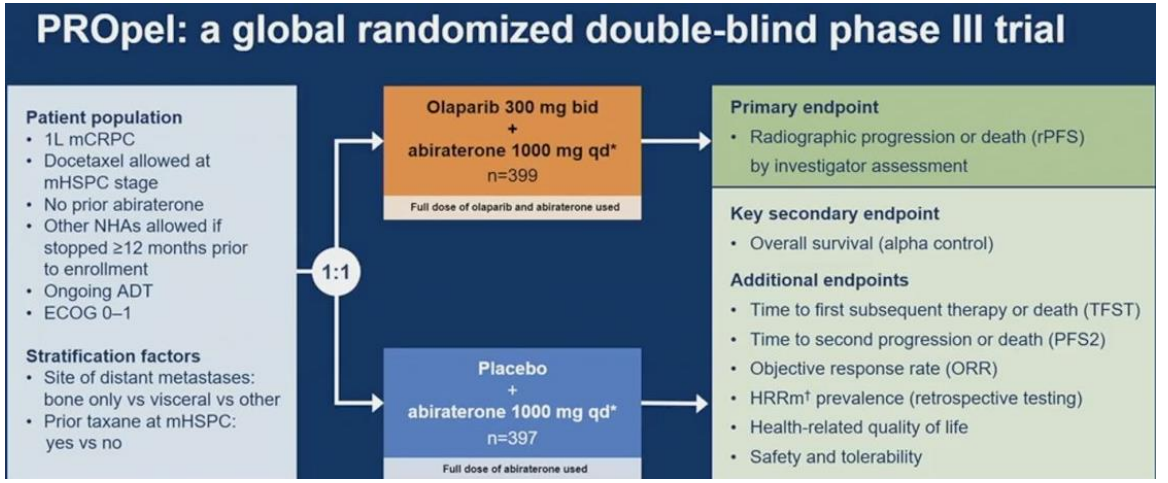

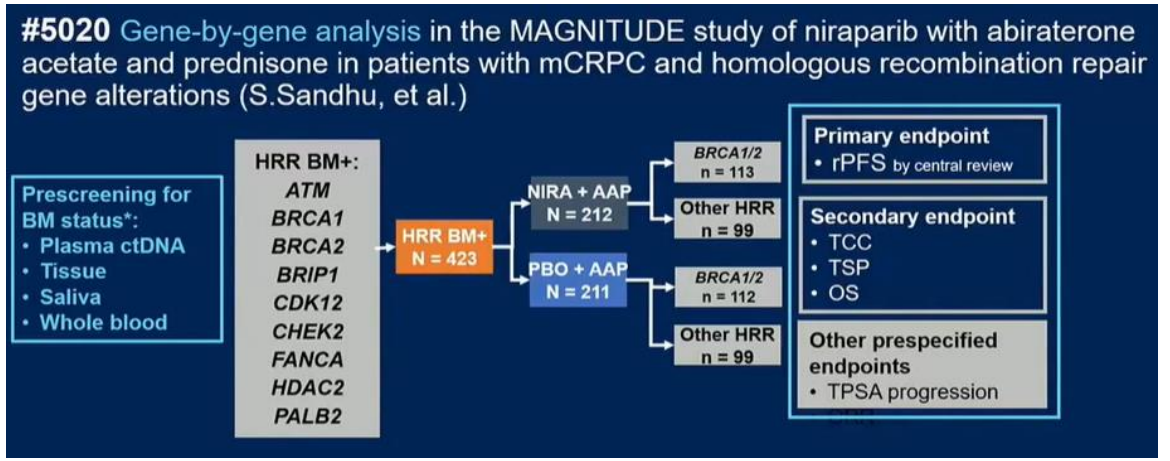

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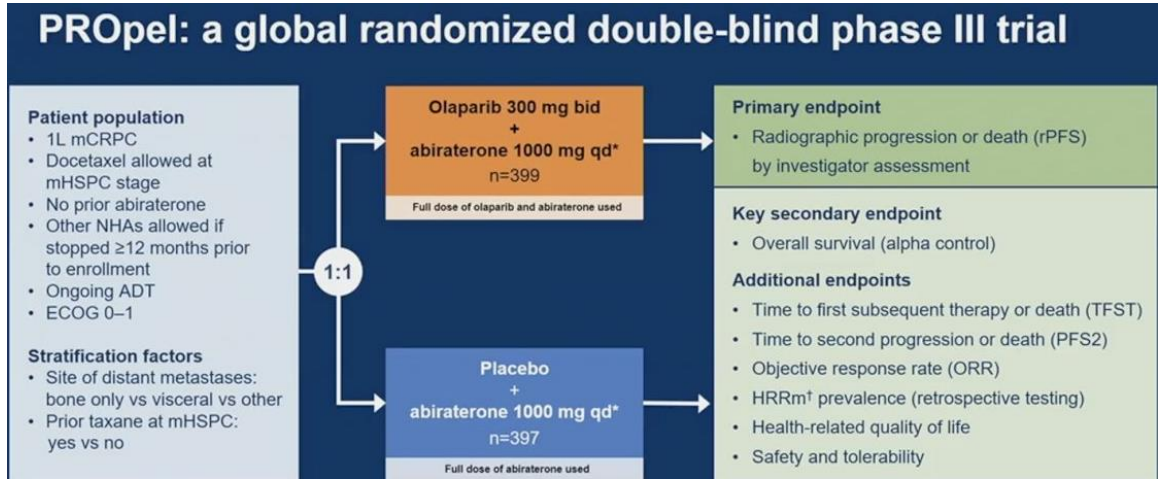
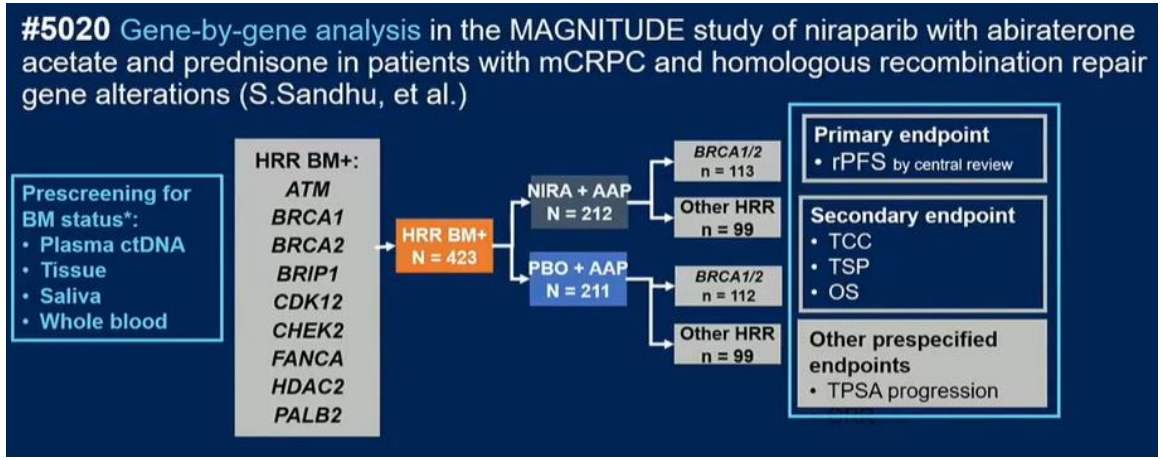
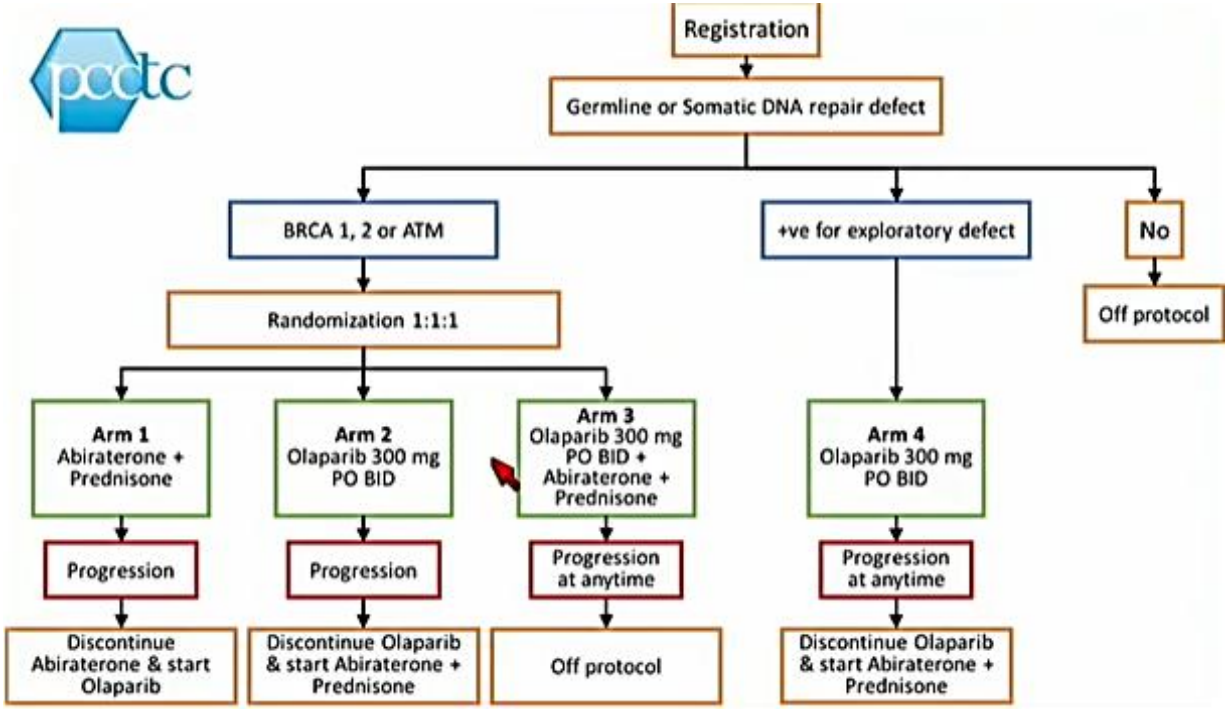
1L mCRPC	Ph3 PROpel [2, 3]	Ph3 MAGNITUDE [4, 5]
Eligibility	Allowed: ✗ NO prior AAP • Other ARi, if >/=12 mos • Prior doce (mCSPC)	Allowed: • AAP </= 4mos for 1L mCRPC • Prior ARi (nmCRPC/mCSPC) • Prior taxane (mCSPC)
Biomarker considerations	Unselected (retrospective HRRm testing)	Prospective HRRm stratification (*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)





Phase 2 BRCAAway



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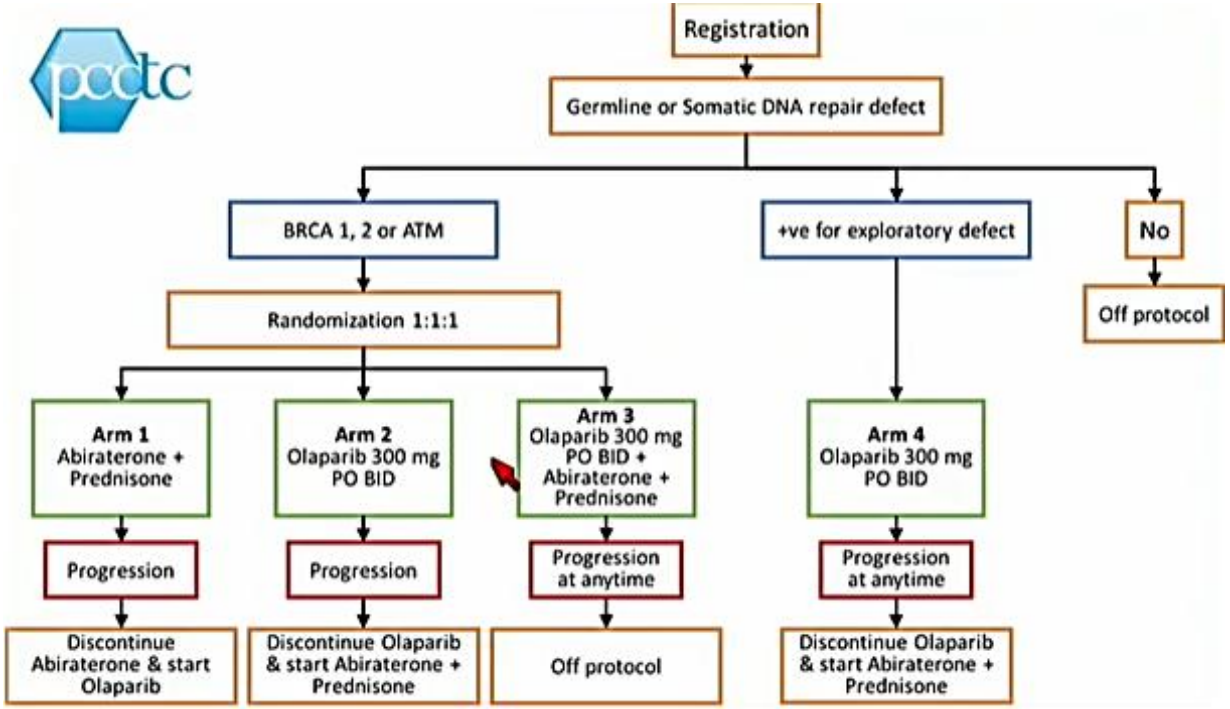
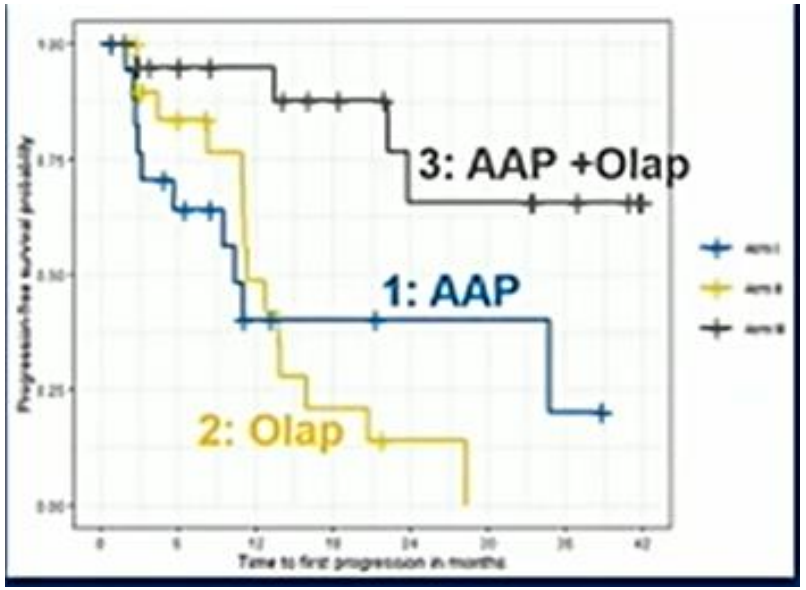
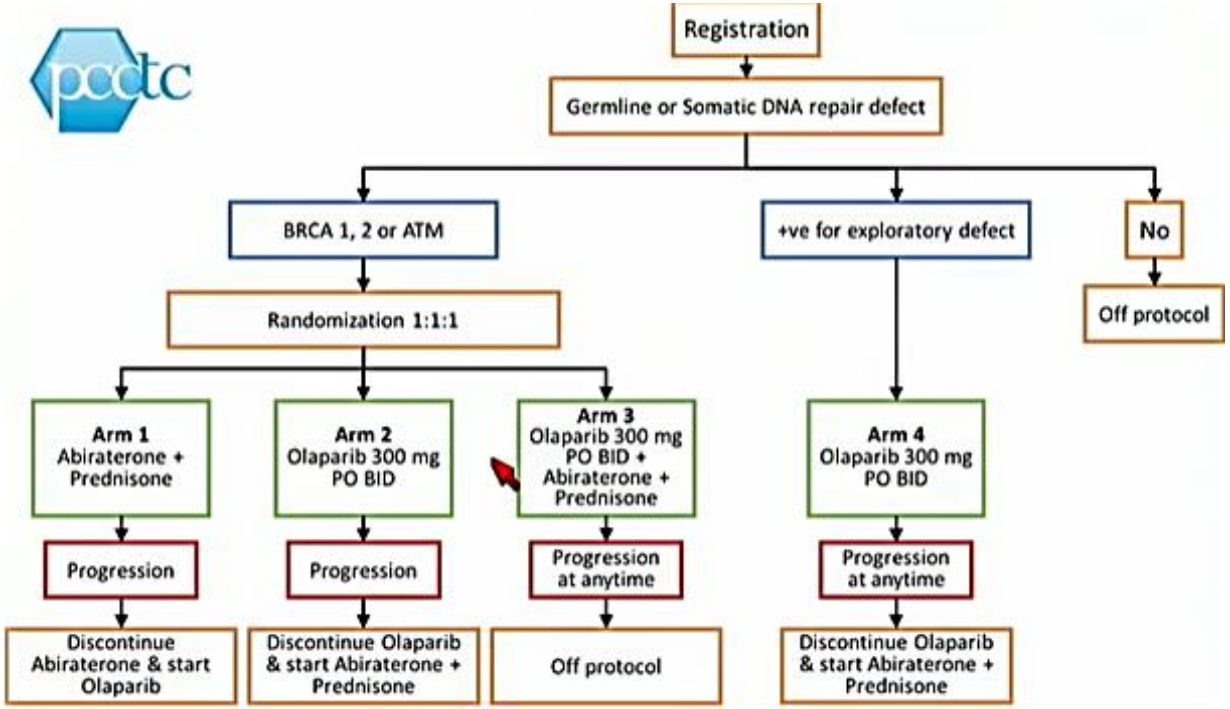
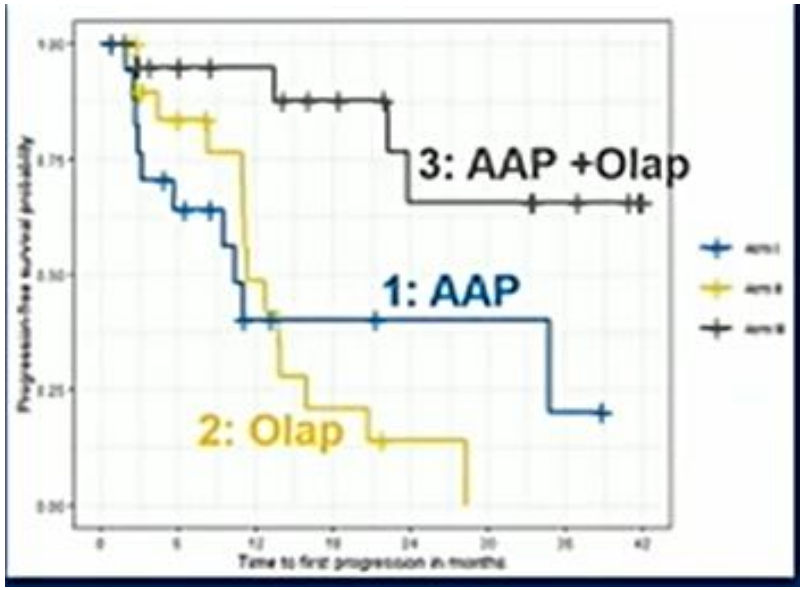




1L mCRPC	Ph2 BRCAAway [1]
Eligibility	Allowed: X NO prior AAP X NO prior ARi • Prior taxane (mCSPC)
Biomarker considerations	Prospective HRRm selection (*BRCA1, BRCA2, ATM*)
Treatment	AAP vs Olap 300BID vs Olap 300BID +AAP
rPFS AAP vs AAP+PARPi	*(preliminary results)* 10.4 mos (AAP) vs 11.3 mos (olap) vs Not reached (AAP +olap)

Phase 2 BRCAAway





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Data de + en + nombreuses validant que l'association NHT+PARPi fait mieux dans une population mutée HHR

PARPi : pour quelle mutation ? Quelle tolérance?

Quelles mutations ?

- Validation BRCA1/2
- MAGNITUDE

Quelle tolérance?

- PROpel

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1. *PALB2 (12), CHEK2 (38)* and *HDAC2 (5)* each showed benefit across all endpoints

2. *CDK12 (27),* no benefit in primary endpoint or >1 secondary endpoint. *ATM (43),* mixed bag

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Quelle tolérance?

- PROpel

Anemia was managed primarily by dose modifications

	Abiraterone plus olaparib (N=398)	Abiraterone plus placebo (N=396)
Any anemia AE,* n (%)	183 (46)	64 (16)
Event rate (per 1000 patient years), n	508	136
CTCAE grade ≥3, n (%)	60 (15)	13 (3)
Fatal, n (%)	0	0
Dose interruption, n (%)	62 (16)	7 (2)
Dose discontinuation, n (%)	15 (4)	3 (1)
Dose reduction, n (%)	42 (11)	2 (1)
Received erythropoiesis stimulating agent, n (%)	2 (0.5)	1 (0.3)
Received blood ≥1 blood transfusion, n (%)	62 (16)	15 (4)

*Grouped term.

PARPi: tous les candidats ne sont pas identifiés mais leur toxicité en association est gérable

Merci de votre attention

Place aux questions !