Nouveautés dans le cancer du sein métastatique en routine

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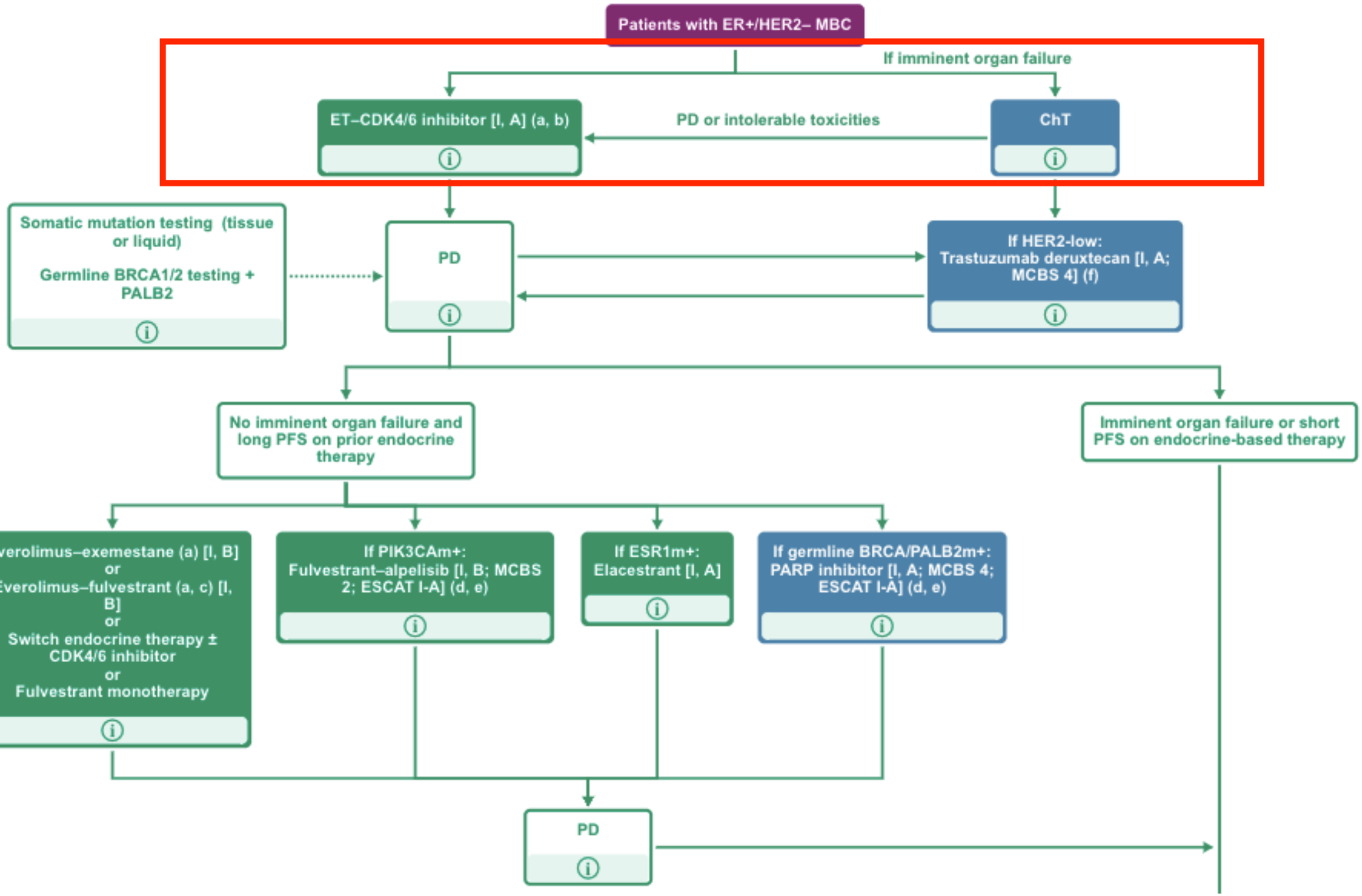
CH Périgueux

Chez les RH+



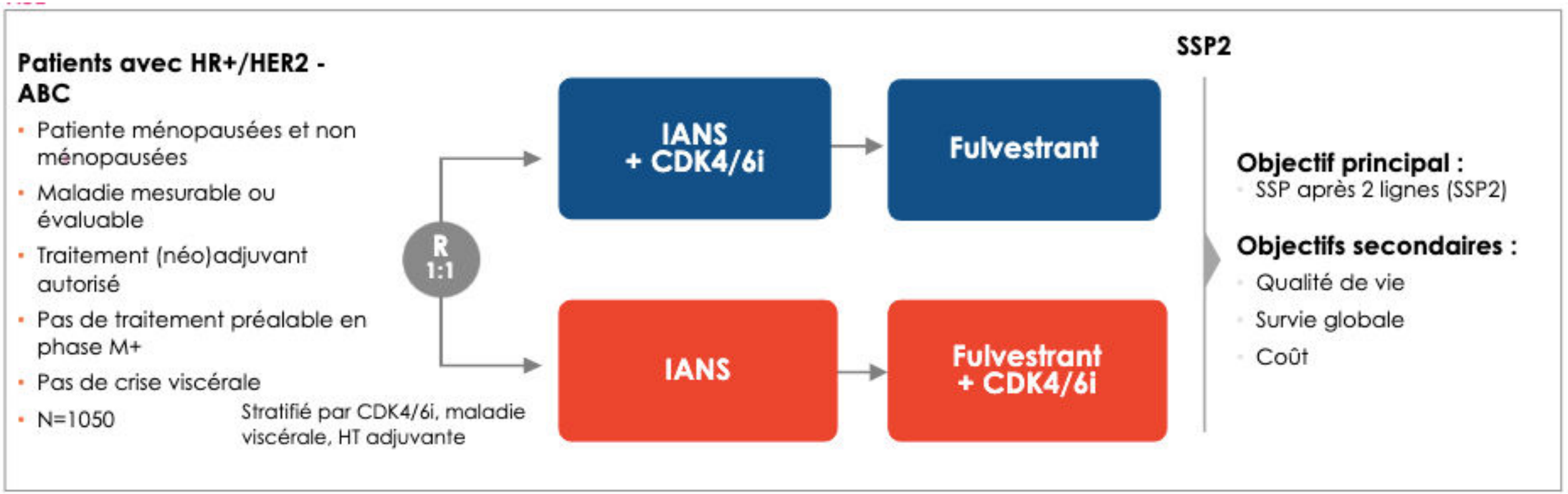
Esmo guidelines mai 2023

Confirmation intérêt des CDK 4-6 en 1ère ligne

- Résultat en SG des CDK 4-6 en 1ère ligne
- Analyse finale de MONARCH-3
- 8 ans de recul
- Gain en SG de 66 mois

MONALEESA-2 Ribociclib+/- IA)	PALOMA-2 palbociclib +/- IA	MONARCH-3 abemaciclib +/- IA
PFS 25,3m vs13m HR=0,56 SG 63,9 mois vs 51,4 mois, HR à 0,76	PFS 24,8m vs 14,5 m HR=0,58 53. m vs 49.8 m en ITT HR=0,92 SG 51,6 m vs 44,6m HR=0.956	PFS 29m vs 14,8m HR = 0,54 SG 66.8 vs 53.7m en ITT HR = 0.804

Etude SONIA : schéma de l'étude

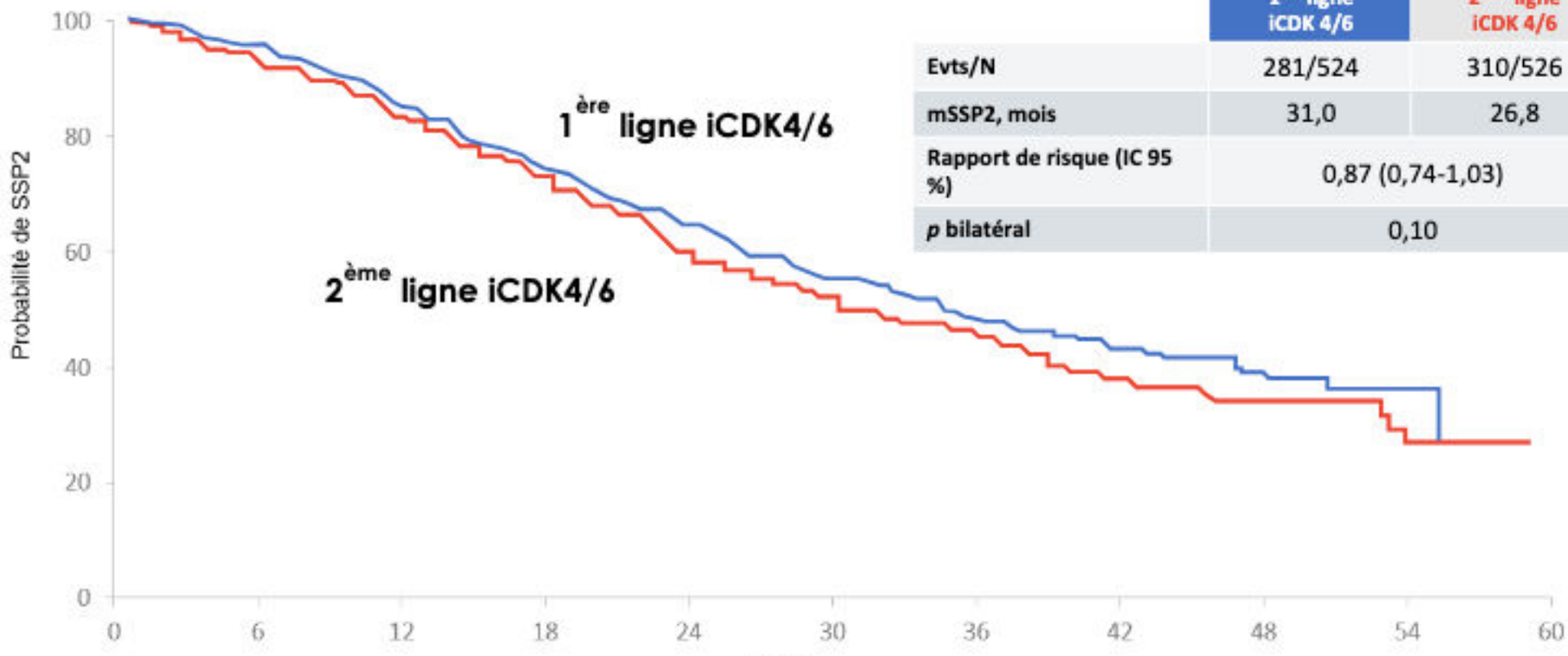


- **Evaluation tumorale toutes les 12 semaines**
- **SSP évaluées localement par RECIST v1.1**
- **Analyse primaire après 574 SSP2 évts**
  - Puissance = 89% pour détecter une supériorité selon ESMO® MCBS (HR ≤ 0,65 et Δ ≥3 mois) avec two-sided α=5% [1]

NM*, récepteurs hormonaux positifs HER2-, HER2+ négatifs ; ABC, cancer du sein avancé, AI, inhibiteur de l'aromatase ;
PFS, progression free survival *intervalle sans maladie après inhibiteur non stéroïdien de l'aromatase >12 mois. ClinicsTrials.gov (NCT03425838)
[1]Cherny NI, *at al.* Ann Oncol 2017

G.S. Sonke et al. ASCO® 2023, Abs. #LBA1000

Résultats : SSP en 2ème ligne

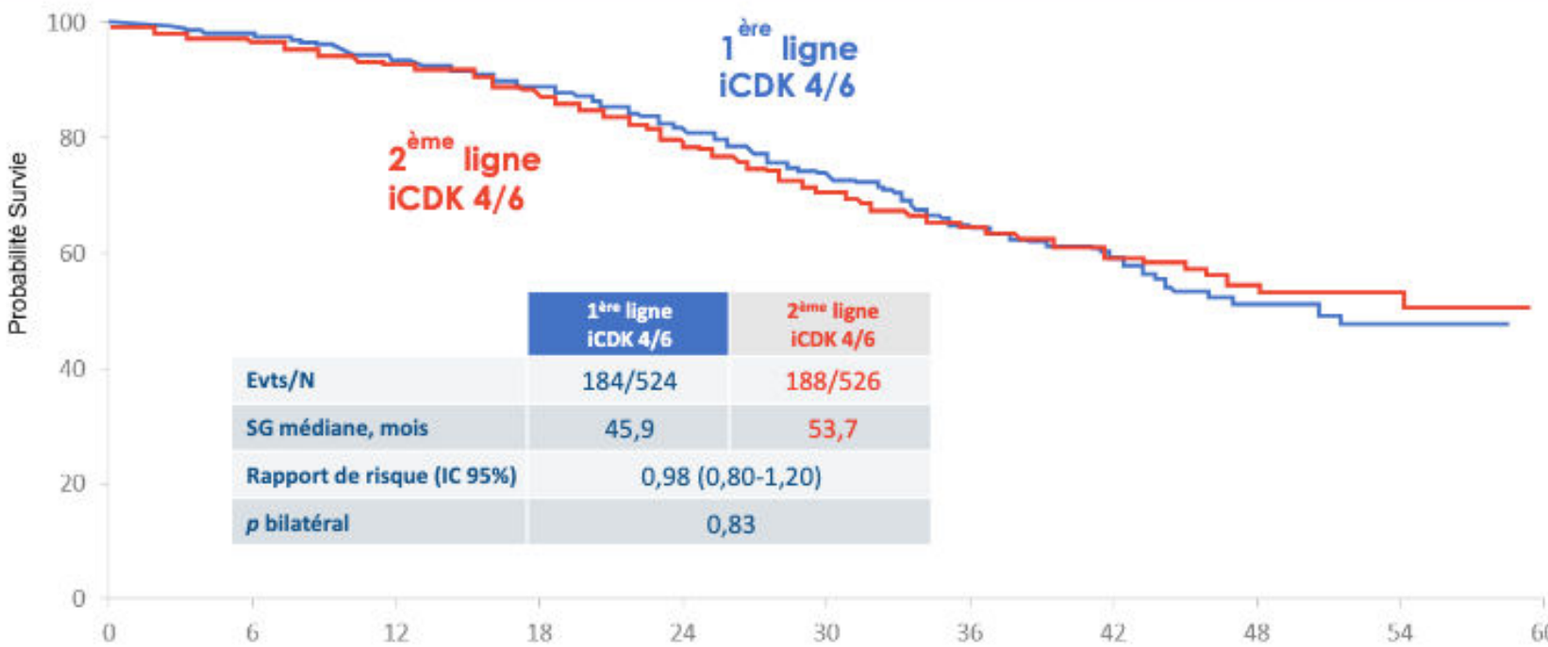


	1ère ligne iCDK 4/6	2ème ligne iCDK 4/6
Evts/N	281/524	310/526
mSSP2, mois	31,0	26,8
Rapport de risque (IC 95 %)	0,87 (0,74-1,03)	
p bilatéral	0,10	

Nombre à risque (censurés)

1ère ligne	524 (0)	491 (3)	429 (5)	339 (34)	244 (84)	167 (123)	118 (148)	69 (184)	31 (215)	5 (239)	0 (243)
2ème ligne	526 (0)	478 (2)	418 (6)	330 (35)	225 (76)	164 (105)	115 (133)	65 (161)	30 (190)	9 (207)	0 (216)

Résultats en SG



	1ère ligne iCDK 4/6	2ème ligne iCDK 4/6
Evts/N	184/524	188/526
SG médiane, mois	45,9	53,7
Rapport de risque (IC 95%)	0,98 (0,80-1,20)	
p bilatéral	0,83	

Nombre à risque (censurés)

1ère ligne	524 (0)	510 (3)	485 (4)	427 (37)	324 (103)	240 (157)	171 (197)	104 (250)	42 (300)	7 (333)	0 (340)
2ème ligne	526 (0)	506 (2)	483 (2)	426 (32)	328 (89)	242 (139)	175 (186)	112 (236)	52 (287)	16 (322)	0 (338)

- SG bras controle plus basse que dans les autres études (45 mois vs 65 mois)
- Fulvestrant seul en 2ème ligne
- IA seul est une possibilité en 1ère ligne
- Penser au CDK 4-6 en 2ème ligne si non reçu en 1ère ligne
- Enjeux économiques

Etude Sonia : recommandations ABC7

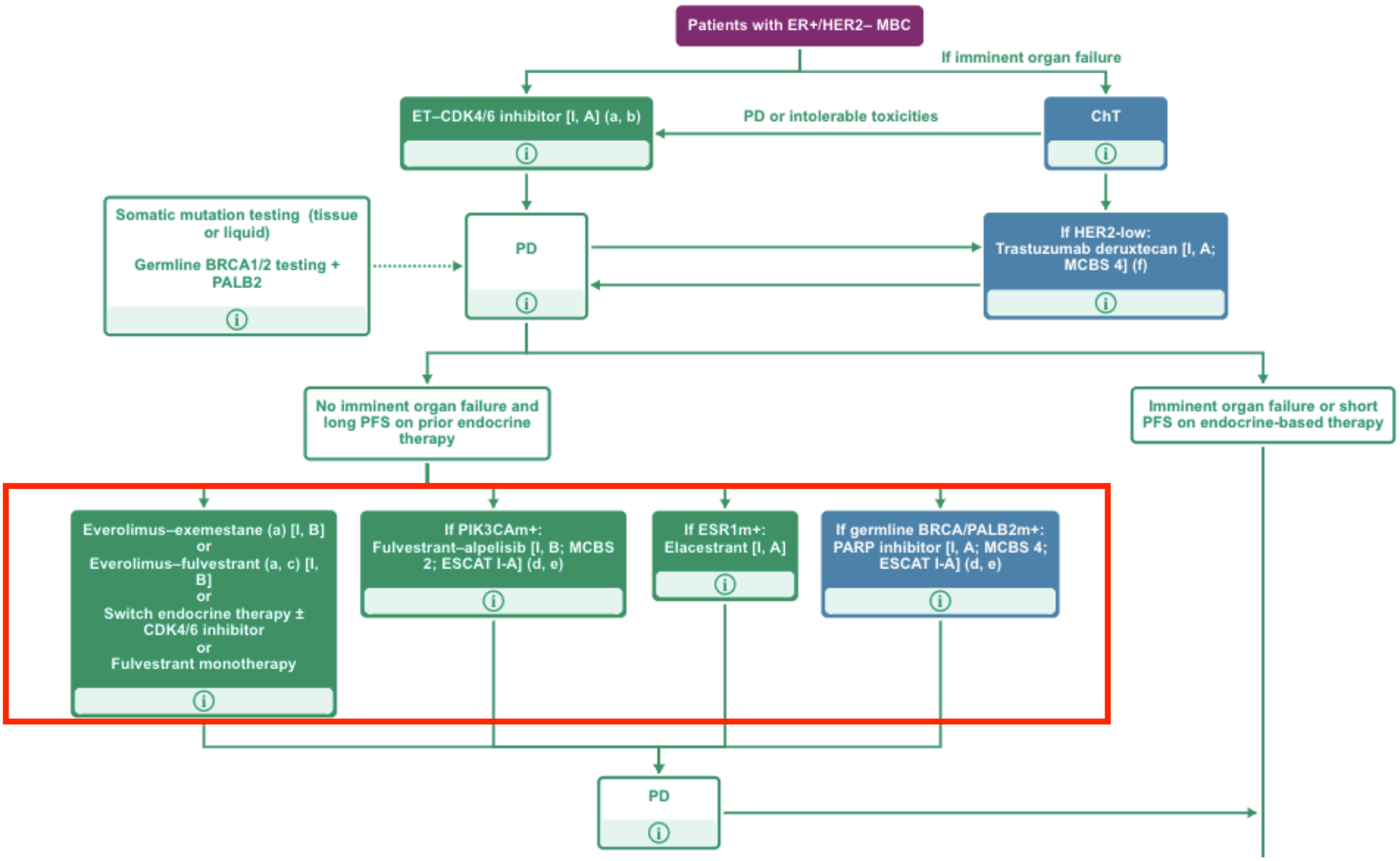
F. Cardoso et al, The Breast 2024, in preparation

It is currently unknown if the results would be the same with ribociclib or abemaciclib.

Based on these results, it is an acceptable option to use ET alone as 1st line therapy for selected patients (e.g. low volume of disease, long DFI, patient preferences, accessibility constraints) with ER+/HER-2 neg ABC.

However, in view of the totality of data (OS benefit and different 2nd line options), the panel still favors the use of a CDK4/6i + ET as 1st line therapy for the majority of patients with this ABC subtype.

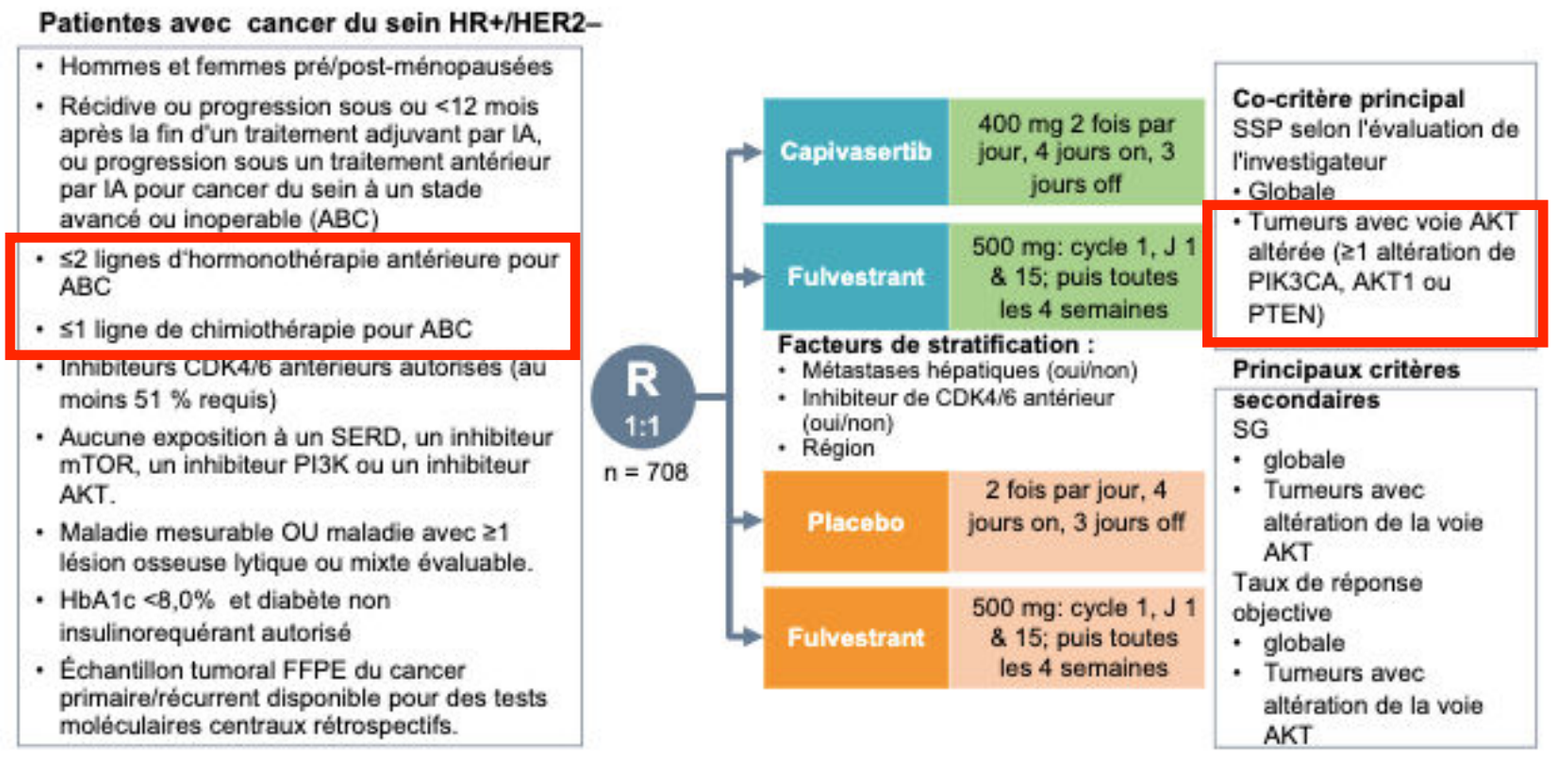
En 2ème ligne ?



Voie PIK3CA

- SOLAR-1 : intérêt de l'alpelisib chez les patientes avec mutations PIK3CA
- Gain en PFS ; pas de gain significatif en SG
- **Etude Capitello** : Fulvestrant +/- Capivasertib (pan-AKT inhibitor)

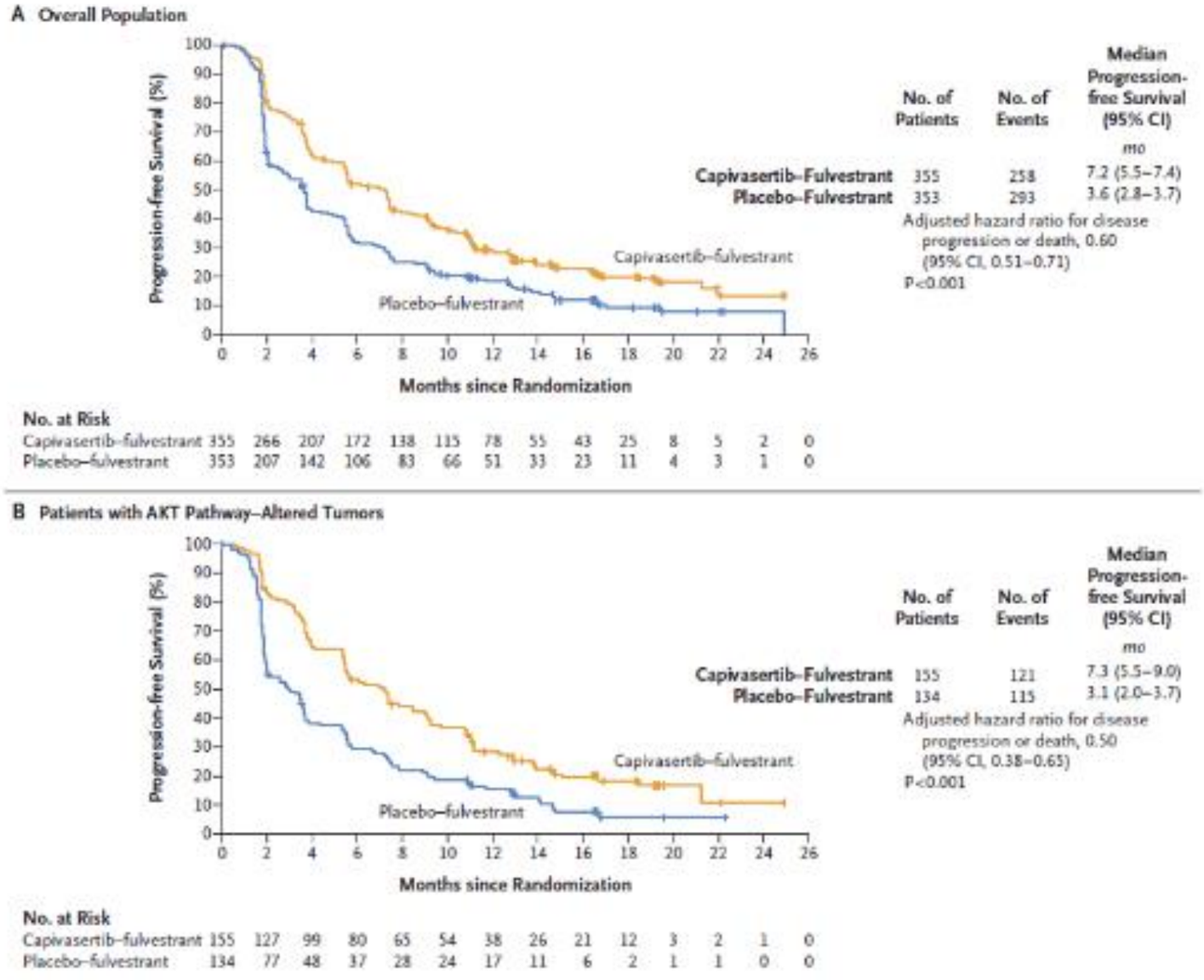
- *Étude de phase III, randomisée, en double aveugle, contrôlée par placebo, pour le traitement du cancer du sein avancé HR+/HER2- après récidive ou progression sous traitement antérieur par inhibiteur de l'aromatase*



Etude Capitello : capivasertib

Post CDK=70%

Les mutations activatrices dans les gènes PIK3CA et AKT1 et les altérations inactivatrices dans les gènes PTEN ont été déterminées de manière centralisée (après randomisation) au moyen du séquençage de nouvelle génération en utilisant le test FoundationOneCDx (Foundation Medicine) dans tous les pays à l'exception de la Chine (OncoScreen Plus, Burning Rock Biotech).



Turner et al, NEJM 2023

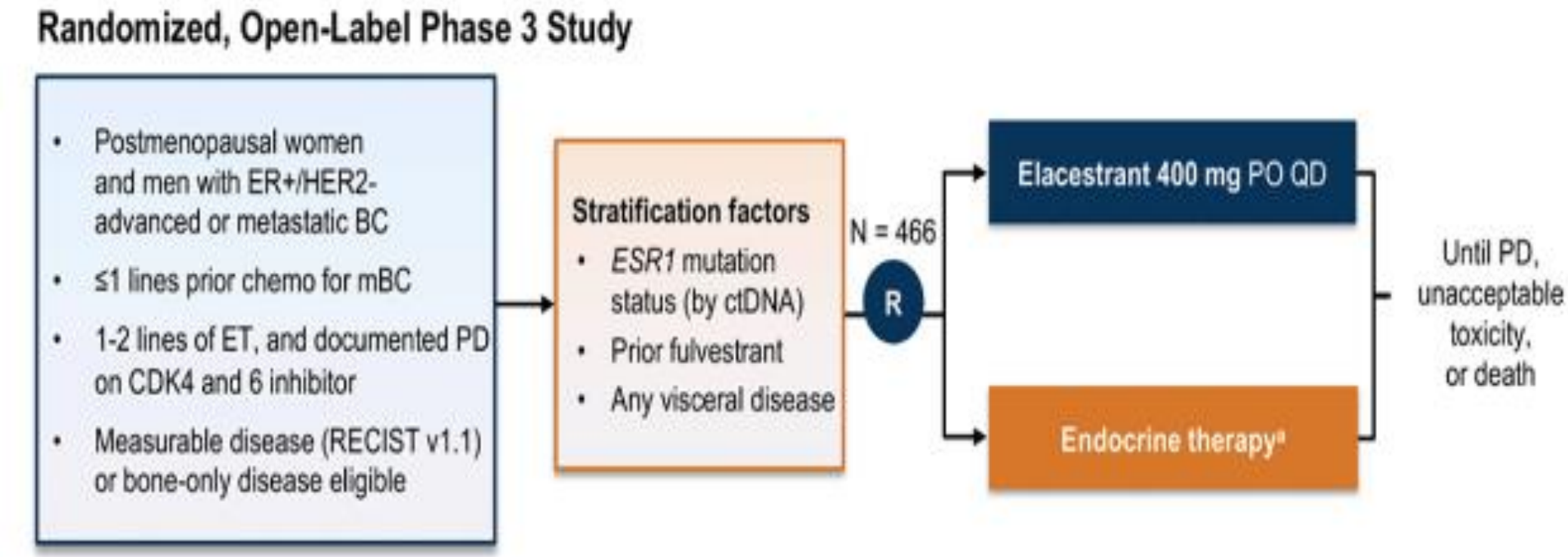
Voie PIK3CA/AKT/mTOR : en 2ème ligne

- Potentiellement un impact clinique
- Aucune étude n'a à ce jour montré un bénéfice en SG
- Toxicités avec effet de classe des PIK3CA : hyperglycémie, diarrhée, stomatite, rash…
  - Alpelisib : plus d'accès
  - Capivasertib : pas encore d'accès
- A suivre

Place des SERDS : mutation ESR1

- Les mutations ESR1 altèrent le domaine de liaison au ligand, rendant le Rc constitutionnellement actif entrainant la carcinogenèse
- Mutation qui apparait au cours de la maladie
- Voie de résistance aux IA
- Analyse sur biopsie liquide
- Lors de la progression sous hormonothérapie
- SERD : antagoniste compétitif des récepteurs aux oestrogènes qui se fixe sur le Rc aux oestrogènes et entraine leur dégradation
  - Plusieurs études, plusieurs molécules

Etude Emerald : Elacestrant vs ET



- **Primary endpoint:** PFS by BICR in all patients and in patients with mutant *ESR1*
  - Overall population (power ≥90% for HR of 0.667) or *ESR1*-mutated subset (power ≥80% for HR of 0.610) at an overall α level of 5%
- **Secondary endpoints:** OS, PFS by BICR in patients with WT *ESR1*, PFS by investigator review, ORR, DOR, CBR, safety, PK, and QoL

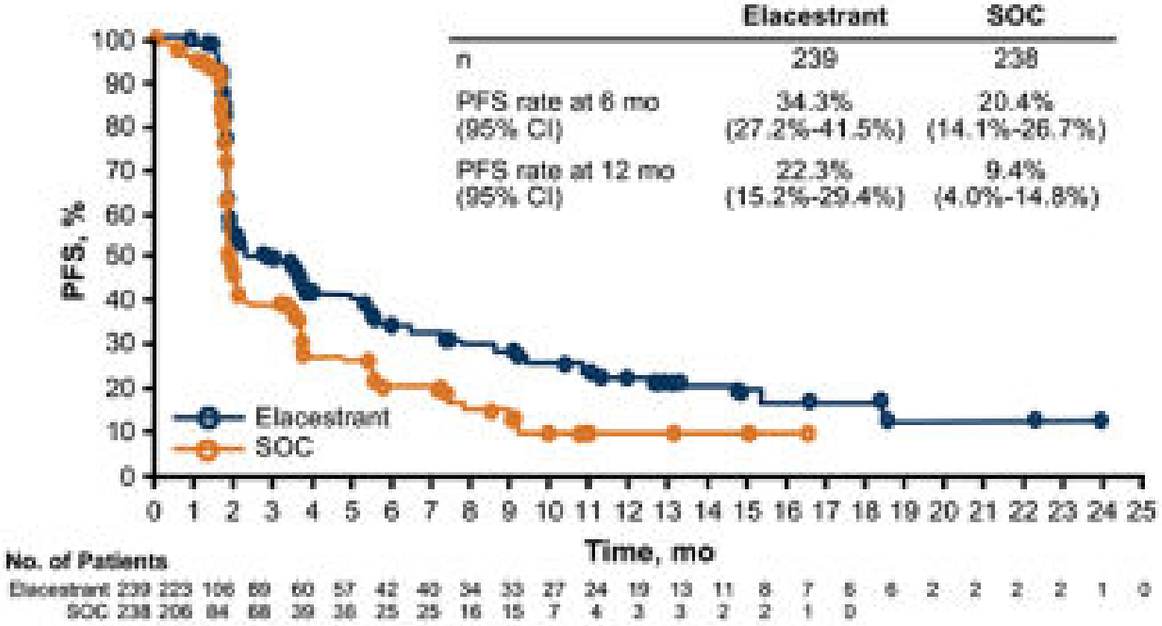
[a] Investigator's choice of fulvestrant 500 mg IM on days 1 and 15 of cycle 1 and then on day 1 of 28-day cycles or an AI (continuous dosing of anastrozole 1 mg/day, letrozole 2.5 mg/day, or exemestane 25 mg/day).

1. Bardia A et al. ASCO 2019. Abstract TPS1104. 2. Bidard F-C et al. *J Clin Oncol*. 2022;JCO2200338.

Résultats : PFS à 6 et 12 mois

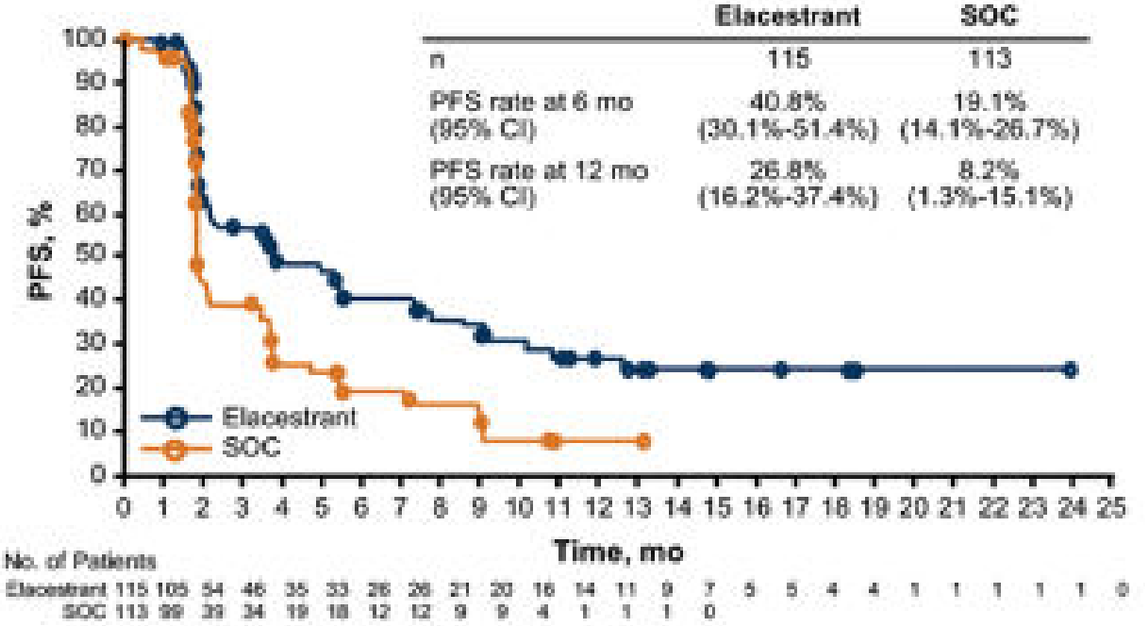
All Patients

	Elacestrant	SOC
n	239	238
PFS rate at 6 mo (95% CI)	34.3% (27.2%-41.5%)	20.4% (14.1%-26.7%)
PFS rate at 12 mo (95% CI)	22.3% (15.2%-29.4%)	9.4% (4.0%-14.8%)



Patients With Tumors Harboring *ESR1*mut

	Elacestrant	SOC
n	115	113
PFS rate at 6 mo (95% CI)	40.8% (30.1%-51.4%)	19.1% (14.1%-26.7%)
PFS rate at 12 mo (95% CI)	26.8% (16.2%-37.4%)	8.2% (1.3%-15.1%)



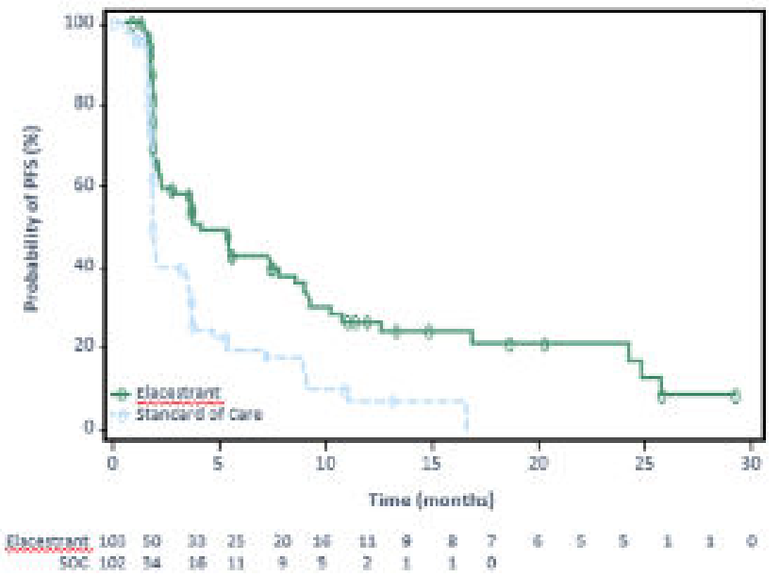
Elacestrant demonstrated a higher PFS rate at 6 and 12 months versus SOC ET in patients with ER+/HER2- advanced/metastatic breast cancer following prior CDK4/6i therapy

1. Bardia A et al. SABCS 2021. Abstract GS2-02. 2. Bidard F-C et al. *J Clin Oncol*. 2022;JCO2200338.

Analyses exploratoires

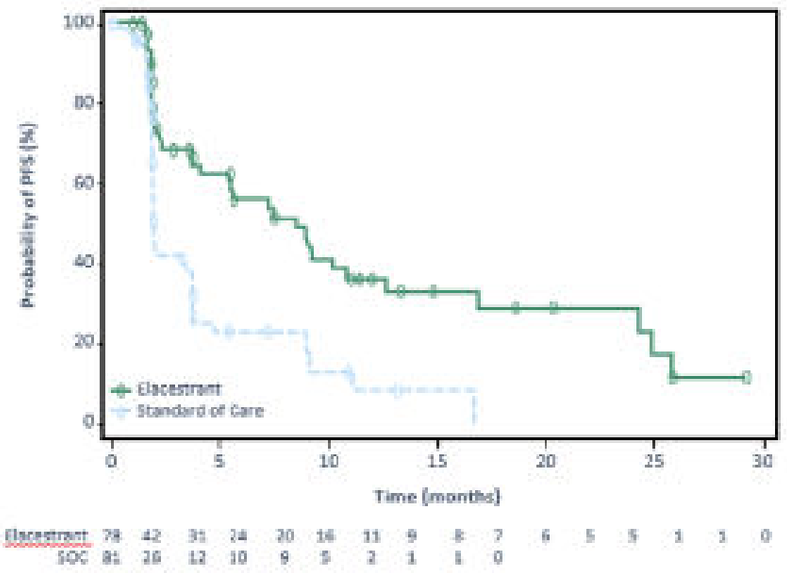
ESR1mut patients

At least 6 mo CDK4/6i



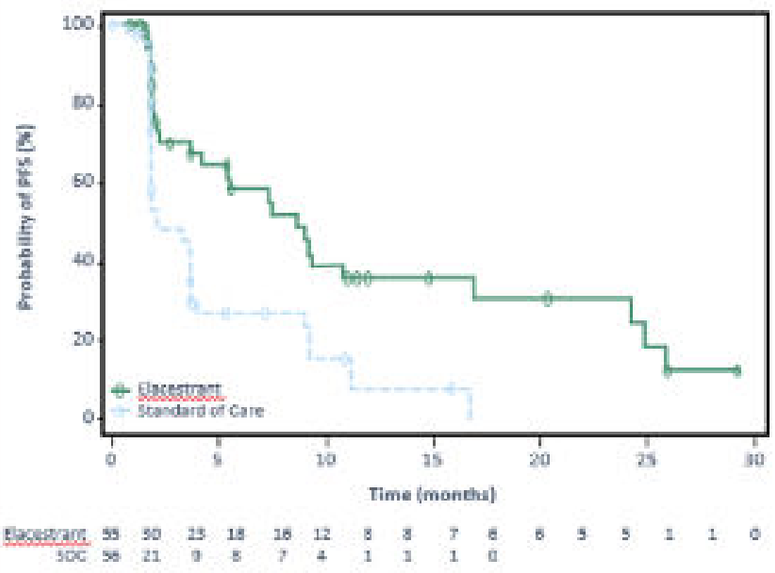
	Elacestrant	SOC Hormonal Therapy
Median PFS, months (95% CI)	**4.14** (2.20 - 7.79)	**1.87** (1.87 - 3.29)
PFS rate at 12 months, % (95% CI)	26.02 (15.12 - 36.92)	6.45 (0.00 - 13.65)
Hazard ratio (95% CI)	**0.517** (0.361 - 0.738)	

At least 12 mo CDK4/6i



	Elacestrant	SOC Hormonal Therapy
Median PFS, months (95% CI)	**8.61** (4.14 - 10.84)	**1.91** (1.87 - 3.68)
PFS rate at 12 months, % (95% CI)	35.81 (21.84 - 49.78)	8.39 (0.00 - 17.66)
Hazard ratio (95% CI)	**0.410** (0.262 - 0.634)	

At least 18 mo CDK4/6i



	Elacestrant	SOC Hormonal Therapy
Median PFS, months (95% CI)	**8.61** (5.45 - 16.89)	**2.10** (1.87 - 3.75)
PFS rate at 12 months, % (95% CI)	35.79 (19.54 - 52.05)	7.73 (0.00 - 20.20)
Hazard ratio (95% CI)	**0.466** (0.270 - 0.791)	

Kaklamani et al., SABCS 2022

Les SERDs en Pratique

Elacestrant, an oral SERD, has been approved by the US FDA as 2nd/3rd line therapy for patients with ER+/HER2 negative ABC with an ESR1 mutation, based on a randomized phase III trial demonstrating a 1.9 months median PFS advantage (HR: 0.546). This advantage was most notable in patients who were previously treated with a CDK4/6 inhibitor for more than 6 months.

Where available, Elacestrant is an option for patients in 2nd/3rd line setting with an ESR1 mutation.

F. Cardoso et al, The Breast 2024, in preparation

Reco ABC7

- Analyse sur biopsie liquide
- En cas de progression sous hormonothérapie (guidelines ASCO2023)
- Profil de tolérance acceptable
- En pratique : pas d'AMM encore en France

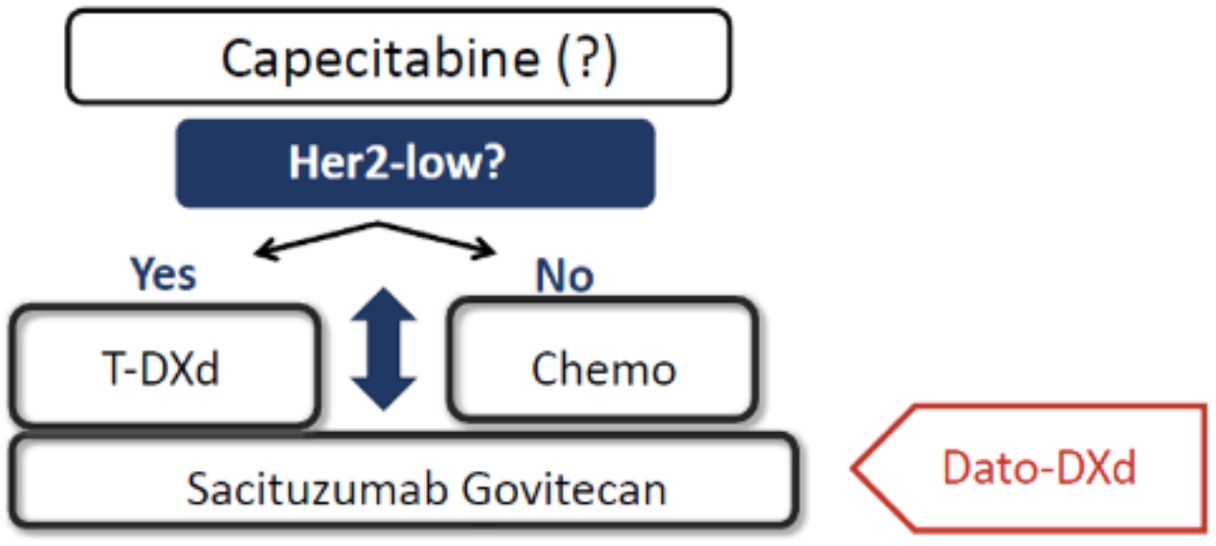
Cancer du sein RH+
en résumé

- 1st line setting **ET+ CDK 4/6i**

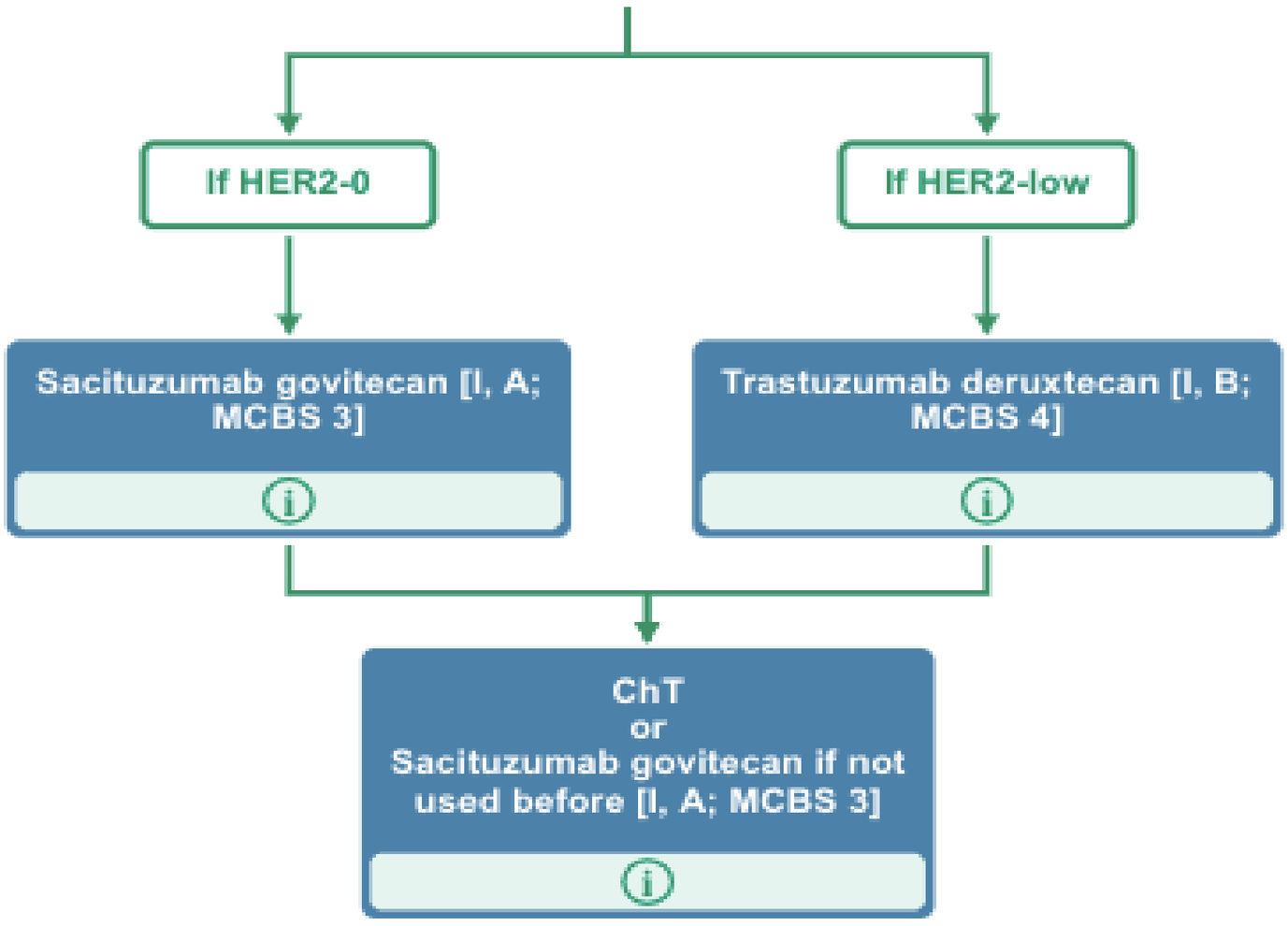
Inavolisib- for selected patients

  - Consider prior ET and response duration (ET sensitivity, CDK4/6i duration)
  - No CDKi beyond progression
  - Somatic mutations – ESR1, PIK3CA, AKT, PTEN and Germline *BRCA*

g*BRCA*m- iPARP	*ESR1*m Elacestrant	PIK3CA Alpelisib + Fulv	PIK3CA, AKT, PTEN Capivasertib + Fulv	no alterations Exe + Everolimus



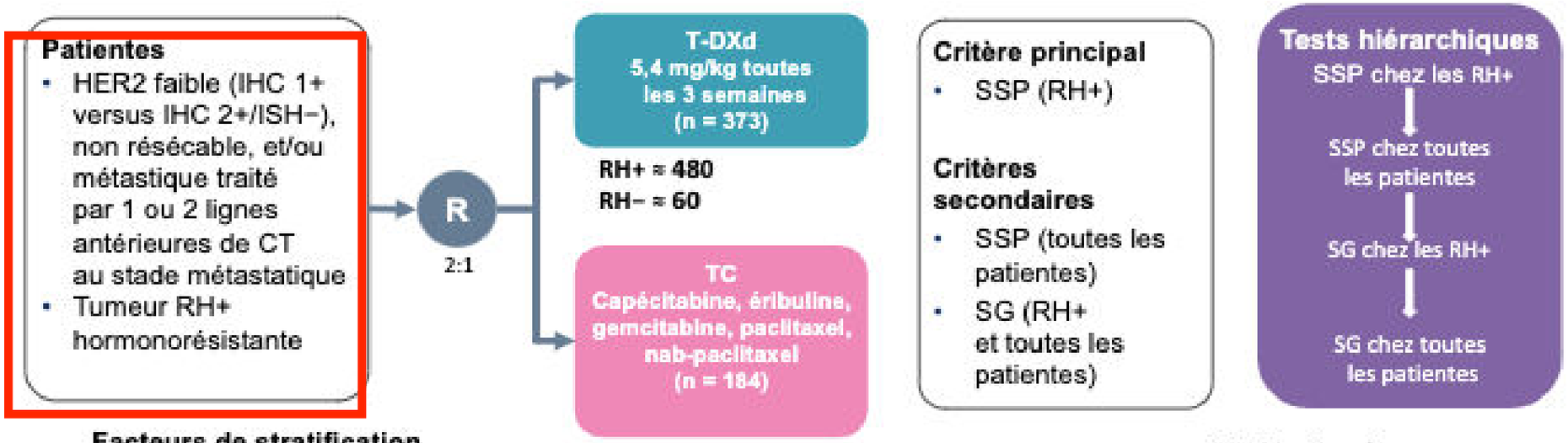
Et après ? l'ère des ADC



Her2 low

DESTINY-Breast04

A phase 3, multicenter, randomized, open-label, active-controlled trial of trastuzumab deruxtecan (T-DXd; formerly DS-8201a) vs investigator's choice for patients with HER2 low, unresectable, and/or metastatic breast cancer



Facteurs de stratification

- Statut HER2 évalué de manière centralisée (IHC 1+ versus IHC 2+/ISH–)
- 1 ou 2 lignes antérieures de chimiothérapie
- RH+ (avec ou sans traitement antérieur par un inhibiteur de CDK4/6)
  Cohorte RH–

Limite d'arrêt pour la première analyse intermédiaire de la SG :
limite d'efficacité pour la supériorité : p < 0,0075

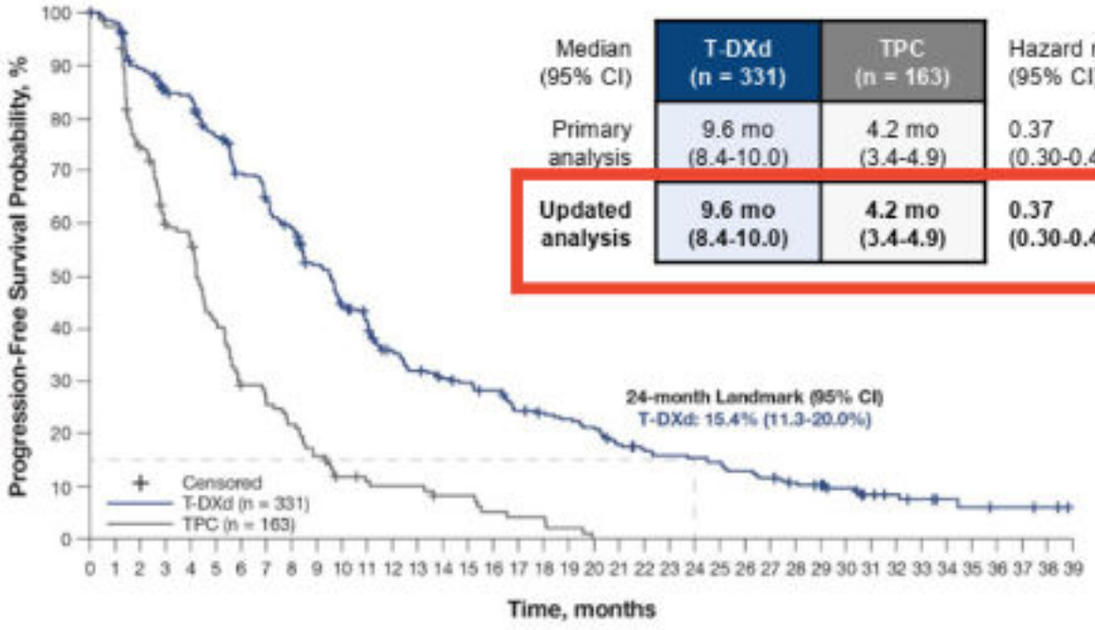
RH : récepteur hormonal ; IHC : immunohistochimie ; ISH : hybridation in situ ; T-DXd : trastuzumab déruxtécan; TC : traitement au choix de l'investigateur.

Congrès américain en oncologie clinique 2022 - D'après Modi S et al., abstr. LBA03, actualisé

Résultats chez les RH+

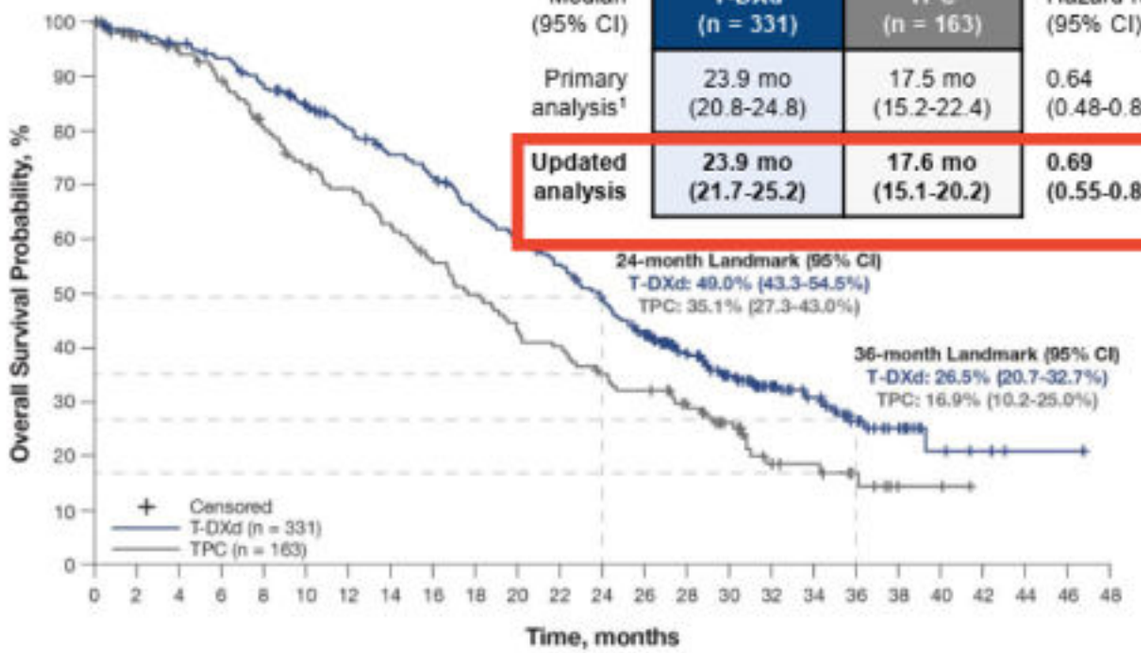
PFS in HR+ patients

Median (95% CI)	T-DXd (n = 331)	TPC (n = 163)	Hazard ratio (95% CI)
Primary analysis	9.6 mo (8.4-10.0)	4.2 mo (3.4-4.9)	0.37 (0.30-0.47)
Updated analysis	**9.6 mo (8.4-10.0)**	**4.2 mo (3.4-4.9)**	**0.37 (0.30-0.46)**



OS in HR+ patients

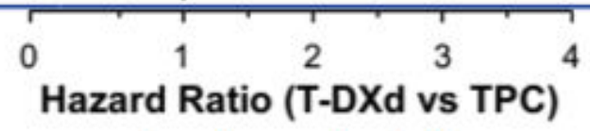
Median (95% CI)	T-DXd (n = 331)	TPC (n = 163)	Hazard ratio (95% CI)
Primary analysis[1]	23.9 mo (20.8-24.8)	17.5 mo (15.2-22.4)	0.64 (0.48-0.86)
Updated analysis	**23.9 mo (21.7-25.2)**	**17.6 mo (15.1-20.2)**	**0.69 (0.55-0.87)**



Modi et al, *ESMO* 2023

Median PFS by Tumor Sample Characteristics in DESTINY-Breast04

Subgroup	Number of Events T-DXd	Number of Events TPC	Median PFS, Months (95% CI) T-DXd	Median PFS, Months (95% CI) TPC	Hazard Ratio (95% CI)
Tumor location					
Primary (n = 196)	96/136	43/60	9.6 (7.1-11.3)	4.2 (1.6-6.4)	0.47 (0.32-0.70)
Metastases (n = 359)	145/235	84/124	10.9 (9.5-12.3)	5.4 (4.3-7.1)	0.50 (0.38-0.66)
Specimen type					
Biopsy (n = 448)	189/299	103/149	10.9 (9.6-12.0)	5.3 (4.2-6.9)	0.46 (0.35-0.59)
Excision/resection (n = 108)	53/73	24/35	7.5 (5.7-9.9)	3.0 (1.4-11.0)	0.57 (0.33-1.0)
Archival tissue (n = 482)	**203/324**	**109/158**	**10.3 (8.6-12.0)**	**5.3 (4.2-7.0)**	**0.48 (0.37-0.61)**
Newly obtained tissue (n = 75)	40/49	18/26	9.7 (5.6-10.9)	4.8 (2.8-6.9)	0.57 (0.30-1.1)
Tumor specimen collection date					
2013 and earlier (n = 29)	11/19	9/10	7.0 (2.8-NE)	6.8 (1.4-11.1)	0.78 (0.24-2.54)
2014-2018 (n = 175)	76/126	33/49	11.4 (9.5-15.1)	4.3 (1.6-7.0)	0.44 (0.28-0.70)
2019 or later (n = 310)	137/203	75/107	9.8 (8.4-11.3)	5.1 (4.1-7.1)	0.49 (0.37-0.66)
Missing (n = 43)	19/25	10/18	6.6 (2.8-10.8)	2.8 (1.2-8.3)	0.54 (0.20-1.4)



- 35% primary tumors, 65% metastatic tumors (10% new biopsy)
- Efficacy of T-DXd compared with TPC was consistent regardless of tumor sample characteristics

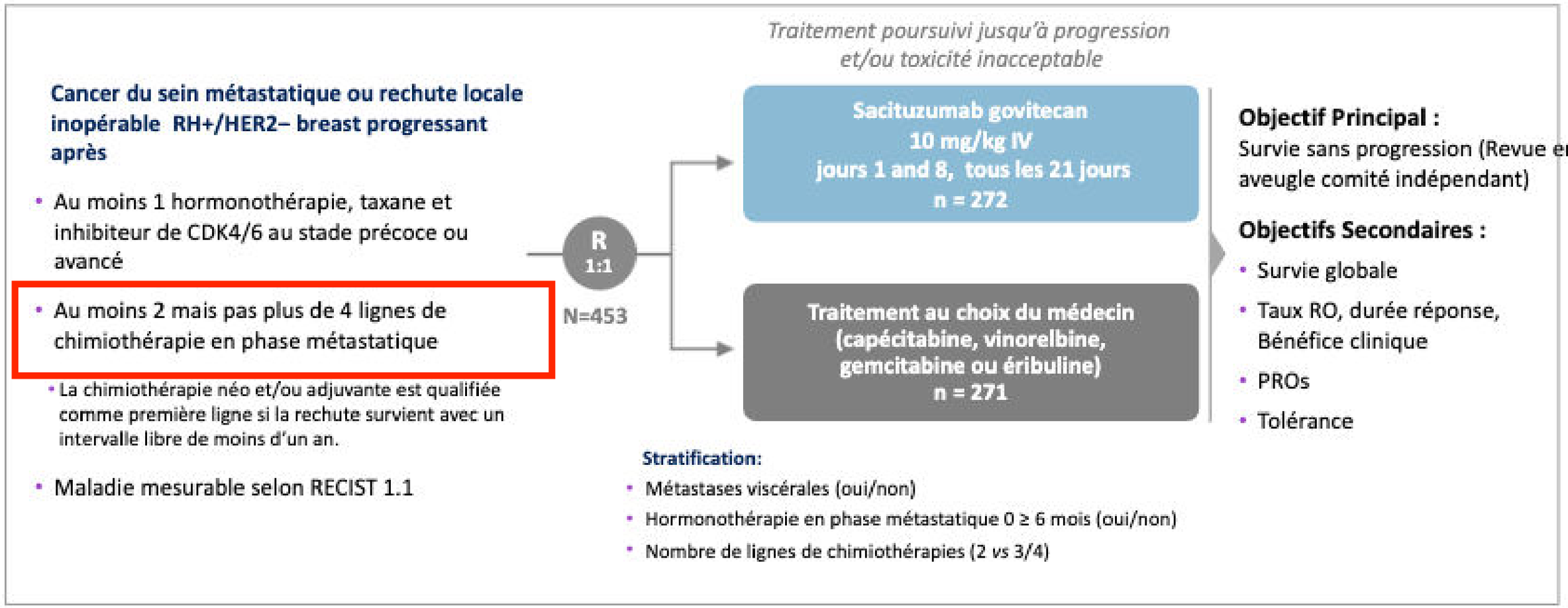
Prat et al, *SABCS* 2022

En pratique

- Confirmation intérêt du **Trastusumab Deruxtecan**
- Chez les RH+ Her2low : **en accès précoce**
  - Maladie hormonoresistante + 1ère ligne de chimio
- Statut HER2 low peut être obtenu sur un échantillon tissulaire à n'importe quel moment de la maladie
- Attention aux pneumopathie interstitielles
  - Destiny breast 06 : en 1ère ligne d'hormonoresistance

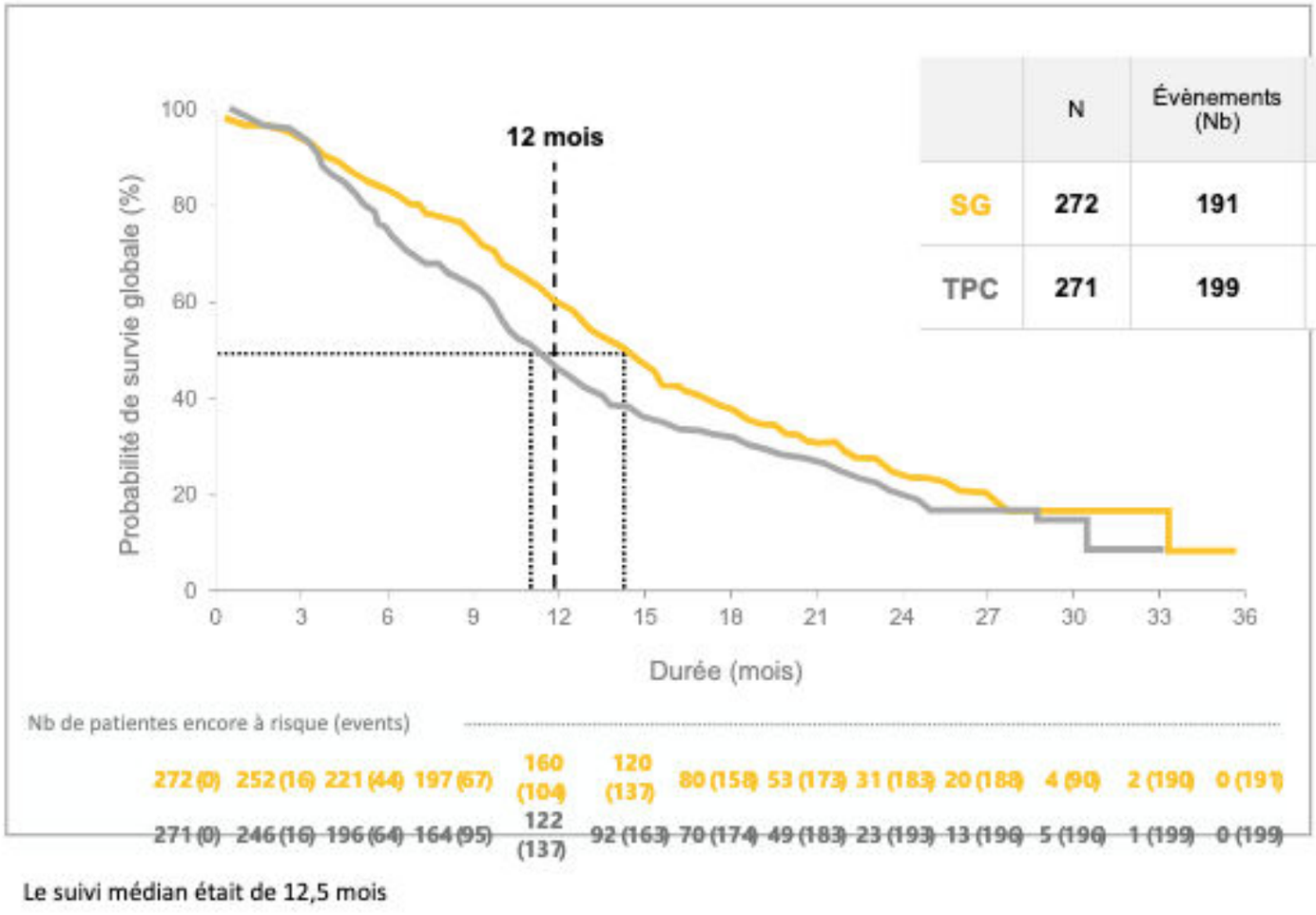
ADC ciblant Trop2 : le Sacituzumab Govitecan

Etude TROPICS-02 : schéma de l'étude



H. S. Rugo, et al., ASCO® 2022, Abs. #LBA1001

TROPiCS-02 : Survie globale (2ème analyse intermédiaire ESMO 2022)



	N	Évènements (Nb)	SG Médiane, Mois (95% CI	SG à 12 mois, % (95% CI)	HR (95% CI)	*valeur-p*
SG	272	191	14,4 (13,0-15,7)	61 (55-66)	0,79 (0,65-0,96)	0,020
TPC	271	199	11,2 (10,1-12,7)	47 (41-53)		

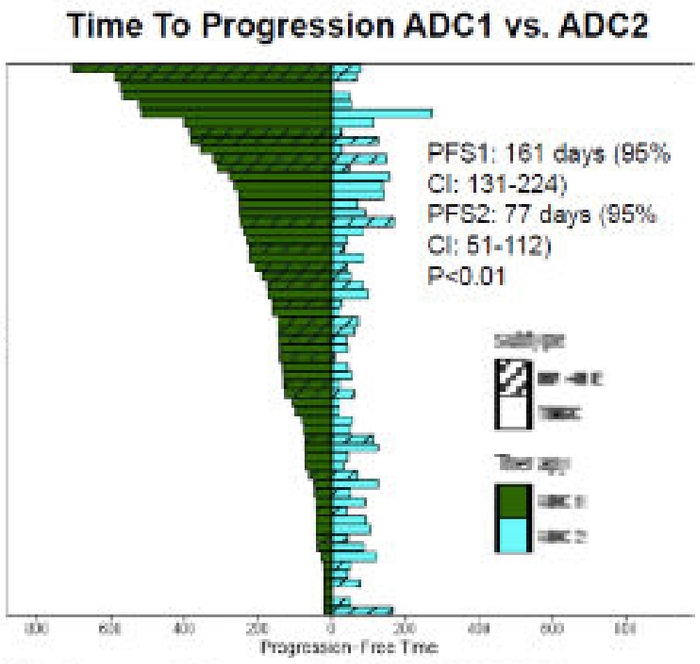
Le suivi médian était de 12,5 mois

- **Le Sacituzumab Govitecan a démontré une amélioration statistiquement significative de 3,2 mois de la SG par rapport à la chimiothérapie (TPC), avec une réduction de 21% du risque de décès**

- En **accès précoce**, après 2 lignes de chimiothérapie
- Se place après le T-Dxd chez les patientes HER2 low, RH+

Rechallenge des ADC

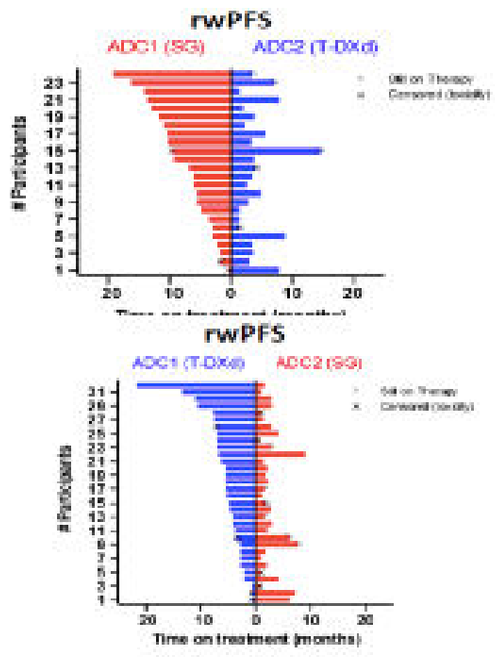
Série rétrospective, n= 74
SSP d'un ADC après l'autre



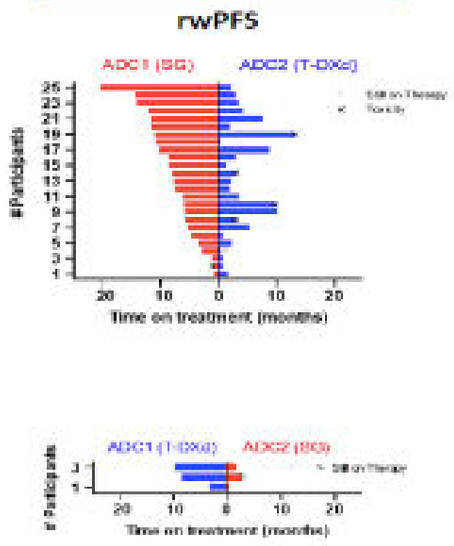
Abelman RO et al., SABCS 2023

Série rétrospective, n= 84 CSM HER2 low
SSP du T-DXd après Sav Gov et vice versa

RH+, n= 56

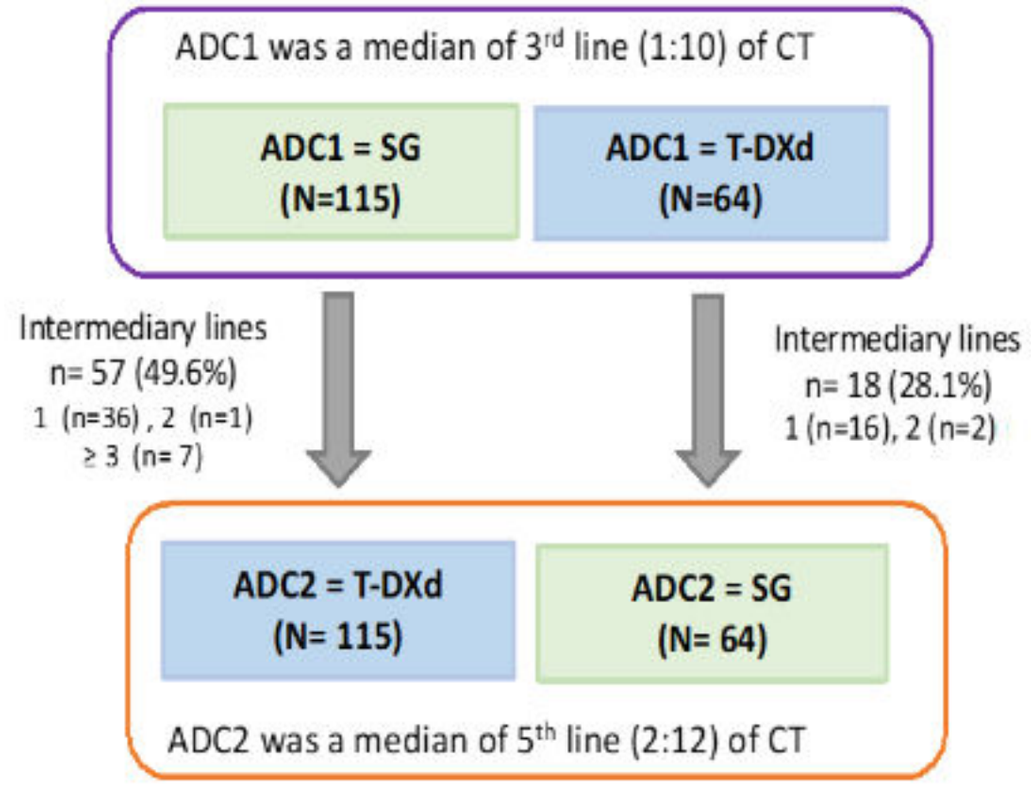


RH- n= 28



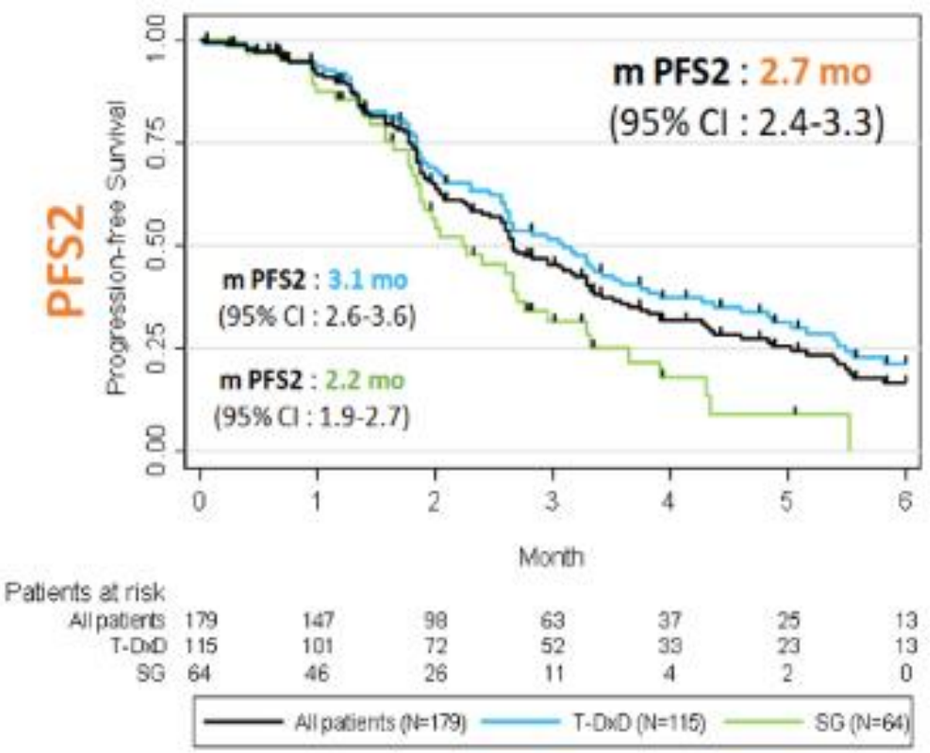
Hupper LA et al., SABCS 2023

Etude rétrospective, multicentrique, française, n=179

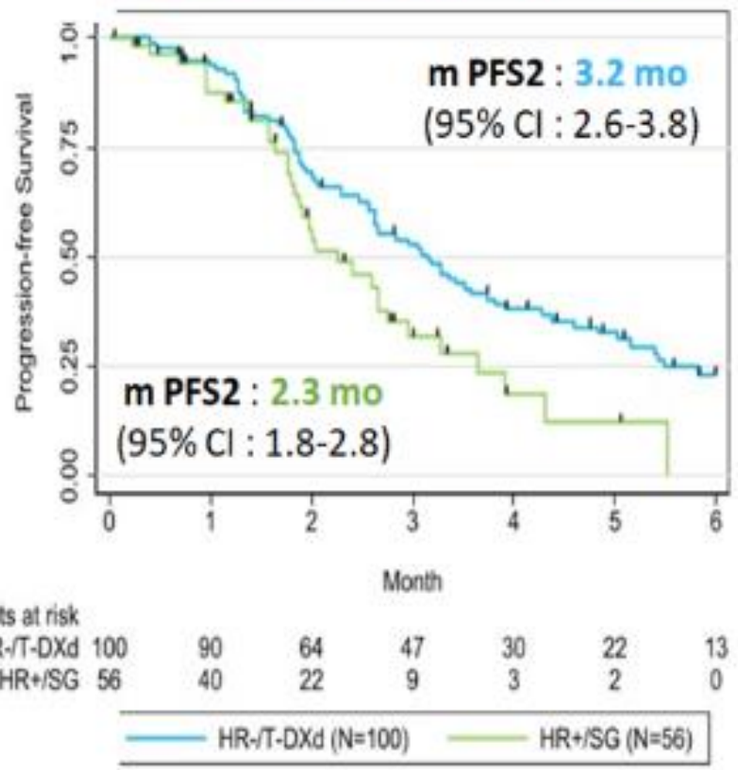


Poumeaud F et al., SABCS 2023

All patients



By HR/ADC combination



ADC après ADC ?

- Peu de données (séries rétrospectives)
- Signaux de moindre efficacité
- Mais quelques patientes semblent en bénéficier
- Possibilité de répondre à l'un et pas à l'autre
- Intérêt d'une chimiothérapie intercalaire ?

Chez les HER2+

Trastuzumab Deruxtecan in “second-line”
Destiny-Breast 03 study: UPDATED at SABCS

Clinical Trial Design (DB03)

Patients
- Unresectable or metastatic HER2-positive[a] breast cancer
- Previously treated with trastuzumab and taxane in advanced/metastatic setting[b]
- Could have clinically stable, treated brain metastases

Stratification factors
- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

R 1:1

- T-DXd 5.4 mg/kg Q3W (n = 261)
- T-DM1 3.6 mg/kg Q3W (n = 263)

Primary endpoint
- PFS (BICR)

Key secondary endpoint
- OS

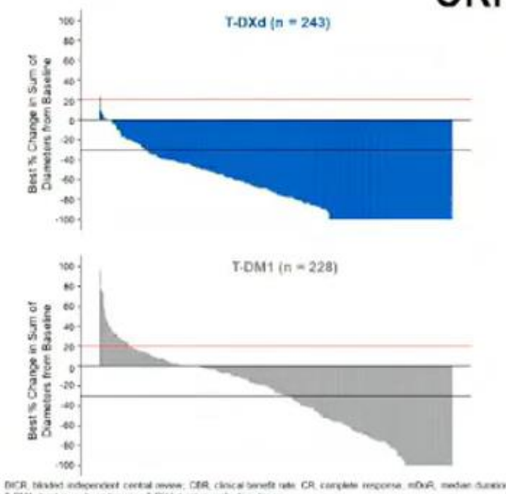
Secondary endpoints
- ORR (BICR and investigator)
- DOR (BICR)
- PFS (investigator)
- Safety

Interim analysis for PFS (data cutoff: May 21, 2021)
- Efficacy boundary for superiority: $P < 0.000204$ (based on 245 events)
- IDMC recommendation to unblind study (July 30, 2021)

Key secondary endpoint, OS: boundary for efficacy: $P < 0.000265$ (based on 86 events)

PFS

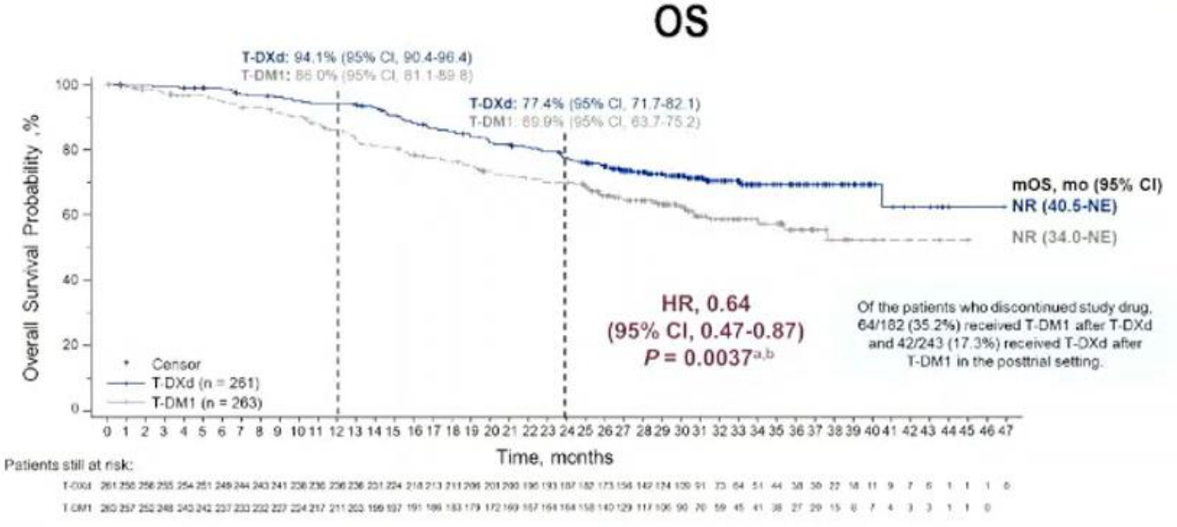
ORR



	T-DXd n = 261[a]	T-DM1 n = 263[a]
Confirmed ORR by BICR		
n (%)	205 (**78.5**)	92 (**35.0**)
[95% CI]	[73.1-83.4]	[29.2-41.1]
Nominal *P* value	< 0.0001	
CR, n (%)	55 (**21.1**)	25 (**9.5**)
PR, n (%)	150 (57.5)	67 (25.5)
SD, n (%)	47 (18.0)	110 (41.8)
PD, n (%)	3 (1.1)	47 (17.9)
NE, n (%)	6 (2.3)	14 (5.3)
CBR, n (%) [95% CI]	233 (89.3) [84.9-92.8]	122 (46.4) [40.2-52.6]
Nominal *P* value	< 0.0001	
mDoR by BICR, months (95% CI)	**36.6** (22.4-NE)	**23.8** (12.6-34.7)

BICR, blinded independent central review; CBR, clinical benefit rate; CR, complete response; mDoR, median duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Red line at 20% indicates progressive disease; black line at −30% indicates partial response.
[a]Only patients with measurable disease at baseline and at least 1 postbaseline target lesion assessment were included.

OS

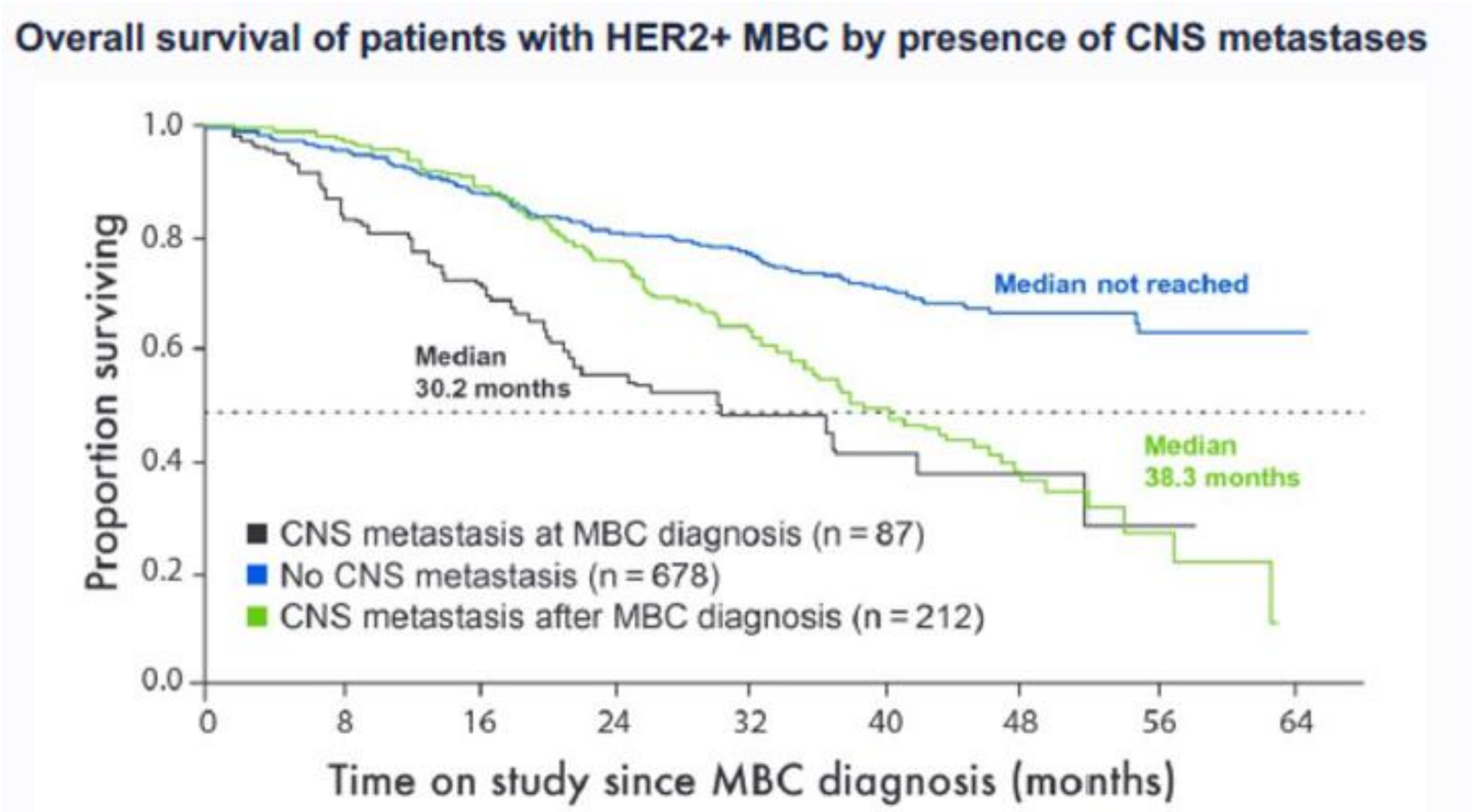


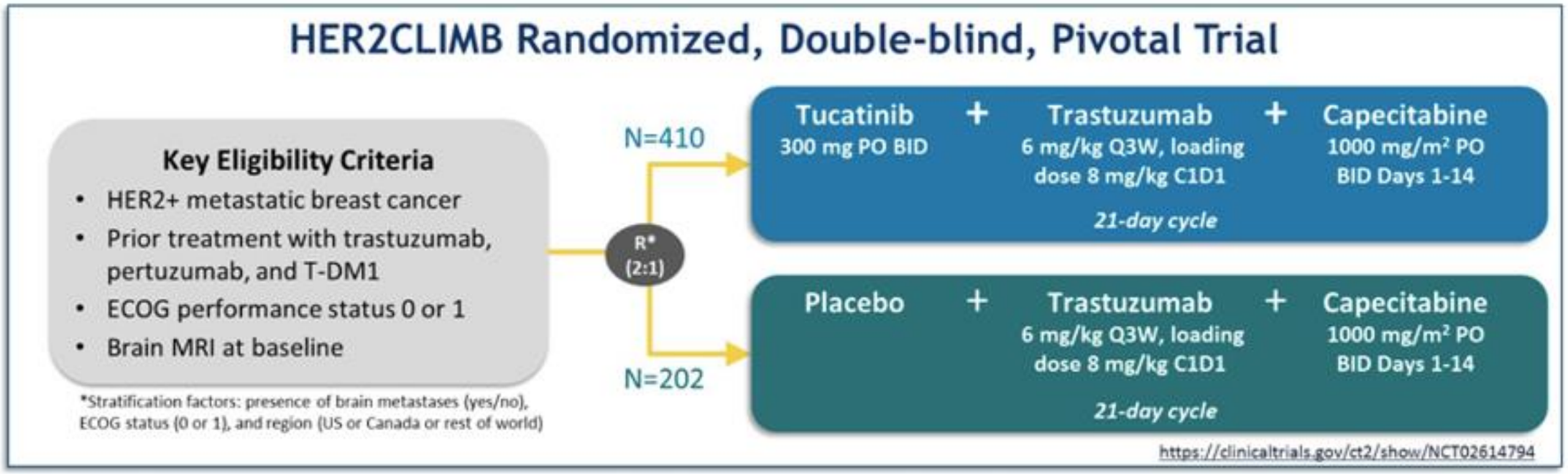
Hurvitz S, et al. SABCS 2022; Lancet 2022

=> Standard en 2ème ligne

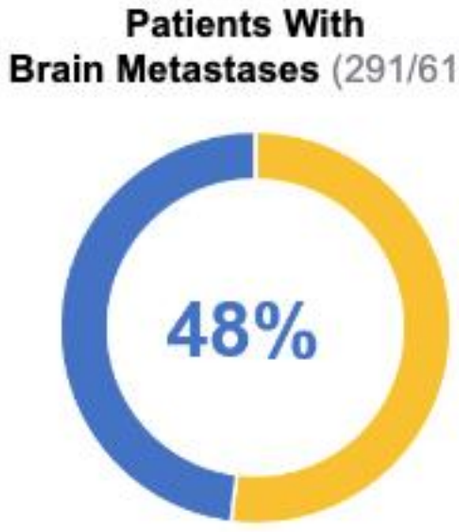
Particularité des métastases cérébrales

- Jusqu'à 50% des patientes atteintes de maladie HER2 métastatique vont connaitre une évolution cérébrale





- Seule étude incluant des patientes avec métastases cérébrales actives



Of those patients who had brain metastases at baseline:

40% **had stable brain metastases**

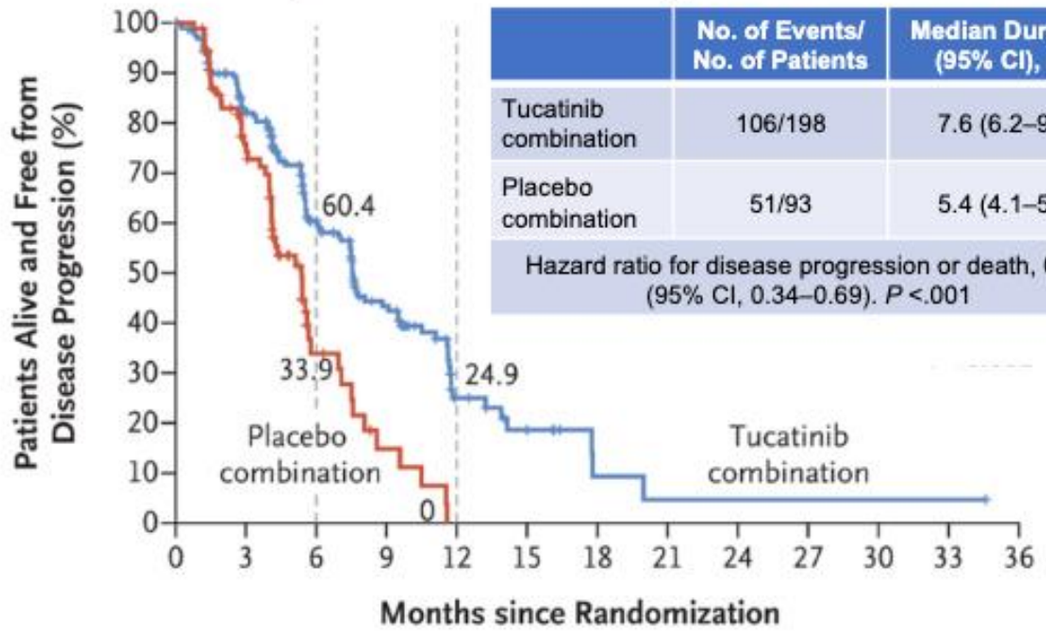
60% **had active brain metastases**

- 23% had untreated progressing brain metastases
- 37% had treated but progressing brain metastases

Intracranial Response	Tuc +Tras + Cape (n = 55)	Pbo + Tras + Cape (n = 20)
Patients with objective response of confirmed complete response or partial response, n	26	4
Confirmed ORR-IC, % (95% CI)	47.3 (33.7–61.2)	20.0 (5.7–43.7)
DOR-IC, median (95% CI), mo	8.6 (5.5–10.3)	3.0 (3.0–10.3)

Résultats dans la population avec méta cérébrales

Kaplan–Meier Estimates of Progression-free Survival among Patients with Brain Metastases[1]



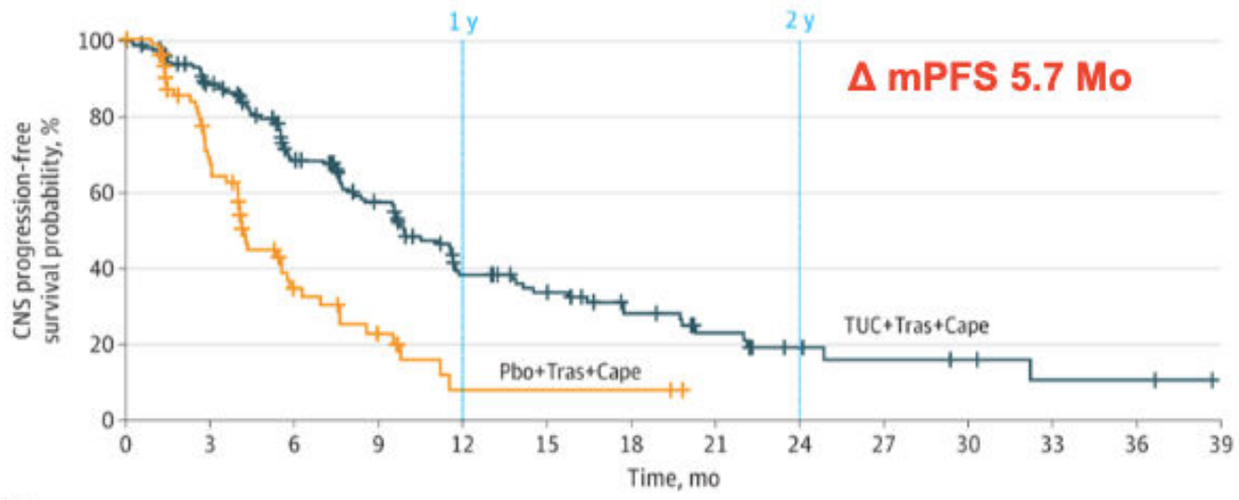
	No. of Events/ No. of Patients	Median Duration (95% CI), mo
Tucatinib combination	106/198	7.6 (6.2–9.5)
Placebo combination	51/93	5.4 (4.1–5.7)
Hazard ratio for disease progression or death, 0.48 (95% CI, 0.34–0.69). *P* <.001		

No. at Risk

Tucatinib combination	198	144	78	45	14	8	2	1	1	1	1	1	0
Placebo combination	93	49	12	4	0	0	0	0	0	0	0	0	0

Intracranial Progression-free Survival[2]
Exploratory Analysis

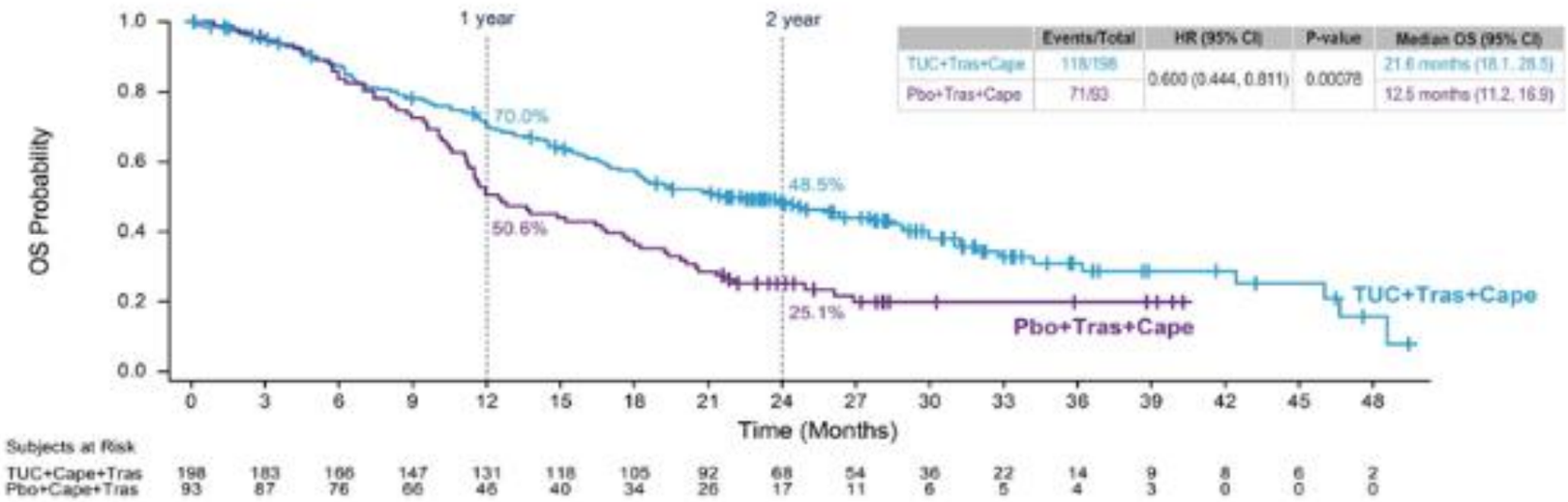
Median PFS (95% CI), months	
T + C + Tras (n = 198)	P + C + Tras (n = 93)
9.9 (8.4–11.7)	**4.2** (3.6–5.7)
HR (95% CI): 0.39 (0.27–0.56) ***P* <.001**	



No. at risk

TUC+Tras+Cape	198	132	91	65	37	29	19	12	7	5	4	2	2	0
Pbo+Tras+Cape	93	41	16	8	2	2	2	0	0	0	0	0	0	0

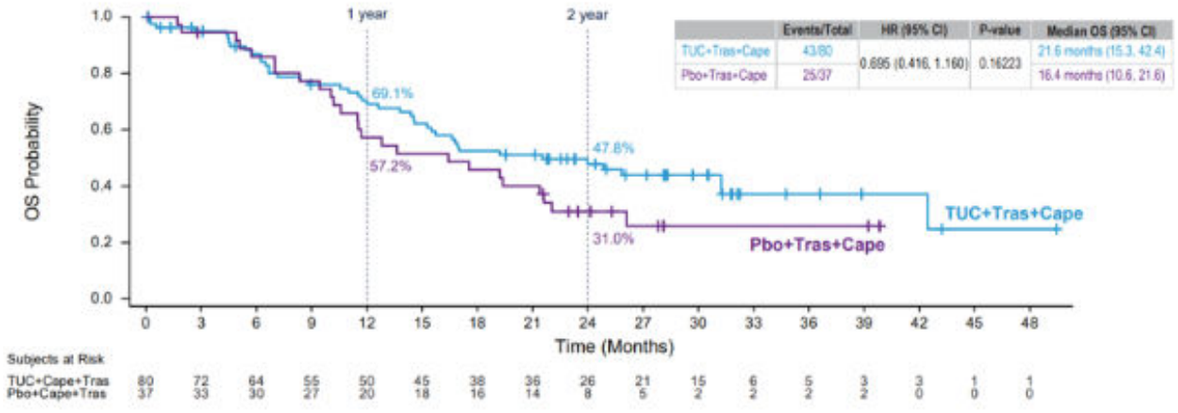
HER2CLIMB: OS Benefit in Patients with BCBM



	Events/Total	HR (95% CI)	P-value	Median OS (95% CI)
TUC+Tras+Cape	118/198	0.600 (0.444, 0.811)	0.00078	21.6 months (18.1, 28.5)
Pbo+Tras+Cape	71/93			12.5 months (11.2, 16.9)

9.1-month absolute improvement in OS associated with tucatinib

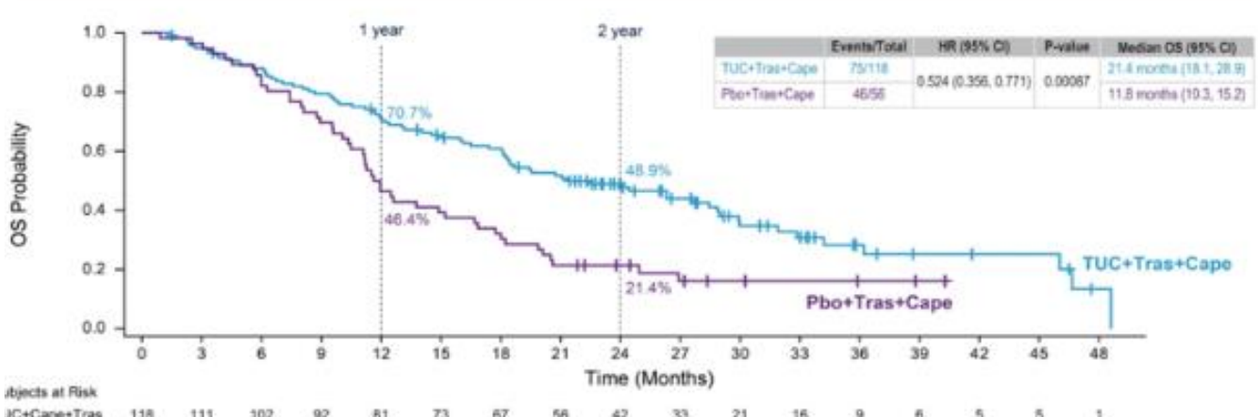
OS for Patients with Treated Stable Brain Metastases



	Events/Total	HR (95% CI)	P-value	Median OS (95% CI)
TUC+Tras+Cape	43/80	0.695 (0.416, 1.160)	0.16223	21.6 months (15.3, 42.4)
Pbo+Tras+Cape	25/37			16.4 months (10.6, 21.6)

Median OS was 5.2 months longer in the tucatinib arm compared with the control arm in patients with treated stable brain metastases

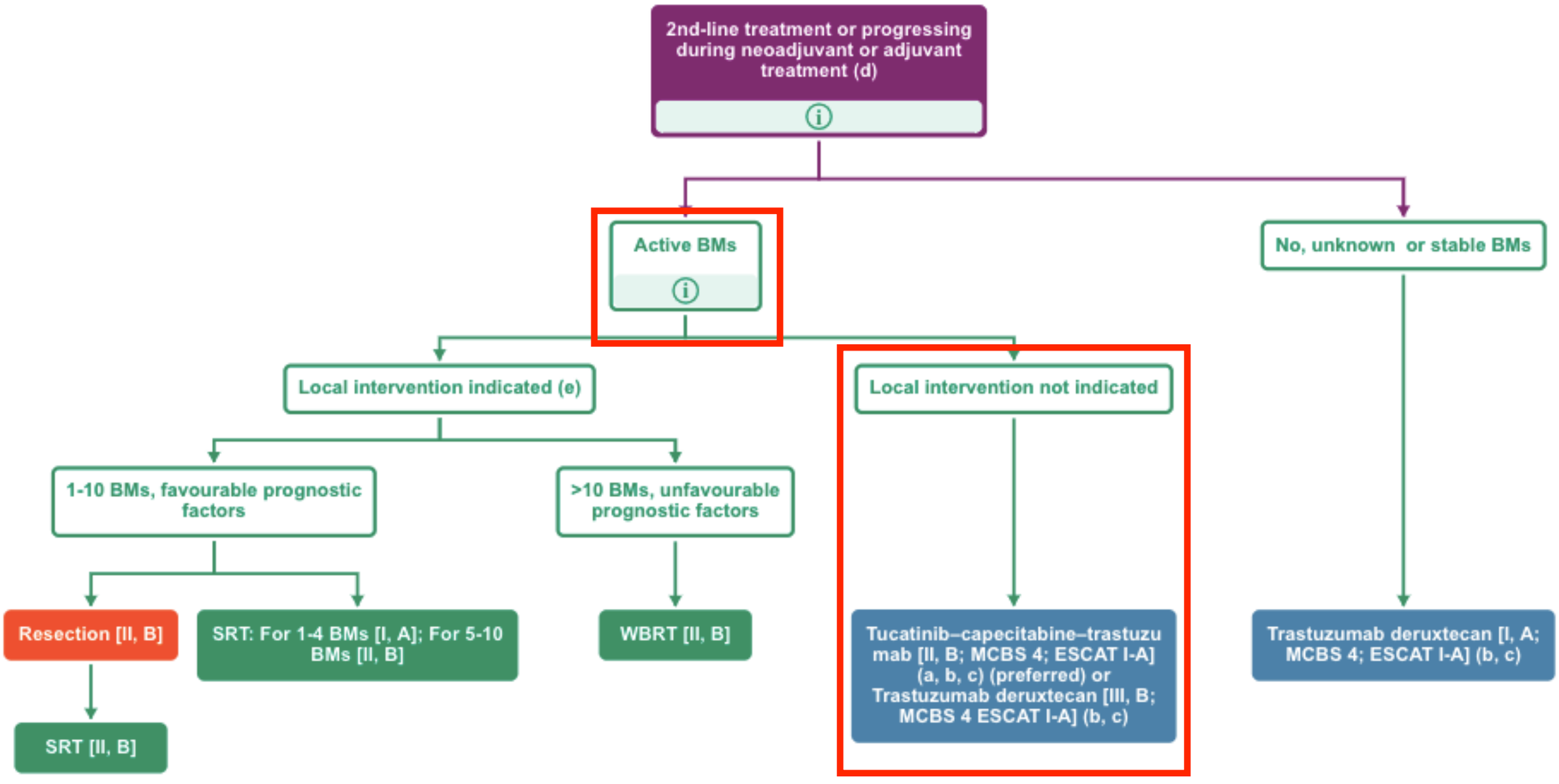
HER2CLIMB: OS Benefit in Patients with Active BCBM



	Events/Total	HR (95% CI)	P-value	Median OS (95% CI)
TUC+Tras+Cape	75/118	0.524 (0.356, 0.771)	0.00087	21.4 months (18.1, 28.9)
Pbo+Tras+Cape	46/56			11.8 months (10.3, 15.2)

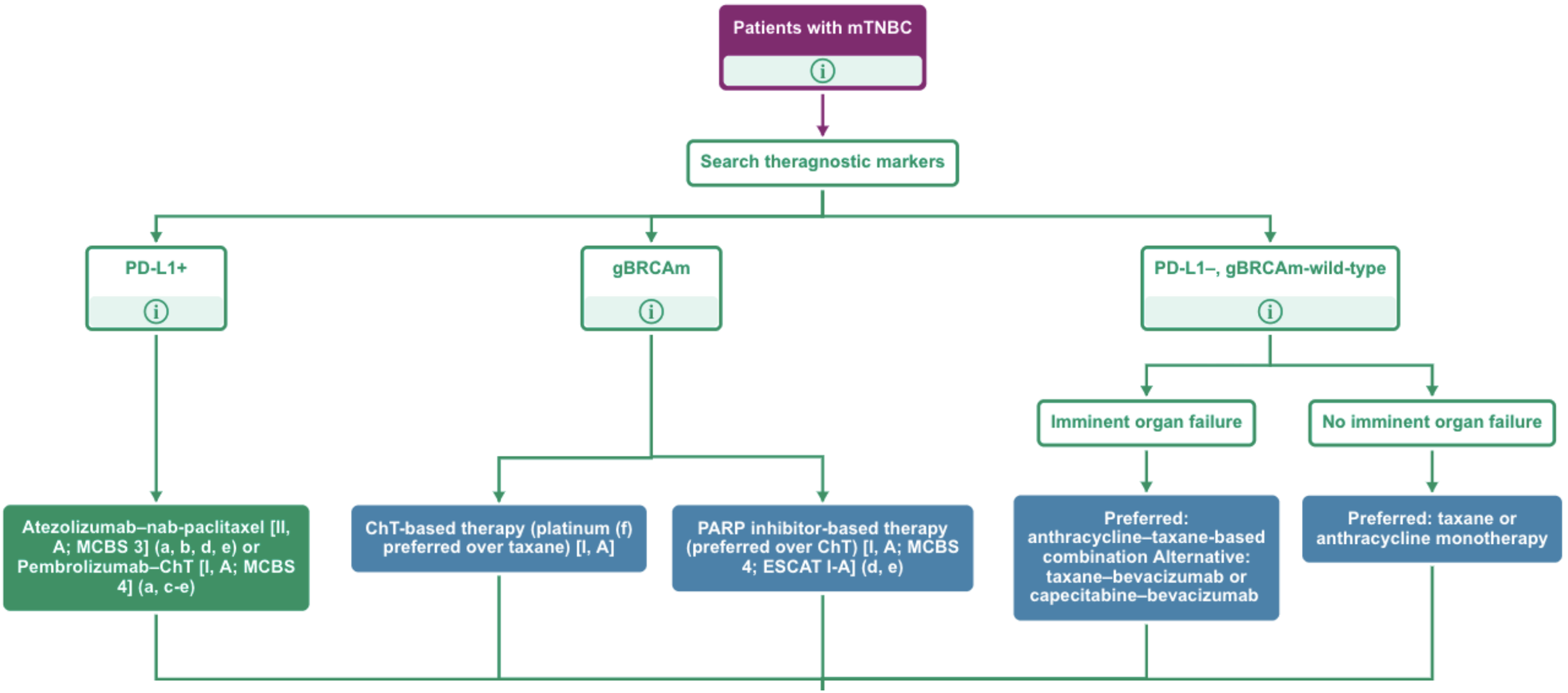
9.6 month-absolute improvement in OS associated with tucatinib

Reco ESMO 2023, HER2+



Triple négatif

v1.1 - May 2023



Pembrolizumab+chimio en 1ère ligne : Keynote 355

Critère d'éligibilité
- Âge ≥ 18 ans
- Détermination centralisée des cancers TN et de l'expression de PD-L1 (score CPS)
- Cancer en rechute inopérable ou cancer TN métastatique
- Traitement adjuvant terminé ≥ 6 mois avant la 1ère rechute
- Statut de performance ECOG 0 ou 1
- Espérance de vie ≥ 12 semaines
- Fonctions organiques conservées
- Absence de corticothérapie
- Absence de métastases évolutives du SNC
- Absence de maladies auto-immunes

R (2:1)

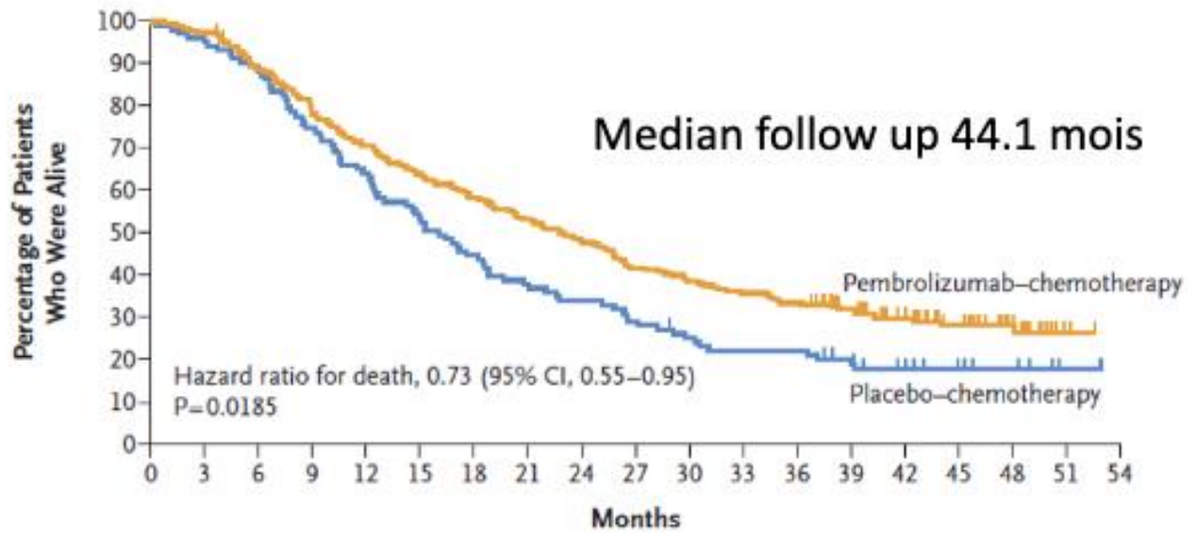
- Pembrolizumab 200 mg (i.v.) toutes les 3 sem. + chimiothérapie[a]
- Placebo + chimiothérapie[a]

→ Progression de la maladie/ arrêt du traitement

Facteurs de stratification
- Chimiothérapie durant l'étude (taxane vs gemcitabine/carboplatine)
- Expression tumorale de PD-L1 (CPS ≥ 1 vs CPS < 1)
- Chimiothérapie néoadjuvante ou adjuvante avec la même classe de cytotoxique (oui vs non)

Cortes et al. Lancet 2020: 396:1817

Actualisation SG PD-L1 CPS ≥ 10
(40% des patientes)



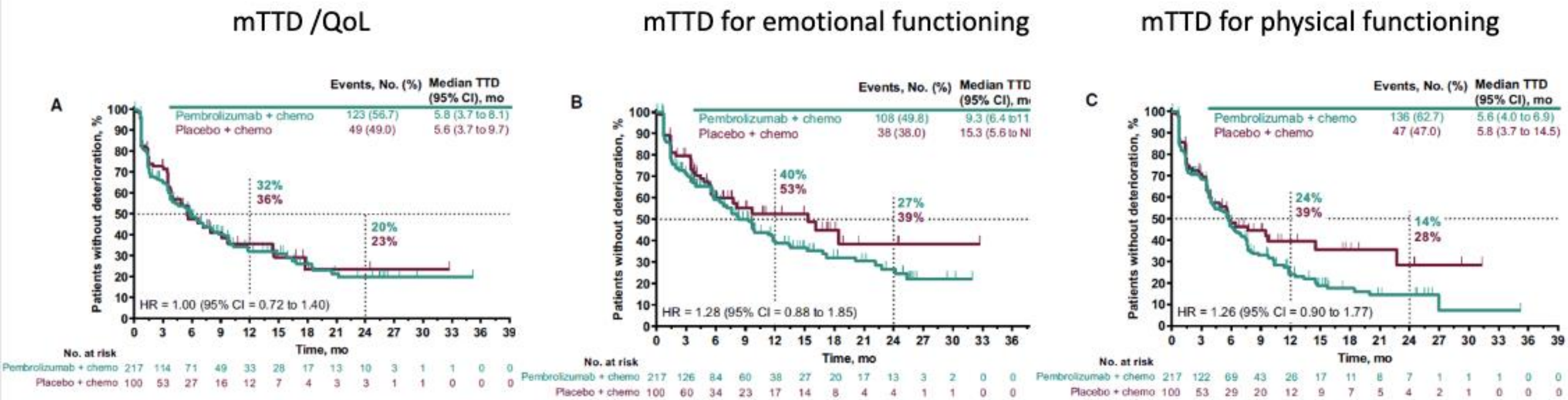
No. at Risk

Pembrolizumab–chemotherapy	220	214	193	171	154	139	127	116	105	91	84	78	73	59	43	31	17	2	0
Placebo–chemotherapy	103	98	91	77	66	55	46	39	35	30	25	22	22	17	12	8	6	2	0

Cortes *et al.* NEJM 2022

Median SG : 23 mois vs 16 mois

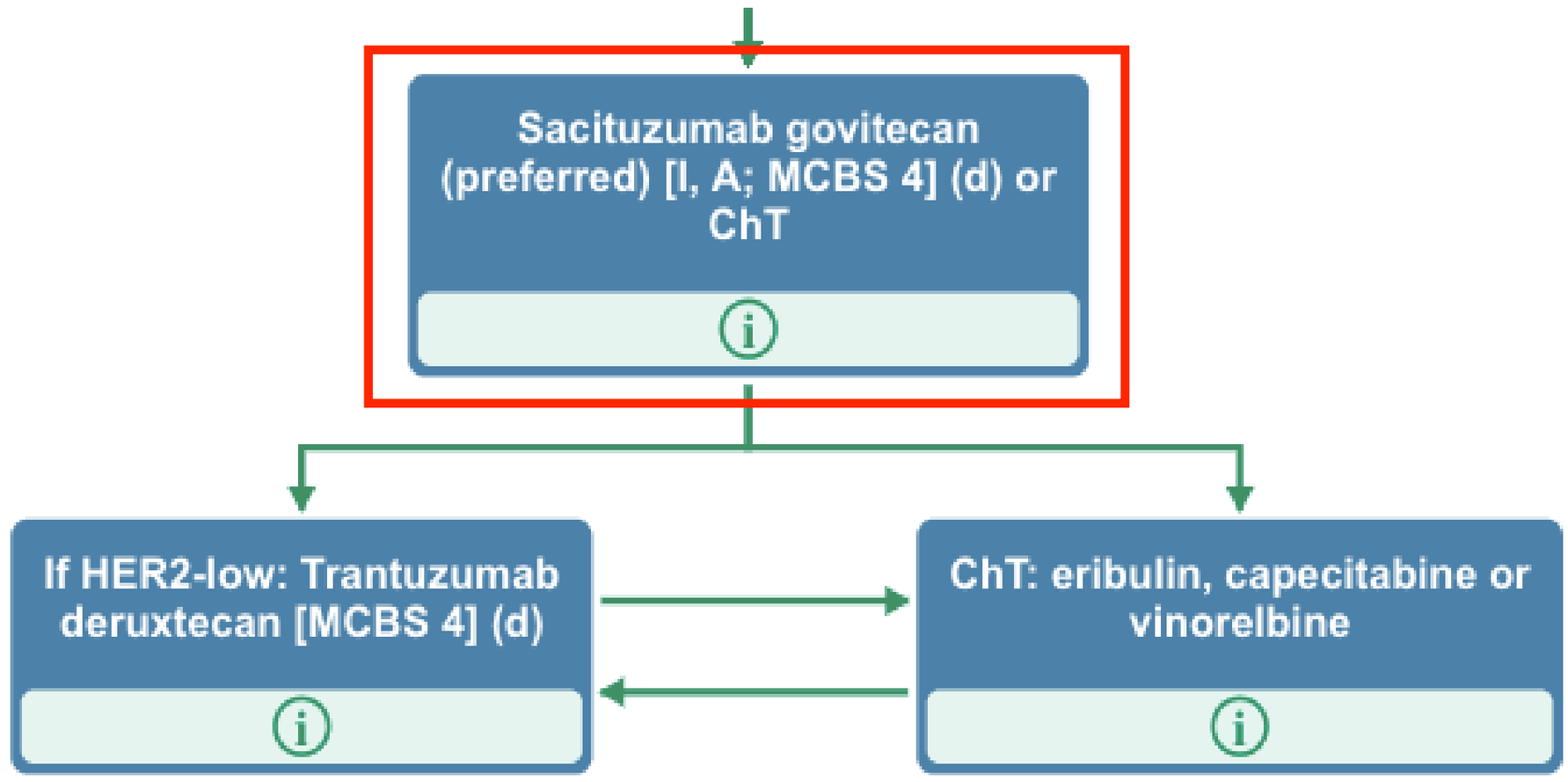
Résultats en qualité de vie



No major differences in QoL parameters

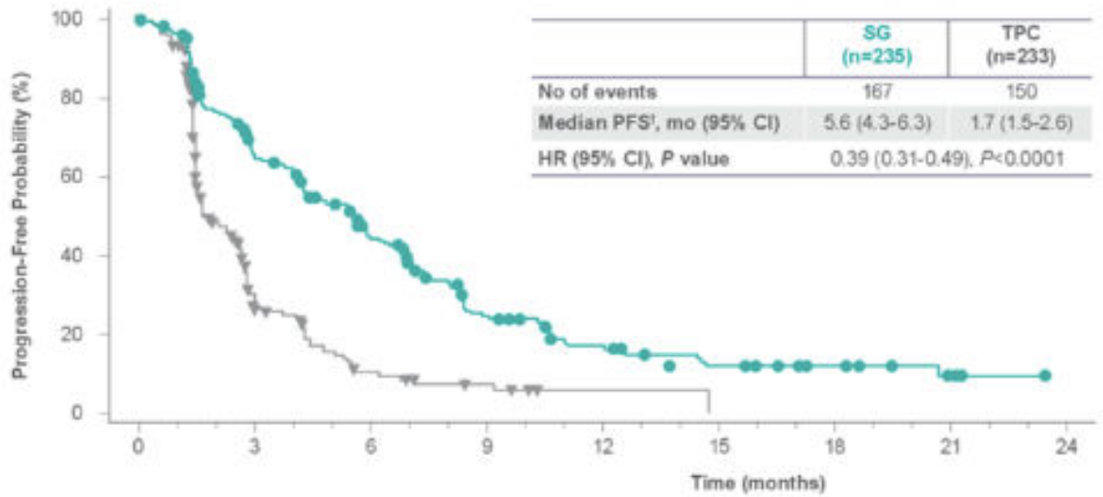
Cescon et al. JNCI. December 2023

En ≥ 2ème ligne : place des ADC



Etude Ascent : SG en ≥ 2ème ligne

PFS (BMneg population)

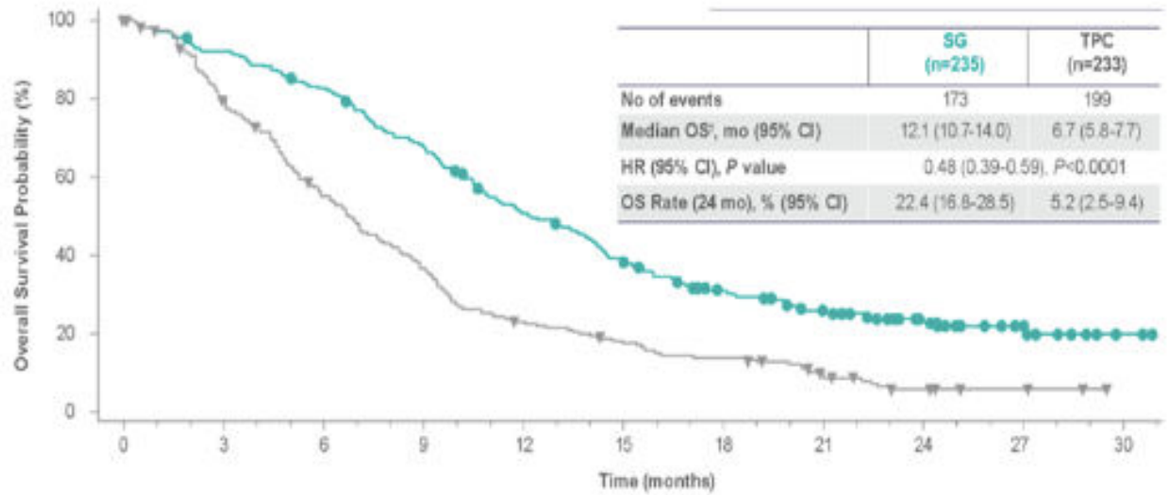


	SG (n=235)	TPC (n=233)
No of events	167	150
Median PFS[1], mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P* value	0.39 (0.31-0.49), *P*<0.0001	

No. of Patients Still at Risk

Time (months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
SG	235	222	166	134	127	104	81	63	54	37	33	24	22	17	16	13	11	10	8	6	5	3	1	1	0
TPC	233	178	77	34	31	18	11	8	6	5	3	1	1	1	1	0	0	0	0	0	0	0	0	0	0

OS (BMneg population)



	SG (n=235)	TPC (n=233)
No of events	173	199
Median OS[1], mo (95% CI)	12.1 (10.7-14.0)	6.7 (5.8-7.7)
HR (95% CI), *P* value	0.48 (0.39-0.59), *P*<0.0001	
OS Rate (24 mo), % (95% CI)	22.4 (16.8-28.5)	5.2 (2.5-9.4)

No. of Patients Still at Risk

Time (months)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
SG	235	228	220	214	206	197	191	177	164	156	140	122	113	105	97	85	74	65	59	56	46	40	35	30	25	17	14	11	7	4	2
TPC	233	214	200	173	156	134	117	101	90	77	58	53	47	44	40	35	30	28	27	24	22	13	11	7	6	4	3	3	2	1	0

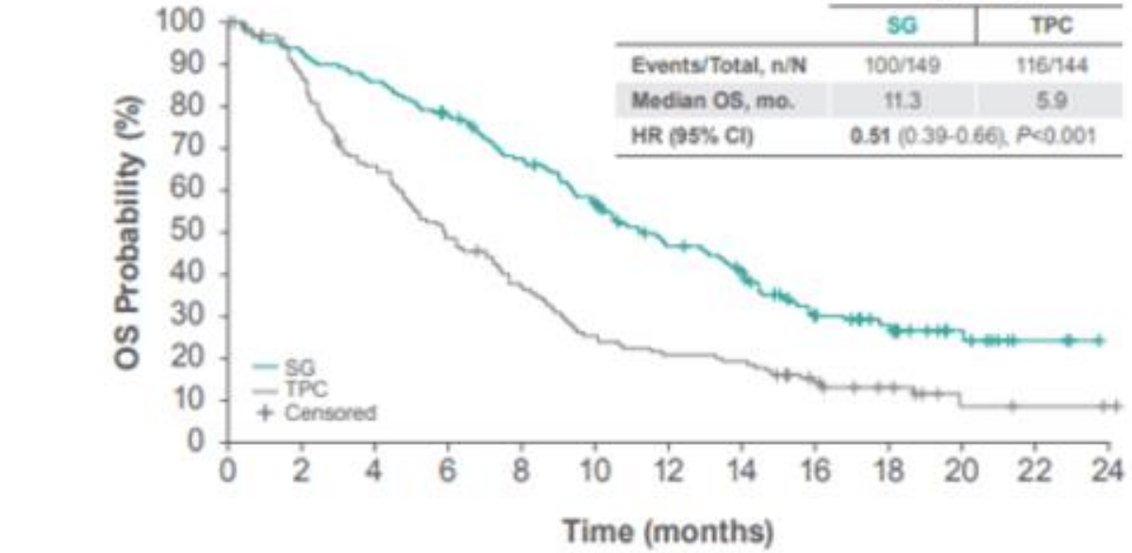
Bardia et al. ASCO 2022

- Remboursement du sacituzumab govitecan dans les cancers du sein triple négatif métastatiques
  - Après au moins deux traitements systémiques, dont au moins un pour une forme avancée de la maladie

Résultats selon le statut HER2

SG selon statut HER2 (0 vs low)

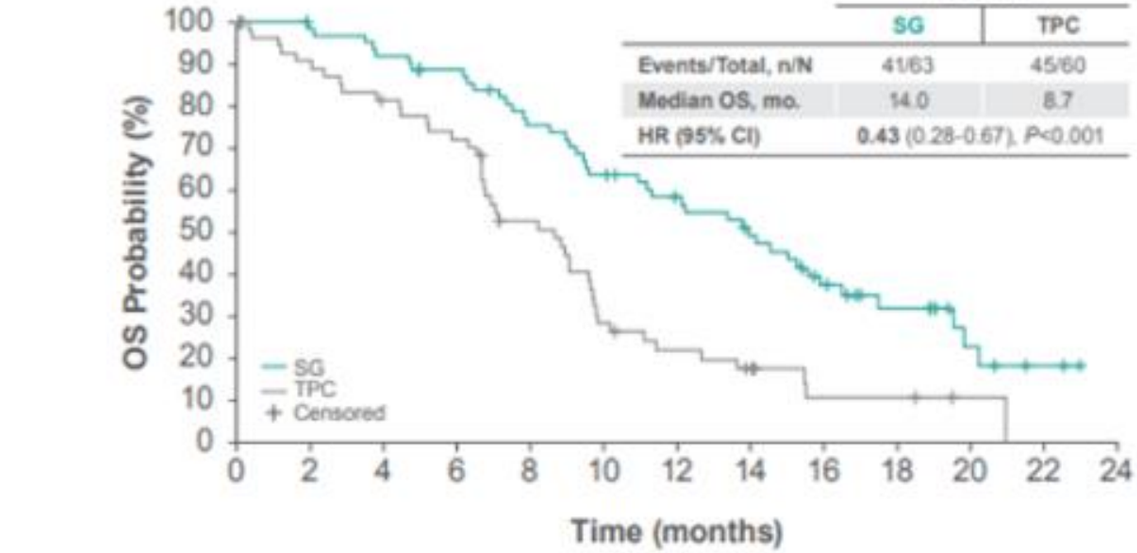
A



No. of Patients Still at Risk

SG, HER2 IHC0	149	139	128	115	98	80	62	52	29	22	11	4	0
TPC, HER2 IHC0	144	118	88	64	48	33	27	25	15	9	3	2	1

B



No. of Patients Still at Risk

SG, HER2-Low	63	61	57	54	45	38	32	26	17	10	5	2	0
TPC, HER2-Low	60	49	43	38	26	14	10	7	3	3	1	0	0

Hurvitz et al, ESMO Breast 2022 abstr. 168P

Trastuzumab Deruxtecan chez les TN
Analyses exploratoires

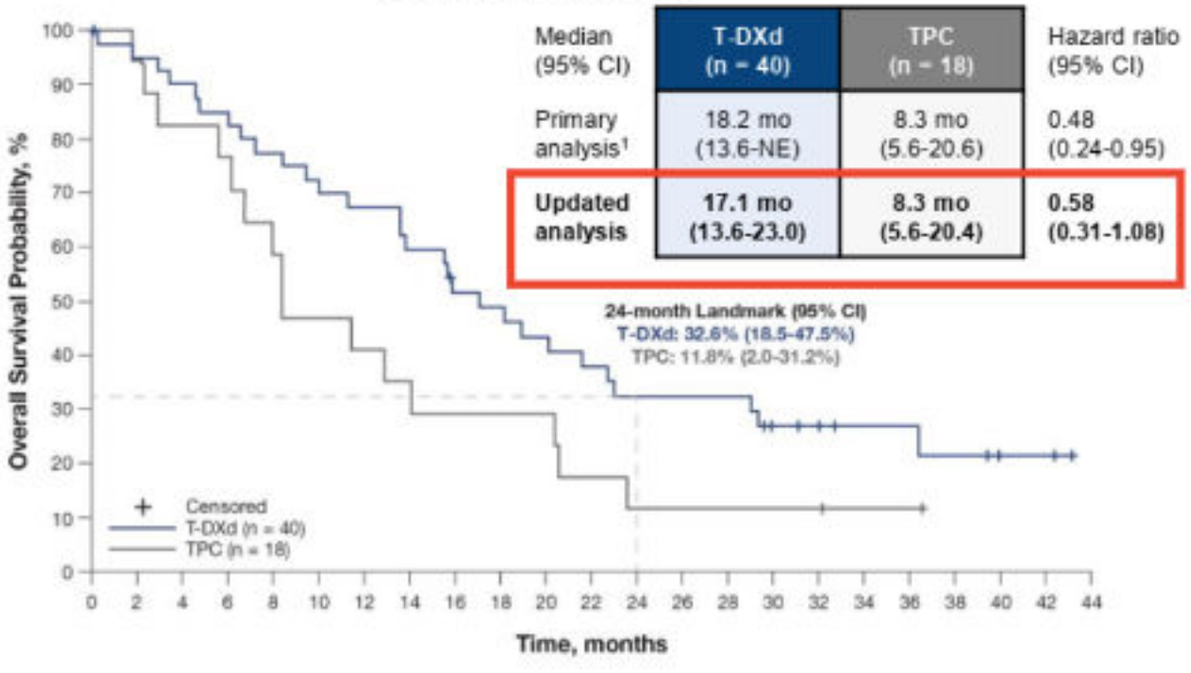
DESTINY-Breast04

Efficacy in the HR− Cohort (Exploratory Analyses)

N= 58 pts

Overall Survival

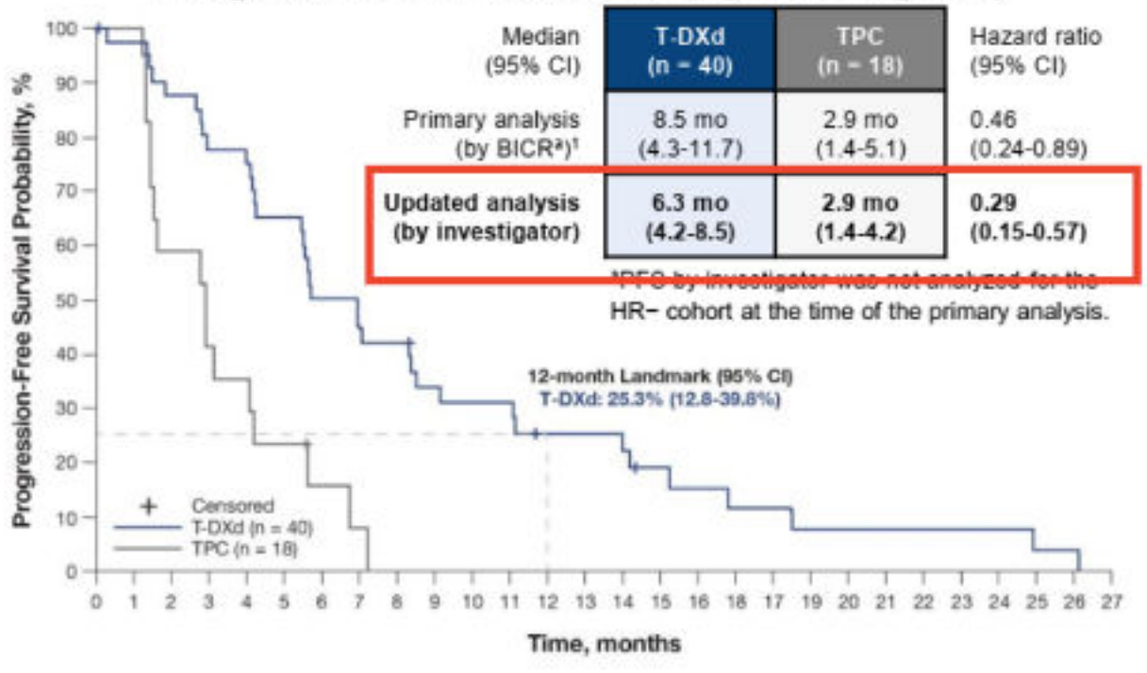
	T-DXd (n = 40)	TPC (n = 18)	Hazard ratio (95% CI)
Median (95% CI)			
Primary analysis[1]	18.2 mo (13.6-NE)	8.3 mo (5.6-20.6)	0.48 (0.24-0.95)
Updated analysis	**17.1 mo (13.6-23.0)**	**8.3 mo (5.6-20.4)**	**0.58 (0.31-1.08)**



Progression-Free Survival (by Investigator)

	T-DXd (n = 40)	TPC (n = 18)	Hazard ratio (95% CI)
Median (95% CI)			
Primary analysis (by BICR[a])[1]	8.5 mo (4.3-11.7)	2.9 mo (1.4-5.1)	0.46 (0.24-0.89)
Updated analysis (by investigator)	**6.3 mo (4.2-8.5)**	**2.9 mo (1.4-4.2)**	**0.29 (0.15-0.57)**

[a]PFS by investigator was not analyzed for the HR− cohort at the time of the primary analysis.



Modi et al, *ESMO* 2023

En pratique

There are very few data regarding the best sequence of administration of ADCs for ER negative/ HER2 low ABC.

In view of the results of the trials of T-Dxd and sacituzumab govitecan in this patient population, the panel believes that sacituzumab govitecan should be used in earlier than T-Dxd.

F. Cardoso et al, The Breast 2024, in preparation

Reco ABC7

T-DXD chez les TN HER2 low : accès précoce, après 1ère ligne de chimio

Merci