NOUVELLES RECOMMANDATIONS POUR LES TRAITEMENTS ADJUVANTS

Pr ELISE DELUCHE

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Déclaration publique de liens d’intérêts

- Advisory Boards : Novartis, Pfizer, GSK, Lilly, MSD, AZ, ROCHE,
- Congrès : Pfizer, Amgen, Roche, Novartis, GSK, Lilly, MSD,
- Honoraires: Astrazeneca-Daiichi, Lilly, Novartis, Pfizer, Fresubin, GSK, MSD, BMS, Menarini,

Quelques chiffres...

Figure 5a. Délai attendu entre la chirurgie et le 1er traitement complémentaire pour les patientes atteintes d'un carcinome du sein canalaire *in situ* (strate A)

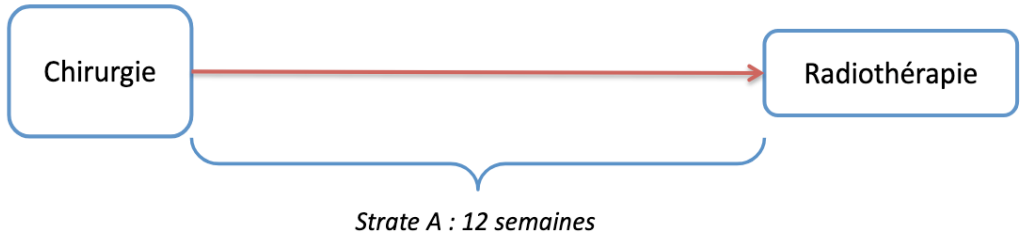
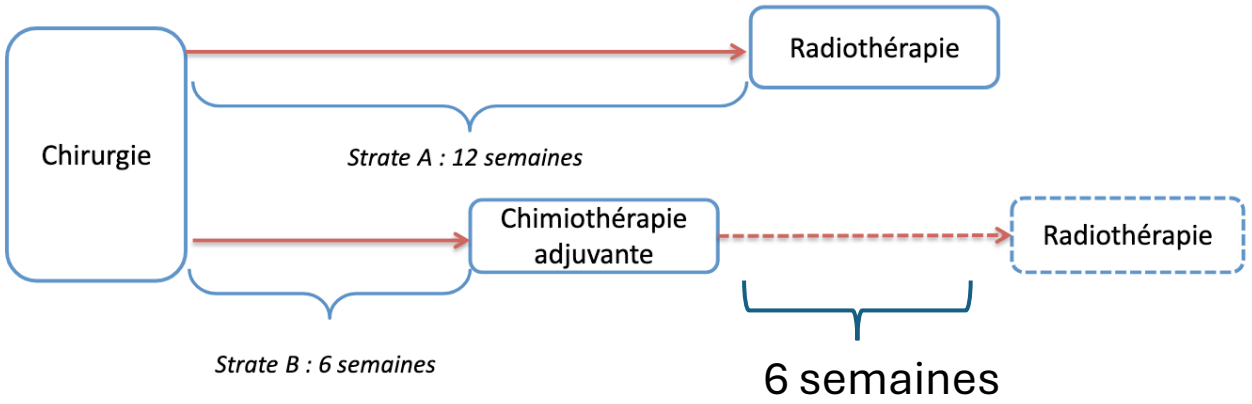
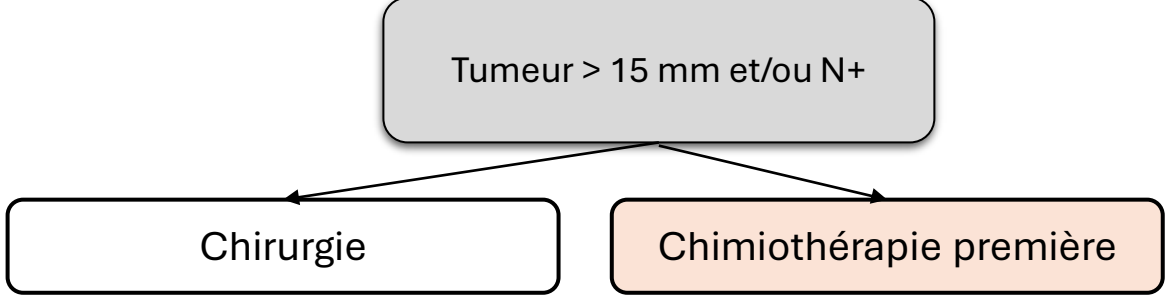


Figure 5b. Délais attendus entre la chirurgie et le 1er traitement complémentaire pour les patientes atteintes d'un carcinome du sein invasif non métastatique selon les strates A et B.

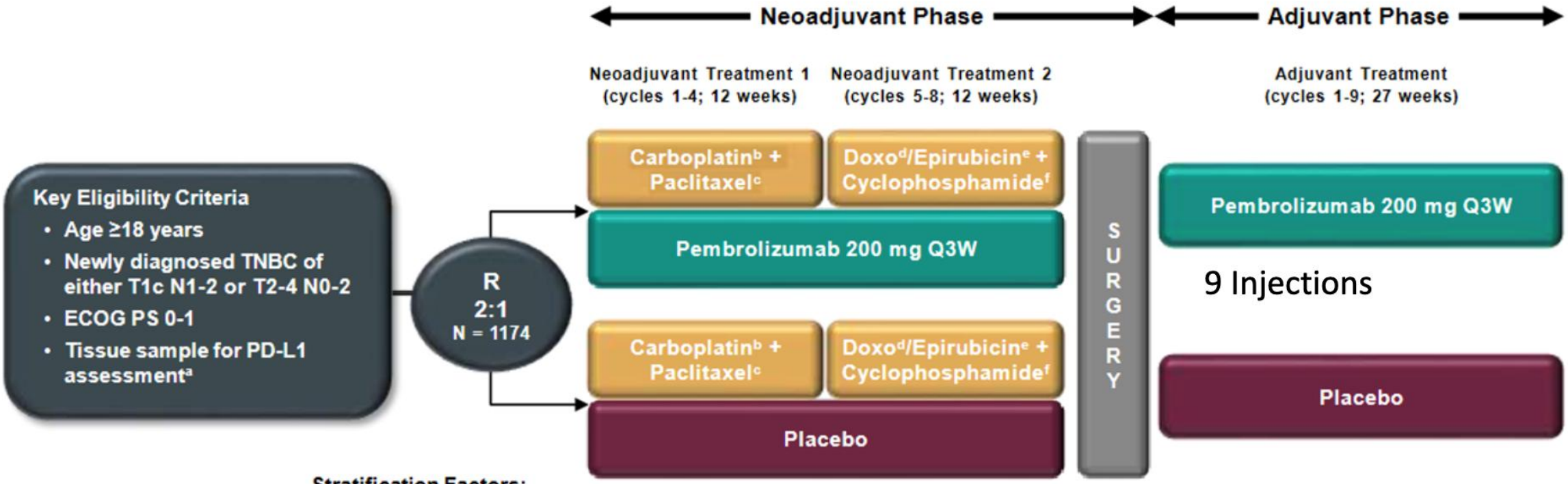


Cancers triple négatifs



En fonction de l’âge, des comorbidités…

KEYNOTE 522



Stratification Factors:
- Nodal status (+ vs -)
- Tumor size (T1/T2 vs T3/T4)
- Carboplatin schedule (QW vs Q3W)

Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)

Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

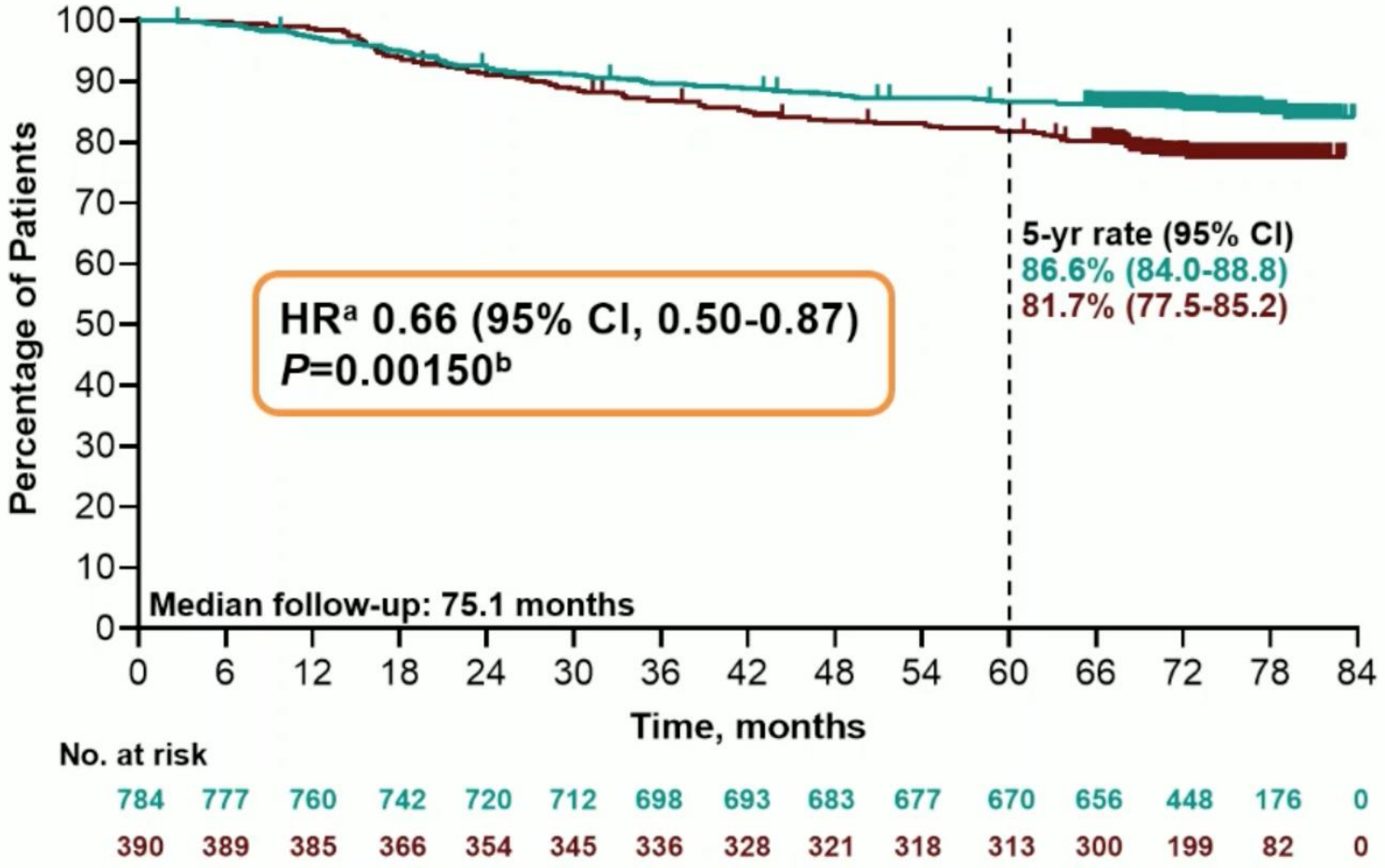
[a]Must consist of at least 2 separate tumor cores from the primary tumor.
[b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.
[c]Paclitaxel dose was 80 mg/m^2 QW.
[d]Doxorubicin dose was 60 mg/m^2 Q3W.
[e]Epirubicin dose was 90 mg/m^2 Q3W.
[f]Cyclophosphamide dose was 600 mg/m^2 Q3W.

Schmid et al, NEMJ 2020

Pembrolizumab = benefice en OS

Traitement de reference en néo-adjuvant

Key Secondary Endpoint: Overall Survival



	Pts w/ Event
Pembro + Chemo/Pembro	14.7%
Placebo + Chemo/Placebo	21.8%

[a]The unstratified piecewise HR was 0.87 (95% CI, 0.57-1.32) before the 2-year follow-up and 0.51 (95% CI, 0.35-0.75) afterwards. The weighted average HR with weights of number of events before and after 2-year follow-up was 0.66. With 200 events (67.3% information fraction), the observed *P*-value crossed the prespecified nominal boundary of 0.00503 (1-sided) at this interim analysis. Data cutoff date: March 22, 2024.

Schmid P *et al*. ESMO 2024 Schmid et al, NEMJ 2024

Quel traitement en adjuvant ?

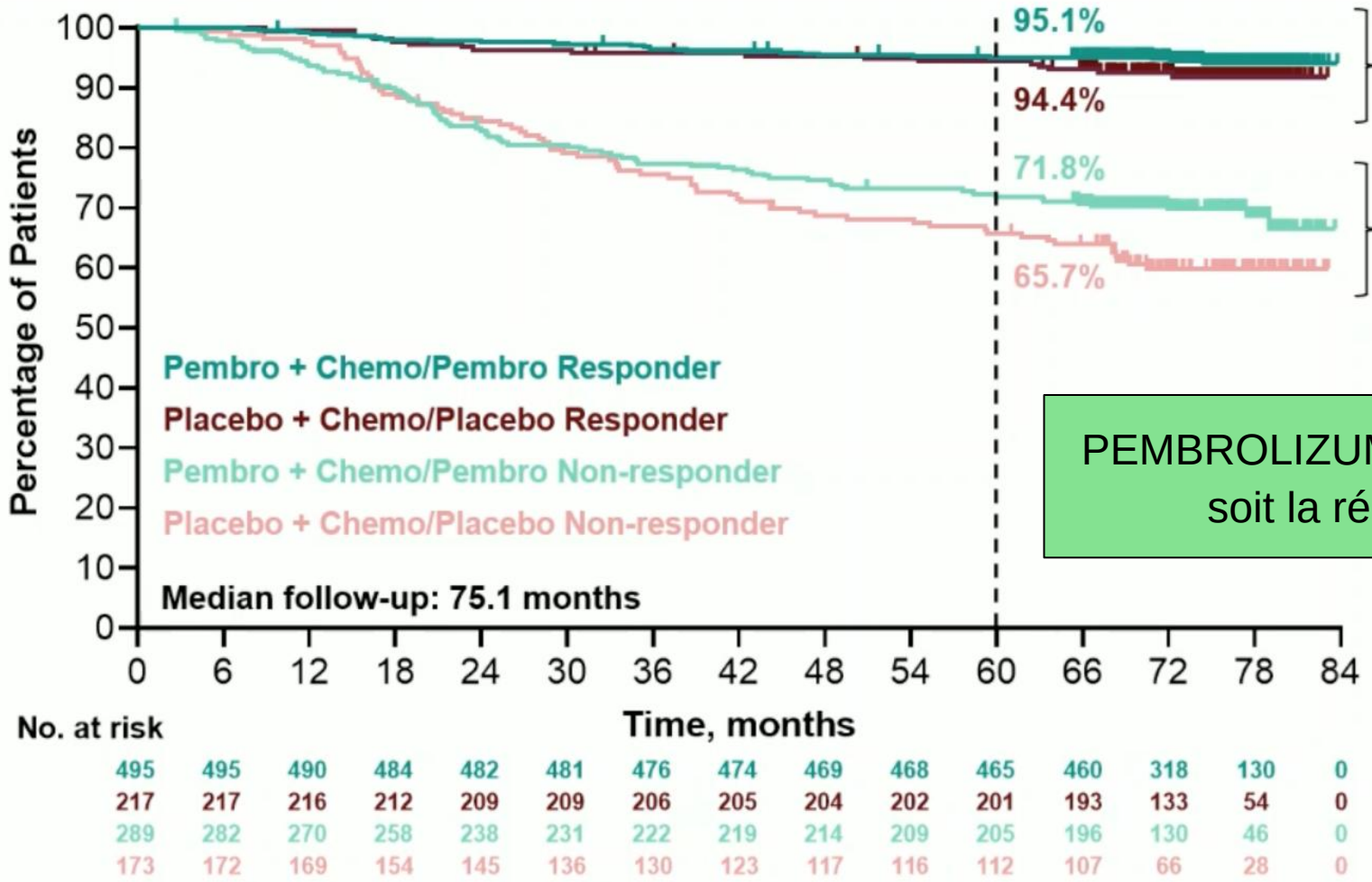
- 4 acteurs :
  - Immunothérapie
  - Chimiothérapie par Capécitabine
  - Inhibiteur de PARP
  - Chimiothérapie par sel de platine

Quel traitement en adjuvant ?

- 4 acteurs :
  - Immunothérapie
  - Chimiothérapie par Capécitabine
  - Inhibiteur de PARP
  - Chimiothérapie par sel de platine


Chimiothérapie
néo-adjuvante
+ IO
Chirurgie
Chimiothérapie
adjuvante IO

Overall Survival by Pathologic Complete Response (yp T0/Tis ypN0)



PEMBROLIZUMAB en adjuvant quelque soit la réponse histologique

This is a non-randomized subgroup analysis based on the post-treatment outcome of pCR and HRs should therefore be interpreted with caution. Data cutoff date: March 22, 2024.

Schmid P *et al.* ESMO 2024 Schmid et al, NEMJ 2024

Groupe UNICANCER - UCBG
Protocole n°: UC-BCG-2401
EudraCT n°: 2024-515787-31-00

OPT-PEMBRO

Eligibilité (N= 2454)

- Carcinome mammaire invasif confirmé localement
- Cancer du sein précoce, non métastatique
- ER≤10%/ PR≤10%/ HER2- negative
- pCR après **chimiothérapie néoadjuvante (NAC)** et **pembrolizumab**

R 1:1

Pembrolizumab (9 cycles) 200 mg Q3W

Stratifié par:
- Statut ganglionnaire (N0 vs N1-3) [cN]
- Taille de la tumeur(T1 to T2 or T3 to T4) [cT]
- Anthracyclines en neoadjuvant (oui ou non)
- Région géographique

Observation

Critère d'évaluation principal
Survie sans récidive

Critère d'évaluation secondaire principal
- QoL (ePROs); AEs grade ≥ 2

Critères d'évaluation secondaires
- IBCFS/DRFS/Second cancer/OS
- Economique /analyse HTA
- Translationnel - TILs

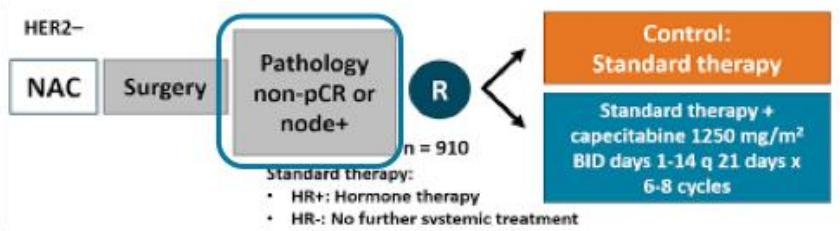
Investigateur Coordonnateur : Dr Joana MOURATO RIBEIRO & Dr Olivier TREDAN

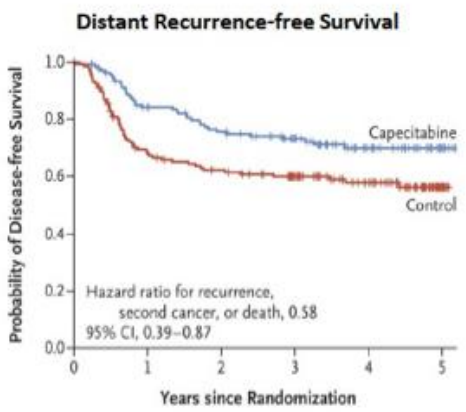
Quel traitement en adjuvant ?

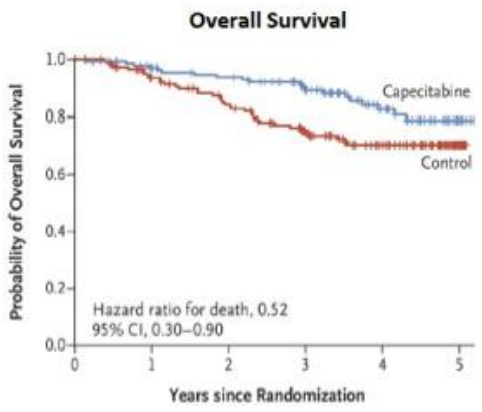
- 4 acteurs :
  - Immunothérapie
  - Chimiothérapie par Capécitabine
  - Inhibiteur de PARP
  - Chimiothérapie par sel de platine

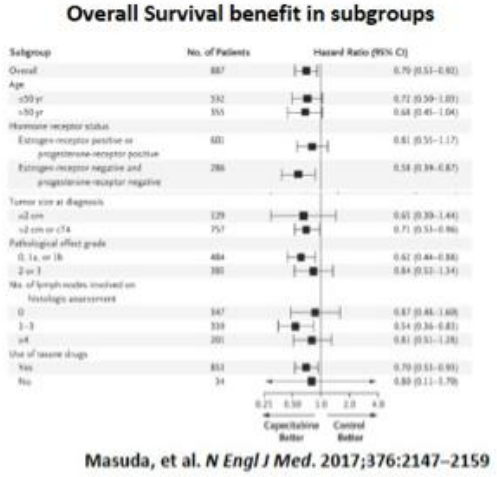
Chimiothérapie néo-adjuvante sans IO → Chirurgie / Non pCR → **Chimiothérapie adjuvante par CAPECITABINE**

Etude CREATE- X









Masuda, et al. *N Engl J Med*. 2017;376:2147–2159

Masuda et al. NEMJ 2017

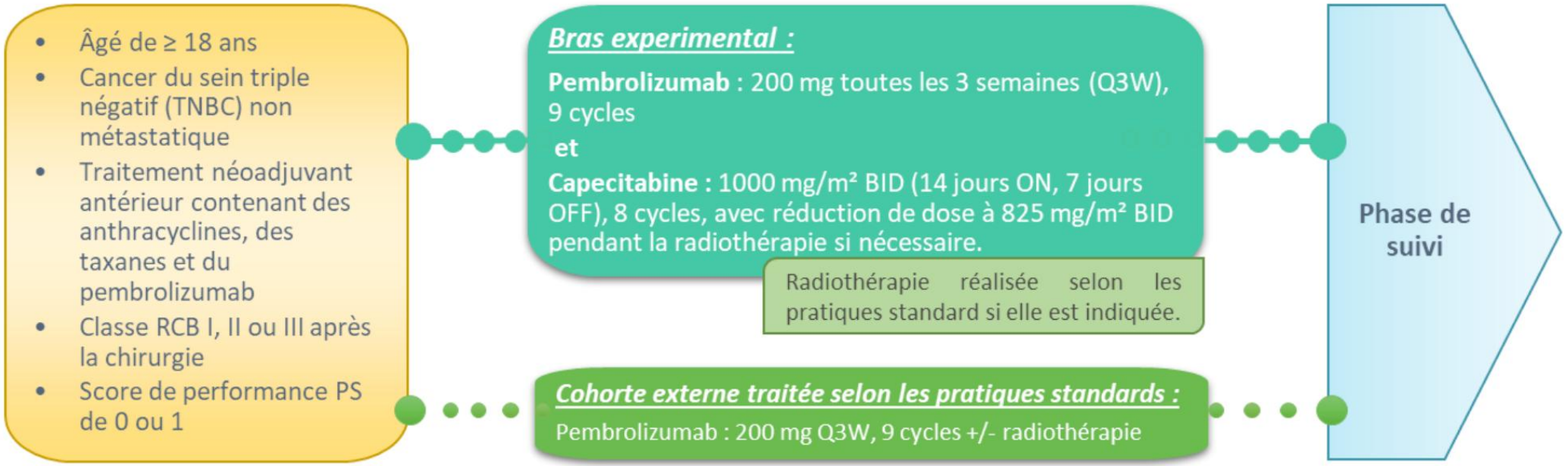

Chimiothérapie néo-adjuvante + IO
Chirurgie / Non pCR
Chimiothérapie adjuvante par CAPECITABINE + IO ?

Quelles données pour capécitabine + IO ?

Aucune donnée publiée

Etude en cours CAPPA:

Étude de phase II, visant à évaluer l'association CAPécitabine et Pembrolizumab en tant que thérapie post-opératoire Adjuvante pour le cancer du sein triple négatif avec maladie résiduelle après une chimio-immunothérapie néoadjuvante.



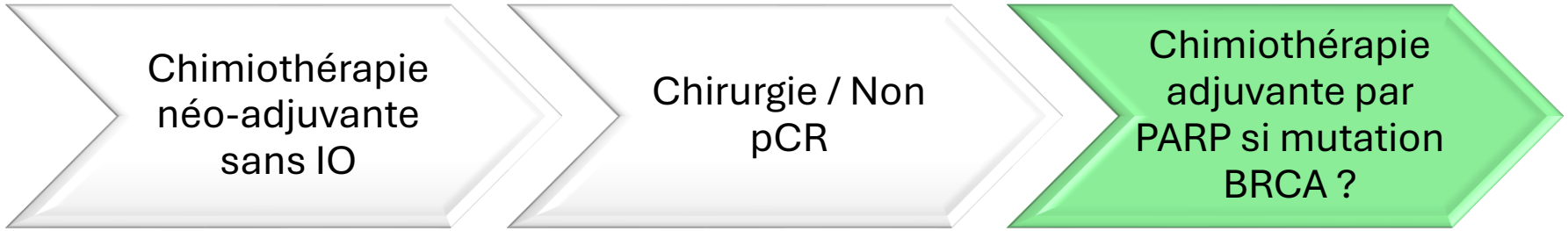
Dr Delphine LOIRAT

Après traitement néoadjuvant selon les modalités de l'étude KEYNOTE-522 et en cas de maladie résiduelle, il est acceptable après discussion en RCP du rapport bénéfice/risque et discussion avec la patiente, d'initier un traitement par capécitabine pour une durée de 6 mois concomitamment à la poursuite du pembrolizumab adjuvant.

	D'accord	Pas d'accord	Abstention
Votes experts	100%	0%	0%
Votes participants	94%	4%	2%

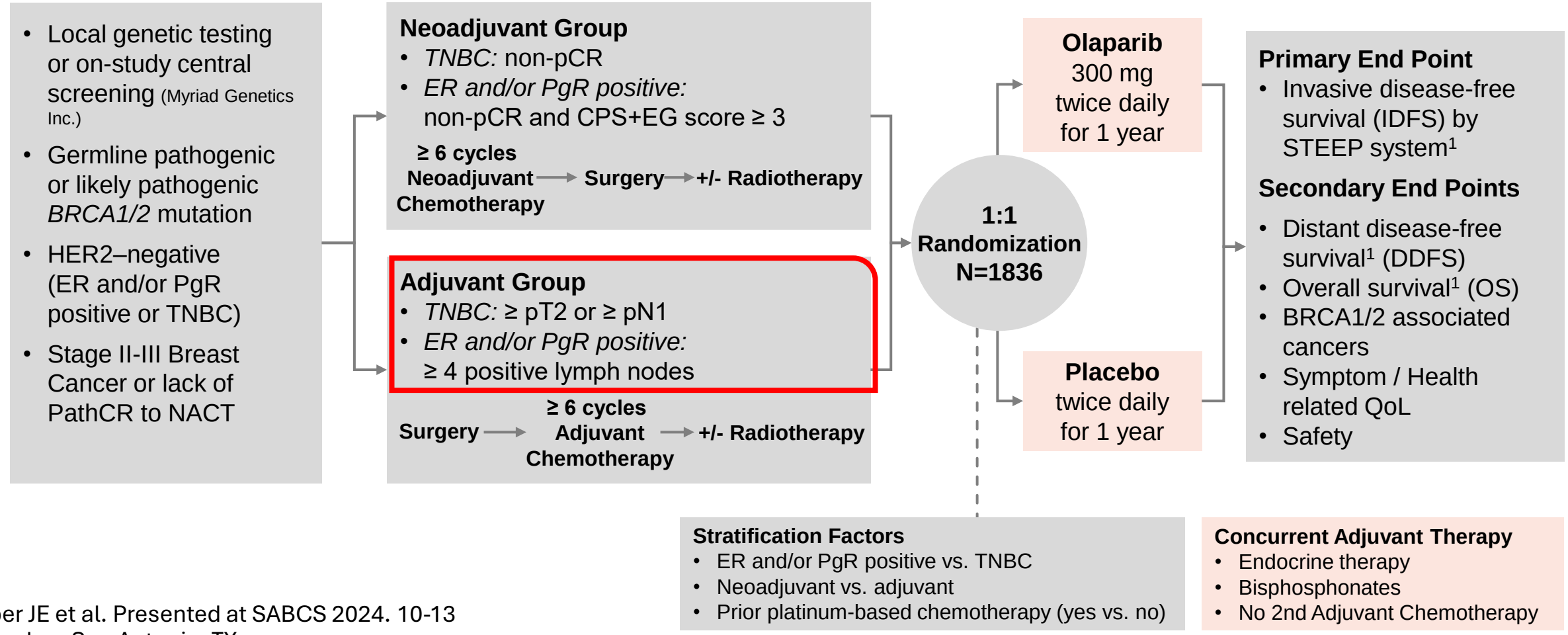
Quel traitement en adjuvant ?

- 4 acteurs :
  - Immunothérapie
  - Chimiothérapie par Capécitabine
  - Inhibiteur de PARP
  - Chimiothérapie par sel de platine


Chimiothérapie néo-adjuvante sans IO
Chirurgie / Non pCR
Chimiothérapie adjuvante par PARP si mutation BRCA ?

OlympiA: Trial schema

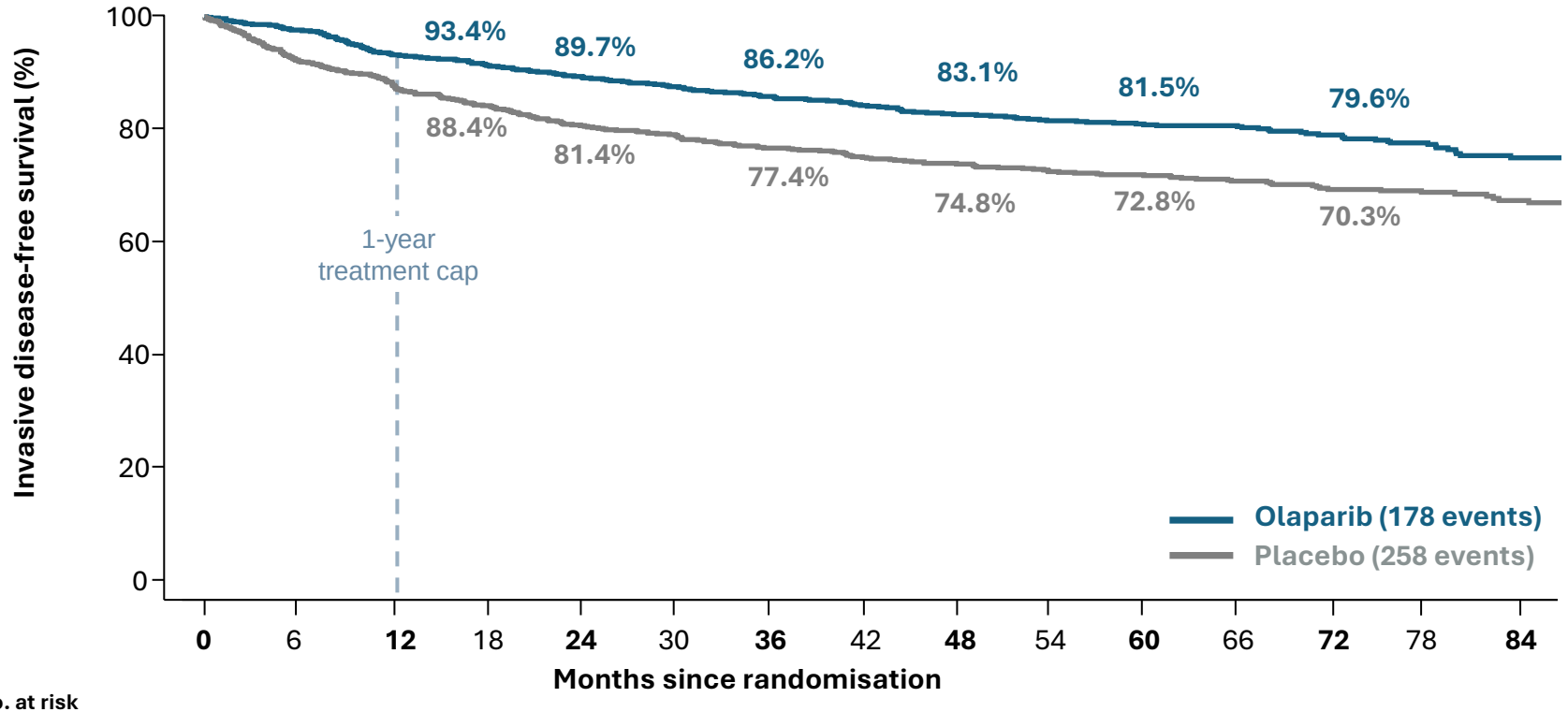
- Triple Negative Breast Cancer = 751 (81.5%) - 758 (82.8%)
- Adjuvant / néo-adjuvant = equivalent



Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

At 6.1 years median follow-up, one year of adjuvant olaparib after (neo)adjuvant chemotherapy continues to demonstrate clinically meaningful improvements in IDFS

Exploratory analysis: invasive disease-free survival (descriptive)



No. at risk								
Olaparib	921	778	712	670	632	570	361	194
Placebo	915	766	683	628	588	512	327	181

IDFS at DCO3

HR 0.65
95% CI 0.53–0.78

6-year IDFS rate

Olaparib (n=921) **79.6%**

Placebo (n=915) **70.3%**

Difference 9.4%
95% CI 5.1–12.7

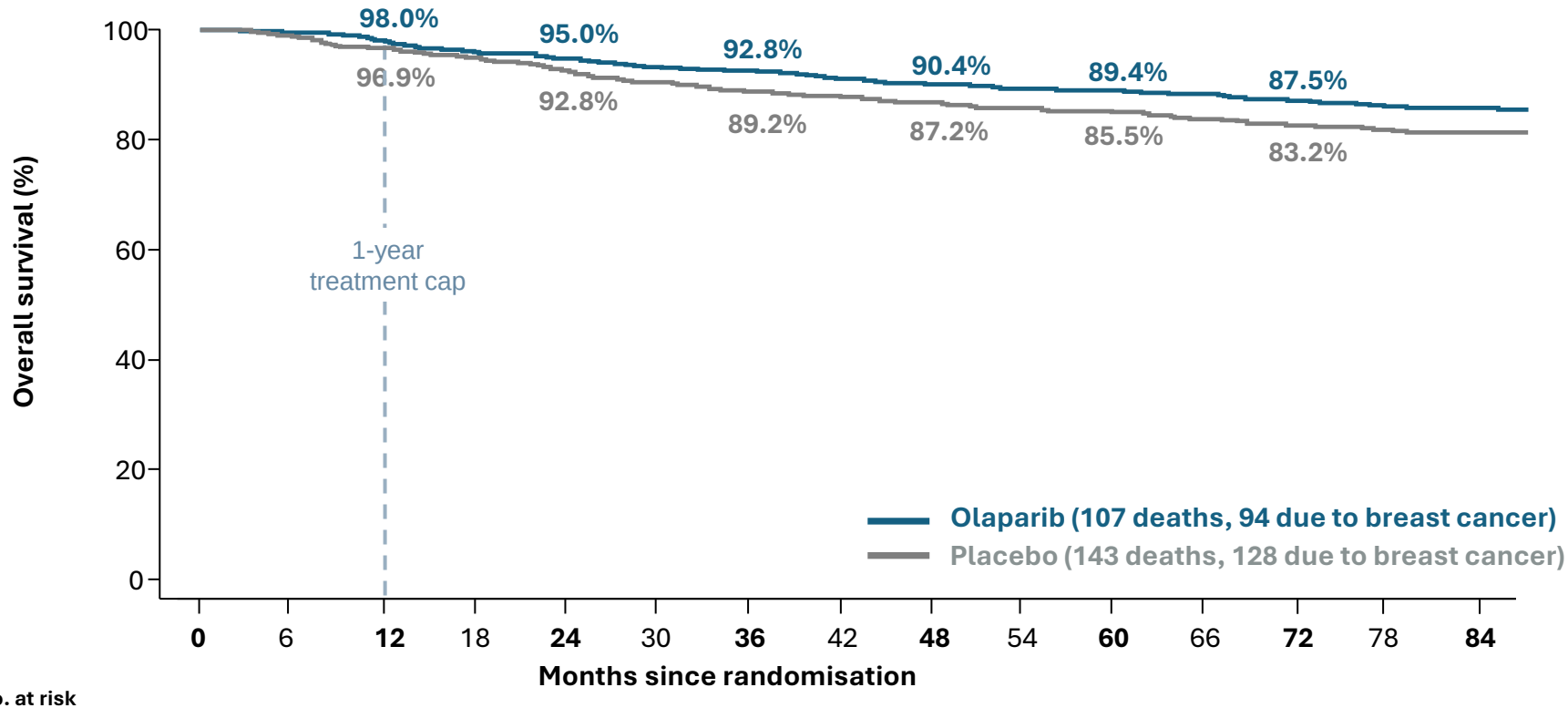
DCO3 June 2024; median follow-up 6.1 years.

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Olaparib = benefice en OS à 6 ans

OLAPARIB - Statut de mutation *gBRCA* indispensable

Secondary endpoint: overall survival



No. at risk								
Olaparib	921	846	795	765	728	660	420	224
Placebo	915	843	788	739	698	616	390	221

OS at DCO3

HR 0.72
95% CI 0.56–0.93

6-year OS rate

Olaparib (n=921) **87.5%**

Placebo (n=915) **83.2%**

Difference 4.4%
95% CI 0.9–6.7

DCO3 June 2024; median follow-up 6.1 years.

Garber JE et al. Presented at SABCS 2024. 10-13 December. San Antonio, TX.

Question 3
Testing *BRCA1/2* (2)

2025

En l'absence d'histoire familiale, **et en situation adjuvante**, une analyse de ADNt circulant ou de la tumeur suffit pour décider de l'intérêt d'un traitement par PARPi.

Réponse: NON, analyse germinale préférée

	D'accord	Pas d'accord	Abstention
Votes experts	17%	83%	0%
Votes participants	28%	65%	8%

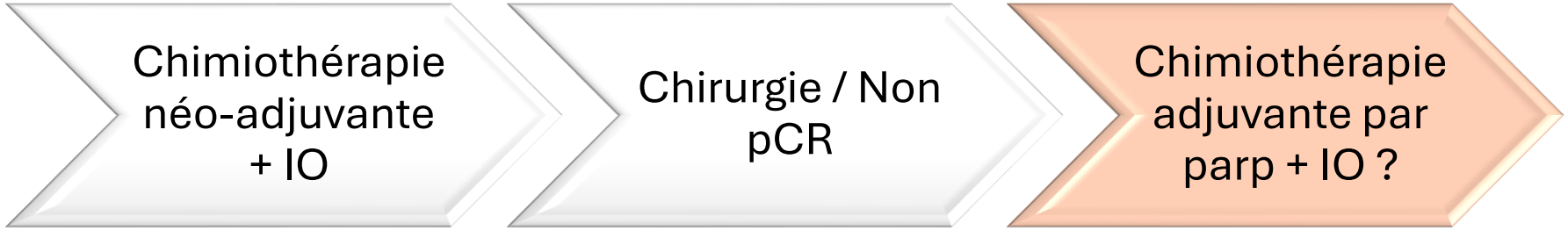
Question 4
Testing *BRCA1/2* (3)

2025

L'existence d'une mutation *gPALB2* peut permettre de prescrire l'olaparib en adjuvant (selon les critères d'inclusion d'OLYMPIA par analogie avec les patientes *gBRCA1/2* mutées).

Réponse: NON (pas de consensus)

	D'accord	Pas d'accord	Abstention
Votes experts	50%	45%	5%
Votes participants	38%	45%	17%



Quelles données pour l'olaparib + IO ?

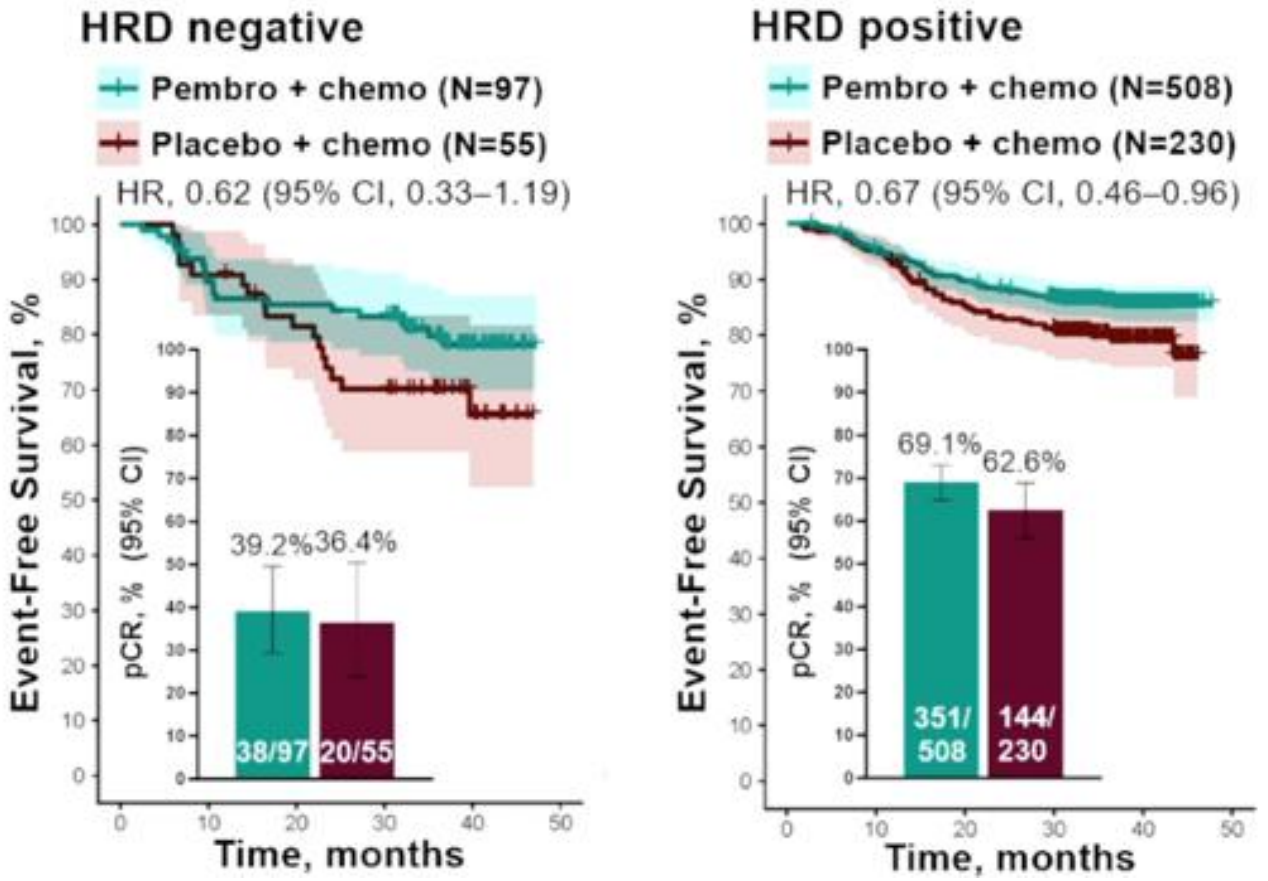
- Aucune donnée en adjuvant publié
- Données en métastatique sur la tolérance

- En attente : étude OPERETTA (*étude japonaise*)

A phase II study evaluating neoadjuvant and adjuvant olaparib plus pembrolizumab following platinum-based chemotherapy plus pembrolizumab for germline BRCA mutated triple negative breast cancer.

Quid des patientes BRCA en cas de traitement par pembrolizumab ? Analyse exploratoire

Pas de stratification selon le statut BRCA



HRD : Définie par la présence de mutations *BRCA* (21% dont 17% de *gBRCAm)* et/ou de LOH ≥16%

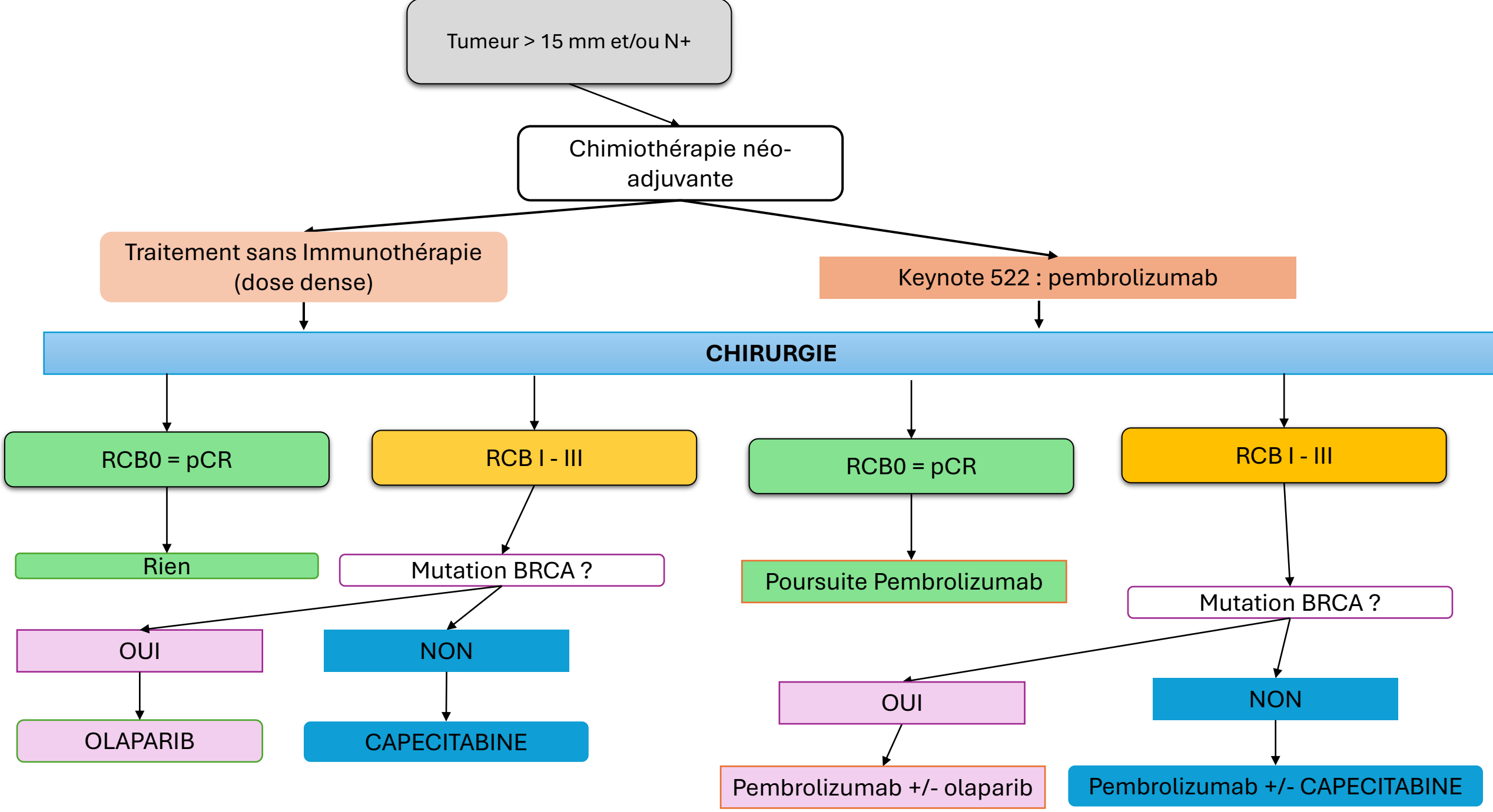
Joyce O'Shaughnessy et al., SABCS® 2024, Abs # - LB1-07

Question 47
Cancers du sein précoces RH négatifs et HER2 négatifs (3)

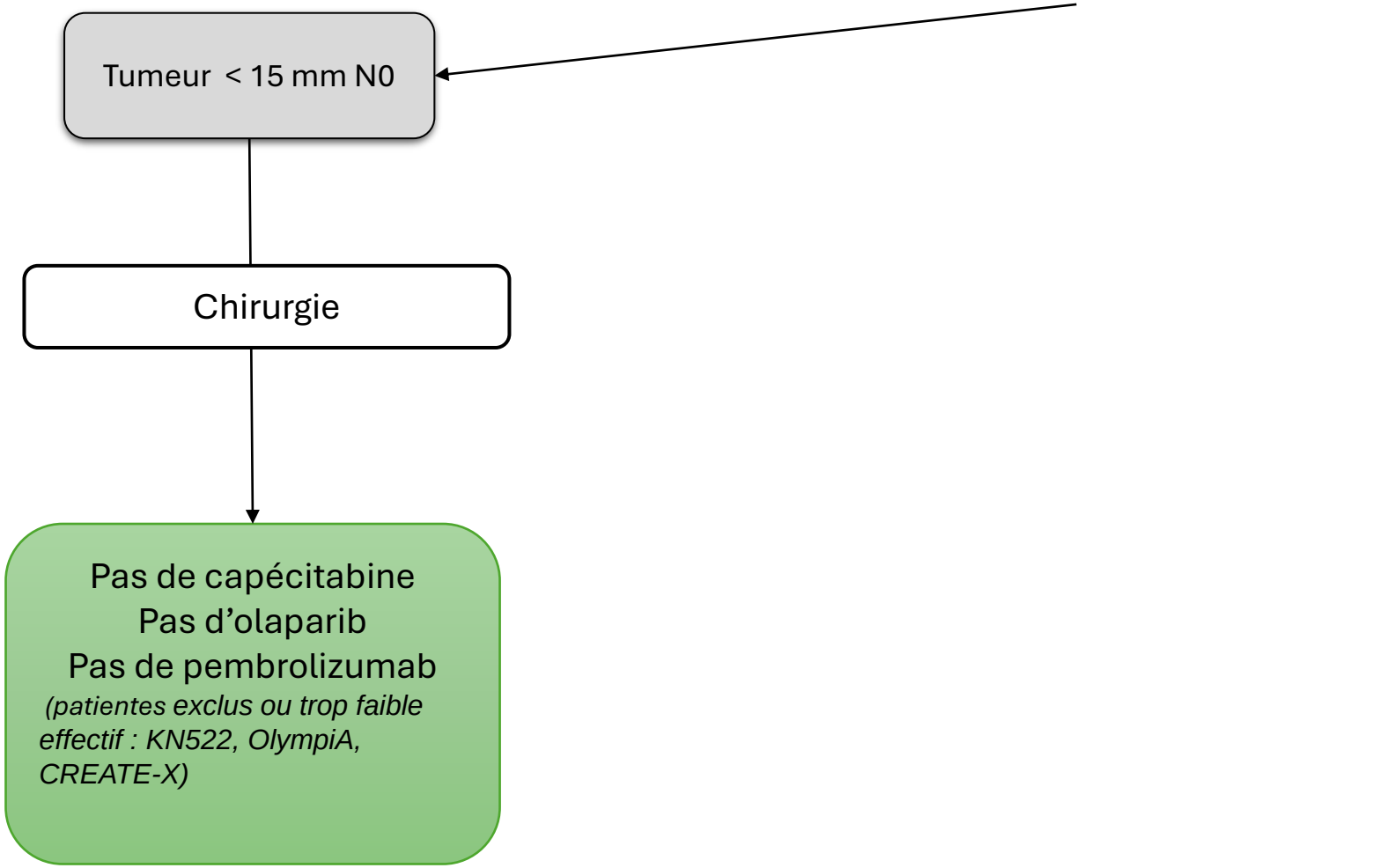
CANAL ST-PAUL

- Chez une patiente porteuse de mutation *gBRCA1/2,* après traitement néoadjuvant selon les modalités de l'étude KEYNOTE-522 et avec maladie résiduelle, il est acceptable, d'initier un traitement par olaparib pour une durée d'un an concomitamment à la poursuite du pembrolizumab adjuvant, après évaluation en RCP du rapport bénéfice/risque et discussion avec la patiente.

	D'accord	Pas d'accord	Abstention
Votes experts	**100%**	**0%**	**0%**
Votes participants	**91%**	**4%**	**6%**


Tumeur > 15 mm et/ou N+
Chimiothérapie néo-adjuvante
Traitement sans Immunothérapie (dose dense)
Keynote 522 : pembrolizumab
CHIRURGIE
RCB0 = pCR
RCB I - III
RCB0 = pCR
RCB I - III
Rien
Mutation BRCA ?
Poursuite Pembrolizumab
Mutation BRCA ?
OUI
NON
OUI
NON
OLAPARIB
CAPECITABINE
Pembrolizumab +/- olaparib
Pembrolizumab +/- CAPECITABINE

TAKE HOME MESSAGE



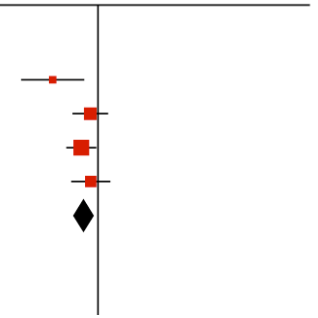
PLATINE en adjuvant

Analysis 2.1. Comparison 2: Adjuvant, Outcome 1: Disease-free survival

Study or Subgroup	log[Hazard Ratio]	SE	Platinum Total	Control Total	Weight	Hazard Ratio IV, Fixed, 95% CI
2.1.1 Adjuvant						
Li 2020 (1)	-1.171183	0.417558	70	73	9.0%	0.31 [0.14 , 0.70]
Nasr 2015 (2)	-0.198451	0.235707	78	80	28.2%	0.82 [0.52 , 1.30]
PATTERN (3)	-0.430783	0.199024	325	322	39.5%	0.65 [0.44 , 0.96]
Zheng 2022 (4)	-0.18633	0.258992	154	154	23.3%	0.83 [0.50 , 1.38]
Subtotal (95% CI)			**627**	**629**	**100.0%**	**0.69 [0.54 , 0.88]**

Heterogeneity: Chi² = 4.81, df = 3 (P = 0.19); I² = 38%

Test for overall effect: Z = 3.00 (P = 0.003)



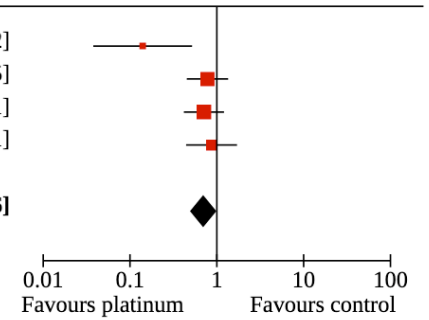
Analysis 2.2. Comparison 2: Adjuvant, Outcome 2: Overall survival

Study or Subgroup	log[Hazard Ratio]	SE	Platinum Total	Control Total	Weight	Hazard Ratio IV, Fixed, 95% CI
Li 2020 (1)	-1.966113	0.668645	70	73	6.1%	0.14 [0.04 , 0.52]
Nasr 2015 (2)	-0.248461	0.280263	78	80	34.5%	0.78 [0.45 , 1.35]
PATTERN (3)	-0.34249	0.272033	325	322	36.6%	0.71 [0.42 , 1.21]
Zheng 2022 (4)	-0.139262	0.344804	154	154	22.8%	0.87 [0.44 , 1.71]
Total (95% CI)			**627**	**629**	**100.0%**	**0.70 [0.50 , 0.96]**

Heterogeneity: Chi² = 6.34, df = 3 (P = 0.10); I² = 53%

Test for overall effect: Z = 2.20 (P = 0.03)

Test for subgroup differences: Not applicable

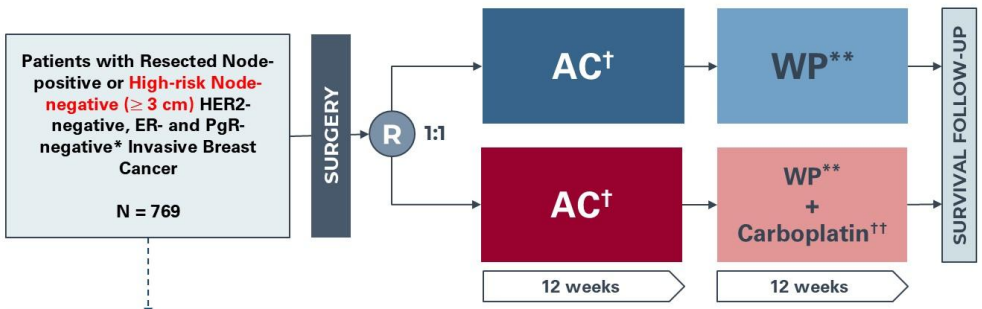


Pas de franc bénéfice des sels de platine en adjuvant

Mason et al, Cochrane Library 2023

PLATINE en adjuvant

NRG-BR003 Study Design



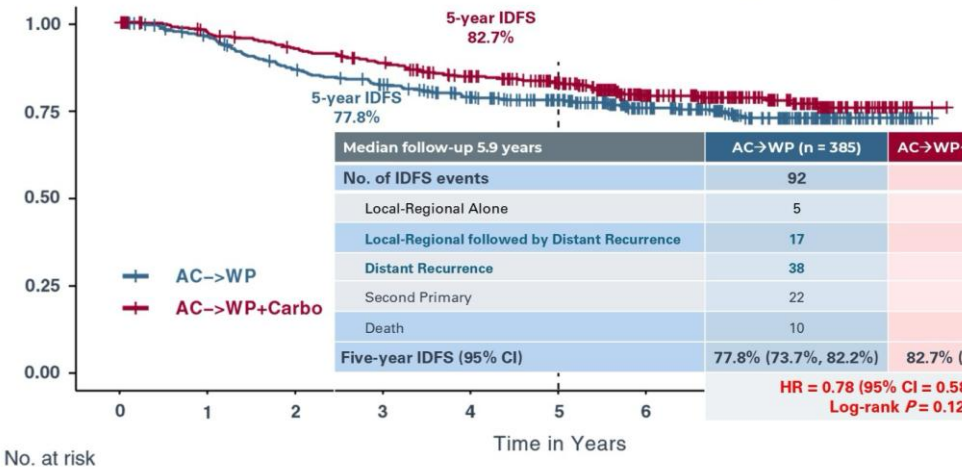
* Patients are eligible if the tumor staining meets one of the following criteria:
- ER-negative and PgR-negative by ASCO/CAP guidelines, OR
- ER or PgR stains are positive in 1-9% of cells and neither is positive in ≥10% of cells

† Doxorubicin (A) 60 mg/m2 IV + cyclophosphamide (C) 600 mg/m2 IV every 2 weeks for 4 cycles (dose-dense schedule)

** Paclitaxel 80 mg/m2 IV weekly for 12 doses

†† Carboplatin AUC of 5 IV every 3 weeks for 4 cycles

Invasive Disease-Free Survival

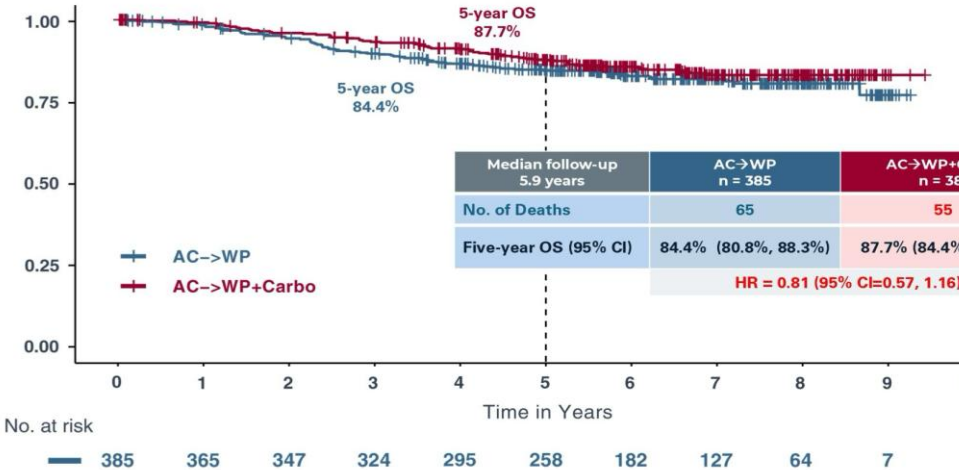


Median follow-up 5.9 years	AC→WP (n = 385)	AC→WP+Carbo (n = 384)
No. of IDFS events	92	77
Local-Regional Alone	5	5
Local-Regional followed by Distant Recurrence	17	8
Distant Recurrence	38	36
Second Primary	22	19
Death	10	9
Five-year IDFS (95% CI)	77.8% (73.7%, 82.2%)	82.7% (78.9%, 86.7%)
	HR = 0.78 (95% CI = 0.58, 1.06) Log-rank *P* = 0.12	

No. at risk

AC–>WP	385	356	318	296	267	238	168	117	58	7	0
AC–>WP+Carbo	384	362	342	323	292	256	174	121	57	4	0

Overall Survival



Median follow-up 5.9 years	AC→WP n = 385	AC→WP+Carbo n = 384
No. of Deaths	65	55
Five-year OS (95% CI)	84.4% (80.8%, 88.3%)	87.7% (84.4%, 91.2%)
	HR = 0.81 (95% CI=0.57, 1.16)	

No. at risk

AC–>WP	385	365	347	324	295	258	182	127	64	7	0
AC–>WP+Carbo	384	370	355	340	315	273	192	132	66	4	0

Dogme initial : pas de platine en adjuvant

Valero et al. ASCO 2025

Adjuvant Epirubicin Plus Cyclophosphamide Followed by Taxanes With or Without Carboplatin in Early-Stage Triple-Negative Breast Cancer (RJBC 1501): A Randomized Phase III Trial

Critères d'inclusion :

- Stade I-III TNBC[1]
- Chirurgie d'emblée
- Candidate pour une chimio adjuvante
- Sans traitement systémique préalable
- ECOG PS 0-1

Facteur de stratification

Envahissement ganglionnaire (N0 vs N1 vs N2-3)[2]

R 1:1

EC-T

Epirubicin 90 mg/m² ET Cyclophosphamide 600 mg/m² q3w 4 cycles

Paclitaxel 80 mg/m² qw x12 OU Docetaxel 80 -100 mg/m² q3w 4 cycles

EC-TCb

Epirubicin 90 mg/m² ET Cyclophosphamide 600 mg/m² q3w 4 cycles

Paclitaxel 80 mg/m² + Carboplatine AUC 2 D1, 8, 15, q4w 4 cycles OU Docetaxel 75 mg/m² + Carboplatine AUC 5-6 q3w 4 cycles

Objectif primaire :

- Survie Sans Maladie (SSM)[3]

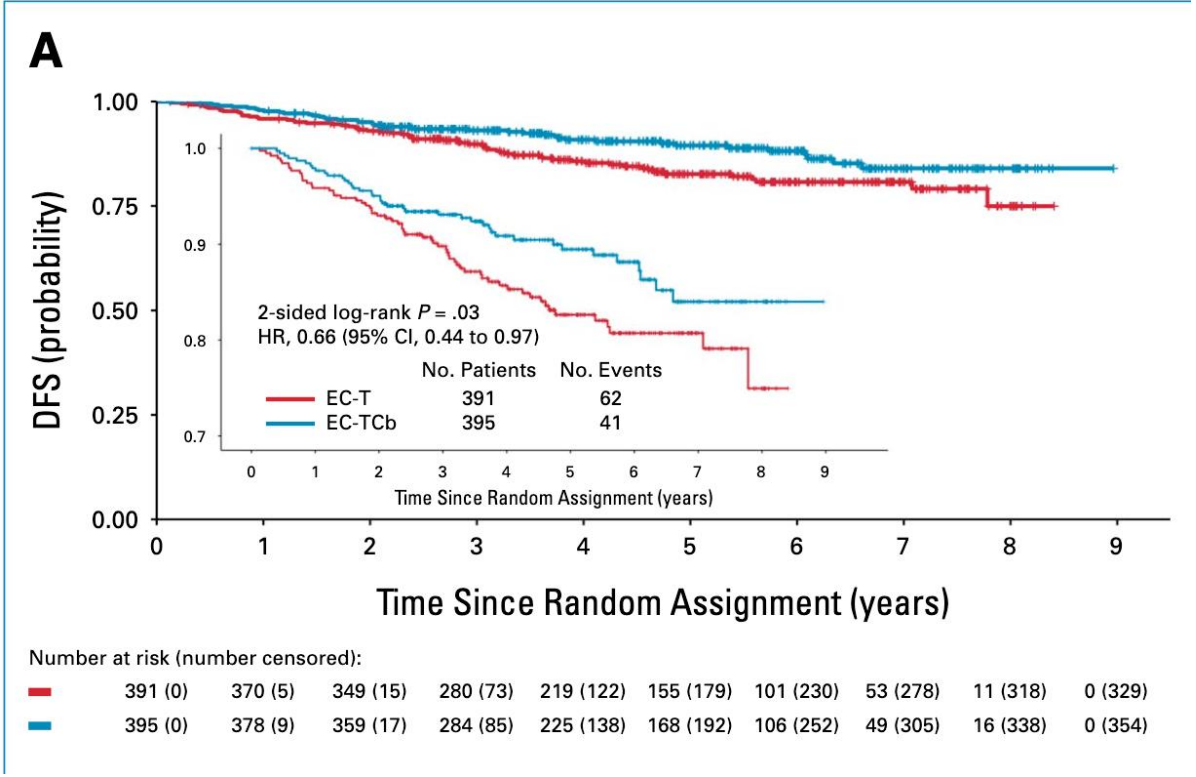
Objectifs secondaires :

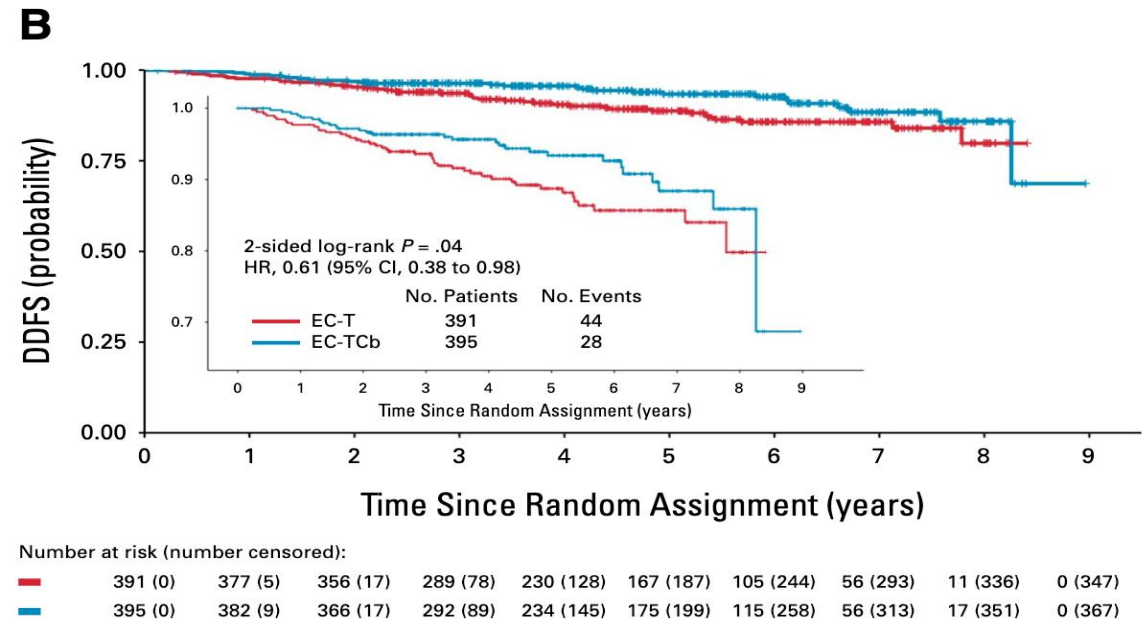
- Survie Sans Métastase[3]
- Survie globale (SG)
- Toxicités

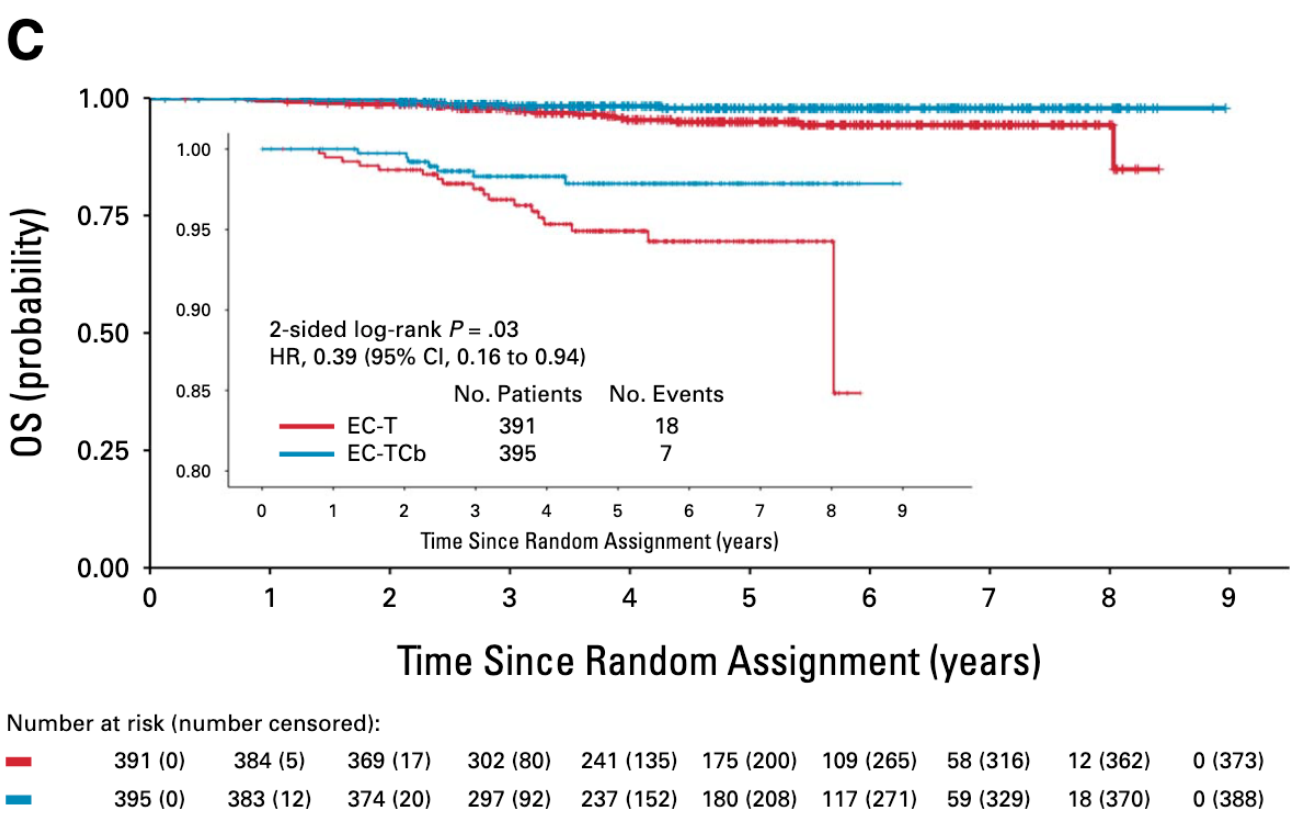
X. Chen et al. JCO décembre 2025/ SABCS 2025

TABLE 1. Demographic and Baseline Clinical Characteristics

Characteristic	EC-T (n = 391)	EC-TCb (n = 395)
Age at diagnosis, No. (%)		
≤50 years	191 (48.8)	199 (50.4)
>50 years	200 (51.2)	196 (49.6)
BMI, No. (%)		
≤24 kg/m^2	253 (64.7)	266 (67.3)
24.1-27.9 kg/m^2	110 (28.1)	109 (27.6)
≥28 kg/m^2	28 (7.2)	20 (5.1)
Breast surgery, No. (%)		
BCS	152 (38.9)	166 (42.0)
Mastectomy	239 (61.1)	229 (58.0)
Axillary surgery, No. (%)		
SLNB	214 (54.7)	234 (59.2)
ALND	177 (45.3)	161 (40.8)
Histology type, No. (%)		
IDC	362 (92.6)	367 (92.9)
ILC and others	29 (7.4)	28 (7.1)
Grade, No. (%)		
G1-2	81 (20.7)	70 (17.7)
G3	291 (74.4)	303 (76.7)
Not applicable/unknown	19 (4.9)	22 (5.6)
Pathologic T stage, No. (%)		
T1	181 (46.3)	185 (46.8)
T2-3	210 (53.7)	210 (53.2)
Lymph node involvement, No. (%)		
N0	282 (72.1)	286 (72.4)
N1	76 (19.4)	81 (20.5)
N2-3	33 (8.4)	28 (7.1)
Ki67 expression		
%, median (IQR)	70.0 (40.0-80.0)	70.0 (40.0-80.0)
No. (%)		
<30%	47 (12.0)	50 (12.7)
≥30%	344 (88.0)	345 (87.3)
ER expression, No. (%)		
0%	376 (96.2)	379 (95.9)
1%-9%	15 (3.8)	16 (4.1)
PR expression, No. (%)		
0%	380 (97.2)	385 (97.7)
1%-9%	11 (2.8)	9 (2.3)
HER2 IHC, No. (%)		
0	247 (63.2)	256 (64.8)
1+ to 2+	144 (36.8)	139 (35.2)
Chemotherapy regimen, No. (%)		
Docetaxel	300 (76.7)	292 (73.9)
Paclitaxel	86 (22.0)	96 (24.3)
Not applicable[a]	5 (1.3)	7 (1.8)

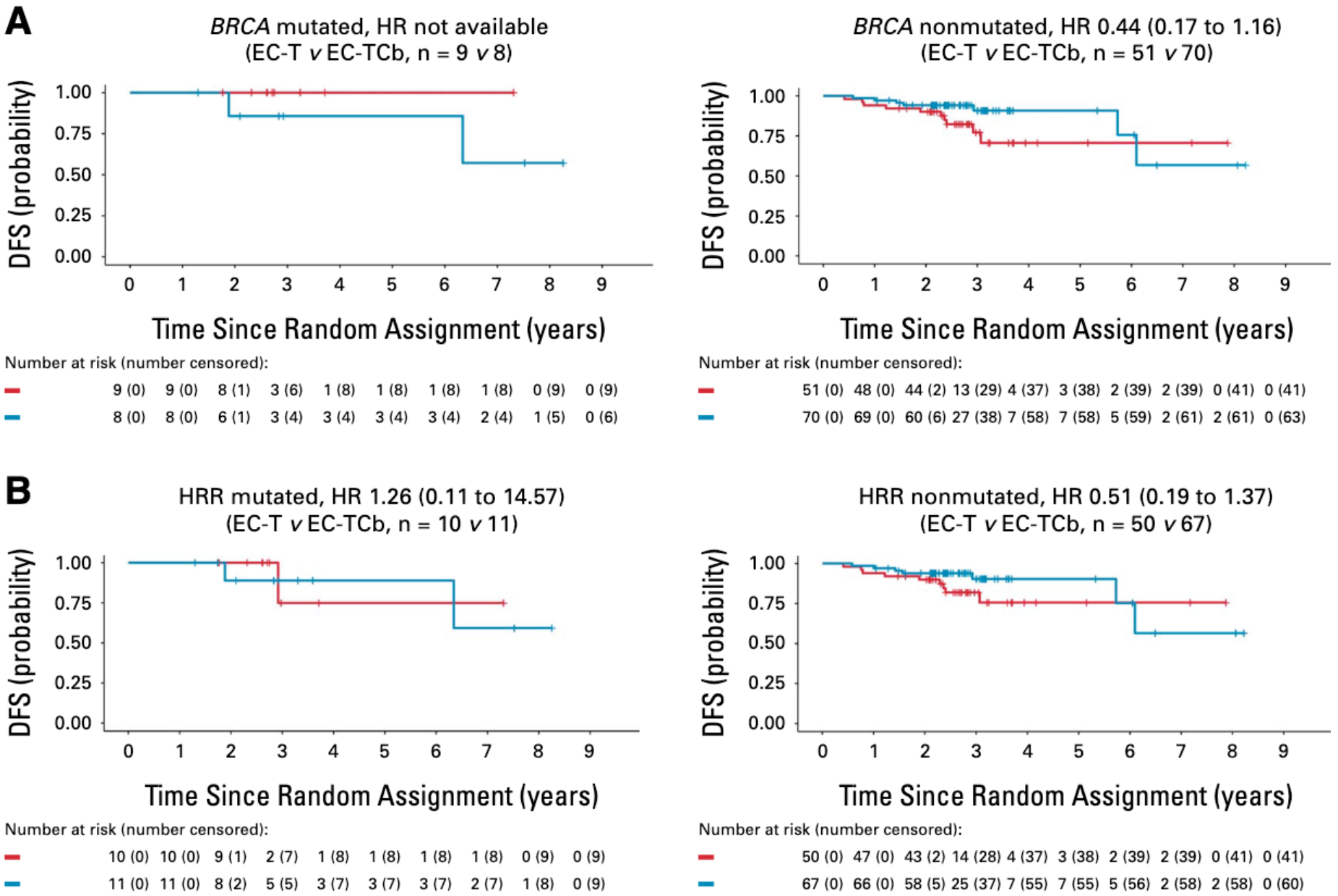






L'ajout de carboplatine augmente la survie sans maladie, sans métastase et globale

X. Chen et al. JCO décembre 2025



X. Chen et al. JCO décembre 2025

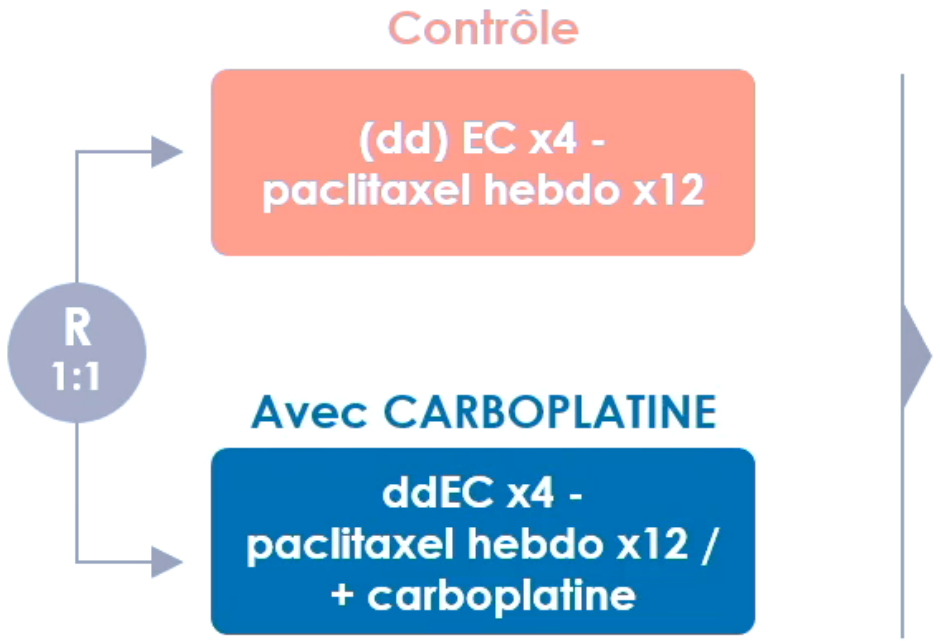
Effect of adjuvant carboplatin intensified chemotherapy versus standard chemotherapy on survival in women with high risk, early stage, triple negative breast cancer (CITRINE): randomised, open label phase 3 trial

- TNBC
- Age : 18-70
- ECOG 0-1
- En situation adjuvante
- Envahissement ganglion

ou pN0 avec Ki67 ≥ 50%

N=808

Préménopausée	**61%**
N+	**38%**
Stade I	**34%**
Chimio dose-dense	**94%**



Objectif primaire :

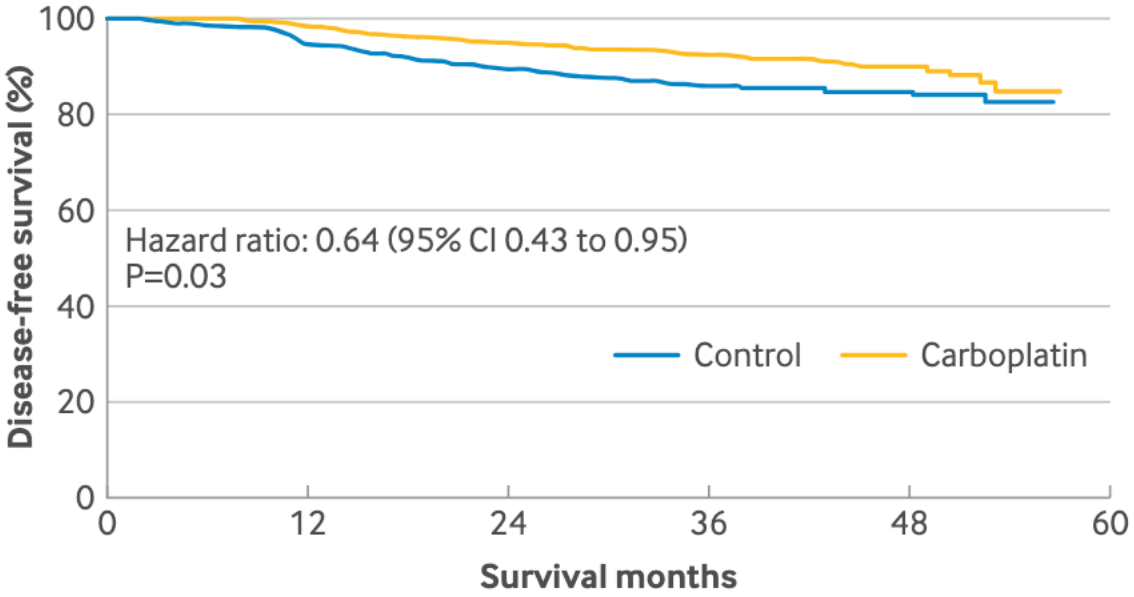
- Survie Sans Maladie (SSM)

Objectifs secondaires :

- Survie sans métastase (DDFS)
- Survie Globale (SG)
- Toxicité

Liu et al. SABCS 2025/*BMJ décembre 2025*

Characteristics	Control (n=404)	Carboplatin (n=404)
Median (range) age, years	48 (24-70)	47 (22-70)
Menopausal status:		
Premenopausal	240 (59.4)	251 (62.1)
Postmenopausal	164 (40.6)	153 (37.9)
Histological grade:		
I-II	38 (9.4)	41 (10.1)
III	366 (90.6)	363 (89.9)
Pathological T stage:		
pT1	183 (45.3)	184 (45.5)
pT2	209 (51.7)	206 (51.0)
pT3	12 (3.0)	14 (3.5)
Pathological N stage:		
pN0	255 (63.1)	257 (63.6)
pN1	99 (24.5)	109 (27.0)
pN2	38 (9.4)	28 (6.9)
pN3	12 (3.0)	10 (2.5)
Pathological tumour stage:		
I	132 (32.7)	125 (30.9)
II	218 (54.0)	237 (58.7)
III	54 (13.4)	42 (10.4)
Lymphovascular invasion:		
Negative	271 (67.1)	273 (67.6)
Positive	133 (32.9)	131 (32.4)
Ki-67 index:		
<50%	48 (11.9)	45 (11.1)
≥50%	356 (88.1)	359 (88.9)
EC schedule:		
Every 2 weeks	381 (94.3)	404 (100.0)
Every 3 weeks	23 (5.7)	0 (0.0)
BRCA1/2 genes:		
Deleterious variant	30 (7.4)	19 (4.7)
No deleterious variant	70 (17.3)	71 (17.6)
Unknown	304 (75.2)	314 (77.7)
HRR related genes		
Deleterious variant	21 (5.2)	20 (5.0)
No deleterious variant	79 (19.6)	70 (17.3)
Unknown	304 (75.2)	314 (77.7)



No at risk

Control					
	404	384	361	306	122
Carboplatin					
	404	396	383	329	133

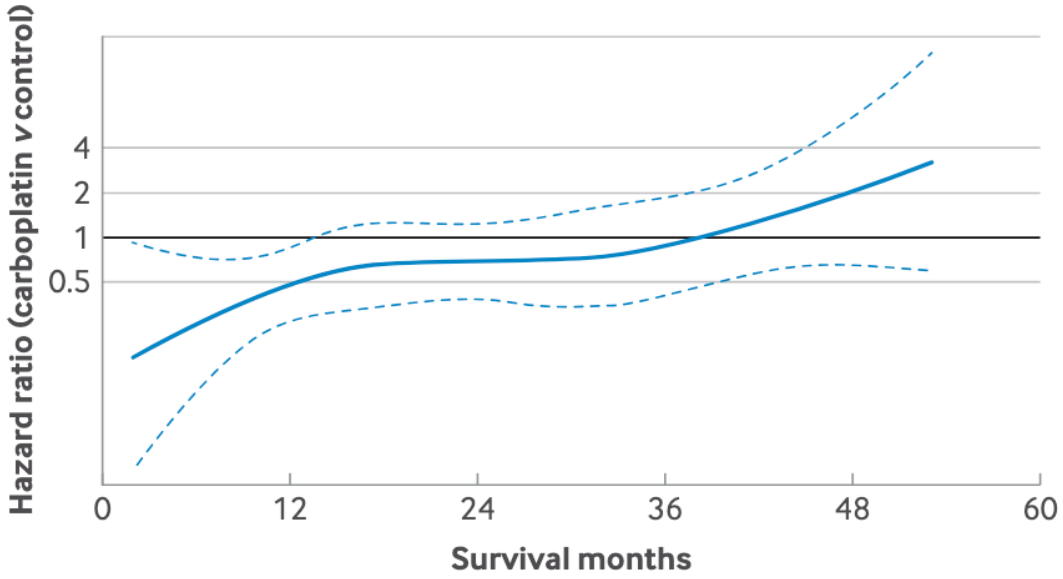
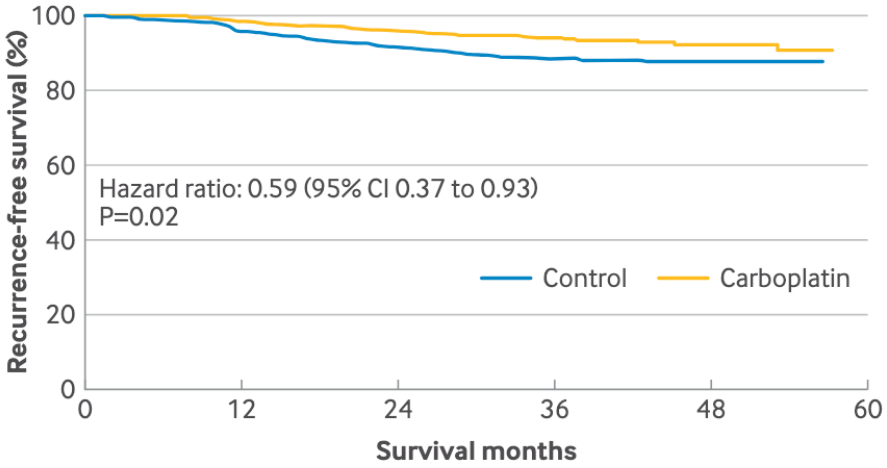
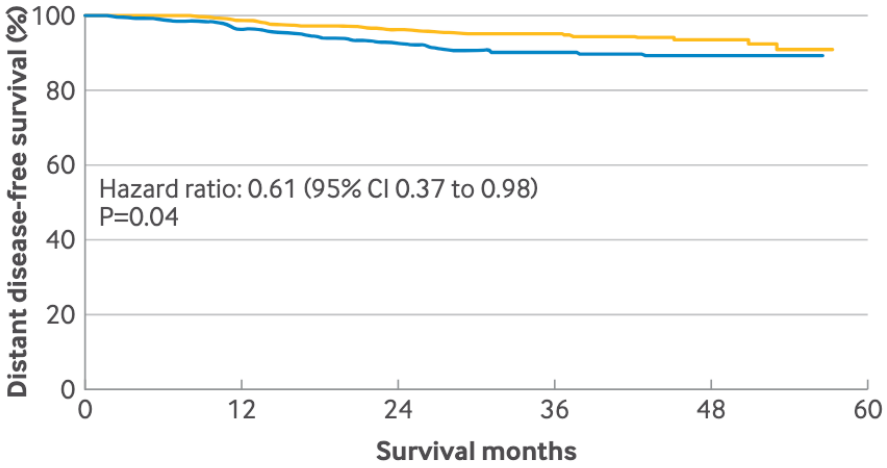


Fig 2 | Primary efficacy outcome. Top: Kaplan-Meier plot showing disease-free survival for patients. Bottom: non-linear plot showing hazard ratio (HR) over time derived from natural spline (df=4) smooth of scaled Schoenfeld residuals on original timescale with y axis relabelled in HR units. CI=confidence interval



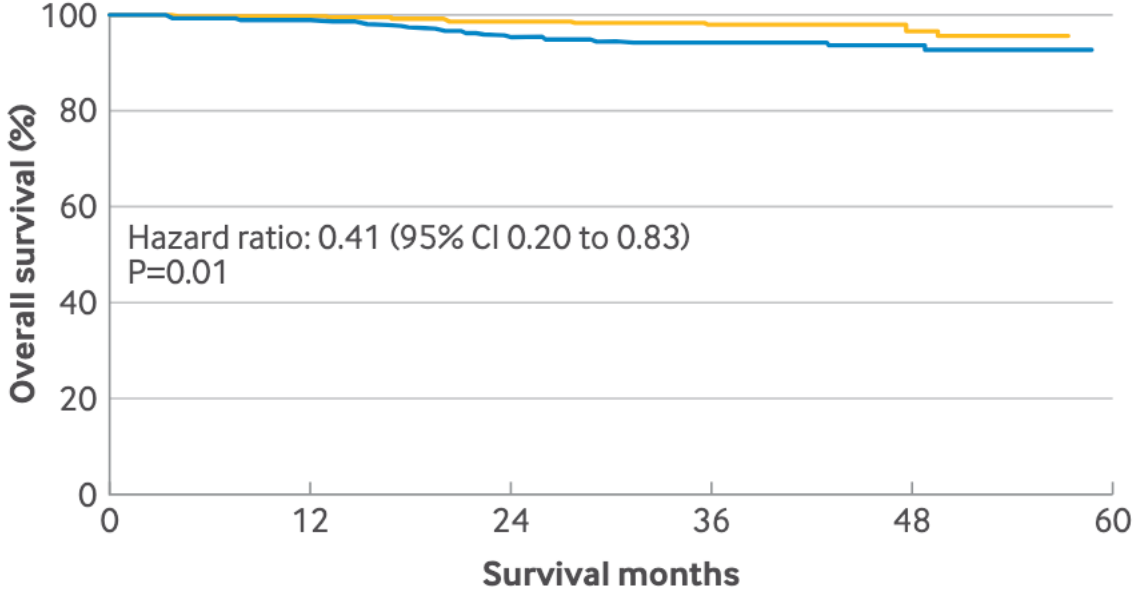
No at risk

Control	404	388	369	316	127
Carboplatin	404	397	387	335	140



No at risk

Control	404	389	373	322	129
Carboplatin	404	397	388	339	143



No at risk

Control	404	399	385	335	133
Carboplatin	404	404	397	345	144

L'ajout de carboplatine augmente la survie sans maladie, sans métastase et globale

Liu et al. SABCS 2025/*BMJ décembre 2025*

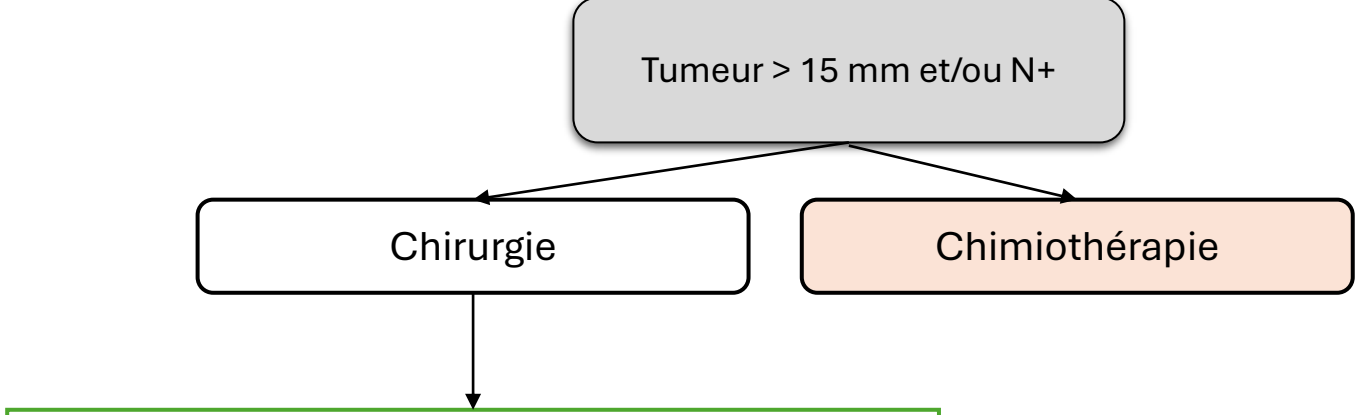
TAKE HOME MESSAGE

Tumeur < 15 mm N0

Chirurgie

Pas de capécitabine
Pas d'olaparib
Pas de pembrolizumab
(patientes exclus ou trop faible effectif : KN522, OlympiA, CREATE-X)

Carboplatine, un nouveau standard si facteur de risque ? (grade 3, Ki67 > 20%, N1 fortuit)



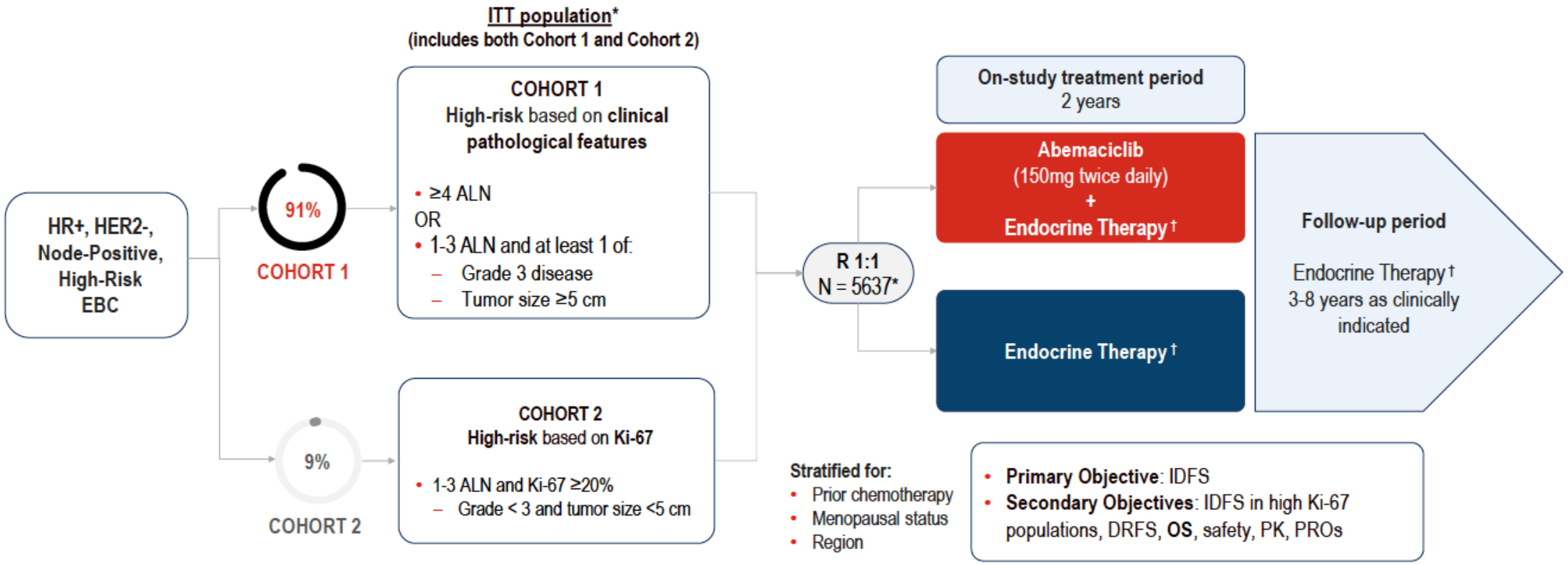
En fonction de l'âge, des comorbidités…

Carboplatine, un nouveau standard si facteur de risque ?
T1 avec grade 3, Ki67 > 20%
T2
N1

Si mutation *gBRCA* : olaparib → T2 et N1

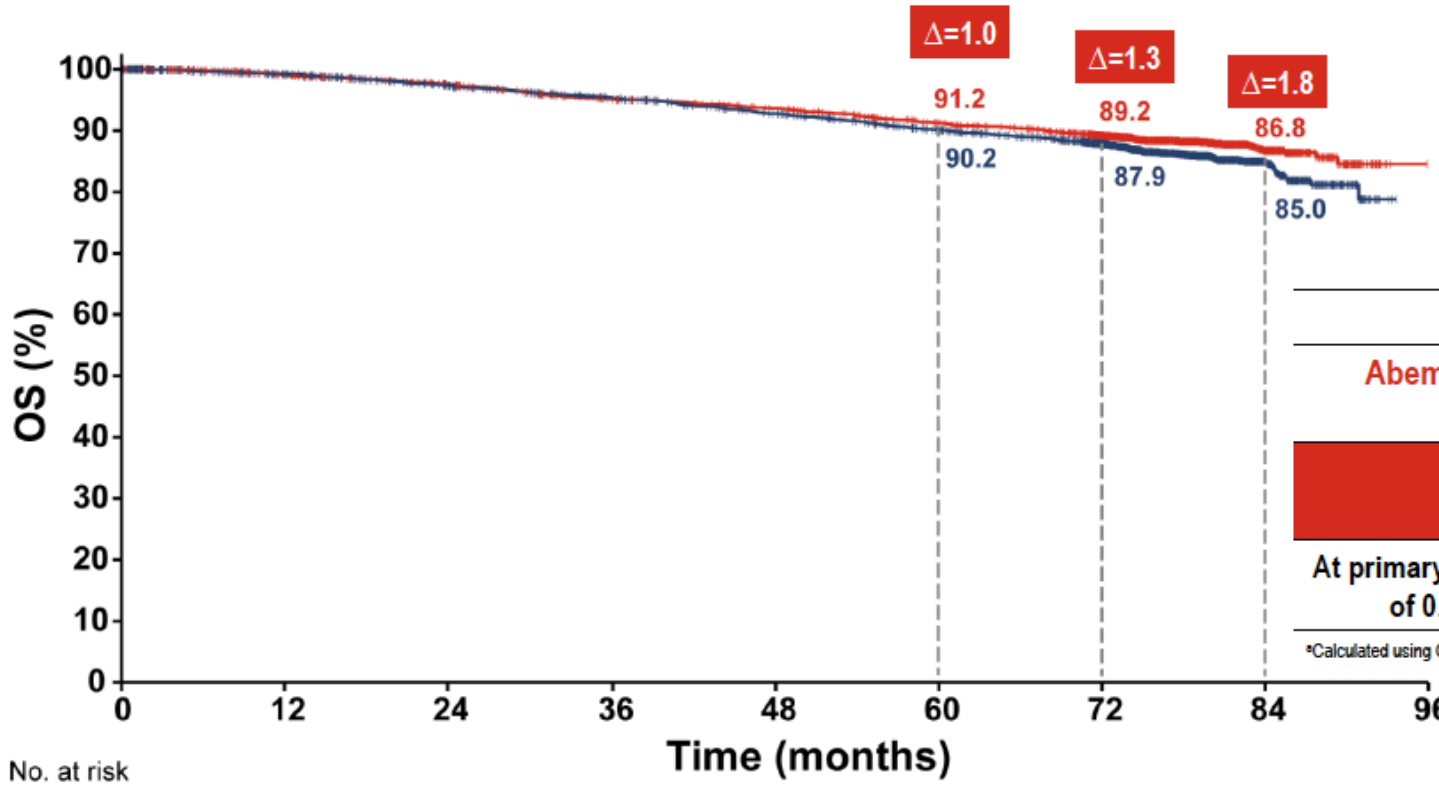
Cancers RH+

monarchE Trial Design (NCT03155997)



*Recruitment from July 2017 to August 2019. †Endocrine therapy of physician's choice (e.g. AI, Tamoxifen, GnRH). Data for the monarchE Cohort 1 population that forms the basis of multiple global approvals is in the supplement.
AI: aromatase inhibitor; ALN: axillary lymph nodes; DRFS: distant relapse-free survival; EBC: Early Breast Cancer; GnRH: gonadotropin-releasing hormone; HER2-: human epidermal growth factor receptor 2 negative; HR+: hormone receptor positive; IDFS: invasive disease-free survival; ITT: Intent-to-treat population; OS: overall survival; PK: pharmacokinetics; PRO: patient-reported outcome; R: randomized.

Key Secondary Endpoint: Overall Survival in ITT



Number of OS events	
Abemaciclib + ET	ET
301	360

HR (95% CI): 0.842 (0.722, 0.981)
P=0.0273

At primary OS testing, OS in ITT met the critical boundary of 0.0434 (2-sided)[a] for statistical significance

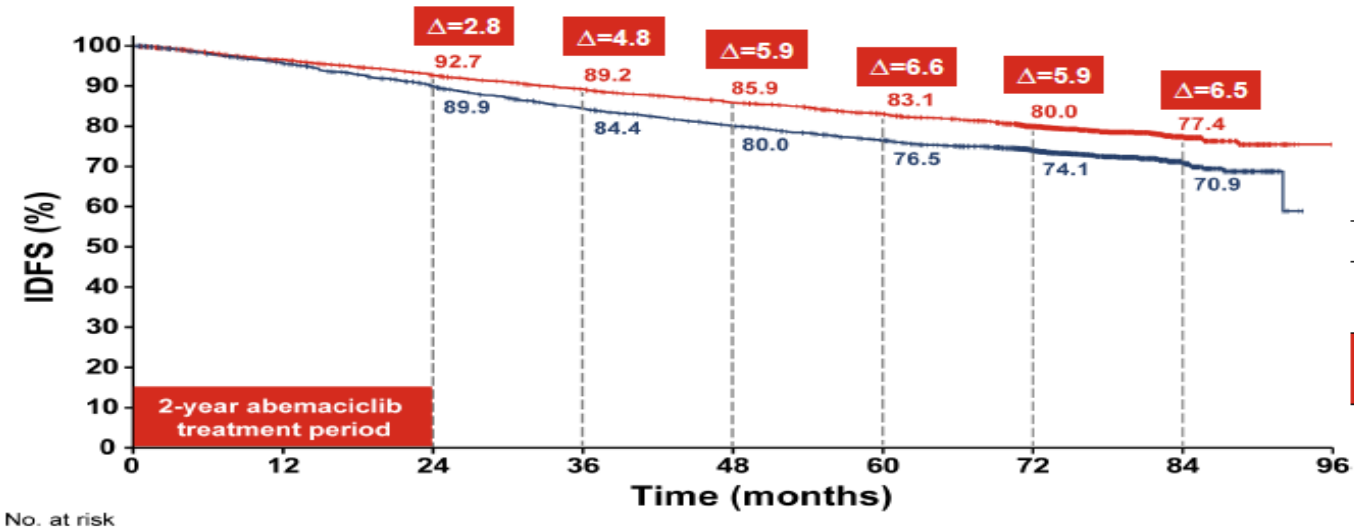
[a]Calculated using O'Brien-Fleming type stopping boundary based on the observed number of events

At a median follow-up of 6.3 years, abemaciclib + ET reduced the risk of death by 15.8% compared to ET alone

Stephen Johnston, MD, PhD

Effet carry-over au fil du temps

Sustained IDFS Benefit in ITT: Evolution of Yearly Rates



No. at risk

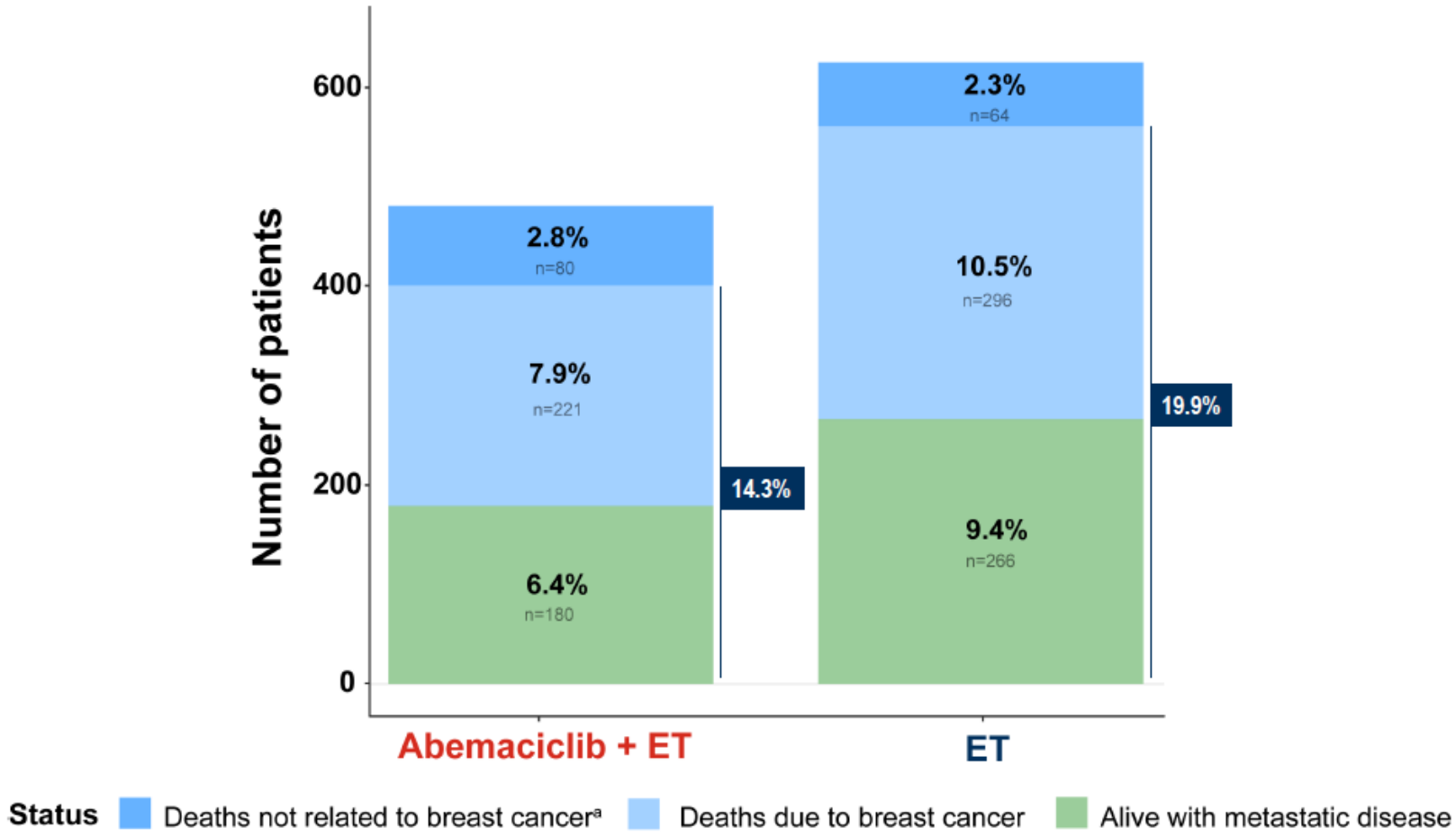
Abemaciclib + ET	2808	2549	2406	2285	2173	2056	1763	369	0
ET	2829	2573	2374	2193	2057	1923	1621	363	0

Number of IDFS events	
Abemaciclib + ET	ET
547	722

HR (95% CI): 0.734 (0.657, 0.820)
Nominal *P*<.0001

Abemaciclib + ET reduced the risk of IDFS events by 26.6% compared to ET alone

~30% Fewer Patients in Abemaciclib Arm Living with Metastatic Disease



Percentages based on ITT populations (abemaciclib + ET, N=2808; ET, N=2829). [a]Deaths due to AEs and due to unknown cause.

Stephen Johnston, MD, PhD

Systemic Anticancer Therapy in First-Line Metastatic Setting

Patients with distant recurrence who entered post 2-yr treatment follow-up[a]	Abemaciclib + ET n=407	ET n=565
Any first systemic therapy[b], %	**78.9**	**83.4**
Chemotherapy	**32.7**	**23.7**
ET[c]	46.7	58.4
Targeted therapy	33.2	48.8
CDK4/6i	**30.0**	**47.3**
PI3K/AKT/mTORi	3.2	0.7
Other[d]	5.2	4.8
No systemic therapy documented[e]	21.1	16.6

Subgroups based on time to distant recurrence	Early recurrence[f] n=191	Later recurrence[g] n=216	Early recurrence[f] n=313	Later recurrence[g] n=252
Any systemic therapy, %	**83.2**	**75.0**	**85.3**	**81.0**
Chemotherapy	**43.5**	**23.1**	**26.8**	**19.8**
ET[c]	44.0	49.1	59.1	57.5
Targeted therapy	19.9	44.9	46.3	52.0
CDK4/6i	**15.2**	**43.1**	**44.7**	**50.4**
No systemic therapy documented[e]	16.8	25.0	14.7	19.0

Difference in CDK4/6 inhibitors and chemotherapy use between arms primarily observed in early recurrences, with a less pronounced difference in later recurrences

[a]14 patients in abemaciclib + ET arm versus 17 patients in ET arm did not enter follow up after documentation of distant recurrence; [b]Includes systemic therapies which were started after distant recurrence as first-line metastatic setting; [c]Monotherapy and in combination; [d]Antibody drug conjugates excluded as did not meet 2% threshold; [e]Data collection ongoing. Reasons reported for no new systemic therapy captured post-distant recurrence include recent progression with information pending on subsequent therapy, lost to follow-up and rapid deterioration; [f]Distant recurrence on treatment or ≤1-year post-treatment; [g]Distant recurrence >1-year post-treatment.

Stephen Johnston, MD, PhD

TRADE: Design

- HR-positive, HER2-negative, early breast cancer
- Adjuvant abemaciclib is indicated based on patient risk/stage

Screening

N=90

Adjuvant Endocrine Therapy

Abemaciclib 50mg BID	Abemaciclib 100mg BID	Abemaciclib 150mg BID
Days 1 – 14	Days 15 – 28	> 28 Days

→ **Endocrine Therapy + up to 2 years Abemaciclib**

Intra-patient dose escalation requirements: Absence of ongoing grade 3/4 or persistent grade 2 toxicity

Supportive care, including anti-diarrhea medication, provided as needed

PRIMARY ENDPOINT:

- **Composite Adverse Event Rate**: Discontinuation of adjuvant abemaciclib for any reason and/or inability to reach or maintain target dose of 150 mg BID by 12 weeks of therapy

SECONDARY ENDPOINTS:

- Treatment-emergent adverse effects, discontinuation / hold rates, incidence of grade ≥2 diarrhea, quality of life, adherence, dose intensity, correlative science

STATISTICAL DESIGN:

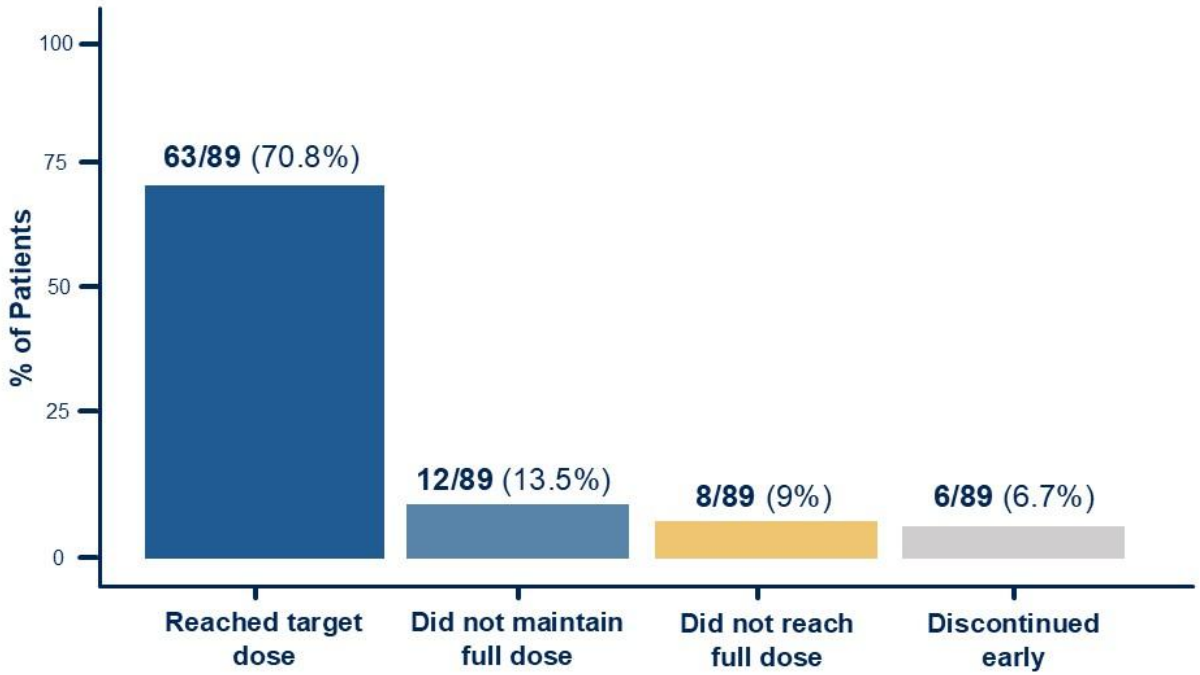
- **Experimental hypothesis**: **a dose-escalation schedule will significantly reduce the composite adverse event rate at 12 weeks from a baseline of 40%, based on monarchE**
- **Sample size**: 90 patients provides 92% power, against an alternative of 25%, with a 1-sided test at a significance level of 0.07, assuming drop-out rate of 10%

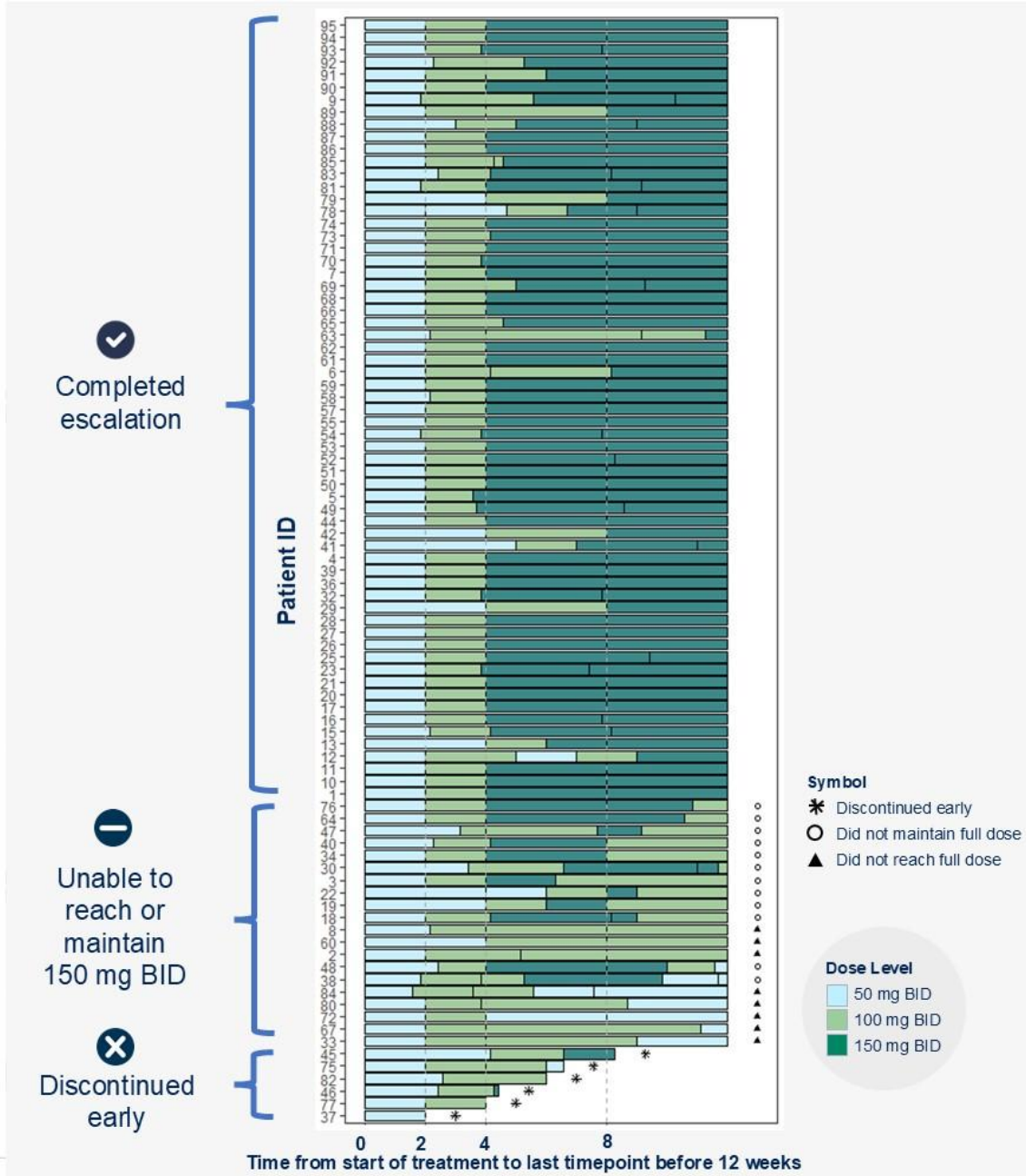
PRESENTED BY: Erica L. Mayer, MD, MPH

TRADE: Primary Results

Of 89 evaluable patients, 26 (29.2%; 90% CI [21.3-38.2]; p=0.046) **met the primary endpoint at 12 weeks:**

- 12 (13.5%) for inability to maintain target dose of 150 mg BID
- 8 (9.0%) for inability to reach 150 mg BID
- 6 (6.7%) for early discontinuation (3 [3.4%] for toxicity)





PRESENTED BY: Erica L. Mayer, MD, MPH

Futur ? En attente pour le ribociclib

Positive lymph nodes	Histological grade	Tumour size, cm		
		≤2	>2 and ≤5	>5
0	2		RIB (Ki-67 ≥20% or high genomic risk)	RIB
	3		RIB	RIB
1–3	1–2	RIB	RIB	RIB, ABE*
	3	RIB, ABE	RIB, ABE	RIB, ABE
≥4	Any	RIB, ABE	RIB, ABE	RIB, ABE

*Abemaciclib can be given if the tumour size is ≥5 cm.
ABE=abemaciclib; CDK=cyclin-dependent kinase; eBC=early breast cancer; Ki-67=antigen Kiel-67; RIB=ribociclib.
Slamon DJ, et al. *Ther Adv Med Oncol.* 2023;15:17588359231178125.

Chez une patiente porteuse de mutation gBRCA1/2, éligible à la fois à un traitement adjuvant par olaparib et par inhibiteurs de CDK4/6, il est acceptable de proposer un traitement par olaparib pendant un an suivi d'un traitement par inhibiteurs de CDK4/6, après évaluation en RCP du rapport bénéfice/risque et discussion avec la patiente

	D'accord	Pas d'accord	Abstention
Votes experts	87%	7%	7%
Votes participants	88%	10%	2%

Avis personnel : à discuter en RCP car risque de toxicités non évaluées – pas de données - PHRC demandée

Merci de votre attention