Institut de Cancérologie de l'Ouest

unicancer PAYS DE LA LOIRE

Faut-il rediscuter la place des hormonothérapies en prévention ?

SFSPM
07/11/2024

Pr Jean-Sebastien Frenel, Institut de Cancérologie de l'Ouest

CENTRE D'EXCELLENCE EUROPÉEN

OECI COMPREHENSIVE Cancer Centre

UN CENTRE D'EXCELLENCE

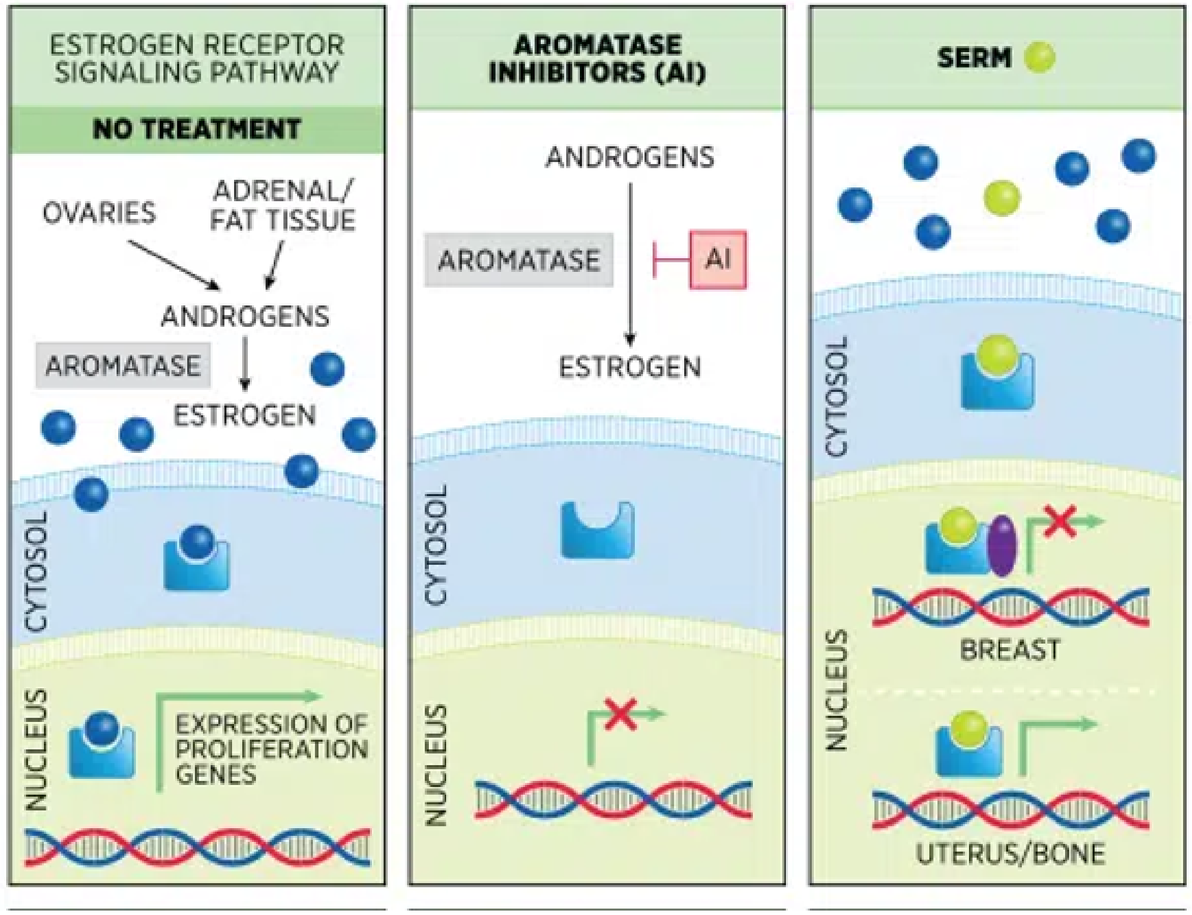
UN ACCÈS POUR TOUS

CONTEXTE ET OBJECTIFS

Quelle évidence?

Quelles perspectives à l'heure des nouvelles hormonothérapies et des nouveaux outils d'évaluation de risque?

QUELLES HORMONOTHERAPIES?



QUELLE EVIDENCE?

		POPULATION	N			IAL		PRINCIPAUX RESULTATS
TAM	**NSABP P1 (Fisher et al, 2005)**	≥60 ans ou 35–59 ans et risque à 5 ans: BC ≥ 1.66%(score de Gail) ou ATCD CLIS ou atypie	13388	Tamoxifene 20mg vs placebo	5 ans	IBC	7 ans	↓ risque de cancer invasif de 43% (RR: 0.57, 95% CI: 0.46–0.70). 42,5/1000 (placebo) versus 24,8 cas /1000 (tamoxifene) Significatif que pour les cancers RH+
	IBIS-I trial (Cuzick et al, 2015)	RRX2 de CS si âge 45–70 ans, RRX4 de CS si âge 40–44 ans, RRX10 de CS si âge 35–39 ans (Cuzick)	7154	Tamoxifene 20mg vs placebo	5 ans	IBC DCIS	7 ans	↓ risque de cancer invasif et DCIS de 29% (HR: 0·71, 95% CI: 0·60-0·83, p < 0·0001)
	Italian Randomized Tamoxifen Prevention Trial (Veronesi et al., 2007)	Toute femme ayant eu une hystérectomie	5408	Tamoxifene 20mg vs placebo	5 ans	IBC	16 ans	Pas de bénéfice dans la population globale Si haut risque (13%) : T>1.6 , au moins 1 ovaire intact, âge au1ere règle <14 ans, pas de grossesse avant l'âge de 24 ans ↓ risque CSI de 76% (RR: 0.24, 95% CI: 0.10–0.59).
	Royal Marsden trial (Powles et al., 2007)	1 ATCD de cancer du sein au 1 degré <50 ans ou bilatéral ou 2 ATCD famou 1 ATCD de biopsie benine+ 1 ATCD au 1er degré	2471	Tamoxifene 20mg vs placebo	8 ans	IBC	13 ans	Pas de bénéfice sauf ↓ risque de CSI ER+ de 39% (HR: 0.61, 95% CI: 0.43–0.86, p = 0.005).

QUELLE EVIDENCE?

RAL	**MORE trial (Cummings et al., 1999)**	Femmes ménopausées avec ostéoporose	7705	Raloxifene 120 m/j ou raloxifene 60 mg/j ou placebo	4 ans	Tx Fr IBC	3 ans	↓ risque de CSI de 76% (RR: 0.24, 95% CI: 0.13–0.44, p = 0.001) (qql soit le dosage) Significatif pour les ER+ (NS pour ER-)
	CORE trial (Martino et al, 2004)	Patientes de l'essai MORE	4011	Raloxifene 60 mg versus placebo	+ 4 ans	IBC	7.9 ans	↓ risque de CSI de 66% (HR: 0.34, 95% CI: 0.22–0.50) ER+IBC : 76% (HR: 0.24, 95% CI: 0.15– 0.40)
	RUTH trial (Barrett-Connor et al., 2006)	Femme ménopausée avec maladie coronarienne ou à risque de maladie coronarienne avec risque>1,66% (score degail)	10101	Raloxifene 60 mg versus placebo	5.5 ans	IBC	5.6 ans	↓ risque de CSI de 44% (HR: 0.56, 95% CI: 0.38–0.83).Réduction de 1,2 cancer pour 1 000 femmes traitées pendant 1 an.

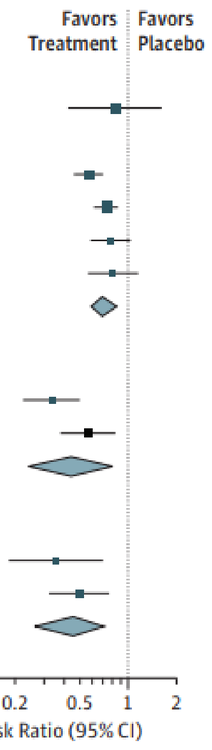
QUELLE EVIDENCE?

IA	**Exemestane** **MAP.3 trial** **(Goss et al.,2011)**	Femme ménopausée ≥ 35 ans et au moins un FdR: age ≥ 60 ans; risque 5 ans≥ 1.66%, ATCD atypie ou CLIS ou DCIS	4560	Exemestane 25 mg /j vs placebo	5 ans	IBC	3 ans	↓ du risque annuel de cancer du sein invasif de 65% (HR: 0.35, 95% CI: 0.18–0.70, p = 0.002)
	Anastrozole IBIS-II trial (Cuzick et al.,2020)	Femme ménopausée ≥ 45–60 ans avec RRX2 ou agée de 60–70 ans avec RRx 1·5 ou agée 40–44 ans avec RRx4	3864	Anastrozole 1 mg /j vs placebo	5 ans	IBC and DCIS		↓ risque de cancer du sein invasif et CCIS de 49% (HR 0·51, 95% CI 0·39- 0·66, p < 0·0001) ↓ risque de C invasif RH+ de 54% (HR0·46, 95% CI 0·33–0·65, p<0·0001) Pas de différence en SG

SYNTHESE DES RESULTATS ANCIENS

Figure 3. Risk Reduction of Invasive Breast Cancer: Meta-analysis of Primary Prevention Trials

Source	Trial	Mean, y: Intended Treatment Duration	Mean, y: Total Follow-up	No. With Invasive Breast Cancer/Total Participants (%): Treatment	No. With Invasive Breast Cancer/Total Participants (%): Placebo	Rate per 1000 Women-Years: Treatment	Rate per 1000 Women-Years: Placebo	Risk Ratio (95% CI)
Tamoxifen, low dose								
DeCensi et al,[41] 2013	HOT	5	6.2	18/938 (1.9)	22/946 (2.3)	3.13	3.78	0.83 (0.42-1.62)
Tamoxifen								
Fisher et al,[82] 2005	NSABP-1	5	6.1	145/6681 (2.2)	250/6707 (3.7)	3.59	6.29	0.57 (0.46-0.70)
Cuzick et al,[74] 2015	IBIS-I	5	16.0	214/3579 (6.0)	289/3575 (8.1)	3.86	5.29	0.73 (0.61-0.87)
Powles et al,[83] 2007	Marsden	5	13.2	82/1238 (6.6)	104/1233 (8.4)	4.80	6.10	0.78 (0.58-1.04)
Veronesi et al,[84] 2007	Italian	4[a]	11.2	53/2700 (2.0)	66/2708 (2.4)	1.77	2.21	0.80 (0.56-1.15)
Combined I^2 = 38.7%; Q = 4.9 for heterogeneity; P = .18								0.69 (0.59-0.84)
Raloxifene								
Martino et al,[45] 2004	MORE/CORE	4 or 8[b]	5.4[b]	40/5129 (0.8)	58/2576 (2.3)	1.40	4.20	0.34 (0.22-0.50)
Barrett-Connor et al,[48] 2006	RUTH	5.1[a]	5.6	40/5044 (0.8)	70/5057 (1.4)	1.43	2.49	0.56 (0.38-0.83)
Combined I^2 = 66.4%; Q = 3.0 for heterogeneity; P = .08								0.44 (0.24-0.80)
Aromatase inhibitor								
Goss et al,[44] 2011	MAP.3	5[c]	2.9	11/2285 (0.5)	32/2275 (1.4)	1.66	4.85	0.35 (0.18-0.70)
Cuzick et al,[4] 2014	IBIS-II	5	5	32/1920 (1.7)	64/1944 (3.3)	3.29	6.62	0.50 (0.32-0.76)
Combined I^2 = 0.0%; Q = 0.8 for heterogeneity; P = .39								0.45 (0.26-0.70)



US Preventive Services Task Force JAMA 2019

SYNTHESE DES RESULTATS ANCIENS

Table. Benefits and Harms of Risk-Reducing Medications Estimated From Meta-analysis of Randomized, Placebo-Controlled Trials[a,b]

Outcome	Tamoxifen	Raloxifene	Aromatase Inhibitors
Benefits: Events Reduced (95% CI)[c]			
Breast cancer			
Invasive	7 (4-12)	9 (3-15)	16 (8-24)
ER+	8 (4-13)	8 (4-13)	15 (8-20)
ER−	ND	ND	ND
Noninvasive	ND	ND	ND
Mortality			
Breast cancer	ND	NR	NR
All-cause	ND	ND	ND
Fracture			
Vertebral	ND	7 (5-9)	ND
Nonvertebral	3 (0.2-5)	ND	ND
Harms: Events Increased (95% CI)[c]			
Vascular			
Venous thromboembolic event	5 (2-9)	7 (0.3-17)	ND
Deep vein thrombosis	ND	ND	NR
Pulmonary embolism	ND	ND	NR
Coronary heart disease events	ND	ND	ND
Other			
Endometrial cancer	4 (1-8)	ND	ND
Cataracts	26 (5-50)[d]	ND	ND

Abbreviations: ER−, estrogen receptor–negative; ER+, estrogen receptor–positive; ND, no difference; NR, not reported.

[a] See Nelson et al.[3,4]

[b] Trials included women whose 5-year risk of breast cancer may have been lower than 3%.

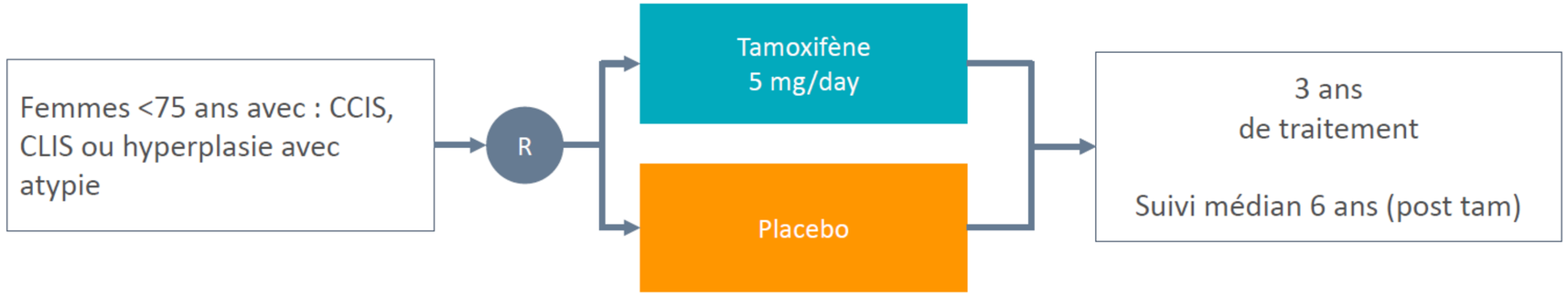
[c] Per 1000 women over 5 years of use.

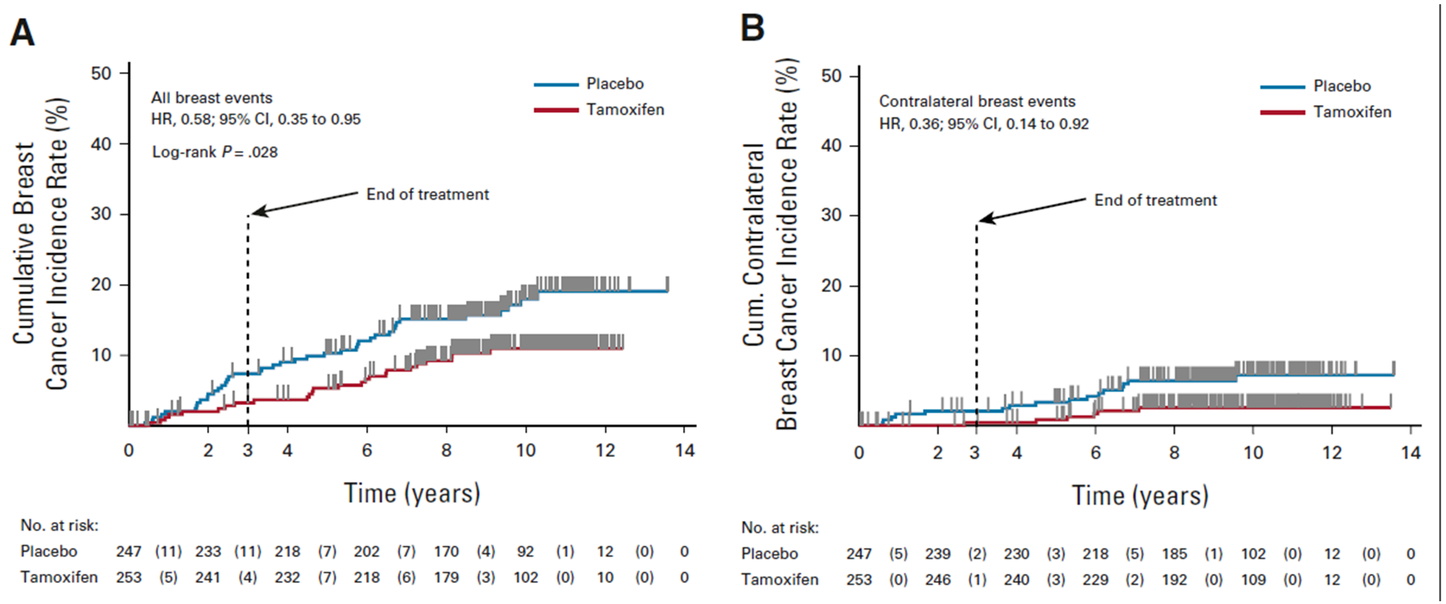
[d] Results from the National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene (STAR) trial.

US Preventive Services Task Force JAMA 2019

DONNEES RECENTES: BABY TAM

Effet intéressant avec une excellente tolérance (mais: 70% intracanalaire et 30% de lésions atypiques)





US Preventive Services Task Force JAMA 2019

Lazzeroni et al J Clin Oncol 2023

DONNEES RECENTES: LIBER

Background:

- Women with germline BRCA1/2 mutations (BRCAm) have a 70% lifetime-risk of breast cancer (BC)
- Hormone prevention by aromatase inhibitors (AI) is effective in high-risk patients, including those with familial risk
- Hormone prevention has not been specifically addressed in women carrying a BRCAm

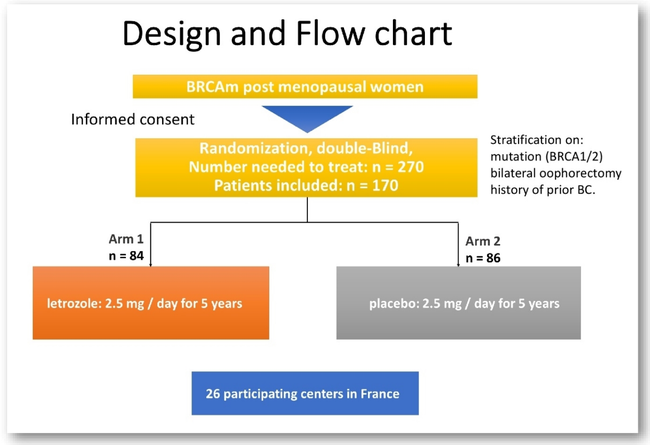
Objective:

Evaluate the preventive effect of letrozole in postmenopausal BRCAm women

- Primary endpoint: 5-years invasive BC-free survival (BC-FS).
- Secondary endpoints: Toxicity (CTCAE V3.0), Safety including Quality of Life (QoL, menopause rating scale, SF36) and bone mineral density (BMD).

Methods:

- Double blind randomized phase III trial, NCT: 00673335
- Eligible women: aged 40-70, postmenopausal or oophorectomized, BRCA1/2 germline m, No BC or prior unilateral BC > 5 years ago: included from 05/2008 to 08/2013
- Surveillance include : Annual breast MRI and mammogram, baseline and longitudinal clinical and bloods parameters, QOL, questionnaire, BMD.

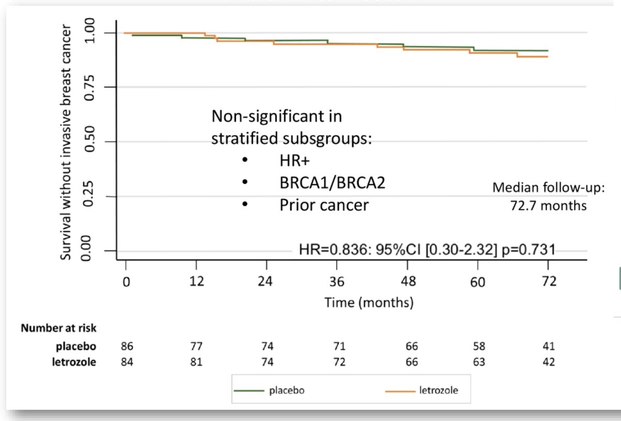


Results:

Patients characteristics

	Placebo arm N = 86	Letrozole arm N = 84	p
Age median [range]	54.5 [40-70]	55.0 [41-70]	NS
BRCA1 n(%)	52 (60)	48 (57)	NS
BRCA2 n(%)	34 (40)	35 (32)	NS
Prior Cancer n(%)	41 (48)	36 (43)	NS
Oophorectomy n(%)	79 (92)	75 (89)	NS

Breast cancer-free survival



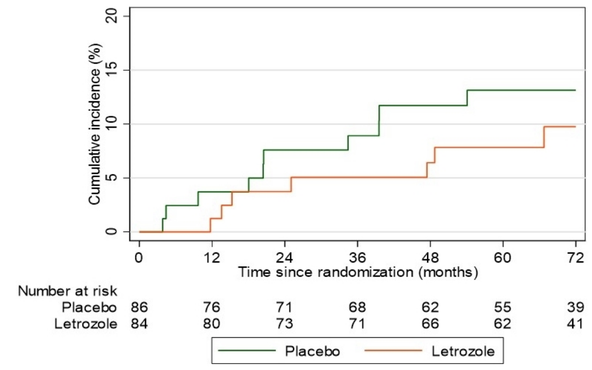
Compliance and adverse effects

	Placebo arm N = 86	letrozole arm N = 84	p
Treatment Stoped prematurely n(%)	37 (43)	35 (42)	NS
Serious adverse event	37	23	0.05
number of patients with at least one event			
No	56 (65)	66 (79)	
Yes	30 (35)	18 (21)	
Bone density (Spine/Hip)			
inclusion med	-0.9 / -0.7	-0.9 / -0.8	NS
12 months med	-0.8 / -0.9	-1.3 / -1.1	NS
60 months med	-1.2 / -1.1	- 1.6 / -1.1	NS

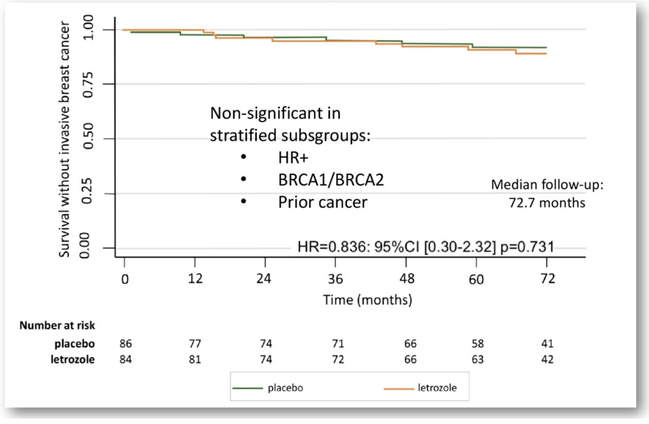
Quality of Life	Placebo arm N = 86	letrozole arm N = 84	p
Hot flashes			
Baseline n (missing)*	80 (0)*	80 (5)*	
I n(%)	66 (83.5)	60 (80)	NS
II n(%)	14 (17.5)	15 (20)	NS
6 months n	62 (2)*	74 (1)*	
I n(%)	49 (82)	64 (88)	NS
II n(%)	11 (18)	9 (12)	NS
24 months n	53 (2)*	61(1)*	
I n(%)	40 (78)	54 (90)	NS
II n(%)	11 (22)	6 (10)	NS
Atralgia			
Baseline n (missing)*	80 (1)*	80 (4)*	
I n(%)	70 (89)	68 (90)	NS
II n(%)	9 (11)	8 (10)	NS
6 months n	62 (3)*	74 (7)*	
I n(%)	49 (83)	54 (81)	NS
II n(%)	10 (17)	13 (19)	NS
24 months n	53 (5)*	61 (2)*	
I n(%)	37 (77)	42 (71)	NS
II n(%)	11 (23)	17 (29)	NS

I: None, Light, Moderate; II: Strong, Very strong

- 5-year incidence of invasive BC 13.1% with placebo vs 7.8% with letrozole. HR 0.70 (95% CI, 0.29 to 1.66), *P* = .416.
- Trial acceptability < 20%
- 5 year compliance: 58% in both arms



Breast cancer-free survival



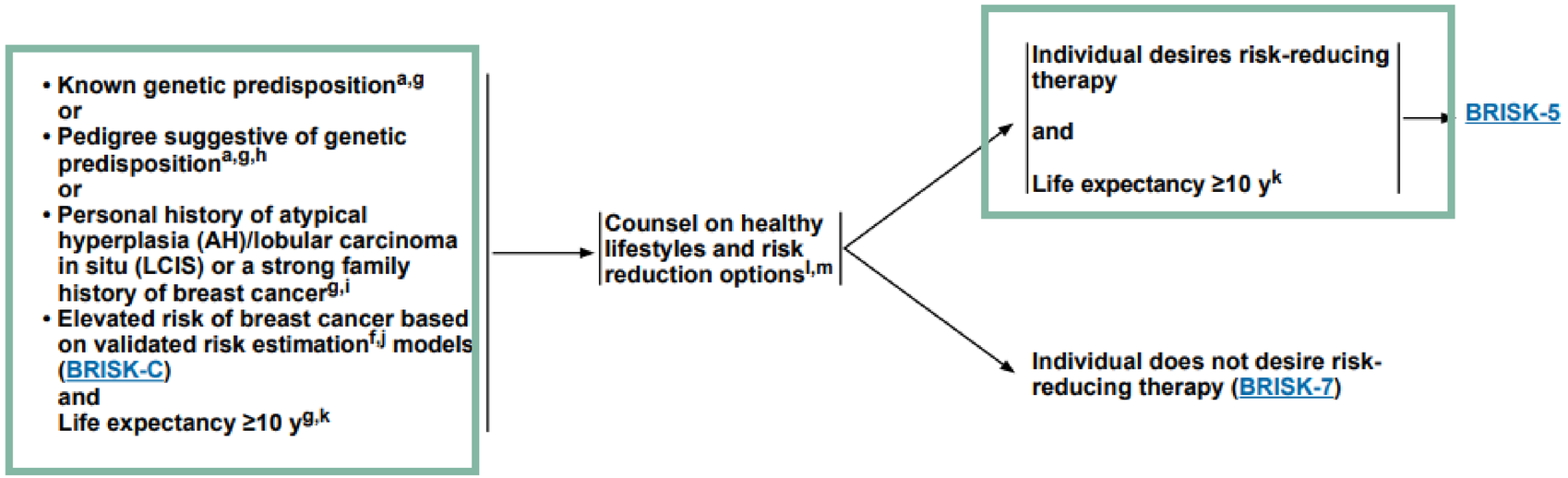
QUE NOUS DISENT LES GUIDELINES? NCCN

BREAST CANCER RISK-REDUCING AGENTS

Tamoxifen[a,b,c]	Raloxifene[a,b]	Aromatase Inhibitors (exemestane and anastrozole)
• Data regarding tamoxifen risk reduction are limited to pre- and postmenopausal individuals ≥35 years of age with a Gail Model 5-year breast cancer risk of ≥1.7% or a 10-year risk by IBIS/ Tyrer-Cuzick[e] of ≥5% or a history of LCIS. • Tamoxifen: 20 mg per day for 5 years was shown to reduce risk of breast cancer by 49%. Among individuals with a history of AH, this dose and duration of tamoxifen were associated with an 86% reduction in breast cancer risk. Low-dose tamoxifen (5 mg per day or 10 mg every other day for 3–5 years)[d] is an option if patient is symptomatic on the 20-mg dose or if patient is unwilling or unable to take standard-dose 20 mg per day tamoxifen.[1] This low dosage needs further investigation in premenopausal individuals. • The efficacy of tamoxifen risk reduction in individuals who are carriers of *BRCA1/2* and other pathogenic mutations is less well studied than in other risk groups. Limited data suggest there may be a benefit, likely a larger benefit, for *BRCA2* carriers. • For healthy, premenopausal individuals at elevated risk for breast cancer, data regarding the risk/benefit ratio for tamoxifen appear relatively favorable (category 1). • For postmenopausal individuals at elevated risk for breast cancer, data regarding the risk/ benefit ratio for tamoxifen are influenced by age, presence of uterus, or comorbid conditions (category 1). There are insufficient data on ethnicity and race.	• Data regarding raloxifene risk reduction are limited to postmenopausal individuals ≥35 years of age with a Gail Model 5-year breast cancer risk ≥1.7% or a 10-year risk by IBIS/Tyrer-Cuzick[e] of ≥5% or a history of LCIS. • Raloxifene: 60 mg per day was found to be equivalent to tamoxifen for breast cancer risk reduction in the initial comparison. While raloxifene in long-term follow-up appears to be less efficacious in risk reduction than tamoxifen, consideration of toxicity may still lead to the choice of raloxifene over tamoxifen in individuals with an intact uterus. • There are no data regarding the use of raloxifene in individuals who are carriers of *BRCA1/2* and other pathogenic mutations or who have had prior thoracic radiation. • For postmenopausal individuals at elevated risk for breast cancer, data regarding the risk/benefit ratio for raloxifene are influenced by age or comorbid conditions (category 1). There are insufficient data on ethnicity and race. • Use of raloxifene for breast cancer risk reduction in premenopausal individuals is inappropriate unless part of a clinical trial.	• Data regarding exemestane are from a single large randomized study limited to postmenopausal individuals ≥35 years of age with a Gail Model 5-year breast cancer risk ≥1.7% or a 10-year risk by IBIS/Tyrer-Cuzick[e] of ≥5% or a history of LCIS. • Data regarding anastrozole are from a single large randomized study limited to postmenopausal individuals 40 to 70 years of age with the following risk compared with the general population: ▸ Aged 40 to 44 years - 4 times higher ▸ Aged 45 to 60 years - ≥2 times higher ▸ Aged 60 to 70 years - ≥1.5 times higher Individuals who did not meet these criteria but had a Tyrer-Cuzick[e] model 10-year breast cancer risk >5% were also included. • Exemestane: 25 mg per day was found to reduce the relative incidence of invasive breast cancer by 65% from 0.55% to 0.19% with a median follow-up of 3 years. • Anastrozole: 1 mg per day was found to reduce the relative incidence of breast cancer by 53% with a median follow-up of 5 years. • There are retrospective data that aromatase inhibitors can reduce the risk of contralateral breast cancer in *BRCA1/2* patients with ER-positive breast cancer who take aromatase inhibitors as adjuvant agents. • For postmenopausal individuals at elevated risk for breast cancer, data regarding the risk/benefit ratio for aromatase inhibitor agents are influenced by age and comorbid conditions such as osteoporosis (category 1). There are insufficient data on ethnicity and race. • Use of aromatase inhibitors for breast cancer risk reduction in premenopausal individuals is inappropriate unless part of a clinical trial.

Footnotes and references on BRISK-B 2 of 2

QUE NOUS DISENT LES GUIDELINES? NCCN

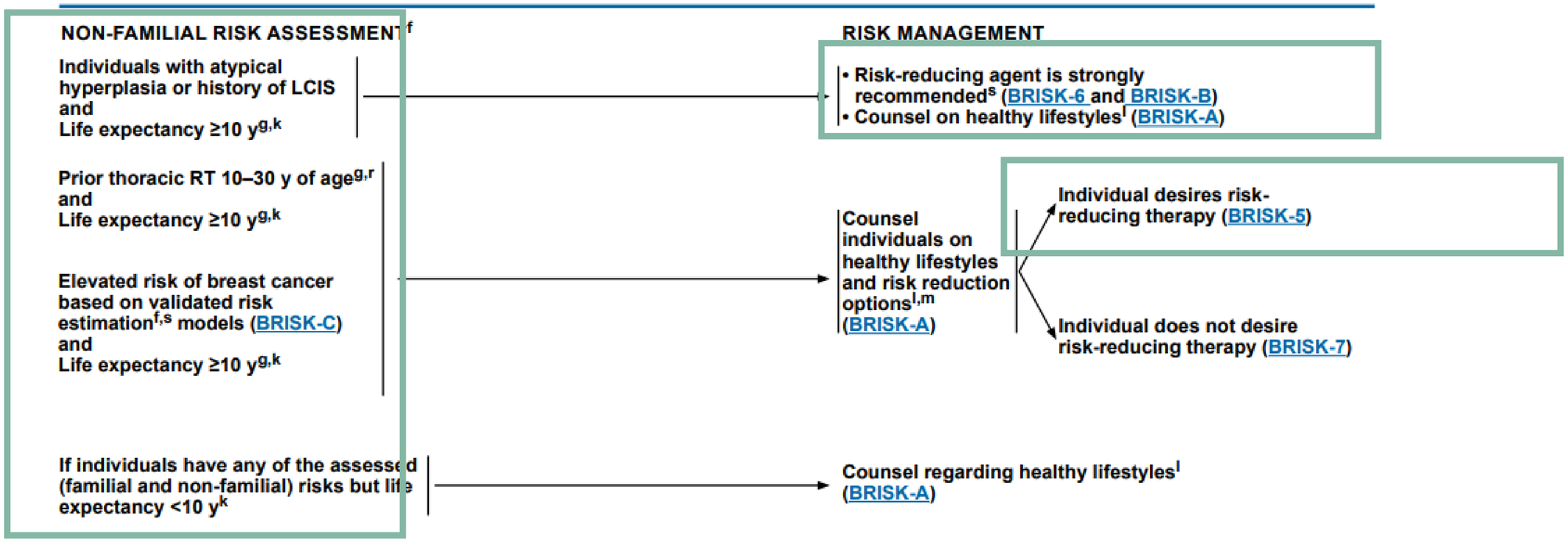


[a] NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.
[f] The routine use of polygenic risk scores (PRS) in breast cancer risk assessment is discouraged. Further validation is required to understand interaction of single nucleotide polymorphisms (SNPs) with environmental or hormonal risk factors and disease subtype in diverse populations. Ongoing research will shed light on utility of PRS in comprehensive risk assessment models to guide personalized therapy.
[g] In patients with at least one intact breast for whom risk-reducing therapy is recommended.
[h] Individual meets one or more of the familial risk criteria (BRISK-1).
[i] For risk models that are largely dependent on family history (eg, Tyrer-Cuzick, BRCAPro, CanRisk/BOADICEA), see Comparison of Risk Assessment Models (BRISK-C). For breast cancer screening recommendations, see NCCN Guidelines for Breast Cancer Screening and Diagnosis.
[j] A change in family history, or a recent breast biopsy, would affect risk estimate and should prompt re-calculation of breast cancer risk. Consider periodic re-calculation of risk as individual ages.
[k] See life expectancy calculator (www.eprognosis.com). For a reference point, the life expectancy of the average 78-year-old patient assigned female at birth (AFAB) in the United States is 10.2 years. See NCCN Guidelines for Older Adult Oncology.
[l] Components of Risk/Benefit Assessment and Counseling (BRISK-A).
[m] See BRISK-B for risk reduction agents and details on dosing.

Note: All recommendations are category 2A unless otherwise indicated.

BRISK-2

QUE NOUS DISENT LES GUIDELINES? NCCN



[f] The routine use of PRS in breast cancer risk assessment is discouraged. Further validation is required to understand interaction of SNPs with environmental or hormonal risk factors and disease subtype in diverse populations. Ongoing research will shed light on utility of PRS in comprehensive risk assessment models to guide personalized therapy.
[g] In patients with at least one intact breast for whom risk-reducing therapy is recommended.
[k] See life expectancy calculator (www.eprognosis.com). For a reference point, the life expectancy of the average 78-year-old patient AFAB in the United States is 10.2 years (NCCN Guidelines for Older Adult Oncology).
[l] Components of Risk/Benefit Assessment and Counseling (BRISK-A).
[m] See BRISK-B for risk reduction agents and details on dosing.
[r] These individuals are at a significantly elevated risk for breast cancer and risk reduction options should be strongly considered. Bhatia S, et al. Clin Cancer Res 2021;27:967-974.
[s] Individuals with AH have an 86% reduction in risk with an endocrine agent. LCIS has a >50% reduction in risk with an endocrine agent. Risk-reducing endocrine agents should be strongly recommended for individuals with AH and LCIS (for risk-reducing endocrine therapy agent options, see BRISK-6).

Note: All recommendations are category 2A unless otherwise indicated.

BRISK-4

QUE NOUS DISENT LES GUIDELINES? NCCN

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2025
Breast Cancer Risk Reduction

NCCN Guidelines Index
Table of Contents
Discussion

RISK-REDUCING AGENT

Premenopausal[y] → **Clinical trial[z]** or **Tamoxifen[m,y] (category 1)[aa]**

Postmenopausal[u,y] → **Clinical trial[z]** or **Tamoxifen[m,z] (category 1)[aa]** or **Raloxifene[m] (category 1)[aa]** or **Aromatase inhibitors[m] (category 1)[aa]**

SURVEILLANCE

- Surveillance according to NCCN Guidelines for Breast Cancer Screening and Diagnosis for those at increased risk for breast cancer
- Routine age-appropriate gynecologic screening (for individuals with intact uterus on tamoxifen)[bb]
- Ophthalmology exam if cataracts or vision problems
- For management while on endocrine agent, see BRISK-8
- Monitor bone density while on aromatase inhibitors

QUE NOUS DISENT LES GUIDELINES? ESMO

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO Clinical Practice Guideline☆

C. Sessa[1], J. Balmaña[2], S. L. Bober[3], M. J. Cardoso[4], N. Colombo[5,6], G. Curigliano[7,8], S. M. Domchek[9], D. G. Evans[10,11], D. Fischerova[12], N. Harbeck[13], C. Kuhl[14], B. Lemley[15,16], E. Levy-Lahad[17], M. Lambertini[18,19], J. A. Ledermann[20], S. Loibl[21], K.-A. Phillips[22] & S. Paluch-Shimon[23], on behalf of the ESMO Guidelines Committee*

BRCA1/2 PV carriers is less clear.[34,37,38] Although alcohol is associated with increased risk for breast cancer in the general population,[39] studies have not demonstrated a clear association for *BRCA1/2* PV carriers.[34,40]

Recommendations

- Physical exercise most days at moderate or strenuous intensity should be encouraged if appropriate (more is better); avoid being overweight or obese and encourage breastfeeding [B].
- Minimise alcohol intake [C].
- Decisions about hormonal contraception should weigh the possible increase in breast cancer risk against contraceptive efficacy, convenience and reduction in risk of ovarian cancer [C].

Risk-reducing medication

RRMed is an option for women who postpone, or do not undergo, elective bilateral RRM (BRRM). In randomised placebo-controlled trials for women with an elevated lifetime risk (LTR) of breast cancer (genetic status was only available in a very small subset of these women), the selective estrogen receptor modulators, tamoxifen and raloxifene, and the aromatase inhibitors, anastrozole and exemestane, reduced breast cancer incidence by ~30%-60%, especially estrogen receptor-positive disease. The absolute risk of serious side-effects was low, particularly for premenopausal women.[41] Five years of daily tamoxifen (20 mg) or anastrozole (1 mg) reduces risk for at least 20 and 10 years, respectively. Lower dose, shorter-duration tamoxifen is an option if the 20 mg dose is not tolerated. Tamoxifen is the only option for premenopausal women. Side-effect profiles should be considered when choosing between agents for postmenopausal women, including risks of thrombosis, endometrial cancer and osteoporosis.

Data pertaining specifically to women with PVs in germline predisposition genes are extremely limited. The underpowered LIBER trial showed no reduction in first breast cancers in carriers of *BRCA1/2* PVs randomised to letrozole versus placebo.[42] A subgroup analysis of the effect of tamoxifen for individuals with *BRCA1* and *BRCA2* in the NSABP-P1 trial was too small and thus uninterpretable.[43] Observational studies of tamoxifen and aromatase inhibitors for risk reduction of contralateral breast cancer have suggested benefits for carriers of both *BRCA1* and *BRCA2* PVs.[44] There are no data pertaining to PVs in other breast cancer predisposition genes.

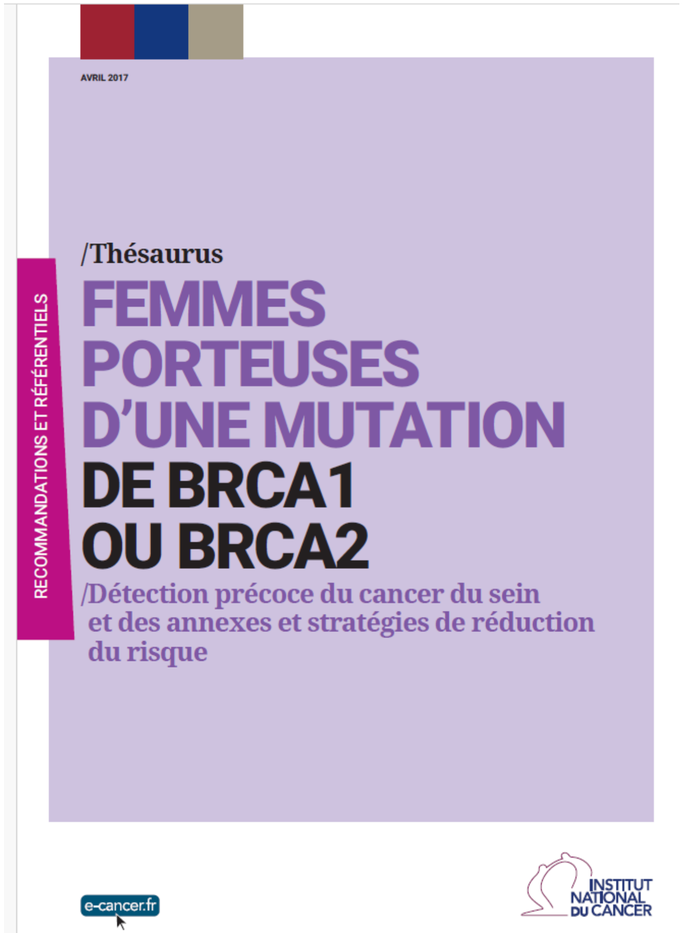
Recommendation

- RRMeds can be considered for primary risk reduction of breast cancer and risk reduction of contralateral disease in women who decline BRRM, or who have a risk level that does not warrant surgery [C].

Risk-reducing surgery

BRRM is the most effective method for reducing breast cancer risk among *BRCA1/2* PV carriers.[45] High-risk carriers

QUE NOUS DISENT LES GUIDELINES? INCA HAS



RECOMMANDATIONS

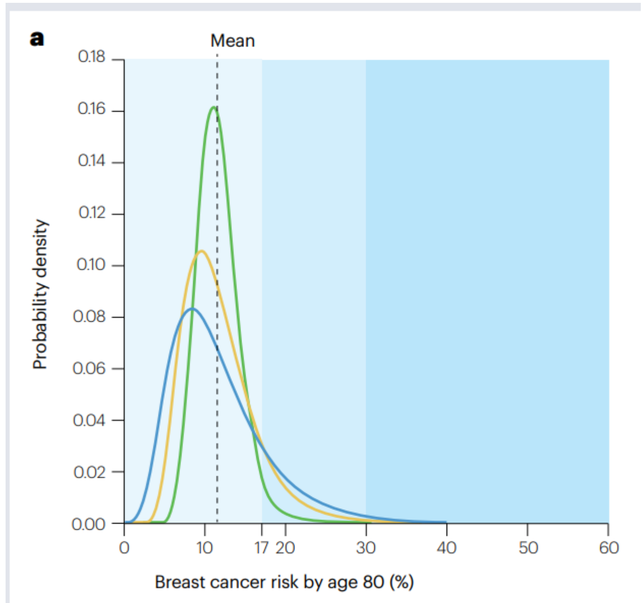
Hormonoprévention

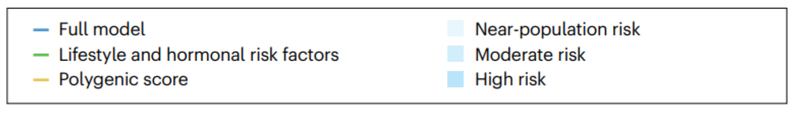
- Bien qu'il y ait des données avec un niveau de preuve élevé pour les femmes à haut risque de cancer du sein, il n'y a pas de données sur le bénéfice des SERM et des inhibiteurs de l'aromatase sur la réduction du risque de cancer du sein chez les femmes porteuses d'une mutation de BRCA1/2 et indemnes de cancer. Par conséquent, ces traitements hormonaux en prévention primaire du cancer du sein chez ces femmes doivent s'envisager dans le cadre d'essais cliniques.
- Pour les femmes porteuses d'une mutation de BRCA1/2 et atteintes d'un cancer du sein (avec ou sans récepteurs hormonaux) : les données disponibles ne concernent que les SERM et les inhibiteurs de l'aromatase administrés en situation adjuvante. Les utilisations de ces traitements hormonaux chez les femmes n'ayant pas reçu un traitement hormonal en situation adjuvante ne peuvent donc pas faire l'objet de recommandations faute de données.
- Les experts recommandent la mise en place et la poursuite d'études cliniques pour évaluer l'efficacité et préciser la balance bénéfice-risque à long terme de ces traitements hormonaux à visée préventive chez les femmes porteuses d'une mutation de BRCA1/2.

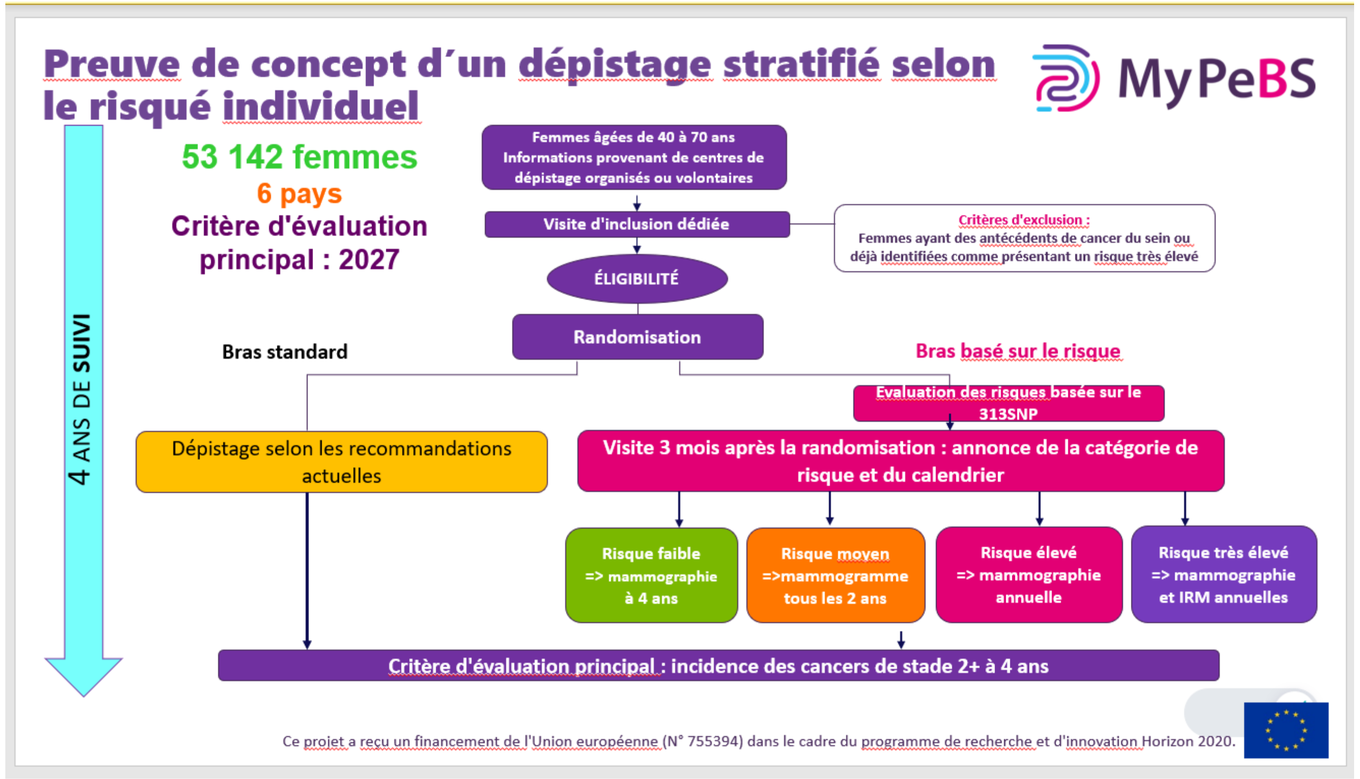
QUEL AVENIR?

DEPISTAGE DE PRECISION >> PREVENTION DE PRECISION?

313 SNP polygenic model

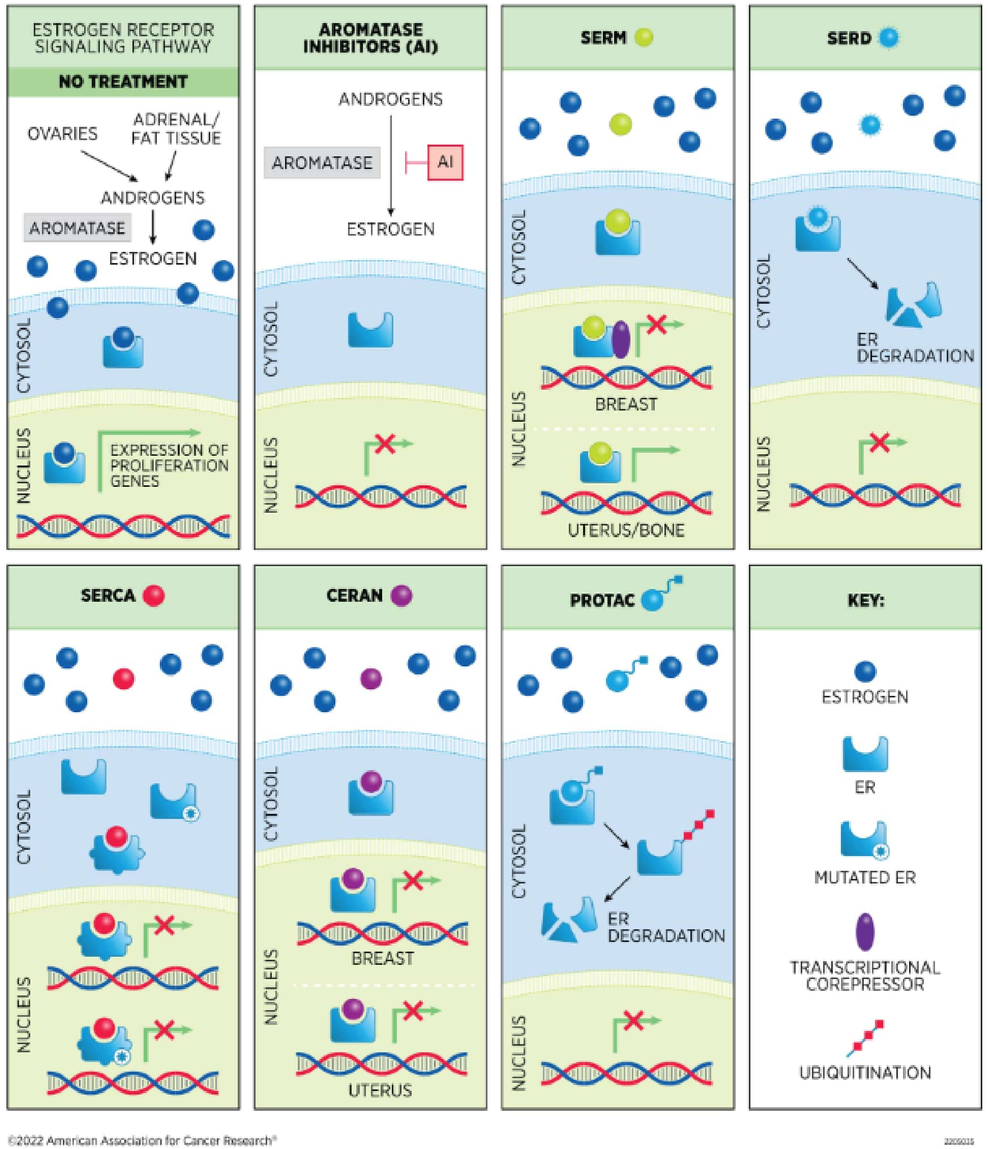




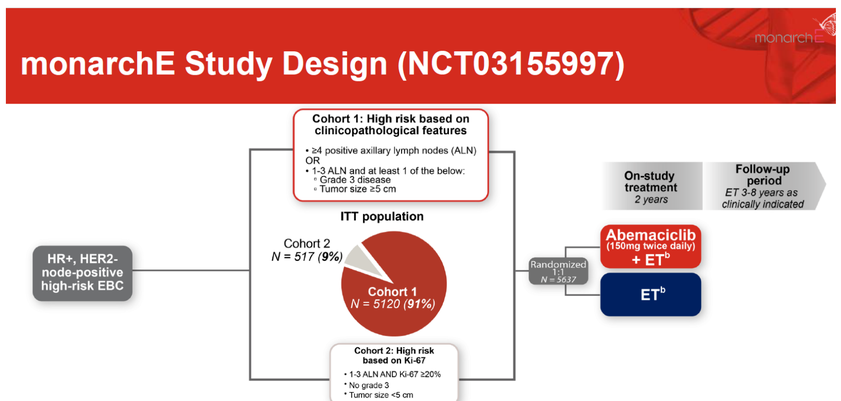


Yang, nature review cancer 2023

QUID NOUVEAUX TRAITEMENTS ANTI-HORMONAUX?



IMPACT HT + ICDK4/6? MONARCHE



Detailed study design previously described [Johnston SRD, et al. J Clin Oncol. 2020;38(34):3987-3998]

Cohort 2 recruitment started 1 year after Cohort 1

Abbreviations: ALN = positive axillary lymph nodes; ET = Endocrine Therapy; HER2 = human epidermal receptor 2; HR = hormone receptor; ITT = intent-to-treat population; N = number of patients in the ITT population; R = randomized; SOC = standard of care

Summary of IDFS events **ITT population**	**Abemaciclib + ET** **N=2808**	**ET alone** **N=2829**
Number of IDFS events, n (%)	336 (12·0)	499 (17·6)
Death without invasive disease	30 (1·1)	20 (0·7)
Invasive disease recurrence	306 (10·9)	479 (16·9)
Local/regional recurrence	48 (1·7)	76 (2·7)
Distant recurrence	225 (8·0)	364 (12·9)
Contralateral recurrence	9 (0·3)	14 (0·5)
Second primary neoplasm	29 (1·0)	38 (1·3)

Note: Tumour locations at the first occurrence were summarised in this table.

IMPACT HR + ICDK4/6? NATALEE

Table S5. Type and Site of First Invasive Disease-Free Survival Event[a]

	RIB + NSAI (N=2549) n (%)	NSAI Only (N=2552) n (%)
Type of first iDFS event		
Invasive IBTR	8 (0.3)	7 (0.3)
Local/regional invasive recurrence	19 (0.7)	35 (1.4)
Distant recurrence	120 (4.7)	170 (6.7)
Invasive contralateral breast cancer	7 (0.3)	9 (0.4)
Death	13 (0.5)	7 (0.3)
Primary cause of death adverse event	12 (0.5)	3 (0.1)
Primary cause of death disease recurrence/progression	1 (<0.1)	0
Primary cause of death other	0	4 (0.2)
Second primary non-breast invasive cancer	30 (1.2)	28 (1.1)
Site(s) of iDFS event recurrence (excluding death and second primary non-breast invasive cancer)		
Ipsilateral breast	8 (0.3)	6 (0.2)
Ipsilateral chest wall/skin	10 (0.4)	15 (0.6)
Ipsilateral axilla	4 (0.2)	7 (0.3)
Regional lymph nodes	9 (0.4)	17 (0.7)
Contralateral breast (with or without contralateral lymph nodes)	7 (0.3)	9 (0.4)
Bone	71 (2.8)	96 (3.8)
Liver	34 (1.3)	53 (2.1)
Lung/pleura	22 (0.9)	37 (1.4)
Central nervous system	11 (0.4)	16 (0.6)
Distant lymph nodes	17 (0.7)	23 (0.9)
Other	11 (0.4)	8 (0.3)

IBTR, ipsilateral breast tumor recurrence; iDFS, invasive disease-free survival; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.

[a] Patients may have multiple iDFS recurrence sites counted in the table but are only counted once per patient.

PARP inhibiteurs?

OLYMPIA TRIAL BREAST CANCER	Olaparib (N=921)	Placebo (N=915)
	no. of patients (%)	
Contralateral invasive breast cancer	15 (1.6)	18 (2.0)
Second primary malignancies	11 (1.2)	23 (2.5)
Second primary invasive non-breast ovarian/fallopian tube malignancy	2 (0.2)	10 (1.1)
Second primary invasive non-breast non-ovarian malignancies	9 (1.0)	13 (1.4)

SOLO1 TRIAL OVARIAN CANCER	Olaparib (N=260)	Placebo (N=131)
	no. of patients (%)	
Breast cancer events	1.2%	2.3%

Geyer et al Ann Oncol 2023, Moore et al New Engl J Med 2018

CONCLUSION

Des recommandations internationales variables

Pas de recommandation d'hormonoprévention en FRANCE

Avenir: Prévention de précision?