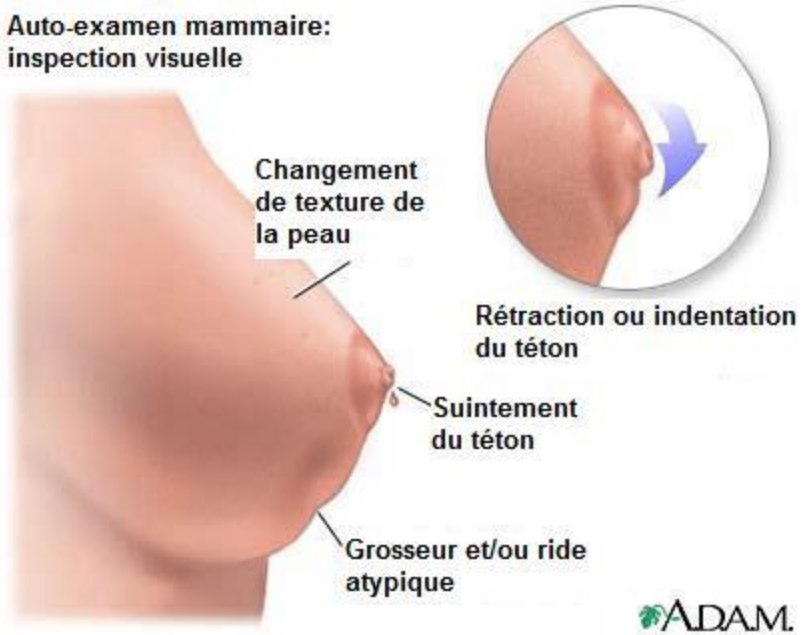
Génétique et cancer du sein

Marie Mailleux
24/03/2017

Cancer du sein

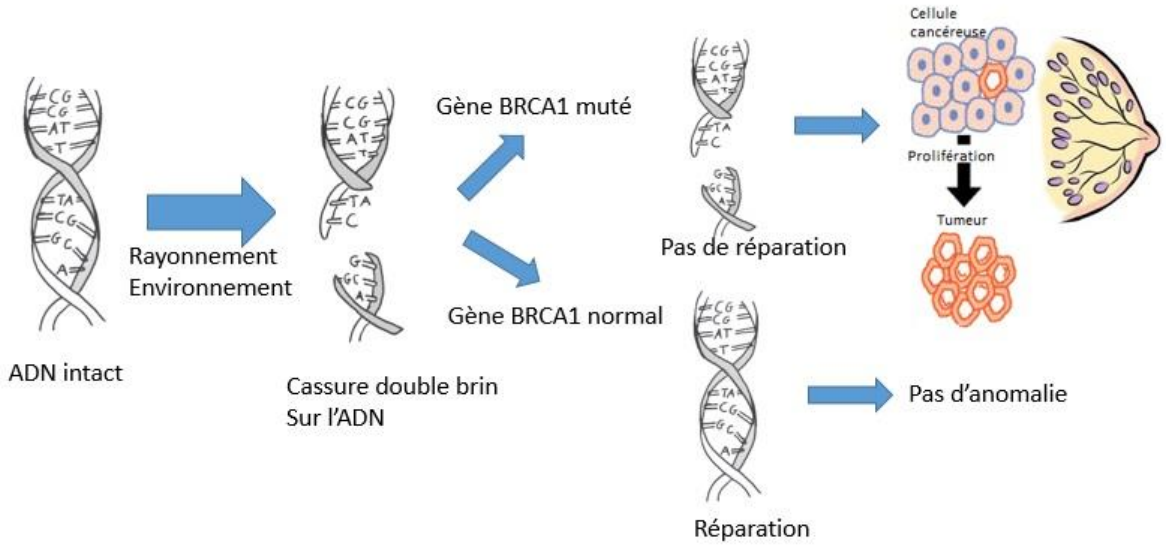
- 1 femme sur 8.
- 1er cancer féminin en terme de fréquence
- 1ère cause de décès féminin par cancer
- 5 à 10% héréditaires;

Mutations BRCA = 30% des familles à risque élevé de cancer du sein



Etiologie du cancer?

- Mutation dans certains gènes surtout ceux impliqués dans la régulation de la croissance cellulaire et/ou réparation de l'ADN.
- Mutation germinale → cancers héréditaires ou familiaux.
- Mutation sporadique



Introduction :

• Susceptibilité familiale pour le cancer du sein : <25% de tous les cas de cancers du sein. Dans > 70% des cas : pas de cause identifiée.
• Mutations BRCA1-2 : environ 20-30% des cas familiaux.
• Mutations germinales au niveau des gènes TP53, PTEN et SKT11 : <1% des familles de cancer du sein; association avec des syndromes rares (Li-Fraumeni, Cowden, syndrome de Peutz-Jeghers respectivement), avec autres caractéristiques (manifestations cutanéo-muqueuses dans le syndrome de Cowden, macrocéphalie et anomalie thyroïdienne dans le syndrome de Cowden).

Cas clinique 1

- Patiente de 54ans
- Cancer du sein bilatéral diagnostiqué en 09/06 : carcinome canalaire infiltrant SBRII de 19mm à droite (pT1cN0) et de grade SBRI de 9mm à gauche (pT1bN) → radiothérapie →hormonothérapie.
- 2 filles de 30 et 29 ans et un fils de 20 ans.
- Cancer du sein chez une tante paternelle âgée de 50 ans qui en est décédée à 60 ans → avis génétique

Mutations recherchées le + fréquemment :

- BRCA1
- BRCA2
- CHECK2
- PALB2
- …

Panel de 26 gènes impliqués dans les cancers héréditaires en particulier du sein recherché.

BREAST AND OVARIAN MANAGEMENT BASED ON GENETIC TEST RESULTS[a,b]

The inclusion of a gene on this table below does not imply the endorsement either for or against multi-gene testing for moderate-penetrance genes.

Gene	Breast Cancer Risk and Management	Ovarian Cancer Risk and Management	Other Cancer Risks and Management
ATM	**Increased risk of BC** • Screening: Annual mammogram and consider breast MRI with contrast starting at age 40 y[c] • RRM: Consider based on family history	**No increased risk of OC**	Unknown or insufficient evidence for pancreas or prostate cancer
	Comments: Insufficient evidence to recommend against radiation therapy. The 7271T>G missense mutation may act in a dominant–negative fashion, resulting in a lifetime breast cancer risk as high as 60% by age 80 (which is higher than truncating mutations, where risks are in the range of 30-40%). Counsel for risk of autosomal recessive condition in offspring.		
BRCA1	**Increased risk of BC** • See BRCA Mutation-Positive Management	**Increased risk of OC** • See BRCA Mutation-Positive Management	Prostate cancer • See BRCA Mutation-Positive Management
BRCA2	**Increased risk of BC** • See BRCA Mutation-Positive Management	**Increased risk of OC** • See BRCA Mutation-Positive Management	Pancreas, Prostate, Melanoma • See BRCA Mutation-Positive Management
BRIP1	**No increased risk of BC**	**Increased risk of OC** • Consider RRSO at 45–50 y	N/A
	Comments: Counsel for risk of autosomal recessive condition in offspring. Based on estimates from available studies, the lifetime risk of ovarian cancer in carriers of mutations in *BRIP1* appears to be sufficient to justify consideration of risk-reducing salpingo-oophorectomy. The current evidence is insufficient to make a firm recommendation as to the optimal age for this procedure. Based on the current, limited evidence base, a discussion about surgery should be held around age 45–50 y or earlier based on a specific family history of an earlier onset ovarian cancer.		
CDH1	**Increased risk of lobular BC** • Screening: Annual mammogram and consider breast MRI with contrast starting at age 30 y[c] • RRM: Consider based on family history	**No increased risk of OC**	Diffuse gastric cancer • See NCCN Guidelines for Gastric Cancer

BC: Breast cancer
OC: Ovarian cancer
RRM: Risk-reducing mastectomy
RRSO: Risk-reducing salpingo-oophorectomy

[a]Tung N, Domchek SM, Stadler Z, Nathanson KL, Couch F, Garber JE, Offit K, Robson ME. Counselling framework for moderate-penetrance cancer-susceptibility mutations. Nat Rev Clin Oncol 2016;13:581-588.

[b]The following genes and others are found on some of the panels but there is insufficient evidence to make *any* recommendations for breast MRI, RRSO, or RRM: BARD1, FANCC, MRE11A, MUTYH heterozygotes, RECQL4, RAD50, RINT1, SLX4, SMARCA4, or XRCC2.

[c]May be modified based on family history or specific gene mutation.

Continued

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

BREAST AND OVARIAN MANAGEMENT BASED ON GENETIC TEST RESULTS[a]

The inclusion of a gene on this table below does not imply the endorsement either for or against multi-gene testing for moderate-penetrance genes.

Gene	Breast Cancer Risk and Management	Ovarian Cancer Risk and Management	Other Cancer Risks and Management
CHEK2	**Increased risk of BC** • Screening: Annual mammogram and consider breast MRI with contrast age 40 y[c] • RRM: Evidence insufficient, manage based on family history.	**No increased risk of OC**	Colon • See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal
	Comments: Risk data are based only on frameshift mutations. The risks for most missense mutations are unclear.		
MSH2, MLH1, MSH6, PMS2, EPCAM	**Unknown or insufficient evidence for BC risk[d]** • Manage based on family history	**Increased risk of OC** • See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal	See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal
NBN	**Increased risk of BC** • Screening: Annual mammogram and consider breast MRI with contrast age 40 y[c] • RRM: Evidence insufficient, manage based on family history	**Unknown or insufficient evidence for OC risk**	Unknown or insufficient evidence
	Comments: Management recommendations are based on data derived from the 657del5 Slavic truncating mutation. Although risks for other mutations have not been established it is prudent to manage patients with other truncating mutations similarly to those with 657del5. Counsel for risk of autosomal recessive condition in children.		
NF1	**Increased risk of BC** • Screening: Annual mammogram starting at age 30 y and consider breast MRI with contrast from ages 30–50 y • RRM: Evidence insufficient, manage based on family history.	**No increased risk of OC**	• Malignant peripheral nerve sheath tumors, GIST, others • Recommend referral to NF specialist for evaluation and management.
	Comments: At this time, there are no data to suggest an increased breast cancer risk after age 50 y.		

[a]Tung N, Domchek SM, Stadler Z, Nathanson KL, Couch F, Garber JE, Offit K, Robson ME. Counselling framework for moderate-penetrance cancer-susceptibility mutations. Nat Rev Clin Oncol 2016;13:581-588.
[c]May be modified based on family history or specific gene mutation.
[d]There have been suggestions that there is an increased risk for breast cancer in LS patients; however, there is not enough evidence to support increased screening above average-risk breast cancer screening recommendations.

BC: Breast cancer
OC: Ovarian cancer
RRM: Risk-reducing mastectomy
RRSO: Risk-reducing salpingo-oophorectomy

Continued

BREAST AND OVARIAN MANAGEMENT BASED ON GENETIC TEST RESULTS[a]

The inclusion of a gene on this table below does not imply the endorsement either for or against multi-gene testing for moderate-penetrance genes.

Gene	Breast Cancer Risk and Management	Ovarian Cancer Risk and Management	Other Cancer Risks and Management
PALB2	**Increased risk of BC** • Screening: Annual mammogram and consider breast MRI with contrast at 30 y • RRM: Consider based on family history.	**Unknown or insufficient evidence for OC risk**	Unknown or insufficient evidence
	Comments: Counsel for risk of autosomal recessive condition in offspring.		
PTEN	**Increased risk of BC** • See Cowden Syndrome Management	**No increased risk of OC**	See Cowden Syndrome Management
RAD51C	**Unknown or insufficient evidence for BC risk**	**Increased risk of OC** • Consider RRSO at 45–50 y	N/A
	Comments: Counsel for risk of autosomal recessive condition in offspring. Based on estimates from available studies, the lifetime risk of ovarian cancer in carriers of mutations in *RAD51C* appears to be sufficient to justify consideration of RRSO. The current evidence is insufficient to make a firm recommendation as to the optimal age for this procedure. Based on the current, limited evidence base, a discussion about surgery should be held around age 45–50 y or earlier based on a specific family history of an earlier onset ovarian cancer.		
RAD51D	**Unknown or insufficient evidence for BC risk**	**Increased risk of OC** • Consider RRSO at 45–50 y	N/A
	Comments: Based on estimates from available studies, the lifetime risk of ovarian cancer in carriers of mutations in *RAD51D* appears to be sufficient to justify consideration of RRSO. The current evidence is insufficient to make a firm recommendation as to the optimal age for this procedure. Based on the current, limited evidence base, a discussion about surgery should be held around age 45–50 y or earlier based on a specific family history of an earlier onset ovarian cancer.		
STK11	**Increased risk of BC** • Screening: See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal • RRM: Evidence insufficient, manage based on family history.	**Increased risk of non-epithelial OC** • See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal	See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal
TP53	**Increased risk of BC** • See Li-Fraumeni Syndrome Management	**No increased risk of OC**	See Li-Fraumeni Syndrome Management

[a]Tung N, Domchek SM, Stadler Z, Nathanson KL, Couch F, Garber JE, Offit K, Robson ME. Counselling framework for moderate-penetrance cancer-susceptibility mutations. Nat Rev Clin Oncol 2016;13:581-588.

BC: Breast cancer
OC: Ovarian cancer
RRM: Risk-reducing mastectomy
RRSO: Risk-reducing salpingo-oophorectomy

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Syndrome de Li-Fraumeni:

• Mutation germinale TP53, suppresseur de tumeur sur le chromosome 17; guardien du génome, jouant un rôle important dans le contrôle du cycle cellulaire et de l'apoptose.
• 1sur 5000 à 1 sur 20.000
• 1% des cancers du sein héréditaires
• Incidence cumulative de cancer de 100% : sarcomes des tissus mous, ostéosarcomes, cancer du sein en pré-ménopause (surtout Her-2+), tumeurs cérébrales, cancer du colon, carcinome surrénalien…

Syndrome de Cowden/ PTEN hamartoma tumor syndrome :

- 1 sur 200.000; pénétrance 80%
- Autosomique dominant
- Incidence cumulative de cancer du sein de 25 à 50%, avec une moyenne d'âge au dignostic de 38 à 50 ans
- + risque de cancer endométrial, rénal, mélanomes…
- Maladie thyroïdienne (goitre, multinodulaire, nodule adénomateux, cancer)
- Polypes gastro-intestinaux → cancers.
- Tumeurs cérébrales et malformations vasculaires.
- Lésions cutanées bénignes : hamartomes muco-cutanées, trichilemmomes

Risque de cancer :

- BRCA1 : Risque cumulatif de cancer du sein à 70 ans : 80%; risque cumulatif chez un homme : 4%; risque de cancer des ovaires : 15 à 45%
- BRCA 2 : Risque cumulatif de cancer du sein à 70 ans : 60%; risque cumulatif chez un homme : 4 à 7%; risque de cancer des ovaires : 11 à 17%.
+ risque majoré de cancer du pancréas, mélanome, prostate et colon.
- PALB2 : Risque cumulatif de cancer du sein à 70 ans : 35 à 60%.

Patients à screener :

- Femme avec cancer du sein < ou = 35 ans (<50ans)
- Femme avec cancer du sein bilatéral, <50ans
- Femme avec cancer sein <50 ans + parent avec cancer de l'ovaire ou cancer du sein < 50 ans ou cancer du sein chez un homme
- Femme avec cancer du sein triple négatif ou de type carcinome médullaire <50ans
- 3 ou + de cas de cancers du sein dans la famille avec au moins un cas < 50 ans
- 2 cas de cancers du sein <40 ans
- Juif Ashkénaze avec cancer du sein < 60ans
- Femme avec un cancer de l'ovaire, de haut grade épithélial séreux ou papillaire, à tout âge
- Cancer du sein chez un homme
- Cancer du pancréas multiples ou avec histoire familiale.

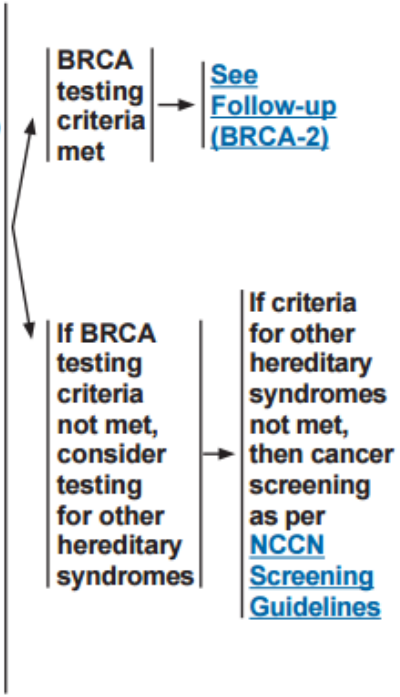
NCCN Guidelines Version 2.2017
BRCA-Related Breast and/or Ovarian Cancer Syndrome

NCCN Guidelines Index
Table of Contents
Discussion

BRCA1/2 TESTING CRITERIA[a,b]

Meeting one or more of these criteria warrants further personalized risk assessment, genetic counseling, and often genetic testing and management. Testing of an individual without a cancer diagnosis should only be considered when an appropriate affected family member is unavailable for testing.

- Individual from a family with a known deleterious *BRCA1/BRCA2* gene mutation
- Personal history of breast cancer[b] + one or more of the following:
  - Diagnosed ≤45 y
  - Diagnosed ≤50 y with:
    - An additional breast cancer primary[c]
    - ≥1 close blood relative[d] with breast cancer at any age
    - ≥1 close relative with pancreatic cancer
    - ≥1 relative with prostate cancer (Gleason score ≥7)
    - An unknown or limited family history[a]
  - Diagnosed ≤60 y with:
    - Triple negative breast cancer
  - Diagnosed at any age with:
    - ≥2 close blood relatives with breast cancer, pancreatic cancer, or prostate cancer (Gleason score ≥7) at any age
    - ≥1 close blood relative[d] with breast cancer diagnosed ≤50 y
    - ≥1 close blood relative[d] with ovarian[e] carcinoma
    - A close male blood relative[d] with breast cancer
    - For an individual of ethnicity associated with higher mutation frequency (eg, Ashkenazi Jewish) no additional family history may be required[f]
- Personal history of ovarian[e] carcinoma
- Personal history of male breast cancer
- Personal history of prostate cancer (Gleason score ≥7) at any age with ≥1 close blood relative[d] with ovarian carcinoma at any age or breast cancer ≤50 y or two relatives with breast, pancreatic, or prostate cancer (Gleason score ≥7) at any age
- Personal history of pancreatic cancer at any age with ≥1 close blood relative[d] with ovarian carcinoma at any age or breast cancer ≤50 y or two relatives with breast, pancreatic cancer, or prostate cancer (Gleason score ≥7) at any age
- Personal history of pancreatic cancer and Ashkenazi Jewish ancestry
- *BRCA1/2* mutation detected by tumor profiling in the absence of germline mutation analysis
- Family history only (significant limitations of interpreting test results for an unaffected individual should be discussed):
  - First- or second-degree blood[d] relative meeting any of the above criteria
  - Third-degree blood[d] relative who has breast cancer[b] and/or ovarian[e] carcinoma and who has ≥2 close blood relatives[d] with breast cancer (at least one with breast cancer ≤50 y) and/or ovarian[e] carcinoma



[a]For further details regarding the nuances of genetic counseling and testing, see BR/OV-A.

[b]For the purposes of these guidelines, invasive and ductal carcinoma in situ breast cancers should be included.

[c]Two breast cancer primaries includes bilateral (contralateral) disease or two or more clearly separate ipsilateral primary tumors either synchronously or asynchronously.

[d]Close blood relatives include first-, second-, and third-degree relatives on same side of family. (See BR/OV-B)

[e]Includes fallopian tube and primary peritoneal cancers. *BRCA*-related ovarian cancers are associated with epithelial non-mucinous histology. Lynch syndrome can be associated with both nonmucinous and mucinous epithelial tumors. Be attentive for clinical evidence of Lynch syndrome (see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal). Specific types of non-epithelial ovarian cancers and tumors can also be associated with other rare syndromes. Examples include an association between sex-cord tumors with annular tubules and Peutz-Jeghers syndrome or Sertoli-Leydig tumors and DICER1-related disorders.

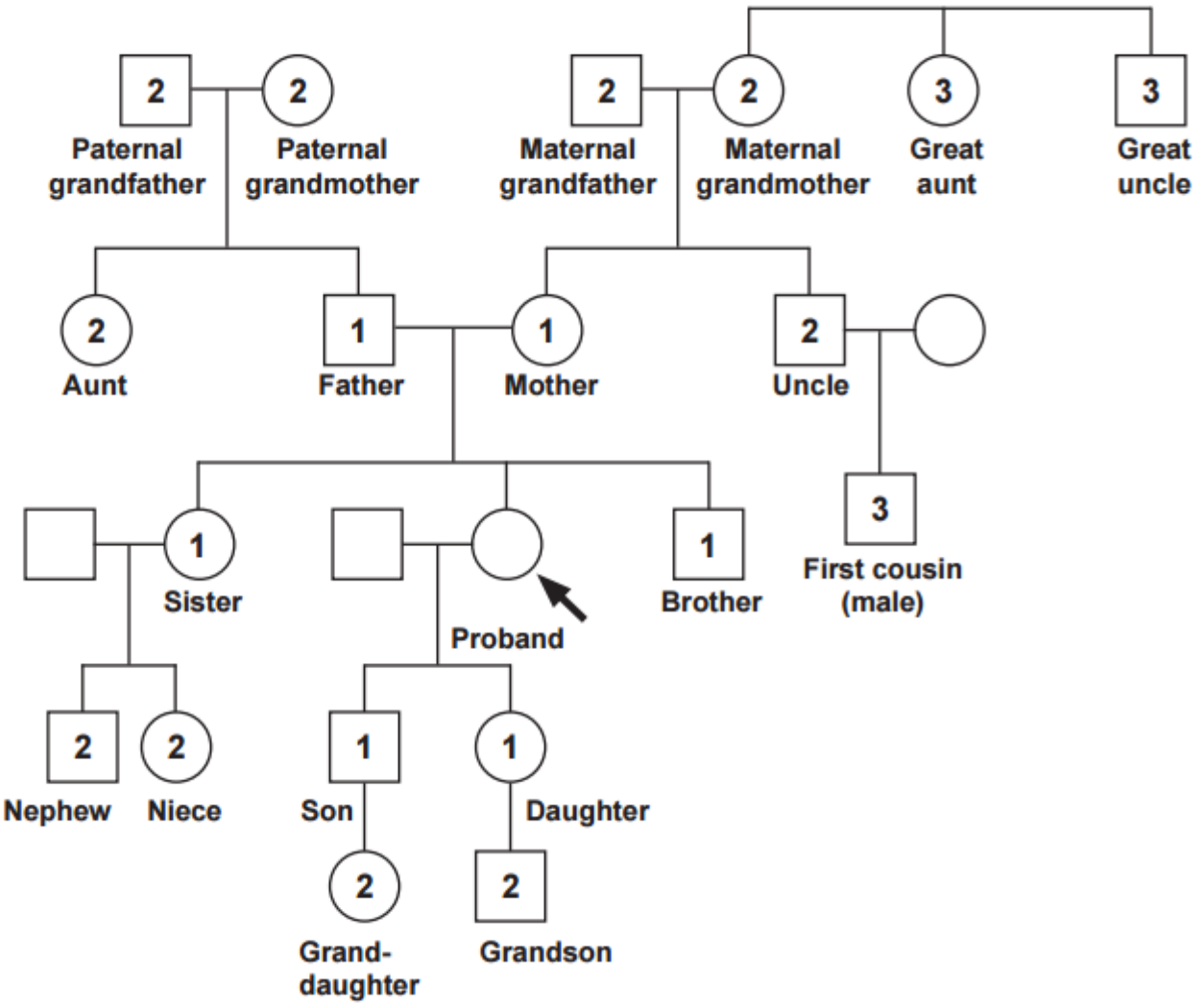
[f]Testing for Ashkenazi Jewish founder-specific mutation(s) should be performed first. Comprehensive genetic testing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or if other *BRCA*-related criteria are met. Founder mutations exist in other populations.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Avant screening:

- Chez adultes
- Conseil génétique pré-test :
  - Collecte de l'histoire familiale; tableau familial
  - Evaluation du risque de cancer chez le patient
  - Générer un diagnostic différentiel
  - Expliquer au patient les conséquences d'un test positif ou négatif, avec les incertitudes
  - Obtenir le consentement du patient
- Conseil génétique post-test :
  - Donner les résultats et leur signification + impact avec explications des options médicales
  - Interprétation des résultats en tenant compte du contexte d'histoire personnelle et familiale de cancer
  - Information et testing des membres de la famille
  - Option en cas de désir de grossesse.

PEDIGREE: FIRST-, SECOND-, AND THIRD-DEGREE RELATIVES OF PROBAND[a]



[a]First-degree relatives: parents, siblings, and children;
second-degree relatives: grandparents, aunts, uncles, nieces, nephews, grandchildren, and half-siblings;
third-degree relatives: great-grandparents, great-aunts, great-uncles, great-grandchildren, and first cousins.

NCCN Guidelines Version 2.2017
Breast and/or Ovarian Cancer Genetic Assessment

NCCN Guideline
Table of C
Dis

ASSESSMENT

Patient needs and concerns:
- Knowledge of genetic testing for cancer risk, including benefits, risks, and limitations
- Goals for cancer family risk assessment

Detailed family history:
- Expanded pedigree, particularly around individuals with a diagnosis of cancer, to include a three-generational pedigree (See BR/OV-B)
- Types of cancer, bilaterality, age at diagnosis
- History of chemoprevention and/or risk-reducing surgery
- Medical record documentation as needed, particularly prior genetic testing results for patient and their family members and pathology reports of primary cancers

Detailed medical and surgical history:
- Any personal cancer history (eg, age, histology, laterality)
- Carcinogen exposure (eg, history of radiation therapy)
- Reproductive history
- Hormone or oral contraceptive use
- Previous breast biopsies and pathology results
- History of salpingo-oophorectomy

Focused physical exam (conducted by qualified clinician):
- Cowden syndrome/PTEN Hamartoma Tumor Syndrome (PHTS) specific:
  - Dermatologic,[k] including oral mucosa
  - Head circumference
  - Thyroid (enlarged or nodular on palpation)

GENE TESTING[l]

See Targeted Testing Criteria for
BRCA-Related Breast/Ovarian Cancer Syndrome (BRCA-1)

Li-Fraumeni Syndrome (LIFR-1)

Cowden Syndrome/PHTS (COWD-1)

See Multi-Gene Testing (GENE-1)

[k]For Cowden syndrome dermatologic manifestations, see COWD-1 and for PJS dermatologic manifestations, see NCCN Guidelines for Genetic/Familial High-Ri
Assessment: Colorectal.
[l]In some cases, multi-gene testing may be a preferable way to begin testing over the single-gene testing process.

Technique de screening:

- DNA sequencing
- Au niveau sanguin
- Sur la tumeur

Mutations BRCA 1 et BRCA2

Mutations BRCA1/2:

- Prévalence et pénétrance :
- Fréquence de mutation dans la population des gènes BRCA1/2 : 1/800 à 1/1000 par gène. 15-20% du risque familial accru.
- Prévalence des mutations germinales variant selon groupes ethniques et aires géographiques. Mutations spécifiques et récurrentes décrites chez juifs Ashkenazes (1 femme sur 500).
- Transmission autosomique dominante.

Mutations BRCA1/2:

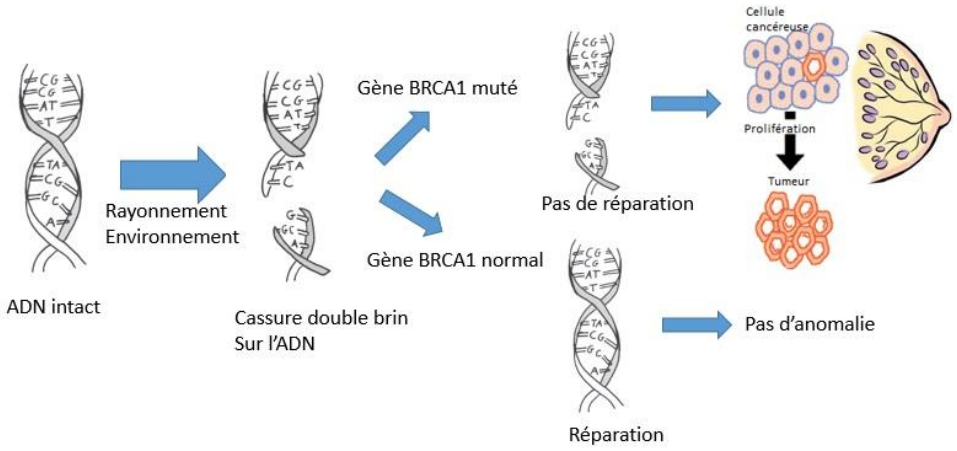
- Prévalence et pénétrance :
- Fréquence des mutations basse dans population non sélectionnée : <1-7% pour BRCA1 et 1-3% pour BRCA2.
- Risque relatif de mutations pour les 2 gènes en cas de cancer chez un homme, surtout pour BRCA2 + élevé : 6%.

Mutations BRCA1/2:

• Gènes codant pour des protéines qui sont des suppresseurs de tumeur : impliquées dans la réparation de l'ADN endommagé et la régulation du cycle cellulaire.

•BRCA1 sur chromosome 17 et BRCA2 sur le chromosome 13.

•Pénétrance : variable. Pourquoi?



Mutations BRCA1/2:

• Spécificités histo-pathologiques et cliniques:
-Triple negative : ER-/PR- et Her2-négatif
- Pronostic moins bon pour le cancer du sein?
(Inverse pour le cancer de l'ovaire?)
- Age de diagnostic + jeune
- Meilleure sensibilité aux platines
- Sensibilité aux PARP-inhibiteurs?

Suivi chez BRCA-mutés:

- Auto-examen clinique 1x/mois dès 18 ans
- Examen clinique médical 2x/an dès 25 ans
- Bilan sénologique (écho+mammo) + IRM mammaire 1x/an dès l'âge de 25-30 ans → 75ans min
→ Sensibilité IRM supérieure
- (Echographie transvaginale des ovaires vers 30-35 ans +/- CA 125)
- Pas de prévention primaire par tamoxifène qui diminue le risque de cancer controlatéral (en traitement adjuvant).
- Activité physique + réduction consommation d'alcool.

- Diagnostic pré-implantatoire (+/-FIV).

Options chirurgicales prophylactiques chez BRCA-mutés :

- But : réduire le risque de cancer et la mortalité.
- Mammectomie prophylactique bilatérale : réduction du risque de cancer d'au moins 90%; pas de bénéfice en survie. Découverte d'un cancer occulte dans +/-5%. Reconstruction à proposer. Risque de cancer controlatéral chez patiente BRCA 1-2 : 40 ans à 10 ans.
- Ovariectomie bilatérale après l'âge de 35-40 ans (voire 40-45 ans pour BRCA-2 mutées) et désir d'enfants accompli : diminue le risque de cancer du sein chez préménopausées (surtout BRCA2+), de cancer de l'ovaire et réduction de la mortalité.
- Thérapie hormonale substitutive de courte durée.

Traitement du cancer du sein chez BRCA-mutés :

- Mammectomie versus chirurgie conservative?
- Chimio-sensibilité surtout par rapport aux agents « DNA-damaging », notamment les platines.

Etudes en cours : probable meilleure sensibilité aux platines en cas de cancer triple négatif précoce. A envisager rapidement chez une patiente métastique.

- PARP-inhibiteurs : à l'étude.

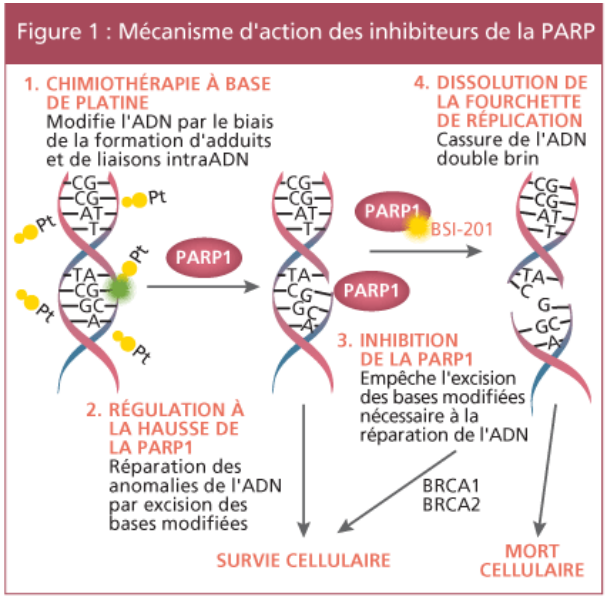
Traitement du cancer de l'ovaire chez BRCA-mutés :

• Poly (ADP-ribose) polymerase (PARP) inhibiteurs:

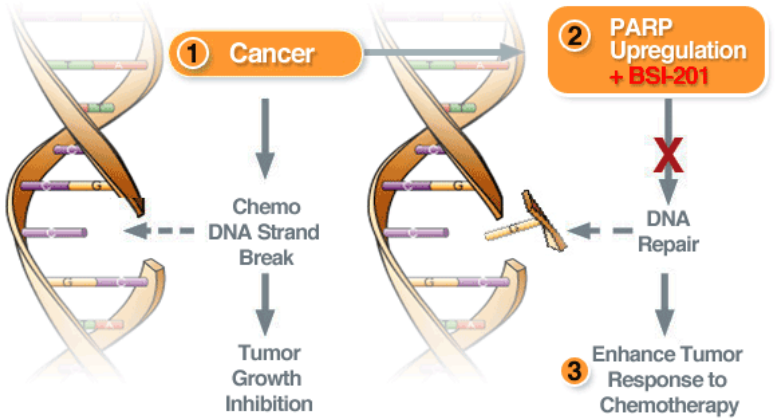
- Développés de façon privilégiée chez patients BRCA-mutés.
- Inhibition la réparation des cassures d'ADN simple brin → apoptose des cellules cancéreuses BRCA-déficientes qui ont déjà un déficit de « homologous recombination repair »

Traitement du cancer de l'ovaire chez BRCA-mutés :

- Olaparib (Lynparza) : cancer épithélial séreux de haut grade récidivant et sensible aux platines, chez une patiente BRCA-mutée, comme traitement d'entretien.



O'Shaughnessy J et al. Congrès annuel 2009 de la Société américaine d'oncologie clinique (ASCO 2009). Sommaire 3.



1. Many commonly utilized cancer chemotherapy regimens target tumor cells via fatal DNA lesions
2. Key DNA repair pathways (such as PARP) are upregulated in tumor cells - may lead to resistance
3. Inhibiting PARP may potentiate chemotherapy or be used as monotherapy in conditions with pre-existing DNA repair defects (such as BRCA negative)

Cas clinique 2

• Antécédents familiaux : plusieurs cancers du sein dans la famille du père avec mutation BRCA 1 connue ; cancer du sein chez la mère <50 ans.
• 2011 : Carcinome canalaire infiltrant SBRII de 2cm triple négatif Ki67 à 75%. BRCA1 positif. Chimiothérapie néoadjuvante (4ACdd+ 2Taxotère) → Tumorectomie + curage axillaire gauche ypT0N0 (0/12) → radiothérapie adjuvante.

Cas clinique 2

• 07/2014 : Métastase sternum avec extension dans le médiastin et adénopathies sus-claviculaires. Radiothérapie 50Gy
• 01/2015 : Métastase C4 et micronodules pulmonaires. Radiothérapie cervicale puis 3FEC suivis de 3TC
• 10/2015 : Progression osseuse (C7) et pulmonaire (micronodules) : xeloda
• 15/07/2016 : 2 métastases cérébrales et légère progression des nodules pulmonaires (max 11mm).
• 4 et 5/08/2016 : radiothérapie stéréotaxique cérébrale.

Cas clinique 2

- 21/11/2016 : nouvelle progression pulmonaire. Inclusion dans le protocole BRAVO, bras investigationnel donnant accès au PARP-inhibiteur (Niraparib).
- 16/02/2017 : Carboplatine-Gemcitabine.


Merci pour votre attention!