Multidisciplinary treatment

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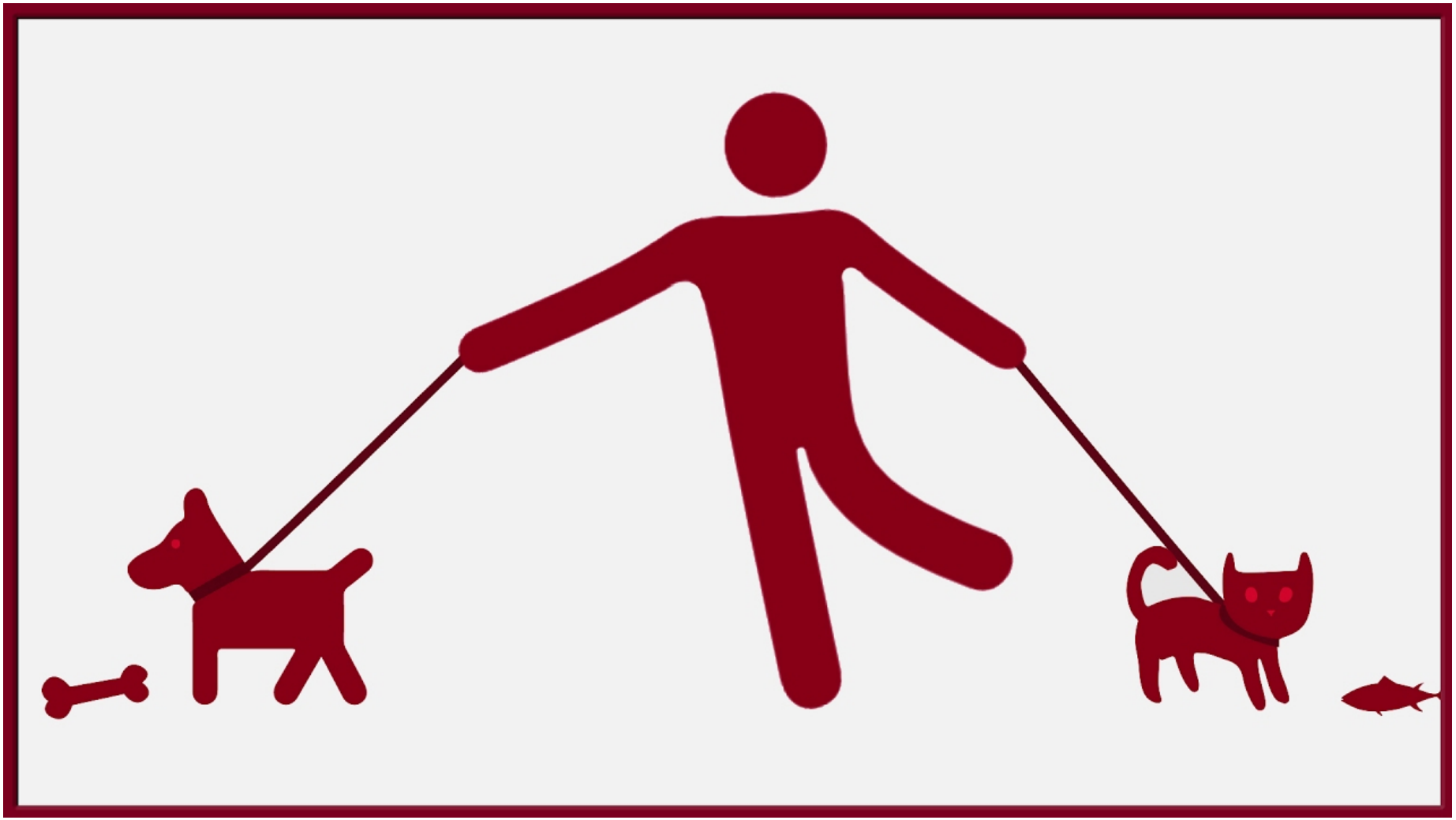
I have no COI

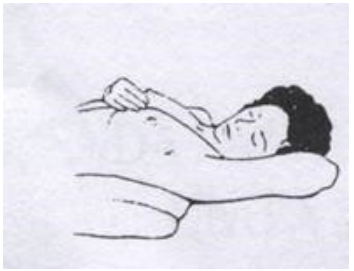


G.M. 9.9.1960 ♀

Personal history

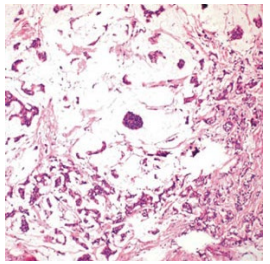
- Nulliparous, university teacher (chemistry)
- Never smoking, moderate alcohol consumption
- No previous Estro-Progestins
- Normal weight, ECOG 0, regular physical activity (Basket, mountain walking)
- No concomitant illnesses (uterine fibroids)
- **Positive family history for breast cancer**
  Maternal aunt BC at 45 years
  Maternal grandmother BC at 55 years
  Father AML at 50 years

Clinical history



- **<u>07.2001</u>**
  Self-examination: nodule right breast
  Clinical stage: T1, N0
  Ductal infiltrating carcinoma with mucinous aspects G2, ER 95%, PgR 80%, Ki-67 20%, HER2 0 (Luminal A)

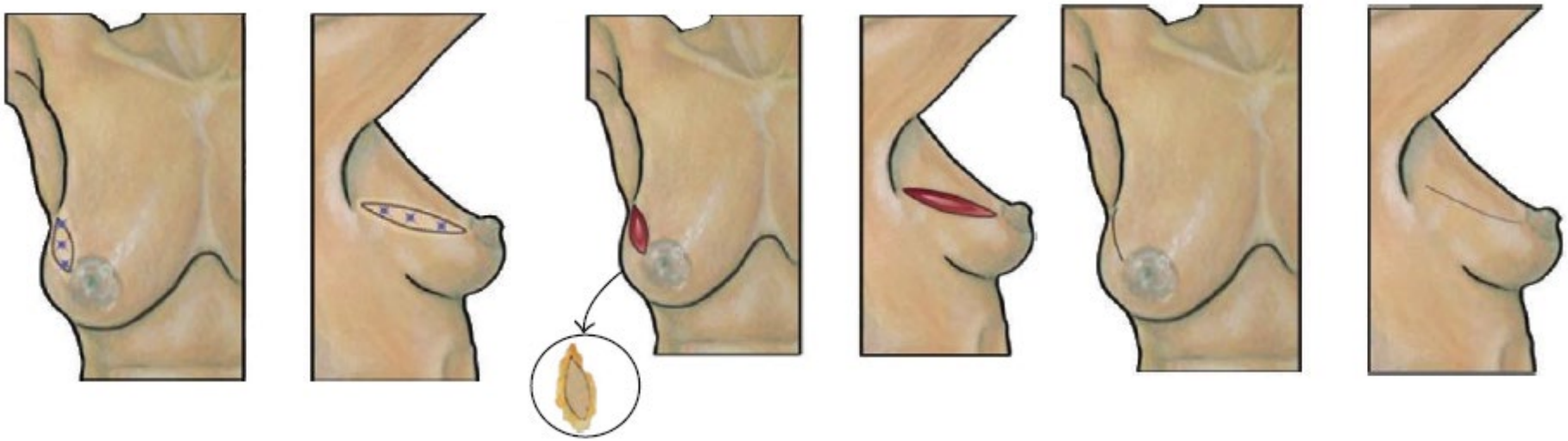
- **Quadrantectomy right breast + SN biopsy (2/2)**
  + axillary dissection
  pT1c (1.5 cm) pN1bi (**2/22**) M0
  Free margins



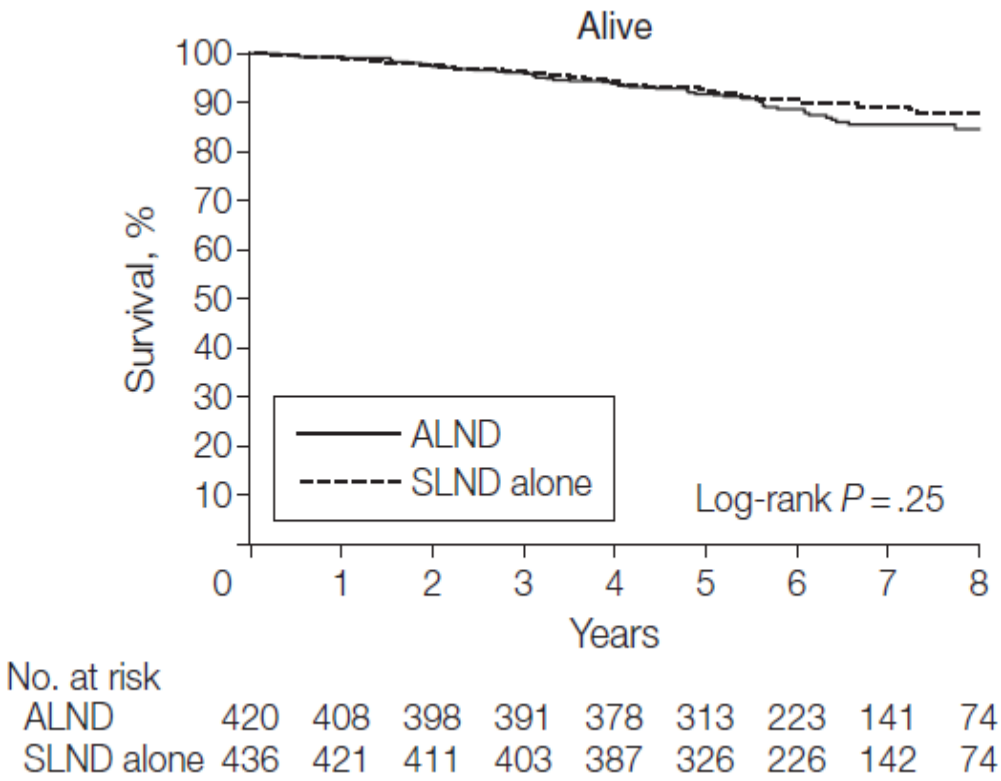
- **Breast radiotherapy** (50 Gy in 25 fractions)
  + 10 Gy boost to the tumor bed

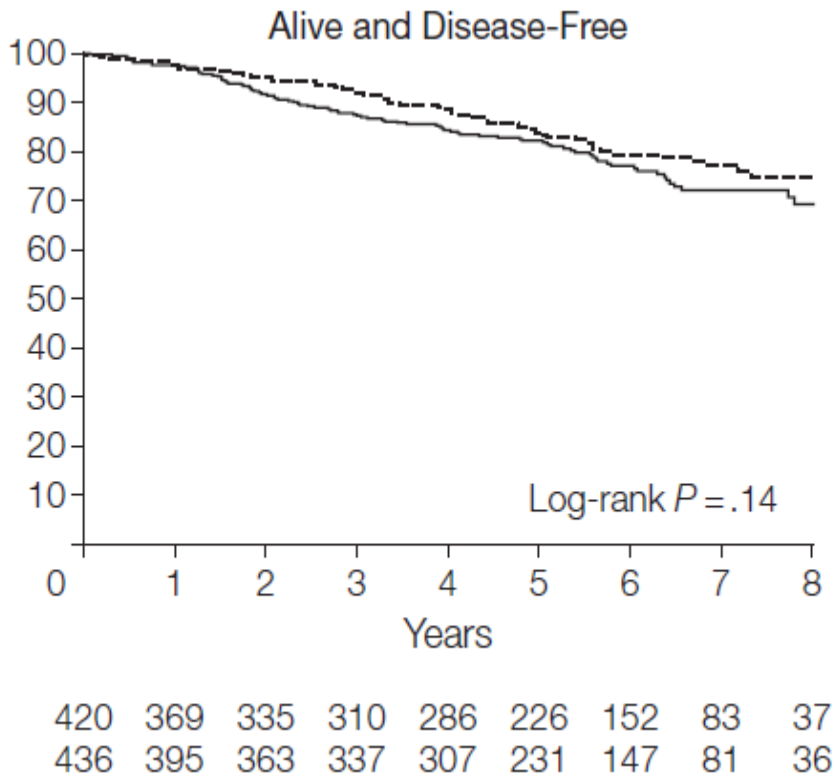
What would we do differently today?

- No axillary dissection
- We would have discussed loco-regional radiation therapy



Z0011 trial



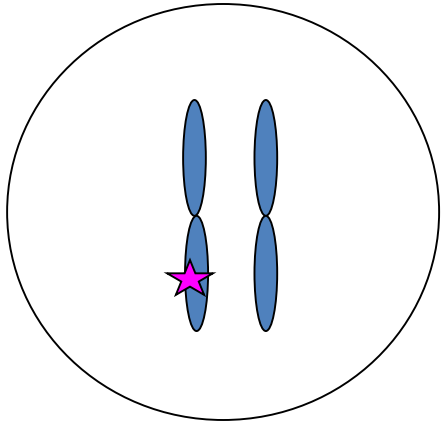


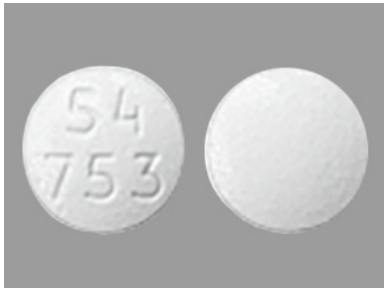
Giordano, JAMA. 2011; 305 (6):569

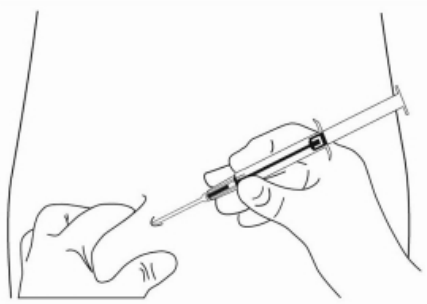
Clinical history

- **No pathogenic mutation in BRCA 1 and 2**

- 8.2001 - **8.2006**
  Adjuvant endocrine therapy:
  Tamoxifen 20 mg/daily
  + monthly LH-RH analogue







What would we do differently today?

- Genetic counselling before surgery?
  Multigene panel testing?
- Endocrine therapy
  LH-RH analog + Exemestane
- Adjuvant Chemoterapy?
- Extended Endocrine therapy ?
  Nobody knows and will ever know….

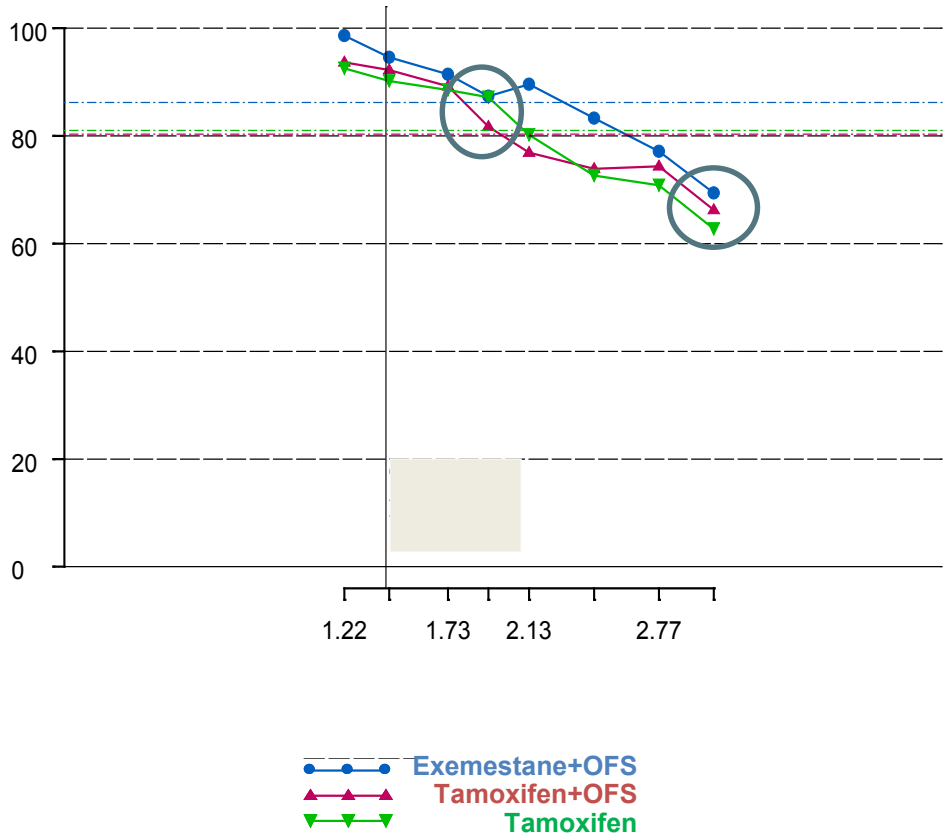
Genetic counseling and testing

Genes to be tested for depend mainly on personal and family history. Although BRCA1/2 are the most frequently mutated genes, other additional low/moderate- to high-penetrance genes should be considered, if deemed indicated by the geneticist/genetic counsellor.

Multi-gene panel testing should be proposed when either a hereditary cancer syndrome is suspected and a pathogenic gene variant in BRCA1/2 has not been identified and/or if the personal/family history can be explained by more than one gene.

Risk communication and clinical recommendations need to be adapted to the increased complexity and uncertainty of multi-gene testing.
(LoE: Expert opinion)

STEPP of 8-yr Freedom from Distant Recurrence according to Composite Risk



Grade 2 or 3 ER ≥50% N+ 1-3 ≥40 yrs
Ki-67 ≥20% PgR≥50% T≤2cm

86.2% E+OFS
80.3% T+OFS
81.0% T
5.2% improvement **E+OFS vs T**

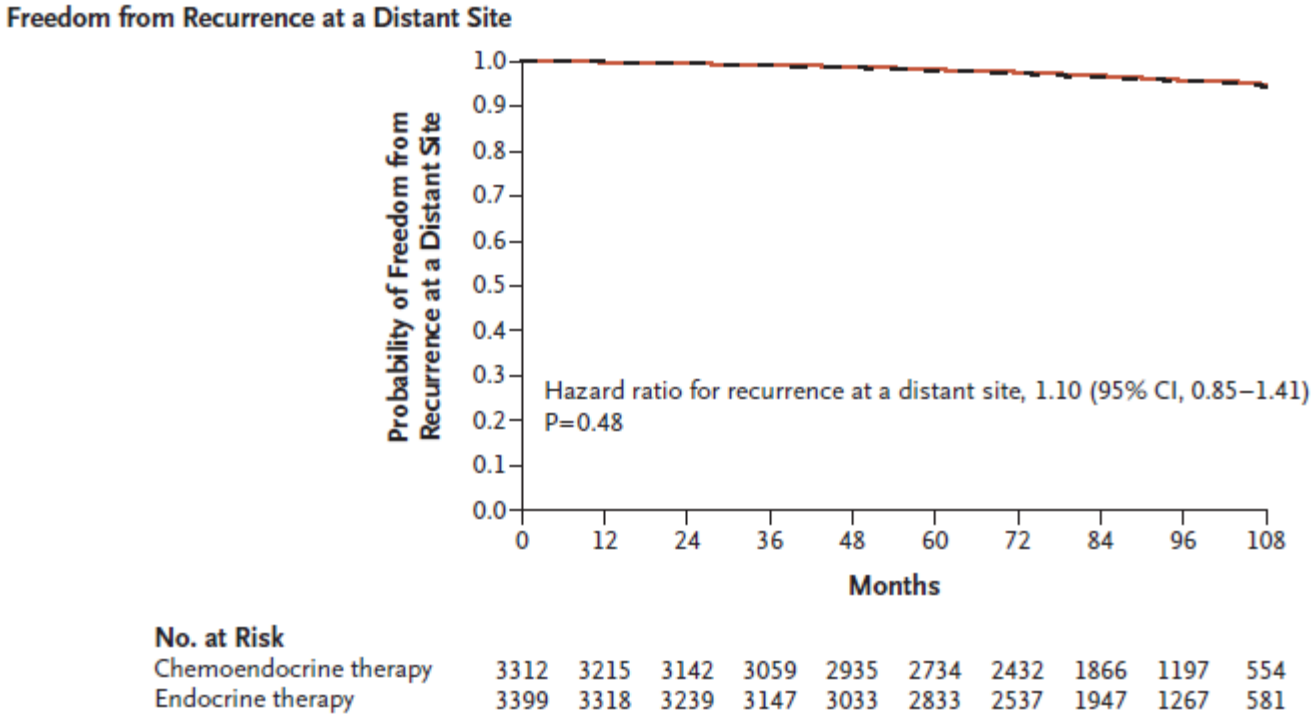
Grade 2 or 3 ER ≥50% N+ 1-3 <40 yrs
Ki-67 ≥20% PgR<50% T>2cm

E+OFS vs T,
max 10% for higher composite risks

Regan M, Pagani O, Francis P, ASCO 2018

TAILORx RS 11 to 25

Characteristic	Recurrence Score of ≤10	Recurrence Score of 11–25		Recurrence Score of ≥26
	Endocrine Therapy (N=1619)	Endocrine Therapy (N=3399)	Chemoendocrine Therapy (N=3312)	Chemoendocrine Therapy (N=1389)
Median age (range) — yr	58 (25–75)	55 (23–75)	55 (25–75)	56 (23–75)
Age ≤50 yr — no. (%)	429 (26)	1139 (34)	1077 (33)	409 (29)
Menopausal status — no. (%)†				
Premenopausal	478 (30)	1212 (36)	1203 (36)	407 (29)
Postmenopausal	1141 (70)	2187 (64)	2109 (64)	982 (71)



Sparano et al, NEJM, 2018

Who are the players at early breast cancer diagnosis?

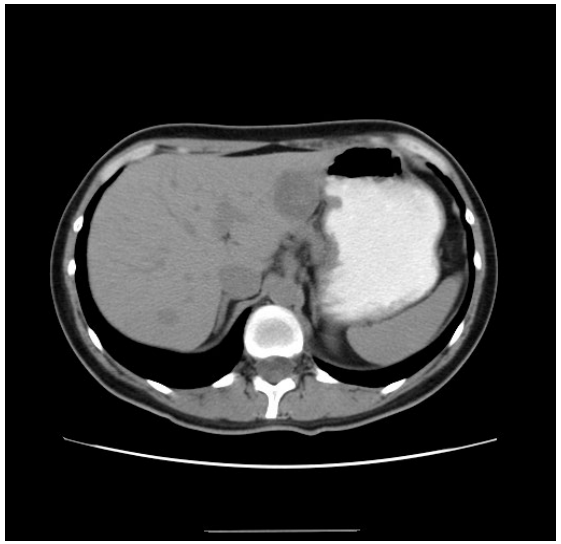
1. The radiologist
2. The pathologist
3. The breast surgeon/plastic surgeon
4. The nuclear medicine expert
5. The radiation oncologist
6. The medical oncologist
7. The psycho-oncologist
8. The fertility expert
9. The geriatrician

Clinical history

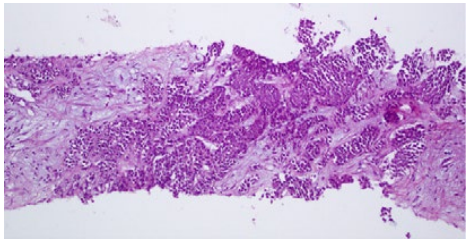
- **<u>November 2006</u>**
  3 months after end of 5 years adjuvant
  combined endocrine therapy
  Patient asymptomatic
  Abdominal ultrasound to follow uterine fibroids
  Suspicious liver lesion
  Normal blood tests and tumor markers (CEA, CA 15-3, αFP)

Clinical history

- CT Scan
  Isolated liver metastasis
  (segment III, ø 3.2 cm)
  PET-CT:
  No additional lesions



- Biopsy:
  Metastasis of breast cancer
  ER 90%, PgR 70%, Ki-67 15%, HER2 0



What would we do differently today?

- Different Follow-up?

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JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Breast Cancer Follow-Up and Management After Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update

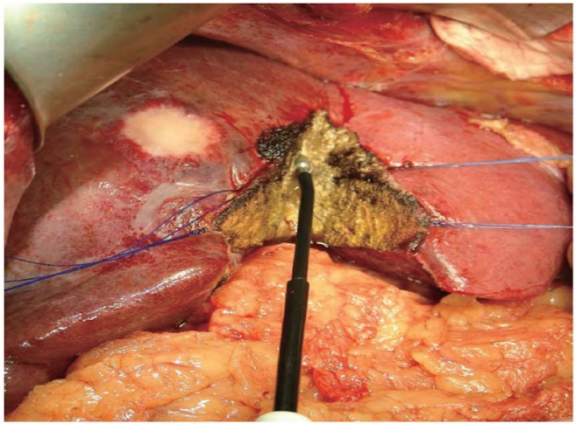
Recommendations

Regular history, physical examination, and mammography are recommended for breast cancer follow-up. Physical examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter. For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiation therapy. Thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed. The use of complete blood counts, chemistry panels, bone scans, chest radiographs, liver ultrasounds, pelvic ultrasounds, computed tomography scans, [^{18}F]fluorodeoxyglucose–positron emission tomography scans, magnetic resonance imaging, and/or tumor markers (carcinoembryonic antigen, CA 15-3, and CA 27.29) is not recommended for routine follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.

Khatcheressian JL et al; J Clin Oncol 2013

Clinical history

- November 2006 – **February 2007**
  LH-RH analogue + Letrozole (2.5 mg/day)
  Liver PD: Ø 4 cm
  No new lesions
- March 2007
  Liver resection segment III
- March 2007 – currently
  LH-RH analogue + Letrozole (2.5 mg/day)
  Ongoing complete remission



What would we do differently today?

- Chemotherapy?
- Endocrine therapy + CDK4-6 inhibitor?
- Surgery first?

ER POSITIVE / HER-2 NEGATIVE MBC

Endocrine therapy (ET) is the preferred option for hormone receptor positive disease, even in the presence of visceral disease, unless there is visceral crisis or concern/proof of endocrine resistance. (LoE: 1 A)

Many trials in ER+ ABC have not included pre-menopausal women. Despite this, we recommend that young women with ER+ ABC should have adequate ovarian suppression or ablation (OFS/OFA) and then be treated in the same way as post-menopausal women with endocrine agents with or without targeted therapies.
(LoE/GoR: Expert Opinion/A) (95%)

Future trials exploring new endocrine-based strategies should be designed to allow for enrollment of both pre- and post-menopausal women, and men.
(LoE/GoR: Expert Opinion/A) (92%)

OLIGOMETASTATIC DISEASE

A small but very important subset of patients with ABC, for example those with oligo-metastatic disease or low volume metastatic disease that is highly sensitive to systemic therapy, can achieve complete remission and a long survival.
A multimodal approach, including local-regional treatments with curative intent, should be considered for these selected patients (LoE: Expert opinion).

A prospective clinical trial addressing this specific situation is needed.

Who are the players at advanced breast cancer diagnosis?

1. The radiologist
2. “The nuclear medicine expert”
3. The pathologist
4. The medical oncologist
5. **The psycho-oncologist**
6. **The general surgeon**
7. The radiation oncologist
8. **The palliative care expert**

Grazie