Breast cancer

Izabela Glanowska
MD
Plan of the seminar:

- Presentation
- General information
- Risk factors
- Prognostic factors
- Diagnostics and staging system
- Treatment
- Follow up
General information
Breast cancer

- Most masses we can find in breast are benign (fibroadenomas)
- Cancer of the breast can be detected by screening
- Around 200,000 new cases of invasive breast cancer / year in EU (around 2000 in men).
- Crude incidence around 110/100,000 females; mortality 38.4/100,000
RISK FACTORS
What are the risk factors?

- **Sex**
  - The most common cancer among women
  - Women 100 times more often than men (men are at low risk)

- **Age**
  - Breast cancer incidence (look below) and death rates increase with age
    - <0.4% when 30-40 yr
    - 3.7% when 60-70 yr
What are the risk factors?

• **Reproductive factors**
  - Long menstrual history:
    - early menarche (before 12 yr),
    - late menopause (after 55 yr)
  - Never having children
    - (in contrary: breastfeeding is a protective factor)
  - Having first child after 30 yr

• **Race**
  - White women: higher incidence of breast ca. than African women but… after 40 yr
  - In contrary African women: higher incidence of breast ca. before 40 yr;
    also more likely to die because of breast ca. than White women (any age).
What are the risk factors?

- **Breast cancer in relatives**
  - First-degree relative (sister, mother, daughter) with b.c. increases the risk of developing b.c.
  - Second-degree relatives in case of their premenopausal diagnosis

- **Genetic changes**
  - 5-10% of b.c are connected to genetic disorders:
  - **BRCA1** and **BRCA2** (present in less than 1% - no screening tests recommended) → around 70% lifetime risk (!)
  - p53, CHEK2, Rb-1, C-Myc
  - genetic disease: Li-Fraumeni or Cowden syndrome,
What are the risk factors?

- **Benign breast diseases**
  - Ductal hyperplasia
  - Atypical ductal hyperplasia
  (especially when with family history)

- **Previous irradiation**
  - Mantle radiation for HD
What are the risk factors?

- Previous breast cancer

- Other risk factors (dependent on life style):
  
  Postmenopausal hormone therapy
  (estrogen + progesteron)
  Oral contraceptives
  No physical activity
  Diet (being overweight, alcohol consumption)
What are the risk factors?

• **High risk**:  
  - BRCA1/2 gene mutation or first-degree relative with a BRCA1/2 gene mutation  
  - A lifetime risk of breast cancer > 20% (based mainly on a family history)  
  - History of radiation therapy (between 10 ys and 30 yr)  
  - Some genetic disease (Li-Fraumeni syndrome)

• **Increased risk**:  
  - A lifetime risk of breast cancer 15 - 20%, 
  - Personal history of breast cancer, ductal or lobular carcinoma in situ, atypical ductal or lobular hyperplasia  
  - Extremely dense breasts (shown by mammogram)
You examined a 3.5 cm mass in your 31-year old patient’s left breast. A biopsy (fine needle aspiration) revealed carcinoma cells. You know that the patient has a sister (33-year old) with a history of breast cancer. Which risk factor is the most likely to be responsible for this cancer?

A. BRCA1 or 2 mutation
B. Prior intraductal papilloma
C. Early menarche
D. Diet rich in fats
Question

You examined a 3.5 cm mass in your 31-year old patient’s left breast. A biopsy (fine needle aspiration) revealed carcinoma cells. You know that the patient has a sister (33-year old) with a history of breast cancer. Which risk factor is the most likely to be responsible for this cancer?

A. BRCA1 or 2 mutation
B. Prior intraductal papilloma
C. Early menarche
D. Diet rich in fats
What are the **prognostic factors**?

- Size of the tumor
- Lymph nodes involvement
- Histological type
- Grading
What are the prognostic factors?

- **Resections margins status**
  - Resection of the breast tumor with an approximately 1cm-thick rim of surrounding tissue with the expectation that this will yield a microscopic margin of at least 1 to 5 mm on pathologic analysis.
  - In general, a microscopic margin of at least 1-2 mm seems to insure reasonable likelihood that that local failure rates will be less than 5 % at 5 years.

- **Vessel invasion**

- **HER-2 receptor overexpression or amplification**

- **(Estrogen and progesterone receptor expression)**

  Triple negative b.c- tumor with negative receptors for HER-2, ER and PR (10-15%)
What are the prognostic factors?

**HER-2 receptor**

*Human Epidermal growth factor Receptor 2*

- CD340, erbB2, HER2/neu
- Transmembrane oncoprotein
- Belongs to EGF receptors family
- Orphan receptor
- Acts as a dimer
Which of the following you would considered to be a good prognostic factor for breast cancer?

A. HER2 receptor overexpression
B. Well differentiated tumor
C. >4 lymph nodes involved in ca process
D. Vessel invasion
Which of the following would you consider to be a good prognostic factor for breast cancer?

A. HER2 receptor overexpression
B. Well differentiated tumor
C. >4 lymph nodes involved in cancer process
D. Vessel invasion
Histology

- Usually ‘benign’ tumors:
  - Phyllodes tumor
  - Intraductal papilloma
Histology

- Carcinoma in situ:
  - Ductal DCIS
    No invasion of the basement membrane of the breast ducts
  - Lobular LCIS
    Benign-appearing proliferation of terminal ductules,
    Often multifocal and bilateral

Cribiform DCIS with central necrosis (x400).
Histology

- **Infiltrating ca:**
  - **Ductal (NOS)**
    - The most common breast cancer (around 75%)
    - **Scirrhous; Medullary; Mucinous**
    - **Paget disease** is a subtype in which malignant ductal cells extend intraepithelially to the skin of the nipple.

Mucinous carcinoma
Clusters of tumor cells float in a pool of extracellular mucin
Histology

• Infiltrating ca:
  → Lobular

  - About 10% of breast cancers
  - Arises from terminal ductules of the lobules
  - Often multicentric
  - Often bilateral (20%)

Infiltrating lobular carcinoma.
The tumor cells infiltrate in typical linear files
Histology

- Other rare tumors
  - Sarcoma
  - Lymphoma

High grade sarcoma
Question

Which of the following connections is **false**?

A. Phyllodes tumor → usually behaves as benign change
B. LCIS → often multifocal
C. Infiltrating ductal ca. → the most common breast ca.
D. Paget disease → a type of Infiltrating lobular ca.
Which of the following connections is false?

A. Phyllodes tumor $\rightarrow$ usually behaves as benign change
B. LCIS $\rightarrow$ often multifocal
C. Infiltrating ductal ca. $\rightarrow$ the most common breast ca.
D. Paget disease $\rightarrow$ a type of Infiltrating lobular ca.
How do we diagnose breast cancer?

- **Physical examination:**
  - Women in their 20s and 30s - a clinical breast exam (CBE) every 3 years performed by a health professional
  - Women after 40 yr - CBE every 1 year performed by a health professional
  - Breast self-examination (BSE) – every month

! Don’t forget to check if there is nipple discharge!
! Breast cancer occurs most often in the upper outer quadrant of the breast!
movie
How do we diagnose breast cancer?

- **Mammogram** - an x-ray exam of the breast
  - Once a year for every woman > 40 yr who has no symptoms
  - BILATERAL MAMMOGRAPHY
  - Usually 2 x-ray pictures of each breast

- **USG**
- **MRI**
  (in addition to, not instead of mammogram)

Women at high risk should get an MRI and a mammogram every year starting from 30 yr.

Women at moderately increased risk should have additional MRI screening considered and should have a mammogram every year starting from 30 yr.
How do we diagnose breast cancer?

What do we look for on mammograms?

- Calcifications
  - Macrocacifications: usually related to non-cancerous conditions (also usually do not require a biopsy). They are found in about 1/2 of all women > 50 yr, and in 1/10 women < 50 yr.
  - Microcalcifications: tiny specks of calcium, alone or in clusters. If a suspicious look and pattern → a biopsy
- A mass: may be just cysts or non-cancerous solid tumors but also may be a cancer (usually masses should be biopsied if they are not cysts)

A mammogram it cannot prove that an abnormal area is a cancer
Histopathological assessment (a needle biopsy or an open surgical biopsy) is needed

Mammogram reports

The American College of Radiology has developed a standard system of describing mammograms which is called the Breast Imaging Reporting and Data System (BI-RADS).
The best evidence for a mortality benefit for mammography is in women aged:

A. 30 to 39 years
B. 40 to 49 years
C. 50 to 69 years
D. 70 to 89 years
The **best** evidence for a mortality benefit for mammography is in women aged:

A. 30 to 39 years
B. 40 to 49 years
C. 50 to 69 years
D. 70 to 89 years
What else should we do (after receiving a histopathological report) before treatment?

- Blood tests (full blood counts) and routine chemistry
- Chest X-Ray, CT
- Liver USG
- Bone scan
- Ca 15.3
STAGING
TNM staging

**TX** means that the tumour size cannot be assessed

**Tis** means [DCIS](#)

**T1** – The tumour is 2 centimetres (cm) across or less
TNM T

T1 is further divided into 4 groups

- **T1mi** – the tumour is 0.1 cm across or less
- **T1a** – the tumour is more than 0.1 cm but not more than 0.5 cm
- **T1b** – the tumour is more than 0.5 cm but not more than 1 cm
- **T1c** – the tumour is more than 1 cm but not more than 2 cm
T2 – The tumour is more than 2 centimetres, but no more than 5 centimetres across
T3 – The tumour is bigger than 5 centimetres across
TNM T

**T4** is divided into 4 groups
- **T4a** – The tumour has spread into the chest wall
- **T4b** – The tumour has spread into the skin and the breast may be swollen
- **T4c** – The tumour has spread to both the skin and the chest wall
- **T4d** – Inflammatory carcinoma – this is a cancer in which the overlying skin is red, swollen and painful to the touch
N staging

**NX** means that the lymph nodes cannot be assessed (for example, if they were previously removed)

**N0** – No cancer cells found in any nearby nodes

*Isolated tumour cells (ITCs)* are small clusters of cancer cells less than 0.2 mm across, or a single tumour cell, or a cluster of fewer than 200 cells in one area of a lymph node. Lymph nodes containing only isolated tumour cells are not counted as positive lymph nodes

**N1** – Cancer cells are in the lymph nodes in the armpit but the nodes are not stuck to surrounding tissues

**pN1mi** – One or more lymph nodes contain areas of cancer cells called micrometastases that are larger than 0.2 mm or contain more than 200 cancer cells but are less than 2mm
N staging

N2 is divided into 2 groups

N2a – there are cancer cells in the lymph nodes in the armpit, which are stuck to each other and to other structures

N2b – there are cancer cells in the internal mammary nodes (behind breast bone) which have either been seen on a scan or felt by the doctor. There is no evidence of cancer in lymph nodes in the armpit
N staging

N3 is divided into 3 groups

N3a – there are cancer cells in lymph nodes below the collarbone

N3b – there are cancer cells in lymph nodes in the armpit and behind the breast bone

N3c – there are cancer cells in lymph nodes above the collarbone
The M stages (metastases)

**M0** means that there is no sign of cancer spread

**cMo(i+)** means there is no sign of the cancer on physical examination, scans or X-rays but cancer cells are present in blood, bone marrow, or lymph nodes far away from the breast cancer – the cells are found by laboratory tests

**M1** – means the cancer has spread to another part of the body
Metastatic disease

- Bones
- Lungs
- Brain
- Liver
- Breast
- Ovary
- Skin
<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>5-yr Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis N0 M0</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>T1 N0 M0</td>
<td>98%</td>
</tr>
<tr>
<td>II</td>
<td>T0/1 N1 M0 or T2 N0 M0</td>
<td>A 88%</td>
</tr>
<tr>
<td></td>
<td>T2 N1 M0 or T3 N0 M0</td>
<td>B 76%</td>
</tr>
<tr>
<td>III</td>
<td>T0/1/2 N2 M0 or T3 N1/2 M0</td>
<td>A 56%</td>
</tr>
<tr>
<td></td>
<td>T4 Any N M0 or any T N3 M0</td>
<td>B 49%</td>
</tr>
<tr>
<td>IV</td>
<td>Any T Any N M1</td>
<td>16%</td>
</tr>
</tbody>
</table>
Treatment

à Surgery
à Chemotherapy
à Radiotherapy
à Hormone therapy
à Targeted therapy
Surgery

à Tumorectomy
à Breast Conserving Therapy
à Total mastectomy
à Modified mastectomy
à Reconstruction
à Palliative operations

BCT: removing of tumor, sentinel lymph node followed by RTH Radical treatment!

Pathologic diagnosis with fine needle aspiration (FNA) or core needle biopsy (CNB) should be obtained before any surgical procedure.
Primary tumor size less than 5cm

Proper ratio of tumor-to-breast size

Retroareolar localization is a contraindication

Prior therapeutic chest irradiation is a contraindication

Diffuse, malignant-appearing microcalcifications on the preoperative mammogram is a contraindication

Positive lumpectomy margins after resection is a contraindication

Unifocal disease
BCT Complications

- Rib fractures
- Arm edema
- Radiation pneumonitis
- Poor cosmetic outcome
- Second non-breast malignancy
- Brachial plexus lesion
Sentinel lymph node biopsy

A sentinel node
Theoretically, first lymph node collecting cancer cells that metastasize from the tumor

Procedure
An injection with a radionuclide near the tumor →
Scintigraphic imaging →
Just before the biopsy: injection of a blue dye →
During the biopsy: visual detection + radionuclide detection of a sentinel node
Sentinel node biopsy should not be carried out if:

- Palpable axillary nodes
- Multicentric tumors
- Prior axillary surgery
- Breast reconstruction or implantation of a prothesis
- Pregnancy or lactation
- T > T3
- After neoadjuvant systemic treatment
Surgery

Poor cosmetic outcome (poor incision placement, incision size, and hematoma)
Surgery

Metachronous bilateral breast cancers treated with radical mastectomy (left) and modified radical mastectomy (right).

Reconstruction of the breast
Systemic treatment
# St. Gallen consensus

## Systemic Treatment Recommendations for Breast Cancer Subtypes

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Clinico-pathologic definition</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Luminal A | • ER and/or PgR positive  
• HER2 negative  
• Ki-67 low (<14%) | Endocrine therapy alone |
| HER2- | • ER and/or PgR positive  
• HER2 negative  
• Ki-67 high (≥ 14%) | Endocrine ± cytotoxic therapy |
| Luminal B | • ER and/or PgR positive  
• HER2 over-expressed or amplified  
• Any Ki-67 | Cytotoxics + anti-HER2 + endocrine therapy |
| HER2+ | • HER2 over-expressed or amplified  
• ER and PgR absent | Cytotoxics + anti-HER2 |
| HER2+ | • HER2 over-expressed or amplified  
• ER and PgR absent | Cytotoxics |
| Triple-negative | • ER and PgR absent  
• HER2 negative | Cytotoxics |

*St Gallen International Expert Consensus 2011*
Ki-67

- is a protein that in humans is encoded by the MKI67 gene (antigen identified by monoclonal antibody Ki-67).

- is a cellular marker for proliferation.\[^{[5]}\] It is strictly associated with cell proliferation. During interphase, the Ki-67 antigen can be exclusively detected within the cell nucleus, whereas in mitosis most of the protein is relocated to the surface of the chromosomes. Ki-67 protein is present during all active phases of the cell cycle (\(G_1\), \(S\), \(G_2\), and mitosis), but is absent from resting cells (\(G_0\)).
# Systemic Treatment Recommendations for Breast Cancer Subtypes

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Clinico-pathologic definition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A</td>
<td>• ER and/or PgR positive&lt;br&gt;• HER2 negative&lt;br&gt;• Ki-67 low (&lt;14%)</td>
<td>Endocrine therapy alone</td>
</tr>
<tr>
<td>HER2-</td>
<td>• ER and/or PgR positive&lt;br&gt;• HER2 negative&lt;br&gt;• Ki-67 high (≥14%)</td>
<td>Endocrine ± cytotoxic therapy</td>
</tr>
<tr>
<td>Luminal B</td>
<td>• ER and/or PgR positive&lt;br&gt;• HER2 over-expressed or amplified&lt;br&gt;• Any Ki-67</td>
<td>Cytotoxics + anti-HER2 + endocrine therapy</td>
</tr>
<tr>
<td>HER2+</td>
<td>• HER2 over-expressed or amplified&lt;br&gt;• ER and PgR absent</td>
<td>Cytotoxics + anti-HER2</td>
</tr>
<tr>
<td>HER2+</td>
<td>• HER2 over-expressed or amplified&lt;br&gt;• ER and PgR absent</td>
<td>Cytotoxics + anti-HER2</td>
</tr>
<tr>
<td>Triple-negative</td>
<td>• ER and PgR absent&lt;br&gt;• HER2 negative</td>
<td>Cytotoxics</td>
</tr>
</tbody>
</table>
INTRINSIC SUBTYPES

SURROGATE DEFINITIONS OF INTRINSIC SUBTYPES
(St Gallen International Expert Consensus 2013)

<table>
<thead>
<tr>
<th>Intrinsic subtype</th>
<th>Clinico-pathologic surrogate definition</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A-like</td>
<td>all of: ER and PgR + HER2 -</td>
<td>Ki-67 &lt; 14% or 20% PgR ≥20%</td>
</tr>
<tr>
<td>Luminal A</td>
<td>Ki-67 ‘low’</td>
<td></td>
</tr>
<tr>
<td>Luminal B-like (HER2 negative)</td>
<td>ER + HER2 - and at least one of: Ki-67 ‘high’ PgR ‘negative or low’</td>
<td>Ki-67 ≥ 14% or 20% PgR &lt;20%</td>
</tr>
<tr>
<td>Luminal B</td>
<td>Luminal B-like (HER2 positive) ER + HER2 + Any Ki-67, Any PgR</td>
<td></td>
</tr>
<tr>
<td>Erb-B2 overexpression</td>
<td>HER2 positive (non-luminal) ER and PgR absent</td>
<td></td>
</tr>
<tr>
<td>Basal-like</td>
<td>Triple negative (ductal) ER and PgR absent HER2 -</td>
<td>There is an 80% overlap between ‘triple-negative’ and ‘basal-like’ subtype. TNBC also includes some special histological types</td>
</tr>
</tbody>
</table>

A: copy number alteration
B: most commonly mutated cancer-related genes
<table>
<thead>
<tr>
<th><strong>Adjuvant Chemotherapy in ER-negative disease:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>• Triple negative tumor</td>
</tr>
<tr>
<td>• Patients receiving anti-HER2 treatment</td>
</tr>
<tr>
<td><strong>No</strong></td>
</tr>
<tr>
<td>• Rare phenotypes with N0 and no other signs of increased metastatic potential</td>
</tr>
<tr>
<td>• In T1a N0</td>
</tr>
</tbody>
</table>
Relative indications:

- High grading (3)
- Lower hormone receptors level
- > 4 lymph nodes involved
- Extensive peritumoral vascular invasion
- pT> 5cm (T3)
- Patient’s preference

Adjuvant Chemotherapy in ER-positive, HER2-negative disease:
neoadjuvant treatment

» with locally advanced tumors cT3; N2+
Which factor is a relative indication for adjuvant chemotherapy for patients with ER-positive and HER2-negative breast cancer?

A. Low grading (1)
B. > 2 lymph nodes involved
C. Lower hormone receptors level
Which factor is a relative indication for adjuvant chemotherapy for patients with ER-positive and HER2-negative breast cancer?

A. Low grading (1)
B. > 2 lymph nodes involved
C. Lower hormone receptors level
**ADJUVANT SYSTEMIC Chemotherapy USED IN THE TREATMENT OF EARLY BREAST CANCER**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Frequency</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAC</td>
<td>Every 21 days X 6 treatments</td>
<td>Docetaksel, Doxorubicin</td>
</tr>
<tr>
<td>AC</td>
<td>Every 21 days X 4 treatments</td>
<td>Cyclophosphamide, Doxorubicin</td>
</tr>
<tr>
<td>FEC</td>
<td>Every 21 days X 6 times</td>
<td>5FU, Cyclophosphamide, Epirubicin</td>
</tr>
<tr>
<td>AC with Paclitaxel</td>
<td>Every 21 days X 4 treatments</td>
<td>AC -&gt; Paclitaxel</td>
</tr>
<tr>
<td>AC with DTX</td>
<td>Every 21 days X 4 treatments</td>
<td>AC -&gt; Docetaksel</td>
</tr>
</tbody>
</table>
## Hormon therapies

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective estrogen receptor modulators (SERM)</td>
<td>tamoxifen, toremifene</td>
</tr>
<tr>
<td>Luteinizing hormone-releasing hormone analogue (GnRHA – gonadotropin-releasing hormone analogue)</td>
<td>goserelin, lupreolrin, triptorelin, buserelin</td>
</tr>
<tr>
<td>Third-generation aromatase inhibitors (AI)</td>
<td>anastrozole, letrozole</td>
</tr>
<tr>
<td>Progestins</td>
<td>medroxyprogesterone acetate, megestrol acetate</td>
</tr>
<tr>
<td>Estrogen receptor down-regulator</td>
<td>fulvestrant</td>
</tr>
</tbody>
</table>
Adjuvant endocrine therapy:

• Applied in all pts whose tumors show evidence of endocrine responsiveness (the presence of ANY detectable estrogen receptor)
Question

Adjuvant endocrine therapy should be given to the patients:

A. whose tumors show the presence of any detectable estrogen receptor
B. whose tumors show presence the estrogen receptors in at least > 9% of tumor cells
Adjuvant endocrine therapy should be given to the patients:

A. whose tumors show the presence of any detectable estrogen receptor

B. whose tumors show presence the estrogen receptors in at least > 9% of tumor cells
A woman with a 6-cm breast cancer (cT3) and clinically palpable immobile ipsilateral axillary nodes (cN2) would best be served by

A. surgery
B. neoadjuvant chemotherapy
C. adjuvant chemotherapy
D. radiation therapy
A woman with a 6-cm breast cancer (cT3) and clinically palpable immobile ipsilateral axillary nodes (cN2) would best be served by

A. surgery
B. neoadjuvant chemotherapy
C. adjuvant chemotherapy
D. radiation therapy
Adjuvant endocrine therapy (ER+):

Premenopausal patients
- 1. Tamoxifen + ovarian function suppression
  GnRHA
- Contraindicated: aromatase inhibitors!!!

Postmenopausal patients
1. Tamoxifen
2. Aromatase inhibitors!!!
Tamoxifen and Cancer

- Estrogen molecule binds to estrogen receptor
- Estrogen receptor acquires changed shape
- Estrogen receptor binds to coactivators

- Tamoxifen molecule binds to estrogen receptor
- Tamoxifen receptor does not acquire changed shape
- Tamoxifen receptor cannot bind to coactivators
Tamoxifen
side effects therapy

» endometrial cancers
» thromboembolias
» BUT improves bone mass
Figure 2. Mechanism of action of the aromatase inhibitors.

- Androstenedione → Testosterone
- Peripheral tissues (subcutaneous fat, liver, muscle, or brain)
- Aromatase inhibitors → Aromatase
- Estrone
- Estradiol
- Breast cancer cell
- Estrogen receptor
- Tamoxifen

Tamoxifen vs IA

More with tamoxifen:
- Hot flushes
- Ischaemic cerebrovascular event
- Venous thromboembolic event
- Endometrial cancer
- Vaginal bleeding
- Vaginal discharge

More with anastrozole:
- Bone fractures
- Musculoskeletal disorder

Nature Reviews | Cancer
Question

What kind of the adjuvant endocrine therapy is the best option for your premenopausal patients with breast cancer (ER+):

A. Tamoxifen + GnRH
B. Aromatase inhibitor alone
C. Initial treatment with aromatase inhibitor and then Tamoxifen
What kind of the adjuvant endocrine therapy is the best option for your premenopausal menstruating patients with breast cancer (ER+):

A. Tamoxifen + GnRH
B. Aromatase inhibitor alone
C. Initial treatment with aromatase inhibitor and then Tamoxifen
Targeted Therapy

**Herceptin - Trastuzumab**
- Humanized monoclonal antibody against HER2 receptor
- Reduces cancer cells proliferation
- Suppresses angiogenesis
- Side effects: cardiotoxicity (especially when given with antracyclines!); also weakness, nausea, vomiting - rare

**Avastin – bevacizumab** (anti VEGF)
DISRUPTION OF LIGAND-INDEPENDENT HETERODIMERS

Inhibited formation of ligand-dependent heterodimers

Inhibition of ErbB1/2 tyrosine kinase activity

trastuzumab

pertuzumab

lapatinib

ErbB2  ErbB3

ErbB2  ErbB1/3/4

ErbB2  ErbB1/3/4

Inhibition of ligand-independent signaling

Inhibition of ligand-dependent signaling

Inhibition of ligand-dependent & ligand-independent signaling
Anti-HER2 therapy in adjuvant:

- 1 year duration of trastuzumab therapy
- Anti-HER2 + chemotherapy
- Anti-HER2 + endocrine therapy
- No need if HER2+ if T<1cm and N0
Question

A 55-year-old woman noted a mass in her left breast 2 months ago. On examination: 2 to 3 cm mass in the upper outer quadrant, no palpable lymph nodes. BCT is performed. Cancer cells are negative for ER and PR, but positive for HER2. Which of the following additional treatment options is most likely to be effective in this case?

A. Patey’s operation
B. Tamoxifen or anastrozol
C. Cefalosporins
D. Trastuzumab
A 55-year-old woman noted a mass in her left breast 2 months ago. On examination: 2 to 3 cm mass in the upper outer quadrant, no palpable lymph nodes. BCT is performed. Cancer cells are negative for ER and PR, but positive for HER2. Which of the following additional treatment options is most likely to be effective in this case?

A. Patey’s operation
B. Tamoxifen or anastrozol
C. Cefalosporins
D. Trastuzumab
Question

What is the recommended duration for the therapy with Transtuzumab (Herceptin) in patients with breast cancer HER2+?

A. 6 months
B. 1 year
C. 5 years
What is the recommended duration for the therapy with Transtuzumab (Herceptin) in patients with breast cancer HER2+?

A. 6 months
B. 1 year
C. 5 years
FOLLOW UP
**Recommended breast cancer surveillance**

<table>
<thead>
<tr>
<th><strong>MODE OF SURVEILLANCE</strong></th>
<th><strong>SUMMARY OF RECOMMENDATION</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>History / physical examination</td>
<td>Every 3 to 6 months for the first 3 years after primary therapy; every 6 to 12 months for years 4 and 5; then annually</td>
</tr>
<tr>
<td>Referral for genetic counseling</td>
<td>Criteria include: (1) Ashkenazi Jewish heritage, (2) History of ovarian cancer at any age in the patient or any first- or second-degree relatives, (3) Any first-degree relative with a history of breast cancer diagnosed before the age 50 years, (4) Two or more first- or second-degree relatives diagnosed with breast cancer at any age, (5) Patient or relative with diagnosis of bilateral breast cancer, (6) History of breast cancer in a male relative</td>
</tr>
<tr>
<td>Breast self-examination</td>
<td>All women should be counseled to perform monthly breast self-examination</td>
</tr>
<tr>
<td>Mammography</td>
<td>First post-treatment mammogram 1 year after the initial mammogram that leads to diagnosis but no earlier than 6 months after definitive radiation therapy.</td>
</tr>
<tr>
<td>Pelvic examination</td>
<td></td>
</tr>
</tbody>
</table>


### Recommended breast cancer surveillance

<table>
<thead>
<tr>
<th>MODE OF SURVEILLANCE</th>
<th>SUMMARY OF RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>History / physical examination</td>
<td>Every 3 to 6 months for the first 3 years after primary therapy; every 6 to 12 months for years 4 and 5; then annually</td>
</tr>
<tr>
<td>Referral for genetic counseling</td>
<td>Criteria include: (1) Ashkenazi Jewish heritage, (2) History of ovarian cancer at any age in the patient or any first- or second-degree relatives, (3) Any first-degree relative with a history of breast cancer diagnosed before the age 50 years, (4) Two or more first- or second-degree relatives diagnosed with breast cancer at any age, (5) Patient or relative with diagnosis of bilateral breast cancer, (6) History of breast cancer in a male relative</td>
</tr>
<tr>
<td>Breast self-examination</td>
<td>All women should be counseled to perform monthly breast self-examination</td>
</tr>
<tr>
<td>Mammography</td>
<td>First post-treatment mammogram 1 year after the initial mammogram that leads to diagnosis but no earlier than 6 months after definitive radiation therapy.</td>
</tr>
<tr>
<td>Pelvic examination</td>
<td>Regular gynecologic follow-up is recommended for all women. Patients who receive TAM should be advised to report any vaginal bleeding to their physicians.</td>
</tr>
</tbody>
</table>