Chemoprevention and Treatment Update

Dr Angela George
July 2014
500,000 women to be offered breast cancer drugs

Those most at risk should be eligible for preventative treatment to reduce the chances of it developing, NHS told

A consultant analyses a mammogram. Updated advice on familial breast cancer could lead to nearly 550,000 women becoming eligible for preventative drugs.
Green light for breast cancer drug that protects for 20 years: High risk women could get cheap prevention pill

- NHS guidance says tamoxifen will give women at high risk of cancer
- Will be an alternative to having breasts removed and cut risk by third
- Angelina Jolie and Sharon Osbourne both opted for mastectomy

Tamoxifen and raloxifene: Women to be offered daily pill to prevent breast cancer

Women with a family history of the disease will be able to get tamoxifen and raloxifene on the NHS
Breast cancer: women at risk should be given daily pill, say NHS guidelines

Women at high breast cancer risk to be given preventive drugs

Half a million women who are at increased risk of breast cancer will be offered drugs as a preventive measure for the first time under new official guidance which comes into force today.
NICE

• CG164 Familial breast cancer: NICE guidance
  • June 2013

• Recommended discussion (and provision of written materials) to all women with a high or moderate risk of breast cancer seen within a genetics clinic regarding chemoprevention
Background

• FDA approved tamoxifen as chemoprevention in women at a high risk of breast cancer in 1998
  – Defined as 5 year risk of ≥1.66%
  – Age 35-59 yrs
  – Based on NSABP-P1 trial

• First drug to be approved for cancer prevention in USA

• NOT FOR THOSE WITH BREAST CANCER
Based on what?

• NICE considered 4 trials in their guideline:
  – NSABP-P1
  – IBIS-1 trial
  – NSABP – P2 (STAR)
  – MAP3
Who is high risk???

Angelina Jolie has double mastectomy due to cancer gene
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?</td>
<td>No</td>
</tr>
<tr>
<td>2. What is the woman’s age? This tool only calculates risk for women 35 years of age or older.</td>
<td>38</td>
</tr>
<tr>
<td>3. What was the woman’s age at the time of her first menstrual period?</td>
<td>12 to 13</td>
</tr>
<tr>
<td>4. What was the woman’s age at the time of her first live birth of a child?</td>
<td>≥30</td>
</tr>
<tr>
<td>5. How many of the woman’s first-degree relatives - mother, sisters, daughters - have had breast cancer?</td>
<td>&gt;1</td>
</tr>
<tr>
<td>6. Has the woman ever had a breast biopsy?</td>
<td>No</td>
</tr>
<tr>
<td>6a. How many breast biopsies (positive or negative) has the woman had?</td>
<td>Select</td>
</tr>
<tr>
<td>6b. Has the woman had at least one breast biopsy with atypical hyperplasia?</td>
<td>No</td>
</tr>
<tr>
<td>7. What is the woman’s race/ethnicity?</td>
<td>White</td>
</tr>
<tr>
<td>7a. What is the sub race/ethnicity?</td>
<td>Select</td>
</tr>
</tbody>
</table>
**Reminder:** The Breast Cancer Risk Assessment Tool was designed for use by health professionals. If you are not a health professional, you are encouraged to discuss these results and your personal risk of breast cancer with your doctor.

**Race/Ethnicity:**

White

---

**5 Year Risk**

- This woman (age 38) 1.3%
- Average woman (age 38): 0.5%

**Explanation**

Based on the information provided (see below), the woman's estimated risk for developing invasive breast cancer over the next 5 years is 1.3% compared to a risk of 0.5% for a woman of the same age and race/ethnicity from the general U.S. population. This calculation also means that the woman's risk of NOT getting breast cancer over the next 5 years is 98.7%.

**Lifetime Risk**

- This woman (to age 90): 27.1%
- Average woman (to age 90): 12.4%
Problem???

• Did not stratify by BRCA status
  – Does not consider ovarian cancer diagnoses

• Would not recommend chemoprevention for many high risk patients
  – TP53
  – BRCA carriers
Who should take it?
- *BRCA 1* mutation carrier
  On HRT

- History of blood clots
  Under 35 years old

- Hx of breast cancer oophorectomy
  Prior

- Planning pregnancy
  Endometrial cancer

- Bilateral mastectomy
• BRCA 1 mutation carrier

• History of blood clots

• Under 35 years old

• Hx of breast cancer

• Prior oophorectomy

• Planning pregnancy

• Endometrial cancer

• Bilateral mastectomy
• Tamoxifen did not appear to reduce cancer risk in \textit{BRCA1} carriers

• Thought to be due to type of breast cancer
  – \textit{BRCA1} predominantly ER negative
  – This risk was not decreased with tamoxifen
  – ER negative cancer increased in 1 trial in tamoxifen group
Why should I take it?

- Those who took tamoxifen had a relative reduction in ER positive, invasive breast cancer of approximately 50%  
  - Eg those with risk of 60% reduced to 30%

- It may be useful for those with BRCA2 mutations who are considering whether or not to have preventative mastectomy, but are unsure when to have it, and wish to delay it

- It is not a long term alternative to RRM
BUT ...

• There was no difference in mortality (death) rates

• Some died of side effects of tamoxifen

• Those who did develop breast cancer in non-tamoxifen group were successfully treated
How long for?

• The studies gave the drug for 5 years

• The follow-up was short, but suggest some ongoing protection for up to 5 years after taking tamoxifen

• ? Prevents people developing cancer, or delays development???
When should I take it?

- ??????????????????????????????????????????????????

- Based on the trials, NOT before age 35 yrs
- Otherwise, unclear as to best age to use

- Cannot take it while pregnant/breast feeding
Does the breast cancer drug tamoxifen have side-effects?

The British-invented drug has changed the course of breast cancer by preventing recurrences – but it can make life miserable for some. Women must weigh up the risks and benefits for themselves.
Estrogen Targets Tissues

- Brain
- Heart
- Liver
- Breast
- Uterus
- Bone
SERMs

Estrogen receptor in breast cell
Breast receptor not activated
No breast cell proliferation

Estrogen receptor in uterine cell
Uterine receptor activated
Uterine cell proliferation

Artwork by Jeanne Kelly. © 2010.
Tamoxifan as a Cause of Uterine Cancer

- **Estrogen receptor in breast cell blocked**
  - Breast receptor not activated
  - No breast cell proliferation
  - Decreased cancer risk

- **Estrogen receptor in uterine endometrial cell**
  - Uterine receptor activated
  - Endometrial cell proliferation
  - Increased cancer risk

Artwork by Jeanne Kelly. © 2010.
Breast cancer drug's 'brain fog' side effects are real, say researchers

The 'mental fog' effect experienced by users of the drug Tamoxifen has a 'biological basis'...

"For some patients the effects wear off over time, but others experience symptoms that can lead to job loss, depression, and other debilitating events."

The Institute of Cancer Research

The ROYAL MARSDEN
NHS Foundation Trust
The Need for Better SERMs

Tamoxifen

Good effects
• Reduces breast cancer risk
• Lowers LDL cholesterol
• Strengthens bones

Bad effects
• Increases uterine cancer risk
• Increases blood clot risk

+ Menopausal symptoms
Other considerations ...

- No effect on risk of ovarian cancer

- Compliance in trials not well reported, but 60-70%
  - ie ~1 in 3 women stopped taking drug due to side-effects
  - Menopausal side effects –
    - Hot flushes, vaginal drying, dysparunia, mild memory impairment, leg cramps, bladder changes, vaginal bleeding
Breast cancer risk vs. Endometrial cancer
- Blood clots
- Side effects
Breast cancer risk

Endometrial cancer
Blood clots
Side effects
Any questions?