



# ADJUVANT HORMONE THERAPY IN BREAST CANCER

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# HORMONAL TREATMENT FOR BREAST CANCER

## History of Hormonal Therapy

- Oophorectomy - 1896 surgeon George Beatson found he could extend the lives of women with metastatic breast cancer by surgically removing their ovaries
- Tamoxifen – 1966 initially developed as a fertility treatment
- First used in breast cancer in 1971
- Aromatase inhibitors - early 1990s
- Anastrozole
- Letrozole
- Exemestane



# HORMONE RECEPTOR POSITIVE BREAST CANCER

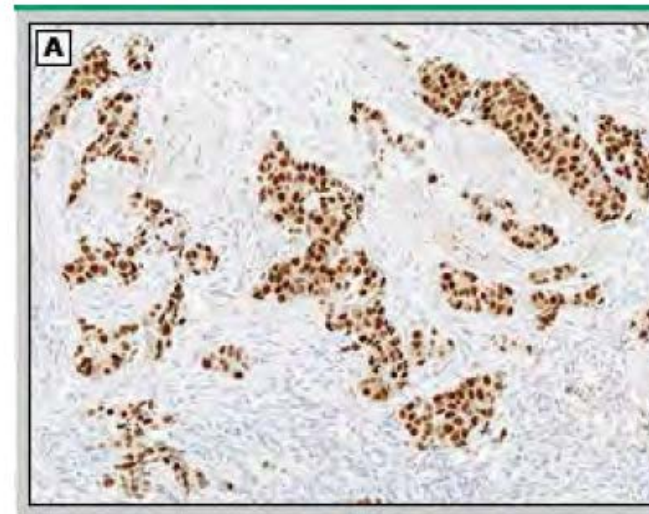
- Breast cancer with receptors to the 2 female hormones (oestrogen and progesterone) on its cells

- 75% of all breast cancers

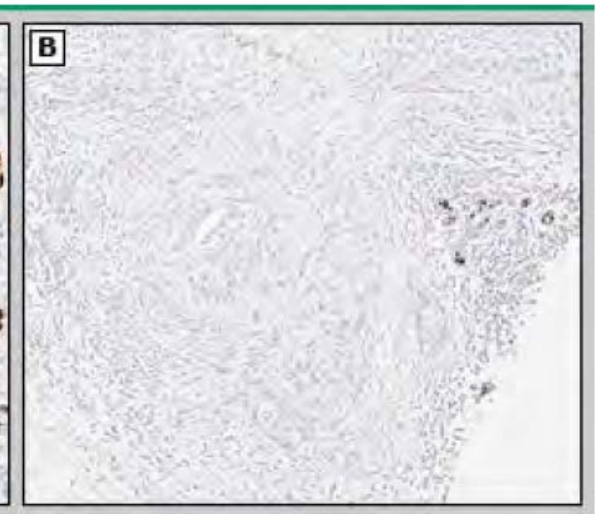
## Testing for Oestrogen Receptors

- Oestrogen (+/-progesterone) can stimulate the growth of hormone receptor positive breast cancer
- Hormone therapies aim to block this stimulation  
***anti-hormone therapy***
- Treatment options depend on whether or not a woman is in menopause

ER positive



ER negative



# MENOPAUSE & SOURCES OF OESTROGEN

## Menopause

- When the ovaries stop producing eggs and menstrual periods end
- Average age is 51 years (range 45 – 55)
- Definitions Peri-menopause (transition) – periods become irregular/ less frequent, can last several years
- Menopause – no periods for 12 months
- Post-menopause – the time after menopause

## Sources of Oestrogen

- Before menopause - ovaries
- After menopause - subcutaneous fat, liver, muscle

# QUIZ TIME

## QUESTION 1

TAMOXIFEN CAN BE USED FOR BOTH PRE AND POST MENOPOSAUL WOMEN

A-T

B-F

## QUESTION 2

AROMATASE INHIBITOR CAN BE USED FOR BOTH PRE AND POST MENOPOSAUL WOMEN

A-T

B-F

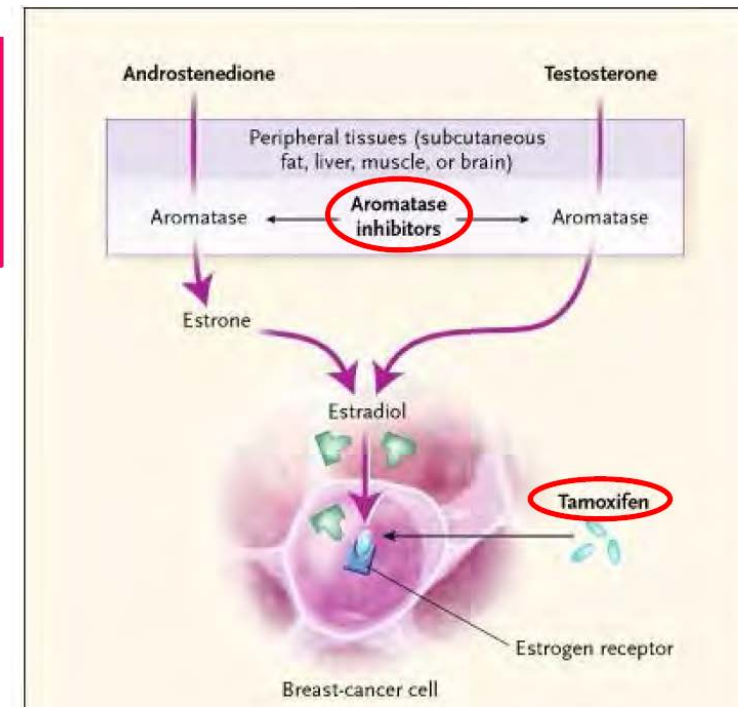
# HORMONE THERAPY

## Options for Anti-Hormone Therapy

- **Pre-menopausal women** Tamoxifen
  - Inhibition of estrogen production from the ovaries temporary - monthly zoladex injections
  - permanent - surgical oophorectomy
- **Post-menopausal women** Tamoxifen
- Aromatase inhibitors

## How Do Hormone Therapies Work?

Aromatase inhibitors decrease production of oestrogen



Tamoxifen stops oestrogen attaching to breast cancer cells

Without oestrogen breast cancer cells are not stimulated to grow



### QUESTION 3

WHAT IS THE DURATION OF ADJUVANT HORMONE THERAPY?

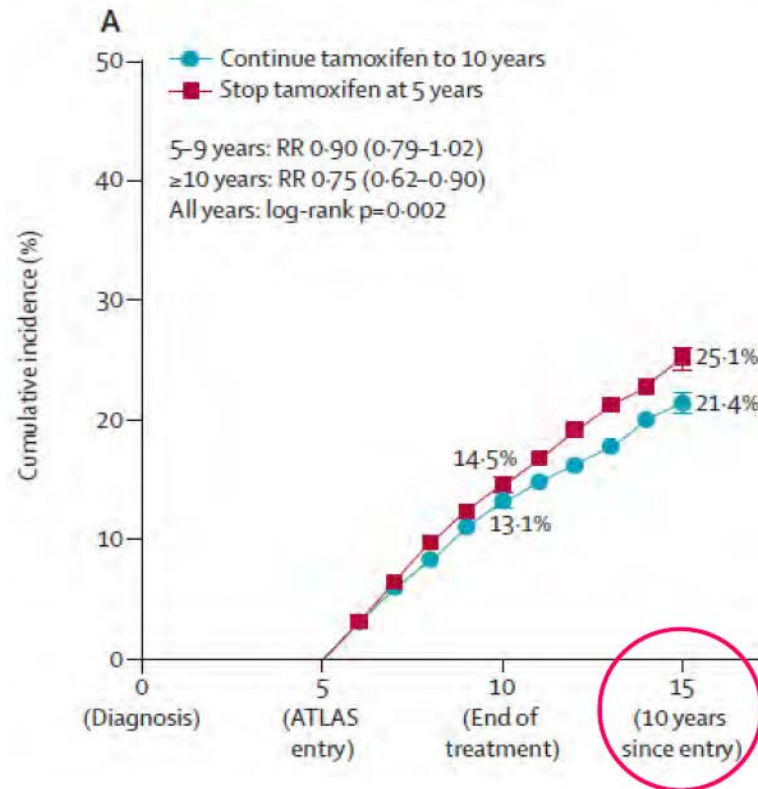
A-2 YEARS

B-5 YEARS

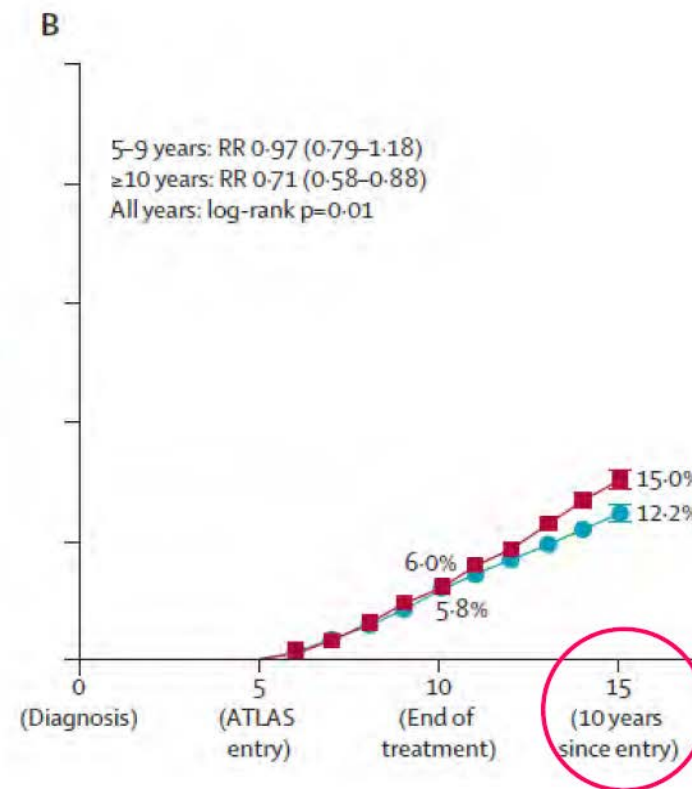
C-10 YEARS

# TAMOXIFEN 5 YRS VS 10 YRS

4% less recurrences

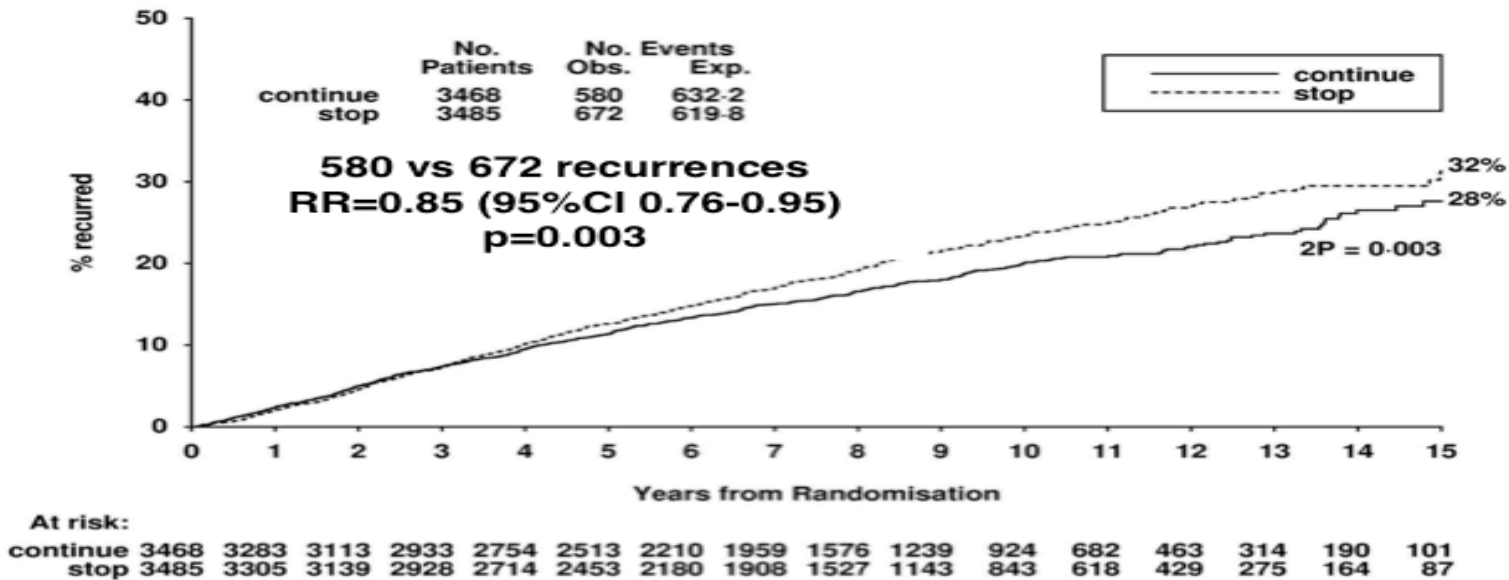


3% less deaths





## aTTom: 6953 women, 10 years vs. 5 years RECURRENCE



Gray, ASCO 2013

# BENEFITS OF ANTI-HORMONE THERAPY

- 5 years of anti-hormone therapy reduces the risk of: breast cancer coming back somewhere else in the body (metastases / secondaries)
- Breast cancer returning in the same breast
- A new breast cancer in the opposite breast
- Death from breast cancer
- The benefits of anti-hormone therapy last well beyond the 5 years you take tablets
- **Tamoxifen** (compared to no hormonal therapy)  
12% reduction in risk of breast cancer coming back
- 9% reduction in risk of death from breast cancer
- **Aromatase Inhibitors** (compared to tamoxifen)  
Further 3% reduction in risk of breast cancer coming back
- Same reduction in risk of death from breast cancer
- All three aromatase inhibitors equivalent efficacy

# WHEN TO START HORMONE THERAPY & DURATION

- 4-6 weeks after surgery
- After chemotherapy
- During or after radiotherapy
- For at least five years
- **Tamoxifen 10 yrs** better than 5 yrs Further reduction in breast cancer recurrence and death
- Especially if large cancer, node positive, high grade
- **Tamoxifen 5 yrs - AI 5 yrs** better than Tamoxifen 5 yrs
- **Aromatase Inhibitor 5 yrs** new data suggested 10 years improves DFS But NOT OS  
MA17 trial

# SIDE EFFECTS OF ANTI-HORMONE THERAPY

## General Side Effects

- Many healthy tissues benefit from oestrogen  
vagina, brain, skin and bones
- Menopausal symptoms can occur when:  
oestrogen is blocked from entering healthy  
tissue by tamoxifen
- Oestrogen levels are reduced by aromatase  
inhibitors

## Aromatase Inhibitor Side Effects

- Common: hot flushes, muscle and joint pains  
and joint stiffness, vaginal dryness, sexual  
dysfunction
- Less common: weight gain, mood change
- Rare: osteoporosis, fractures, cardiovascular  
risk, elevated cholesterol

## Tamoxifen Side Effects

- Common
  - Hot flushes (up to 80%, severe in 30%)
  - Vaginal discharge, sexual dysfunction,  
irregular periods
- Less Common
  - Dry skin, weight gain, mood change
- Rare
  - Blood clots (venous thrombosis) (DVT / PE, 3  
in 100) Risks - smoking, surgery, previous  
blood clots, obesity
  - Cancer of the womb (uterus) (4 in 100)  
women > 50yrs; longer duration on treatment
  - Cataracts

# SIDE EFFECTS AI VS. TAMOXIFEN

- Analysis of 7 studies enrolling 30 023 women

Side Effect	AI %	Tamoxifen %	Risk for AI v tamoxifen	NNH
Broken bone	7.5	5.2	1.5 x	46 (AI)
Cardiovascular (heart attack, high cholesterol)	4.2	3.4	1.3 x	132 (AI)
DVT/PE/blood clot	1.6	3.1	0.5 x	69 (T)
Stroke	1.4	1.5	equal	-
Uterus Cancer	0.1	0.5	0.3 x	250 (T)

NNH = Number of people who must receive treatment for 1 person to develop the side effect

Amir E, J Natl Cancer Inst 2011;103:1299–1309.

# MANAGING THESE SIDE EFFECTS

## General Management

- Changing to a different tablet tamoxifen to aromatase inhibitor
- Aromatase inhibitor to tamoxifen
- One aromatase inhibitor to another
- Take a short break from the tablet “drug holiday”

## Hot Flashes

- Weight loss, exercise
- Avoid triggers – spicy food, caffeine, alcohol
- Loose cotton clothing, layer clothing
- Cold packs, fan
- Medications: venlafaxine , gabapentin , clonidine

# MANAGING THESE SIDE EFFECTS

## Joint Pain and Stiffness

- Exercise
- Acupuncture
- Yoga
- Vitamin D
- Glucosamine
- Paracetamol, anti-inflammatories

## Vaginal Dryness

- Moisturiser (Replens - non-hormonal)
- Lubricants (Sylk, Astroglide)

## Bone Thinning and Osteoporosis

- Aromatase inhibitors can cause thinning of the bones, which may increase the risk of bone fractures and osteoporosis
- Bone mineral density scan measures the strength and thickness of the bone
- Often done when starting an aromatase inhibitor then repeated every 1-2 years while on treatment

# THINGS TO AVOID IN HR POSITIVE BREAST CANCER SURVIVAL

- Systemic and topical oestrogen
- Alcohol
- Weight gain
- Sedentary life style



# MANAGING THESE SIDE EFFECTS & COMPLIANCE

## Keeping Bones Strong

- Calcium: 3 serves of dairy per day, Supplements
- Vitamin D: Sunlight, diet (oily fish), Supplements
- Weight bearing exercise
- Medications – if previous fractures or established osteoporosis: Bisphosphonates , Denosumab

## Compliance

- Many women stop taking anti-hormonal therapy before completing 5 yrs
- One study looked at percentage still on medication at each year from starting therapy – 1 yr 90%, 3 yrs 77% and 5 yrs 51%
- Taking tablets for <80% of the recommended time increases risk of breast cancer returning

# CASE STUDY

Mrs Smith 49 years lady, was diagnosed with early stage breast cancer that was treated with wide local excision and axillary lymph node clearance, Histology confirmed 22mm, G3, Invasive ductal carcinoma, 3/9 LN involved, ER 3+ 90%, PR3+ 90%. HER2 negative, Past medical history include Hysterectomy for menorrhagia .

Completed adjuvant chemotherapy and Radiation therapy.

Presented to discuss hormone therapy

Tamoxifen VS Aromatase Inhibitors ?

# CASE STUDY

- Tamoxifen was started, apart from mild hot flushes she tolerated it well.
- 2 years later she developed unprovoked LL DVT
- Next step ?
- Start anticoagulation
- stop Tamoxifen
- Start Aromatase inhibitor

# CASE STUDY

- Base line Bone Density scan shows osteopenia
- Aromatase inhibitor was started with vitamin D support
- 6 months later she presented with crippling arthralgia and hot flushes, next step?
- Switch back to Tamoxifen
- Switch to different Aromatase inhibitor
- Commence NSAIDs, lifestyle change and SNRIs if symptoms persist
- At her 2 years visit, her follow- up DXA scan reveals osteoporosis now, next step?
- Stop AI

She was commenced on Denosumab 6 monthly , aiming for a total of 10 year hormonal therapy if possible



Thank You!