

**Post treatment concerns
for cancer survivors:
a focus on breast cancer.**

Presentations made by

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of the

Sydney Survivorship Centre.

Hormonal Treatment for Breast Cancer

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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 (Arimidex)
 - letrozole (Femara)
 - exemestane (Aromasin)

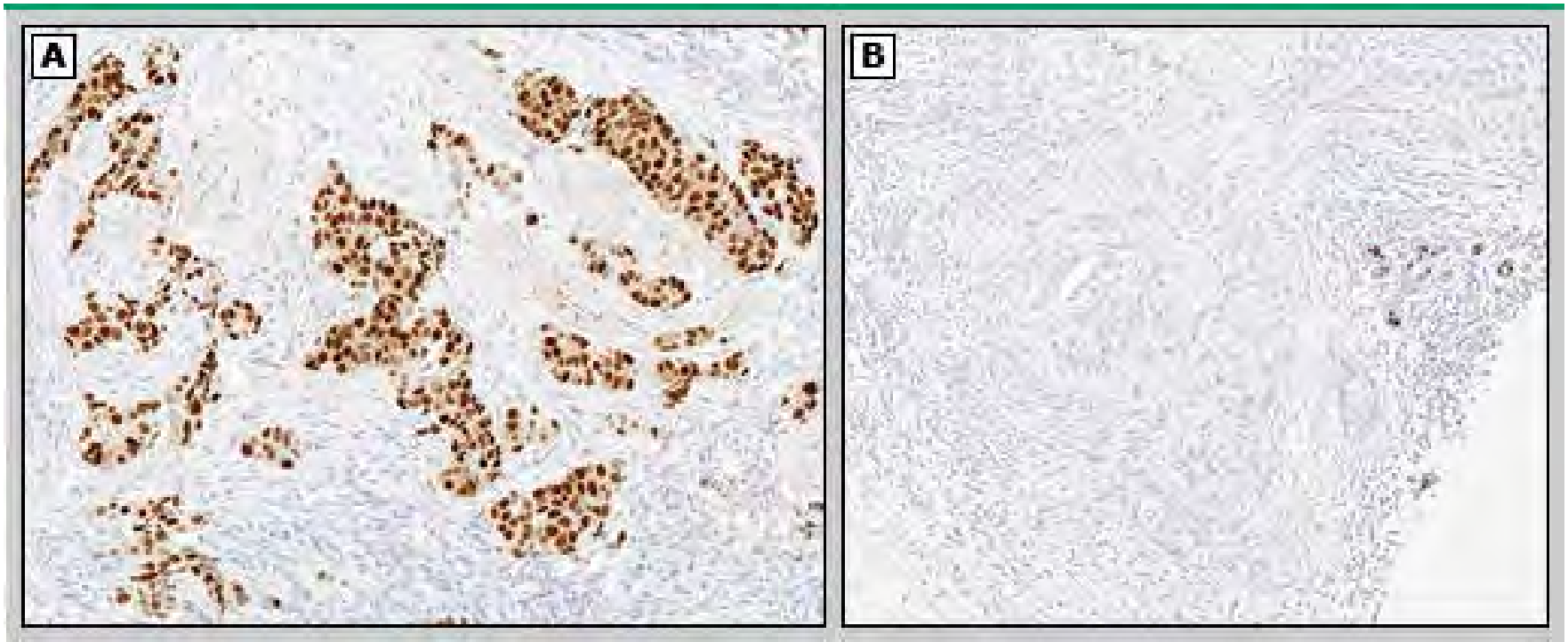
Hormone receptor positive breast cancer

- Breast cancer with receptors to the 2 female hormones – oestrogen and progesterone - on its cells
- 75% of all breast cancers

Testing for oestrogen receptors

ER positive

ER negative



- 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

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

Options for anti-hormone therapy

- **Pre-menopausal women**

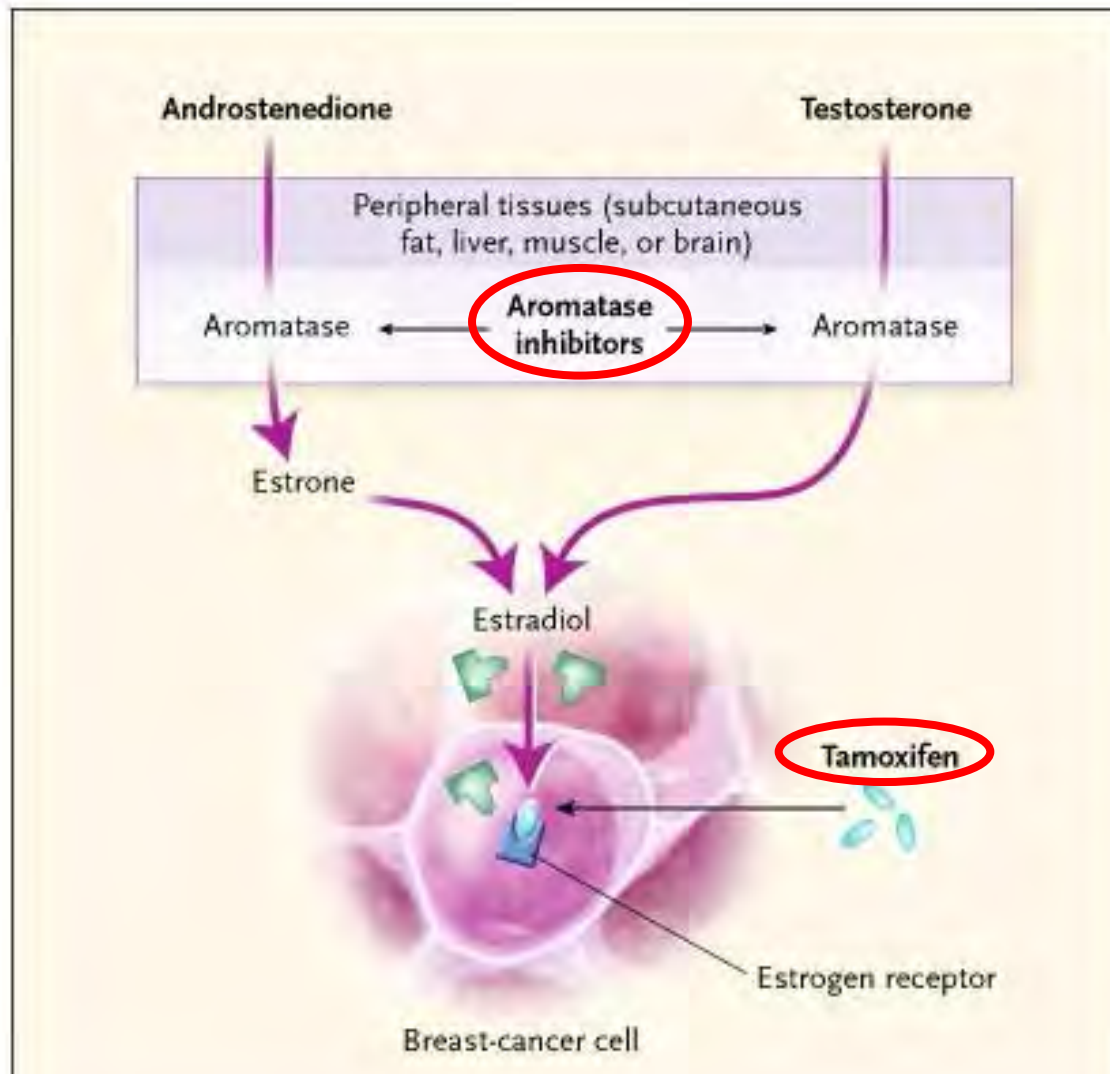
- Tamoxifen
- Inhibition of estrogen production from the ovaries
 - temporary - monthly zoladex injections
 - permanent - surgical oophorectomy

- **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

Benefits of anti-hormone therapy

- 5 yrs 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



Benefits of anti-hormone therapy

- **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 hormonal therapy

- 4-6 weeks after surgery
- After chemotherapy
- During or after radiotherapy

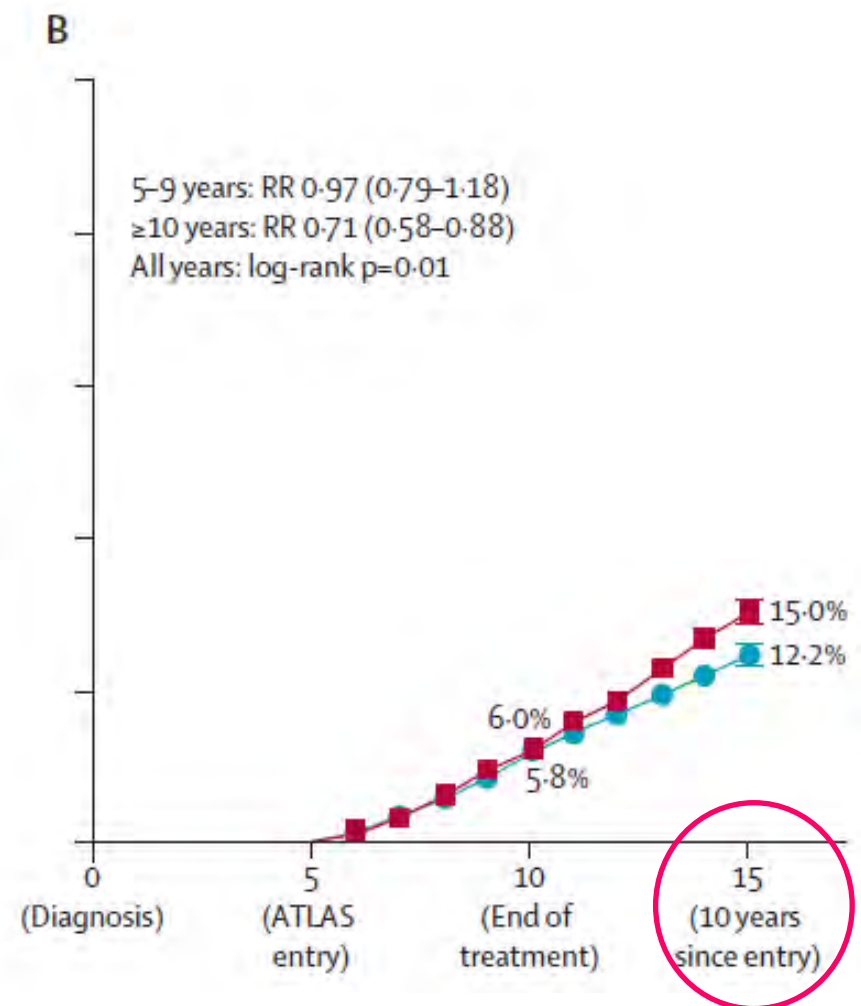
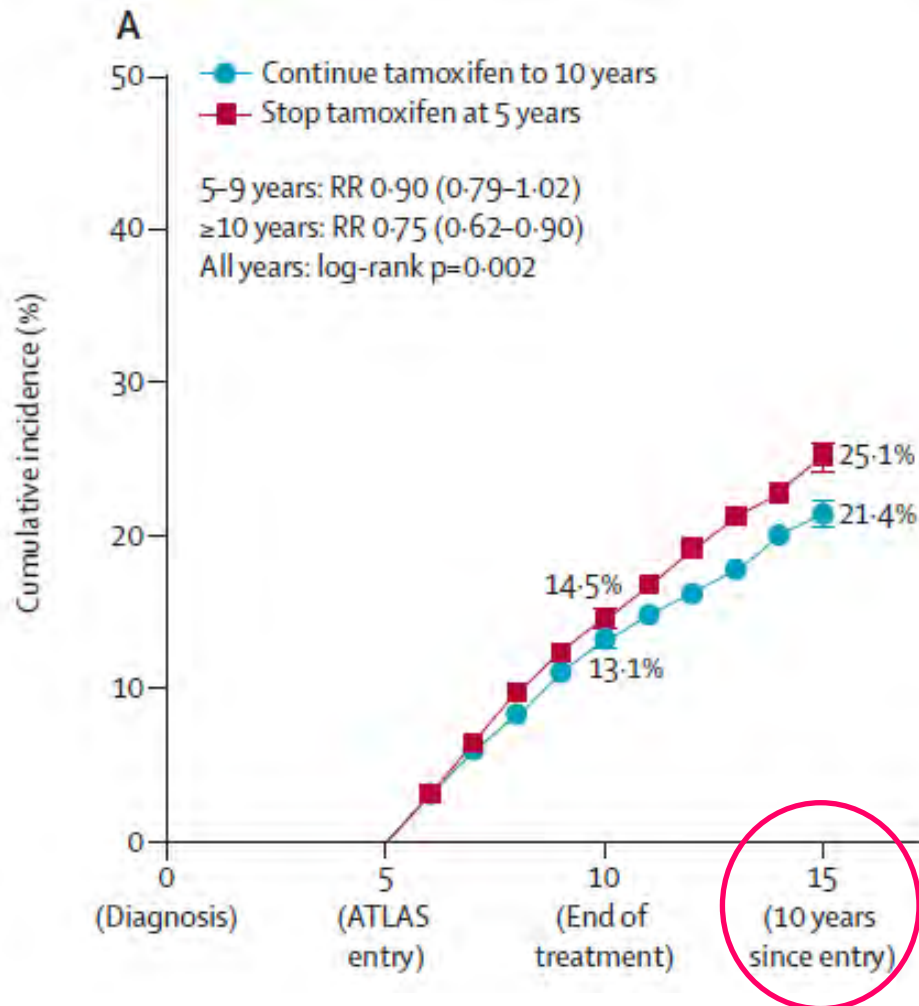
Duration of hormone therapy

- At least 5 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**
 - No data for safety beyond 5 years
 - Trials completed and results awaited

Tamoxifen 5 yrs v 10 yrs

4% less recurrences

3% less deaths





Side Effects of anti-hormone therapy

- 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



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

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

Side Effects: AI v 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

Managing the side effects

- 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 flushes

- weight loss, exercise
- avoid triggers – spicy food, caffeine, alcohol
- loose cotton clothing, layer clothing
- cold packs, fan
- Medications
 - venlafaxine (Efexor),
 - gabapentin (Neurontin)
 - clonidine (Catapress)

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

Keeping bones strong

- Calcium
 - 3 serves of dairy per day
 - Supplements eg caltrate
- Vitamin D
 - Sunlight, diet (oily fish)
 - Supplements eg ostelin, ostevit
- Weight bearing exercise
- Medications – if previous fractures or established osteoporosis
 - Bisphosphonates eg Fosamax, Aclasta
 - Denosumab (Prolia)

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%
 - 5 yrs 51%
- Taking tablets for <80% of the recommended time increases risk of breast cancer returning