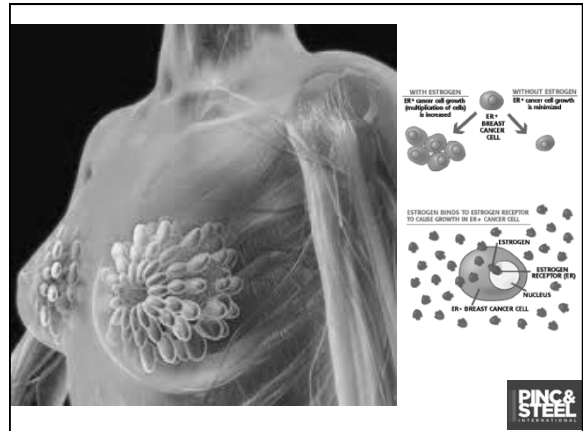


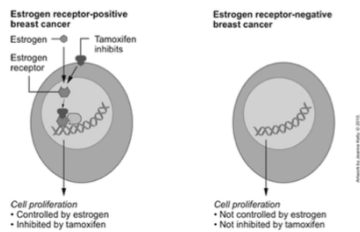
## Managing Side Effects of Estrogen Deprivation in women affected by cancer



Lou James MNZM Founder PINC & STEEL



- **Tamoxifen** – blocks the action of estrogen and is effective in women both before and after the menopause
- **Aromatase inhibitors** (Letrozole, Anastrozole, Exemestane) – reduce non-ovarian production of estrogen, so are effective only in women after menopause.
  - Can only be used in combination with ovarian suppression/ surgical removal in younger women.



## How do Oncologists choose?

- 1) Most effective
- 2) Least harm

Factors in that decision:

- Risk, size, grade, node involvement and ER/PR status
- Genomic information
- Contraindications
- Tamoxifen: DVTs/ pulmonary emboli, risk of endometrial cancer
- AIs: joint pains, osteoporosis risk



## Standard treatment options

- Tamoxifen -> AI ("Switch"/"extended")
- AI -> tamoxifen
- Tamoxifen for 10 years
- What can be tolerated, or made to be tolerable, for as long as possible (up to max effective duration) if a non-standard approach is needed.

**BUT**

...50% of patients do not complete their treatment, mostly due to side effects.



## Mrs T's Story: Tamixofen and me

- Tamixofen was:
  - Extraordinarily difficult and disruptive
- Caused:
  - Cognition/ memory problems
  - Hot flushes
  - Fatigue
  - Weight gain



## Mrs T – What has worked for me

- Sleep hygiene
- My medical team – critical relationship 5+ years
- **PINC & NEXT STEPS** Programs
- Family and friends – must share your goals
- Support groups and online community
- Knowing what to expect helps acceptance
- Professional counselling

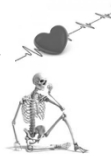


## Side effects of estrogen deprivation

- **Early Effects**
  - Hot flushes, mood swings, hot flushes, vaginal dryness/itch/discharge/bleeding, cognition, weight gain, DVT

- **Late Effects**

- Cardiovascular



- Bone

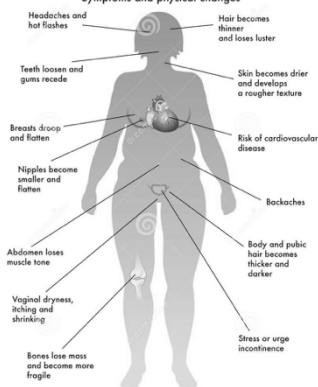


- Brain



## Menopause

Symptoms and physical changes



## The Side effects from either 'lowering' or 'blocking' estrogen need to be assessed in each individual

- When Estrogen levels drop, the membranes of the vagina get thinner, become less flexible, and produce less lubricating fluid. Sexual intercourse may be uncomfortable
- Research studies have shown that if you pay attention to an individual's problems and have targeted interventions for them – you can improve how they do



## Advising patients - managing vaginal dryness

- Women on aromatase inhibitors experience more vaginal dryness than those on Tamoxifen
- **Use a lubricant** that's water-based (not hormone-based) such as Astroglide, Moist Again, or K-Y Liquid during intercourse.
- **Try a vaginal moisturizer** such as Replens, which can help the vaginal walls stay moisturized.
- **Avoid using anything that could be irritating** such as lotions, deodorants, perfumes, harsh or deodorant soaps, in the vaginal area.
- **Try different positions** during sex to ease discomfort
- **Talk to their partner** about how they are feeling.



## Advising patients – managing hot flashes

- **Non-medical treatments include:**
  - keeping well hydrated, wearing all-natural fiber clothes, dressing in layers, using cool packs to get back to sleep, exercising on a regular basis, practicing relaxation exercises, and avoiding triggers
- **Medications:**
  - No hormones – not Estrogen, not Progesterone, not Tibolone – research has shown that women on HRT and Tibolone have an increased risk of breast cancer recurrence
  - Antidepressants, specifically Effexor (Venlafaxine).
  - Started at a low dose (compared to when they are used as antidepressants).
  - Other medications commonly used included gabapentin

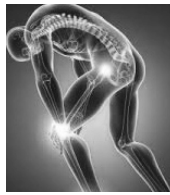


## Cognition problems , mood swings, weight gain, hair loss and DVT



## Aromatase Inhibitors and joint aches

- **What causes AI-related joint symptoms?**
- Not well understood.
- One common theory is that the rapid drop in estrogen levels may be responsible for two reasons:
  - this drop may actually lower the pain threshold, allowing the brain to better "detect" joint symptoms that already exist.
  - the drop in estrogen causes cytokines (proteins released by the body's cells) to be released in high levels, which may hasten bone loss and aging, leading to pain.



## Managing joint aches

- Change medicine from AI to Tamoxifen
- Anti inflammatory medications
- Pain medications
- Physical activity and stretching
- Accupuncture (shown to be helpful in some small studies)



## Late effects of estrogen deprivation on the heart

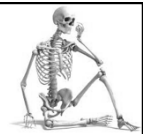


- Women who enter menopause early are at greater risk for **heart disease** and **premature death**
- Meta-analysis of 32 observational studies, involving more than 300,000 women and concluded that:
  - Overall, **heart disease** risk appeared to be **50 percent** greater for the women who were under **45 when menopause began**

Ref: Association of Age at Onset of Menopause and Time Since Onset of Menopause With Cardiovascular Outcomes, Intermediate Vascular Traits, and All-Cause Mortality A Systematic Review and Meta-analysis  
AMA Cardiol. 2016;1(7):767-776. doi:10.1001/jamacardio.2016.2415



## Late effects of estrogen deprivation on bones



- Estrogen has a protective effect on bone, and reduced levels of the hormone trigger bone loss
- **Bone thinning** and an increased risk of **osteoporosis** is a real concern for women on **aromatase inhibitors**, **decreased estrogen production** or **premature menopause** due to surgery or chemotherapy.
- **It is important to note that** tamoxifen increases the risk of osteoporosis in **premenopausal** women, but can actually increase bone density in **menopausal** women.



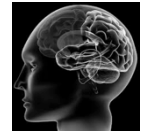
## Advising patients – to preserve bone health



- Exercise – resistance training, weight bearing exercise
- Increase calcium intake
- ... as well as vitamin D...
- ... and supplement as needed
- Cut back on caffeine
- Drink alcohol only in moderation
- Cut down on salt
- Bisphosphonates
- Reduce risk of falls



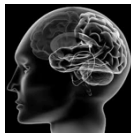
## Advising patients – to help with brain function



- Ask our patients if they are having problems
- Refer for more medical tests if severe
- Find cognitive rehabilitation therapists in your region
- Practicing to be more organised
- Practicing with puzzles
- Using the lumonsity app
- NEXT STEPS program
- Exercise



## Advising patients – to help with brain function



- Ask our patients if they are having problems
- Refer for more medical tests if severe
- Find cognitive rehabilitation therapists in your region
- Practicing to be more organised
- Practicing with puzzles
- Using the lumonsity app
- NEXT STEPS program
- Exercise



## References

- Irwin ML, Carmel R, Gross C, et al. Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer survivors. [doi:10.1093/jco/24.11.3045](http://doi.org/10.1093/jco/24.11.3045)
- Gallard S, Stearns V. Aromatase inhibitor-associated bone and musculoskeletal effects: New evidence defining etiology and strategies for management. *Breast Cancer Res* 13:203, 2011.
- 2. Pritchard CA, Bosseman L, Young T, et al. Aromatase inhibitor-associated arthralgia and/or bone pain: Frequency and characterization in non-clinical trial patients. *Ann Breast Cancer* 7:775-778, 2007.
- Singh S, Guscik J, Mosher D, et al. Effect of baseline serum vitamin D levels on aromatase inhibitors induced musculoskeletal symptoms: Results from the HES-0, chemoprevention study using anastrozole. *Breast Cancer Res Treat* 133:629-629, 2012.
- 13. Crew KD, Capodice A, Greenlee H, et al. Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated pain symptoms in women. *J Clin Oncol* 28:1164-1169, 2010.
- 14. Bao T, Cai L, Giles JT, et al. A dual-center randomized controlled double-blind trial assessing the effect of acupuncture in reducing musculoskeletal symptoms in breast cancer patients taking aromatase inhibitors. *Breast Cancer Res Treat* 138:157-174, 2012.
- 15. Fontaine DB, Seynabev C, Hadji P, et al. Specific adverse events predict survival benefit in patients treated with tamoxifen or aromatase inhibitors: An international tamoxifen/electrometastatic adjuvant multinational trial analysis. [doi:10.1200/JCO.2012.2266.2014](http://doi.org/10.1200/JCO.2012.2266.2014)
- Coleman RE, Bolton WW, Landow M, et al. Aromatase inhibitor-induced arthralgia: clinical experience and treatment recommendations. *Cancer Treat Rev* 34:275-82, 2008.
- Goss JM. Buprenorphine: Improving tolerance of AIs: predicting risk and uncovering mechanisms of musculoskeletal toxicity. *Oncology (Williston Park)* 22:1416, 1424, 2008.
- Henry NH, Giles JT, Ang D, et al. Prospective characterization of musculoskeletal symptoms in early stage breast cancer patients treated with aromatase inhibitors. *Breast Cancer Res Treat* 111:365-72, 2008.
- Henry NH, Giles JT, Stearns V. Aromatase inhibitor-associated musculoskeletal symptoms: etiology and strategies for management. *Oncology (Williston Park)* 22:1407-8, 2008.
- Mao JJ, Bruner DW, Stricker C, et al. Feasibility trial of electroacupuncture for aromatase inhibitor-related arthralgia in breast cancer survivors. *Integr Cancer Ther* 8:123-9, 2009.
- Mao JJ, Stricker C, Bruner D, et al. Patterns and risk factors associated with aromatase inhibitor-related arthralgia among breast cancer survivors. *Cancer* 115:3631-9, 2009.
- Madhwal AA, Spino TP, Chaubey AA, et al. Aromatase inhibitor-related musculoskeletal symptoms: is preventing osteoporosis the key to eliminating these symptoms? *Clin Breast Cancer* 9:34-8, 2009.
- Niravath P. Aromatase inhibitor induced arthralgia: a review. *Annals of Oncology*, 2013. Found at: <http://annonc.oxfordjournals.org/content/early/2013/03/06/annonc.mdt037.full.html>
- **NH Osteoporosis and Related Bone Diseases – National Resource Center**
- Website: <http://www.bonecah.gov>
- **National Cancer Institute**
- Website: <http://www.cancer.gov>
- Alicdar N, Ozkan S, Kucuruk S, Aslay I, Ozkan M. Association of Coping Style, Cognitive Errors and Cancer-related Variables with Depressive Women Treated for Breast Cancer. *Jpn J Clin Oncol*. 2012.

