

## The Gynecologic Implications of Breast Cancer

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## Breast Cancer Epidemiology

- Breast Ca most common invasive cancer in US women
- 178,480 estimated new cases invasive Breast ca in 2007
- 25% diagnosed in reproductive yrs
- More than 25,000 cases per yr in California
- Lifetime risk 1 in 8 at age 85

## Breast Cancer Epidemiology

- 2 million women in US with history of Breast Ca
- Breast cancer rates were increasing since 1980 but recent reports show decline in breast cancer incidence
- Unclear if related to drop in HRT use after publication of WHI, frequency of mammography, or ? other factors

## Breast Cancer Epidemiology

- 80% women diagnosed alive at 5 yrs – 97% alive for localized breast cancer
- Risk of death from Breast Ca 1 in 28
- 40,000 deaths per year
- Second leading cause of cancer deaths after Lung Ca

## Breast Cancer Treatments

- Breast surgery – either breast conserving lumpectomy or modified mastectomy. May also include immediate or delayed reconstructive procedures
- Radiation
- Chemotherapy
- Hormonal Therapies



These treatments can all have gynecologic effects

## Gynecologic Issues Related to Breast Cancer

- Chemotherapy induced menopause
- Side effects of hormonal therapies
- Treatment of menopausal symptoms
  - Hot flashes
  - Vaginal dryness/discomfort
  - Sexuality issues
- Gynecologic uses of hormonal therapies
- Ovarian suppression

## Gynecologic Issues Related to Breast Cancer



- Fertility drugs and breast cancer
- Pregnancy and breastfeeding after breast cancer
- Breast cancer diagnosed during pregnancy
- Hormone replacement therapy after breast cancer
- Ovarian Surveillance: BRCA1/2



## Breast Cancer Treatments and Menopause

Menopausal complaints often more severe

- Surgical treatments may include oophorectomy with immediate onset of menopause
- Premenopausal women with normal menstrual functioning get put into immediate menopause with chemotherapy
- Postmenopausal women abruptly stop their hormones when diagnosed with breast cancer
- Side effects of hormonal drugs like Tamoxifen often severe

## Chemotherapy Induced Menopause

- Incidence of ovarian failure dependent on chemotherapy regimen, cumulative dose and age
- Most due to alkylating agents - cyclophosphamide
  - 10-33% after 1 cycle CMF
  - 33-81% after 6 cycles CMF
- 50% women < 35 resume normal menses post chemotherapy
- 70 -90% women > 40 have permanent ovarian failure post chemotherapy

## Chemotherapy Induced Menopause

- Associated with increased FSH and decreased estradiol
- Symptoms may be more severe given rapid onset
- Women who menstruate post chemotherapy still at increased risk for premature menopause



## Hormonal Treatments and Breast Cancer

- Used to reduce recurrences and overall breast cancer mortality in women with **hormone receptor positive** breast cancer
- Biologic goals of hormonal therapy
  - Block production of estrogen
  - Block action of estrogen
  - Down-regulate the estrogen receptor

## Hormonal Treatments of Breast Cancer

- SERMS: Tamoxifen, Raloxifene, Toremifene
- Estrogen Receptor Downregulators: Fulvestrant
- Aromatase Inhibitors: Anastrozole (Arimidex), Letrozole (Femara), Exemestane (Aromasin)



### Hormonal Treatments of Breast Cancer - Tamoxifen

- Complex drug with estrogen and anti-estrogen properties
- Originally made as contraceptive then found to suppress mammary tumors in rats
- By 1992 shown to increase disease free interval and decrease contralateral breast ca in pre and postmenopausal women

### Tamoxifen – What are the Benefits?

- 5 yrs of Tamoxifen reduces annual risk of breast cancer recurrence by about 40 % and risk of death by about 30 % - independent of age and chemotherapy use. Similar reductions seen over 15 years of follow up
- 5 years of Tamoxifen has been the standard of care for **hormone receptor +** tumors regardless of age of patient, menopausal status, LN status, or tumor size

### Tamoxifen – What about longer treatment?

- Longer treatment may result in resistance and tumor dependence on TAM for growth, updated reports from National Surgery Adjuvant Breast and Bowel Project in US showed slightly lower survival with continued use of TAM beyond 5 yrs
- European trials - International Breast Cancer Intervention Study and the Royal Marsden Hospital trial have shown that the benefits of tamoxifen extend beyond the active treatment period and that longer treatment may provide continued decreases in breast cancer

### Tamoxifen for Breast Cancer Prevention

- Breast Cancer Prevention Trial showed 45% reduction in ER+ breast ca in high risk pts
- Approved by FDA in 1998 for breast cancer **prevention**

## Tamoxifen – Why Don't More Women Use for Prevention?

- Adverse side effects reported in 60% pts
- 20-40% discontinue drug because of poor tolerability and effects on QOL
- Weight gain typically 7-10 lbs

### Common Side Effects:

Hot Flashes  
Vaginal Discharge  
Vaginal Dryness  
Joint Pain  
Headaches



## Tamoxifen – Other Adverse Events

- Increased risks venous thromboembolism, PE and stroke. In NSABP prevention trial:
  - RR 1.6 for DVT
  - RR 3.0 for PE
  - RR 1.59 for stroke
- Updated data show for women who get a stroke, 10% will die and for women with a PE 20% will die

## Tamoxifen - Biologic Effects

- Agonist and Antagonist effects
- Effects of Tamoxifen vary depending on hormonal environment

## Tamoxifen and Premenopausal Women

- Induces estrogen production and ovulation - has been used for ovulation induction for IVF
- Case reports of ovarian cysts – unclear incidence, reports as high as 40%
- Case reports of endometriomas - unknown whether induces new endometriosis or exacerbates existing disease
- No significant estrogenic effects on endometrium – only rare reports of endometrial cancers

## Tamoxifen and Premenopausal Women - Effects on Menses

- 50% pts have menstrual irregularity - oligo and amenorrhea
- Pregnancy: Reports of teratogenicity in rodent studies – although series of women who have conceived on Tamoxifen and had normal pregnancy outcomes
- Nonhormonal forms of contraception indicated

## Tamoxifen and Postmenopausal Women

- Case reports of growth of fibroids
- Case reports of endometriosis and endometriomas
- Increased endometrial proliferation, cystic changes, polyp formation, adenocarcinoma and uterine sarcoma

## Tamoxifen and Endometrial Cancer

- Frequency of cancer dependent on endometrial surveillance: TVS vs. EMB and criteria for surveillance – symptomatic vs. asymptomatic. RR 2-4 in RCT
- RR in the US NSAPB trial was 2.53, seen in women > 50
- Risk thought to increase with longer Tam use - Breast Cancer Trialists' Collaborative Group showed risk doubles with every 2 years of Tam use, and 4-fold higher with 5 years of use

## Tamoxifen and Endometrial Cancer

- Other trials have shown RR of 6.9 for Tam use > 5 yrs
- Absolute risks - about 2 cases of endometrial cancer per 1000 women taking Tam each year
- 95% of Endometrial Cancers present with Vaginal Bleeding
- Most women get a much greater benefit to their breast than risk to their uterus

## Tamoxifen and Endometrial Cancer

- Most studies show histologic type and grade comparable in users and nonusers
- Cochran review suggested higher mortality for Tamoxifen induced endometrial cancers, annual excess of .2 per 1000
- Large review from MD Anderson 8/04 showed Tam users had shorter time to development of endometrial ca compared to nonusers, no difference in clinical or pathological features, no difference in survival

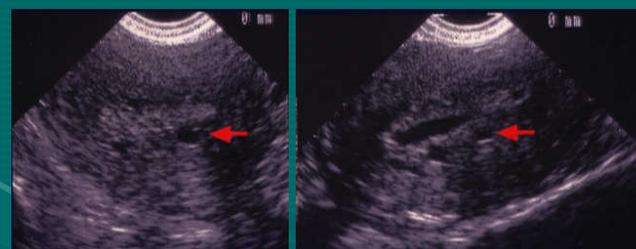
## Tamoxifen and Uterine Sarcomas

- Sarcomas occur in 2-5% of patients with uterine malignancy
- Sarcomas accounted for 10% of uterine malignancies in NSABP trials
- Overall incidence:
  - .01 - .02/ 1000 non Tam users
  - .17/ 1000 in Tam users (in NSABP)
- Survival from sarcomas not affected by Tamoxifen use

## Endometrial Surveillance - Ultrasonography

- Increased endometrial thickness, irregular echoes, cystic changes, polyps and hyperplasia in postmenopausal women
- Findings do not correlate with malignant histology
- Thickened endometrium can be atrophic. Mechanism may be enlargement of subendometrial glands
- Should not use endometrial thickness as an indicator for intervention, high false positive rate even with cutoff of 10mm

## Ultrasound of Patient on Tamoxifen



## Endometrial Surveillance – Other Imaging for patients on Tamoxifen

- Sono-hystero-graphy - high sensitivity and high predictive value
- MRI high sensitivity but poor specificity - role of MR imaging in women on tamoxifen is unproven (American College of Radiology)

Limited published data looking specifically at Tamoxifen

## Tamoxifen – What does ACOG say?

- Updated guidelines published in June 2006
- **Postmenopausal women** should be monitored closely for endometrial hyperplasia or cancer and be informed about the risks associated with the drug
- Abnormal vaginal bleeding, bloody discharge, and staining or spotting should be evaluated

## Tamoxifen – What does ACOG say?

- Because some evidence suggests higher risks in women who had benign endometrial polyps before tamoxifen, consider pretherapy screening
- Routine endometrial surveillance is not recommended unless the patient is at high risk of endometrial cancer
- If atypical endometrial hyperplasia develops, patients should receive appropriate treatment, and reassess tamoxifen use - hysterectomy if tamoxifen must be continued

## Tamoxifen –New Testing in 2006

- Tamoxifen is converted into its active metabolites in the liver by the CYP2D6 liver enzyme, part of the P450 detoxification pathway
- CYP2D6-mediated drug metabolism is highly variable. Some individuals have altered CYP2D6 gene sequences that result in decreased enzyme production
- 7-10% of women with breast cancer may not receive full benefit of tamoxifen, because of altered CYP2D6 genes which could reduce the effectiveness of tamoxifen and increase chance of recurrence

## Metabolism of Tamoxifen –New Changes in 2006

- Polymorphisms associated with CYP2D6 poor metabolizer status are autosomal recessive
- On October 18, 2006 an FDA panel agreed that the CYP2D6 genes are a predictor of tamoxifen efficacy. They recommend relabeling tamoxifen to say that “2D6” poor metabolizers who take tamoxifen have a higher risk for breast cancer recurrence, and that **testing is now available.**

## Tamoxifen and Quality of Life



## Tamoxifen and Hot Flashes

- More than 50% of women have side effects
- Exacerbates vasomotor instability
- Symptoms decrease with increased Tamoxifen use
- For postmenopausal women, severity of symptoms tends to correlate with severity of symptoms when first menopausal



## Hot Flashes - Treatment

- Alternatives to Hormones:
  - Low dose antidepressants – Effexor, Paxil, Prozac, Celexa and Remeron
  - Gabapentin (Neurontin)
  - Antihypertensive Clonidine
  - Vitamin E
  - Soy supplements
  - Herbal Products: best studied Black Cohosh
  - Tibilone (in Europe)
  - Chinese Herbs

## Venlafaxine (Effexor) and Hot Flashes

- Most well studied – RCT's, largest populations and longest trials (13 wks)
- Felt to improve overall well being
- Beneficial effects in days compared to depression
- Side effects - Dry Mouth, Decreased Appetite, Nausea, Sleeplessness

## Venlafaxine (Effexor) and Hot Flashes

- Doses different than depression
  - depression 37.5 - 75 mg BID/TID - max 375 mg/d
  - hot flashes 37.5-75 mg/d - Most effective dose 75 mg/d
- Unclear if sexual dysfunction at these doses
- Not known whether negative effects on vaginal dryness given anticholinergic side effects

## Paroxetine (Paxil) and Hot Flashes

- RCT N=151 showed significant relief of HF's compared to placebo with both 10 and 20 mg/day, less discontinuation with lower dose
- **Use Paxil with caution if on Tamoxifen** - SSRIs may block the therapeutic benefit of tamoxifen, because paroxetine is an effective inhibitor of the CYP2D6 enzyme that is needed to metabolize tamoxifen into the active metabolite endoxifen which is responsible for the anti-estrogenic activity of tamoxifen – new warnings on package insert
- Not an issue for any serotonin norepinephrine reuptake inhibitors (SNRI) like venlafaxine with no significant CYP2D6 inhibitory activity.

## Gabapentin (Neurontin) and Hot Flashes

- Prospective pilot 24 women, 300 to 900 mg/d showed mean 66% reduction in HF frequency compared to baseline  
Loprinzi CL et al. *Mayo Clin Proc* 2002
- RCT 59 PMP pts, 900 mg/d assoc with 45% decrease in HF frequency and 54% reduction in total frequency/severity  
Guttuso T et al. *Obstet Gyn* Feb 2003
- RCT 420 PMP pts, 900 mg/d assoc with 41% decrease in HF frequency and a 49% decrease in HF severity  
Pandya, K. *The Lancet*, Sept. 3, 2005
- RCT gabapentin, titrated to 2,400 mg/daily compared with 625 mg/d of conjugated estrogen found that gabapentin was as effective as estrogen in the treatment of postmenopausal hot flashes – only 12 wks  
Reddy et al., *Obstet Gynecol* 2006

## Antihypertensive Clonidine and Hot Flashes

- Clonidine .1 mg/d PO or patch – 2 RCT have shown slight benefit in reducing number of hot flashes, some improvement in QOL
- Side effects - sleep difficulties, dry mouth, fatigue, dizziness and nausea
- Avoid with low blood pressure

Rymer J, et al (2000) *BMJ*, 321(7275): 1516–1519

Pandya KJ, et al. (2000) *Annals of Internal Medicine*, 132(10): 788–793.

## Vitamin E and Hot Flashes

- Vitamin E 800 IU/day: marginal improvement compared to placebo in Randomized Controlled Trial (1 hot flash/day) No toxicity  
Barton DL, et al. *J Clin Oncol*. 1998;16(2):495-500.
- Should not use when undergoing radiation – concern that antioxidant effects may offset benefits
- Recent meta-analysis raised concerns about megadoses of Vitamin E and increased mortality risk – most patients studied “not healthy”
- Possible interaction of Tamoxifen and Vitamin E – lab data suggested Vit E decreased the inhibitory effects of Tamoxifen in ER+ breast cancer cell lines

### Soy and Hot Flashes

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www.glasbergen.com



**“We’re having soy patties, soy soup, soy salad, soy fries, soy shakes and soy pie...and the same thing for lunch and dinner. Welcome to menopause!”**

## Soy and Treatment of Menopausal Symptoms

- Soy Phytoestrogens – mixed results on relief of hot flashes
- Concern of weak estrogenic effects in the breast - reports of stimulation of nipple aspirate fluid. Concern soy (along with red clover and other herbal preparations) caused proliferation of estrogen-sensitive breast cancer cells (MCF-7) suggesting caution for women with a history of estrogen-sensitive breast cancer

Bodinet et al. *Menopause* (2004)

## Black Cohosh and Treatment of Hot Flashes

- Majority of studies indicate that extract of black cohosh (in Remifemin) improves menopause-related symptoms and is well tolerated

T. Low Dog. *Am J Med* (2005). *Menopause: a review of botanical dietary supplements*

- Possible benefits for depression and anxiety
- Most studies are not RCT



## Black Cohosh and Breast Cancer

- RCT showed Remifemin resulted in statistically significant improvements in menopausal symptoms without affecting hormone levels

Liske et al. *J Womens Health Gend Based Med* (2002)

- Constituents in Black Cohosh inhibited the growth of human breast cancer cells, and “may prove useful in breast cancer prevention or treatment”

Einbond et al. *Breast Cancer Res Treat* (2004)

- Remifemin did not stimulate MCF-7 breast cancer cell growth and exerted inhibitory effects on cellular proliferation showing estrogen-antagonistic effects. “Suggests a favorable safety profile for use in women with a history of breast cancer”

Bodinet et al. *Menopause* (2004)

## Treatment of Hot Flashes - Lifestyle Modifications

- Regular exercise, particularly improves sleep
- Avoid foods or climate changes that trigger hot flashes – alcohol, caffeine, spicy foods
- Stress reduction – yoga, meditation, therapy, massage, “pleasure activities”

### Stress Reduction Kit



Directions:  
 1. Place kit on FIRM surface.  
 2. Follow directions in circle of kit.  
 3. Repeat step 2 as necessary, or until unconscious.  
 4. If unconscious, cease stress reduction activity.  
[www.kurpain.jp](http://www.kurpain.jp)

## Tibolone and Hot Flashes

- New class of agent known as a STEAR - Selective Tissue Estrogenic Receptor Regulator
- Not available in US yet
- As effective as HRT in the relief of hot flashes and vaginal dryness, and significantly improved sexual response - not felt to have endometrial effects

Keneman, Speroff, and the International Tibolone Consensus Group (*Maturitas* (2005)

Hickey et al. (*Lancet* (2005)

## Tibolone and Tamoxifen Induced Hot Flashes

- Found that tibolone decreased frequency and severity of hot flashes compared to placebo in postmenopausal women given tamoxifen without untoward effects on the endometrium (by EMB)

*Kroiss et al. (BJOG (2005): The effect of tibolone in postmenopausal women receiving tamoxifen after surgery for breast cancer: a randomised, double-blind, placebo-controlled trial*

## Tibolone - ? Beneficial for Breast Cancer

- Felt to lower breast tissue concentration of estrogen and not exhibit cellular proliferative activity, potentially protective in breast cancer. The ongoing **LIBERATE (Livial Intervention following Breast cancer Efficacy, Recurrence And Tolerability Endpoints)** trial (presenting first data at end of 2007) seeks to clarify this further, by studying menopausal symptom relief in postmenopausal women with a history of breast cancer

## Tamoxifen vs. Raloxifene for Breast Cancer Prevention – STAR Trial

- Raloxifene currently FDA approved for osteopenia and osteoporosis
- STAR trial: 5 years, one of largest breast cancer prevention studies, took place at more than 500 centers in US, Canada, and Puerto Rico.
- Both drugs reduced the risk of developing invasive breast cancer by about 50 percent
- Tamoxifen was better for decreasing noninvasive breast cancer
- Raloxifene users had lower incidence of uterine cancer
- Raloxifene just got FDA approval for breast cancer prevention (No data looking at effects of Raloxifene on Breast and Endometrium after Tamoxifen treatment)



## Aromatase Inhibitors

- Tamoxifen competes with estrogen at receptor binding site in the breast preventing receptor activation
- Aromatase Inhibitors prevent conversion of androstenedione and testosterone into estrogens and decrease peripheral circulating estrogen
- Not useful in premenopausal women because blocking aromatase in the ovaries results in lower estradiol levels which reduce negative feedback and increase pituitary gonadotropin output, increasing ovarian function

## Aromatase Inhibitors

- Initially first generation AI's used – Aminoglutethimide
  - Inhibited production of all adrenal steroids so needed to be given with hydrocortisone
  - Significant toxicity limited use
- Third generation AI's first approved for metastatic breast ca
  - Found superior to Tamoxifen
  - Orally administered
  - Less toxicity

## Aromatase Inhibitors



- Third generation AI's used:
  - Anastrozole (Arimidex)
  - Letrozole (Femara)
  - Exemestane (Aromasin)

} → **Nonsteroidal - reversible**

→ **Steroidal - irreversible inhibitors**

## Aromatase Inhibitors in Early Breast Cancer Arimidex, Tamoxifen, Alone or in Combination Trial (ATAC)



## Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial

- 9000 PMP women with early stage breast ca, first interim analysis presented in 2001:
  - Arimidex had improved DFS with HR .83
  - Arimidex had improved time to recurrence with HR .79
  - Arimidex had 58% lower incidence of contralateral breast cancer

### Anastrozole vs. Tamoxifen: Rates of Adverse Effects

	Anastrozole	Tamoxifen
Endometrial cancer	0.1%	0.7%
Fractures	7.1%	4.4%
Hot flashes	35.0%	40.3%
Ischemic cerebrovascular events	1.1%	2.3%
Musculoskeletal disorders	30.3%	23.7%
Vaginal bleeding	4.8%	8.7%
Vaginal discharge	3.0%	12.2%
Venous thromboembolic events	2.2%	3.9%

Source: Dr. Richard Sainsbury of the Royal Free and University College Medical School, London, for the ATAC investigators.

### Aromatase Inhibitors

- Updated analysis from ATAC have shown continued longer DFS, improvement in time to recurrence and decreased contralateral breast ca with Arimidex vs. TAM
- Many international trials have now shown efficacy of Aromatase Inhibitors in adjuvant treatment for postmenopausal women
- FDA approved Arimidex as **first-line adjuvant therapy** in PMP women with hormone positive breast cancer
- Gynecologic side effects generally less with AI treatment – fewer hot flashes, but much more vaginal dryness

### Aromatase Inhibitors – What We Don't Know

- Optimal sequence of Tamoxifen and Aromatase Inhibitors in breast cancer treatment
- Long term effects on bone and lipids – preliminary data that pretreating women with bisphosphonate Zoledronic acid may protect bones although some concerns of possible jaw necrosis with prolonged bisphosphonate administration.
- Long term cardiovascular effects



### Aromatase Inhibitors – What's New

- Data in the extended adjuvant setting have continued to show improved time to recurrence and contralateral breast cancer
- Additional trials looking at AI's in adjuvant, neoadjuvant, DCIS and chemoprevention settings
- Trials in premenopausal women looking at AI's with chemotherapy and GnRH suppression

## Aromatase Inhibitors and Uterine Effects

- Study compared expected cases of uterine cancer from registry data in US and Europe to that seen in ATAC trial:
  - Found greater than expected cases for TAM (Standard Incidence Rate, SIR 2.68) and fewer than expected cases for Arimidex (SIR .73)
- Aromatase Inhibitors may actually **PREVENT** uterine cancer

## Aromatase Inhibitors – Other Potential Gynecologic Uses

- Ovulation Induction – studies have shown pregnancy rates similar to gonadotropins
- Treatment of Endometriosis – small study of Letrozole and Norethindrone reported to improve symptoms and histologic diagnosed endometriosis
- Possible treatment for Fibroids – documented aromatase in myoma cells

## What About other Quality of Life Issues after Breast Cancer?

- Vaginal Dryness
- Decreased Libido



## Other Issues – Vaginal Dryness

- Vaginal Moisturizer Replens - Several studies showing improvement in vaginal itching, irritation and dyspareunia - equivalent to vaginal estrogen creams.

Van der Laak, J Clin Pathol (2002)  
Bygdeman & Swahn, Maturitas (1996)  
Nachtigall, Fertil Steril (1994)

- Replens in breast cancer populations - found improvement in vaginal dryness and pain during intercourse, with most of the beneficial effects within the first 2 weeks of treatment and sustained benefit

Pinkerton & Santen Endocr Rev (1999)  
Loprinzi et al. J Clin Oncol (1997)

## Other Issues - Vaginal Dryness

- Water based lubricants for sexual activity: Astroglide, Probe, Silk
- Vaginal Preparations of Estrogens or Testosterones thought to increase vaginal blood flow, improve tone and maintain vaginal moisture: creams, ointments, gels
- Vaginal Estring - a slightly opaque ring placed into the vagina for 3 mos - contains a reservoir of 2 mg estradiol which releases approx. 7.5 µg estradiol/24 hours, in a consistent stable manner over 90 days – almost no systemic absorption
- Vagifem - vaginal tablet containing 25 µgm estradiol inserted 2x per week with minimal systemic absorption
- No long term data in breast cancer patients

## Menopause and Sexual Functioning in the Breast Cancer Patient

- If experiencing sleep disturbances, may influence sexual desire
- Body image changes related to breast cancer surgery may influence desire for both partners
- Other life stressors in addition to breast cancer may affect sexual functioning – job, stressors related to children or aging parents, relationship satisfaction



## Treatment of Sexual Dysfunction - Decreased Desire

- Sexual desire thought to be related in some way to levels of male hormone testosterone
- Herbal remedies thought to improve desire, recent study showed DHEA-S levels were better predictor of low libido compared to Testosterone
- DHEA 25-50 mg/day used – precursor to testosterone
- Herbal products that thought to cause smooth muscle relaxation and improved genital blood flow
- In general lack of good data

## Treatment of Sexual Dysfunction - Decreased Desire

- Low doses of vaginal or oral Testosterone, need to obtain from compounding pharmacies, safety in breast cancer patients not known
- Low doses of antidepressant Wellbutrin – frequently used to counterbalance sexual dysfunction associated with SSRI antidepressants
- Potential new drugs aimed at improving genital blood flow

## Treatment of Sexual Dysfunction - Education

- Open communication important for both partners
- Alter sexual behavior as needed to accommodate for physical, emotional and social changes
- Therapists that specialize in sex therapy



## Ovarian Ablation

Breast Cancer Survival

## Induced Menopause – Ovarian Ablation and Breast Cancer Survival

- Ovarian ablation oldest form of systemic treatment for breast ca, first described 1896
- Many studies looking at ablation as adjuvant therapy, most small, non RCT
- Methods – Surgical, Radiation-Induced, Medical with GNRH analogs (Zoladex)
- Ovarian suppression thought to produce similar benefit to chemotherapy in premenopausal ER+ breast ca, but no clear data suggesting benefit of ovarian ablation to the newer chemo regimens shown to be superior to standard CMF or AC (like Taxane regimens)

## What about Ovarian Ablation plus Chemotherapy/Endocrine Therapy?

- Unclear whether ovarian ablation in addition to chemo or endocrine therapy provides additive benefit
- May be beneficial in subgroups of young women who do not develop amenorrhea after chemotherapy

## Ovarian Ablation

- Randomized trial of adjuvant ovarian suppression in 926 premenopausal patients with early breast cancer treated with adjuvant chemotherapy found that for women < age 40 with ER+ tumors, ovarian suppression significantly decreased risk of recurrence
- Current trials (TEXT, SOFT) looking at ovarian suppression ongoing to determine optimal hormonal therapy for premenopausal women with early breast cancer

## Ovarian Suppression and Fertility

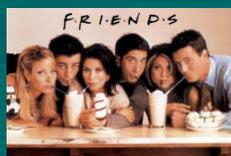
- Preliminary studies looking at ovarian suppression prior to chemotherapy in hopes of preserving ovarian function, mixed results
- Most fertility programs focusing on assisted reproductive techniques to preserve fertility – ovarian stimulation with Tamoxifen or Letrozole and embryo cryopreservation, ovarian tissue or oocyte cryopreservation



## Other Issues – Socialization and Breast Cancer

- Women with good social networks have better survival than those that are socially isolated
- Based on data from Harvard Nurses Health Study 2835 study participants
- Social networks may improve access to care

Kroenke CH et al. Journal of Clinical Oncology. 2006;24: 1105-1111



## Marina Lee Uilani Bermudez Complementary Breast Cancer Treatment Fund

Provides funding for complementary care for women with breast cancer



Thank You!

