Pt’s Who Don’t Follow Treatment

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Standard Breast Cancer Therapy

Advancements in Breast Cancer

- Chemotherapy
  - Full potential was recognized in the 20th century.
  - Several attempts at treating the disease as systemic are evident in our history.
Advancements in Breast Cancer

Chemotherapy
- During World War I and II officials took note of the effect that biological warfare (nitrogen mustard gas) took on toxic changes to the bone marrow on soldiers and civilians that were contaminated.
- The destruction of blood cells and lymphatic tissue was noted from the mustard gas victims.

Advancements in Breast Cancer

Chemotherapy
- Colonel Steward F. Alexander forwarded these observations to Goodman and Gilman of Yale University.
- They began administering the agent to lymphoma patients with dramatic results. Their tumors regressed! (1946)

Metastatic cancer was first cured in 1956 when methotrexate was used to treat a rare tumor called choriocarcinoma.

Advancements in Breast Cancer

Chemotherapy
- The United States Congress created a National Cancer Chemotherapy Service Center (NCCSC) in 1955.
- This was the first federal program to promote drug discovery for cancer
- Unlike now, most pharmaceutical companies were not yet interested in developing anticancer drugs.
Chemotherapy

In the early 1960s, the National Cancer Institute conducted wide-scale tests.

In 1962, an extract of the Pacific Yew Tree bark, Taxol, showed particular promise.

Advancements in Breast Cancer

- Chemotherapy
  - 1965, James Holland, Emil Freireich, and Emil Frei hypothesized that cancer chemotherapy should follow the strategy of antibiotic therapy, with combinations of drugs.
  - Cancer cells could conceivably mutate to become resistant to a single agent, but by using different drugs concurrently it would be more difficult for the tumor to develop resistance to the combination.

Chemotherapy

- Drugs (either alone or in combination) are delivered to kill or maintain cancer cells.
- Can be delivered intravenously, orally, or by injection.
- Most courses are 3-6 months long and can be taken daily, weekly or monthly, depending on the body’s response to the drug.
In many cases, chemotherapy medicines are given in combination, which means you get two or three different medicines at the same time. These combinations are known as chemotherapy regimens. In early stage breast cancer, standard chemotherapy regimens lower the risk of the cancer coming back. In advanced breast cancer, chemotherapy regimens make the cancer shrink or disappear in about 30-60% of people treated. Keep in mind that every cancer responds differently to chemotherapy.

Breastcancer.org

Two groups of chemotherapy medicines for breast cancer therapy

- **Anthracyclines** are chemically similar to an antibiotic. Anthracyclines damage the genetic material of cancer cells, which makes the cells die. Adriamycin, Ellence, and daunorubicin are Anthracyclines.
- **Taxanes** interfere with the way cancer cells divide. Taxol, Taxotere, and Abraxane are taxanes.

Standard chemotherapy regimens include:

- **AT**: Adriamycin and Taxotere
- **AC ± T**: Adriamycin and Cytoxan, with or without Taxol or Taxotere
- **CMF**: Cytoxan, methotrexate, and fluorouracil
- **CEF**: Cytoxan, Ellence, and fluorouracil
- **FAC**: fluorouracil, Adriamycin, and Cytoxan
- **CAF**: Cytoxan, Adriamycin, and fluorouracil
  (The FAC and CAF regimens use the same medicines but use different doses and frequencies)
- **TAC**: Taxotere, Adriamycin, and Cytoxan
- **GET**: Gemzar, Ellence, and Taxol
Abraxane (chemical name: paclitaxel)
Adriamycin (chemical name: doxorubicin)
carboplatin (brand name: Paraplatin)
Cytoxan (chemical name: cyclophosphamide)
daunorubicin (brand names: Cerubidine, Daunoxome)
Doxil (chemical name: doxorubicin)
Ellence (chemical name: epirubicin)
fluorouracil (also called 5-fluorouracil or 5-FU; brand name: Adrucil)
Gemzar (chemical name: gemcitabine)
Halaven (chemical name: eribulin)
Ixempra (chemical name: ixabepilone)
methotrexate (brand names: Amethopterin, Mexate, Folex)
Mitomycin (chemical name: mutamycin)
mitoxantrone (brand name: Novantrone)
Navelbine (chemical name: vinorelbine)
Taxol (chemical name: paclitaxel)
Taxotere (chemical name: docetaxel)
thiotepa (brand name: Thioplex)
vincristine (brand names: Oncovin, Vincasar PES, Vincrex)
Xeloda (chemical name: capecitabine)

New Technology for Chemotherapy treatment of Cancer under trial basis

Magnetic Chemotherapy
Interventional radiologists are currently investigating a new technique in which magnets are used to pull chemotherapy drugs into tumors. Microscopic magnetic particles are attached to the cancer-killing drugs and infused through a catheter into the blood vessel that feeds the tumor.
Magnetic Chemotherapy

- A rare earth magnet is positioned over the patient's body directly above the site of the tumor. The magnet pulls the drug-carrying particles out of the blood vessel so that they lodge in the tumor. Although the technique is still experimental, early research is promising. Physicians are hopeful that it will bolster the effects of chemotherapy while avoiding some of the drugs' side effects, such as hair loss and nausea.

Chemotherapy

- Damages cells that divide, so parts of the body where normal cells divide frequently are commonly the most affected by chemotherapy.
  - Mouth
  - Intestines
  - Hair
  - Skin
  - Bone marrow

Chemotherapy

- Temporary Effects
  - Hair loss
  - Fatigue
  - Nausea
  - Pain
  - Increased risk of infection
  - Depression
  - Increased sun sensitivity
  - Numbness or weakness in the hands and feet
Chemotherapy

- Long-Term Effects
  - Lung damage
  - Heart damage
  - A second cancer in the future
Case Study

- Pt in 2007 had IDC grade 2 to left breast
- Pt refused chemo because she wanted to try a natural approach using diet and exercise.
Today at 7:47 AM

01/09/2008

This 44-year-old lady returns to discuss treatment options for left breast cancer, accompanied by her father, mother, and sister.

The 2 November core biopsy of the left breast processed at the Center shows estrogen receptor 70%, progesterone receptor 20%, HER2/neu FISH ratio 9.68 (amplified). I advised her of this previously by telephone, and discussed the potential significance of it.

Because the HER2/neu is amplified, it is thought that there is a higher risk of developing metastases in the future if she does not have systemic adjuvant treatment including trastuzumab. Because she is premenopausal, adjuvant tamoxifen will be the standard hormonal approach, noting that this may be less effective against HER2/neu amplified breast cancer.

Ms. understands the high risk of developing metastases without systemic treatment, and the significant risk reduction with chemotherapy including trastuzumab (Herceptin) as we discussed before. She would like to have surgery first. The importance of adjuvant radiation treatment after breast-conserving surgery is discussed again, and she is very reluctant to consider this. If she has a mastectomy, radiation probably will not be recommended. If she has preoperative chemotherapy, the volume of the breast needing to be removed at her surgery probably will be decreased, offering a better cosmetic result. She understands this.

She will call me after she recovers from surgery, to make a final decision on systemic adjuvant treatment.

The standard recommendation for her is 24 weeks of trastuzumab, and then trastuzumab every 3 weeks to complete 1 year. During the first 12 weeks, she would be given weekly paclitaxel, and this is followed by 4 courses of FEC (fluorouracil, epirubicin and cyclophosphamide) given at 3-week intervals. The small risk of cardiac toxicity is discussed.

2009
This 45-year-old lady returns for review because of suspected metastasis from her previous left breast cancer.

After her consultation here in December 2007, she had breast conserving surgery at Hospital under the care of Dr. on 24 January 2008. The surgical specimen measured 6.0 x 5.3 x 4.5 cm, containing a 2.6 cm invasive ductal carcinoma with positive estrogen and progesterone receptors. The amplified HER-2/neu result is recalled. The surgical margin was 1.5 mm. Two sentinel nodes were benign.

Dr. reportedly advised Ms. to have adjuvant radiation treatment, but she decided not to. Rather than having standard treatment, she preferred to follow a personal regimen of diet and nutrition.

Reportedly in October 2008, left mammogram suggested a recurrence, and Ms. tells me that a biopsy showed recurrence. On 19 November 2008, a PET scan reportedly showed lung metastases.

Ms. went to California for non-traditional treatment, including a rigorous diet on which she has lost weight. She continues to feel well. On 1 June another PET/CT reportedly showed multiple new metastases, with cancer involving the left breast, lungs, mediastinum, and right iliac bone. She does not have any symptoms. She comes now for further review.
I recommend weekly trastuzumab for 24 weeks, followed by every 3-week treatment. This is given with weekly paclitaxel for the first 12 weeks, and then with every 3-week FEC (fluorouracil, epirubicin, cyclophosphamide) for 4 courses. The small cardiac risk is noted, and an echocardiogram baseline is requested. The first dose of trastuzumab (Herceptin) can cause fever and chills, but subsequent doses are generally well tolerated. Hair falls out, and a prescription is written for a hair prosthesis. Numbness of fingers and toes may be troublesome. Weekly paclitaxel generally is not myelosuppressive, and weekly counts are not needed. A prescription is written for ondansetron 8 mg (dispense 30), noting that this is usually not needed until the FEC phase of chemotherapy when it is best taken every 8 hours for at least 3 days with each dose of every 3-week chemotherapy. The myelosuppressive risk of FEC also is noted, with a risk of infection while the white blood count is low. Menstrual periods are expected to stop, and may not restart.

Ms. favors treatment with chemotherapy, and orders are written tentatively to start on 11 June. She will be given trastuzumab 4 mg/kg or 135 mg intravenously over 90 minutes, and then she will have 2 mg/kg or 120 mg intravenously over 30 minutes in subsequent weeks. She will be given dexamethasone 10 mg intravenously. If she does not have an allergic reaction to paclitaxel, this will not need to be repeated. She will have weekly cimetidine 300 mg and diphenhydramine 50 mg intravenously, followed by paclitaxel 80 mg per meter squared or 135 mg intravenously over 60 minutes.

She will have the first dose of zoledronate 4 mg in 100 cubic centimeters normal saline intravenously over 15 minutes, and this will be repeated every 4 weeks.

Reason for Admission: Altered mental status and headache with new progression of brain metastases.

Attending Physician: Dr. [Redacted]

History of Present Illness: Ms. is a 49-year-old female with metastatic HER-2 positive breast cancer under the care of Dr. [Redacted], currently on treatment with fulvestrant plus Navelbine plus Herceptin. The patient was in her usual state of health until 1 week ago when she noted some pressure-like sensations in the lower part of her head, which she attributed to stiffness of her neck. She reports that on 02/01/2013, she was driving herself to a conference meeting, however, after she arrived, she noticed floaters in both eyes which were not new to her, as well as nausea as well as a headache, which was point tender on the base of the skull on the right side behind the ear. The patient then went to drive herself home after the headache was progressive; however, she could not remember the directions home, even though she had driven this path multiple times. She slowly made her way back home safely. There was no seizure activity, as reported by the patient. The headache continued to progress at which time she asked her boyfriend to bring her to the Emergency Center on 02/02/2013.
ASSESSMENT AND PLAN:
1. Ms.-------- is a 35-year-old premenopausal woman, diagnosed with a left breast upper outer quadrant invasive ductal carcinoma, that is a pT2 (2.1 cm pT2) 5/30 lymph nodes showing metastatic carcinoma, ER 40%, PR 3%, HER-2/neu negative and nonamplified on FISH, Ki-67 of 20%, status post left segmental mastectomy and axillary lymph node dissection, here for further systemic therapy.

2. I discussed in detail the pathology results with the patient. I explained the significance of having extensive lymph node involvement as well as the large size of the tumor.

3. I recommended to her systemic chemotherapy in the form of weekly paclitaxel x 12 followed by dose-dense Adriamycin and cyclophosphamide, once again all side effects were discussed in detail. Written information was once again provided.

4. All questions were answered to the patient and her husband’s satisfaction. Significant amount of time was spent in discussion.

5. However, unfortunately, the patient still declining systemic chemotherapy as she is afraid of the side effects. I tried my best to reassure her fears and to convince her that systemic chemotherapy in the adjuvant setting would significantly decrease the risk of recurrence from her high-risk breast cancer.

6. However, the patient has decided that she does not want any chemotherapy and would like to proceed with radiation therapy followed by surveillance alone.

7. I am respectful of the patient’s wishes and I have provided to her all information and the risk of recurrence associated with her disease.

8. The patient will return to my clinic after completion of adjuvant radiation therapy for continued surveillance.
Results...

- Pt came to the mammography department for her stereotactic breast biopsy, but felt she didn't need to proceed with the biopsy.
- The patient stated she would rather come back for a short term follow up and that will be in November 2016.

Complementary and Holistic Breast Cancer Treatment

- The goal of complementary medicine is to balance the whole person—physically, mentally, and emotionally—while conventional medicine does its work. For many people diagnosed with breast cancer, complementary medicine has helped to:
  - relieve symptoms
  - ease treatment side effects
  - improve quality of life
  - Researchers are working to better understand the value and benefit of complementary medicine in breast cancer.

Complementary Medicine

- Complementary medicine is used to describe therapeutic techniques that are not part of conventional medicine (also called "regular," "standard," or "mainstream" medicine). Complementary therapies are used as a "complement" or addition to conventional medicine. Because complementary medicine can be combined or integrated with conventional medical treatment, it is also called "integrative medicine."
Alternative Medicines

You may not hear about these treatments from your doctor or cancer team, but others may talk about things like traditional Chinese medicine, acupuncture, hypnosis, or machines that are supposed to find or cure cancer. Some people may recommend “body cleansing” with enemas or detoxification diets with special foods and preparation methods.
And even at that time... because all of us in the alternative world, from year to year you know so much more. I can’t do that. The idea of putting chemical poison into my body to cure me just doesn’t make sense. And he [the doctor] said “you’ll die if you don’t.” And I said, “I think I’ll die if I do what you want me to do.”

So I did end up doing radiation because a doctor I respected very much, who is an alternative doctor, said, “Well, you have to do radiation.” And I said, “Really? You would do it, too?” And she said, “Absolutely.”

Hormone Therapy

- Whole-body (systemic) treatment for hormone-receptor-positive breast cancers.
- What are the two systemic systems in the body?
- Used to prevent female hormones (estrogen, progesterone and estradiol) from fueling the growth of breast tumors in some patients.
- If a cancer has receptors for either estrogen or progesterone, it’s considered hormone-receptor-positive. (Estradiol is not only a critical impact on reproductive and sexual function, but also affects other organs including the bones.)
If both estrogen and progesterone receptors are present (ER+, PR+), your chance of responding to hormonal therapy is about 70%.

What percentage of breast cancers are ER+ and PR+?

A. 75%
B. 65%
C. 25%
D. 40%
Why cancers grow with estrogen

Hormone Therapy

Aromatase inhibitors:
- Aromatase inhibitors work differently from tamoxifen and raloxifene. Instead of blocking the estrogen receptors, they stop a key enzyme (called aromatase) from changing other hormones into estrogen. This lowers estrogen levels in the body, taking away the fuel that estrogen receptor-positive breast cancers need to grow.
- These drugs are only useful in women whose ovaries aren't making estrogen (such as those who have already gone through menopause).
Hormone Therapy

- Aromatase inhibitors Effects
  - Bone and joint pain
  - Osteoporosis
  - Nausea
  - Vomiting
  - Hot flashes
  - Weakness/fatigue
  - Headache
  - Insomnia
  - Dizziness
  - Drowsiness
  - High cholesterol
  - Weight gain

SERMs (Selective Estrogen Receptor Modulators):
  - Tamoxifen
  - Evista (chemical name: raloxifene)
  - Fareston (chemical name: toremifene)
Hormone: SERMs are selective estrogen-receptor modulators, or drugs that block the naturally circulating estrogen in breast tissues and other estrogen-sensitive tissues in your body. SERMs block natural estrogen by getting into the estrogen receptors before your own estrogen can get into place and signal the cells to grow and spread.

SERMs are called "selective" because they bind to particular estrogen receptors. This selective binding action is sometimes called estrogen inhibition, or estrogen suppression. SERMs do not prevent the production of estrogen, but they help to slow or stop the growth of estrogen-sensitive cancer cells by starving them of a full dose of natural estrogen.
SERMs’ Effects:
- Increased tumor or bone pain
- Hot flashes
- Nausea
- Fatigue
- Mood swings
- Depression
- Headache
- Hair thinning
- Constipation
- Dry skin
- Loss of libido

Pt before serms  Same pt on Tamoxifen one year later

Hormone Therapy
- Aromatase inhibitors:
  - Arimidex (chemical name: anastrozole)
  - Aromasin (chemical name: exemestane)
  - Femara (chemical name: letrozole)
Arimidex

- Chemical name is Anastrozole
- Approved adjuvant treatment for postmenopausal women with hormone receptor positive breast cancer. Approved in 1996.
- Also a SERM

Aromiasin

- Chemical name is exemestane
- Approved by FDA in 1999
- Can treat early and advanced breast cancers
- A SERM

Femara

- Chemical name is Letrozole
- Approved by FDA originally in 1997 then 2001 for other treatments
- Treats receptor positive/hormone receptor locally advanced and/or metastatic breast cancer
- Also a SERM
Hormone Therapy

ERDs (Estrogen Receptor Downregulators):

- Block the effects of estrogen in breast tissue. ERDs work in a similar way to SERMs. ERDs sit in the estrogen receptors in breast cells, so the cell doesn’t receive estrogen’s signals to grow and multiply.
- ERDs also reduce the number of estrogen receptors and change the shape of the breast cell estrogen receptors, so they don’t work as well.
- Unlike SERMs, ERDs don’t activate estrogen receptors in other parts of the body, such as the bones or the uterus. ERDs only block and destroy estrogen receptors.

ERDs (Estrogen Receptor Downregulators):

- Faslodex (chemical name: fulvestrant)
- Approved by FDA in 2002

ERD’s Effects:

- Nausea
- Vomiting
- Hot flashes
- Headache
- Constipation
- Diarrhea
- Sore throat
- Back/stomach/abdominal pain
- Injection site pain
Before there was medication to prevent the growth of tumors from hormones, doctors relied on the removal of the endocrine organs.

- Oophorectomy: the removal of the ovaries.
- Adrenalectomy: the removal of the adrenal glands.

Biologic Therapy

- A drug treatment that helps the body’s immune system to fight cancer.

Biologic Therapy

- What does HER2/neu stand for?
Biologic Therapy

- Human Epidermal growth factor Receptor 2

4 test to check for HER2

- IHC test (Immunohistochemistry): The ImmunohistoChemistry test finds out if there is too much HER2 protein in the cancer cells. The results of the IHC test can be: 0 (negative), 1+ (also negative), 2+ (borderline), or 3+ (positive — HER2 protein overexpression).

- FISH test (Fluorescence In Situ Hybridization): The Fluorescence In Situ Hybridization test finds out if there are too many copies of the HER2 gene in the cancer cells. The results of the FISH test can be positive (HER2 gene amplification) or negative (no HER2 gene amplification).

- SPoT-Light HER2 CISH test (Subtraction Probe Technology Chromogenic In Situ Hybridization): The SPoT-Light test finds out if there are too many copies of the HER2 gene in the cancer cells. The results of the SPoT-Light test can be positive (HER2 gene amplification) or negative (no HER2 gene amplification).

- Inform HER2 Dual ISH test (Inform Dual In Situ Hybridization): The Inform HER2 Dual ISH test finds out if there are too many copies of the HER2 gene in the cancer cells. The results of the Inform HER2 Dual ISH test can be positive (HER2 gene amplification) or negative (no HER2 gene amplification).

Biologic Therapy

- So what is HER2/neu?
Biologic Therapy

HER2/neu are receptors on the cell membrane that when triggered, transport a signal to cause cell growth.

In HER2+ breast cancer, the cancer cells have an abnormally high number of HER2 genes per cell.

Too much HER2 protein appears on the surface of these cancer cells. (also known as HER2 protein overexpression)

Too much HER2 protein is thought to cause cancer cells to grow and divide more quickly.
In some breast cancers, the cancer cells have many more HER2/neu receptors than normal. These breast cancers are called HER2/neu-positive. Breast cancers with low amounts of the receptor, or none at all, are called HER2/neu-negative.

Herceptin® is a type of biologic therapy that targets cells which produce excessive amounts of the protein called HER2. Herceptin binds to the cells, shutting off HER2 production.
Another type of targeting drugs for HER2neu breast cancers is Tykerb. If Herceptin doesn’t work for the patient then Tykerb is used. It is used in the same manner as Herceptin and is also used in combo with chemo. Herceptin was approved by FDA 1998. Tykerb was approved by the FDA in 2007.

Biologic Therapy
- Effects
  - Nausea
  - Fever
  - Chills
  - Muscle aches

ANY QUESTIONS..............