



Precision Medicine Approaches for Treatment and Early Detection of Breast Cancer

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Precision Medicine

- National Institute of Health Precision Medicine Initiative 2015: “Prevention and treatment strategies that take individual patients into account”...
- Individualizing care based upon genes, environment, and prognosis
- Targeting therapies to specific patients, tumors, and pathways
- Targeting screening strategies to patients at highest risk



Disclosure Information

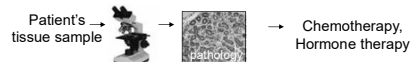
I have the following financial relationships to disclose:

- Grant/research support recipient
 - GlaxoSmithKline -> Novartis
 - Genentech/Roche
- Stock Shareholder
 - Merck
- Consultant fees
 - Bioalta

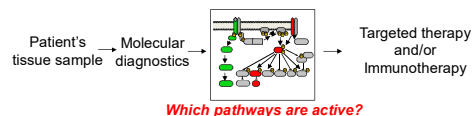


Change in Cancer Treatment Past Decade

Prior Standard of Care



Precision Medicine



Examples: *Her2 amplification, BRAF, KRAS, ALK, EGFR mutations, Microsatellite status*

Modified courtesy of Emile Voest, MD



Outline

- **Breast Cancer and Precision Medicine**
- **Breast Cancer Incidence and Death rates**
- **Treatment Advances**
 - Metastatic breast cancer
 - Early Stage - High Risk cancers
 - Early Stage - Low Risk cancers
- **Athena Breast Health Network**
 - University of California - 5 cancer centers collaboration using precision medicine to advance screening and treatment

Breast Cancer Risk Factors

- Age, Gender, and Race
- Benign Breast Disease
- Personal history of breast cancer
- Lifestyle and diet – migration studies
 - Obesity, poor exercise, alcohol
- Reproductive and hormonal factors
 - Early periods, late menopause, late births
 - Menopause hormonal therapy
- Family history and genetic factors
- Ionizing radiation (Hodgkin’s survivors)

Several Subtypes of Breast Cancer

Subtype Incidence	ER+ Her2 – 65%	Triple Neg 15%	Her2 + 20%
Mammo detected	Yes	Yes	Yes
Interval cancer	No	Yes	Yes
Peak recurrence	> 5 years	< 5 years	< 5 years
Early stage			
Chemo response	Poor	Good	Good
Brain metastases	Uncommon	Common	Common
Course of metastases	Slow: years	Fast: months to years	Slow in 80% Fast in 20%

Diverging Needs To Shift High Risk to Low Risk Cancers

Lower risk cancers

Management challenge

- Careful selection of therapy
- Minimize side effects
- Study use of less toxic therapy
- Improve health care systems
 - Standardization
 - Access
 - Disparities
 - Survivorship
 - Quality metrics
- Integration of multi-disciplinary care

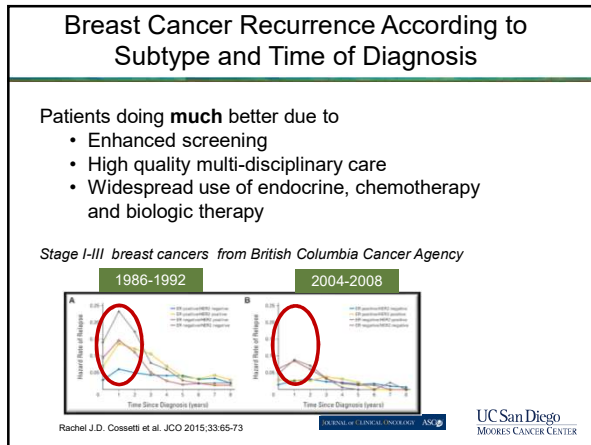
Higher Risk Cancers

Innovation Challenge

- Innovation in tumor and patient selection to guide therapy
- Address subsets of patients
- Therapeutic innovation to reduce recurrence risk and improve survival

Public health initiatives to shift higher risk to lower risk: screening, genetics, prevention, lifestyle risk reduction, education, and models of care

Burstein H, SABCS 2014



- ### Metastatic Breast CA Advances in Treatment
- ER+ Her2 -**
 - New CDK4/6 inhibitors very effective
 - MTOR inhibitors effective
 - Certain mutations (ESR1) predict endocrine resistance
 - Triple negative**
 - Olaparib, a PARP inhibitor, FDA approved for BRCA1/2 carriers
 - Androgen Receptor subset targeting promising
 - Immunotherapy alone or in combination promising
 - Other novel agents promising (e.g. sacituzumab)
 - Her2 +**
 - First line Chemo + two Her2 targeting antibodies
 - Second line: Kadcyla – a drug-antibody conjugate
 - Her2 mutation – targeted therapy under study (neratinib)
 - Lapatinib + Herceptin (non chemo) effective

Diverging Needs

Lower risk cancers

Management challenge

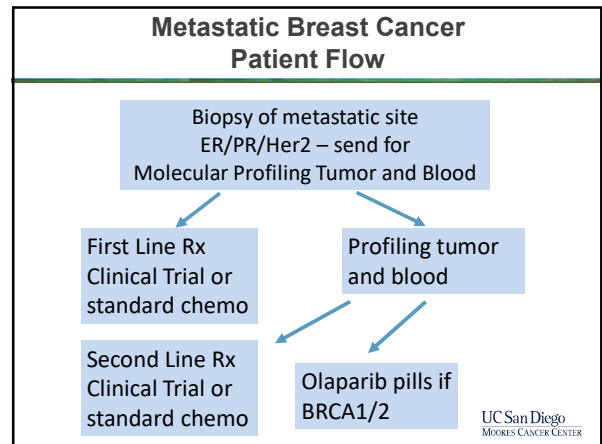
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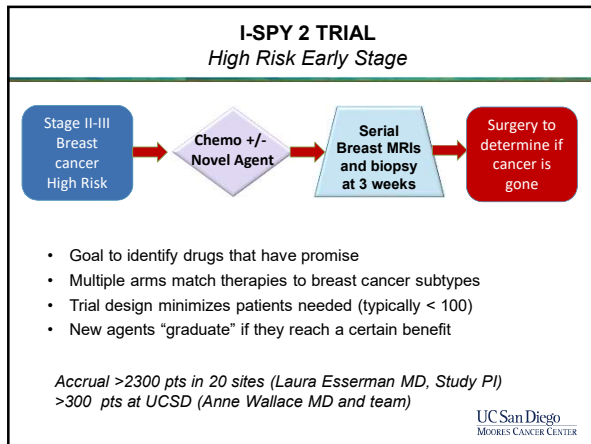
Higher Risk Cancers

Innovation Challenge

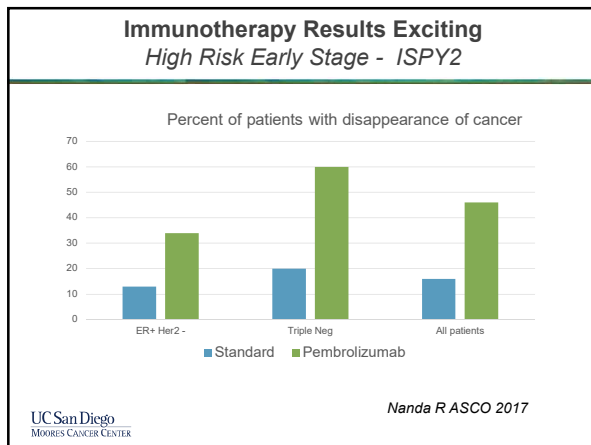
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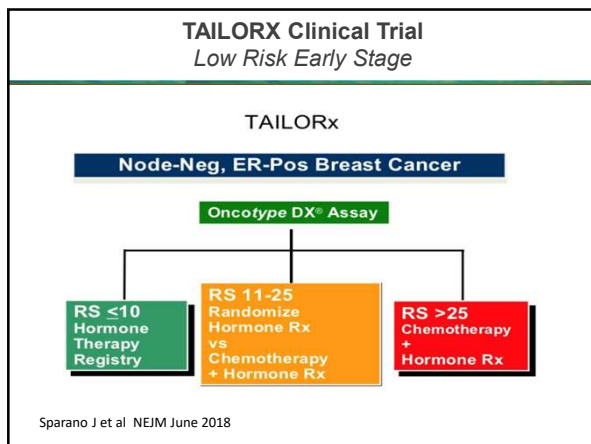




- ### TAILORx Take Home Points
- For patients over the age of 50 with scores less than 26 there is **NO** benefit to adjuvant chemotherapy
 - 75% of patients enrolled in the trial
 - For patients < age 50 (especially with scores of 21-15) there may be a small benefit to chemotherapy
 - Unclear if benefit from induction of menopause
 - Requires careful discussion with patient
 - Results have changed the standard of care



- ### SUMMARY Advances in Breast Cancer Treatment
- Subtype determines treatment
 - Metastatic breast cancer
 - New drugs and novel combinations effective
 - Patients living longer with "chronic disease"
 - Early Stage – High Risk Stage II and Stage III
 - Novel drugs + chemo prior to surgery very promising and may accelerate FDA approval (e.g. ISPY2)
 - Early Stage – Lower Risk Stage I and Stage II
 - Molecular profiling determines the majority of patients who can **avoid** chemotherapy



- ### Athena Breast Health Network
- Purpose is rapid integration of research into clinical care
 - Established network
 - 5 University of California cancer centers
 - 13 Midwest hospitals (Sanford Health)
 - 100+ providers and researchers in multidisciplinary fields
 - Clinical Care and Research Teams
 - 125,000+ women enrolled to date
 - Largest initiative is the **Wisdom Study**
- A UC Davis
 B UC Los Angeles
 C UC Irvine
 D UC San Diego
 E UC San Francisco

PI: Laura Esserman MD

Athena Accomplishments

- 125,000 women completed standardized mammo form
 - >75% agree to have data used for research
 - >60% agree to be contacted for future research
 - About 10% at elevated risk
- Breast oncology standards shared by UCSF and UCSD
 - Automate services and referrals
- Pathology harmonization – Score the Core (Hum Pathol 2015)
- Radiology harmonization – Inter-reader variability (Acad Radiol 2017)
- Radiation Oncology practice patterns – (Clin Breast Cancer 2015)

Athena Strategic Initiatives

