Milliman

Underwriting Nuances in Breast Cancer Progression

Agenda

- Introduction
- Pathophysiology
- Treatment Approaches
- Risk Stratification with Medical Claims

Introduction

Breast cancer is the most common invasive cancer.

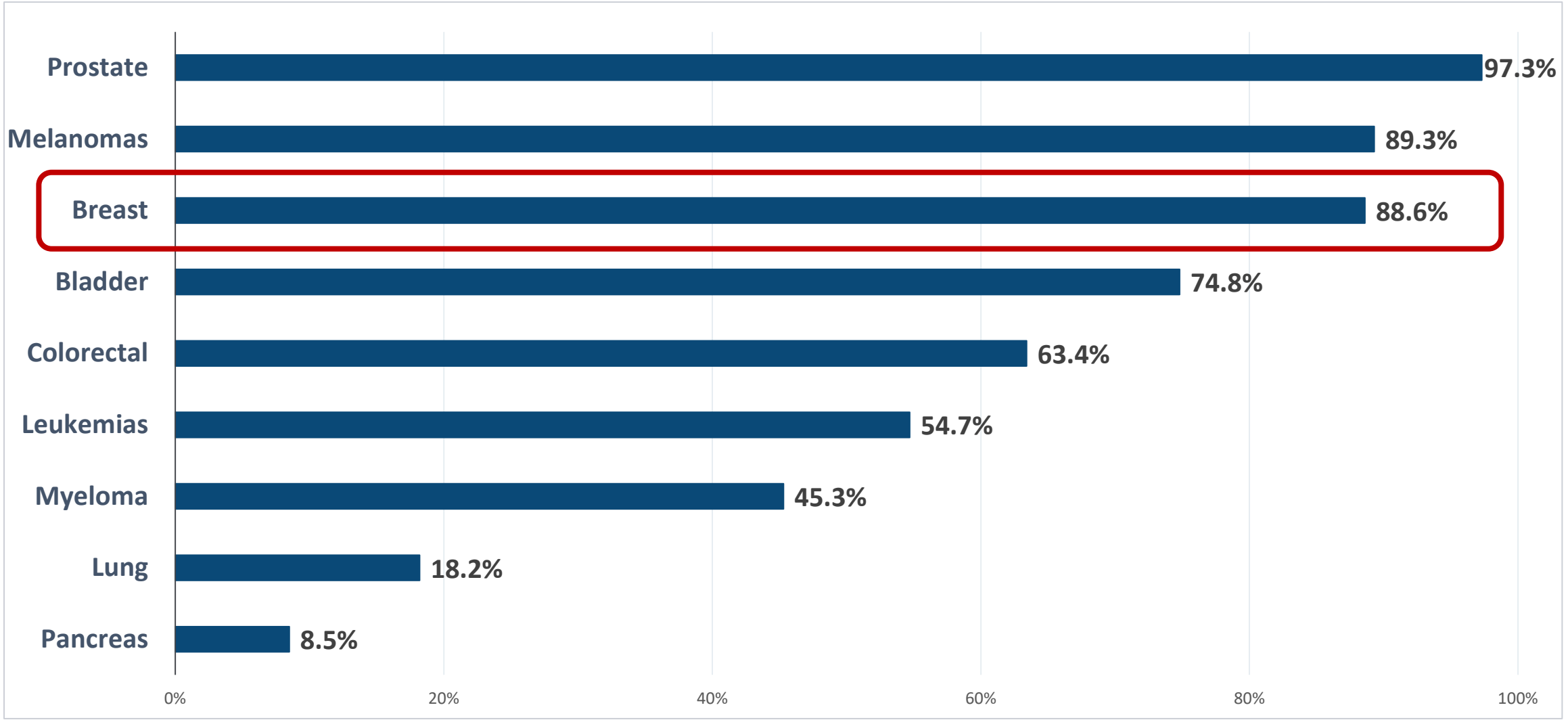
Common Types of Cancer	Estimated New Cases 2019	Estimated Deaths 2019
Breast	268,600	41,760
Lung	228,150	142,670
Prostate	174,650	31,620
Colorectal	145,600	51,020
Melanomas	96,480	7,230
Bladder	80,470	17,670
Leukemia	61,780	22,840
Pancreas	56,770	45,750
Myeloma	32,110	12,960

Surveillance, Epidemiology, and End Results (SEER) Program
https://seer.cancer.gov/statfacts/html/breast.html

Breast cancer represents 15.2% of all new cancer cases in the U.S.

15.2%

Breast cancer has a high survival rate at five years.

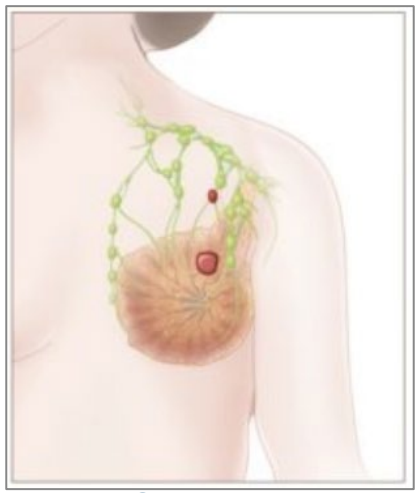


https://gis.cdc.gov/Cancer/USCS/DataViz.html

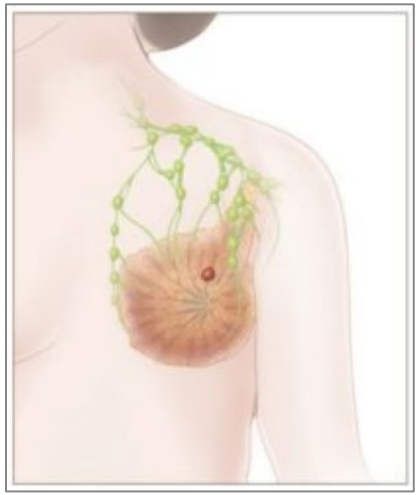
Pathophysiology

Breast cancer staging can be complex.

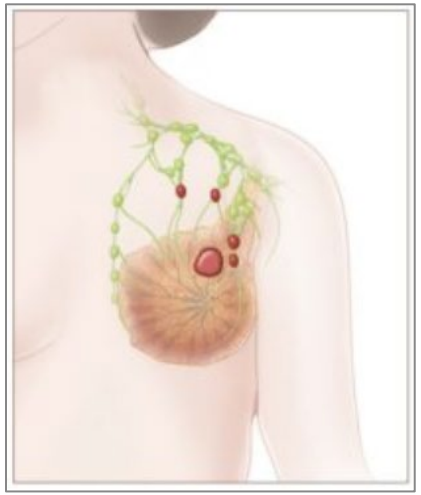
Stage 0



Stage II



Stage I



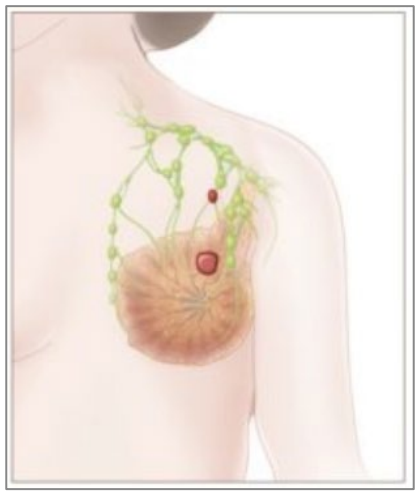
Stage III

Stage IV

https://pathology.jhu.edu/breast/my-results/staging-grade

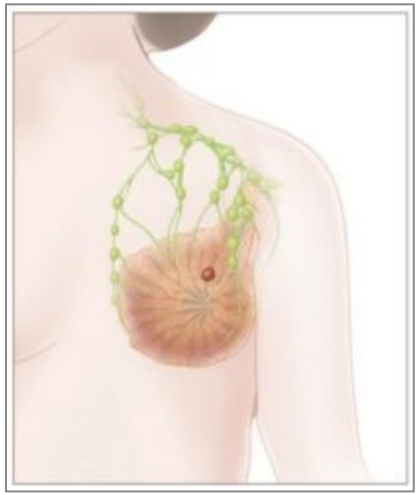
Breast cancer staging can be complex.

D05.12: Ductal Carcinoma in Situ

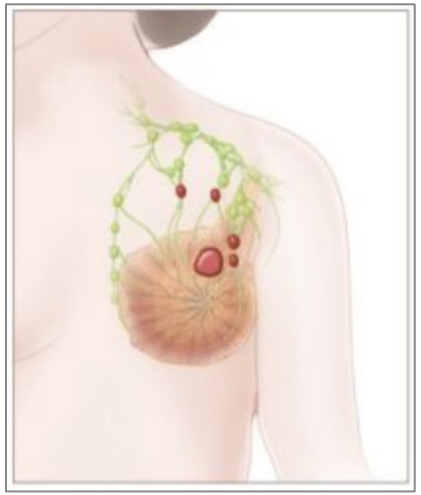


C77.3: Secondary Malignancy Axilla Nodes

C78.7: Secondary Malignancy to Liver



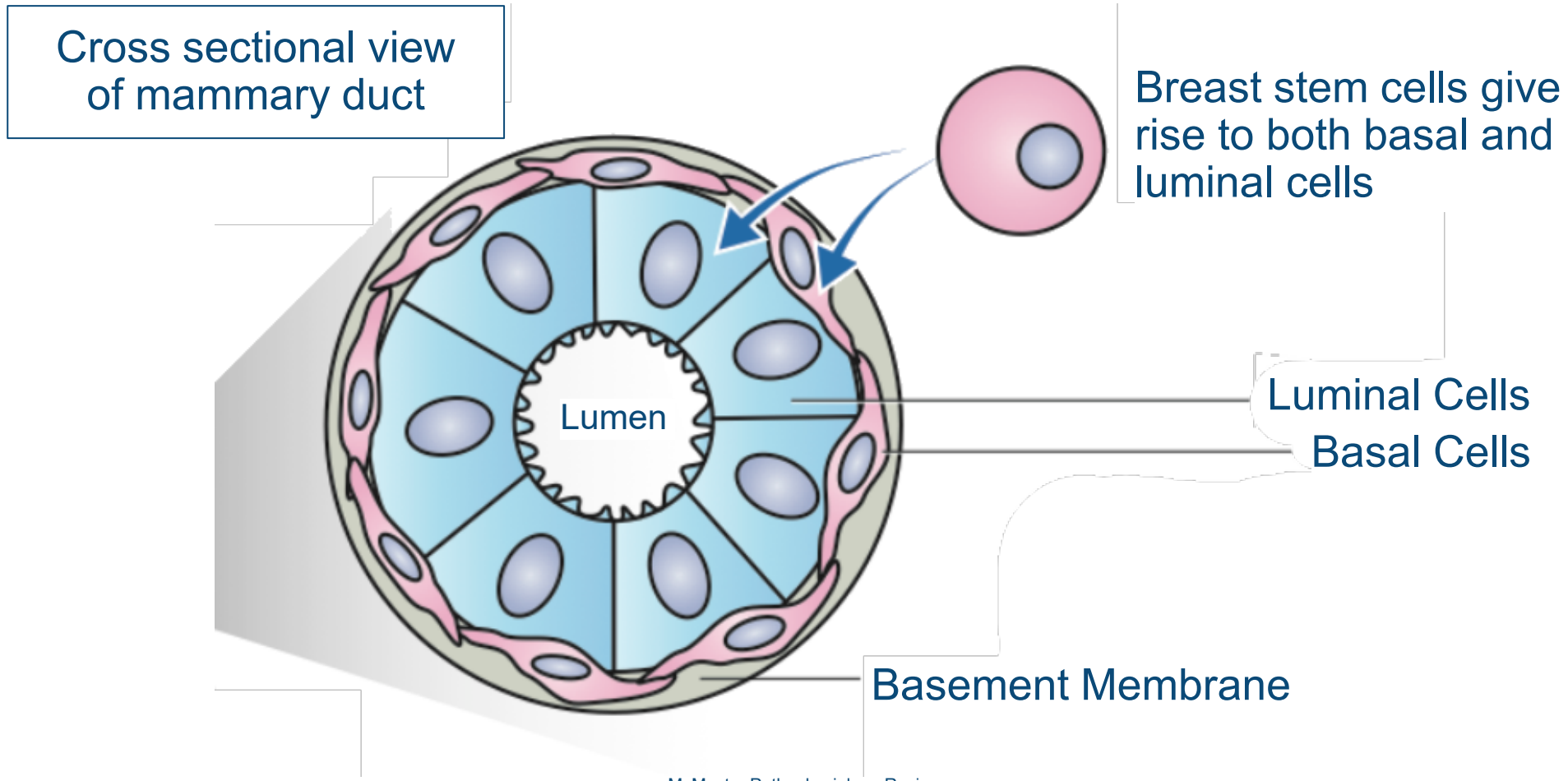
C50.211: Malignant Neoplasm of Breast



C77.8: Secondary Malignancy Multiple Nodes

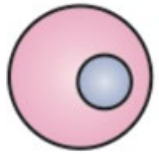
https://pathology.jhu.edu/breast/my-results/staging-grade

Mammary Duct Cell Types



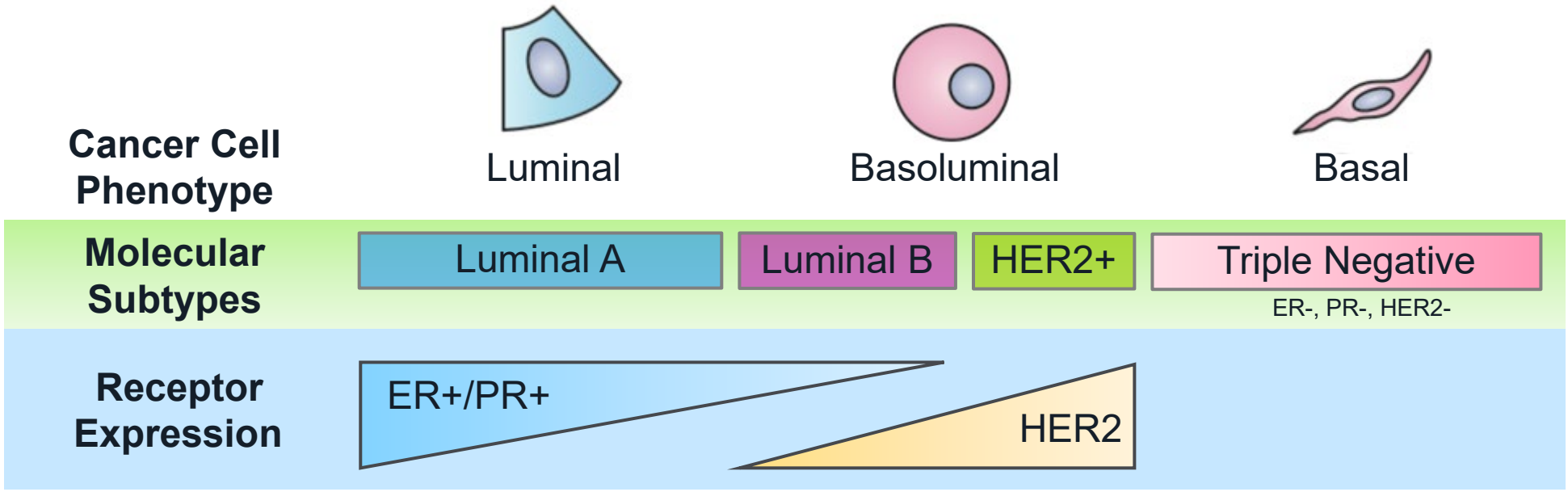
McMaster Pathophysiology Review
http://www.pathophys.org/breast-cancer/

Breast Cancer Molecular Subtypes

Cancer Cell Phenotype	 Luminal	 Basoluminal	 Basal	
Molecular Subtypes	Luminal A	Luminal B	HER2+	Triple Negative ER-, PR-, HER2-

McMaster Pathophysiology Review
http://www.pathophys.org/breast-cancer/

Breast Cancer Molecular Subtypes



McMaster Pathophysiology Review
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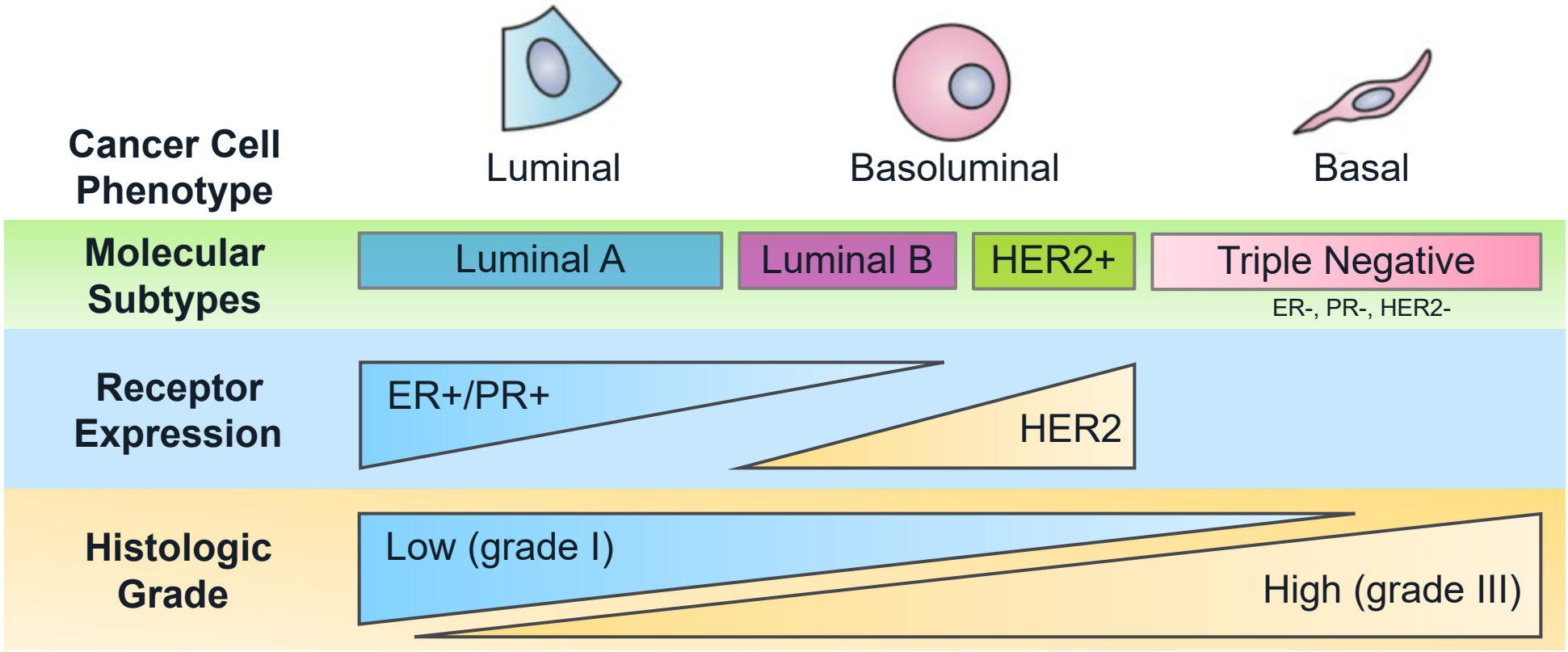
Breast Cancer Molecular Subtypes



McMaster Pathophysiology Review
http://www.pathophys.org/breast-cancer/

Breast cancer has four subtypes.

HR+/HER2- ⟶ Luminal A

70% of all breast cancers

- Low grade
- Slow growth
- Best prognosis

HR-/HER2- ⟶ Triple Negative

15% of all breast cancers

- More common in BRCA1 mutations
- Younger and African-Americans
- Hard to treat (lack targeted treatments)

HR+/HER2+ ⟶ Luminal B

10% of all breast cancers

- Faster growth than A
- More likely lymph node involvement
- Slightly worse prognosis than A

HR-/HER2+ ⟶ HER2 Enriched

5% of all breast cancers

- Grow faster than luminal types
- Targeted treatments aimed at HER2
- Higher risk of recurrence than luminal

Breast cancer survival depends on subtype.

	HR+ (HER2-)
Percent of Cases	70%
Stage I 5-Year Survival	≥99%
Metastatic Median Overall Survival	4-5 years

Breast Cancer Treatment: A Review. JAMA. January 22,2019. 321(3): 288-300.

Breast cancer survival depends on subtype.

	HR+ (HER2-)	HER2+ (HR+/-)
Percent of Cases	70%	15%
Stage I 5-Year Survival	≥99%	≥94%
Metastatic Median Overall Survival	4-5 years	5 years

Breast Cancer Treatment: A Review. JAMA. January 22,2019. 321(3): 288-300.

Breast cancer survival depends on subtype.

	HR+ (HER2-)	HER2+ (HR+/-)	Triple Negative
Percent of Cases	70%	15%	15%
Stage I 5-Year Survival	≥99%	≥94%	≥85%
Metastatic Median Overall Survival	4-5 years	5 years	10-13 months

Breast Cancer Treatment: A Review. JAMA. January 22,2019. 321(3): 288-300.

Treatment Approaches

Breast cancer treatment is becoming more targeted.

	Luminal A	Luminal B	HER2 Enriched	Triple Negative
Percent of Breast Cancer	70%	10%	5%	15%
Receptor Expression	Estrogen and Progesterone	Estrogen and Progesterone, HER2	HER2	

Special section of the Annual Report to the Nation on the Status of Cancer, 1975-2011. JNCI, 107(6) published 03/2015.
Treatment of Advanced Breast Cancer: The Expanding Landscape of Targeted Therapies. J Cancer Biol Res 2(1): 1036.

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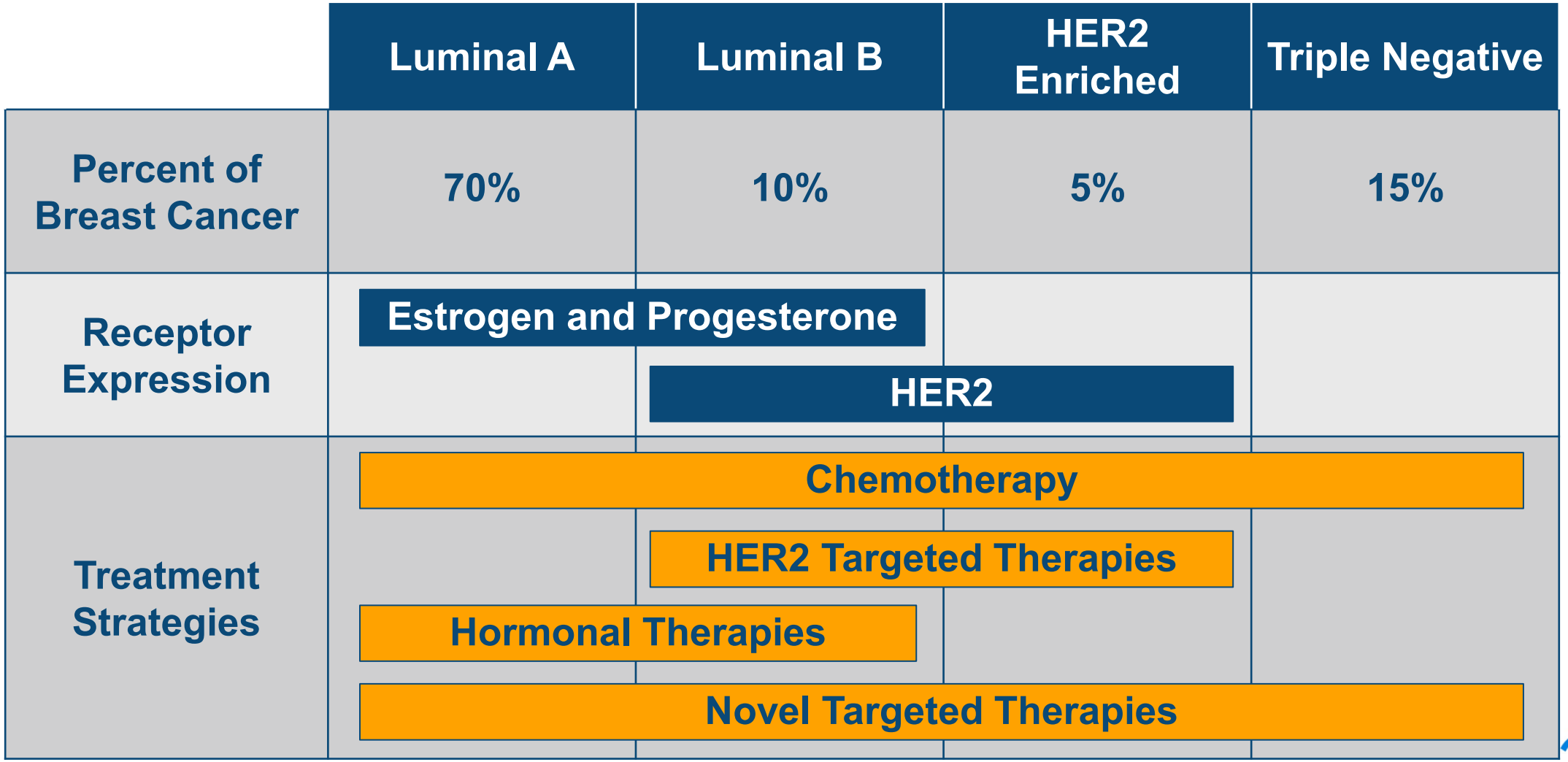
20 YEARS

Breast cancer treatment is becoming more targeted.



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20 YEARS

Drug therapies for breast cancer can be overwhelming.

Tamoxifen
Anastrazole
Letrozole
Exemestane
Fulvestrant
Palbociclib
Ribociclib
Abemaciclib
Everolimus

Trastuzumab
Pertuzumab
Ado-trastuzumab emtansine
Lapatinib
Neratinib
Carboplatin
Cisplatin
Doxorubicin
Cyclophosphamide
Paclitaxel

Olaparib
Talazoparib
Ixabepilone
Vinorelbine
Docetaxel
Nab-paclitaxel
Epirubicin
Gemcitabine
Capecitabine
Atezolizumab

Drug therapies for breast cancer can be overwhelming.

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Neratinib
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Cyclophosphamide
Paclitaxel

Olaparib
Talazoparib

Hormone Receptor Positive Breast Cancer (anti-estrogens)

Drug therapies for breast cancer can be overwhelming.

Tamoxifen

Anastrazole

Letrozole

Exemestane

Fulvestrant

Palbociclib

Ribociclib

Abemaciclib

Everolimus

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Carboplatin

Cisplatin

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Cyclophosphamide

Paclitaxel

Olaparib

Talazoparib

Hormone Receptor Positive Breast Cancer (kinase inhibitors)

Drug therapies for breast cancer can be overwhelming.

Tamoxifen

Anastrazole

Letrozole

Exemestane

Fulvestrant

Palbociclib

Ribociclib

Abemaciclib

Everolimus

Trastuzumab

Pertuzumab

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Lapatinib

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Carboplatin

Cisplatin

Doxorubicin

Cyclophosphamide

Paclitaxel

Olaparib

Talazoparib

Hormone Receptor Positive Breast Cancer (mTOR inhibitor)

Drug therapies for breast cancer can be overwhelming.

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Lapatinib
Neratinib
Carboplatin
Cisplatin
Doxorubicin
Cyclophosphamide
Paclitaxel

Olaparib
Talazoparib

HER2 Positive Breast Cancer (HER2 monoclonal)

Drug therapies for breast cancer can be overwhelming.

Tamoxifen

Anastrazole

Letrozole

Exemestane

Fulvestrant

Palbociclib

Ribociclib

Abemaciclib

Everolimus

Trastuzumab

Pertuzumab

Ado-trastuzumab emtansine

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Neratinib

Carboplatin

Cisplatin

Doxorubicin

Cyclophosphamide

Paclitaxel

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HER2 Positive Breast Cancer (kinase inhibitors)

Drug therapies for breast cancer can be overwhelming.

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Ado-trastuzumab emtansine
Lapatinib
Neratinib
Carboplatin
Cisplatin
Doxorubicin
Cyclophosphamide
Paclitaxel

Olaparib
Talazoparib

Breast Cancer Chemotherapy (platinum-containing)

Drug therapies for breast cancer can be overwhelming.

Tamoxifen
Anastrazole
Letrozole
Exemestane
Fulvestrant
Palbociclib
Ribociclib
Abemaciclib
Everolimus

Trastuzumab
Pertuzumab
Ado-trastuzumab emtansine
Lapatinib
Neratinib
Carboplatin
Cisplatin
Doxorubicin
Cyclophosphamide
Paclitaxel

Olaparib
Talazoparib

Breast Cancer Chemotherapy (broad spectrum)

Drug therapies for breast cancer can be overwhelming.

Tamoxifen
Anastrazole
Letrozole
Exemestane
Fulvestrant
Palbociclib
Ribociclib
Abemaciclib
Everolimus

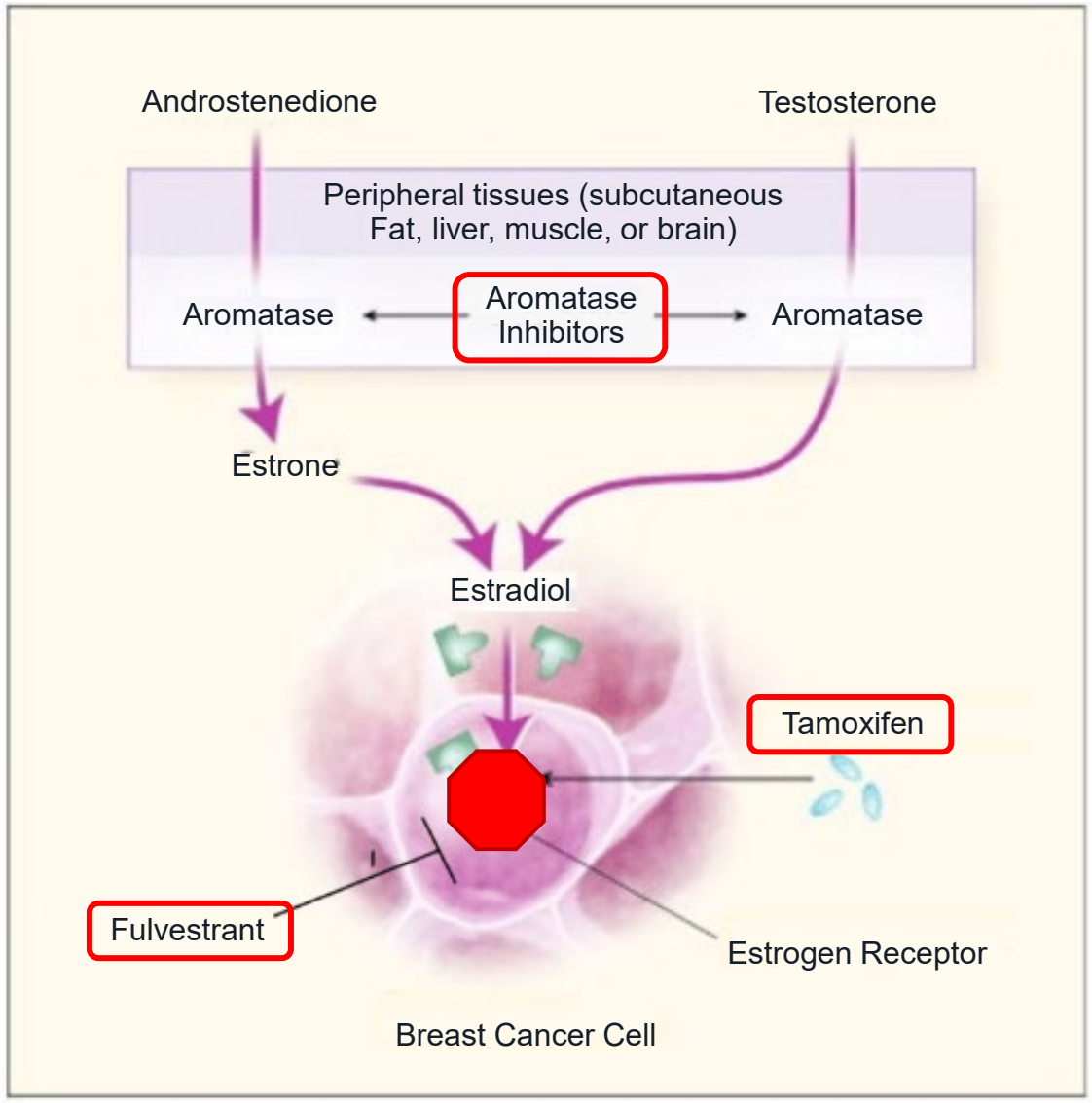
Trastuzumab
Pertuzumab
Ado-trastuzumab emtansine
Lapatinib
Neratinib
Carboplatin
Cisplatin
Doxorubicin
Cyclophosphamide
Paclitaxel

Olaparib
Talazoparib

Breast Cancer Chemotherapy (PARP inhibitors)

Eighty percent of breast cancer is ER positive.

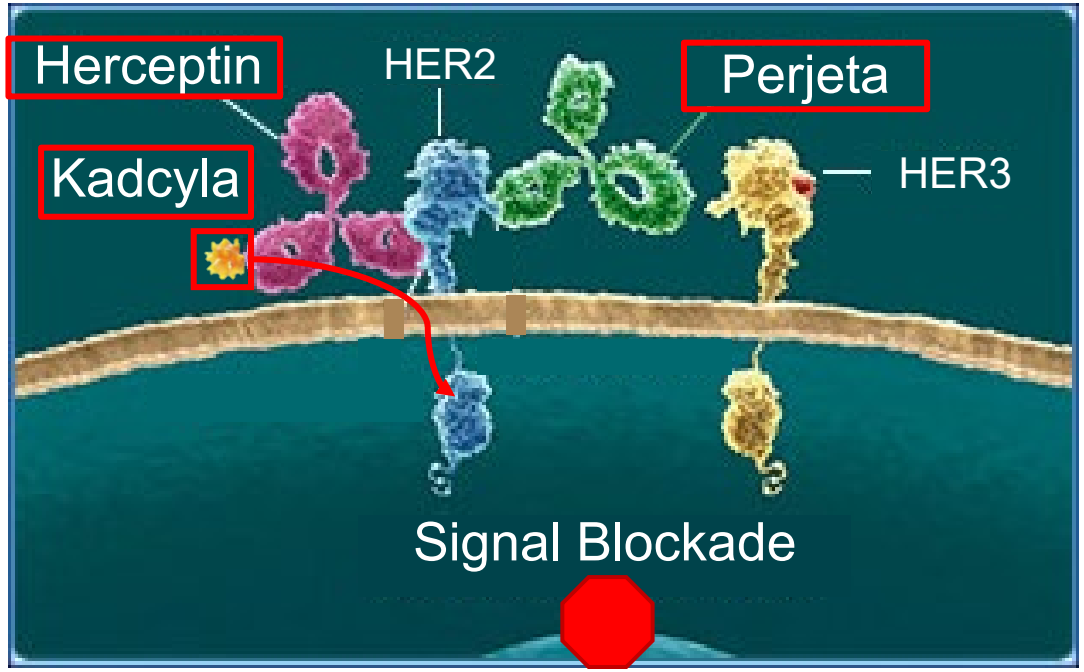
- SERMs
  - Tamoxifen
- Aromatase Inhibitors
  - Letrozole, exemestane, anastrozole
- Fulvestrant
- Kinase Inhibitors (CDK 4/6) if HER2-
  - Palbociclib (Ibrance)
  - Ribociclib (Kisqali)
  - Abemaciclib (Verzenio)
- Everolimus if HER2-



N Engl J Med 2003;248:2431-42.

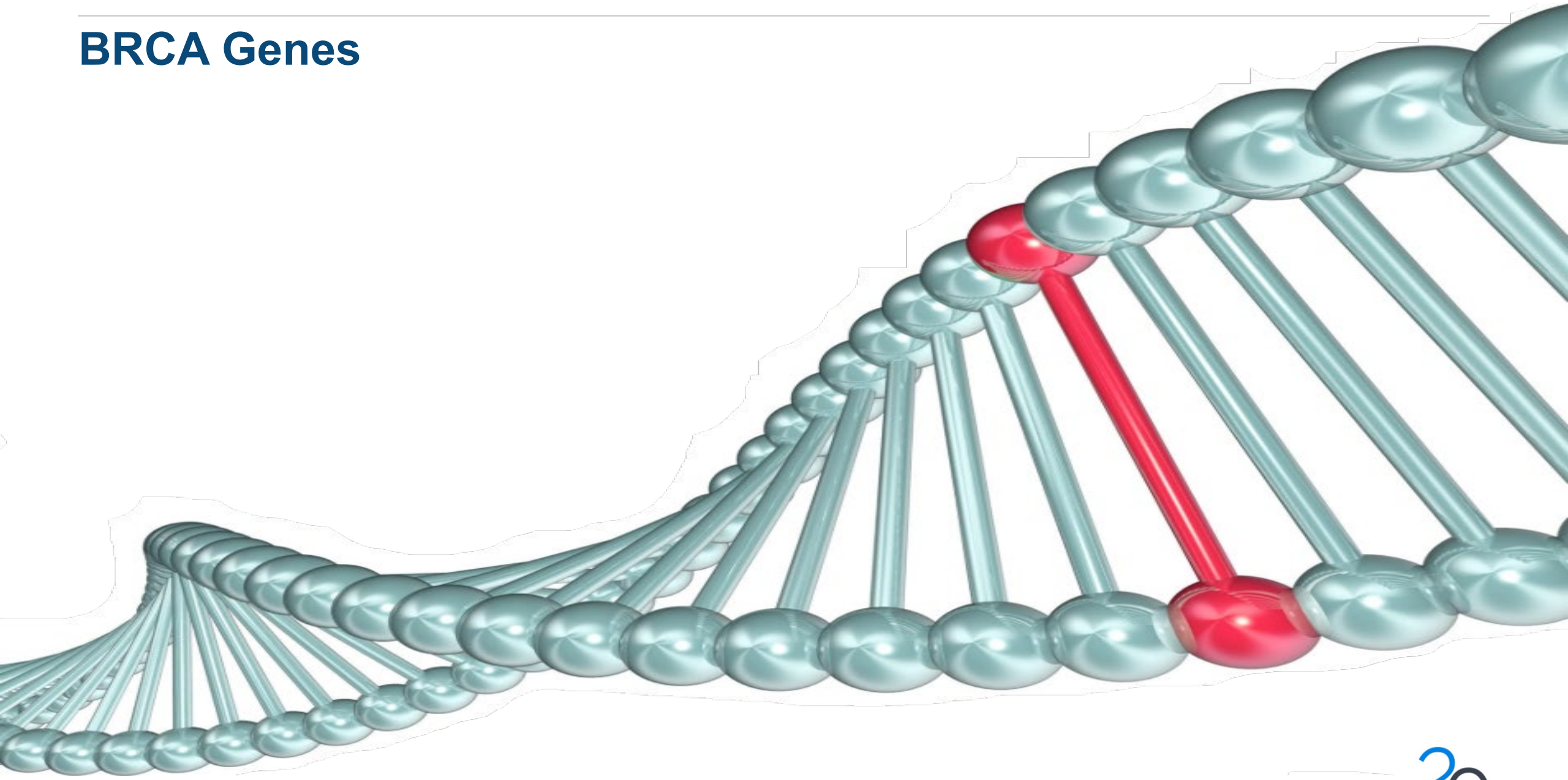
Only fifteen percent of breast cancer is HER2 positive.

- Monoclonal Antibodies
  - Trastuzumab (Herceptin)
  - Pertuzumab (Perjeta)
- Monoclonal/Chemo (T-DM1)
  - Ado-trastuzumab emtansine (Kadcyla)
- Kinase Inhibitors (EGFR)
  - Lapatinib (Tykerb)
  - Neratinib (Nerlynx)

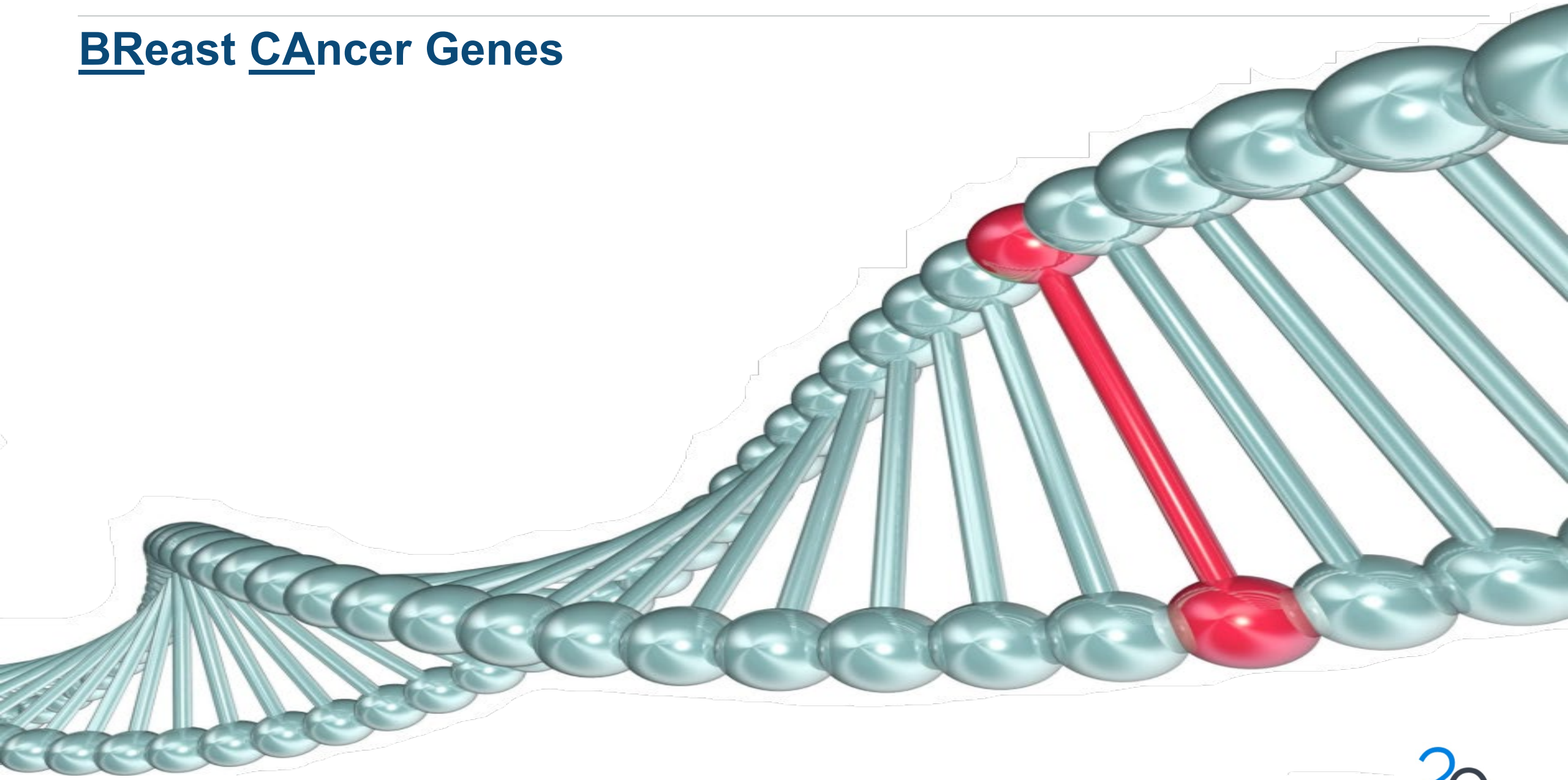


https://www.genomeweb.com/drug-discovery-development/study-suggests-surrogate-endpoint-may-reflect-longer-benefit-early-her2#.XOC7hMhKhhE

BRCA Genes



BReast CAncer Genes



BRCA mutations increase risk of aggressive cancer.

- Most BRCA1 mutations are Triple Negative
  - Over 70% of BRCA1 mutation carriers will develop cancer
  - Tend to develop bilateral breast cancer
  - BRCA1 worse prognosis, BRCA2 little effect

- PARP Inhibitors
  - Talazoparib (Talzenna)
  - Olaparib (Lynparza)

- Platinum Agents – enhanced effect
  - Cisplatin
  - Carboplatin

Risk Stratification with Medical Claims

Medical claims provide a more complete picture of health status.

Identifies conditions

- Morbidity-related conditions
- Substance abuse/psychiatry
- Cancer treatment
- Tobacco

Adds efficiency

- Real-time data
- Interpreted by Irix
- Delivered instantly
- Fewer APS orders

Widely adopted

- Medicare Supplement
- Disability income
- Long-term care
- Life (FUW, SI, FE, accel.)

Instant, indexed, inexpensive

Case 1: Underwriting Considerations

- What subtype?
  - ER+/HER2- (Luminal A)
- Has it spread?
  - No; simple complete mastectomy
- BRCA?
  - No
- Prognosis
  - 10-year overall: 94.1%*

*Long-term survival and stage I breast cancer subtypes. J Cancer Research and Practice; March 2016; 3(1): 1-8.

Case 2: Underwriting Considerations

- What subtype?
  - ER-/HER2+ (HER2 Enriched)
- Has it spread?
  - Yes, to lymph nodes
- BRCA?
  - Genetic susceptibility
- Prognosis
  - 5-year overall: 50.8%*
  - 10-year overall: 25.0%*

*Asian Pac J Cancer Prev. 2018; 19(11): 3167-3174.

Clues about BRCA mutations can be found in medical claims.

- ICD-10 Code Z15.01: Genetic susceptibility to malignant neoplasm of breast
- ICD-10 Code Z15.02: Genetic susceptibility to malignant neoplasm of ovary

- ICD-10 Code Z40.01: Encounter for prophylactic removal of breast
- ICD-10 Code Z40.02: Encounter for prophylactic removal of ovary(s)

- CPT Code 19303: Simple complete mastectomy
- CPT Code 58661: Partial or total oophorectomy/salpingectomy
- CPT Code 58720: Salpingo-oophorectomy, unilateral or bilateral

Case 3: Underwriting Considerations

- What subtype?
  - ER-/HER2- (Triple Negative)
- Has it spread?
  - Yes; bone and liver
- BRCA?
  - Possible (carboplatin)
  - Triple Negative
- Prognosis
  - Median survival: 13 months*

*Survival outcomes for patients with metastatic triple-negative breast cancer: implications for clinical practice and trial design. Clin Breast Cancer. 2009;9(1):29-33.

Summary

- Breast cancer is the most common non-skin cancer.
- Molecular subtype can help determine outcome.
- Prescription histories with medical claims can identify breast cancer.
- A rules engine can consistently interpret breast cancer risk in seconds.

Questions?

Scott Coller, Pharm.D. Director, Health Data Innovation

Scott.Coller@Milliman.com