

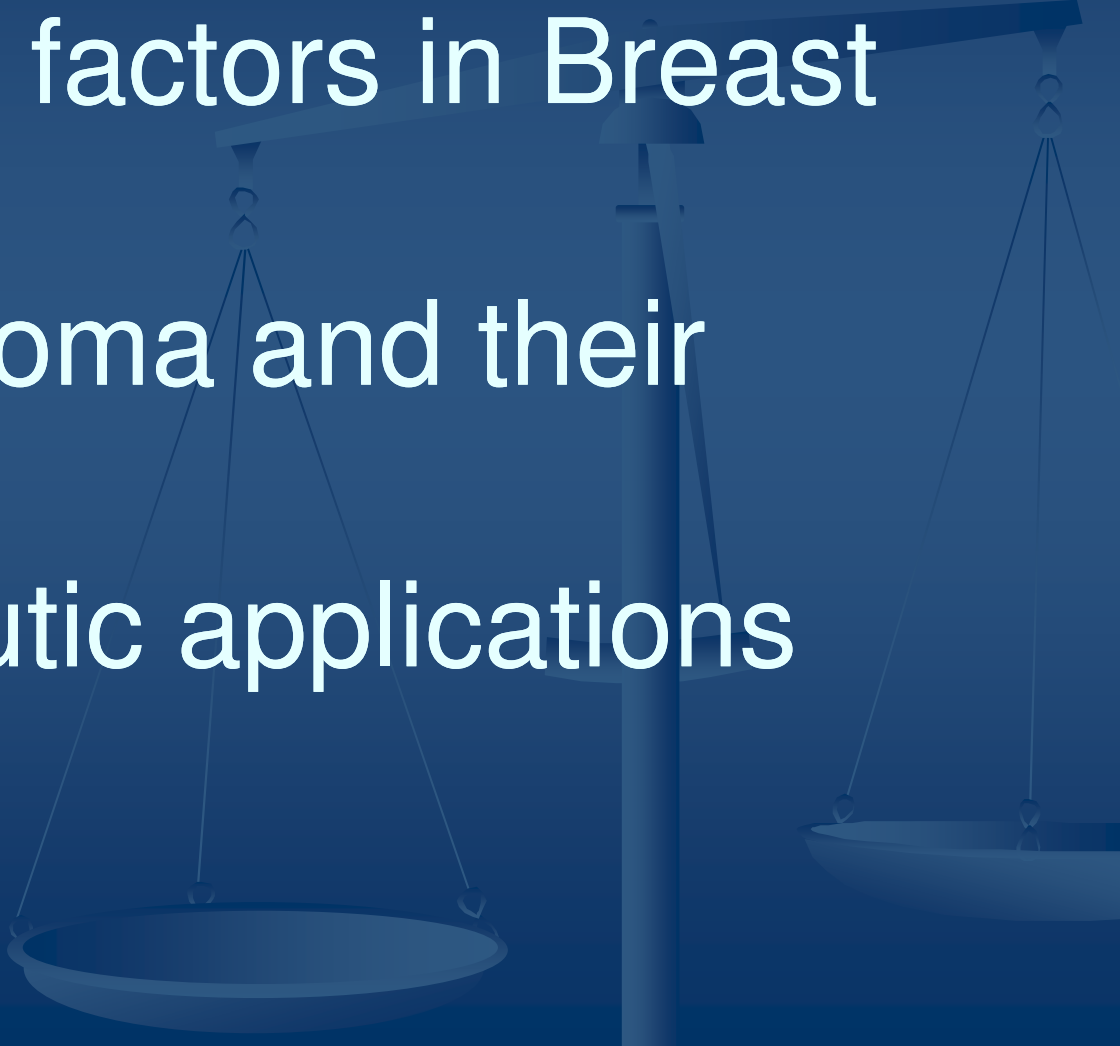


Dr Dehan Gunasekera

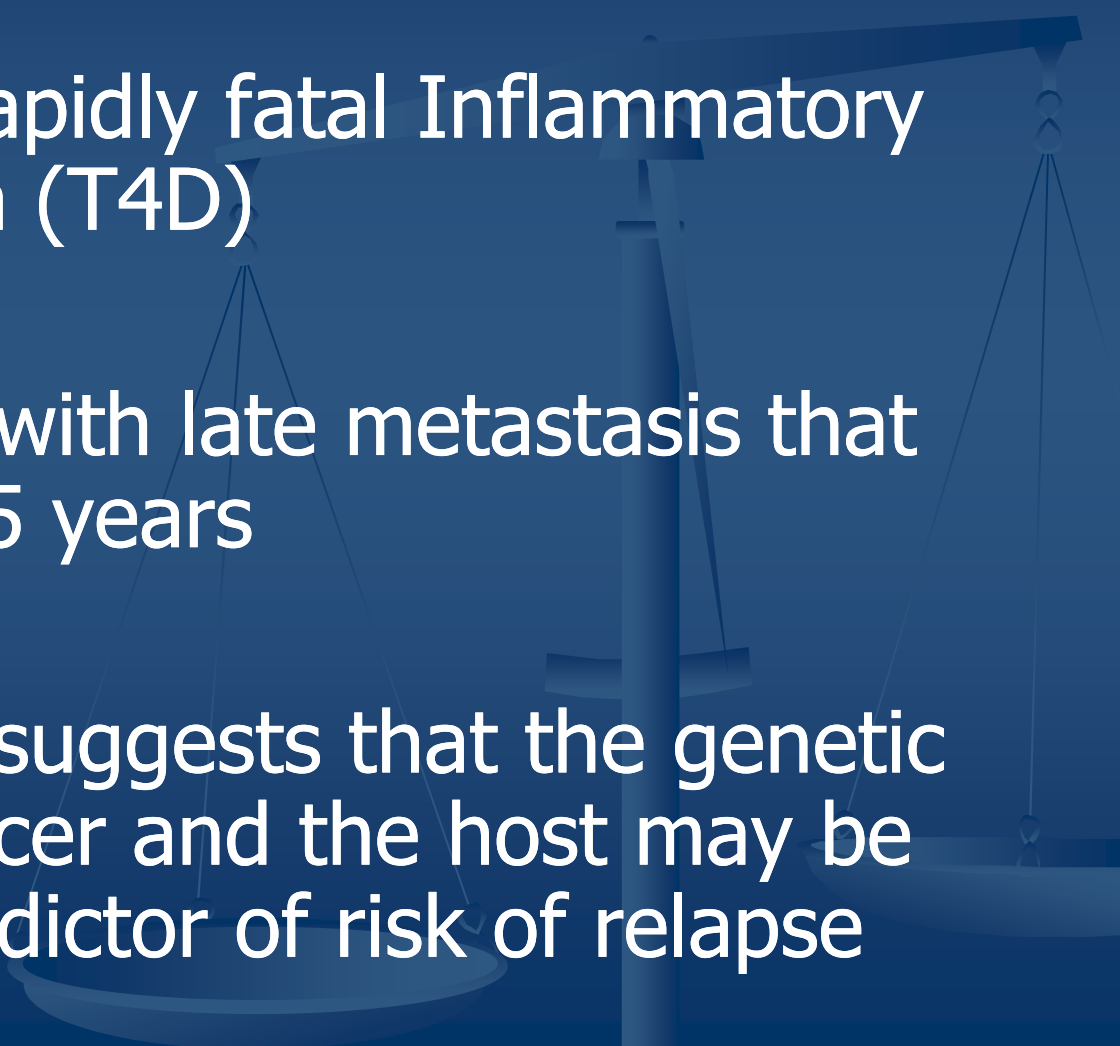
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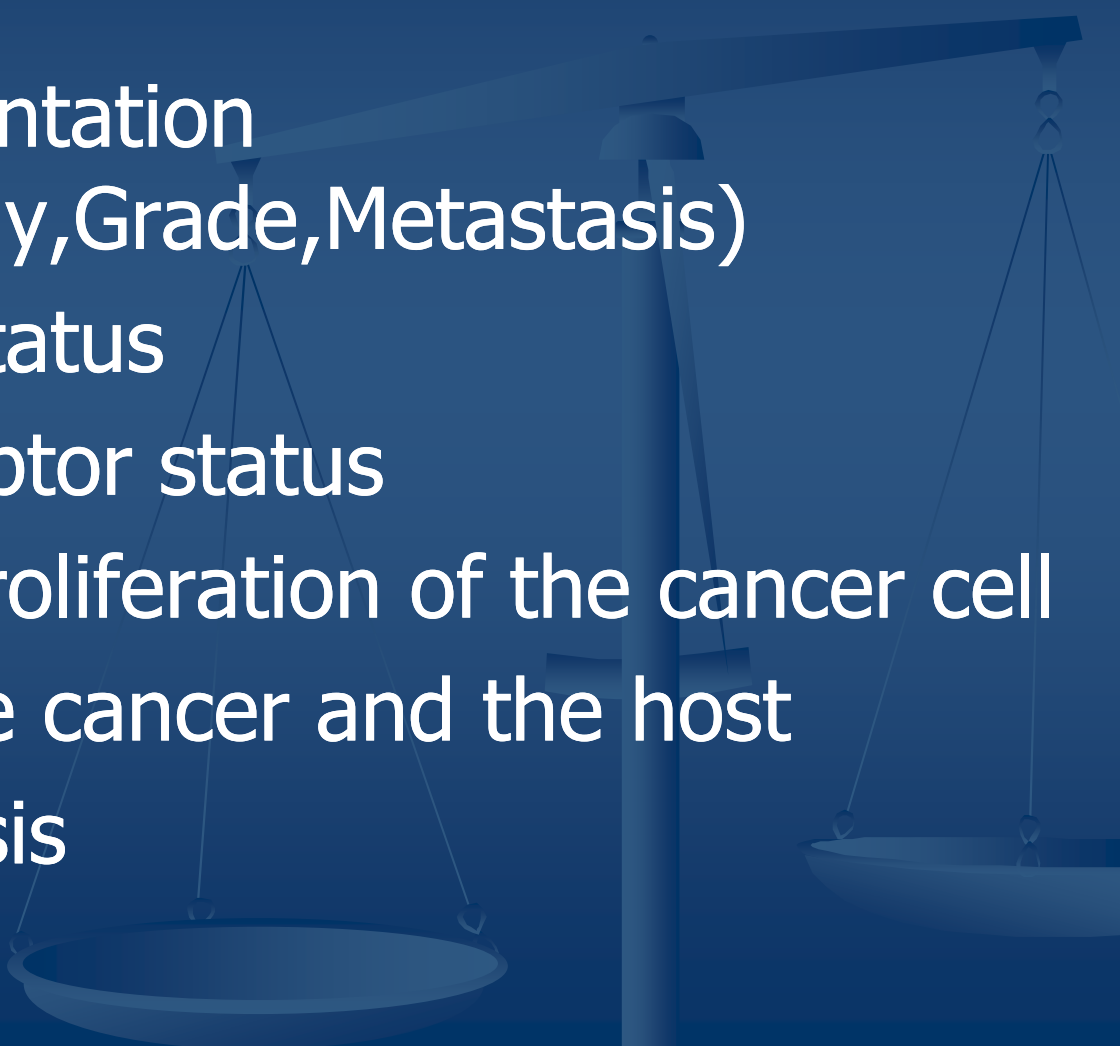
National Cancer Institute of SriLanka



Prognostic factors in Breast Carcinoma and their Therapeutic applications

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- There is a broad spectrum in the Biological behaviour of Breast Carcinoma
 - Aggressive and rapidly fatal Inflammatory Breast Carcinoma (T4D)
 - Indolent disease with late metastasis that occurs in 10 to 15 years
 - Recent evidence suggests that the genetic profile of the cancer and the host may be the strongest predictor of risk of relapse

The occurrence of relapse and survival (Prognosis) are influenced by

- 1. Stage at presentation
(Size, Pathology, Grade, Metastasis)
 - 2. Lymph node status
 - 3. Hormone receptor status
 - 4. Measures of proliferation of the cancer cell
 - 5. Genetics of the cancer and the host
 - 6. Age at diagnosis
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St Galens Recommendations

Low risk

T1

N0

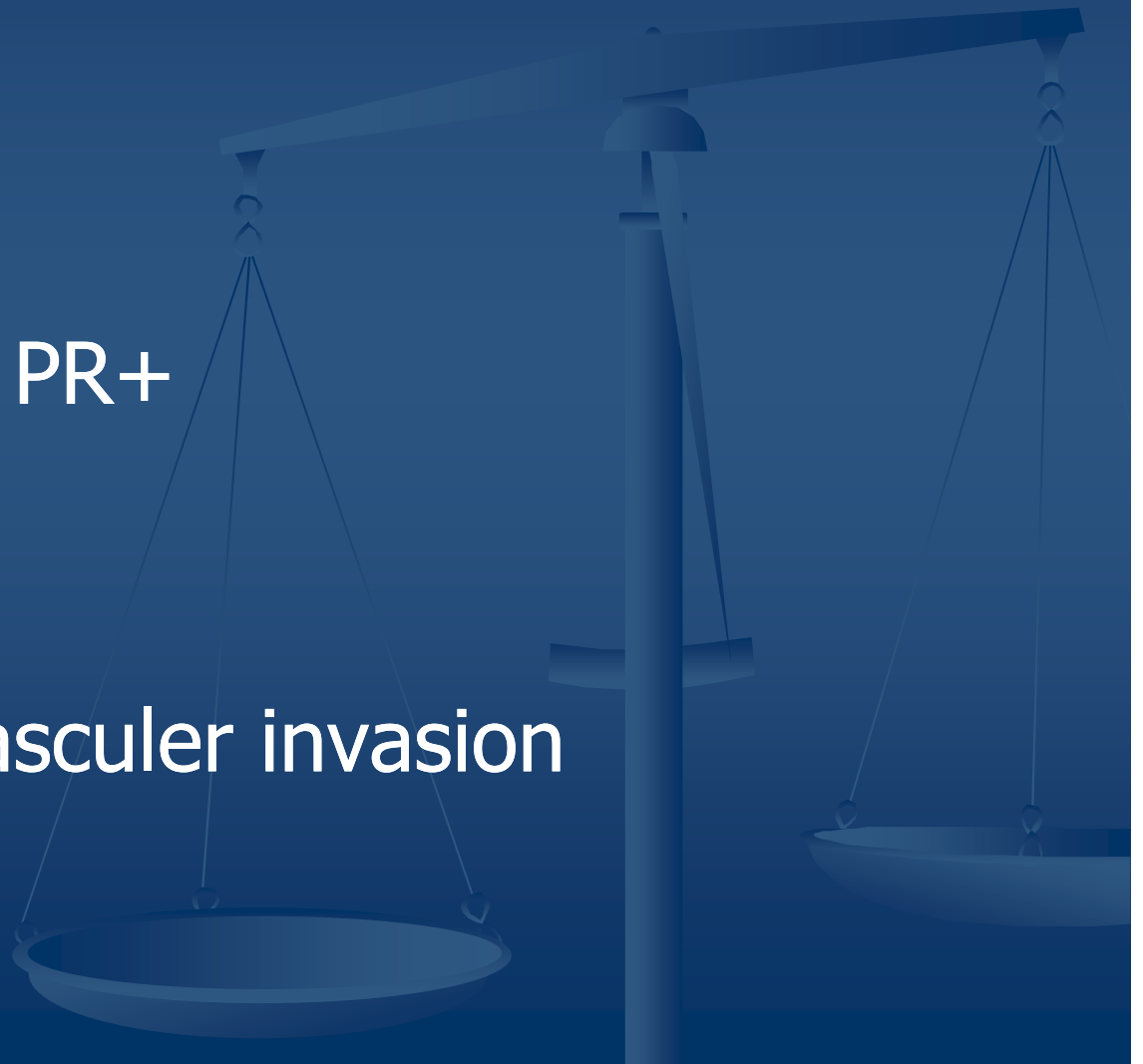
G1

ER+ and /or PR+

Her2 –

>35 years

No lymphovascular invasion



Intermediate risk

ER and/or PR +

Her2 –

N0

No lymphovascular invasion

pT>1 or G2-3

or <35 years

or (1-3) LN+

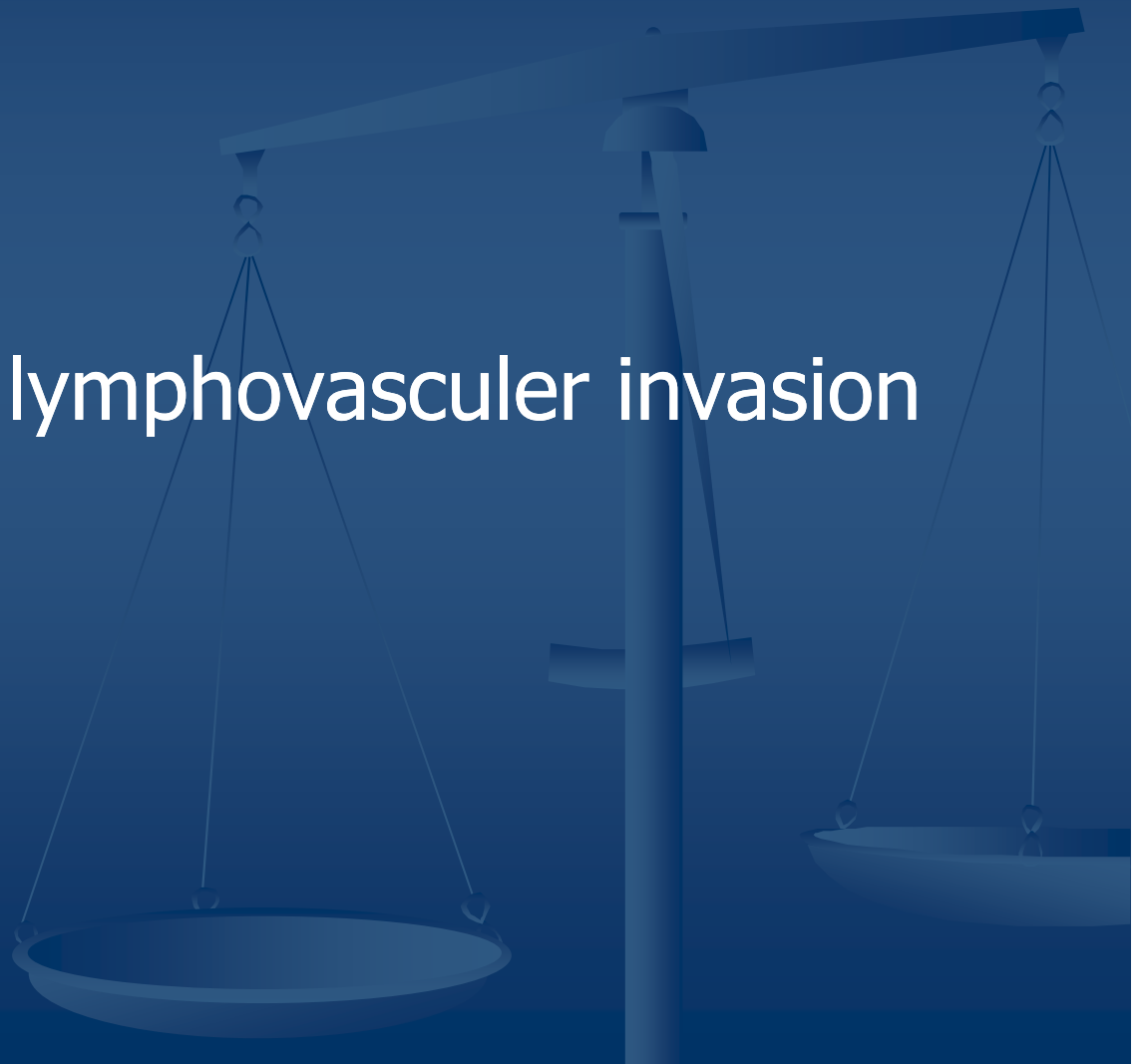
High risk

ER- and PR-

LN >3

Her2+

or LN 1-3 with lymphovascular invasion

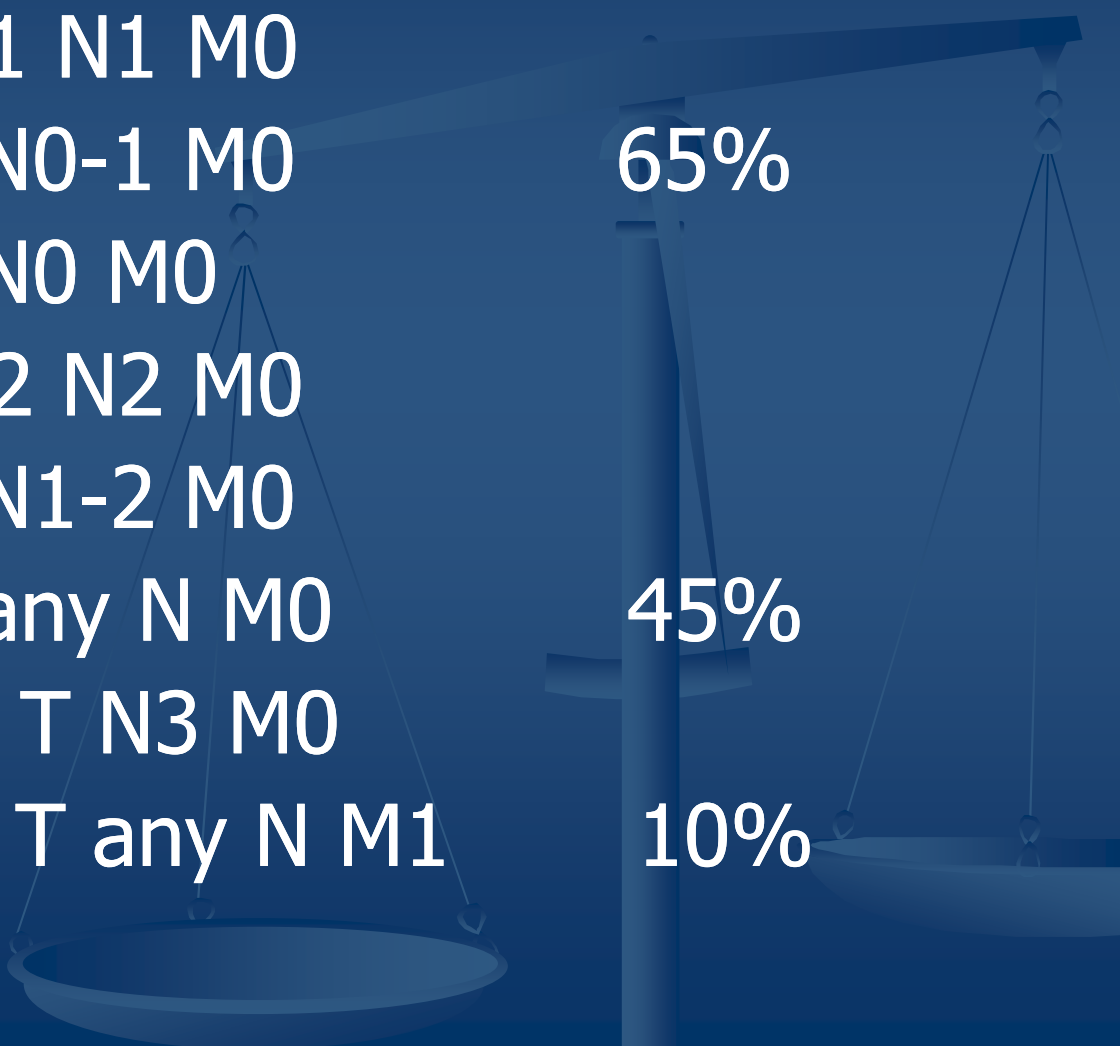


Prognostic relevance is uncertain but valuable

1. Deposits in bone marrow
2. Proliferation marker Ki-67 and thymidine kinase (increase – poor prognosis)
3. Ploidy (euploidy better prognosis)
4. Expression of P53, Cathepsin D
5. Urokinase type Plasminogen activator and Plasminogen activator inhibitor type 1
6. Response to neoadjuvant chemotherapy

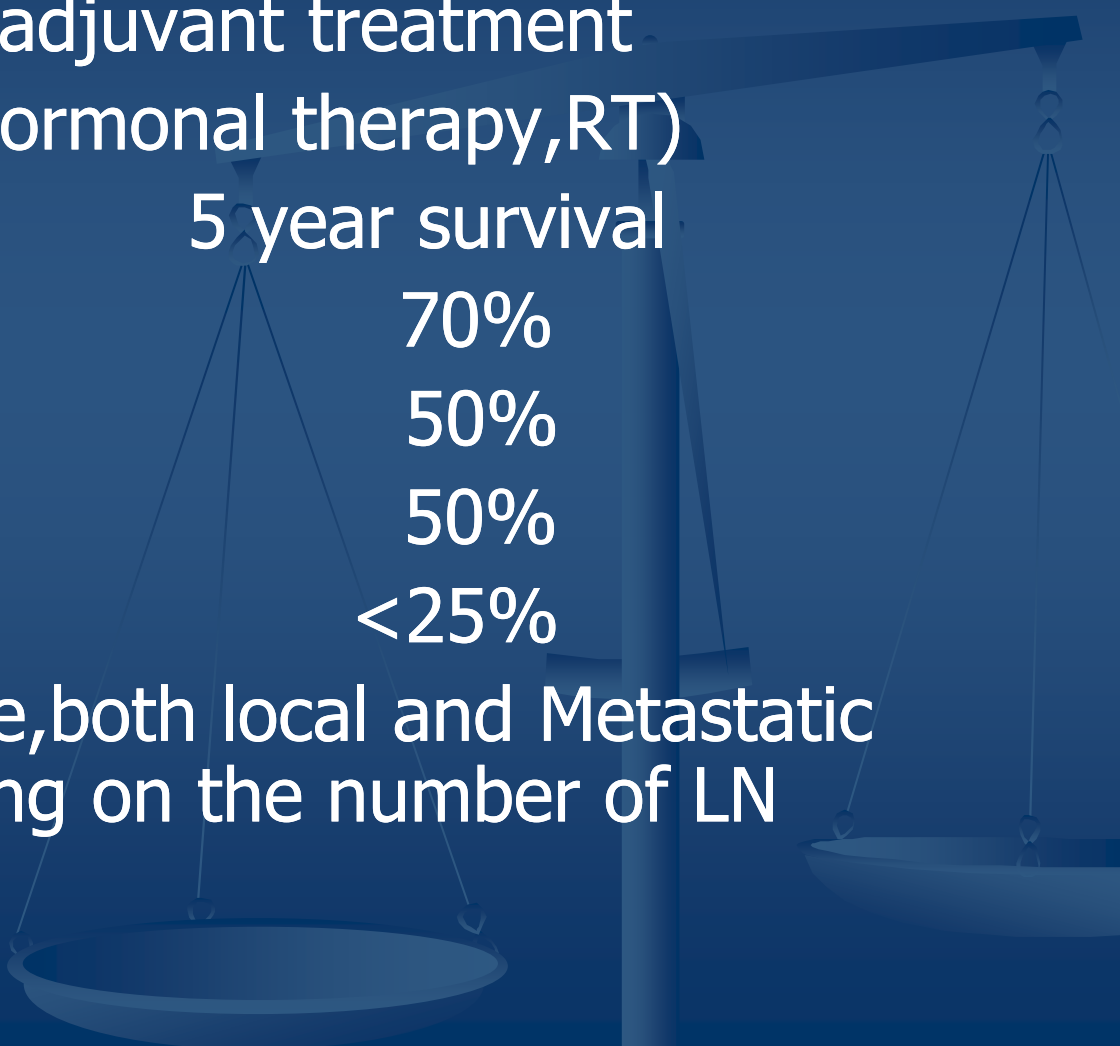
Stage at presentation

- Size and Lymph node status are independent prognostic factors and are major determinants of the likelihood of survival.
- They influence local and regional recurrences as well as distant metastasis
- LN - <1cm 5 year survival 95%-99%
- LN - 1-3cm 5 year survival 90%-95%
- LN - >3cm 5 year survival < 85%



■ Stage		5 year survival
■ Stage I	T1 N0 M0	85%
■ Stage II	T0-1 N1 M0	65%
	T2 N0-1 M0	
	T3 N0 M0	
■ Stage III	T0-2 N2 M0	45%
	T3 N1-2 M0	
	T4 any N M0	
	Any T N3 M0	
■ Stage IV	Any T any N M1	10%

Lymph Node Status

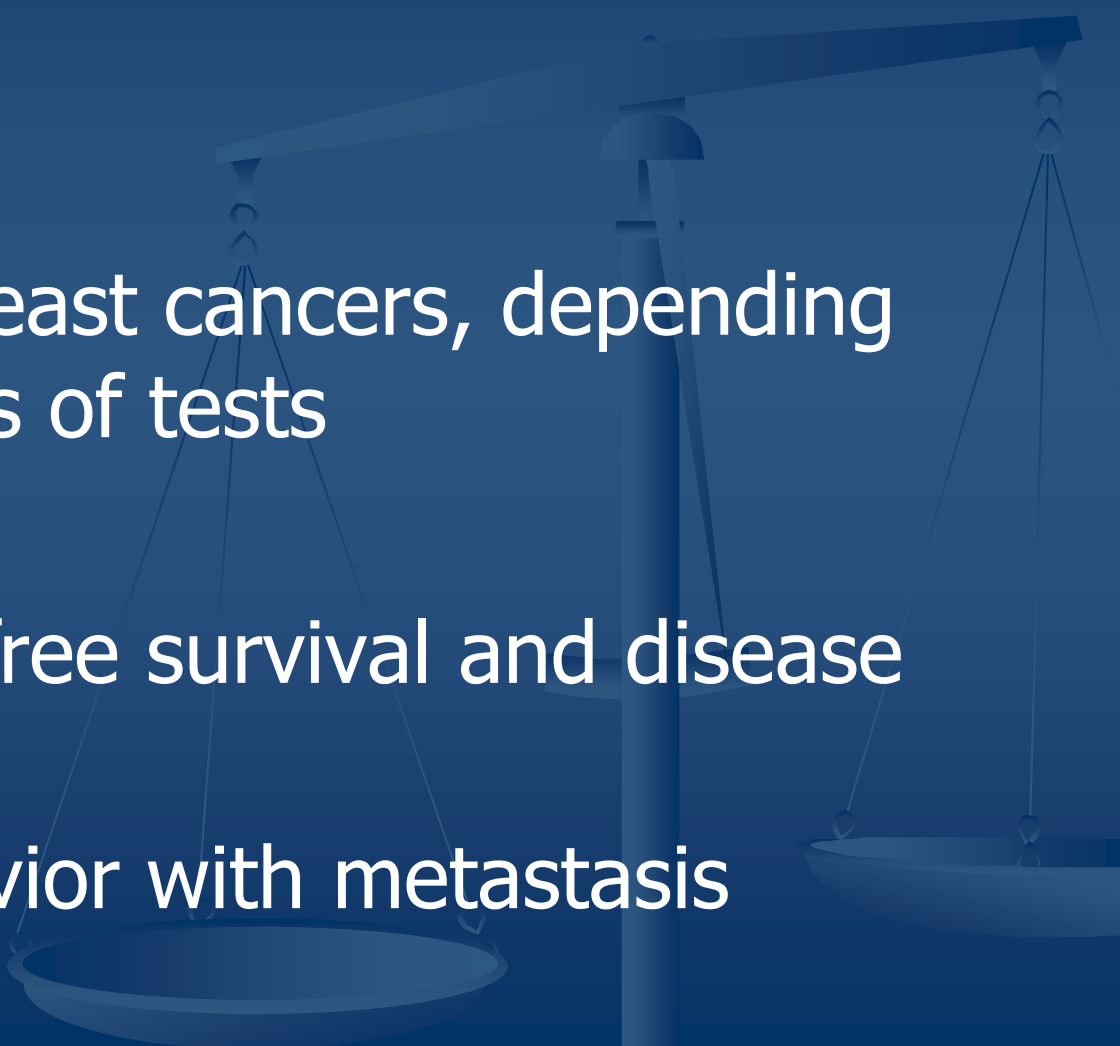
- In the absence of adjuvant treatment (Chemotherapy, Hormonal therapy, RT)
- | | 5 year survival |
|-----------------|-----------------|
| ■ Axillary LN - | 70% |
| ■ Axillary LN + | 50% |
| ■ <4 LN + | 50% |
| ■ >10 LN + | <25% |
- Risk of recurrence, both local and Metastatic increases depending on the number of LN
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Hormone receptor status at diagnosis

- ER-,PR- tumours are twice as likely to relapse during the first 2 years than those who are receptor +

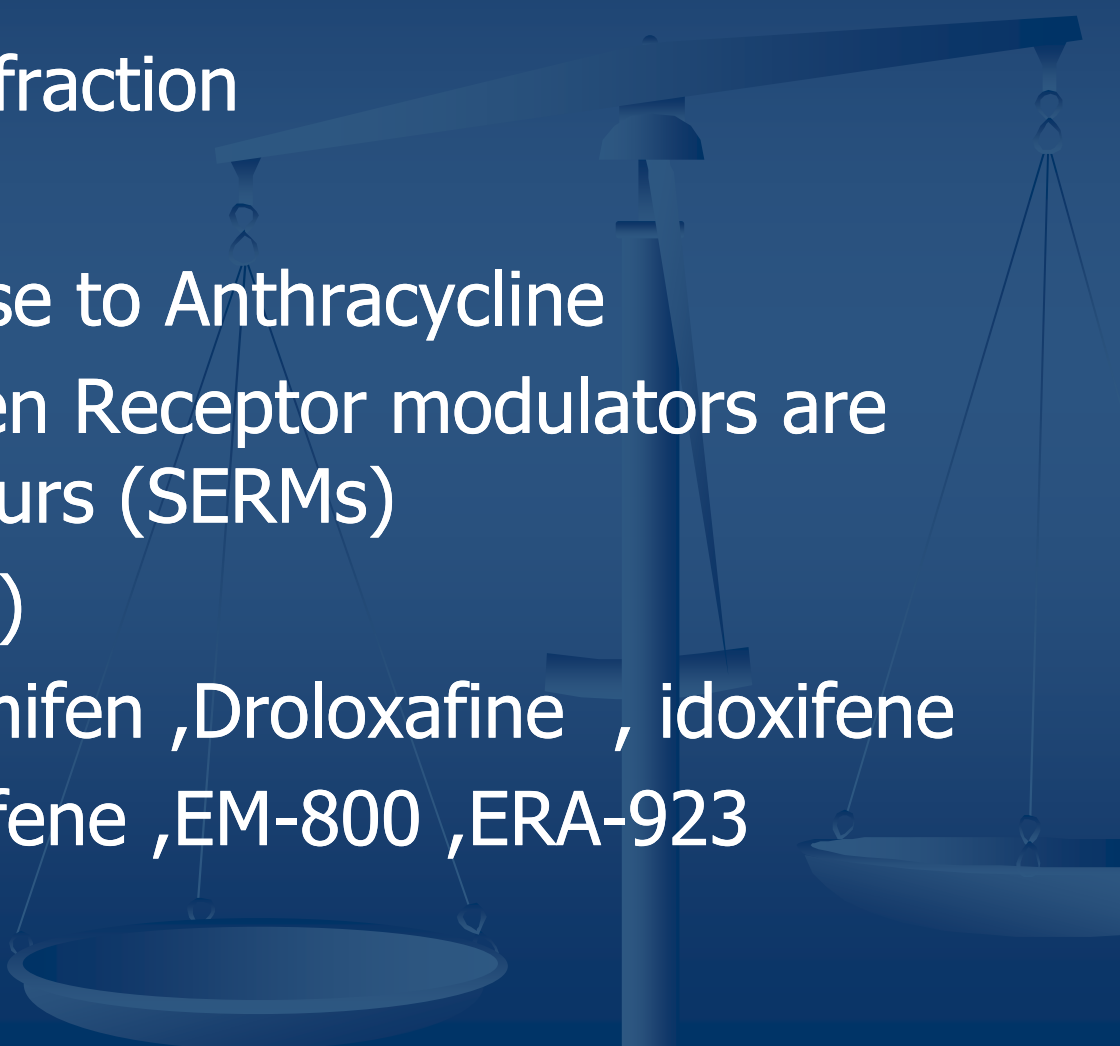
- | | survival |
|--|----------|
| ■ Early stage Breast CA,ER+ | 92% |
| ■ Early stage Breast CA,ER- | 82% |
| ■ Her2/neu amplification is associated with impaired survival in early Breast CA | |

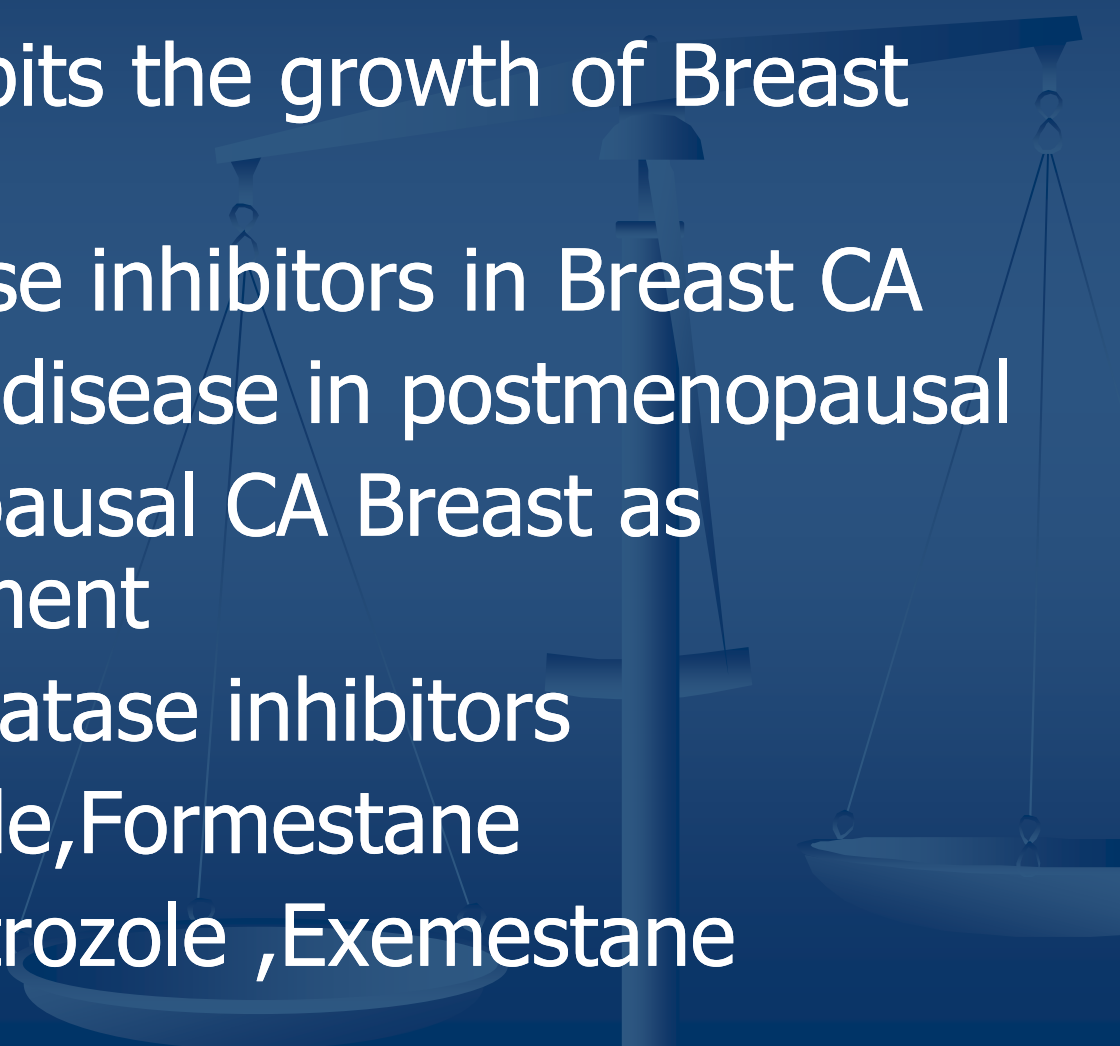
Triple Negative Breast Cancer

- TN: immunophenotypic description
 - ER (-)
 - PR (-)
 - Her-2/neu (-)
 - 10-17% of all breast cancers, depending on the thresholds of tests
 - Younger age
 - Shorter disease free survival and disease specific survival
 - Aggressive behavior with metastasis
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Her2/neu

- Cellular Proto Oncogene that codes for a transmembrane receptor of the epidermal growth factor receptor family
- Amplification is seen in 25% -30% of early breast CA
- Early appearance of Metastatic disease with poor survival
- Trastuzumab (Herceptin) is used in Adjuvant +Metastatic Breast CA which is Her2/neu +

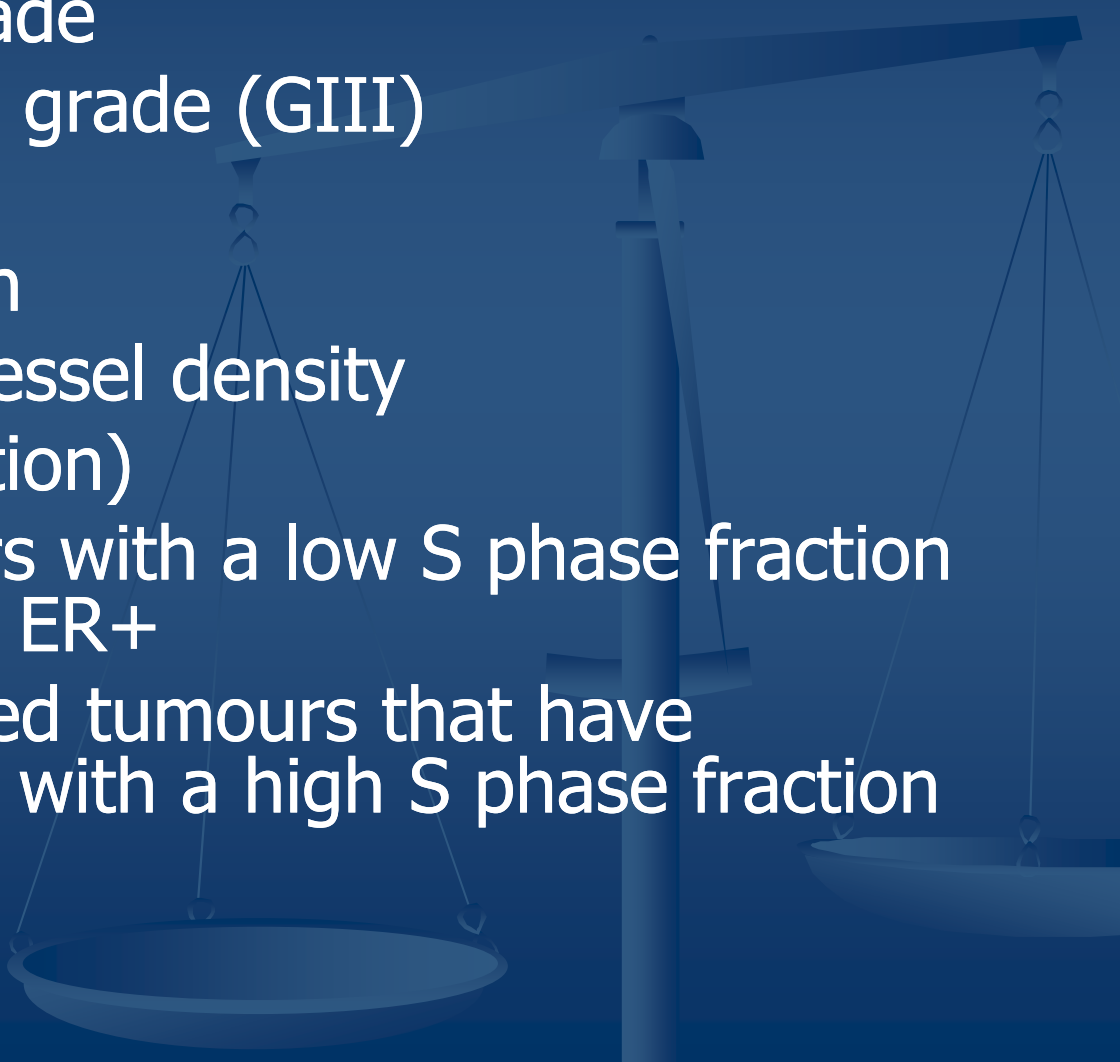
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- Her2/neu over expression is associated
 - Axillary Lymph node +
 - ER -
 - High S phase fraction
 - Poor outcome
 - Better response to Anthracycline
 - Selective Oestrogen Receptor modulators are used in ER+ tumours (SERMs)
 - 2 types of (SERMs)
 - Tamoxifen ,Toremifen ,Droloxafine , idoxifene
 - Raloxafine ,Arzoxifene ,EM-800 ,ERA-923

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- SERMs have cis form and a trans form
 - Cis form stimulates the growth of Breast CA
 - Trans form inhibits the growth of Breast CA
 - Use of Aromatase inhibitors in Breast CA
 - ER+ metastatic disease in postmenopausal
 - ER+ Postmenopausal CA Breast as Adjuvant Treatment
 - 2 types of Aromatase inhibitors
 - Aminoglutamide, Formestane
 - Anastrozole ,Letrozole ,Exemestane

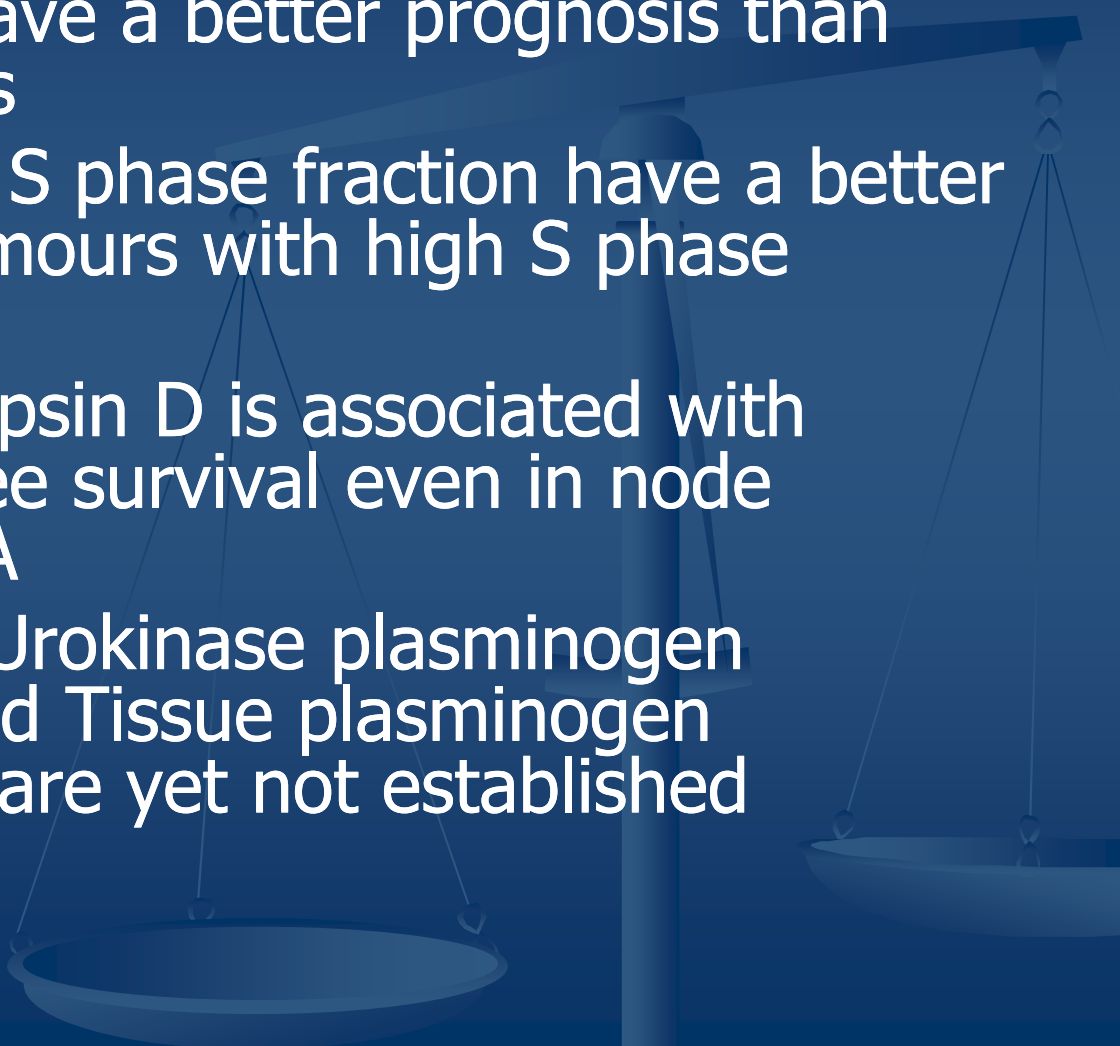
Pathology

- 30% risk of developing invasive Breast CA in 10 years after DCIS
- 35% - 45% risk of developing invasive Breast CA in 10 to 20 years after LCIS
- Invasive duct CA accounts for 80% of Breast CA and DCIS accounts for 20%
- Papillary, Mucinous, Tubular and Medullary CA are less aggressive forms with <10% LN metastasis

Poor prognostic Pathological features

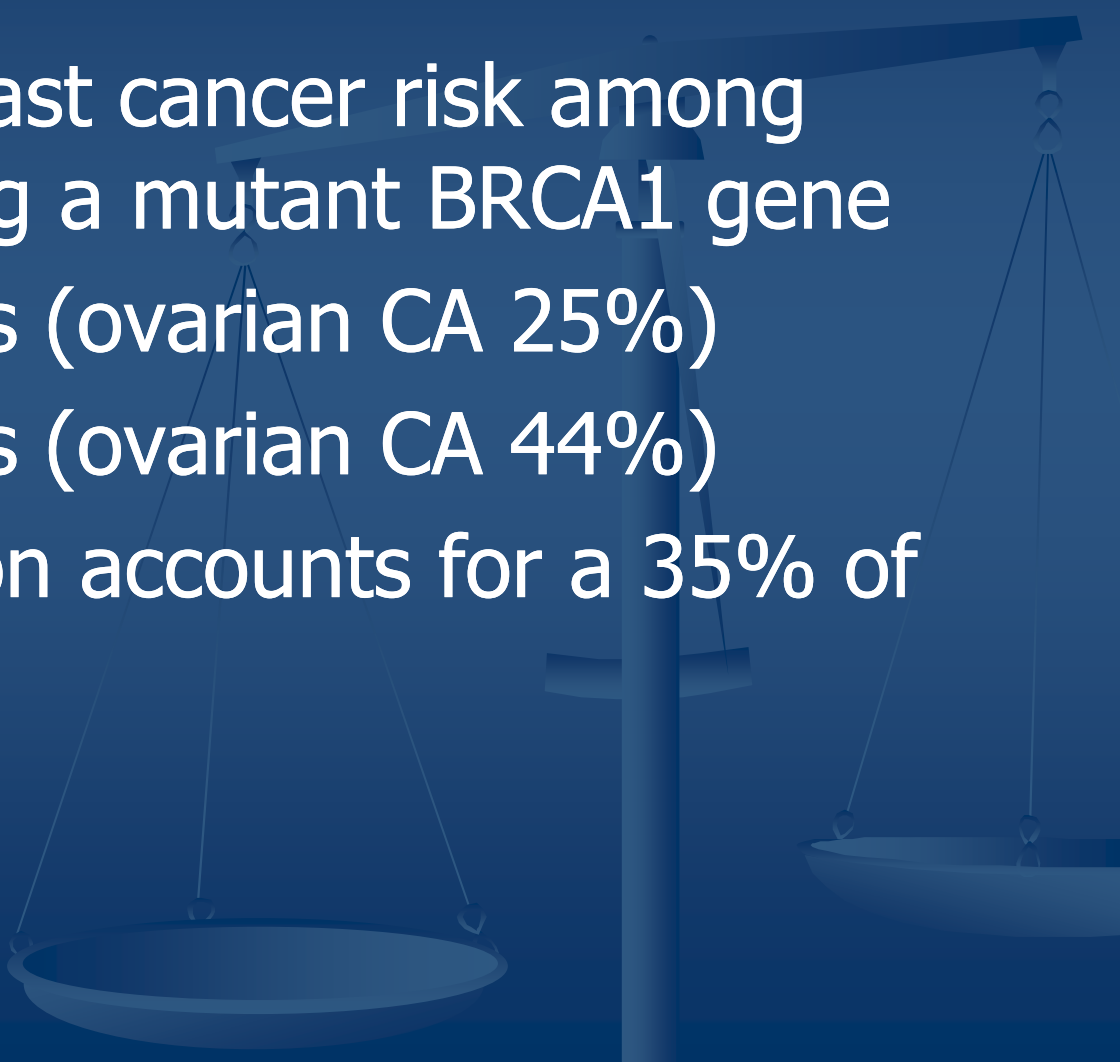
- Higher Nuclear grade
 - Higher histological grade (GIII)
 - Tumour necrosis
 - Lymphatic invasion
 - Increased micro vessel density (Neovascularization)
 - Low grade tumours with a low S phase fraction are nearly always ER+
 - Poorly differentiated tumours that have extensive necrosis with a high S phase fraction are usually ER-
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Measures of Proliferative activity of Cancer cells

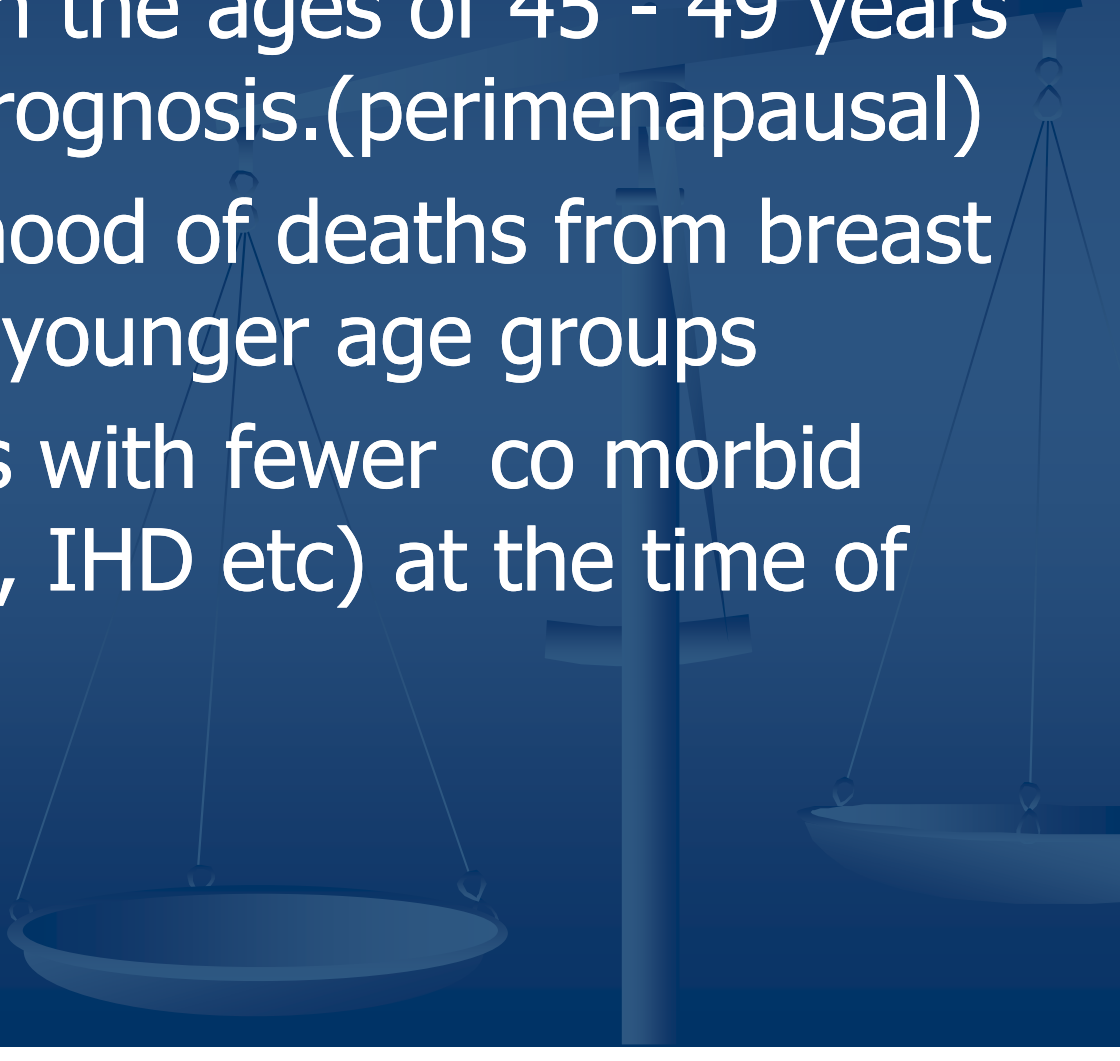
- Diploid tumours have a better prognosis than Aneuploid tumours
 - Tumours with low S phase fraction have a better prognosis than tumours with high S phase fraction. (>6%)
 - Elevation of Cathepsin D is associated with shorter disease free survival even in node negative breast CA
 - Place of CA 15.3, Urokinase plasminogen activator (UPA) and Tissue plasminogen activatorI (TPA-I) are yet not established
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Oncogene Expression

- In sporadic breast CA, P53 is the most frequently mutated gene
- Her2/neu and C-myc amplification with P53 suppressor oncogene expression is associated with early relapse and short survival
- P53 status does not predict response to adjuvant CT but patients with negative P53 benefit from CT
- BRCA1 and 2 mutation have a little effect on prognosis but increases the risk of Breast CA

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- 45% of families with site specific Breast CA have a mutation in BRCA1 gene (17q21)
 - Cumulative breast cancer risk among females carrying a mutant BRCA1 gene
50% at 50 years (ovarian CA 25%)
85% at 70 years (ovarian CA 44%)
 - BRCA2 mutation accounts for a 35% of Breast CA

Age and performance status at Diagnosis

- Women between the ages of 45 - 49 years have the best prognosis.(perimenapausal)
 - Increase likely hood of deaths from breast CA in older and younger age groups
 - Better prognosis with fewer co morbid factors (DM, HT, IHD etc) at the time of diagnosis
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THANKYOU

