



Metastatic Breast Cancer: Medical oncology updates

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Attending physician

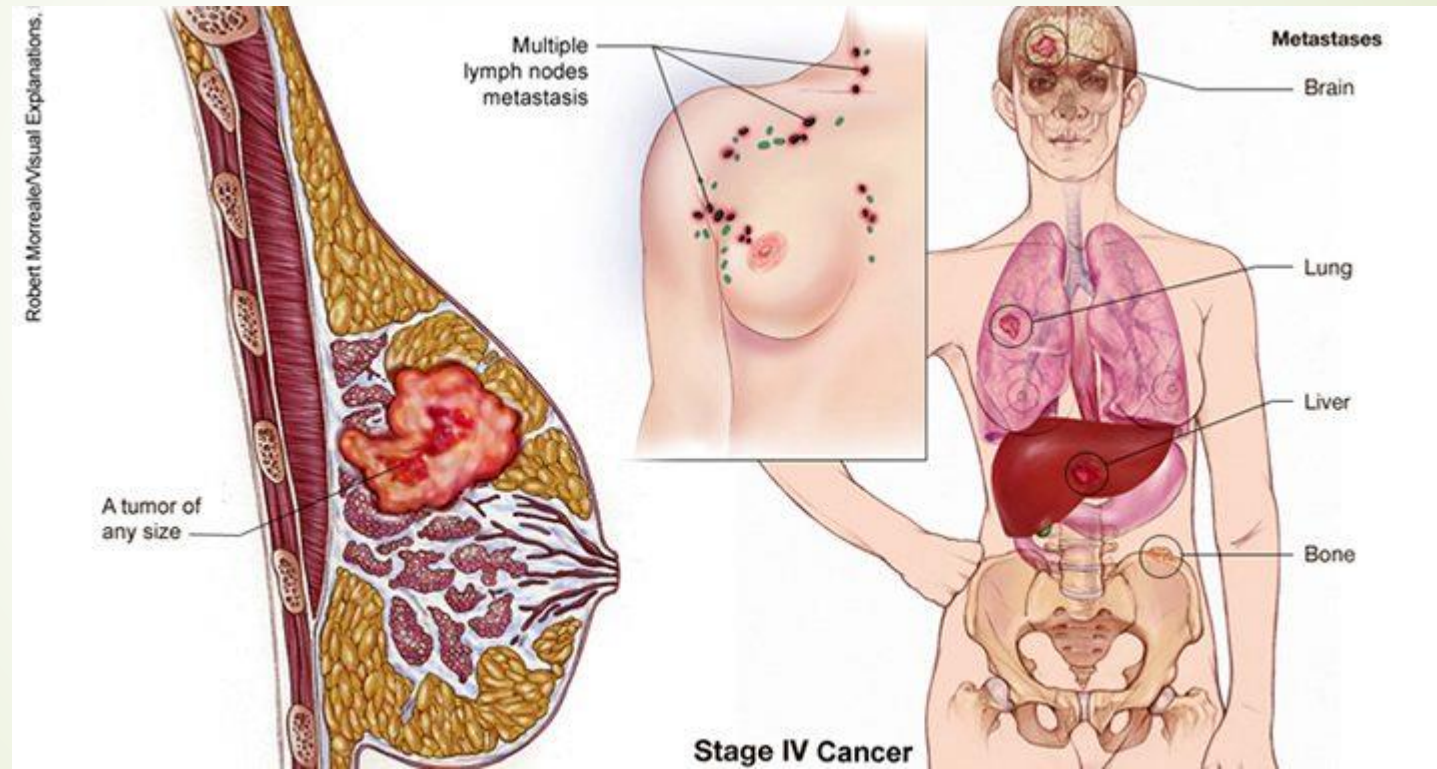
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Agenda: To give an update on medical treatments for the basic subtypes of metastatic breast cancer

- ▶ Review treatments of Er positive(HR positive) breast cancer
- ▶ Review treatments of Her2 positive breast cancer
- ▶ Review treatments for Triple negative breast cancer
- ▶ Review role of next generation sequencing

Metastatic Breast Cancer:

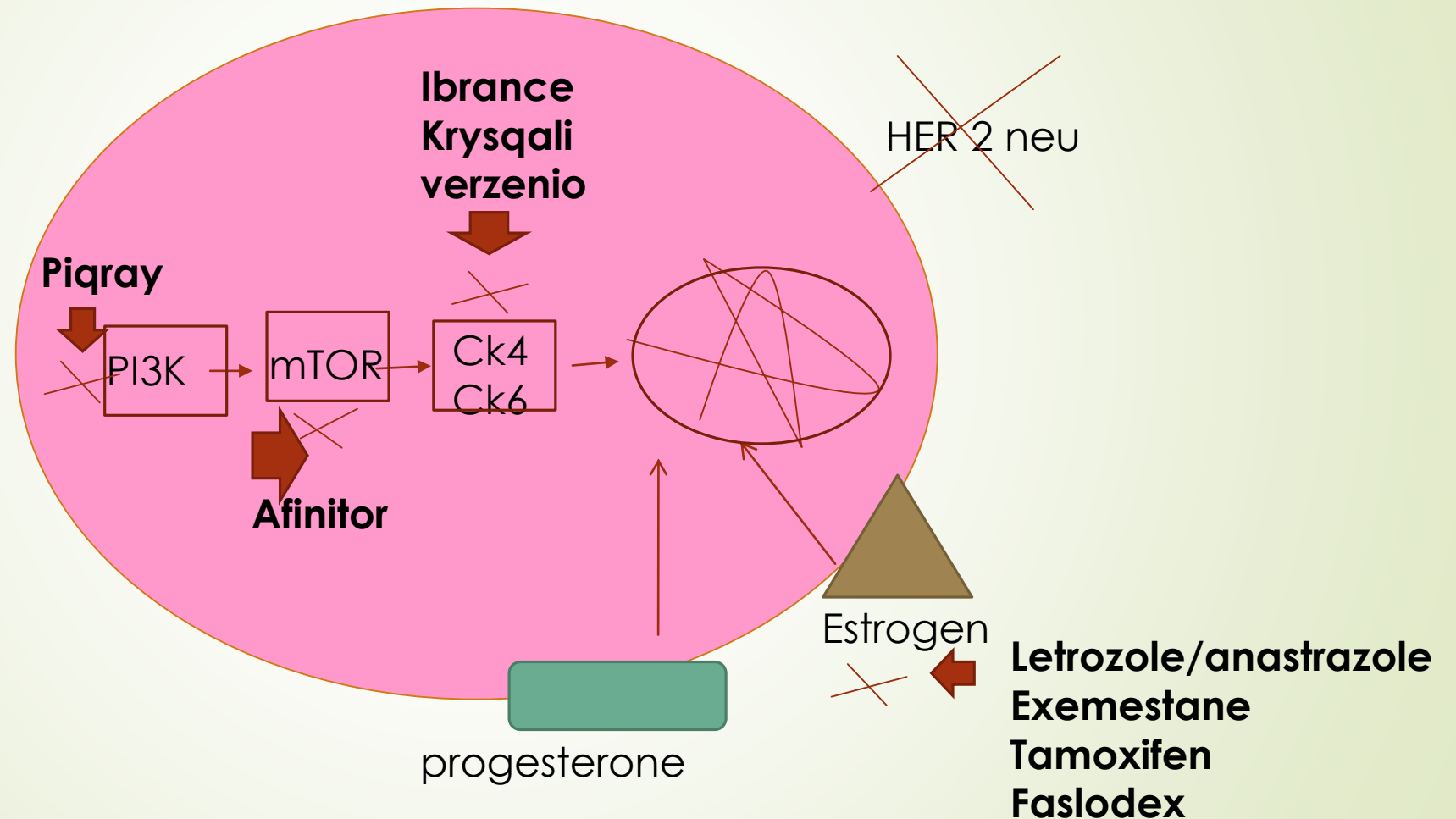




Systemic therapy for Er positive breast cancer:

- ▶ Endocrine therapy is a mainstay of treatment
- ▶ Typically can avoid chemotherapy in most cases
- ▶ Antiestrogen- aromatase inhibitors – letrozole/ansastrazole, aromasin(or tamoxifen), ovarian suppression
- ▶ Faslodex (fulvestrant)
- ▶ Ck4/6 inhibitors + antiestrogen
- ▶ mTOR inhibitor + antiestrogen
- ▶ Importance of next gen sequencing- PI3K mutation, BRCA

Breast cancer cell : Er positive , her2 negative





Her2 positive breast cancer:

- ▶ Anti Her2 therapy is mainstay of treatment
- ▶ First line is usually a low dose chemo (taxol or taxotere) with anti her2 antibodies herceptin and perjeta
- ▶ Second line and beyond include kadcyca , antibody drug conjugate or the newly approved tukysa xeloda and Herceptin or enhertu (another antibody drug conjugate)
- ▶ Tukysa (tucatinib) also has excellent CNS penetration for brain mets

Timeline of targeted agents for Her 2 positive breast cancer:

Her 2 identified as oncogene

1985

Herceptin approved for Metastatic Her 2 positive Breast cancer

1998

Herceptin approved for Use in adjuvant breast cancer

2006

Perjeta for metastatic breast

2007

Perjeta for neo/adjuvant

2012

Kadcyla

2013

Enhertu

2019

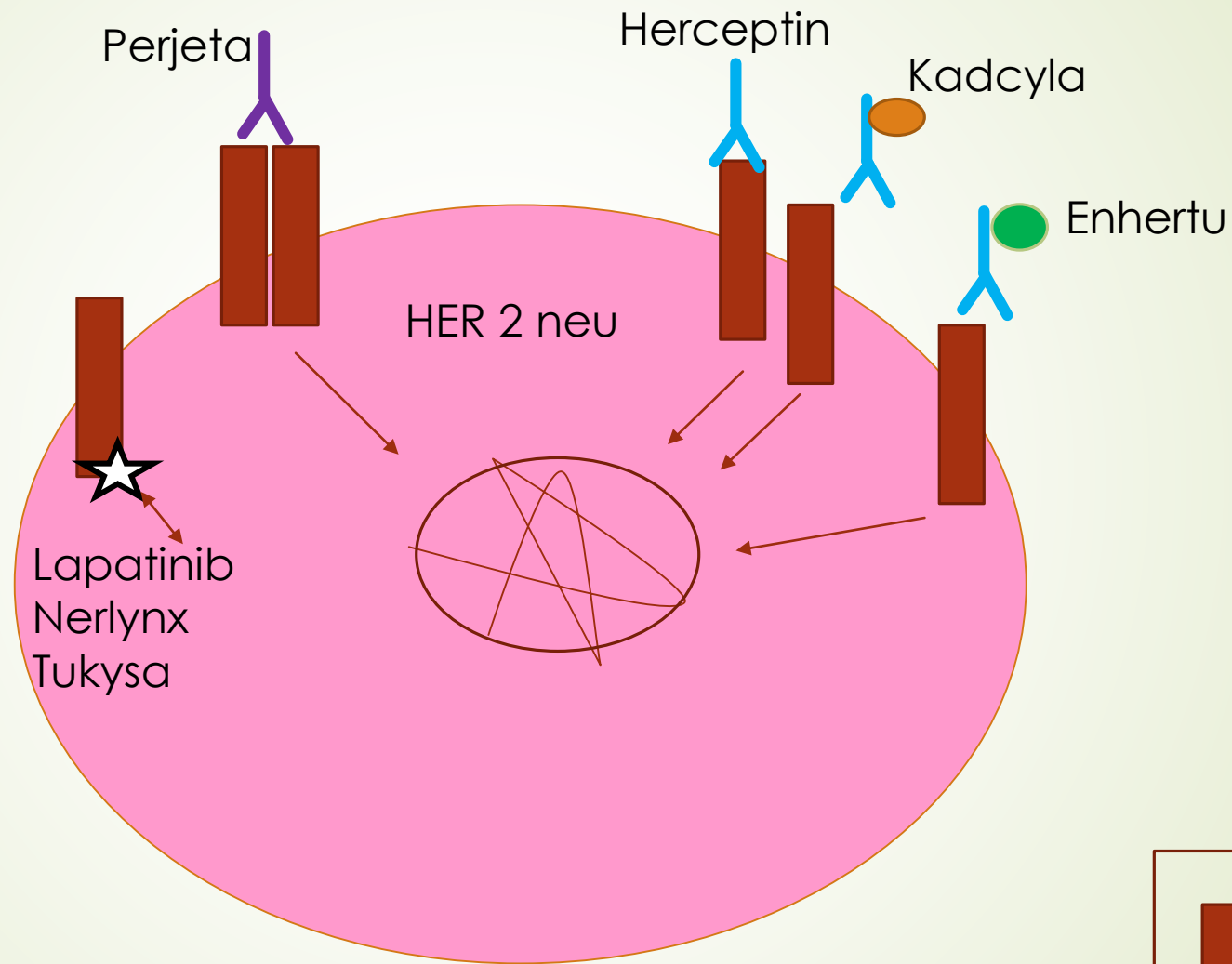
2020

Tucatinib
(Xeloda
Herceptin)

Lapatinib approved For metastatic

Nerlynx +
(xeloda)

Her2 positive Breast cancer cell :



=HER2



Metastatic triple negative breast cancer:

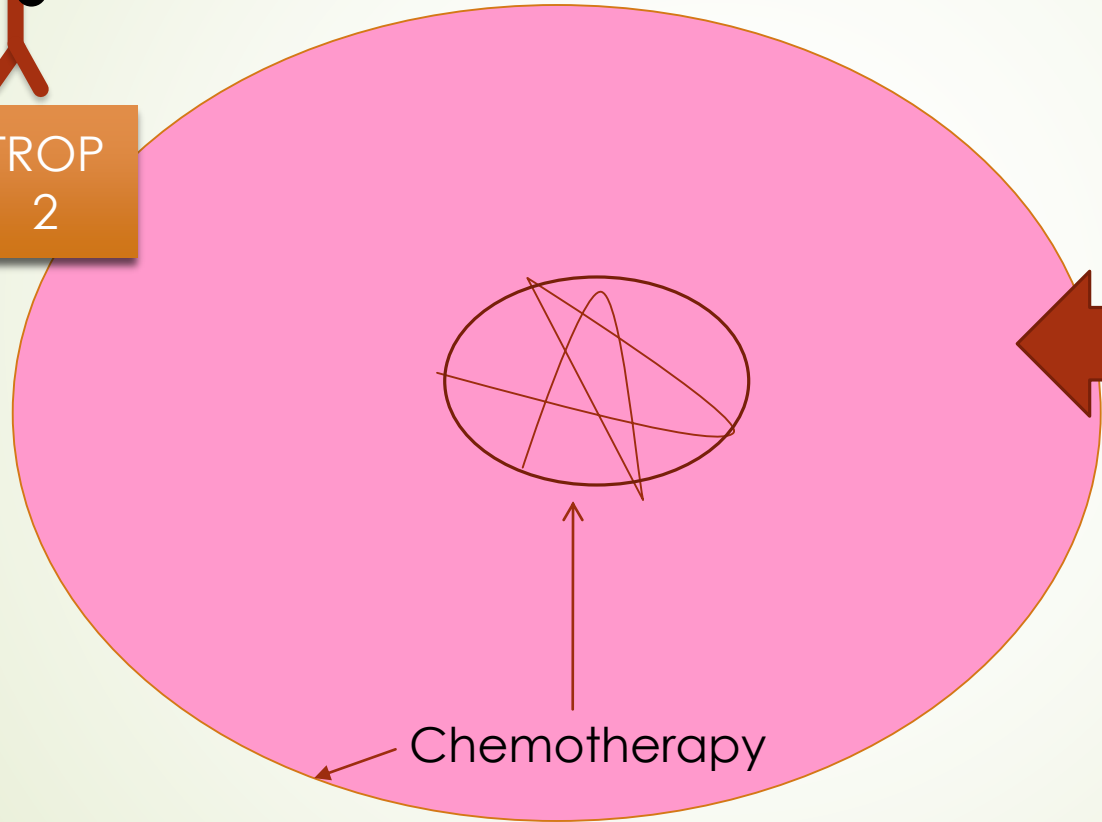
- Usually quite responsive to chemotherapy , this is usually first line
- Problem is resistance
- Now approved is abraxane (low dose chemo) and tecentriq (immunotherapy), tumor lymph must be over 1% PDL1 positive
- For later line therapy – new and first antibody drug conjugate for triple negative breast – sacituzimab
- Always make sure to check brca testing
- Androgen inhibition

Breast cancer cell Triple negative :

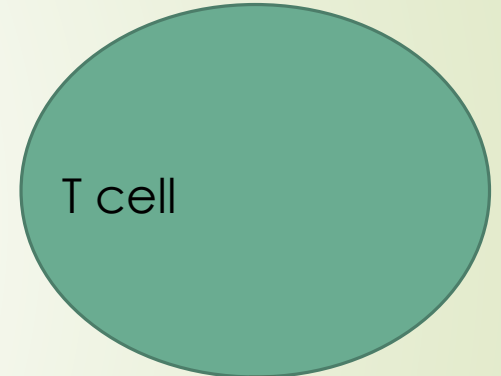
Sacituzumab(todelvy)



TROP
2



Chemotherapy

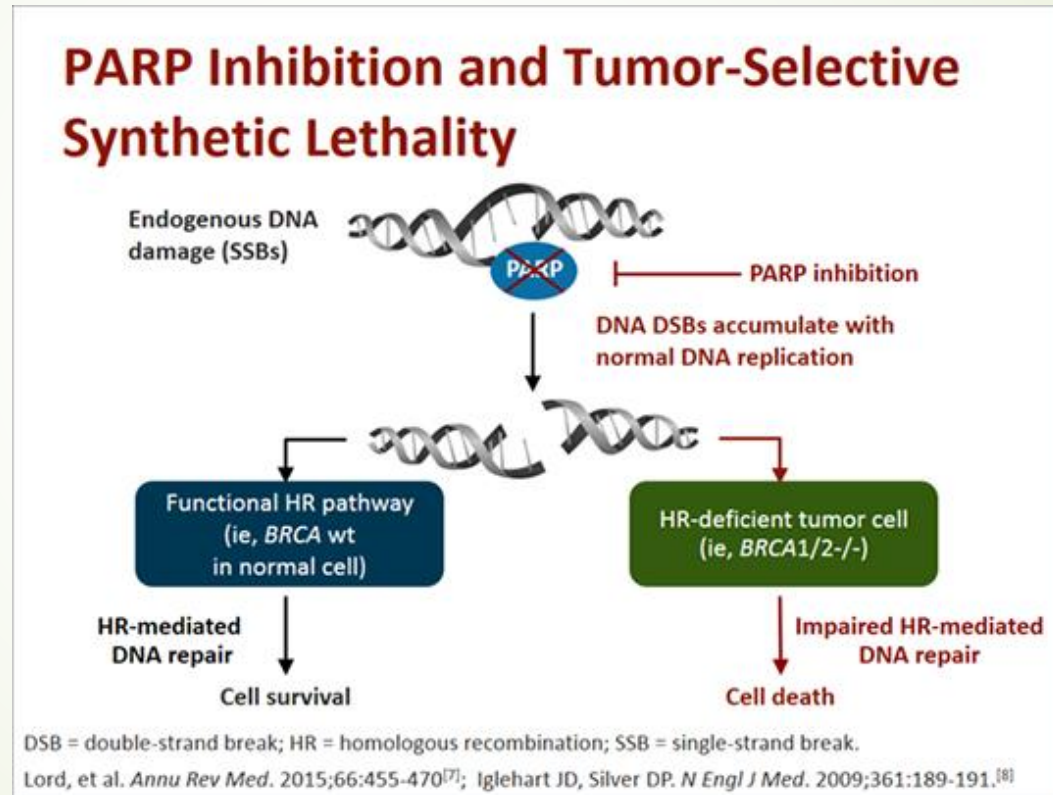



T cell



Tecentriq(attezolizimab)


BRCA positive cells are more sensitive to PARP (poly ADP ribose polymerase) inhibition :





Olaparib approved jan 2018 for metastatic breast cancer with BRCA mutation(germ line)

- Gives further evidence that all woman should have brca testing
- Can test tumor if not able to test patient , blood test is most simple and now affordable
- 302 patient her2 negative , germline(hereditary) BRCA pos , could be ER pos or Negative, had to have prior treatment
- PFS 7 months for olaparib versus 4 months with chemotherapy
- Low blood counts, gi side effects most common
- Rarely secondary MDS and leukemia



VIOLETTE STUDY : BRCA or “other” genes involved in DNA repair

- ▶ Ongoing trial at northwell cancer institute
- ▶ Screen for BRCA and also mutations that make cells more sensitive to inhibition of DNA repair (eg/ CHEK2, PALB, BRIPI) “BRCAness”
- ▶ Testing the effect of parp inhibitor alone versus parp inhibitor + new agent (works on another dna replication check point gene- ATR)
- ▶ Triple negative progressive disease , 1-2 prior treatments, no progression on carboplatin, adequate labs etc