Neoadjuvant Chemotherapy in the Treatment of Breast Cancer

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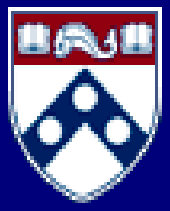

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Overview

- Define
- Why?
- What?
- Where are we going?

Treatment of Early Stage Breast Cancer

- Surgery +/- reconstruction
- Evaluation of axillary lymph nodes
- +/- Chemotherapy
- +/- Anti-hormone therapy
- +/- HER2 targeted therapy
- +/- Radiation

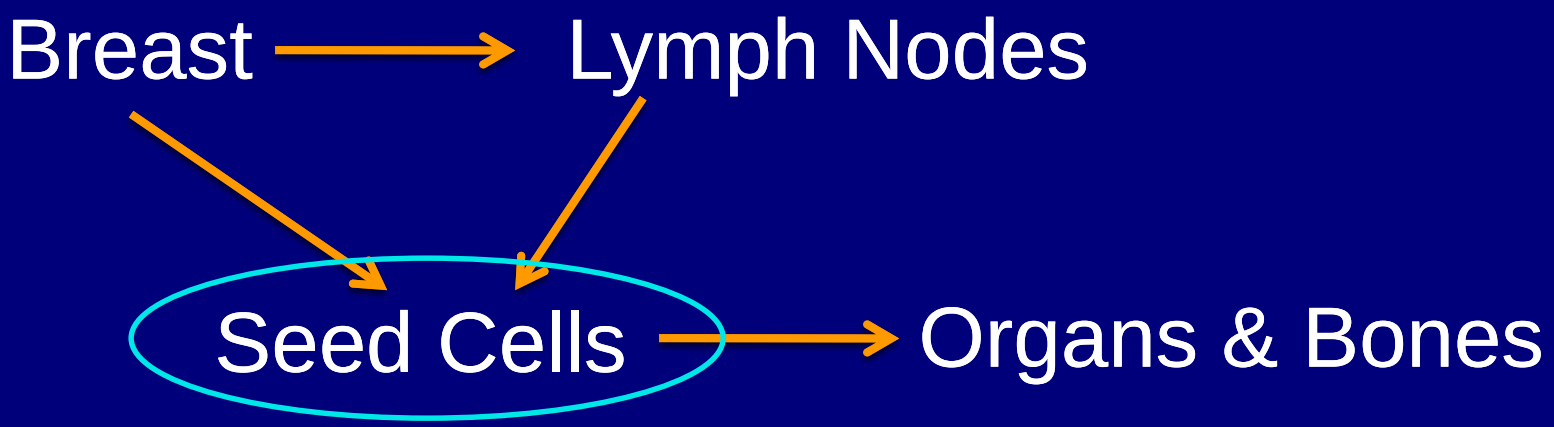
Definitions

- Adjuvant:
  - Any treatment that is given AFTER surgery
- Neoadjuvant
  - Any treatment that is given BEFORE surgery
    - Chemotherapy
    - HER2 directed therapy

Neoadjuvant Therapy

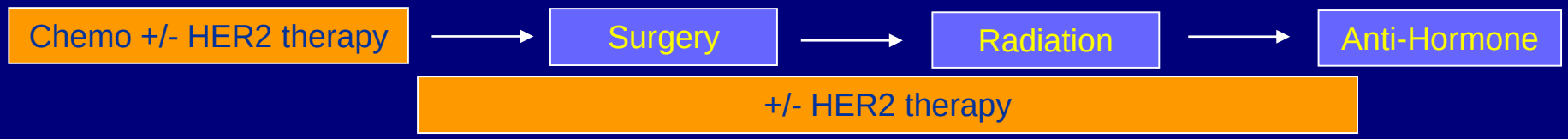
- SAFE: No difference in recurrence
- ER/PR/HER2 status important
- Not appropriate for all
  - Most aggressive chemotherapy combinations used
    - May be more treatment than what some may need

Goal of (neo)Adjuvant Therapy



- Kill seed cells
- Prevent development of metastatic disease
- Risk of seed cells vs side effect/benefit of therapy

Neoadjuvant Therapy: Goal



- SHRINK THE CANCER
  - Enable surgery
    - Inflammatory Breast Cancer
  - Enable a lumpectomy
  - Enable fewer lymph node to be removed
- Goal is pathologic complete response (pCR)
  - No cancer at the time of surgery

Why pCR?

- Those with pCR have lower rate of cancer recurrence
- Determine after surgery
- pCR is the endpoint of some clinical trials

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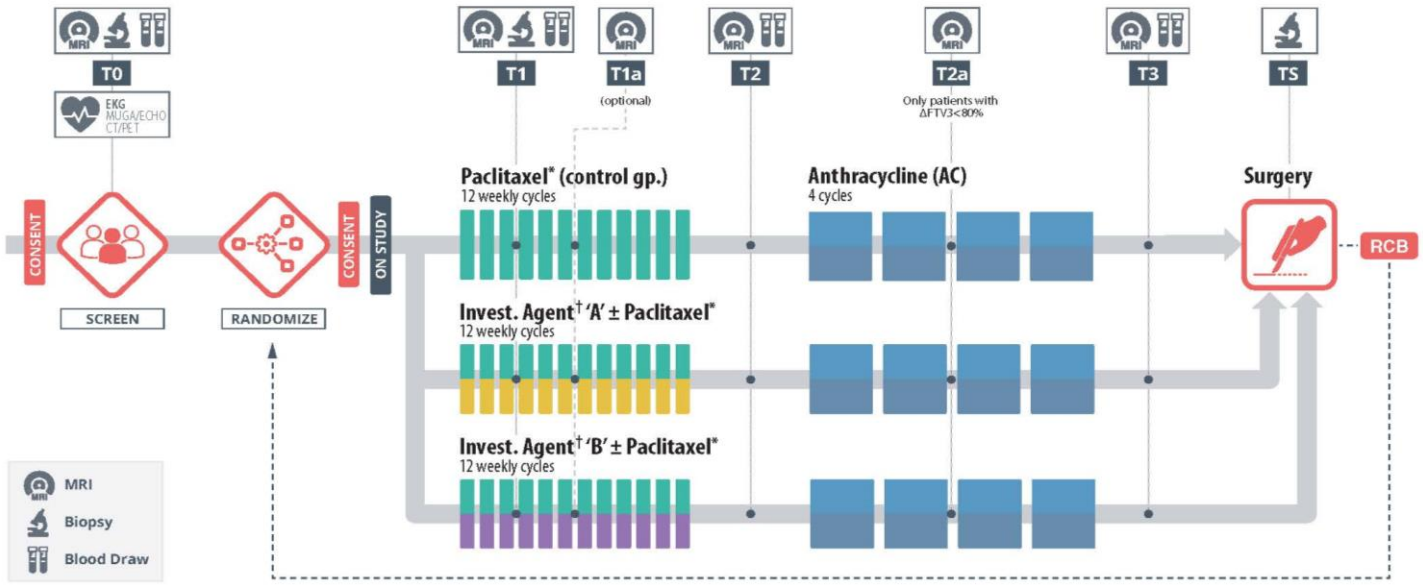
Study Plan



* Patients who are HER2+ may also receive tastuzumab (Herceptin)

† An investigational combination of one or more agents may be used to replace all or some of the standard therapy

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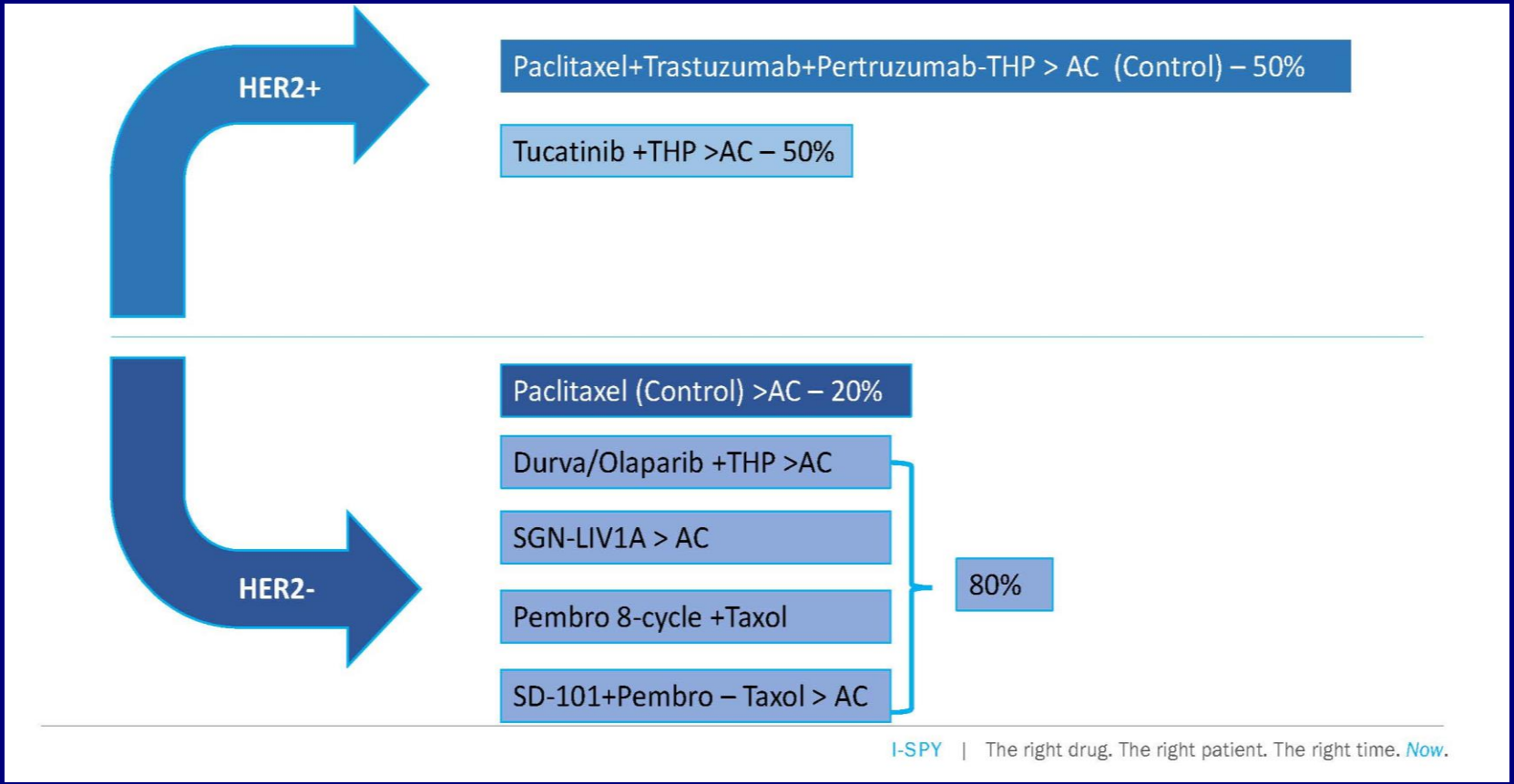
HER2+
Paclitaxel+Trastuzumab+Pertruzumab-THP > AC (Control) – 50%
Tucatinib +THP >AC – 50%
HER2-
Paclitaxel (Control) >AC – 20%
Durva/Olaparib +THP >AC
SGN-LIV1A > AC
Pembro 8-cycle +Taxol
SD-101+Pembro – Taxol > AC
80%
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Inflammatory Breast Cancer ER/PR/HER2 Negative

What About Those with Non-pCR?

- Depends on the ER/PR/HER2 status
- Recent clinical trials have given us additional options
- CREATE X- ER/PR/HER2 negative
- Katherine- HER2 positive
- Penelope- ER/PR+ HER2 negative

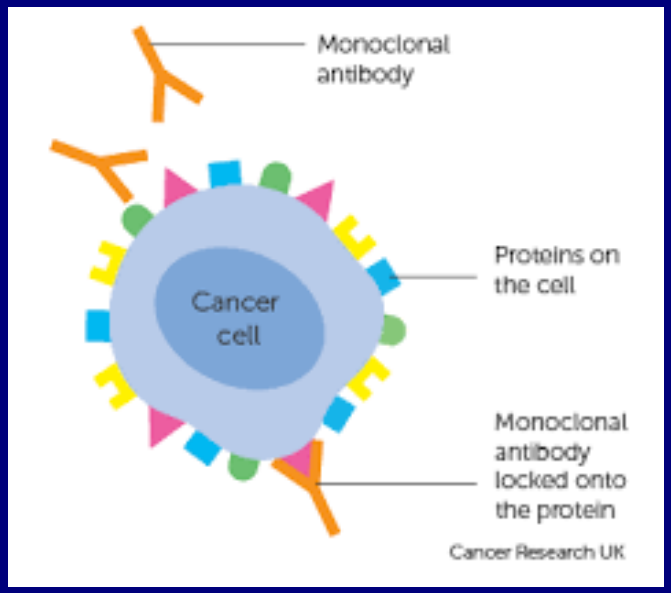
CREATE-X

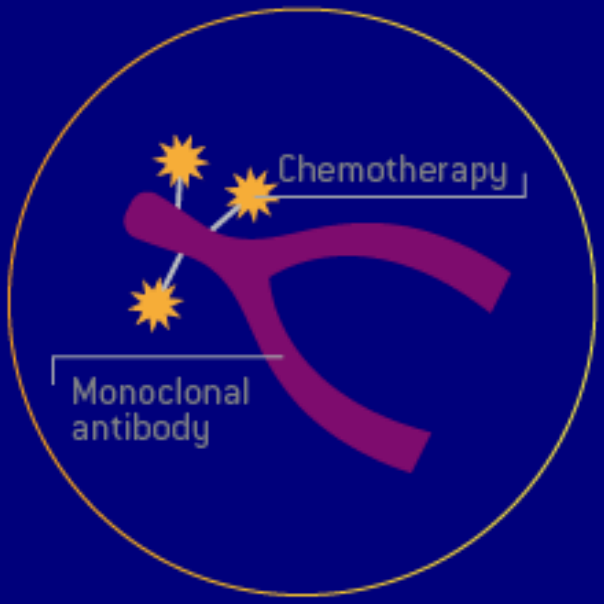
- Residual cancer after neoadjuvant therapy
- ER/PR+ HER2 negative
- ER/PR/HER2 negative
- 6 months of oral chemotherapy or observation

**** Benefit seen with capecitabine for those with ER/PR/HER2- breast cancer*****

KATHERINE: HER2+

- Residual disease
- Trastuzumab (Herceptin) vs TDM-1 (Kadcyla)





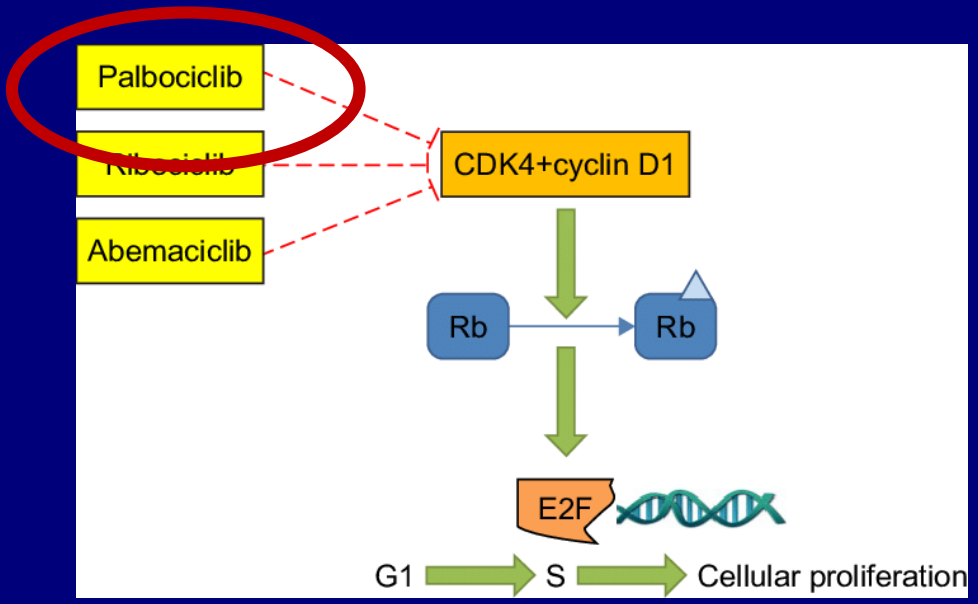
****TDM-1 was better than trastuzumab at preventing recurrent HER2+ breast cancer****

ER/PR+ HER2-

- Lower rates of pCR
- Anti-hormone therapy
- PENELOPE Trial
  - Can we decrease recurrence by adding another medication?
  - Completed
  - Awaiting results

ER/PR+ HER2 Negative

- PENELOPE
  - Anti-hormone therapy OR
  - Anti-hormone therapy with palbociclib for 2 years



Important Note

- Adding these additional therapies can add to side effects
- These other therapies are NOT for everyone
- They add options for consideration
- Risks/benefits should be discussed on a patient by patient basis

Conclusions

- Neoadjuvant therapy is not for everyone
- Help some minimize surgery
- Provides important information about response to therapy
- If response not what we hope, there are different therapies to recommend
  - ER/PR/HER2 status

Future Directions

- Use Neoadjuvant therapy
  - Add more therapy upfront
  - Give more effective therapy after surgery
  - Remove therapy that may not be necessary