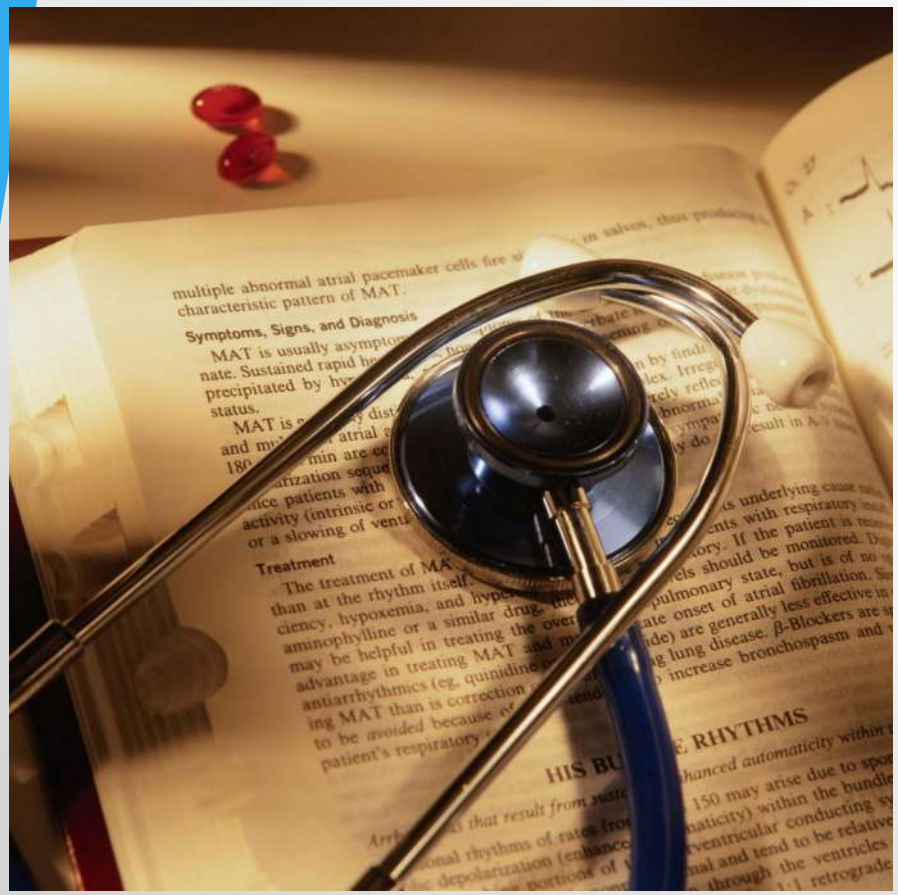
Metastatic breast cancer

Different Names



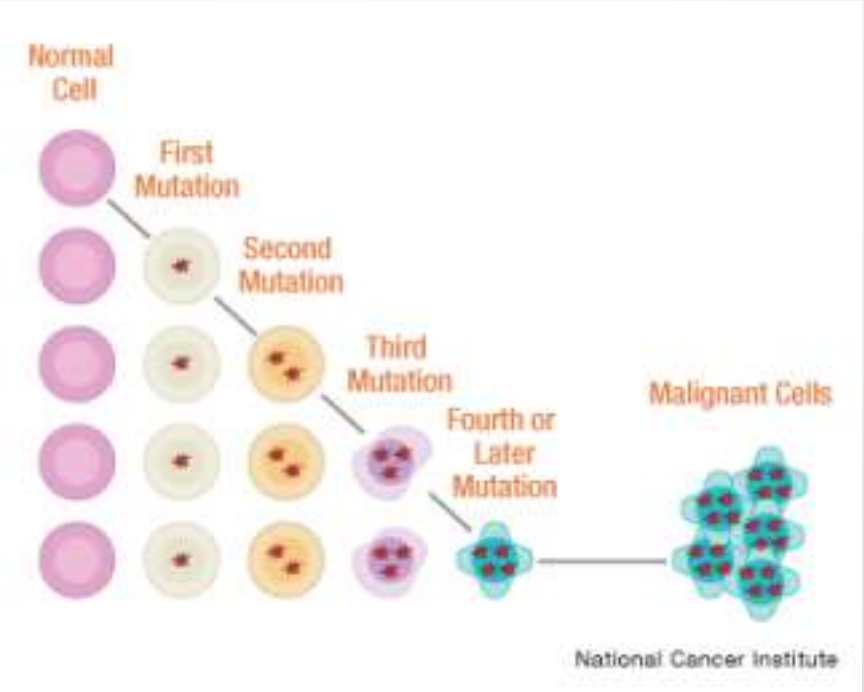
- Advanced
- Metastatic
- Secondaries
- Stage 4 [IV]
- Distant recurrence

What does secondary breast cancer mean?

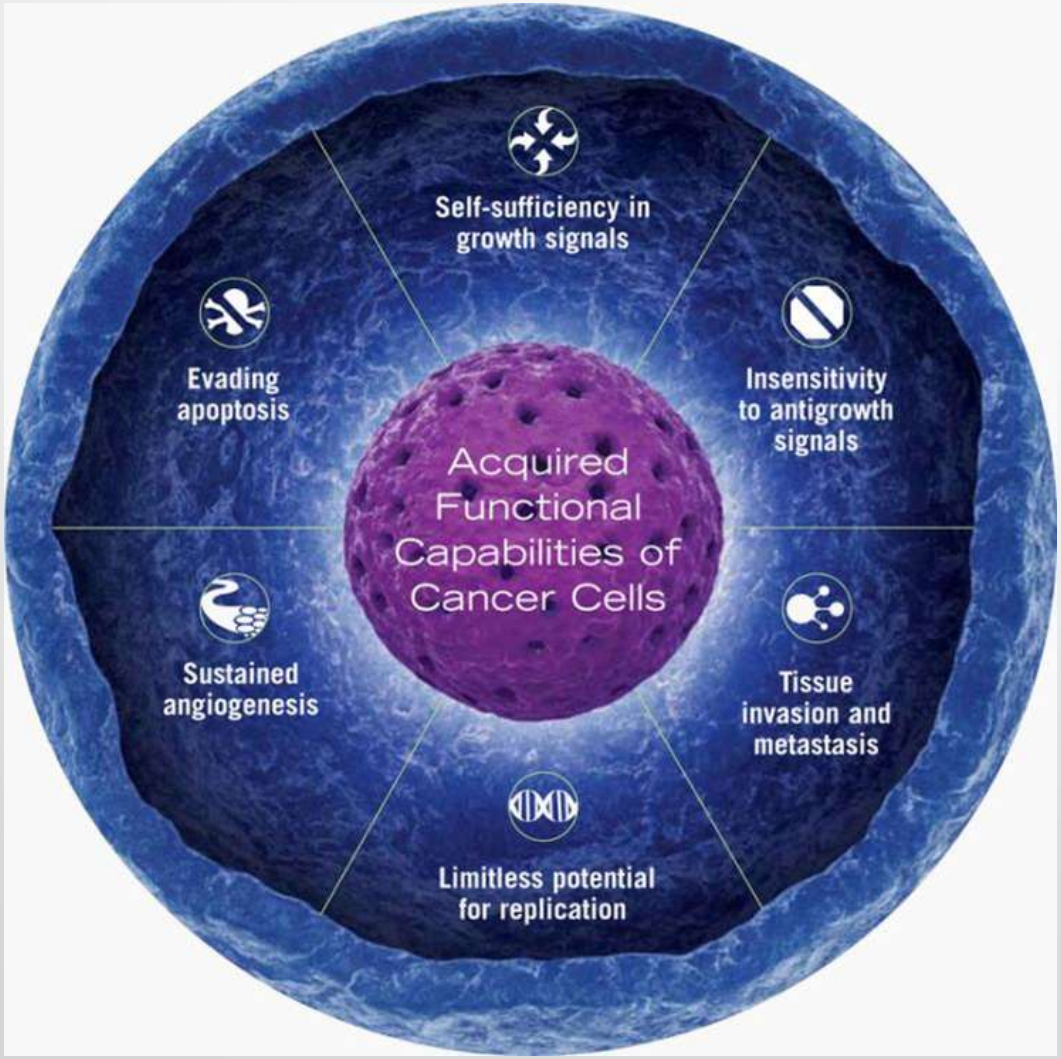
When breast cancer cells spread beyond the breast to other part(s) of the body (it's made up of the same cells as the breast cancer).

Cancer is a genetic disease

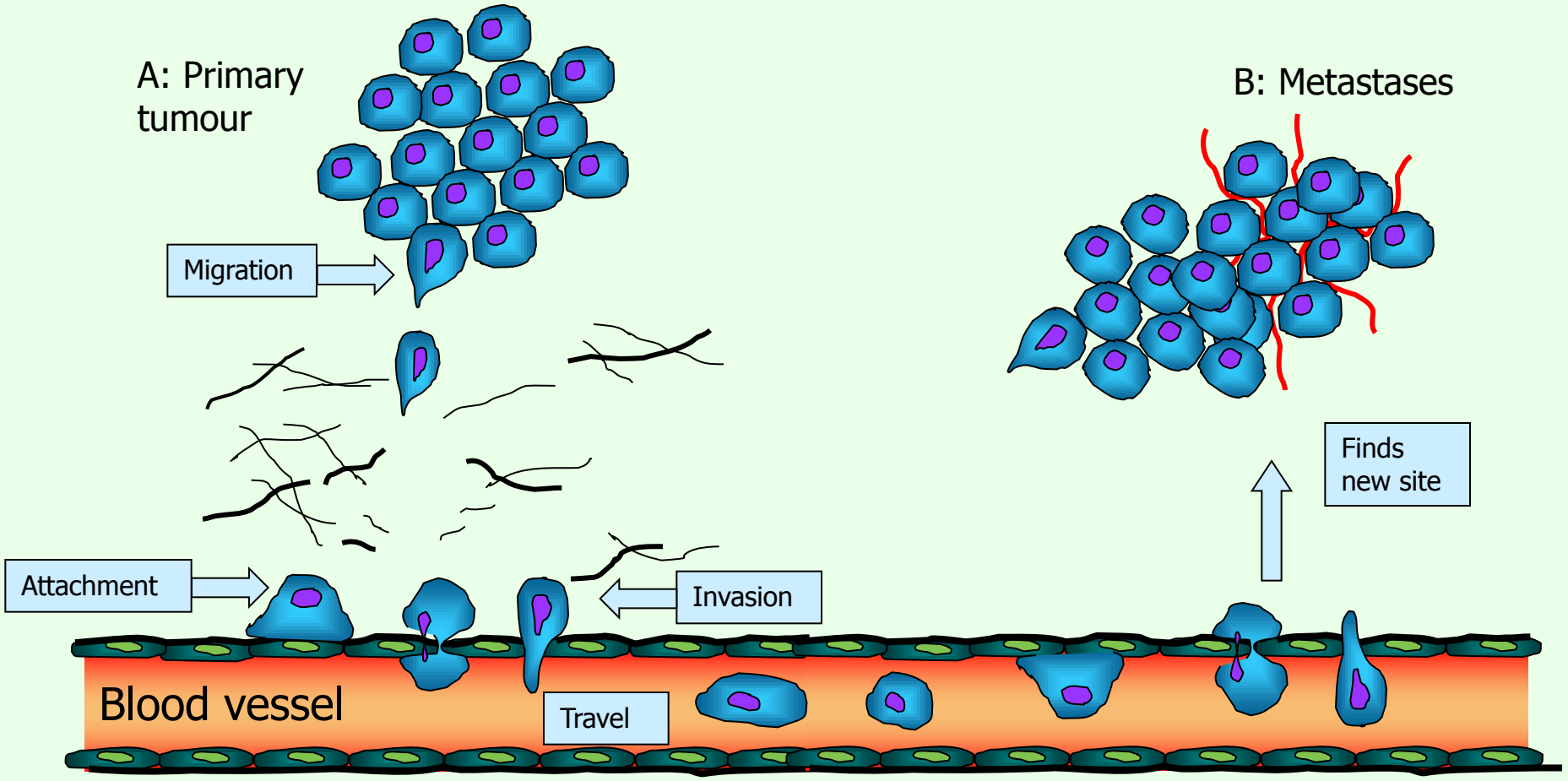
- The transition from a normal cell to a cancer is driven by changes to a cell's DNA, also known as mutations. -- Mutations can accumulate over many years before a cell becomes a cancer.



Cancer is a genetic disease

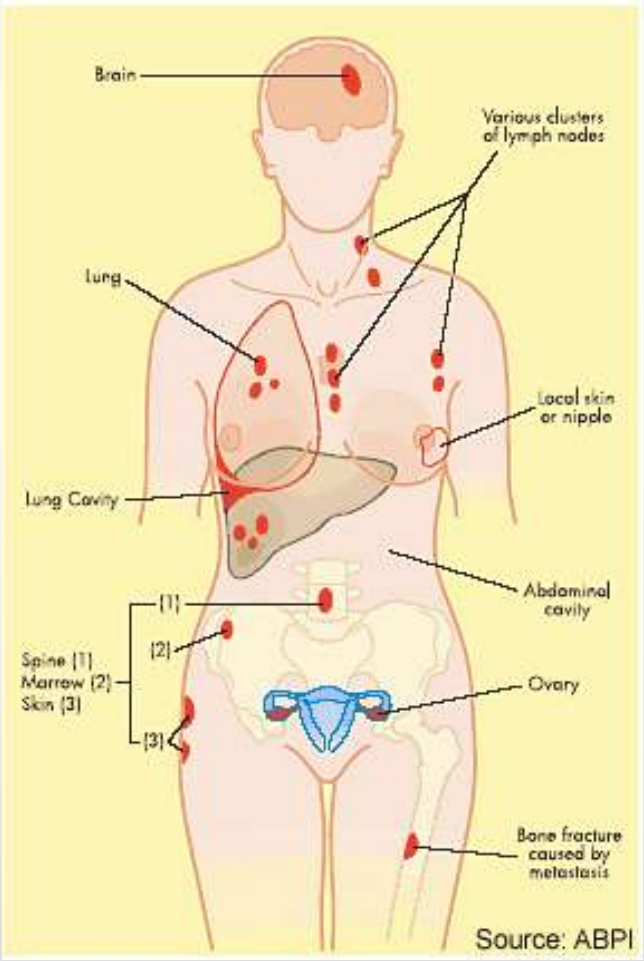


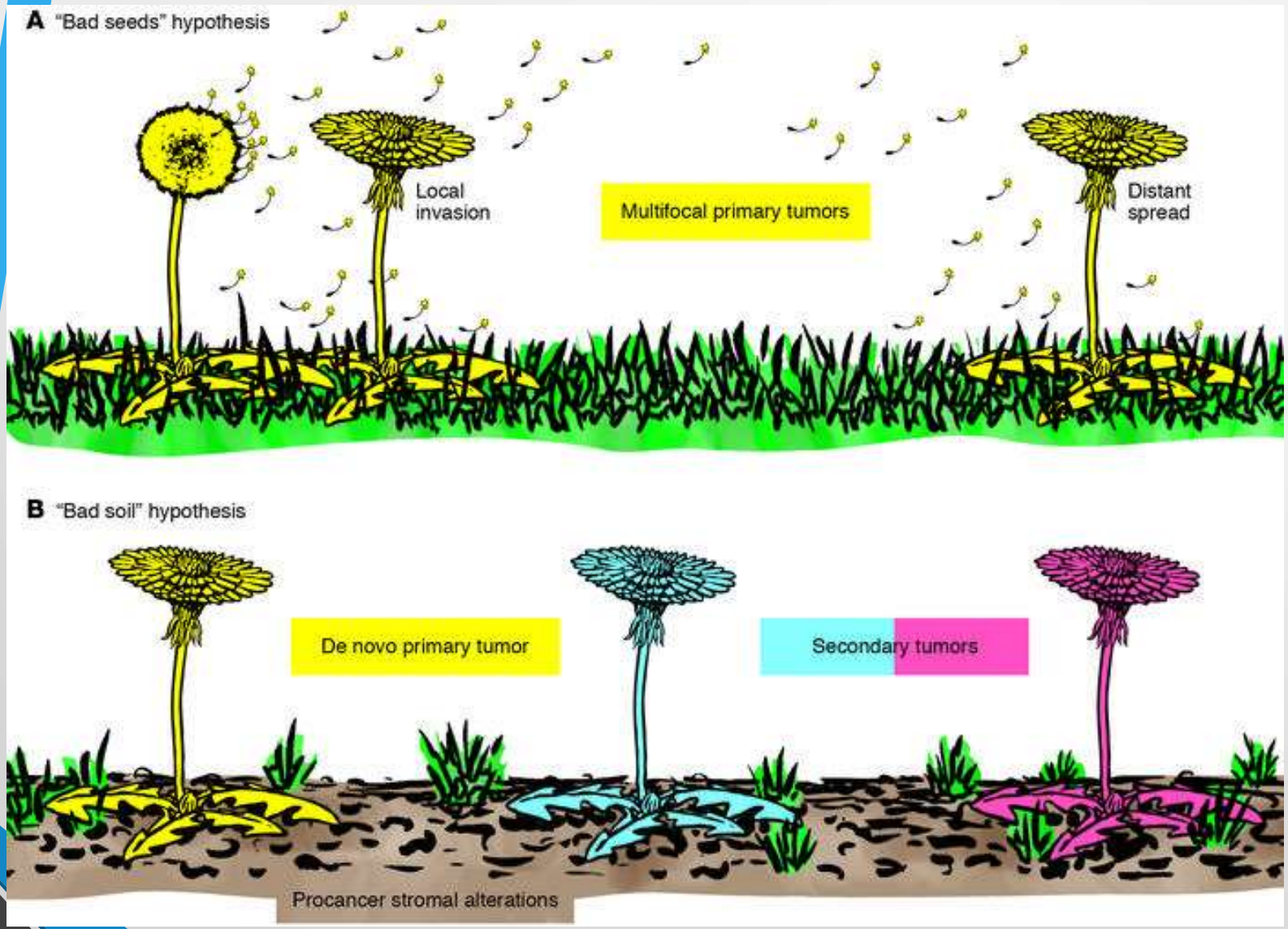
How does breast cancer spread?



Patterns of recurrence

- Common sites
  - Bone
  - Liver
  - Lung
  - Brain
  - Lymph nodes
- Probably driven by biology
- Seed and Soil hypothesis
- Dormancy




A "Bad seeds" hypothesis
Local invasion
Multifocal primary tumors
Distant spread
B "Bad soil" hypothesis
De novo primary tumor
Secondary tumors
Procancer stromal alterations

A changing picture…

- More drugs & Increasing treatment options
- Accessibility
- Longer disease control
- Many people living very active lives

- Not curable but treatable
- Ongoing treatment …always a ‘patient’
- Treatment choices
- Living with uncertainty
- Funding issues/CDF
- Need for information and support to be ‘easily’ available

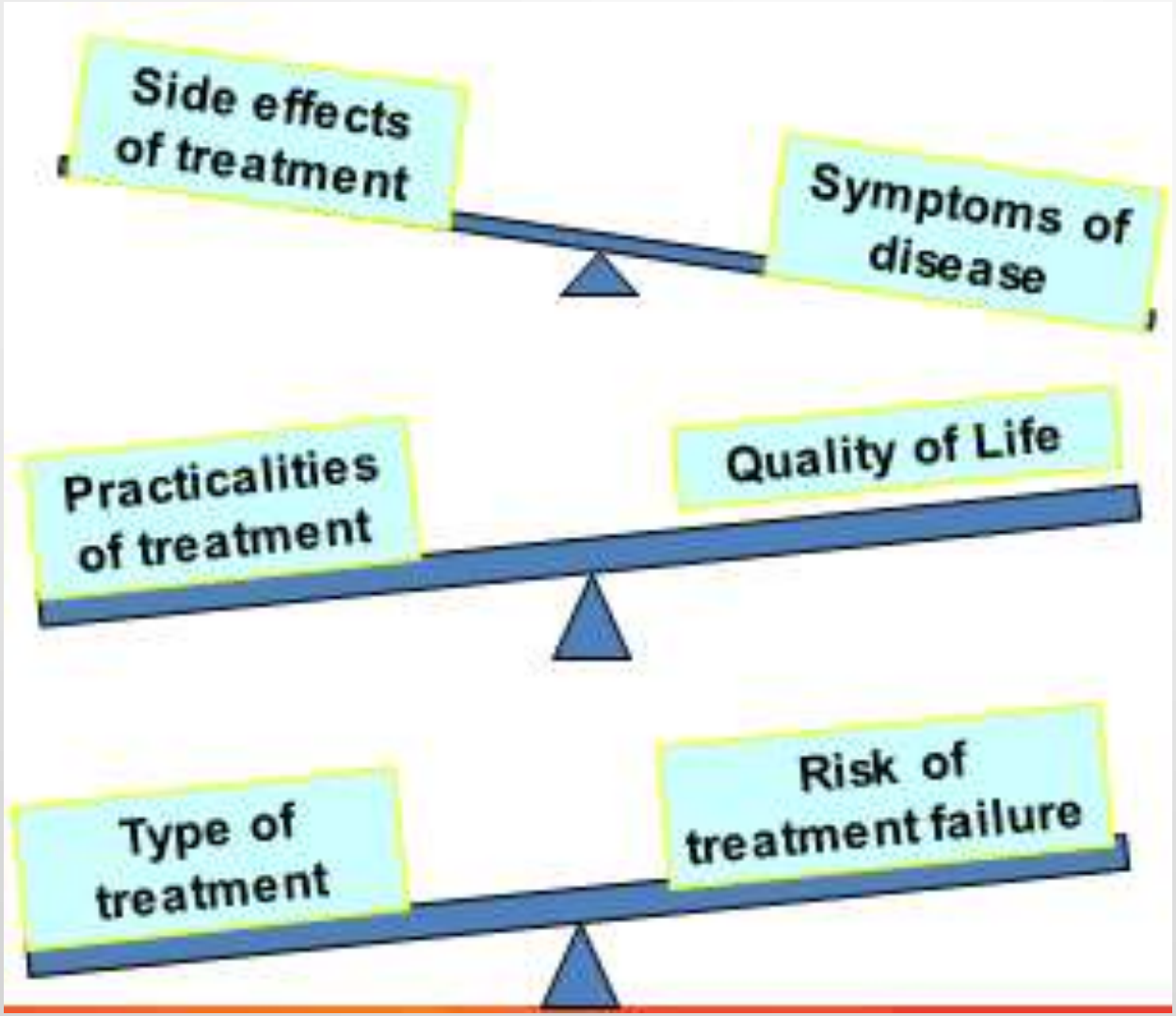
Even if things look the same – they can be different

Treatment guidance

- NICE Advanced Breast Cancer Guidelines (2009) and Update (2014)
- ESMO Advanced breast cancer guidelines (ABC2) (2014)

- 'From the time of diagnosis of ABC, patients should be offered appropriate psychosocial care, supportive care, and symptom-related interventions as a routine part of their care. '

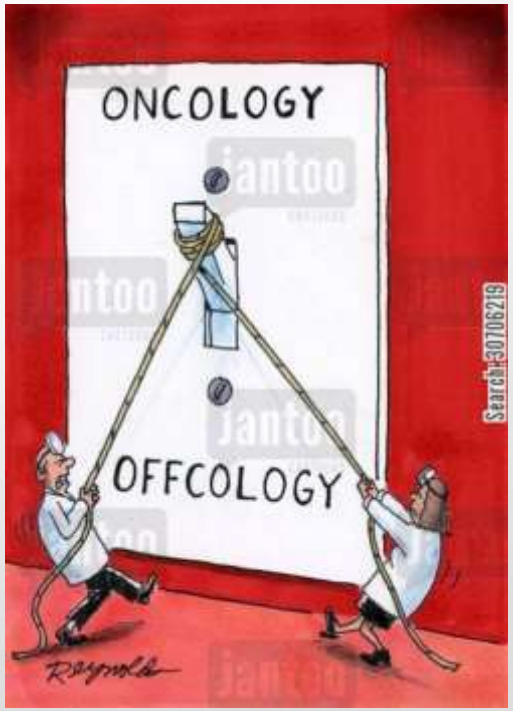
A fine balance



Aims of treatment

Shared decision making

- Reducing growth of the cancer
- Delaying or preventing further spread
- Extend life expectancy
- Improving symptoms & quality of life
- 'Acceptable' side-effects
- Ideally spent some time off treatment



Age

Performance Status

Comorbidities

Menopausal status

Symptoms

Organ function

Choice

Presence or absence of hormone receptors/HER-2

Rate of progression

Disease-free interval

?Repeat biopsy

How long ago?

Build up of toxic effects

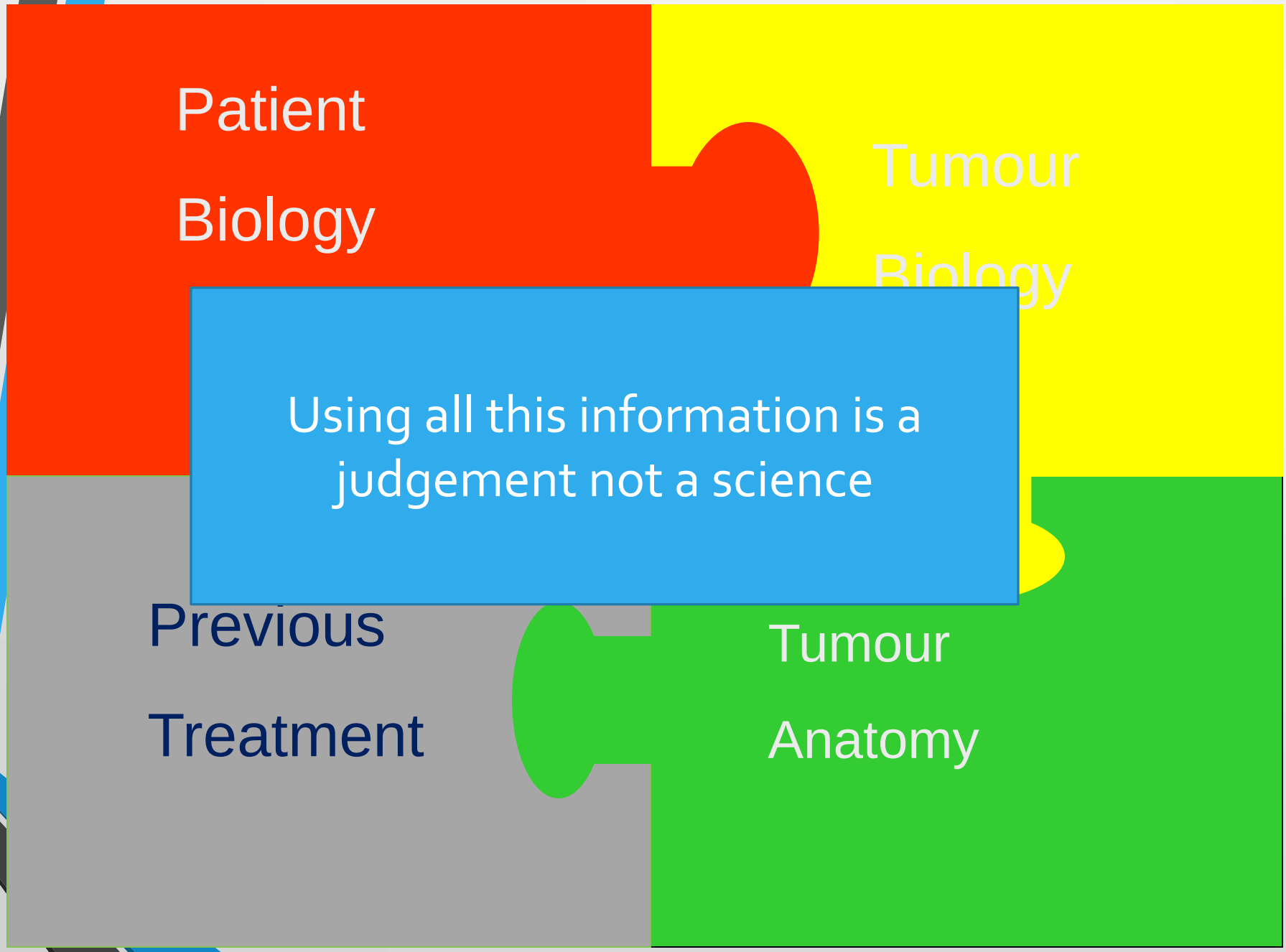
Drug resistance

“Re-challenge”

Site(s)

Extent/ size

Pattern


Patient
Biology
Tumour
Biology
Using all this information is a judgement not a science
Previous
Treatment
Tumour
Anatomy

Hormone Therapy – guiding principles…

- Around 70% of all breast cancers are hormone receptor positive (ER+)
- The preferred option for hormone receptor-positive disease, unless there is disease needing a fast response
- Slower response
- Fewer side effects. Generally well tolerated
- If the cancer responds to one hormone drug it will often respond to another

Hormone therapies

Anti-oestrogens-
- Tamoxifen
- Faslodex

Aromatase Inhibitors-
- Anastrozole (Arimidex)
- Letrozole (Femara)
- Exemestane (Aromasin)

LHRH antagonists-
- Goserelin (Zoladex)

Progestogens-
- megestrol acetate

Chemotherapy – guiding principles

- Triple negative breast cancer
- After progression on hormones
- If a rapid response needed
- Side effects… response rate versus toxicity
- not used continuously
- Single/ combination

Chemotherapy

- **Anthracyclines**

  Damage and disrupt the manufacture of DNA eg Doxorubicin, Epirubicin

- **Microtubule Inhibitors**

  Interfere with cell division eg Taxanes, eribulin, vinorelbine

- **Antimetabolites**

  Bind to DNA eg 5FU, capecitabine, MTX

- **Alkylating Agents -** Damage DNA by adding a chemical to it eg carboplatin, cyclophosphamide

Sequencing chemotherapy

- 'In the absence of medical contraindications or patient concerns, anthracycline- or taxane-based regimens, preferably as a single agent, would usually be considered as first-line for HER-2-negative MBC'
- 'Other treatments are available and effective, such as capecitabine and vinorelbine particularly if avoiding alopecia is a priority for the patient.'
- 'Duration of each regimen and the number of regimens should be tailored to each individual patient.'

Targetted Therapies

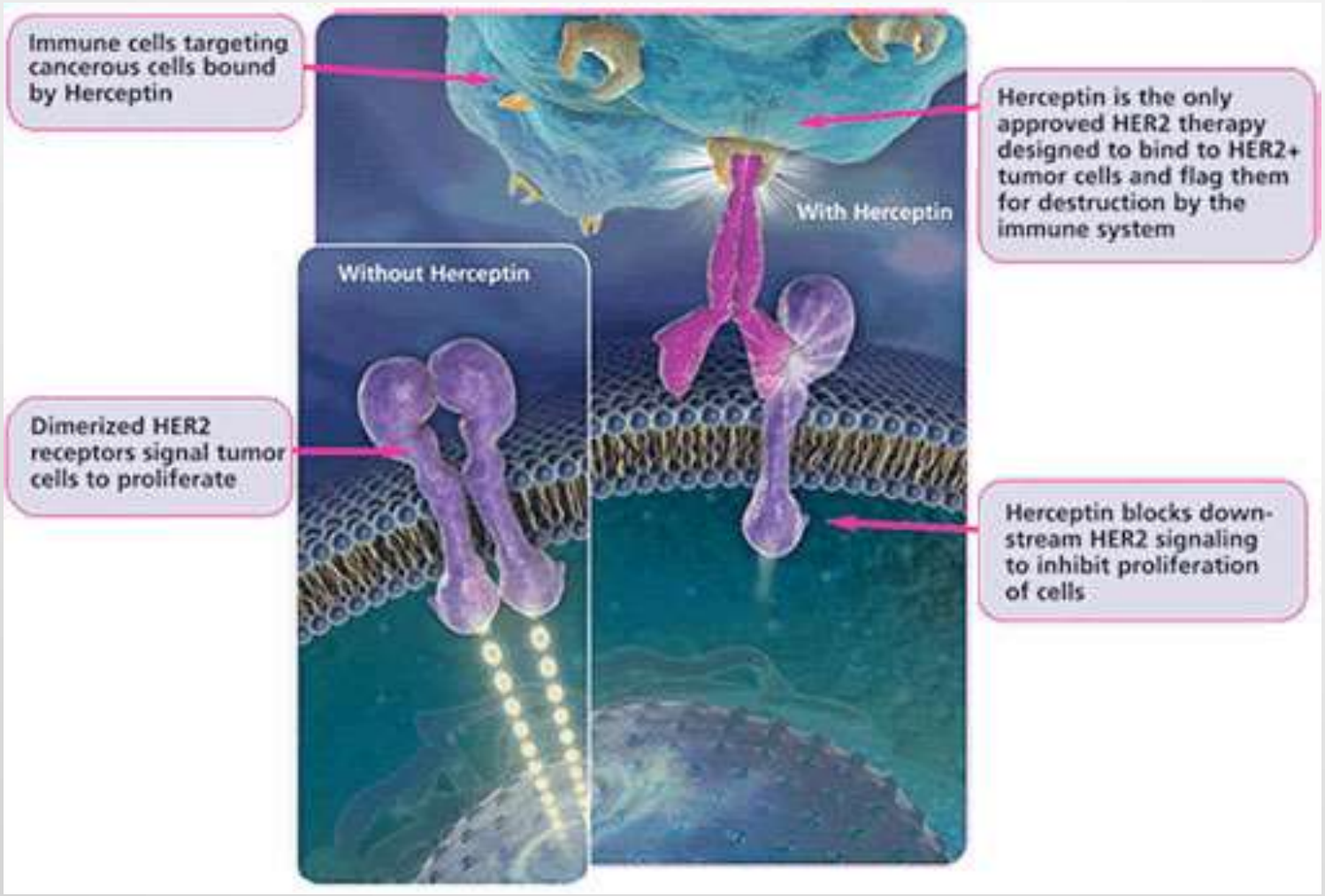
- **Drugs which block the growth and spread of cancer by interfering with specific molecules involved in tumour growth and progression**

- **Include drugs which interfere with:**
- cell growth signalling
- tumour blood vessel development
- trigger specific cancer cell death
- stimulate the immune system
- deliver toxic drugs selectively to cancer cells.

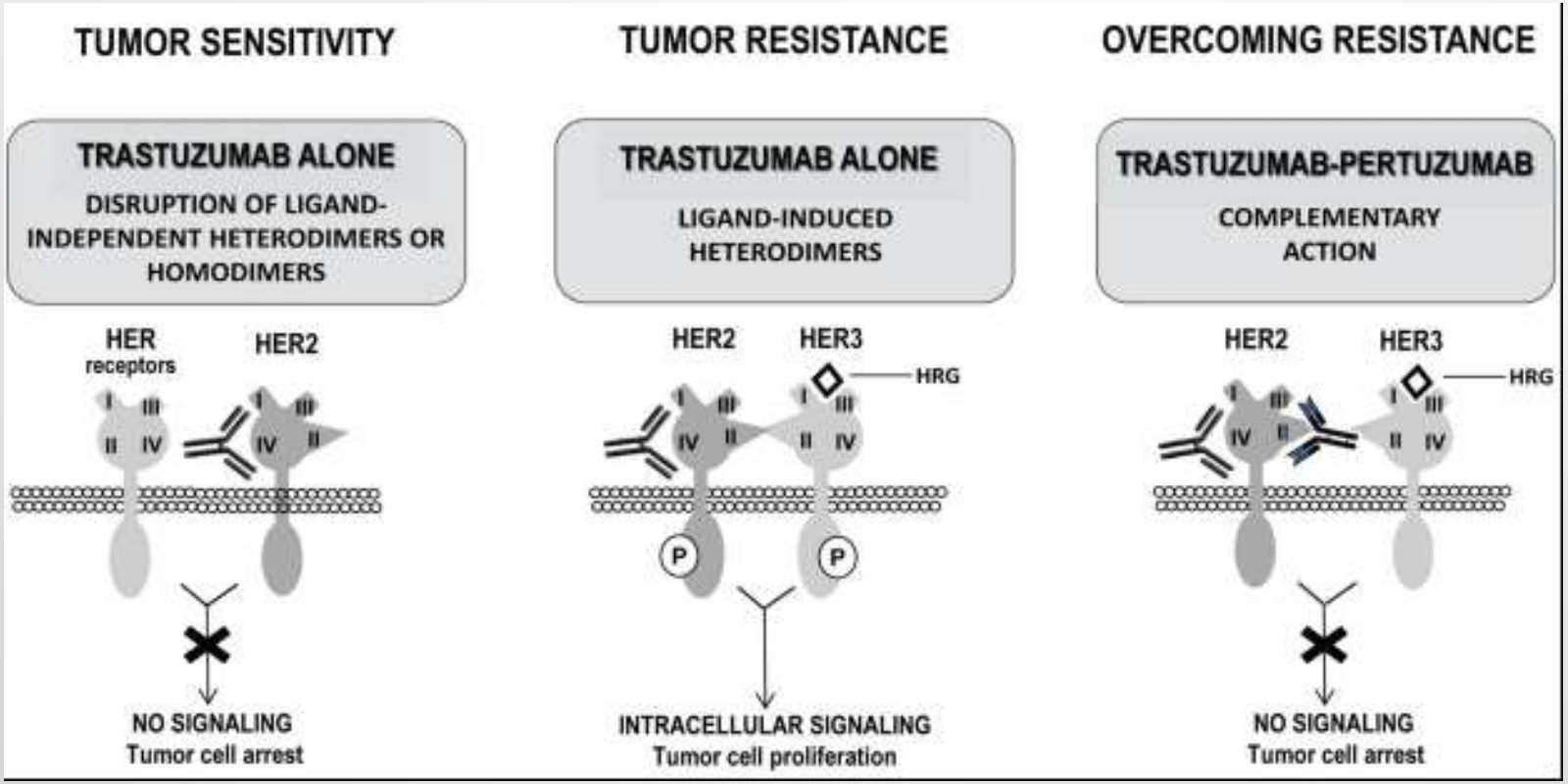
Targetted therapies

- Most commonly used are anti-HER2 agents – herceptin, perjeta, kadcyla
- Other targets include MTOR eg Afinitor.
- Generally well tolerated, but can have side-effects

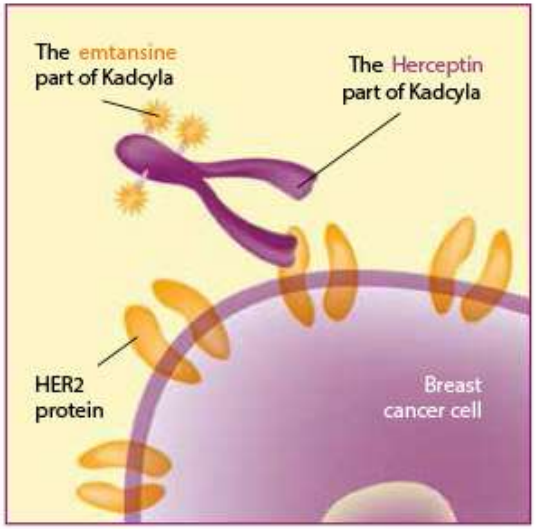
Herceptin


Immune cells targeting cancerous cells bound by Herceptin
Herceptin is the only approved HER2 therapy designed to bind to HER2+ tumor cells and flag them for destruction by the immune system
With Herceptin
Without Herceptin
Dimerized HER2 receptors signal tumor cells to proliferate
Herceptin blocks down-stream HER2 signaling to inhibit proliferation of cells

Pertuzumab


TUMOR SENSITIVITY
TRASTUZUMAB ALONE
DISRUPTION OF LIGAND-INDEPENDENT HETERODIMERS OR HOMODIMERS
HER receptors
HER2
I
II
III
IV
NO SIGNALING
Tumor cell arrest
TUMOR RESISTANCE
TRASTUZUMAB ALONE
LIGAND-INDUCED HETERODIMERS
HER2
HER3
HRG
P
INTRACELLULAR SIGNALING
Tumor cell proliferation
OVERCOMING RESISTANCE
TRASTUZUMAB-PERTUZUMAB
COMPLEMENTARY ACTION
HER2
HER3
HRG
NO SIGNALING
Tumor cell arrest

Trastuzumab emtamsine (kadcyla/TDM-1)



Step 1.

During treatment, Kadcyla attaches to HER2 proteins on HER2-positive breast cancer cells. This tells the cancer cells to stop growing and signals the body's immune system to destroy these cells.

Step 2.

Next, Kadcyla goes inside the cancer cells.

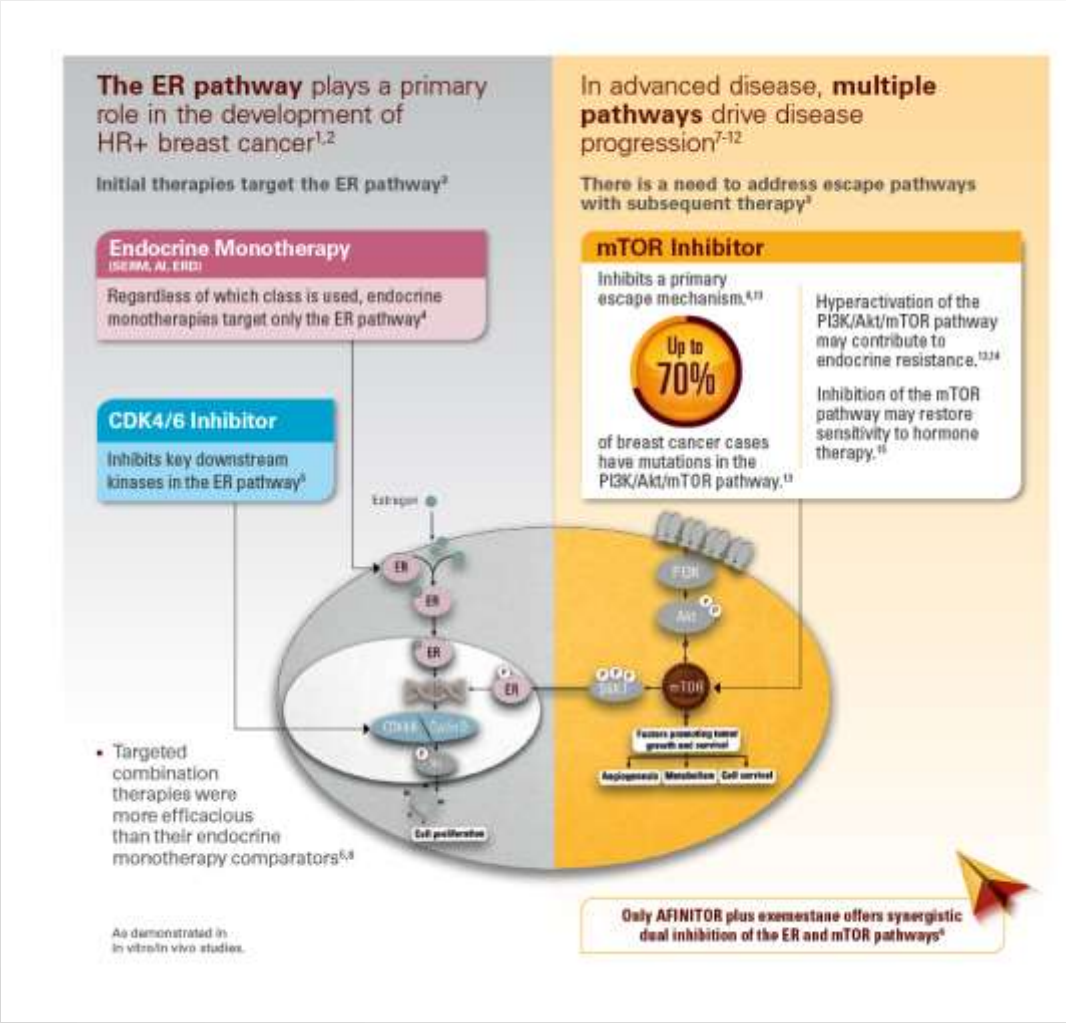
Step 3.

Inside the cancer cell the Herceptin part breaks up, releasing the chemotherapy emtansine.

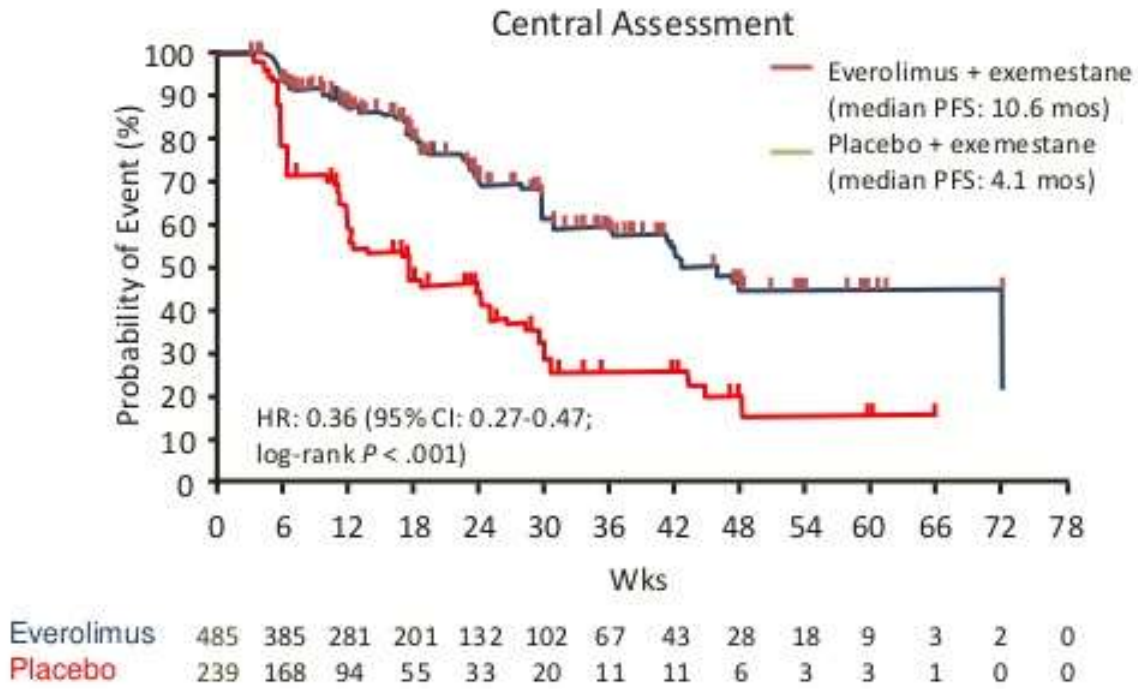
Step 4.

The chemotherapy emtansine attaches to structures inside the cancer cell that help it grow. This stops the cancer cell's ability to grow and divide, eventually leading to cancer cell death.

Overcoming Hormone Resistance

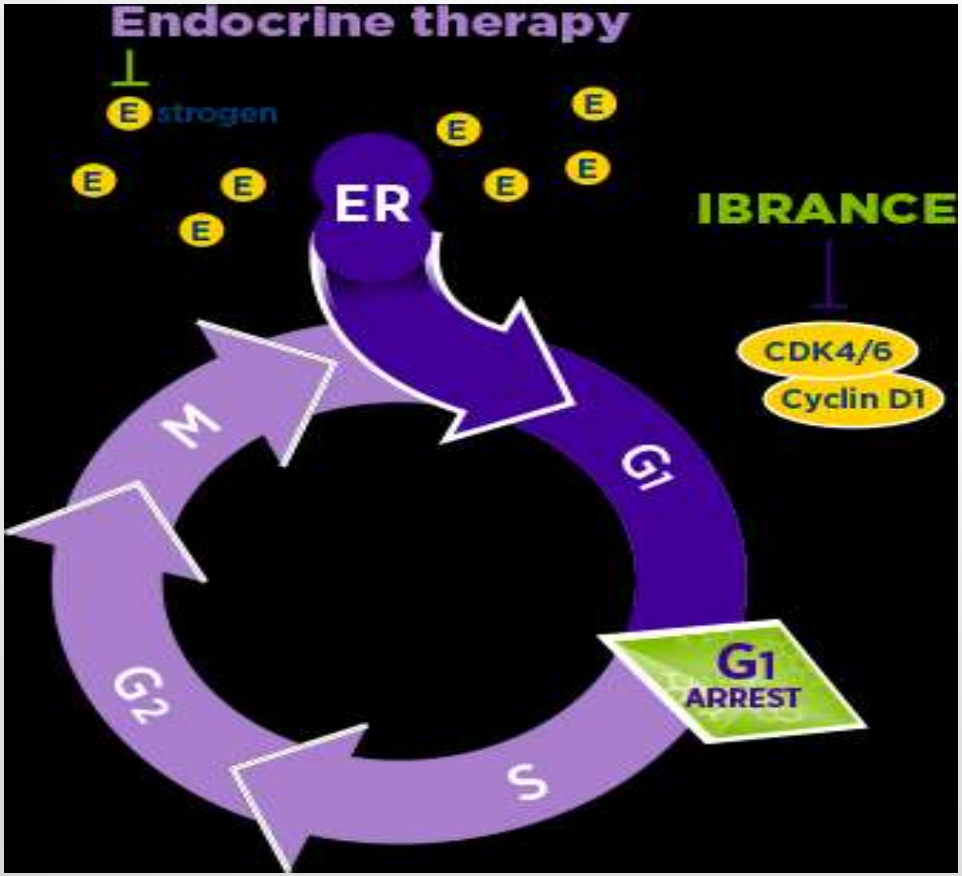


BOLERO-2: Everolimus + Exemestane Improves PFS in HR+ MBC

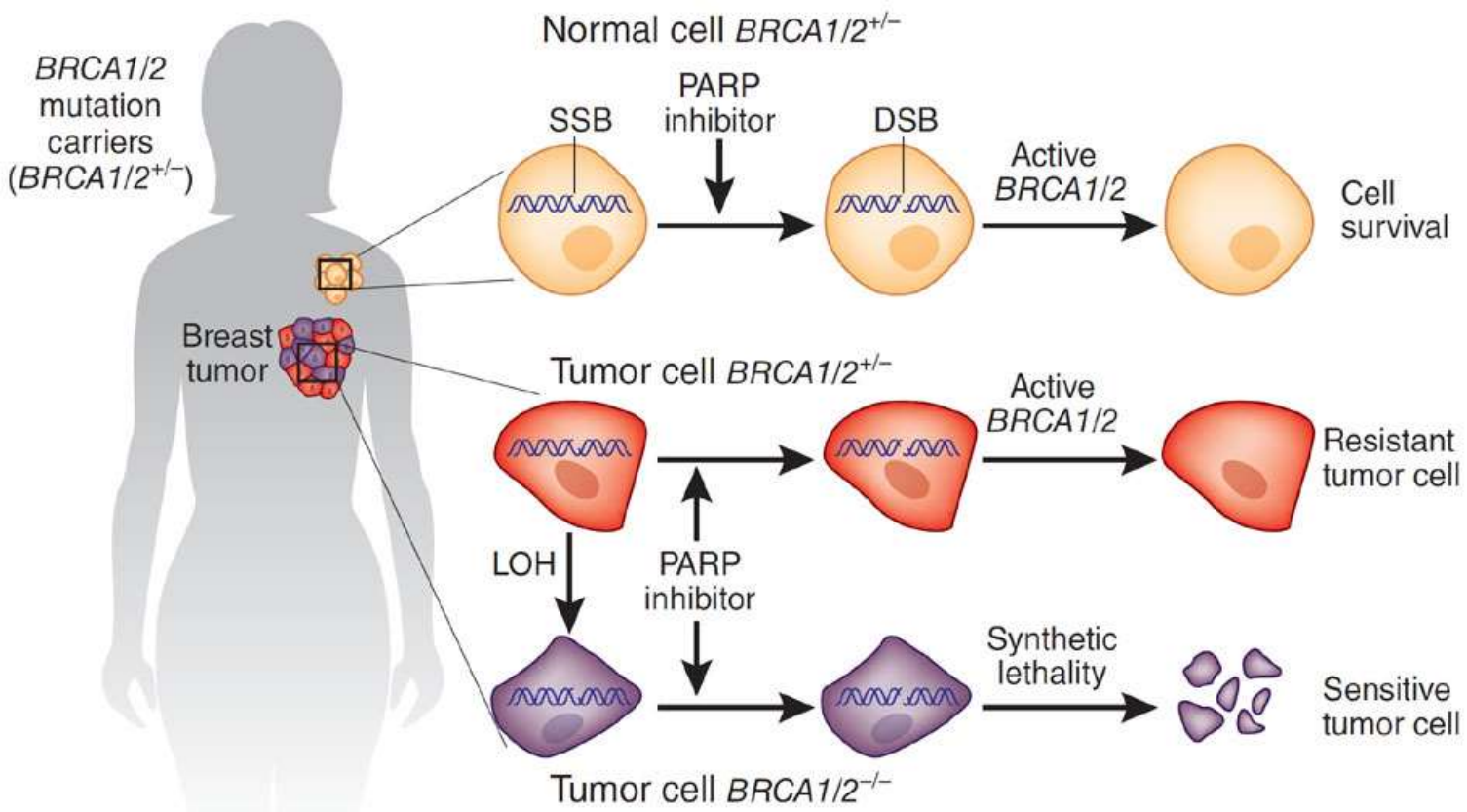


Baselga J, et al. N Engl J Med. 2012;366:520-529.

Palbociclib

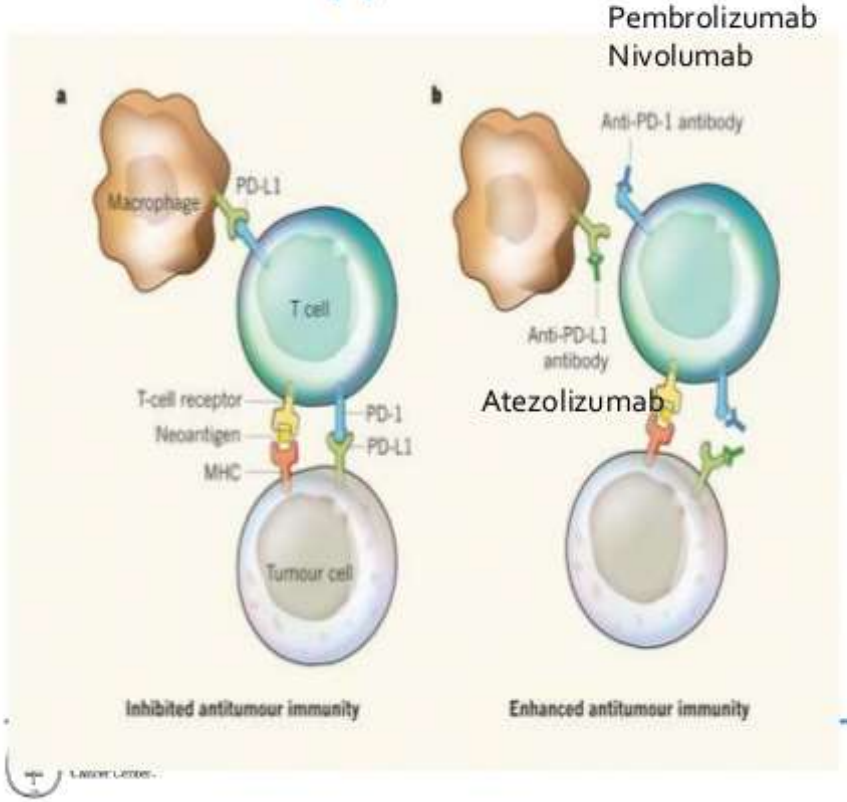


Triple Negative Cancers



Triple Negative Cancers

Immunotherapy rationale



- Normal part of immune regulation
- Antibodies that block the PD-1 pathway can reactivate T-cell activity and proliferation
- Leading to enhanced antitumour immunity

Wolchok & Chan
Nature 2014

Bone metastases

Skeletal problems impact on daily life

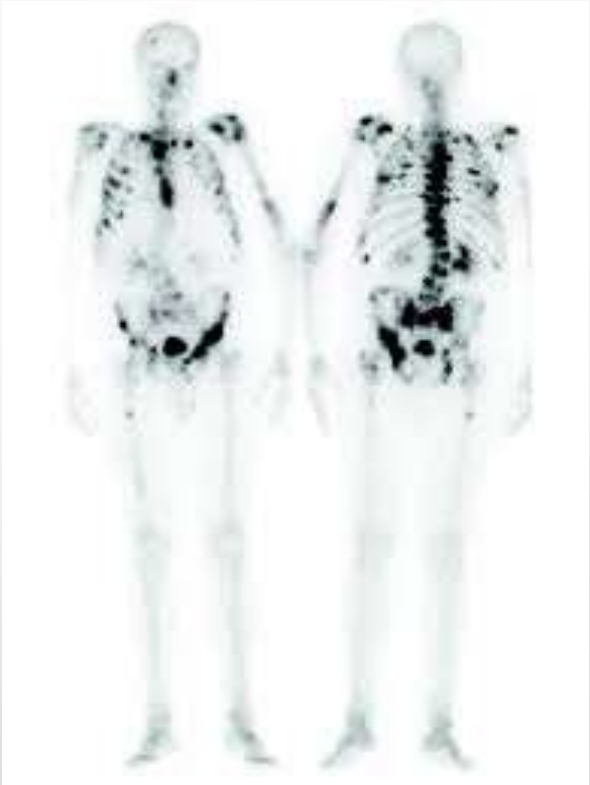
Pain

Risk of Fracture

Spinal Cord Compression

Hypercalcaemia

Report symptoms to hotline



Anti-resorptive agents

- Reduce bony destruction
- Pain relief
- Reduce risk of skeletal events
- Prevent hypercalcaemia

- Pain flare
- Hypocalcaemia
- Teeth/jaw problems

Radiotherapy

- A localised treatment
- Palliative treatment of bony secondaries
- Control locally advanced disease
- Short course

Patient support

breast cancer care
Pink Ribbon 25

What does the future hold?

- Tailored treatment
- Treatments to overcome hormone resistance eg CDK5/6 - palbociclib
- Better anti-HER2 therapies
- Immunotherapies eg PDL-1 directed therapies
- Improvements in supportive care

Summary

- We need to tailor treatment to the patient as well as their disease
- There are a wide range of treatments, but responses and outcomes vary
- Information and psychological support is available
- We want to help the patients live with their disease and with their treatment!


Thank
You
Merci
Gracias
Xièxie
Mèsi
Grazie
Takk
aDank
Chokrane
Oziakuju
Spacibo
Danke
Arigato
Hvala
KamSahHamnida
TerimaKasih
ThintKu
Tak
GraliasAgo
Gracies