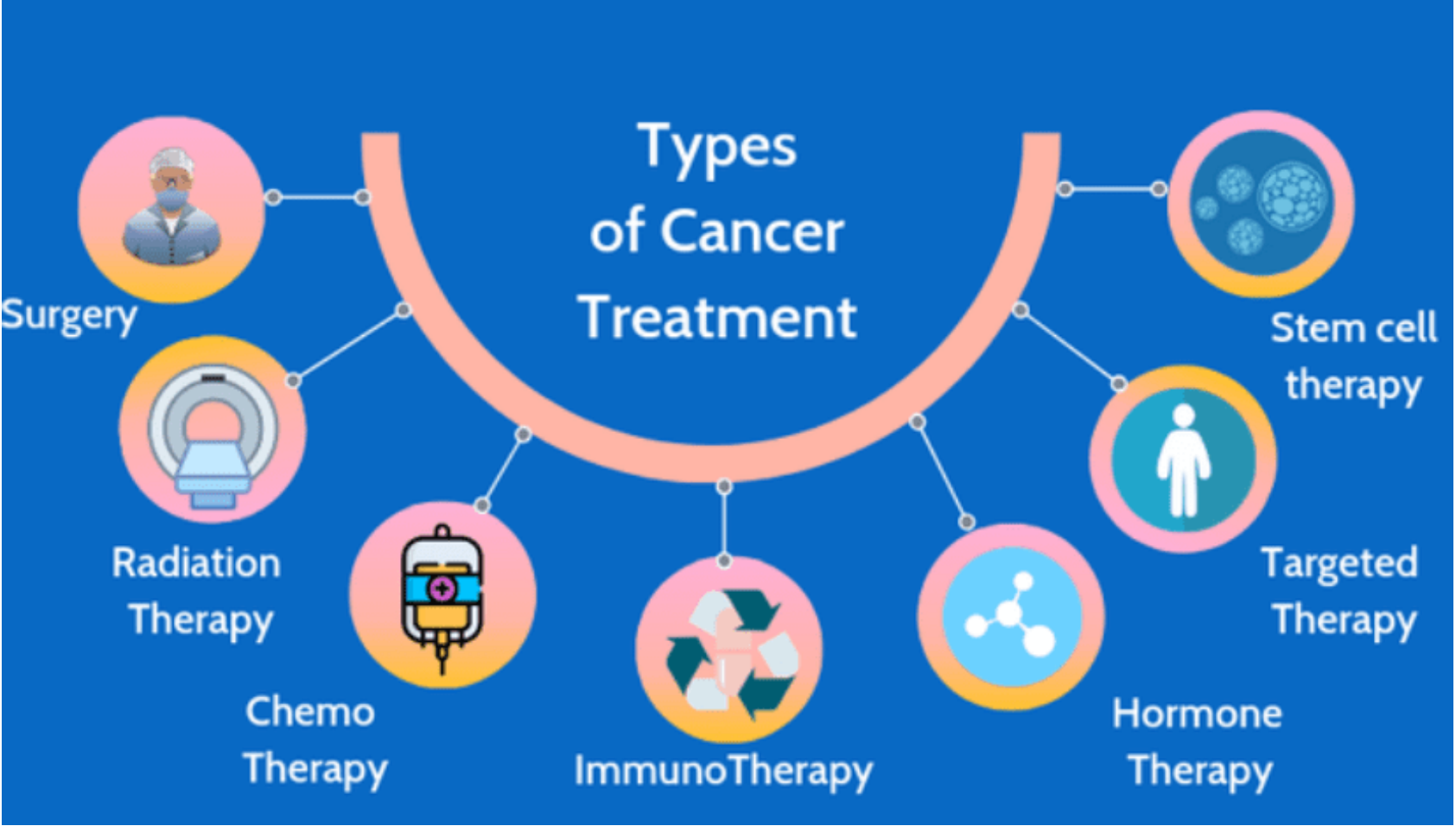


Targeted ofwel doelgerichte therapie en immunotherapie in de oncologie



Disclosure belangen spreker

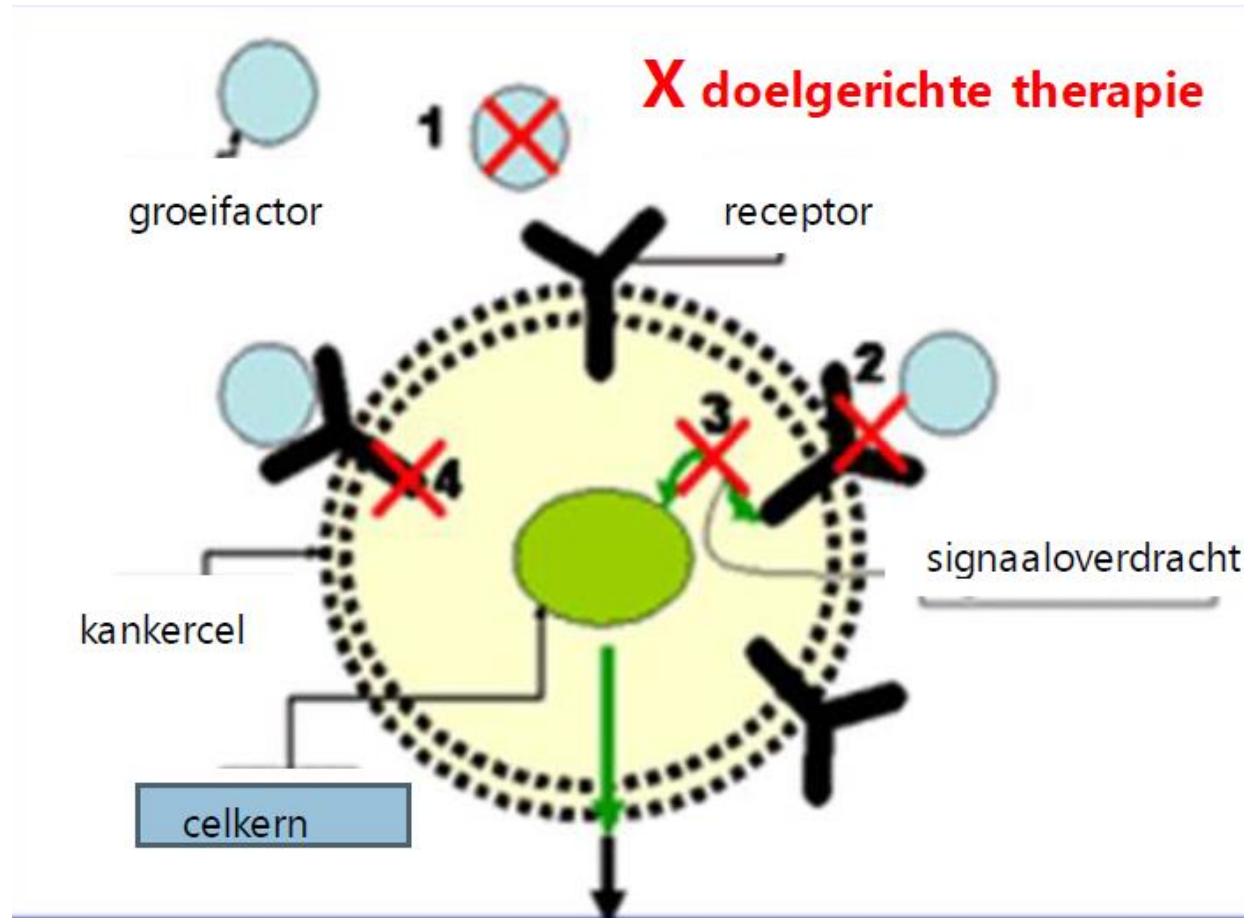
(potentiële) belangenverstrengeling	Geen
Voor bijeenkomst mogelijk relevante relaties met bedrijven	
<ul style="list-style-type: none">• Sponsoring of onderzoeksgeld• Honorarium of andere (financiële) vergoeding• Aandeelhouder• Andere relatie, namelijk ...	<ul style="list-style-type: none">• geen•••

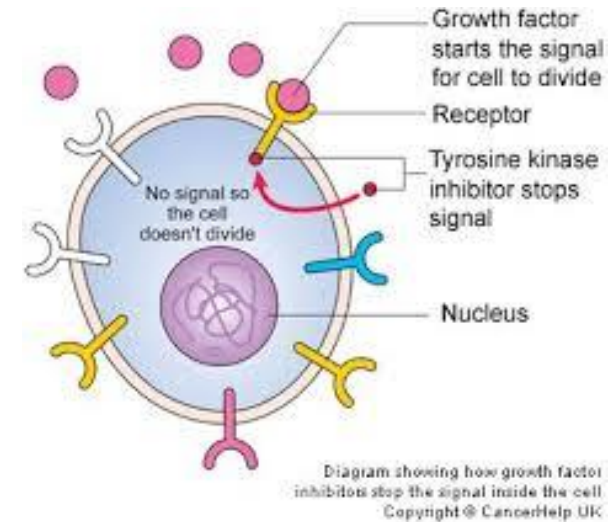
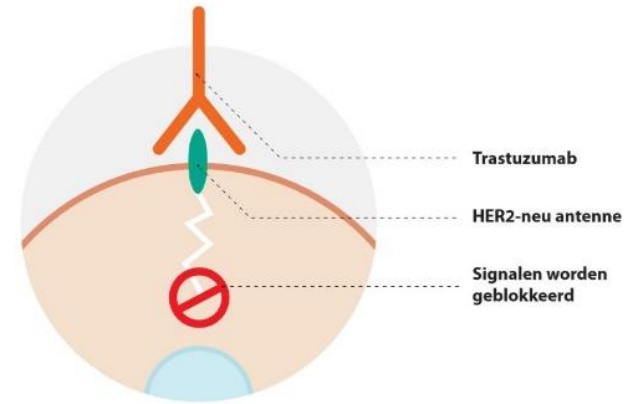
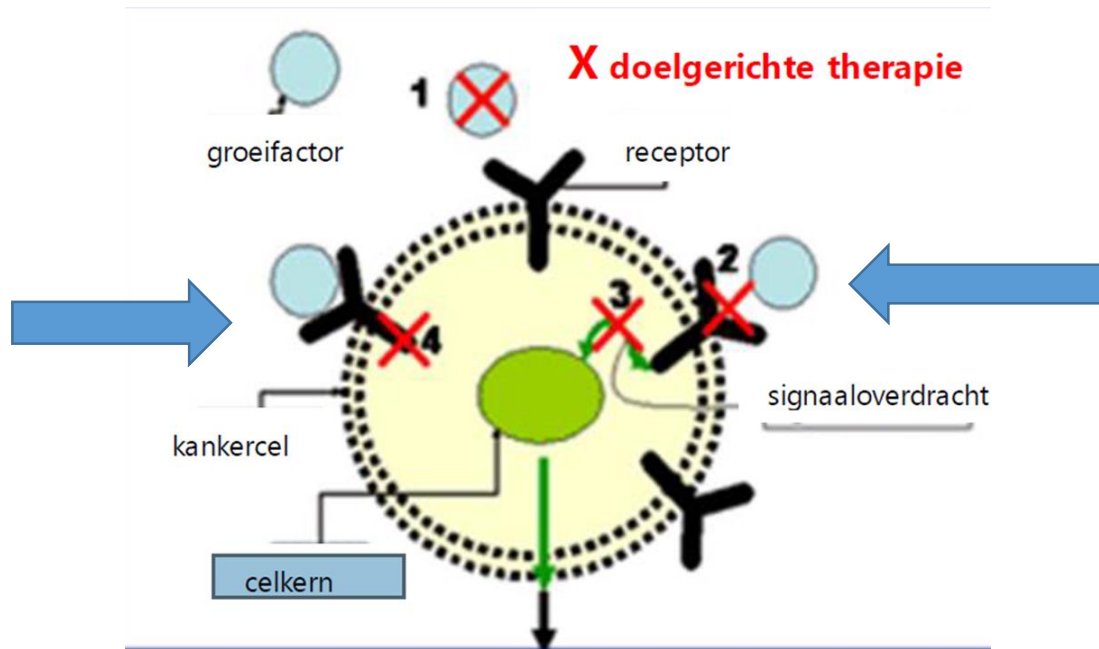


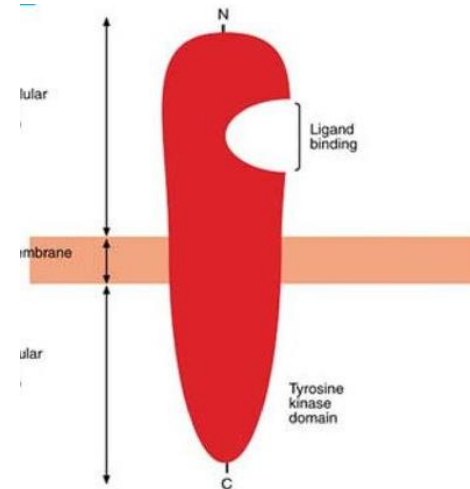
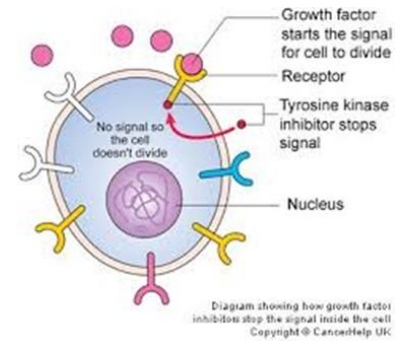
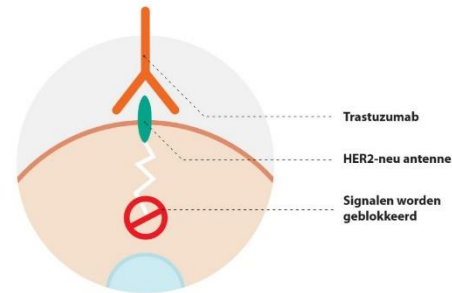
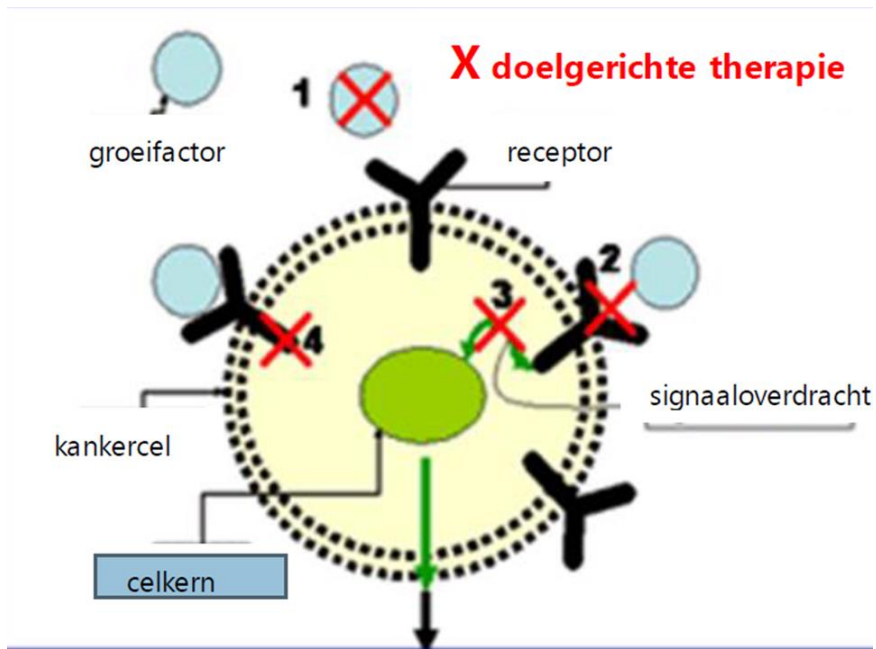
Chemotherapie; werkt maar veel bijwerkingen



Doelgerichte therapie

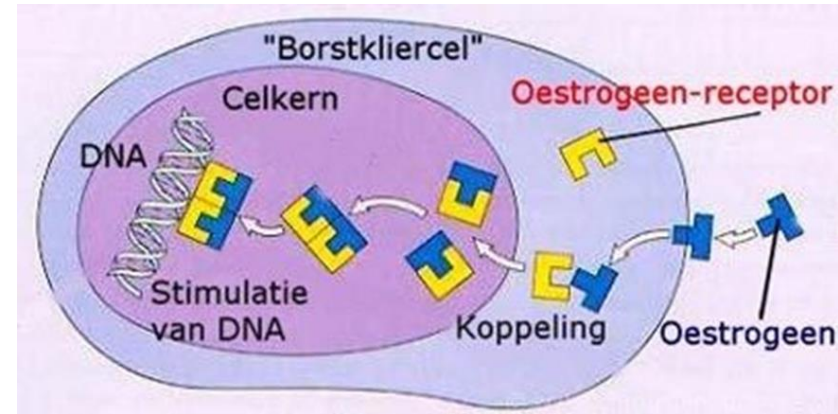
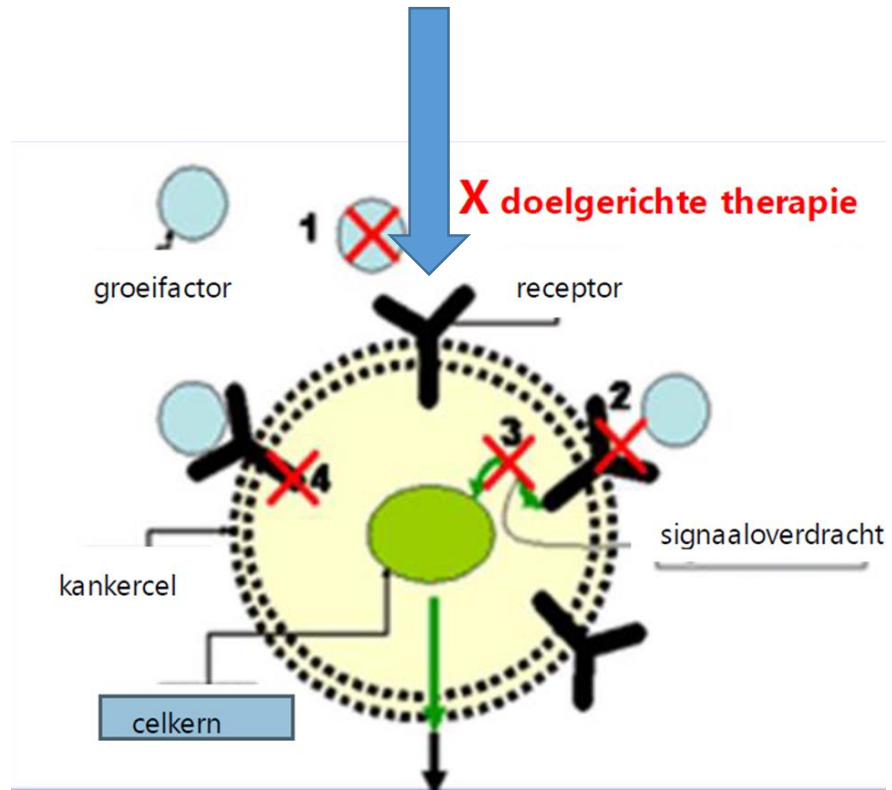


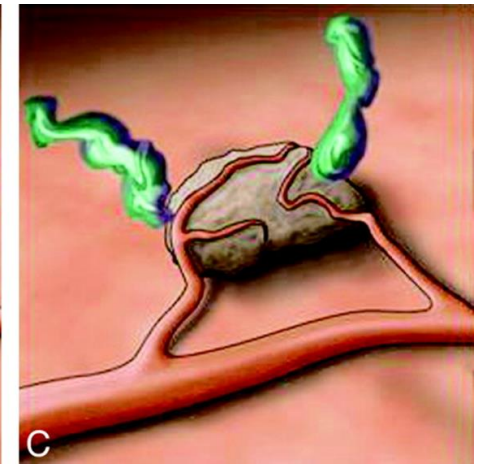
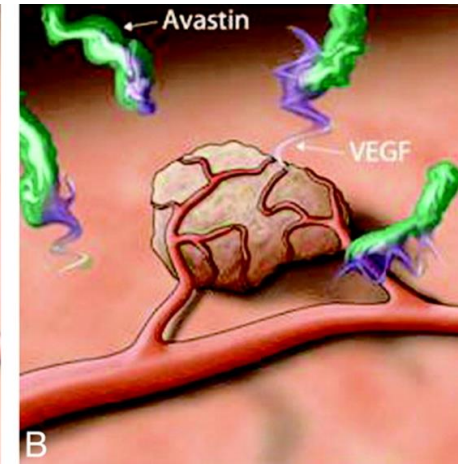
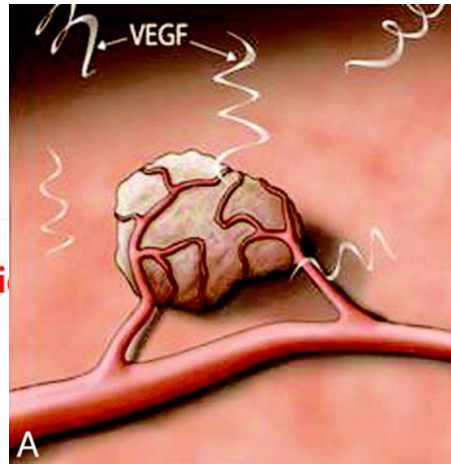
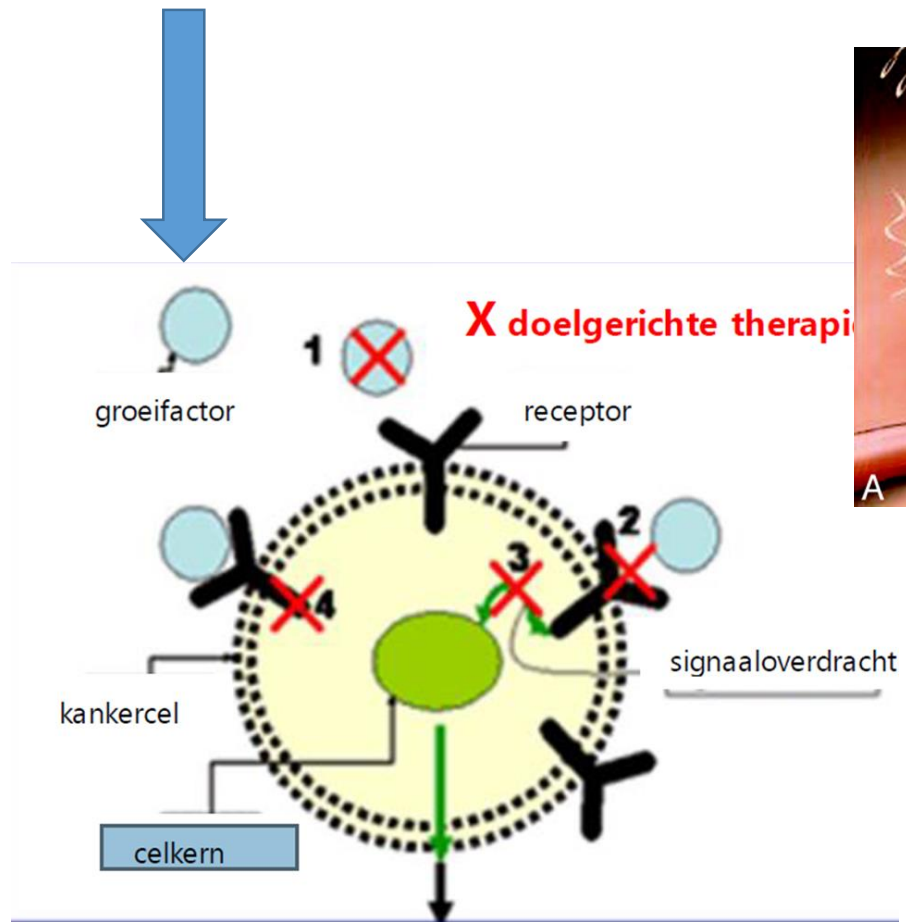




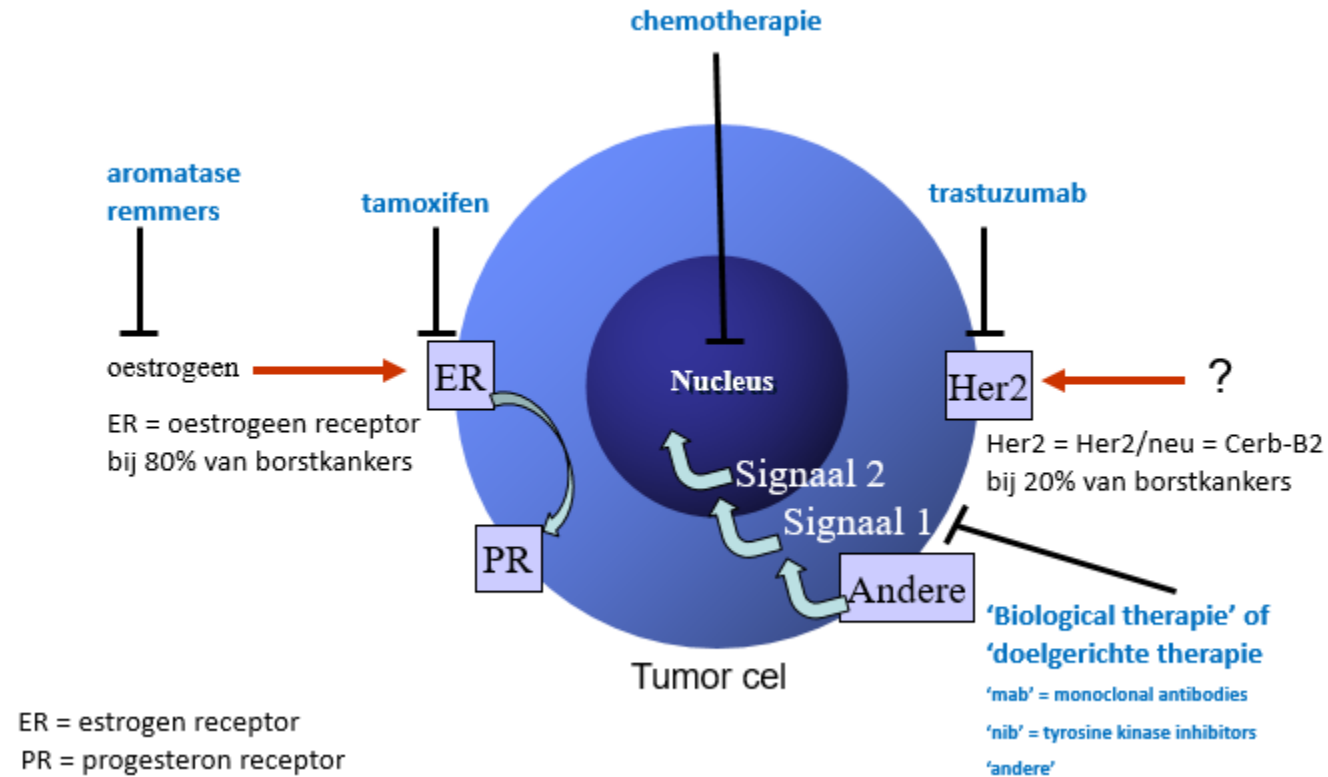
1. Buiten de cel:
Bindingsplaats MAB
(**M**ono**c**lonal **A**nti **B**odies)
= grote moleculen

2. In de cel:
tyrosinekinase domein
IB (tyrosine kinase Inhi**B**itor)
= kleine moleculen

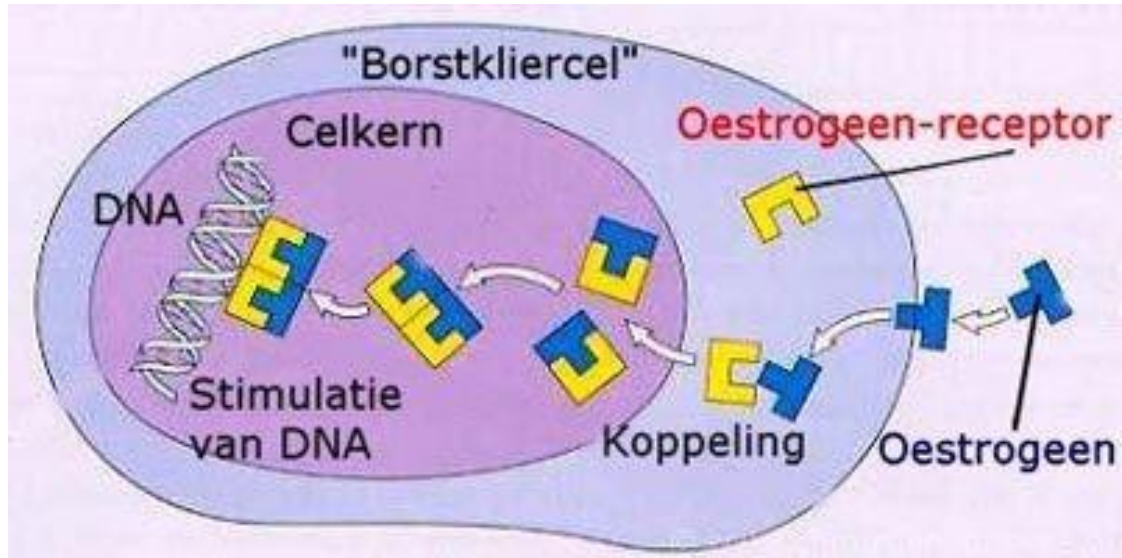




Targeted therapie mammacarcinoom

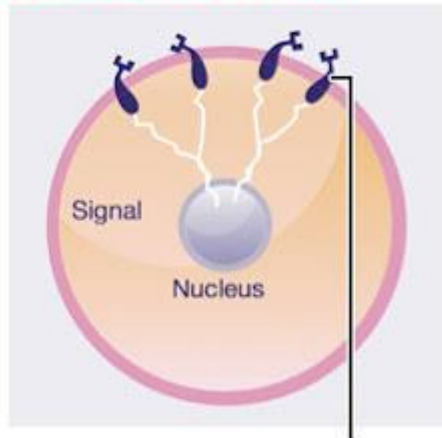


tamoxifen



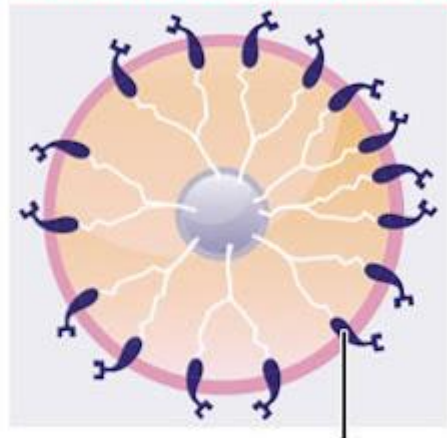
herceptin

Normal breast cancer cell



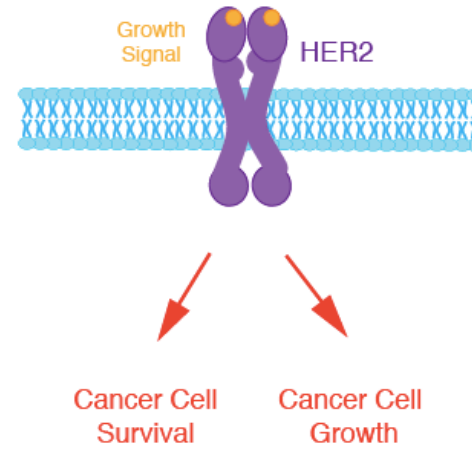
Normal amount of HER2 receptors send signals telling cells to grow and divide.¹

Abnormal HER2+ breast cancer cell

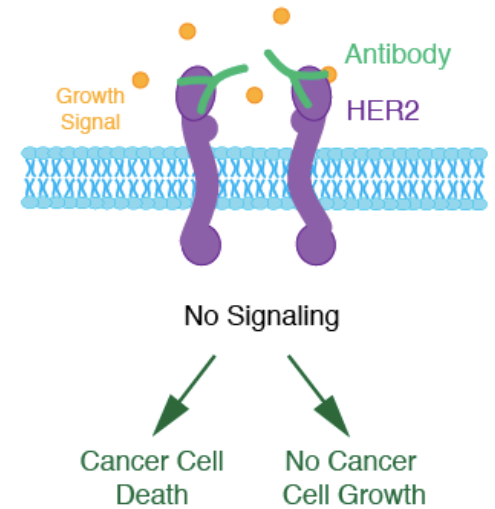


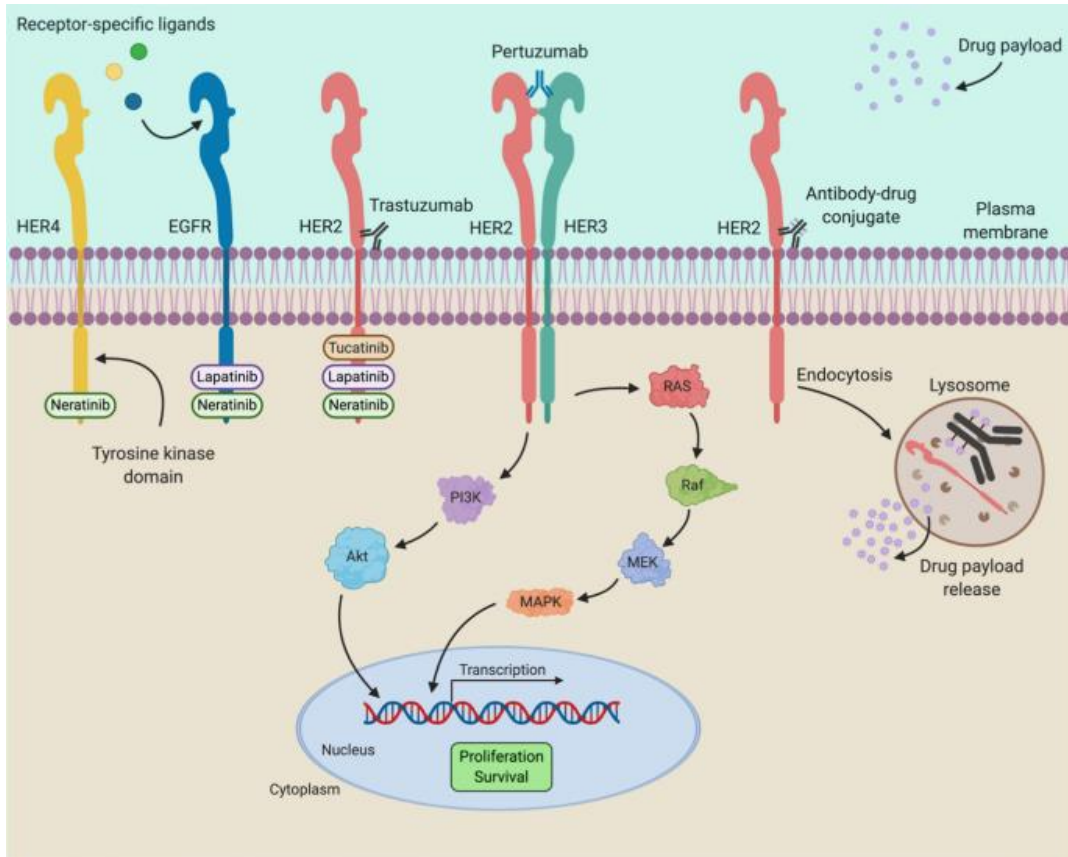
Too many HER2 receptors send more signals, causing cells to grow too quickly.¹

Without Herceptin



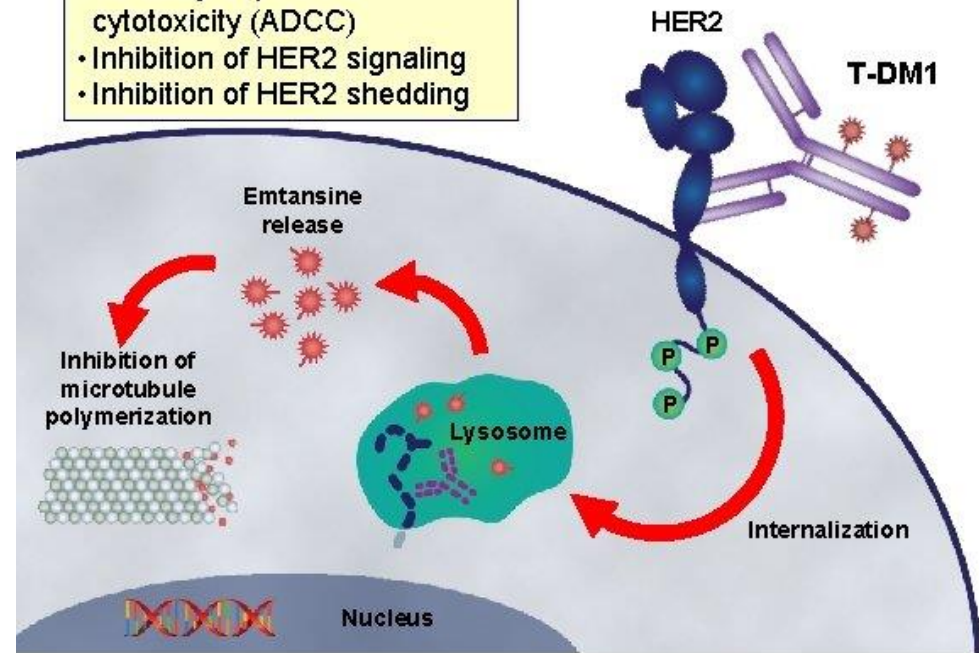
With Herceptin





Trastuzumab Emtansine (T-DM1): Mechanism of Action

- Trastuzumab-specific MOA**
- Antibody-dependent cellular cytotoxicity (ADCC)
 - Inhibition of HER2 signaling
 - Inhibition of HER2 shedding



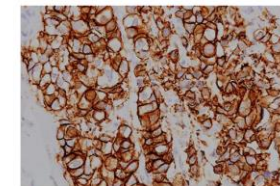
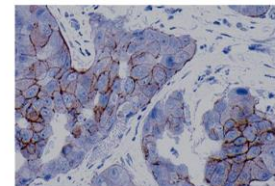
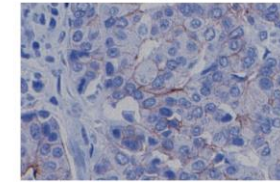
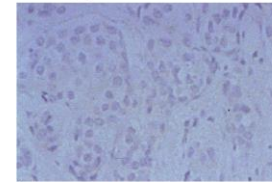
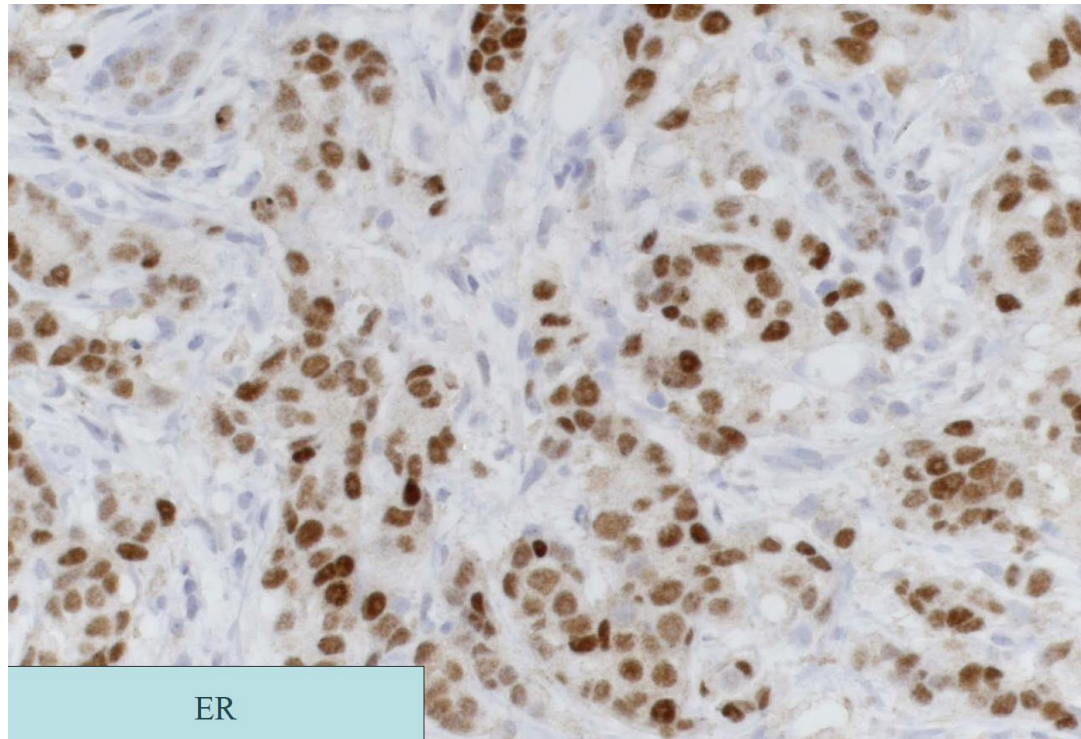
Adapted from LoRusso PM, et al. *Clin Cancer Res* 2011.

Targeted therapie

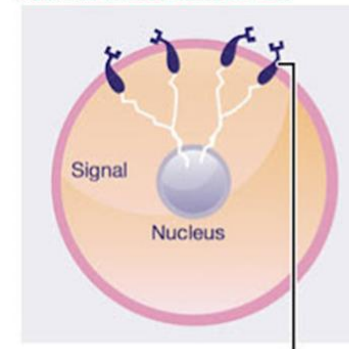
- Minder bijwerkingen dan chemotherapie
- Zo wel ingezet bij gemetastaseerde ziekte als adjuvant
- Biomarker van belang, maar niet altijd

Biomarkers bij mammacarcinoom

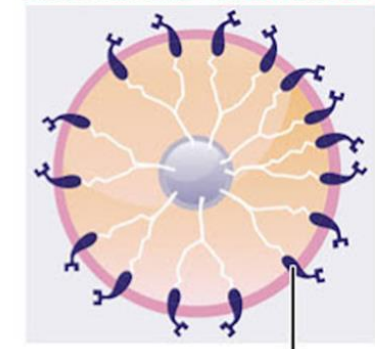
IHC scoring: semi-quantitative interpretation of HER2 expression



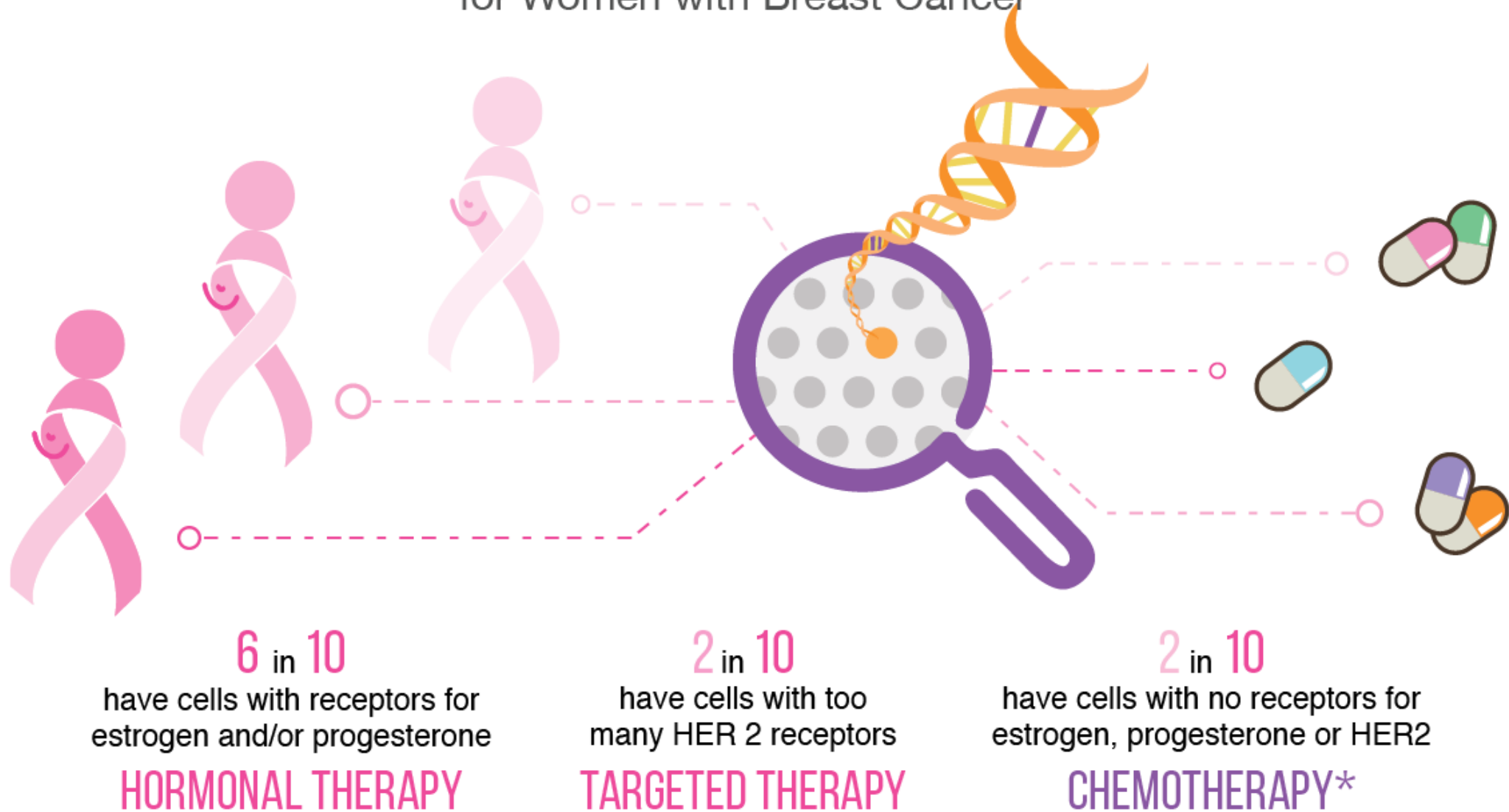
Normal breast cancer cell



Abnormal HER2+ breast cancer cell



Genomic Pattern Leads to Treatment Options and Strategy for Women with Breast Cancer



**chemotherapy is not a targeted treatment option*

DCIS or LCIS only? Yes No

Age at diagnosis
Age must be between 25 and 85

Post Menopausal? Yes No Unknown

ER status Positive Negative

HER2 status Positive Negative Unknown

Ki-67 status Positive Negative Unknown
Positive means more than 10%

Treatment Options

Hormone Therapy No 5 Years 10 Years
Hormone (endocrine) therapy
Available when ER-status is positive

Chemotherapy None 2nd gen 3rd gen

Trastuzumab No Yes
Available with chemotherapy when HER2 status is positive

Bisphosphonates No Yes
Available for post-menopausal women

Invasive tumour size (mm)
If there was more than one tumour, enter the size of the largest tumour. If neo-adjuvant therapy was undertaken, enter the size before neo-adjuvant therapy.

Tumour grade 1 2 3

Detected by Screening Symptoms Unknown

Positive nodes

Micrometastases only Yes No Unknown
Enabled when positive nodes is 1.

Results

Table Curves Chart Texts Icons

Select number of years since surgery you wish to consider:

5 10 15

This table shows the percentage of women who survive at least 10 years after surgery.

Treatment	Additional Benefit	Overall Survival %
Surgery only	-	54%
+ Hormone therapy	10% (5.8% – 13%)	64%
+ Chemotherapy	8.9% (6.5% – 11%)	72%
+ Trastuzumab	5.2% (3.7% – 7.3%)	78%
+ Bisphosphonates	2.3% (0.9% – 3.5%)	80%

If death from breast cancer were excluded, 91% would survive at least 10 years, and 9% would die of other causes. [i](#)

Results

Table

Curves

Chart

Texts

Icons

Select number of years since surgery you wish to consider:

5

10

15

This display shows the number of women who survive at least 10 years after surgery.

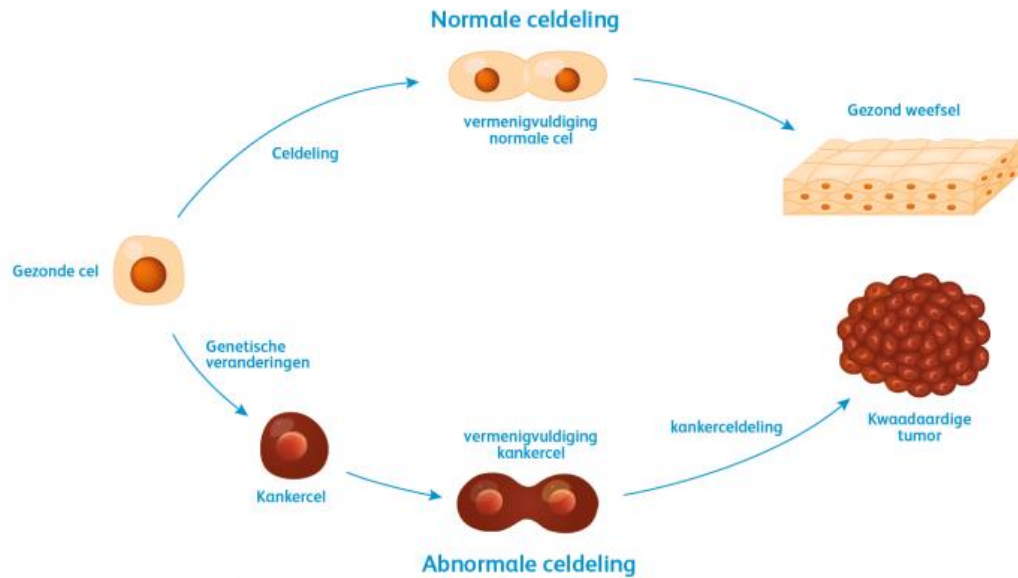


- 9 deaths due to other causes
- 2 extra survivors due to bisphosphonates
- 5 extra survivors due to trastuzumab
- 9 extra survivors due to chemotherapy
- 10 extra survivors due to hormone therapy
- 54 survivors with surgery alone

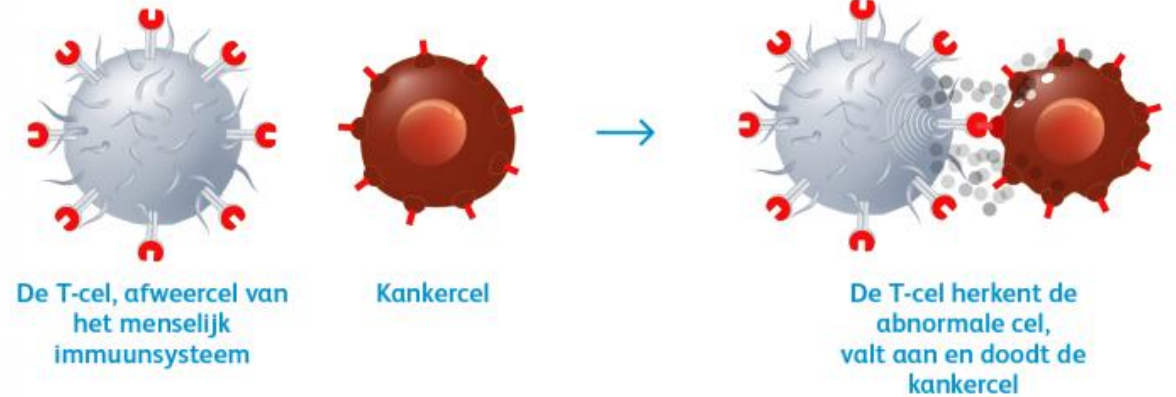
Press and hold for another decimal place to see how the numbers add up.

immunotherapie

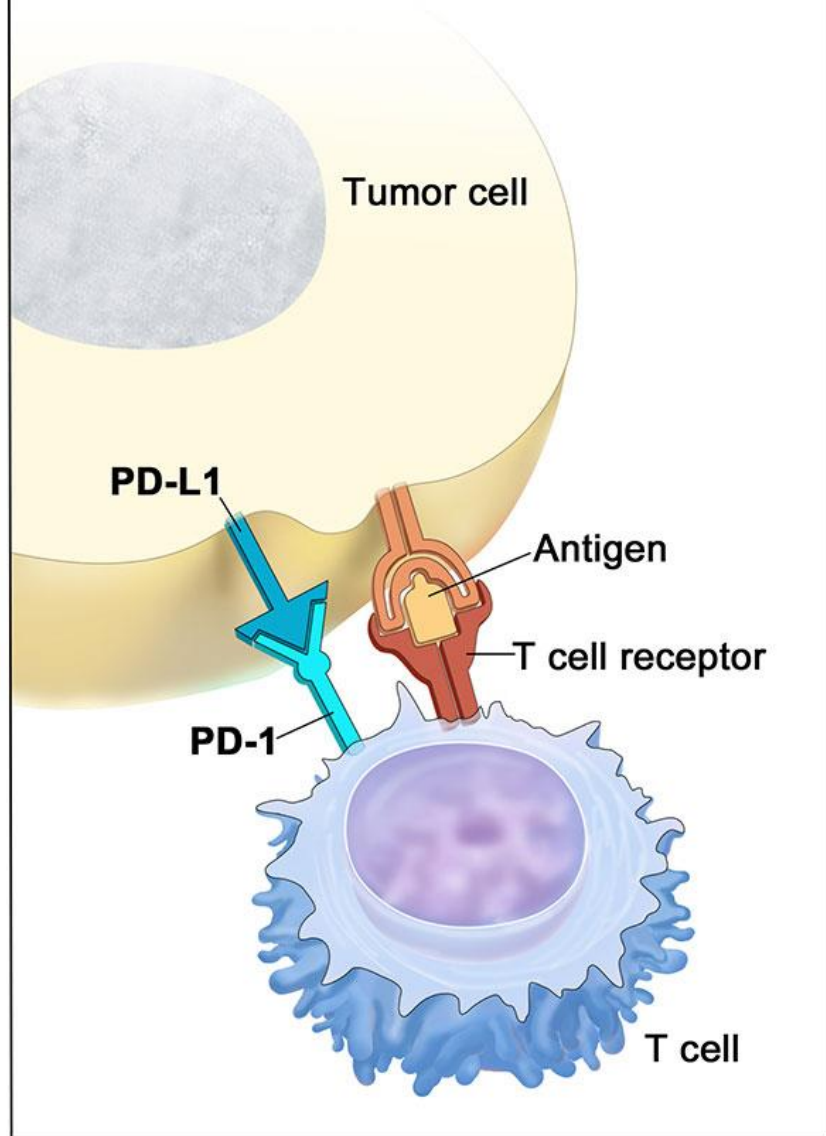
Ontwikkeling kankercellen



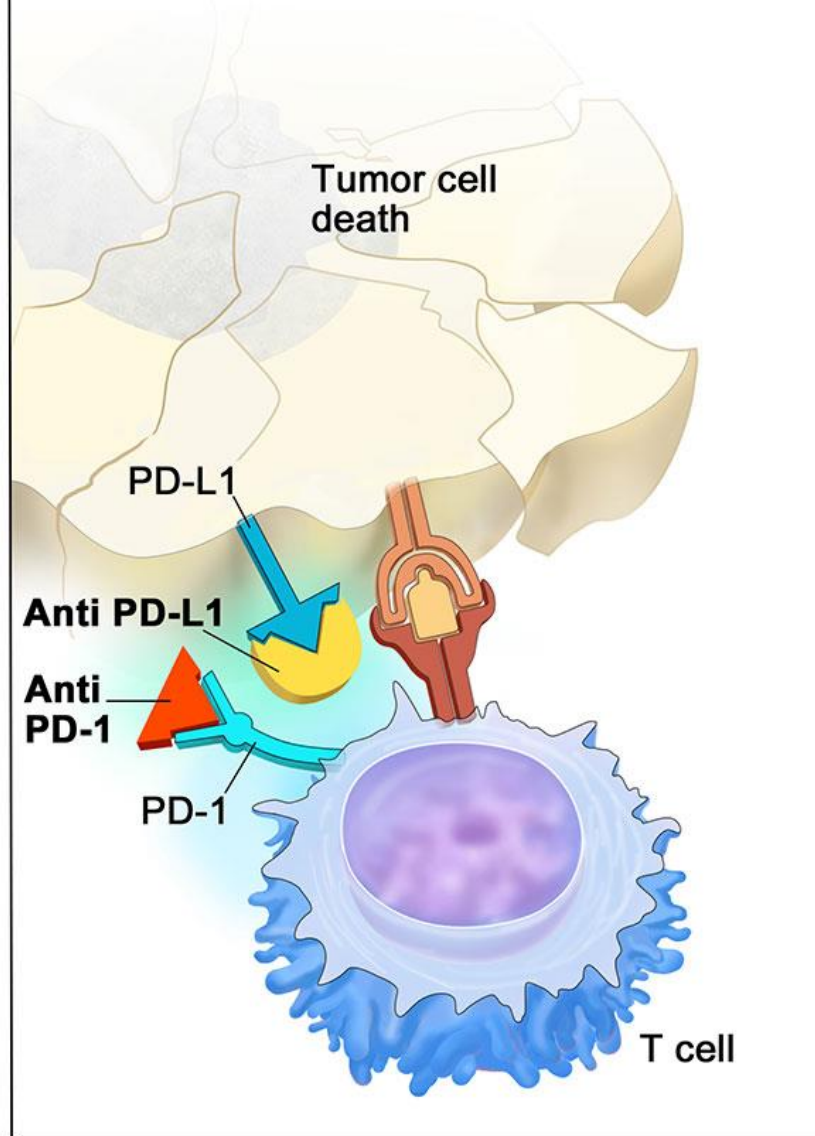
Immuuntherapie

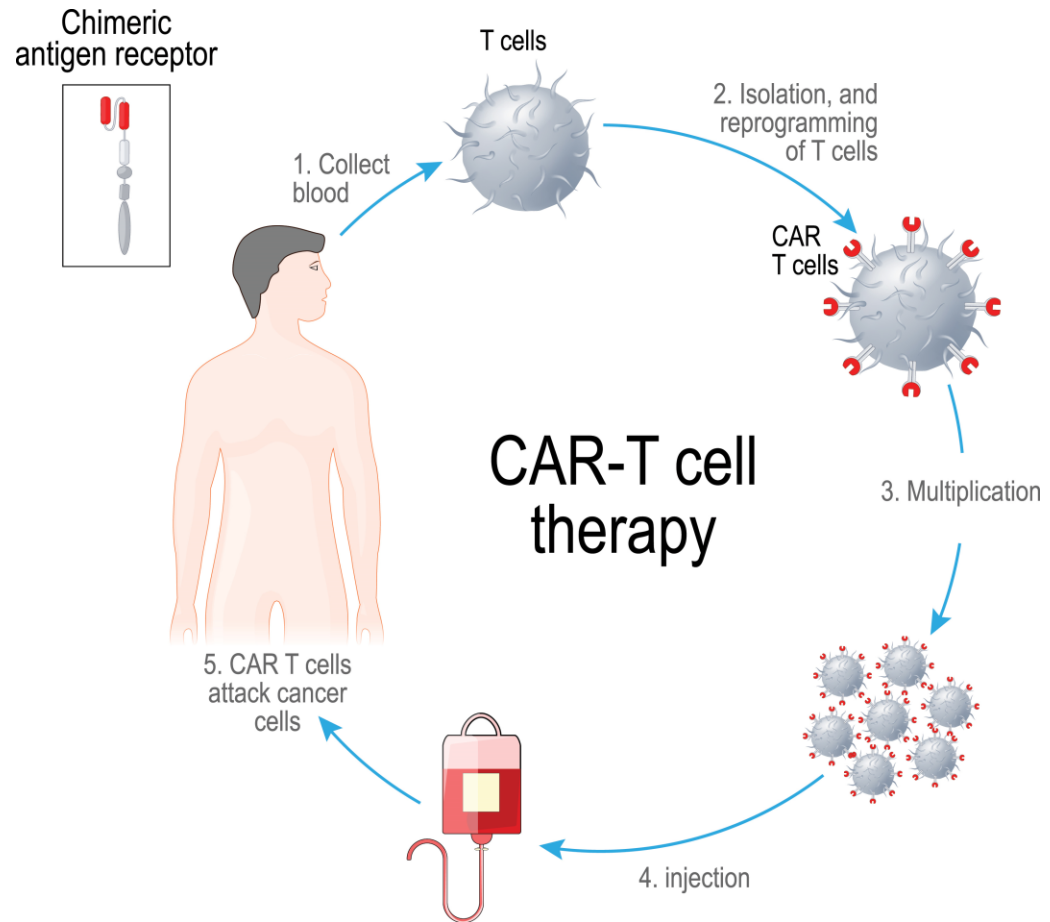


PD-L1/PD-1 binding inhibits T cell killing of tumor cell

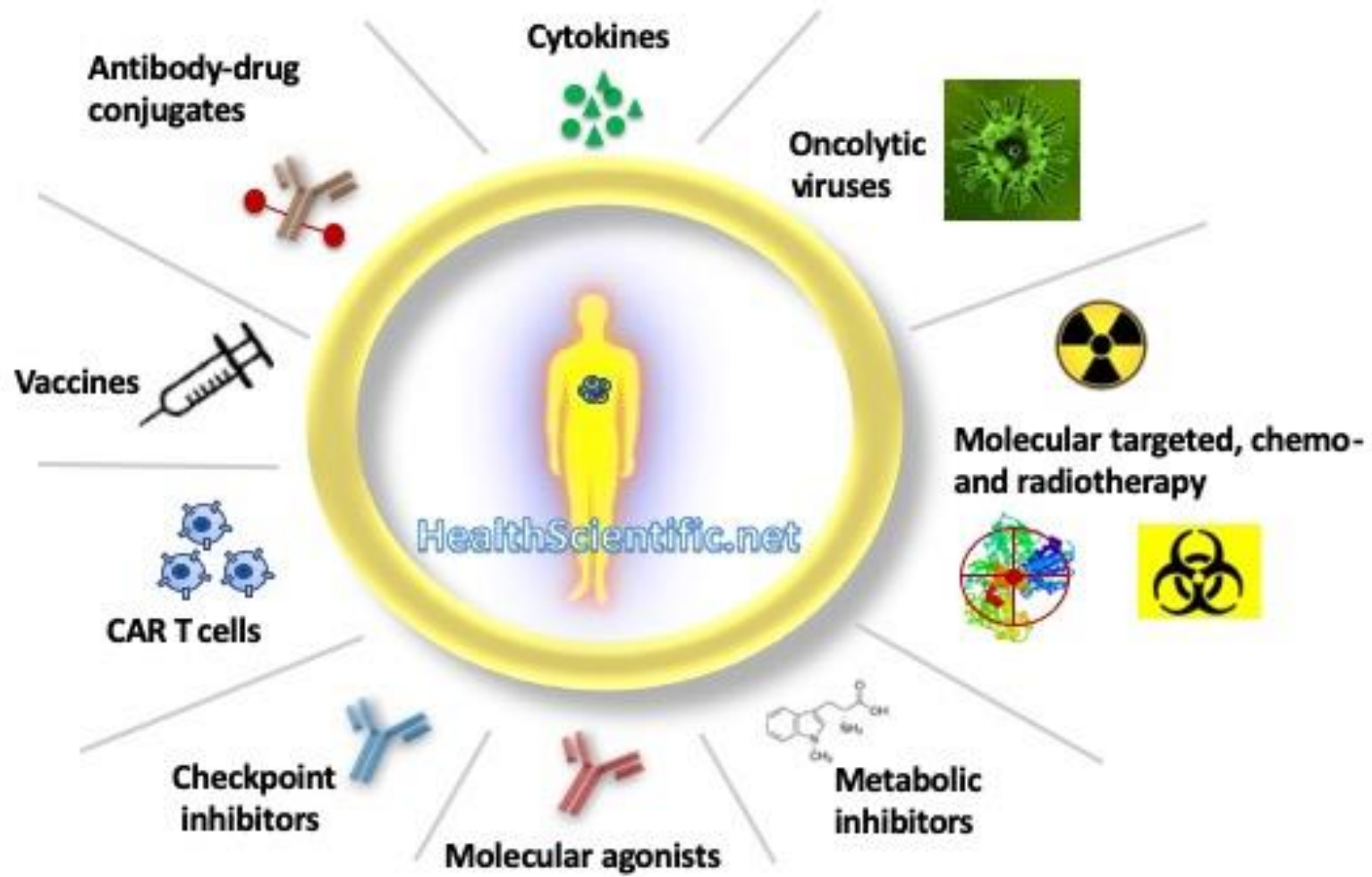


Blocking PD-L1 or PD-1 allows T cell killing of tumor cell

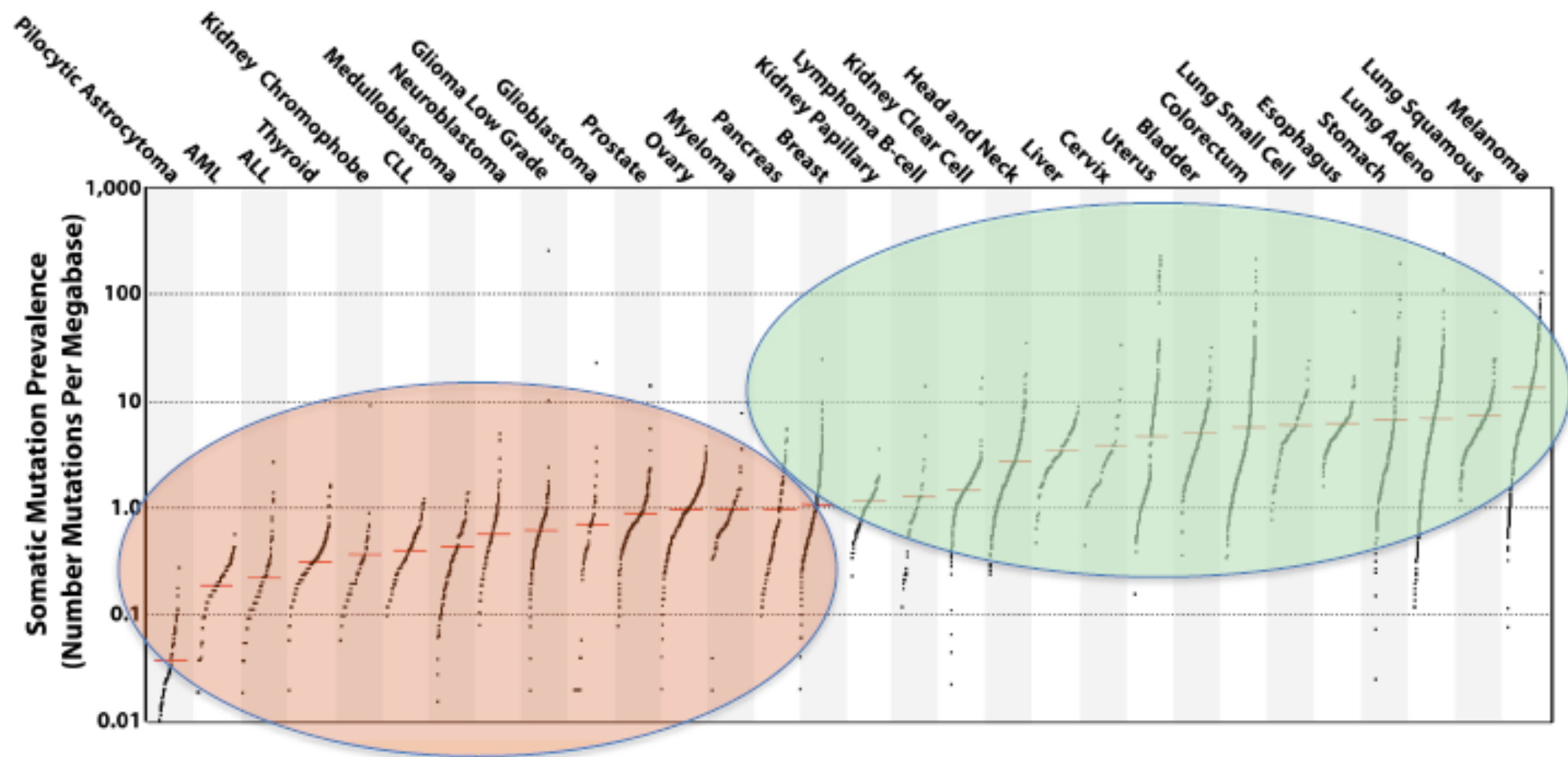




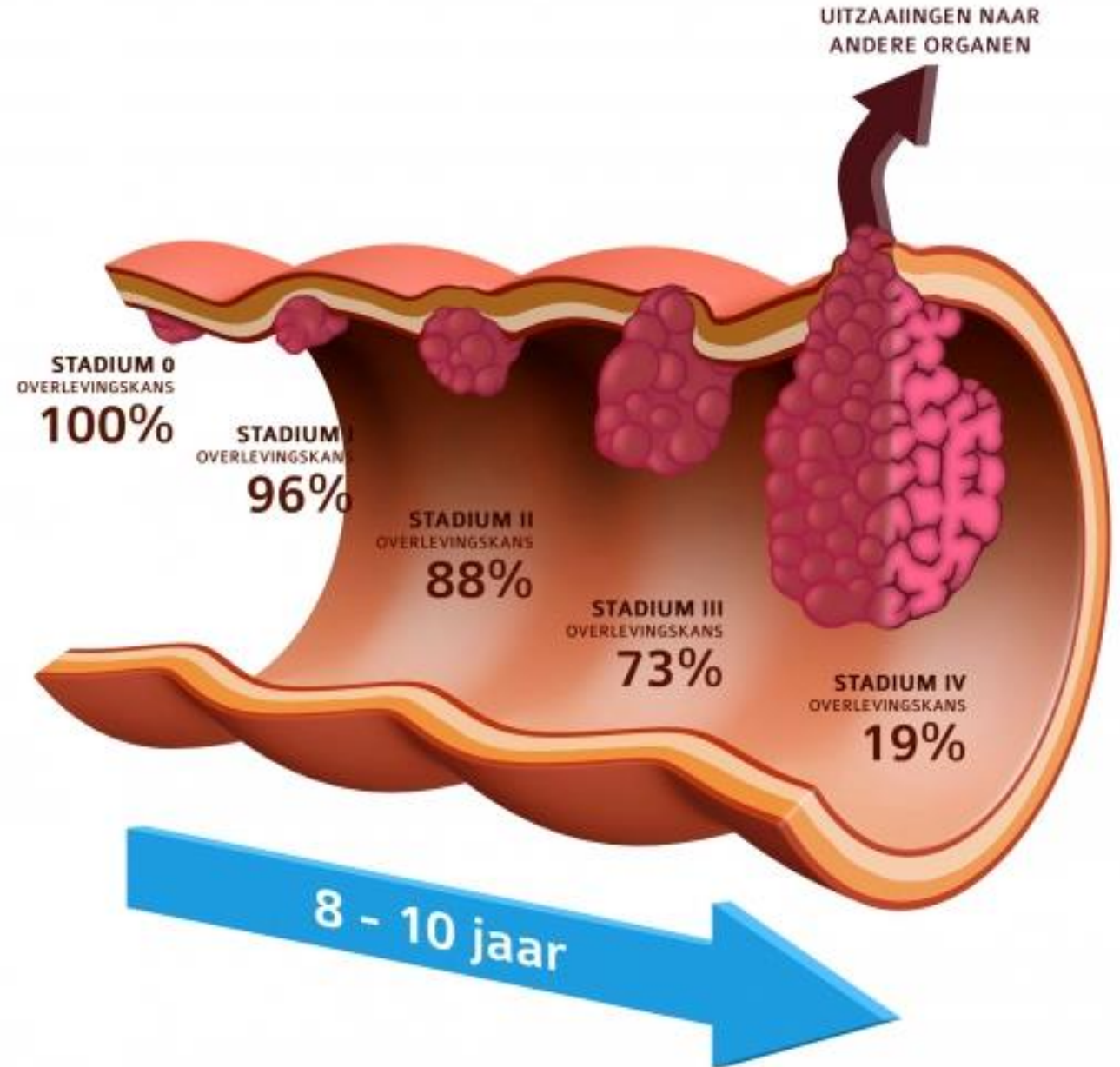
Types of cancer immunotherapy



DNA schade & succes van immunotherapie



Colon carcinoom



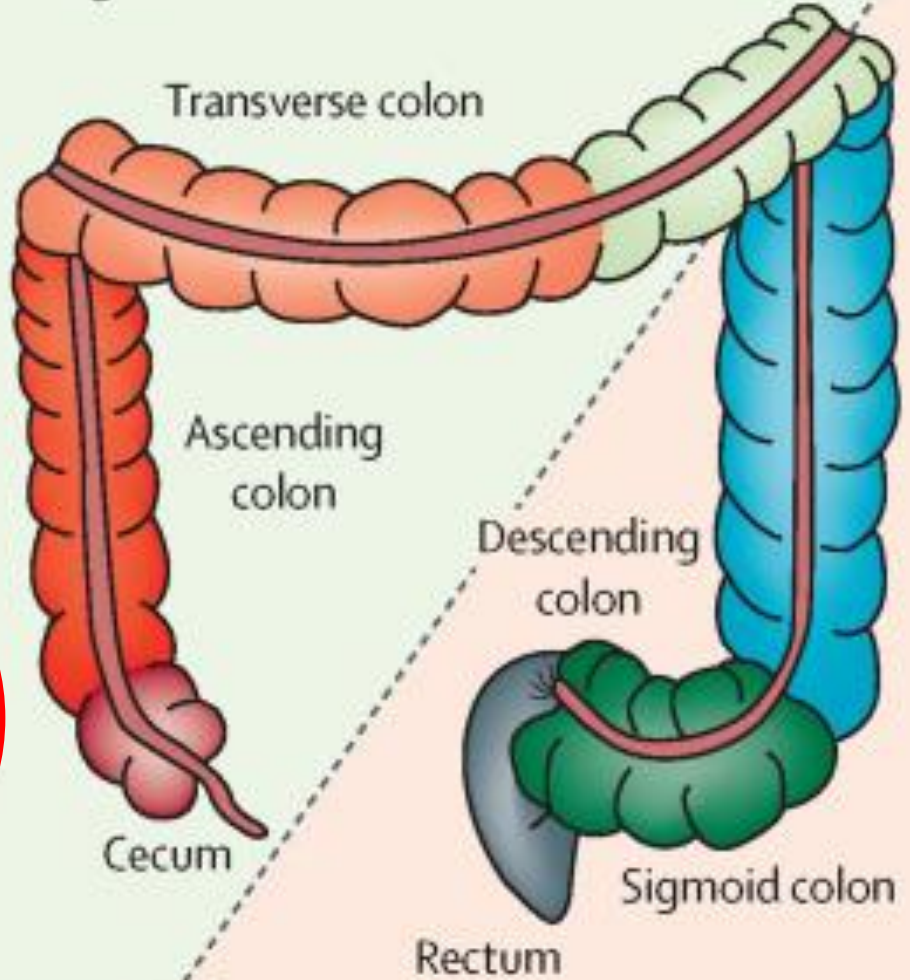
Patient's right ← → Patient's left

Midgut derivative

- ↑ Women
- ↑ Sessile serrated lesions
- ↑ Mucinous tumours

Overall worse prognosis*

- ↑ CIMP-high
- ↑ BRAF
- ↑ MSI-high
- ↑ MSI immune tumours (CMS1)
- ↑ Metabolic tumours (CMS3) (↑ KRAS)



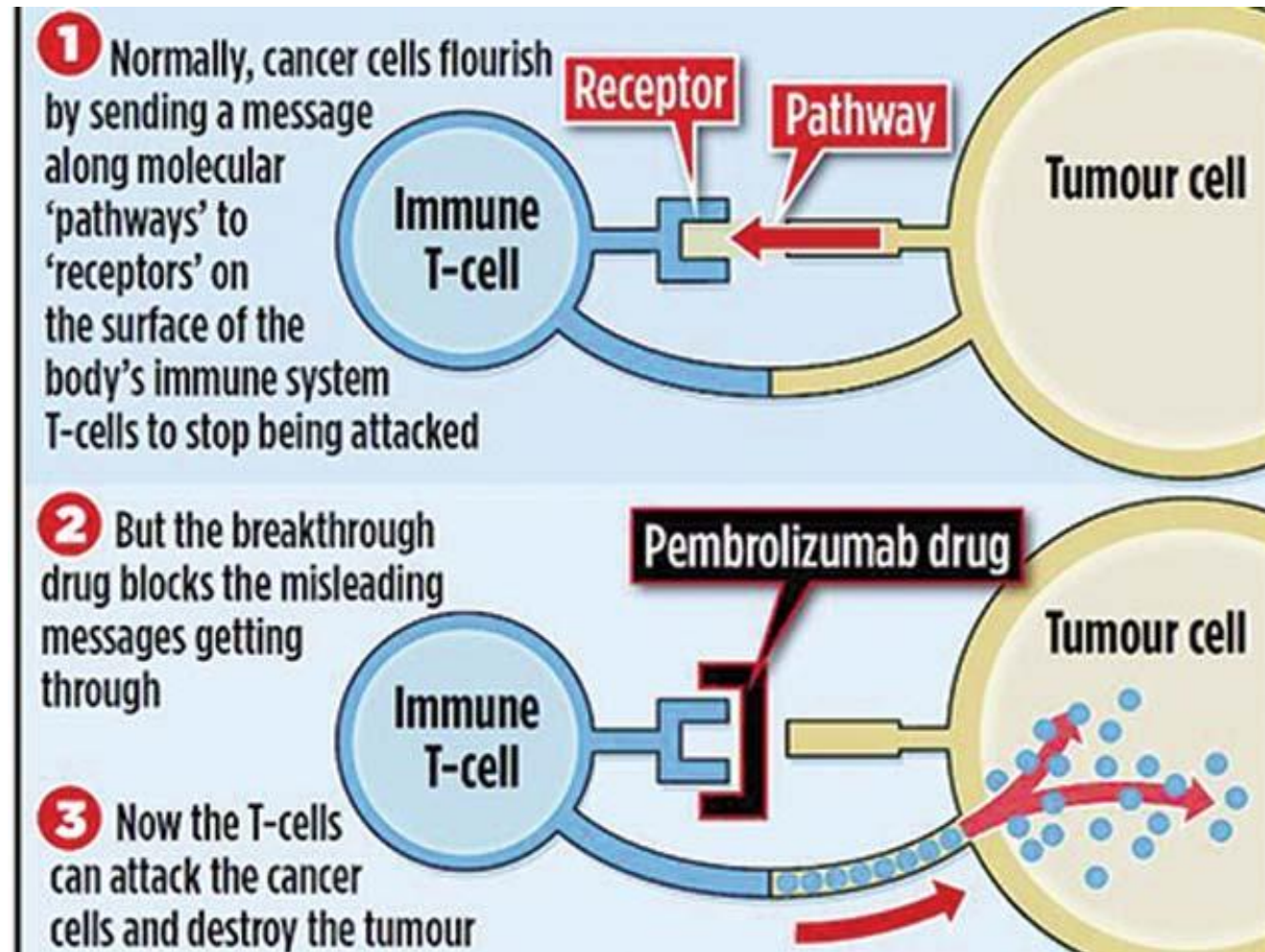
Hindgut derivative

- ↑ Men

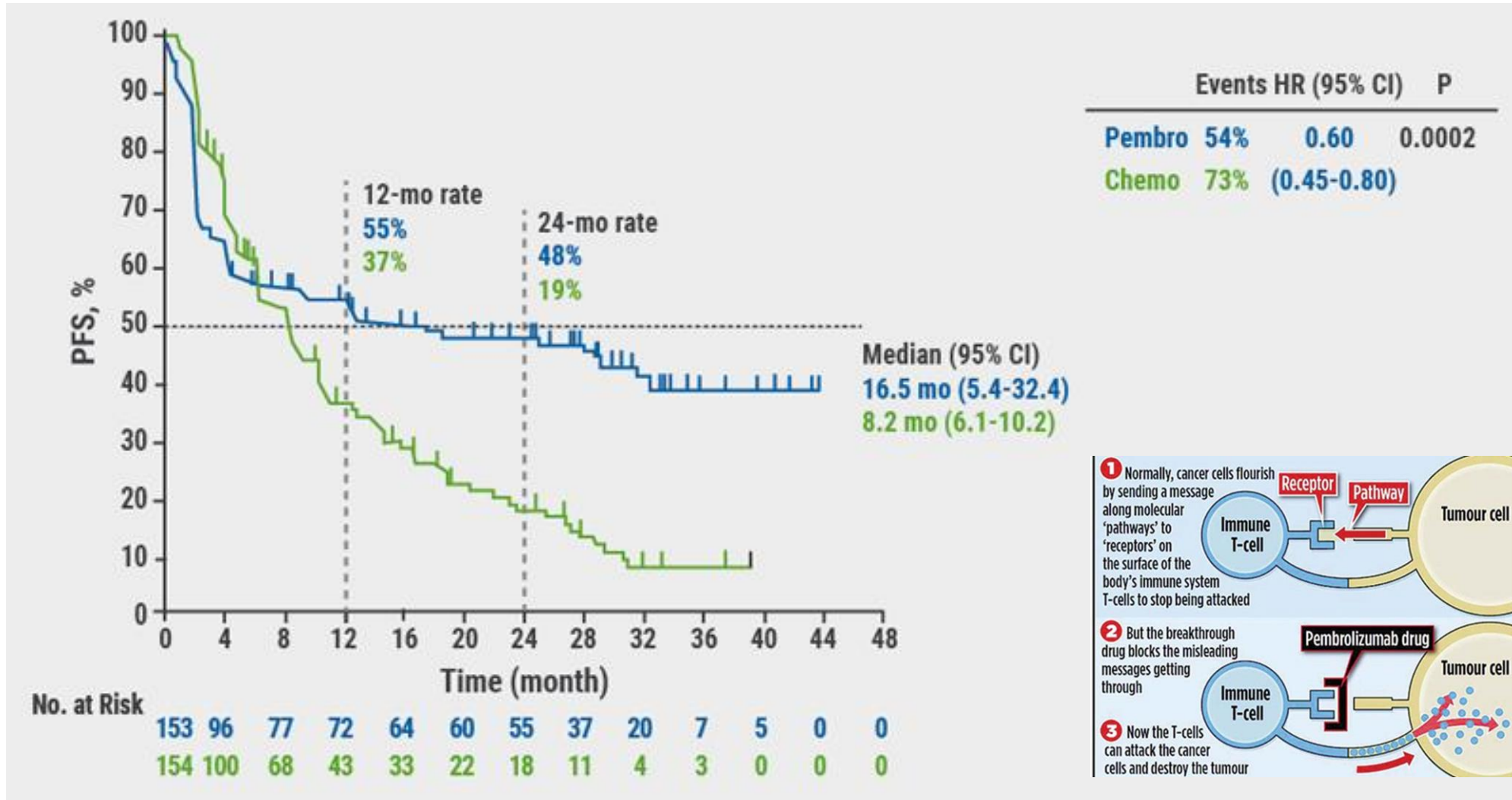
Overall better prognosis*

- ↑ Mesenchymal (CMS4)
- ↑ Canonical (CMS2), distally
- ↑ TP53
- ↑ APC

MMI high tumoren



pembrolizumab



Pembrolizumab for the Treatment of Microsatellite Instability-High Solid Tumors

Leigh Marcus, Steven J. Lemery, Patricia Keegan and Richard Pazdur

Published July 2019

immunotherapie

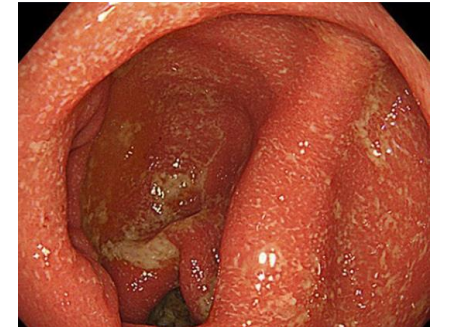
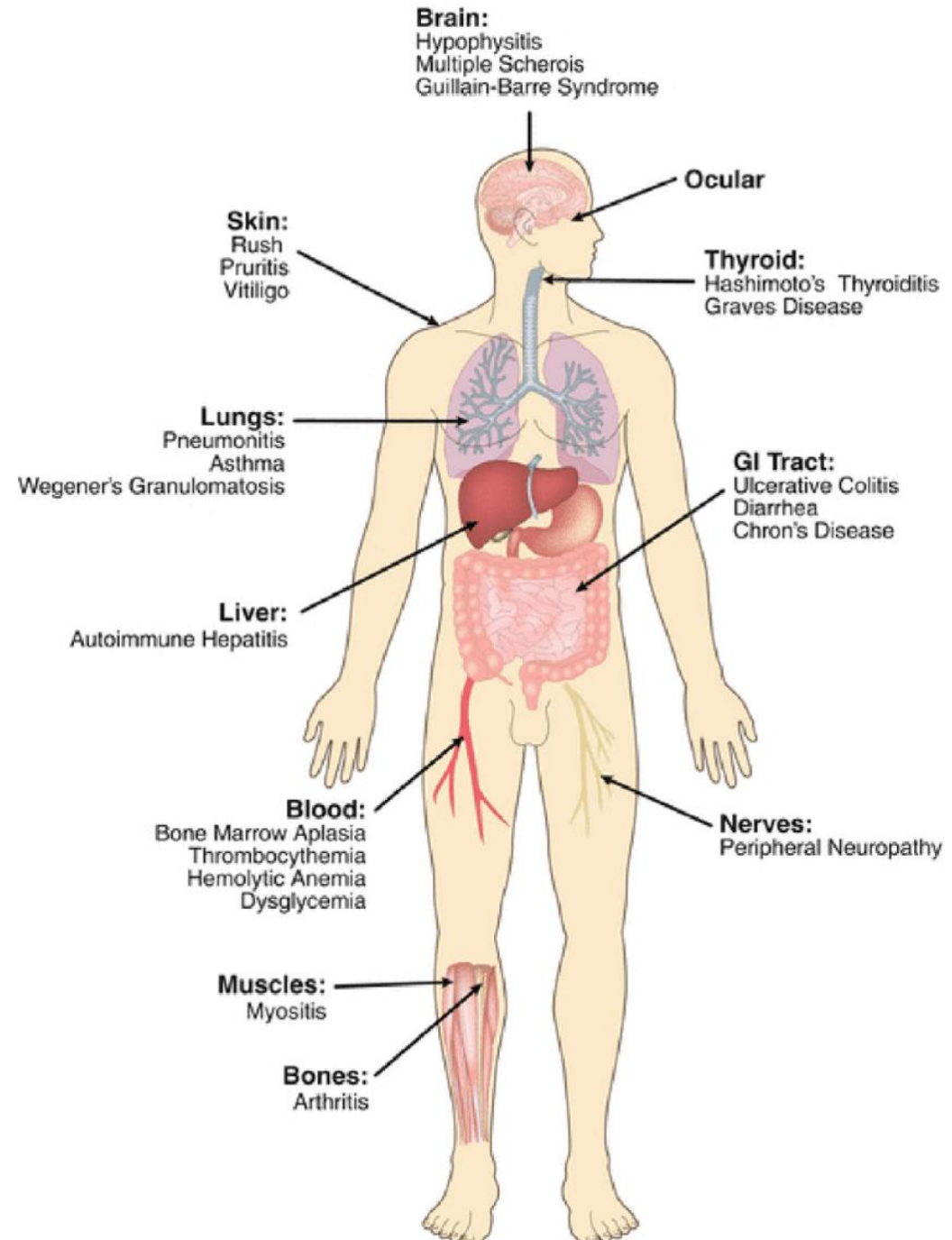
- bij genetisch instabiele tumoren (melanoom, long)
- uitbreidend indicatie gebied (Rechtszijdig coloncarc, blaas)

maar.....

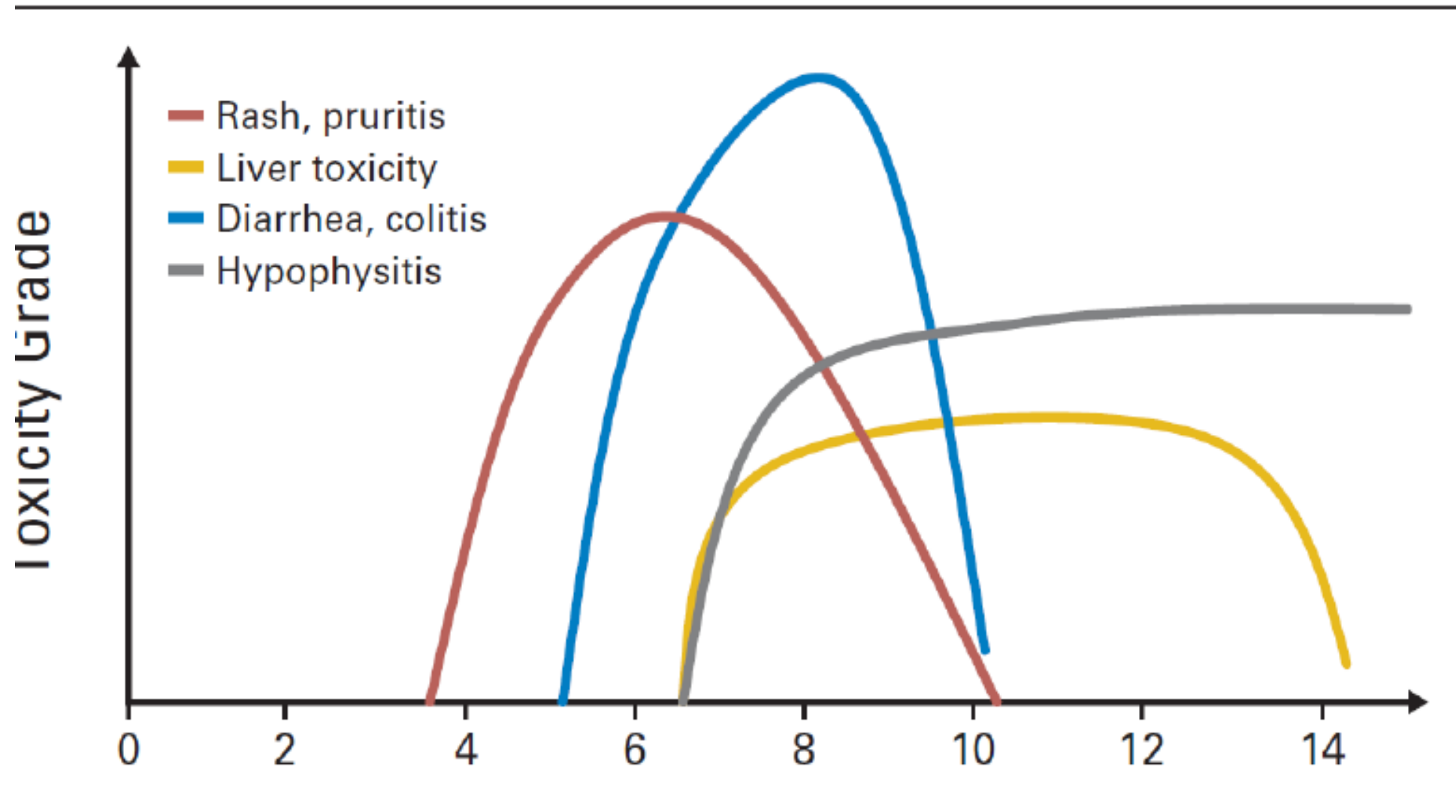
- Heel ander bijwerking profiel
- kunnen vroeg optreden , maar ook pas na maanden



(b)

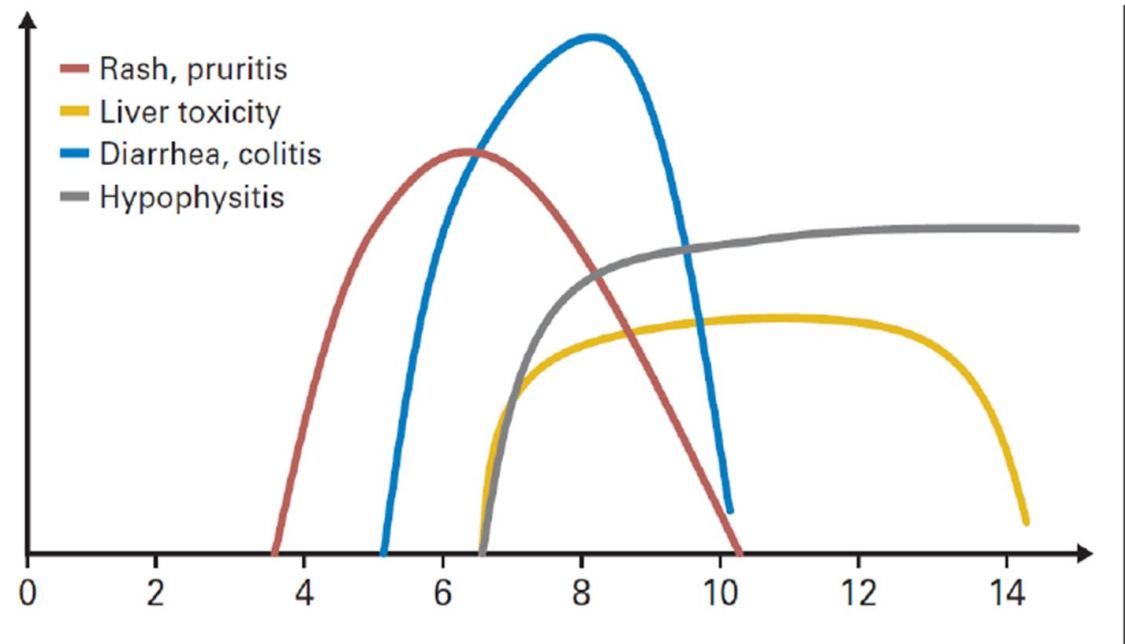


- Gemiddeld 6-12 weken (data ipilimumab)



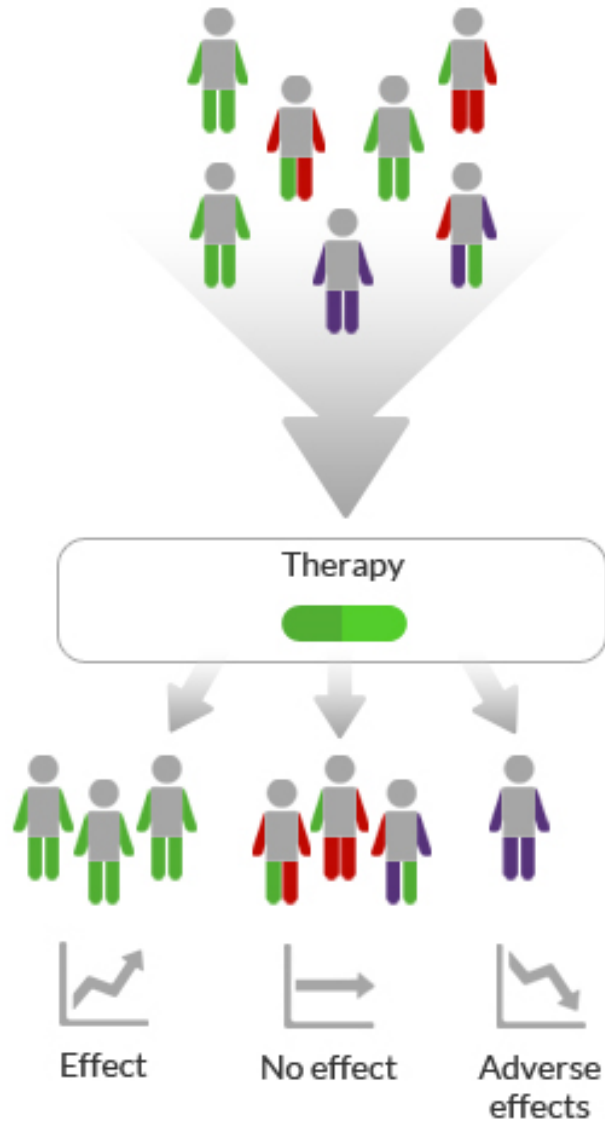
Hypofysitis <1 %

- Kan lange tijd na start behandeling of na behandeling optreden
 - Moe
 - Gewichtsverlies
 - Orthostase
 - hypoglycamie
 - laag cortisol



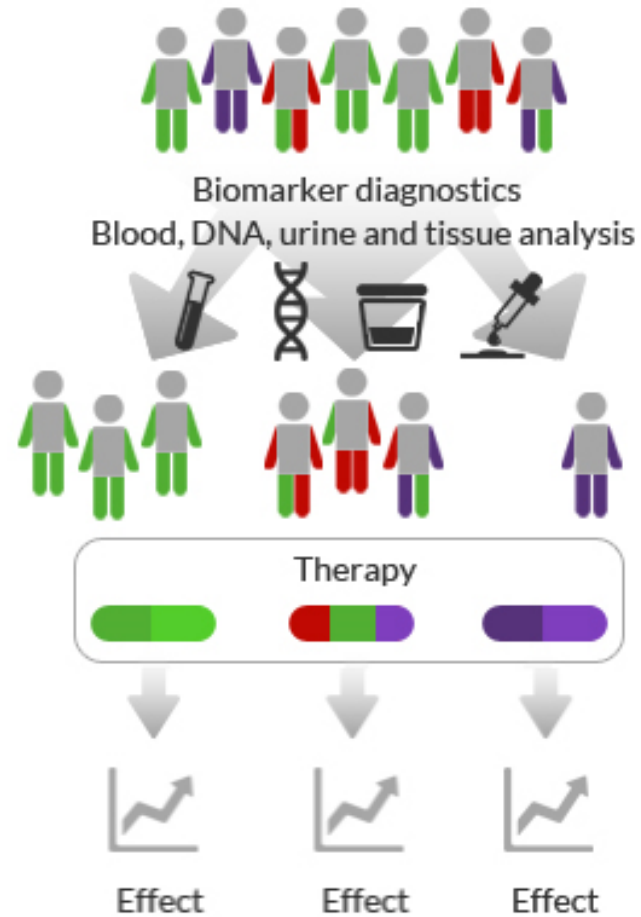
Standard treatment

Cancer patients with e.g. colon cancer



Personalised treatment

Cancer patients with e.g. colon cancer



- Chemotherapie blijft nog steeds belangrijk
 - Voorspelbare bijwerkingen meestal <2 weken
- Doelgerichte therapie
 - mild bijwerkingprofiel, vaak ingezet ogv biomarker
- Immunotherapie
 - indicatie gebied breid uit
 - auto immuun bijwerkingen tot wel 6 maanden na staken