

Nieuwe systemische behandelingen bij het adenocarcinoom van de maag en slokdarm.

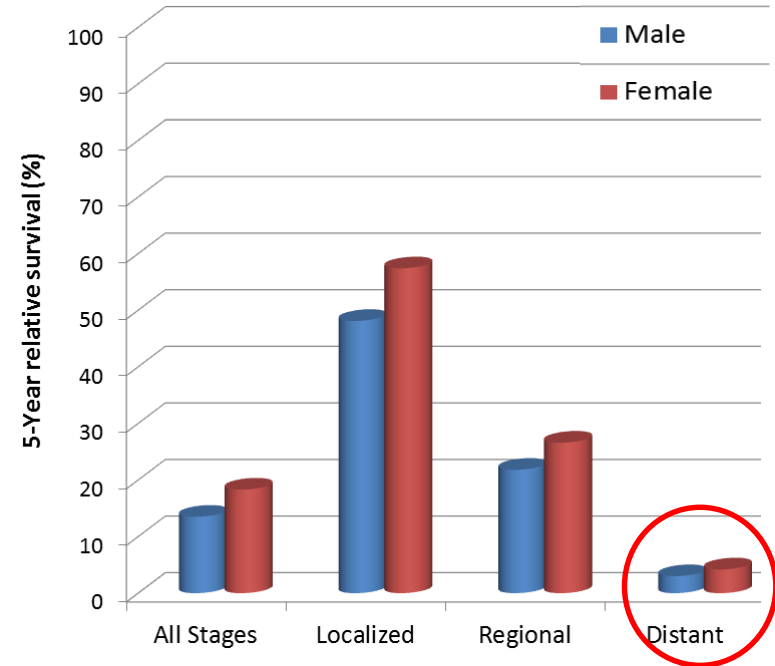
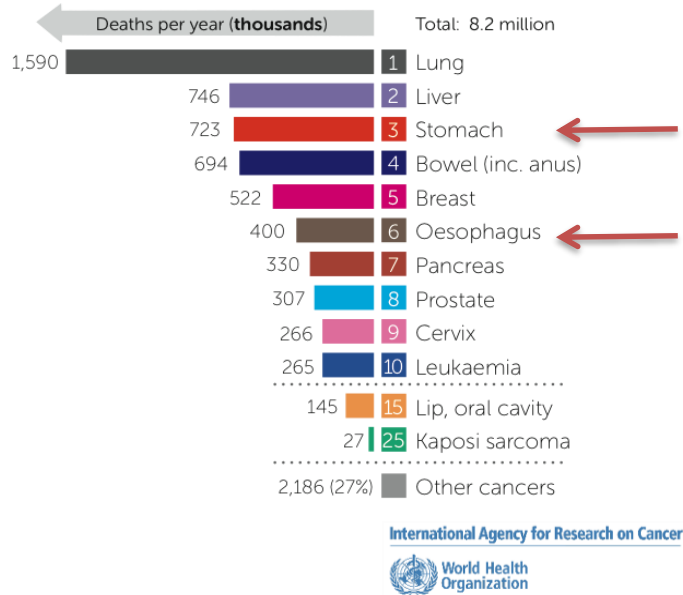
Sarah Derks, Medisch Oncoloog Amsterdam UMC | 28-1-2022





Gemetastaseerd maag- en slokdarmkanker

Most Common Causes of Cancer Death



Sterfte ~3000 patiënten per jaar in NL

Stadium bij diagnose(%)

23%

34%

43%



Vraag 1: hoe wordt uitgezaaid M-S AC behandeld?

A: best-supportive care: chemotherapie doet maar weinig

B: chemotherapie is nog steeds de hoeksteen van de behandeling

C: met gepersonaliseerde therapie



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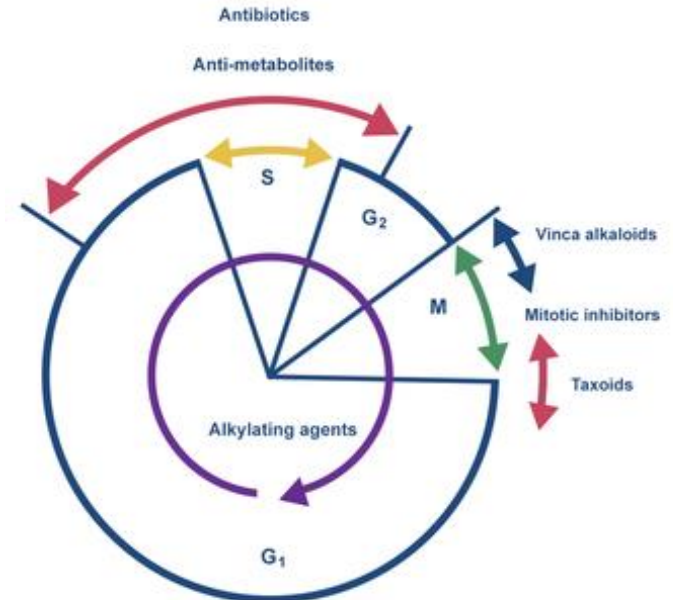
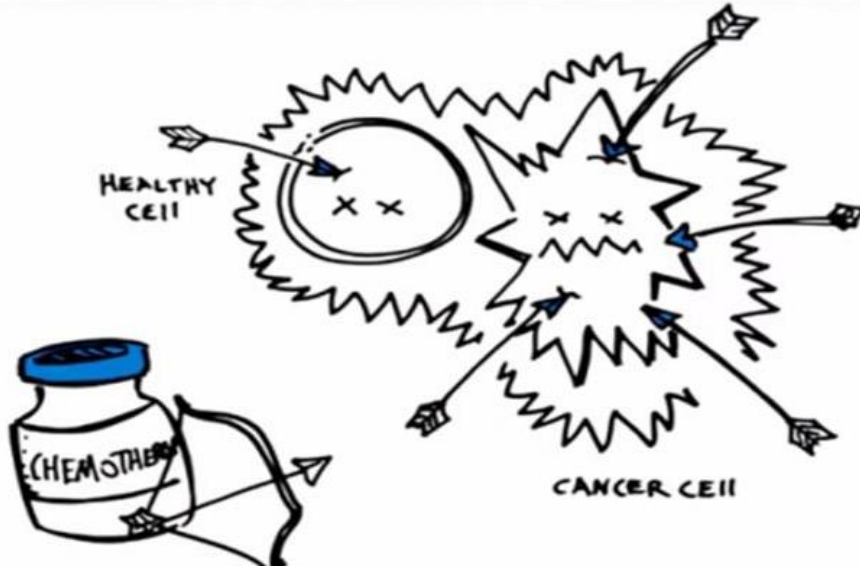
B: chemotherapie is nog steeds de hoeksteen van de behandeling

C: met gepersonaliseerde therapie



Behandeling gemetastaseerde ziekte

chemotherapie en celcyclus



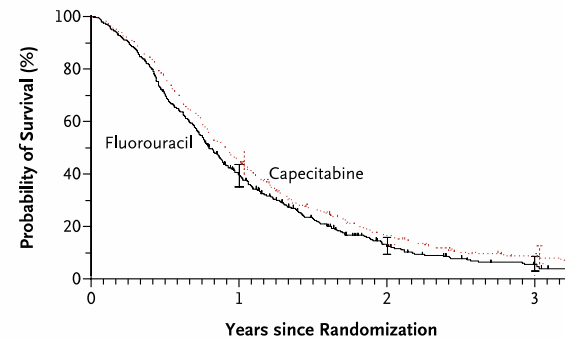


Behandeling gemetastaseerde ziekte

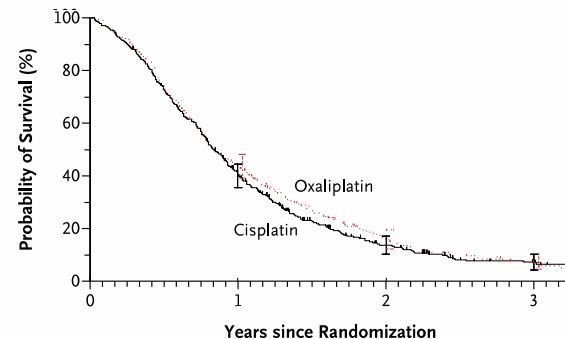
Table 2. Analysis of Efficacy (Intention-to-Treat Population).*

Variable	ECF (N=263)	ECX (N=250)	EOF (N=245)	EOX (N=244)
Death				
No. of patients	225	213	213	199
Hazard ratio (95% CI)		0.92 (0.76–1.11)	0.96 (0.79–1.15)	0.80 (0.66–0.97)
P value		0.39	0.61	0.02
Overall survival				
Median — mo	9.9	9.9	9.3	11.2
At 1 yr — % (95% CI)	37.7 (31.8–43.6)	40.8 (34.7–46.9)	40.4 (34.2–46.5)	46.8 (40.4–52.9)
Progression-free survival				
Median — mo	6.2	6.7	6.5	7.0
Patients who had progression or died	237	231	221	213
Hazard ratio (95% CI)		0.98 (0.82–1.17)	0.97 (0.81–1.17)	0.85 (0.70–1.02)
P value		0.80	0.77	0.07
Response				
Overall — % (95% CI) †	40.7 (34.5–46.8)	46.4 (40.0–52.8)	42.4 (36.1–48.8)	47.9 (41.5–54.3)
P value		0.20	0.69	0.11

A Fluoropyrimidine Comparison



B Platinum Comparison





Behandeling gemetastaseerde ziekte

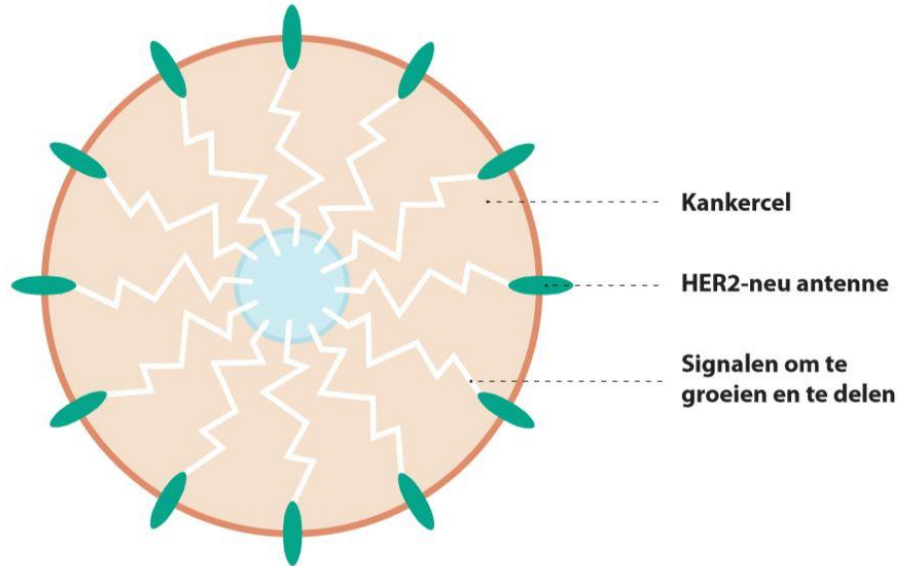
De ene tumor is de andere niet!

- HER2 neu+ tumor kunnen anti-HER2 therapie krijgen (gepersonaliseerde behandeling)
- MSI tumoren lijken het meest gevoelig voor immuuntherapie

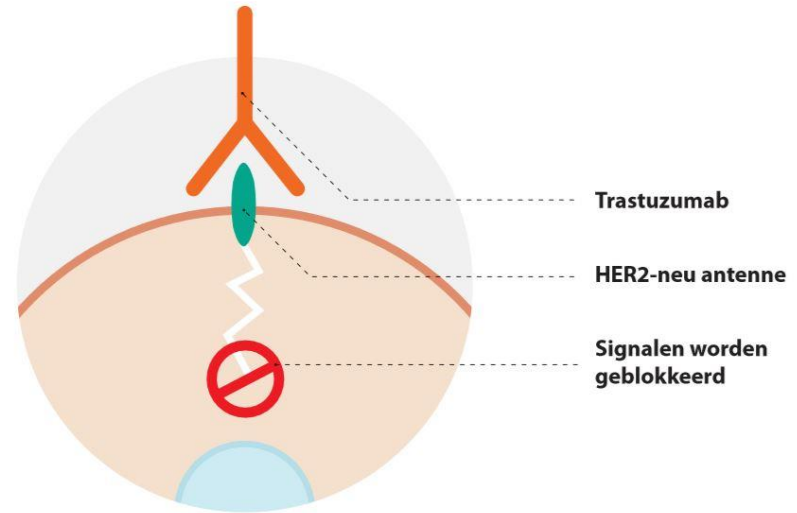


HER2 positieve maag-slokdarm adenocarcinomen

HER2 zet celdeling aan
HER2 +++ in 10-15% van M-S ACs



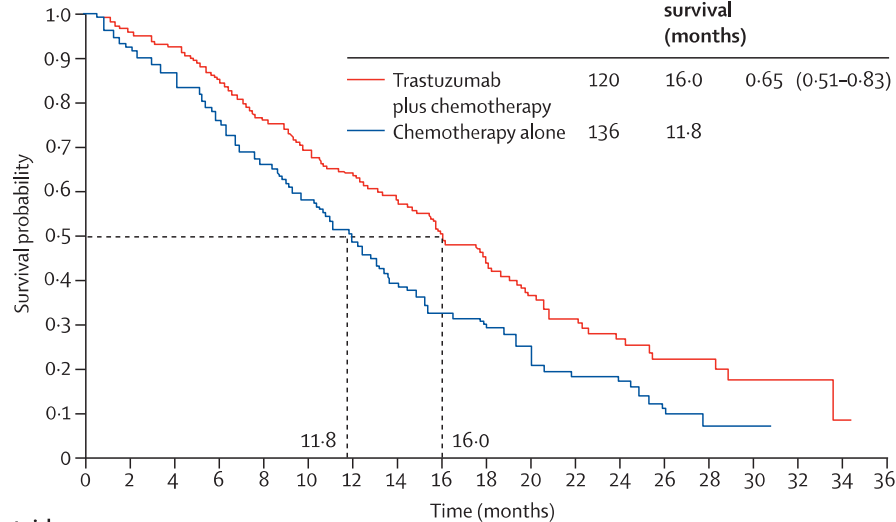
Trastuzumab kan HER2 remmen!





HER2 positieve maag-slokdarm adenocarcinomen

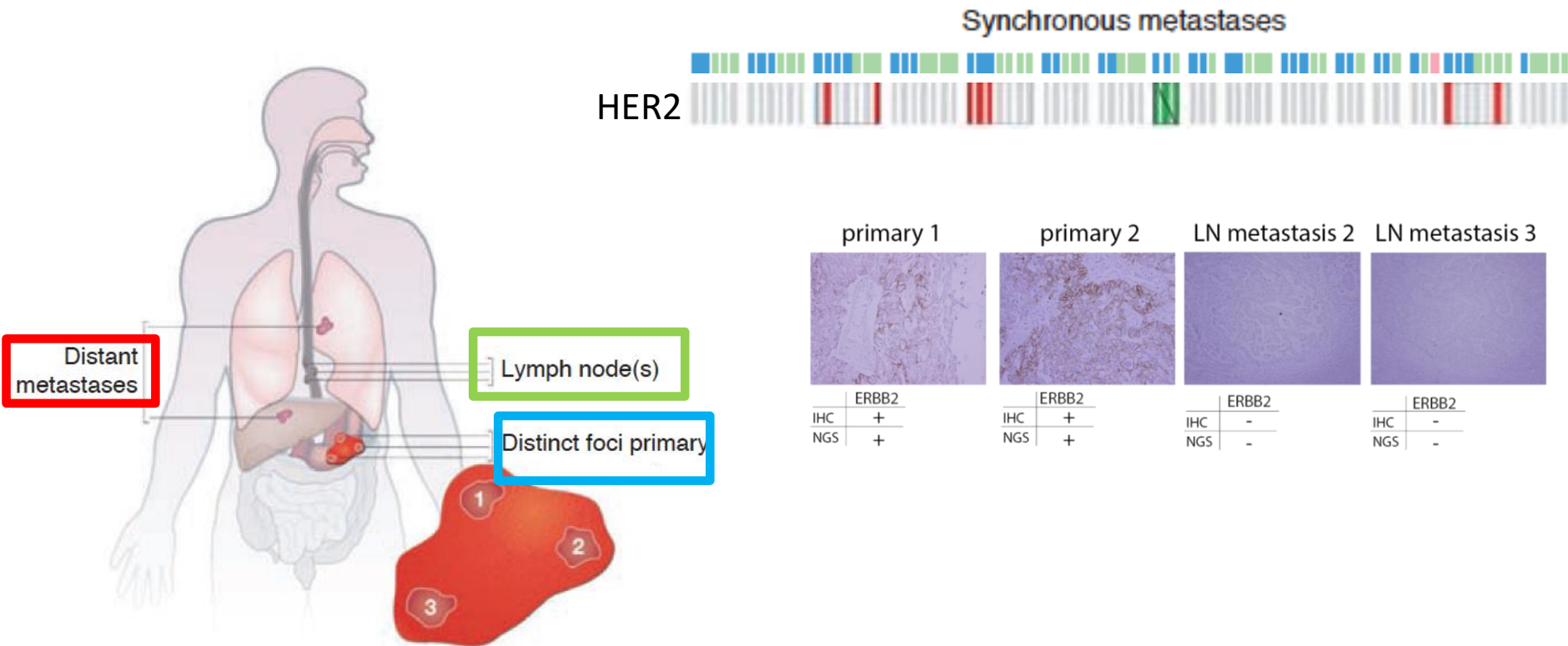
	Trastuzumab plus chemotherapy (n=294)	Chemotherapy alone (n=290)	Non-stratified effect size	Stratified effect size*		Odds ratio	p value
B							
Progression-free survival (months)	6.7 (6-7.3)	6.1 (5.6-6.6)	1.12	Events	Median overall survival (months)		..
Time to progression (months)	7.1 (6.6-7.6)	6.5 (6.0-7.0)	1.09	120	16.0	0.65 (0.51-0.83)	..
Duration of response (months)	6.9 (6.4-7.4)	6.3 (5.8-6.8)	1.10	136	11.8		..
Tumour response							
Overall tumour response rate	139 (47%)	123 (42%)	1.13			0 (1.22-2.38)	0.0017§
Complete response	16 (5%)	16 (5%)	1.00			3 (0.94-5.74)	0.0599§
Partial response	123 (42%)	107 (37%)	1.15			2 (1.09-2.14)	0.0145§
Stable disease	93 (32%)	93 (32%)	1.00				..
Progressive disease	35 (12%)	35 (12%)	1.00				..
Missing	27 (9%)	27 (9%)	1.00				..



	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
Number at risk																			
Trastuzumab plus chemotherapy	228	218	196	170	142	122	100	84	65	51	39	28	20	12	11	5	4	1	0
Chemotherapy alone	218	198	170	141	112	96	75	53	39	28	20	13	11	4	3	3	0	0	0



HER2 positiviteit wisselt nogal per tumor gebied!

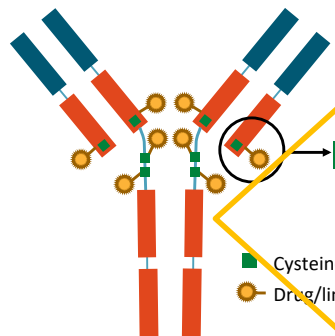




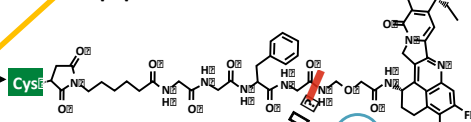
HER2 positieve M-S AC: nieuwe behandelingen!

antilichaam + chemotherapie

Humanized anti-HER2 IgG1 mAb
with same AA sequence as
trastuzumab

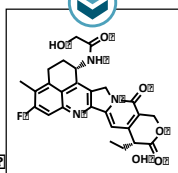


Tetrapeptide-based cleavable linker

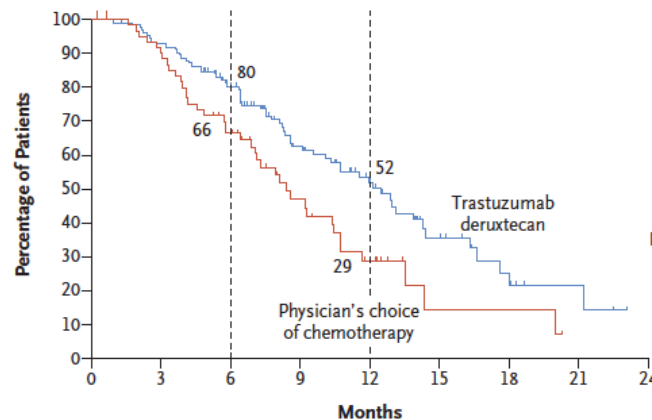


■ Cysteine residue
● Drug/linker

Topoisomerase II inhibitor (Tdx) payload
(exatecan derivative)



A Overall Survival



No. at Risk

Months	0	3	6	9	12	15	18	21	24
Trastuzumab deruxtecan	125	115	88	54	33	14	7	3	0
Physician's choice of chemotherapy	62	54	37	19	10	2	2	0	0



Vraag 2:

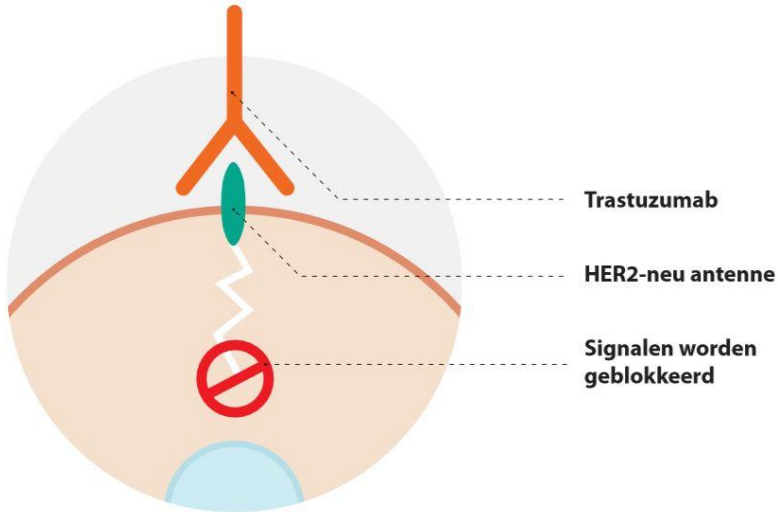
hoe noemen we nu de HER2 gerichte therapie?

A: immuuntherapie

B: doelgerichte therapie

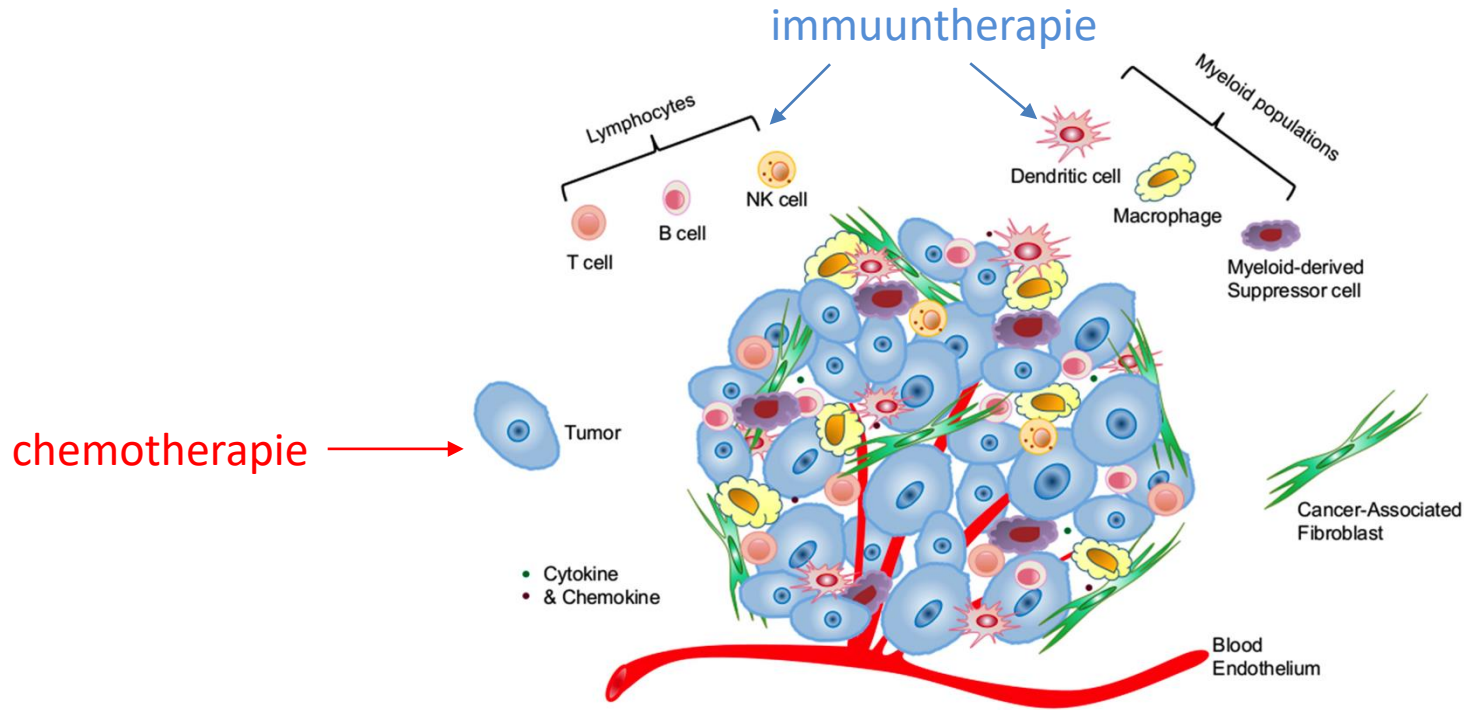


Trastuzumab is geen immuuntherapie maar doelgerichte therapie!



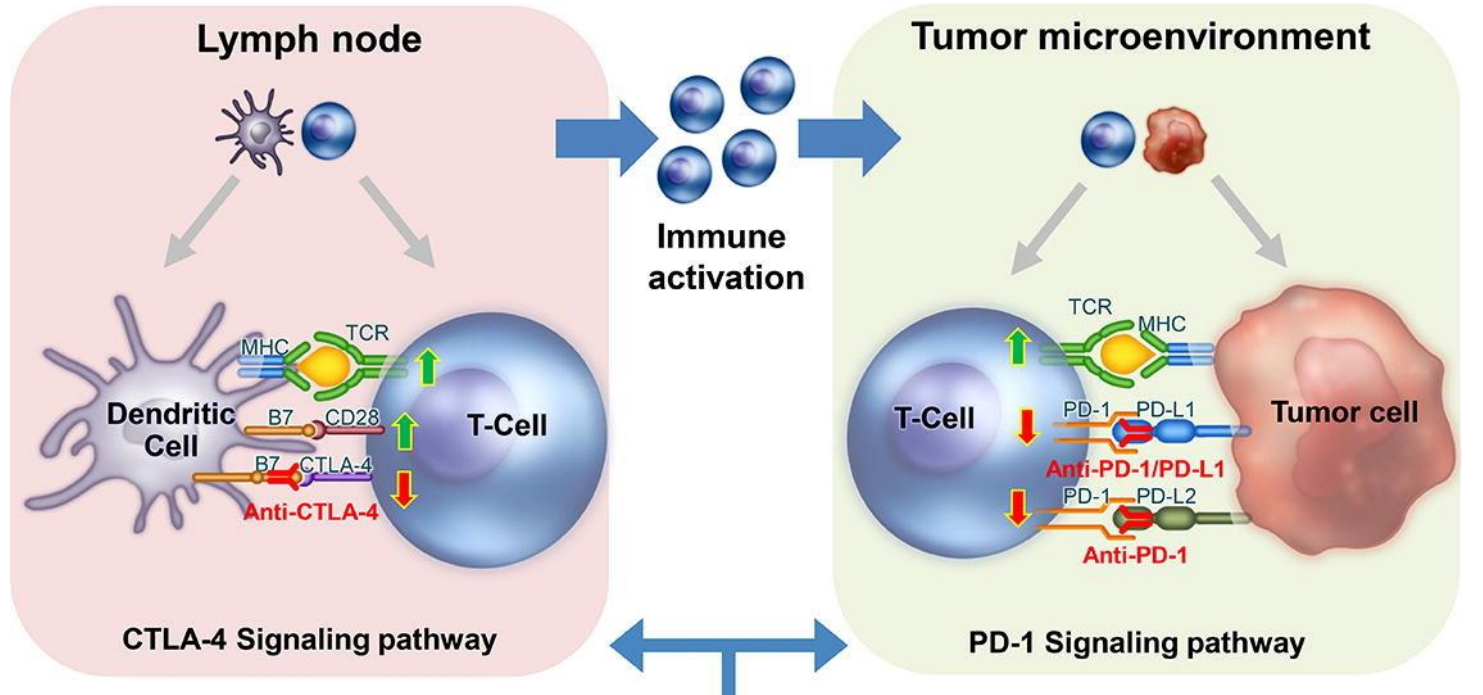


Bij immunotherapie is de immuuncel het doelwit, bij chemotherapie de kankercel





Huidige immunotherapie: checkpointremmers



ipilimumab

pembrolizumab

Nivolumab

retifanlimab

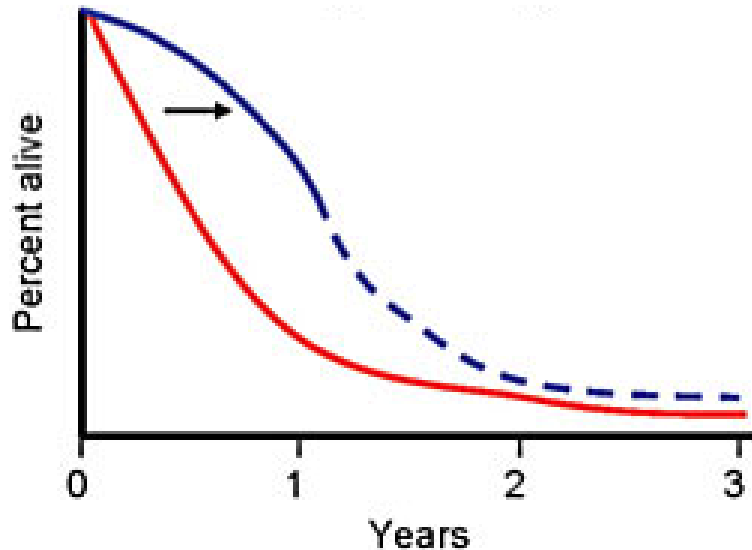
durvalumab

atezoluzimab

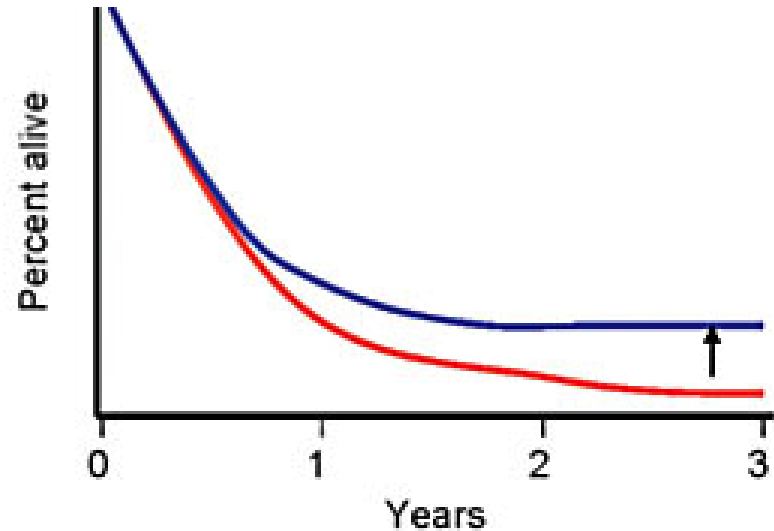


Naast doel ook zeer verschillende respons

Chemotherapie of doelgerichte therapie



Immuuntherapie





Daarnaast ook groot verschil in bijwerkingen

Baseline (Day 0)



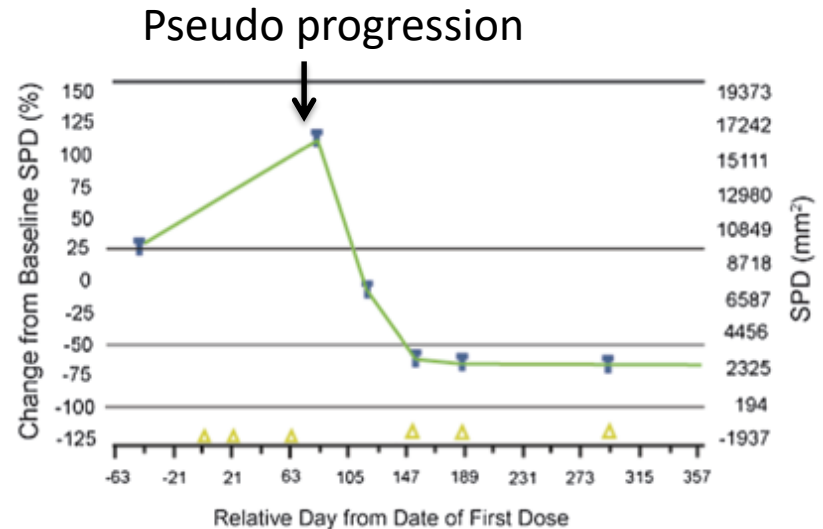
Week 12 (Day 84)



Week 16 (Day 112)



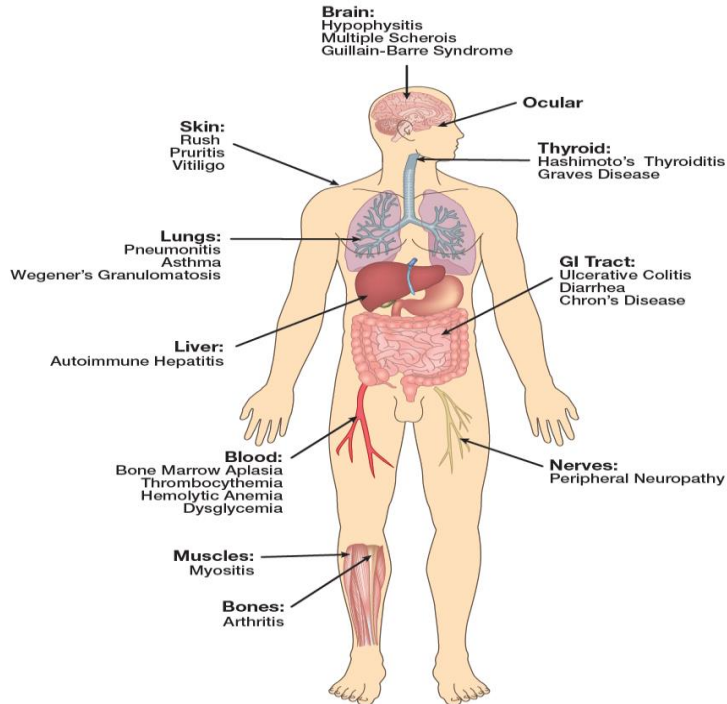
Week 72 (Day 503)



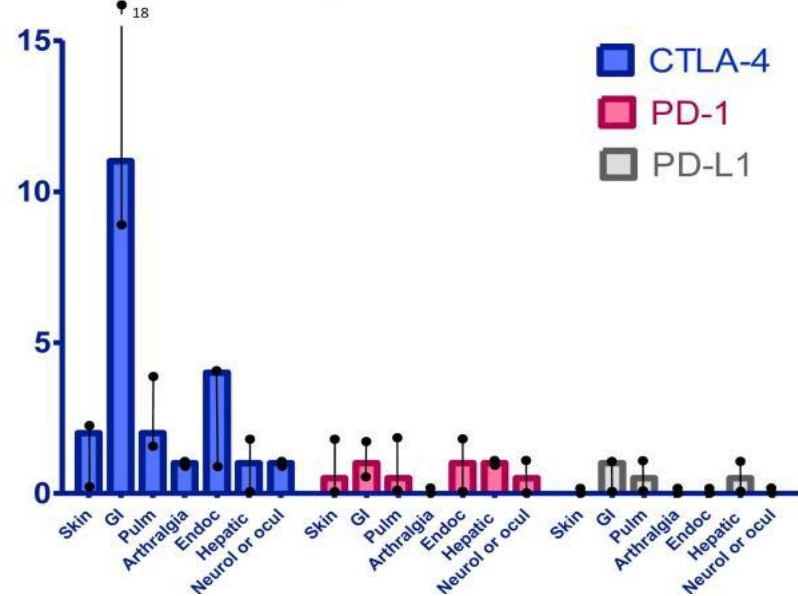


Daarnaast ook groot verschil in bijwerkingen

Auto-immuunziektes!



Distribution of grade 3-5 IRAEs

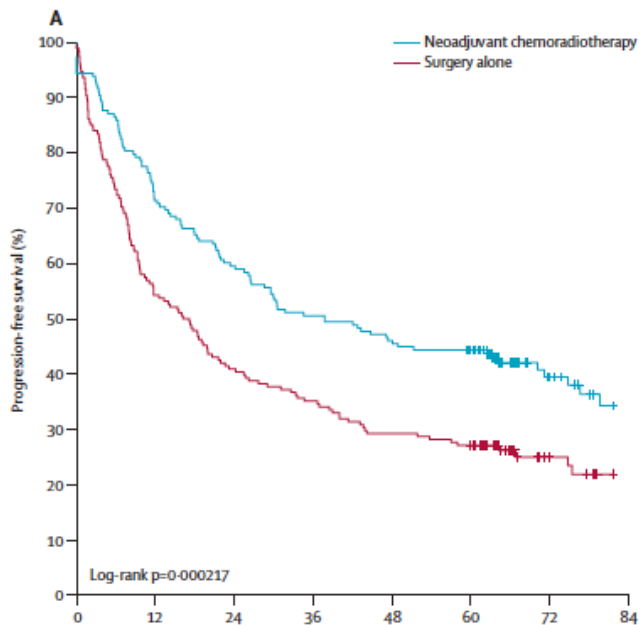




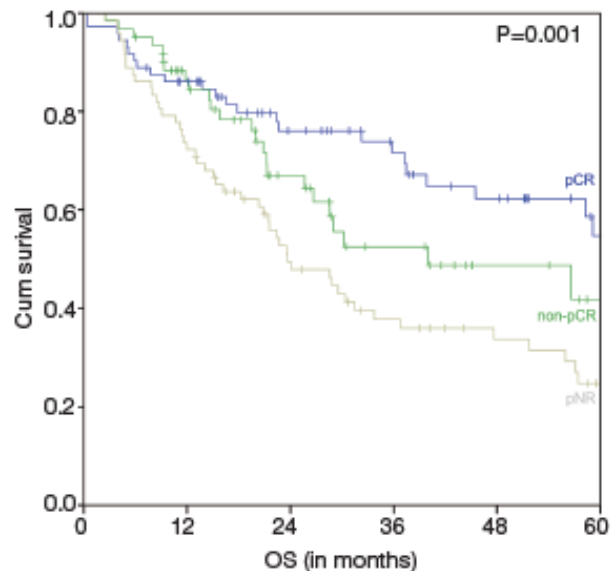
Immuuntherapie bij maag en slokdarmkanker (1)

Adjuvante immuuntherapie voor slokdarmkanker

Neoadjuvant CRT verbetert overleving



Maar overleving hangt af van hoe goed chemoradiatie heeft gewerkt

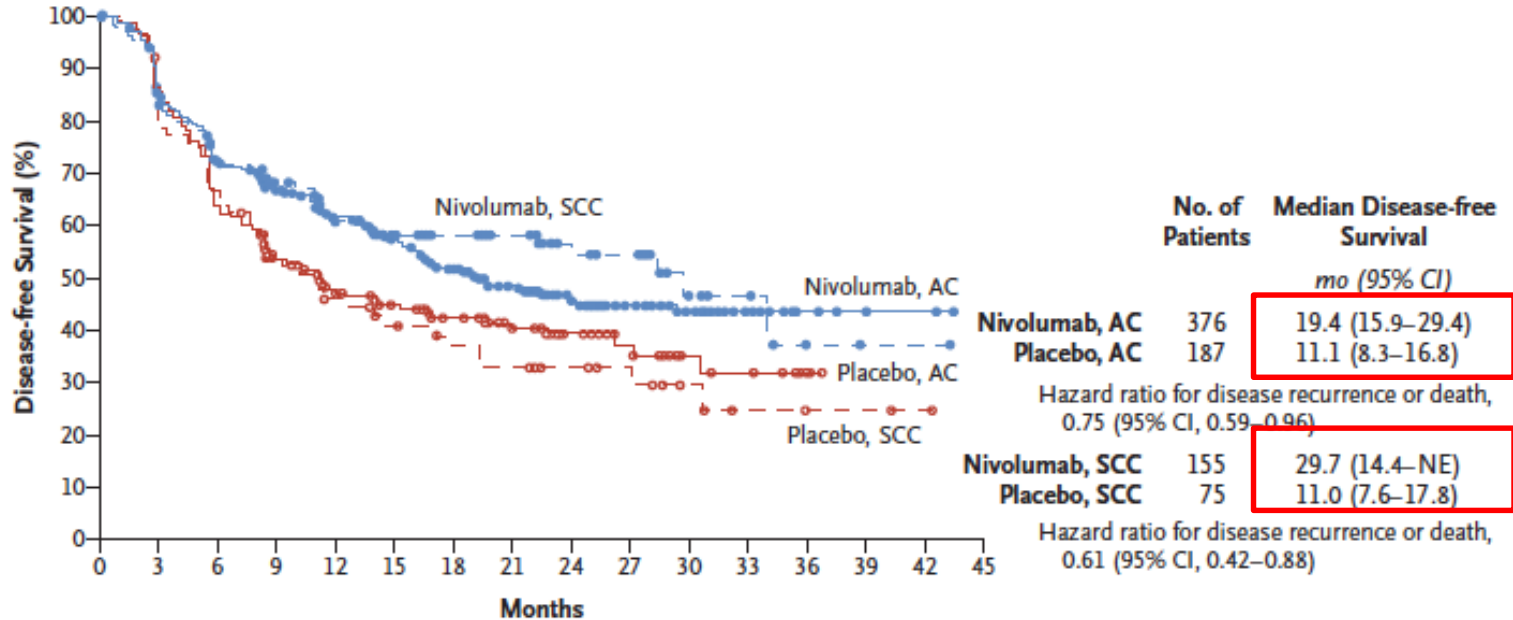




Immuuntherapie bij maag en slokdarmkanker (1)

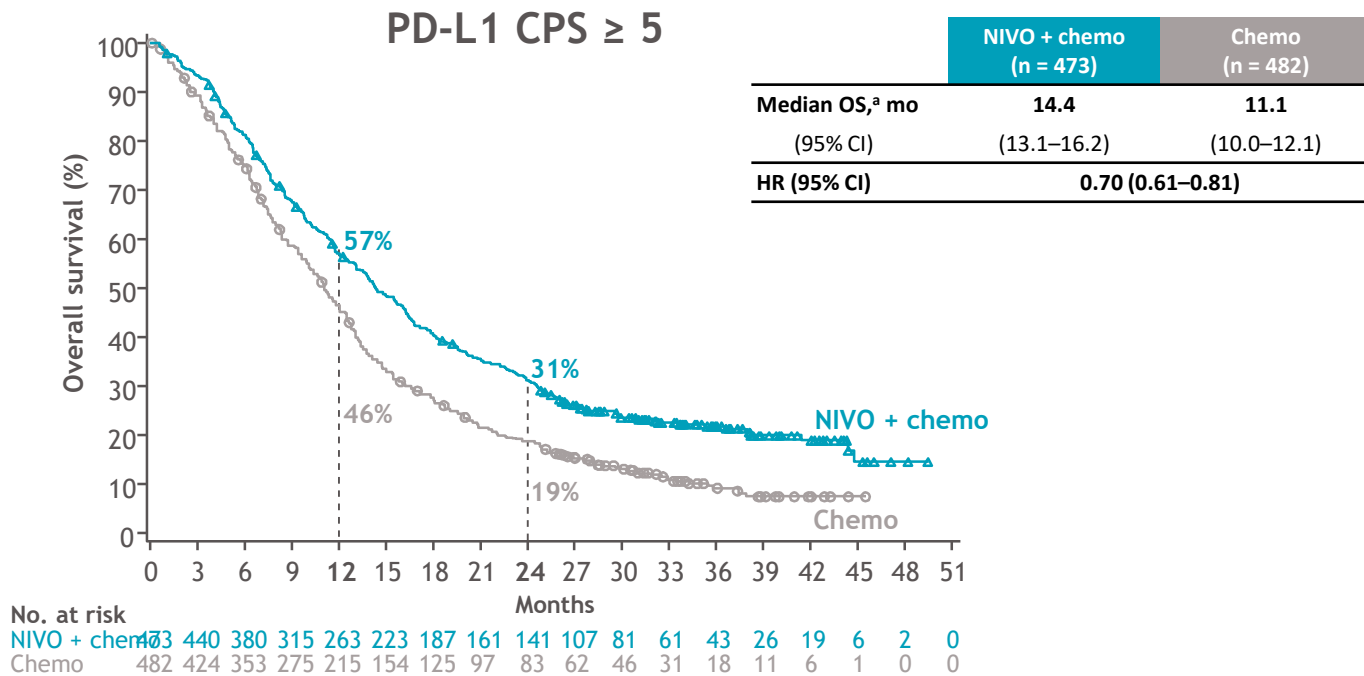
Adjuvante immuuntherapie voor slokdarmkanker

B Disease-free Survival According to Histologic Type





Immunotherapie bij maag en slokdarmkanker (2) immunotherapie wordt toegevoegd aan CAPOX





Conclusie

- Er zijn veel studies gaande die middelen gebruiken die zich op HER2 richten. Dit zal standaardtherapie worden
- Immunotherapie gaat ook op korte termijn gebruikt worden bij maag en slokdarmkanker.
- In het Amsterdam UMC worden veel studies gedaan om de behandeling verder te verbeteren (wat ook echt nodig is...)