Thoracale oncologie anno 2025

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NKI-AVL

Studie sponsoring	MSD
Adviseur	Instituut AsbestSlachtoffers
	Patiëntenvereniging voor Asbestslachtoffers

Vergoedingen zijn voor het :

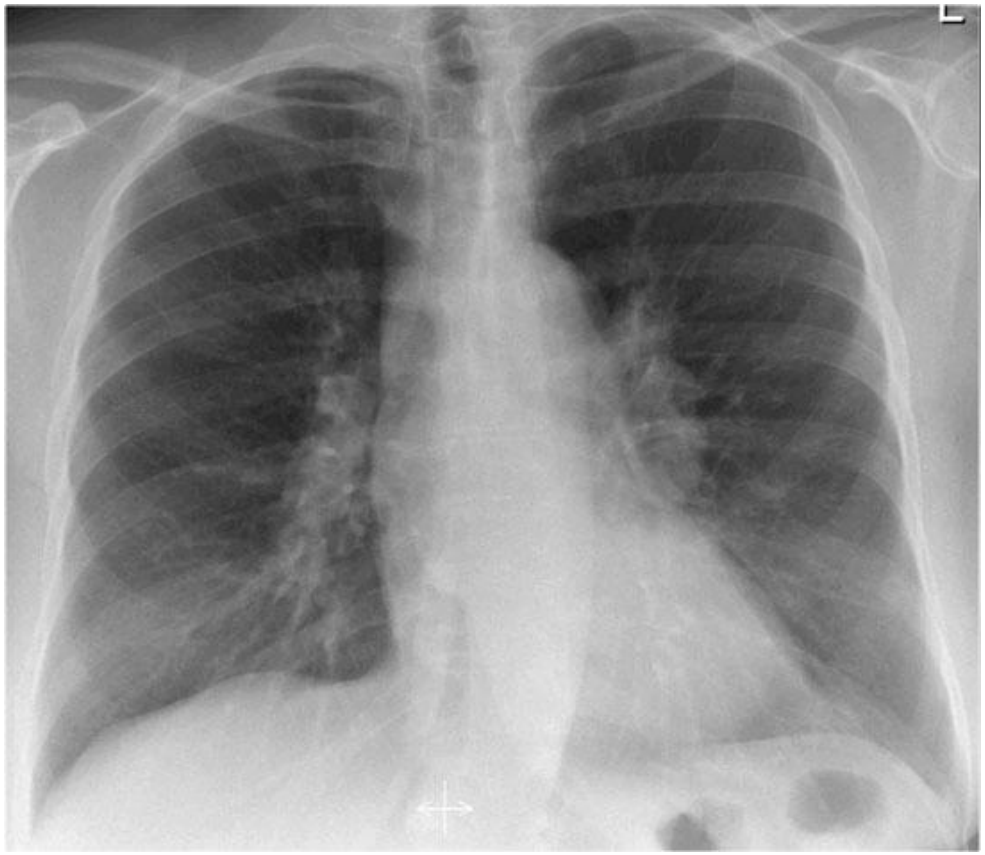
NKI-AVL

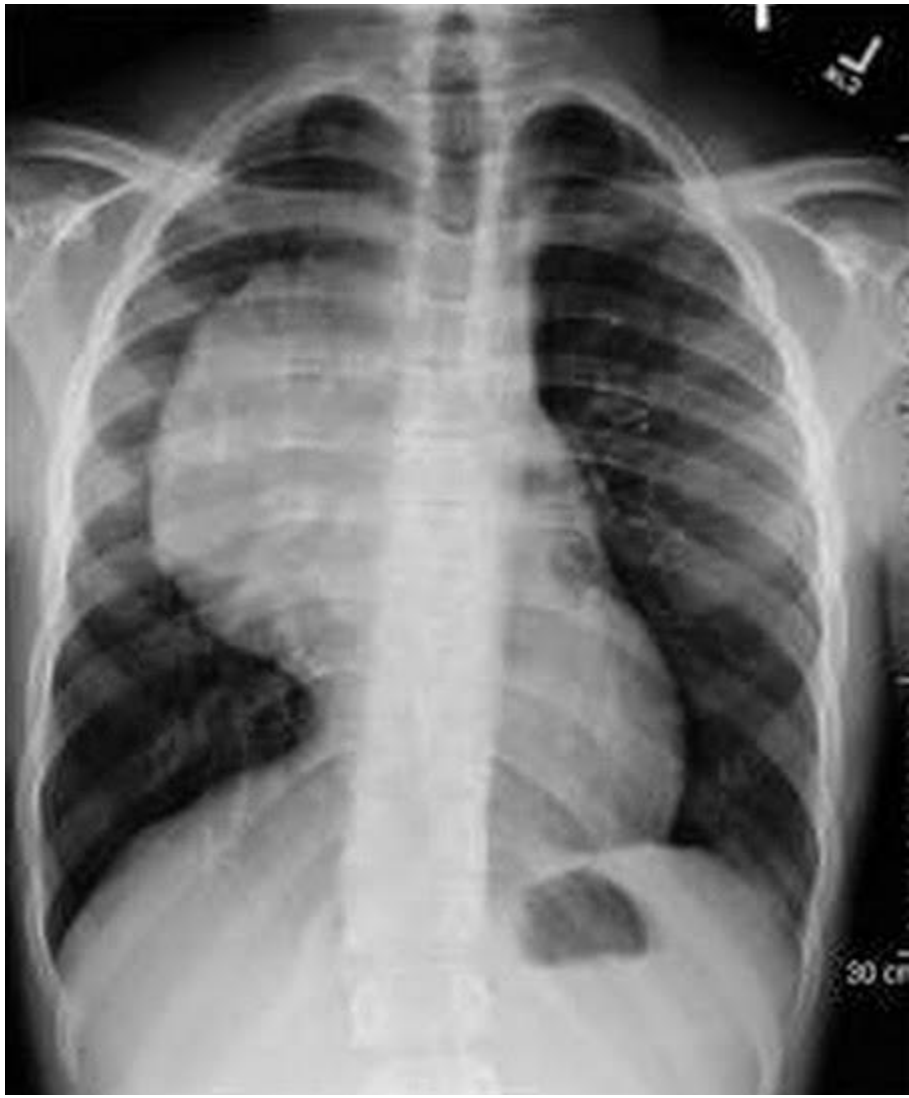
Thoracale oncologie

- Thymoom
- Longkanker
  - Niet-kleincellig
  - Kleincellig
- Mesothelioom

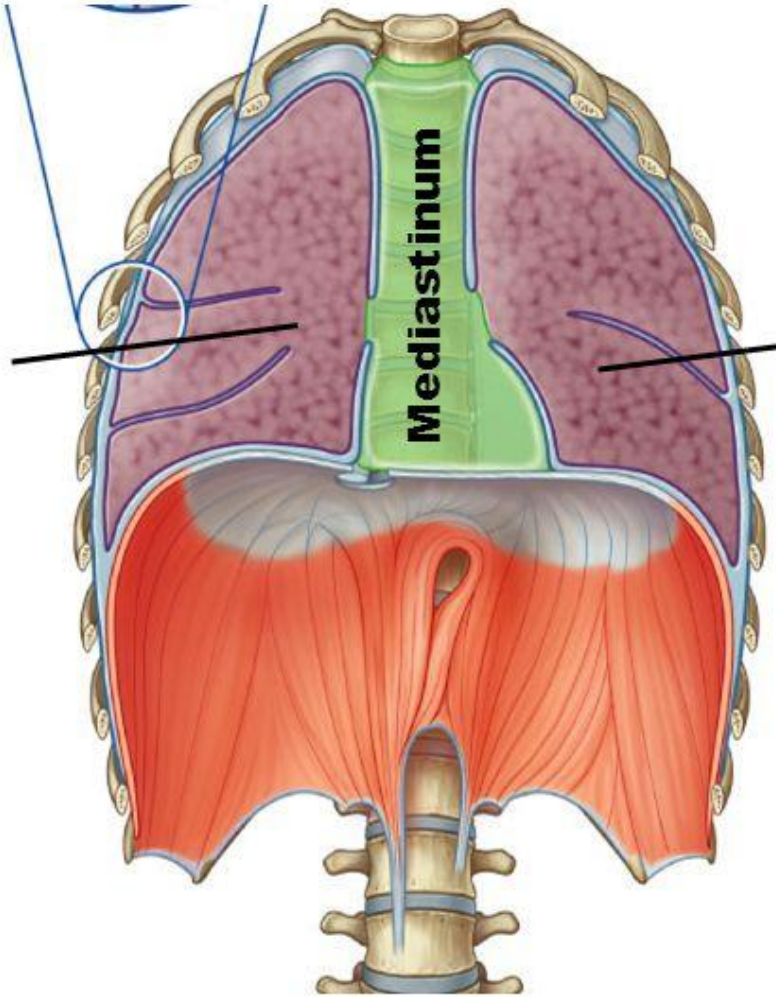
- Oesofagustumoren
- Thoraxwandsarcomen
- Harttumoren

Thymoom - zwezerik tumor



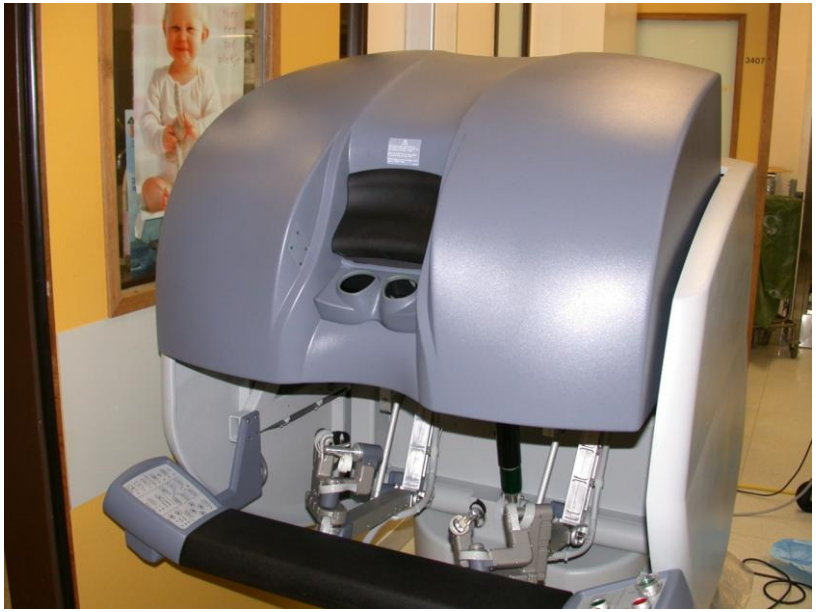


Chest Cavity



pleurae & lungs

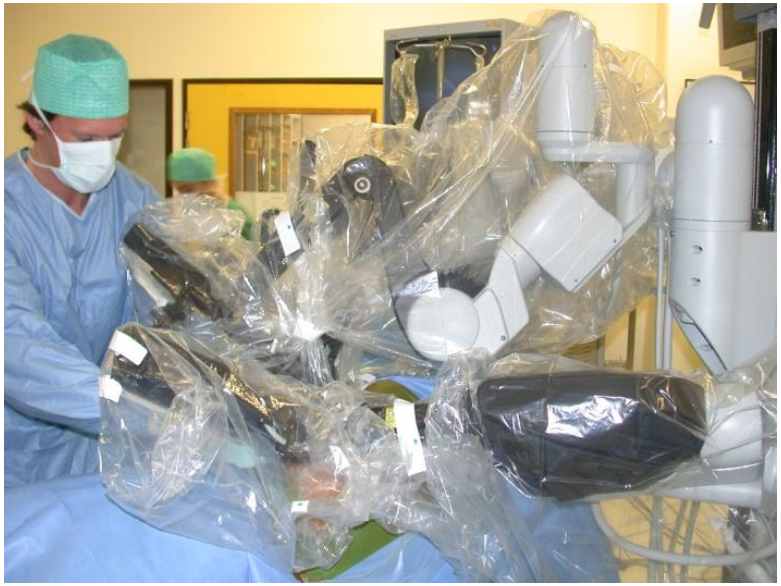
pleurae & lungs

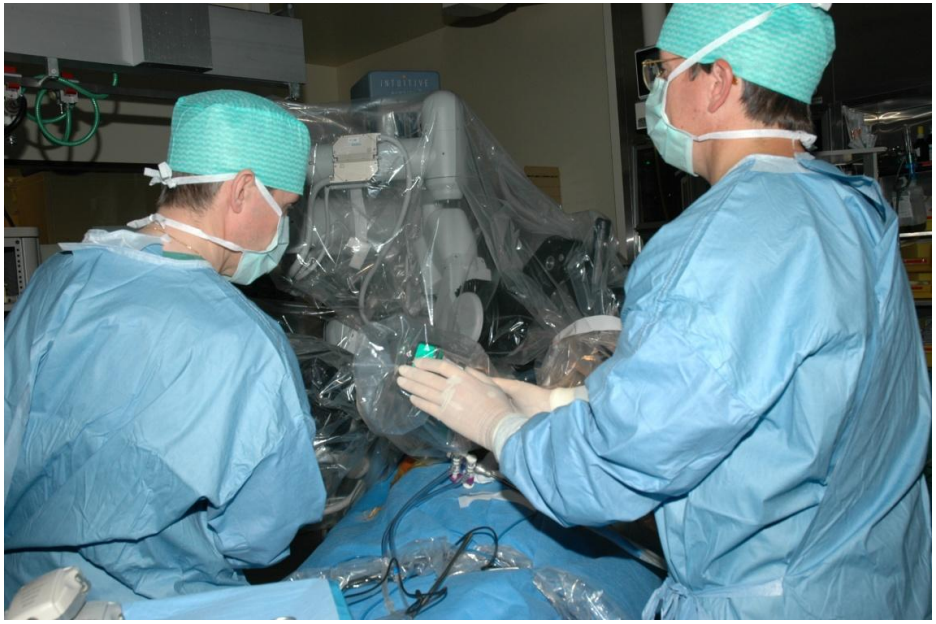


Behandeling

Gericht op resectie

Liefst middels robot-chirurg





Met dank aan Paul van Schil

Chemotherapie

- Etoposide is het enige geregistreerde middel in Nederland

- Meerdere chemotherapeutica hebben een responskans van 10-50%

Targeted therapy

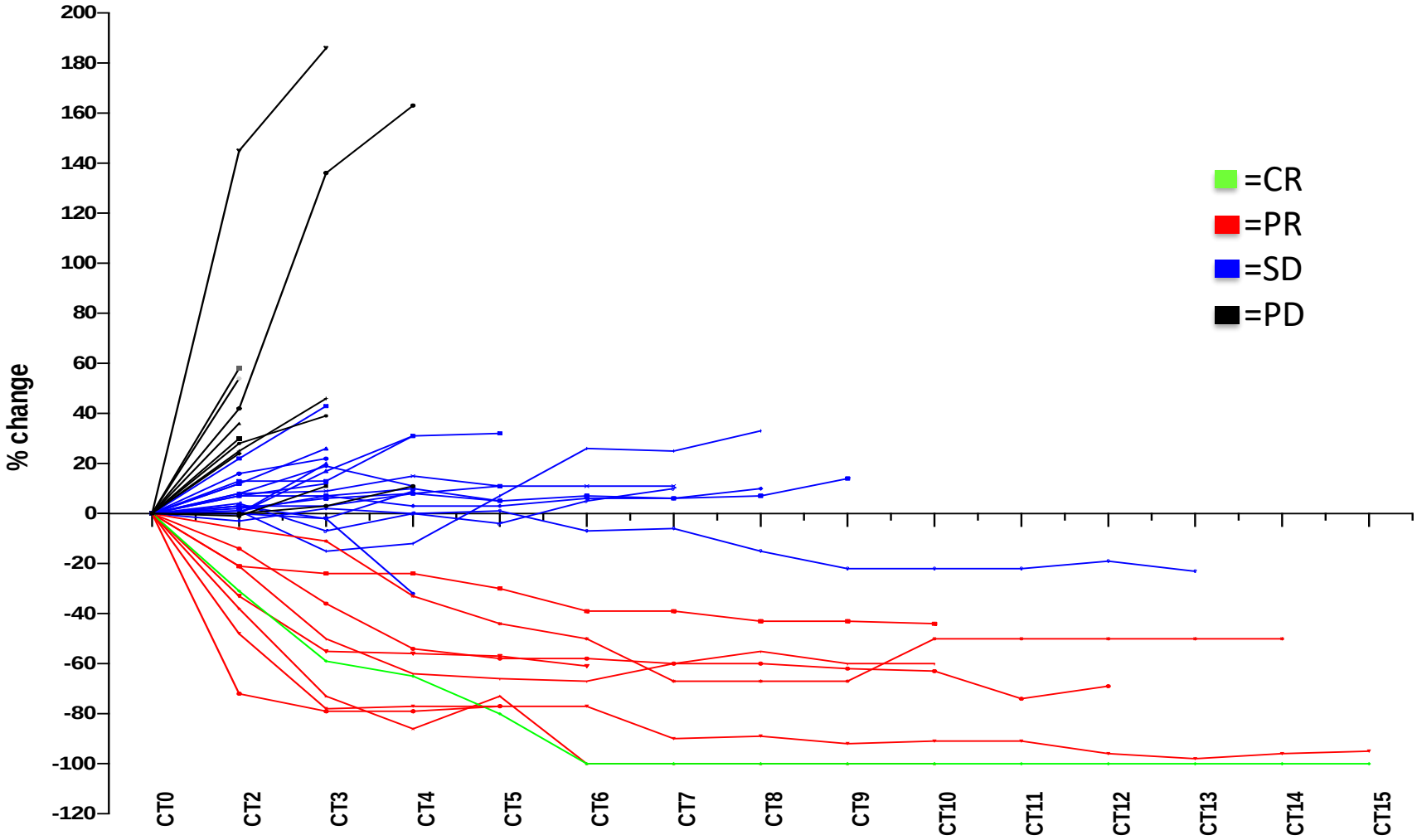
MA10.07: Phase II Trial of Sunitinib in Patients with Type B3 Thymoma or Thymic Carcinoma in Second and Further Lines - STYLE Trial (NCT03449173) – Proto C, et al

- **Key results (cont.)**

Responses	B3 thymoma (n=12) Interim analysis	Thymic carcinoma (n=23) Efficacy analysis	Thymic carcinoma (n=31) ITT analysis
ORR, n (%) [95%CI]	0 [0, 26.5]	5 (21.7) [7.5, 43.7]	6 (21.4) [8.3, 41.0]
BOR, n (%)			
CR	0	1 (4.3)	1 (3.6)
PR	0	4 (17.4)	5 (17.9)
SD	11 (91.7)	15 (65.2)	19 (67.9)
PD	1 (8.3)	3 (13.0)	3 (10.7)
NE	0	0	3 (9.7)
DCR, n (%) [95%CI]	11 (91.7) [61.5, 99.8]	20 (87.0) [66.4, 97.2]	25 (89.3) [71.8, 97.7]

- **Conclusions**
  - In previously treated patients with thymic carcinoma, sunitinib demonstrated clinical activity but accrual in the B3 thymoma cohort was stopped owing to futility

Immunotherapy
Pembrolizumab in Thymic Carcinoma



Giaccone Lancet Oncology 2018; 19:347

Severe IRAEs

- Polymyositis/**myocarditis**
- Hepatitis/pancreatitis/Diabetes mell type 1
- Bullous pemphigoid
- Polymyositis/hepatitis/myocarditis
- **Myasthenia Gravis**
- Polymyositis/hepatitis
- Grade 3 transaminitis

Giaccone Lancet Oncology 2018; 19:347

De boodschap:

- Met uitzondering van studies:

IMMUUNTHERAPIE

IS

GE**CONTRA**-INDICEERD

BIJ THYMUSTUMOREN

Thymomen Nederland vanaf 2022

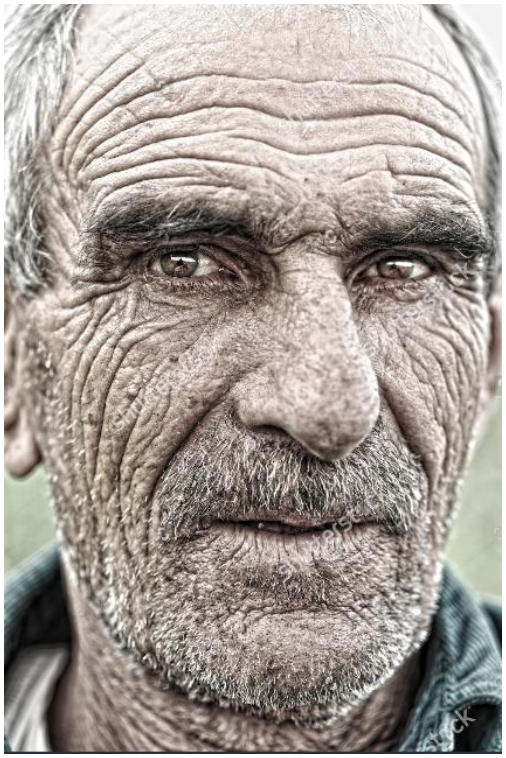
- Het landelijk thymomen-overleg loopt

- Geen nieuwe therapeutische vorderingen

Niet-kleincellig longkanker

Second law of oncology

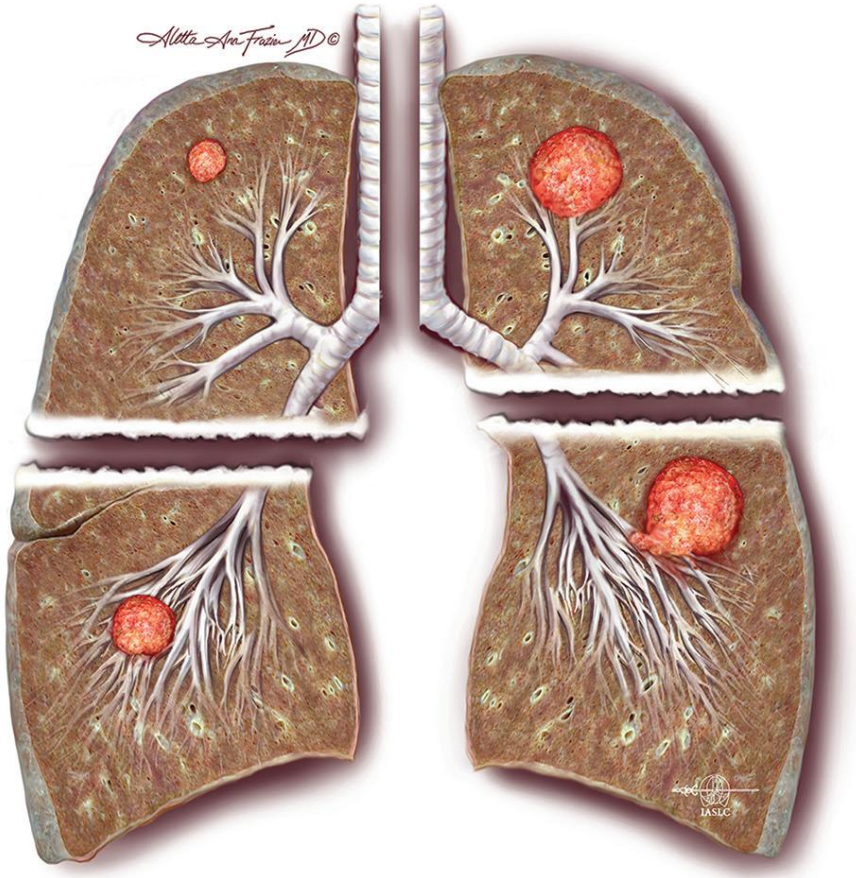
- The tumor has to shrink faster than the patient



Nick Thatcher, oncologist, Manchester

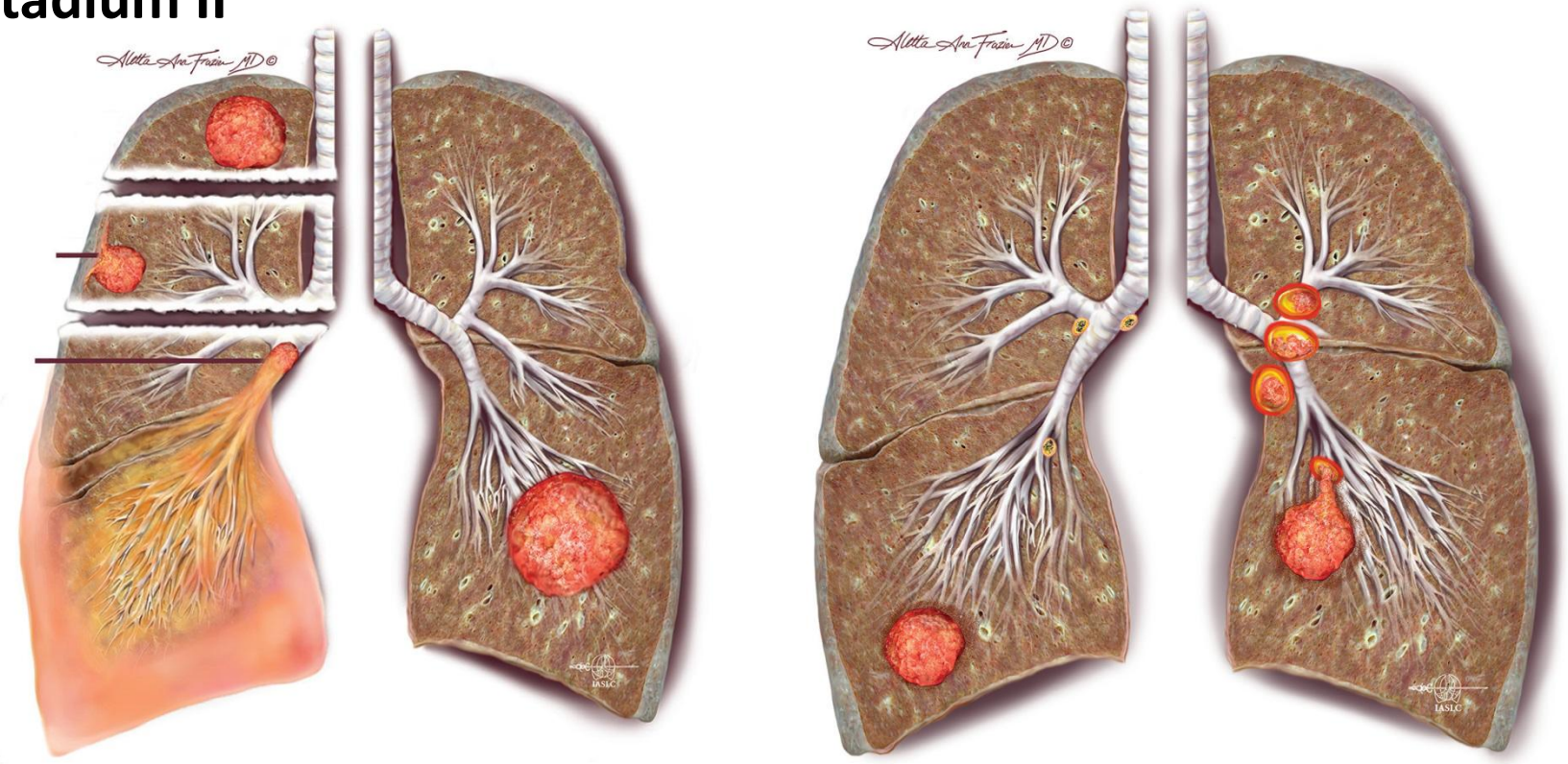
Tumorstadia bij NSCLC

Stadium I



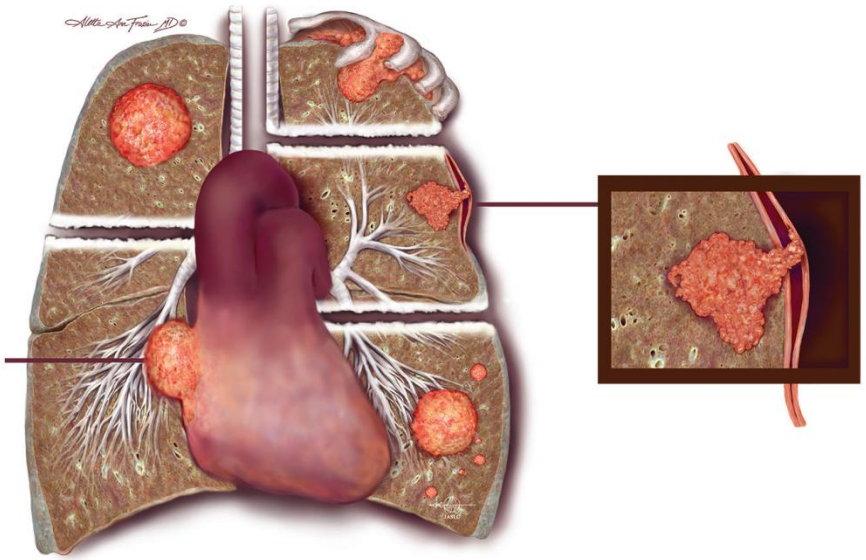
Tumorstadia bij NSCLC

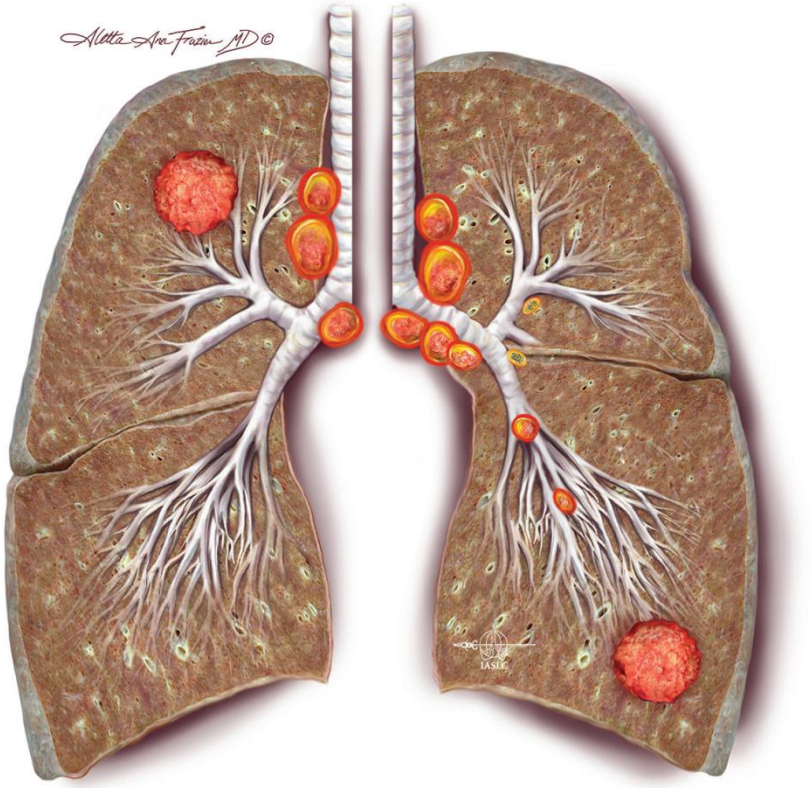
Stadium II



Tumorstadia bij NSCLC

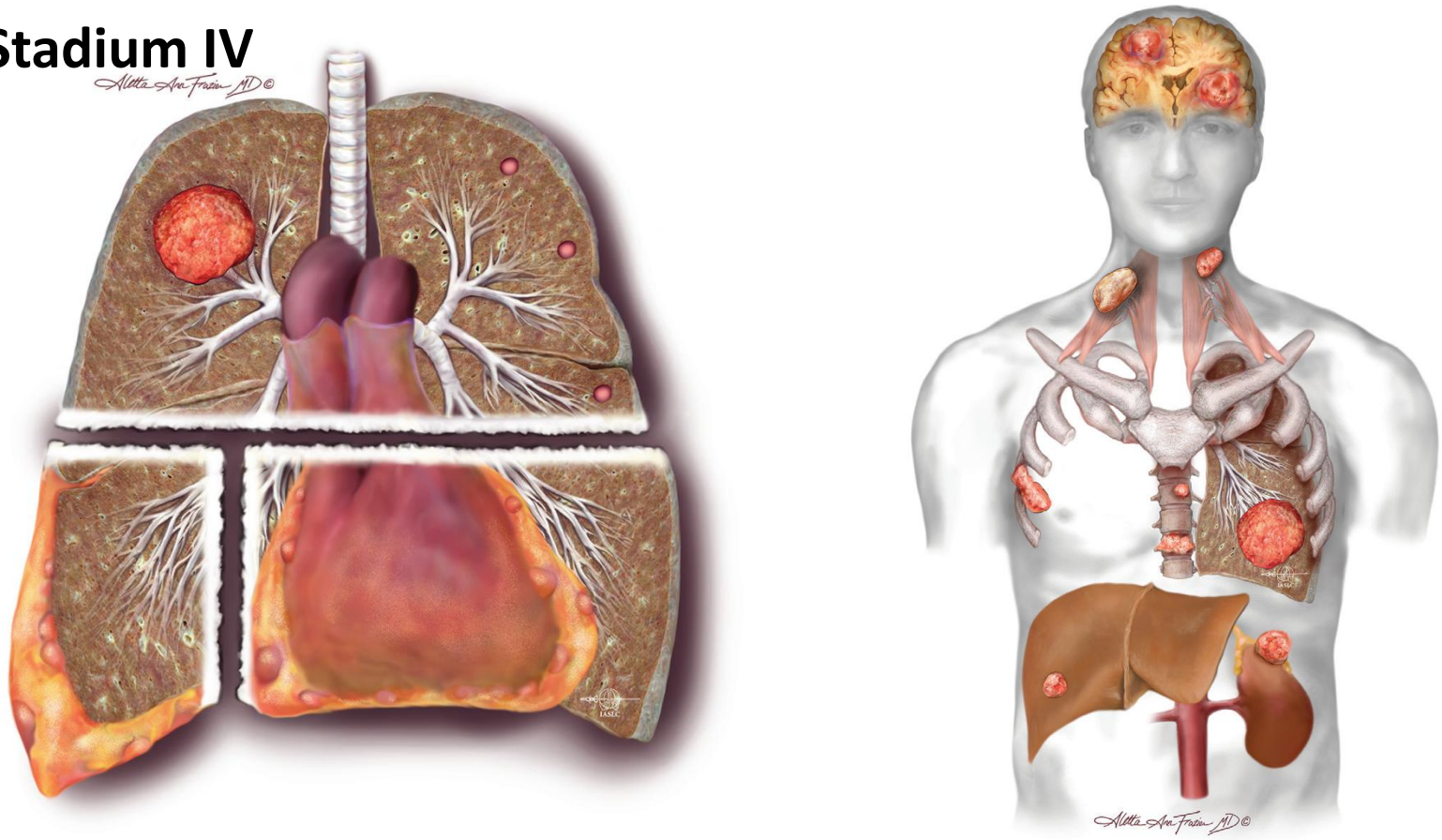
Stadium III



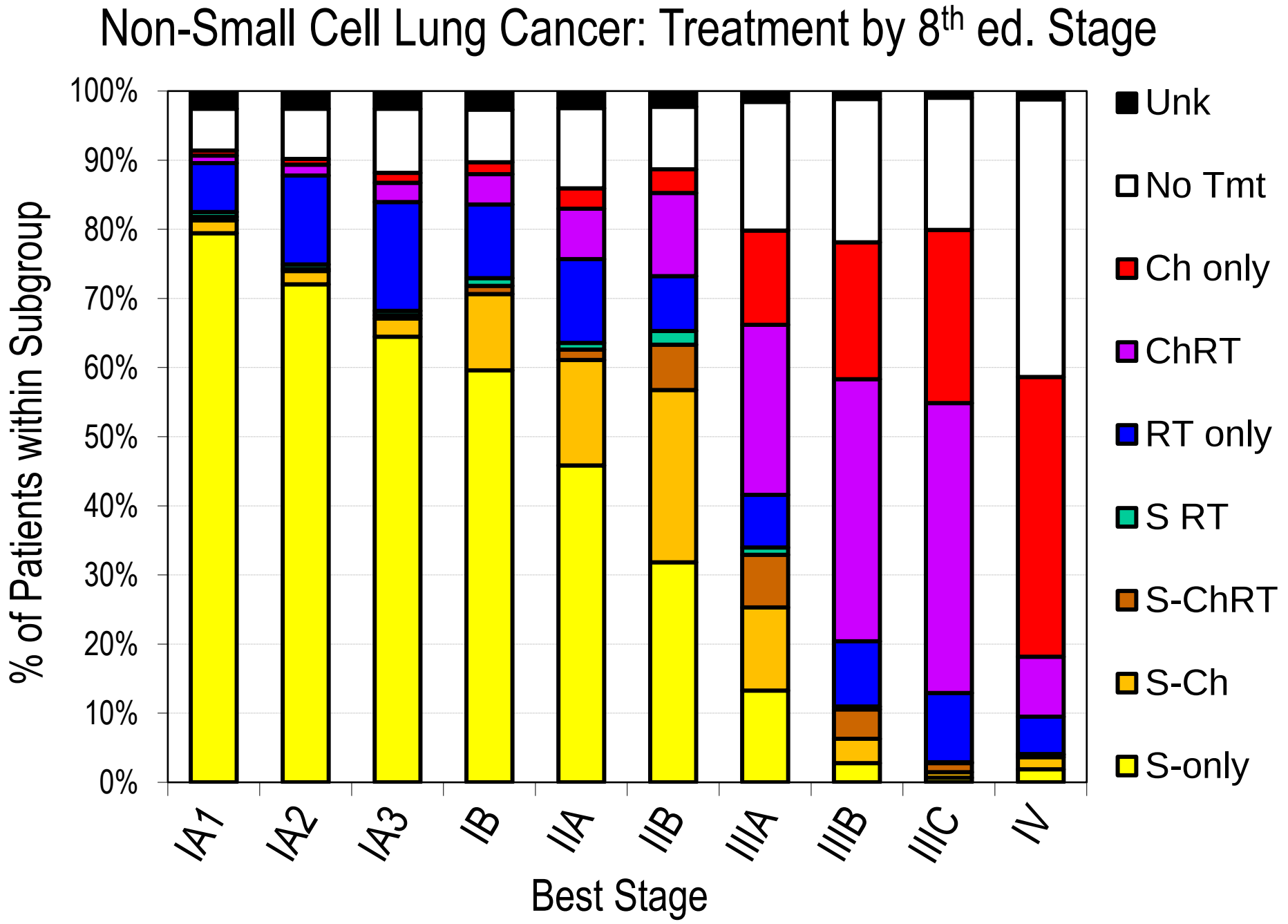


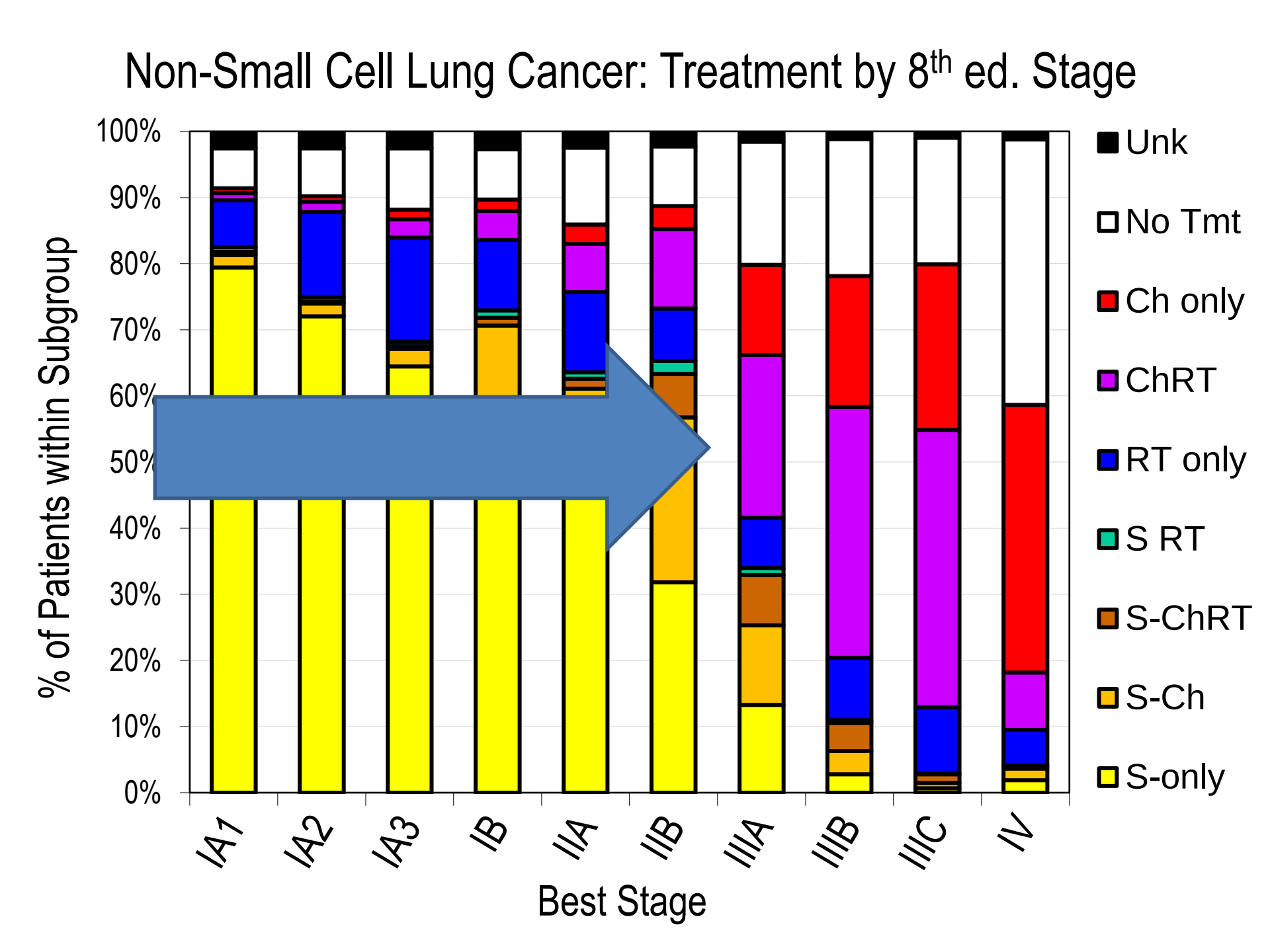
Tumorstadia NSCLC

Stadium IV



Staging manual in Thoracic Oncology. Ed Rami-Porta. IASLC. 2016


Non-Small Cell Lung Cancer: Treatment by 8th ed. Stage
% of Patients within Subgroup
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
IA1
IA2
IA3
IB
IIA
IIB
IIIA
IIIB
IIIC
IV
Best Stage
Unk
No Tmt
Ch only
ChRT
RT only
S RT
S-ChRT
S-Ch
S-only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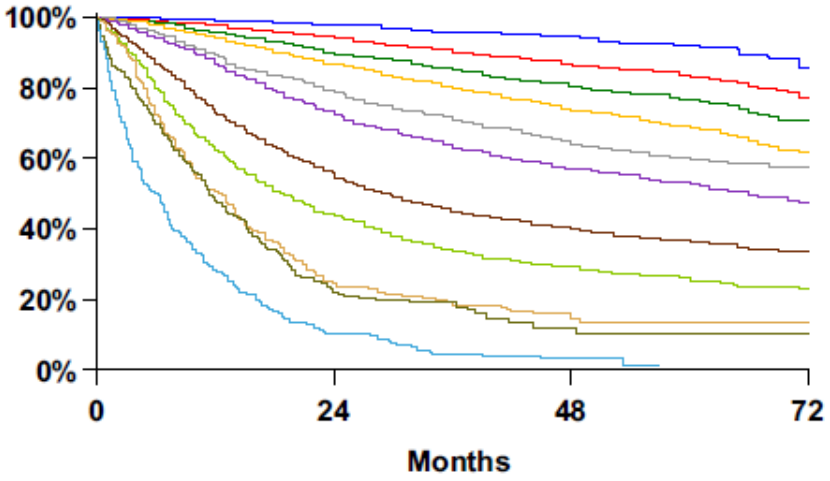
IA3
IB
IIA
IIB
IIIA
IIIB
IIIC
IV
Best Stage
Unk
No Tmt
Ch only
ChRT
RT only
S RT
S-ChRT
S-Ch
S-only

Overleving NSCLC naar tumorstadium



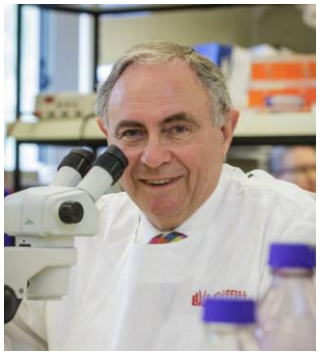
Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

Goldstraw JTO 2015

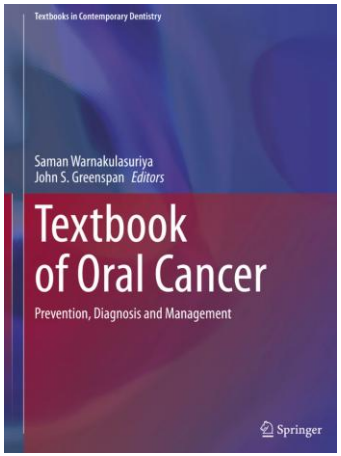
klinisch tumorstadium

First law of oncology

- Every solid neoplasm is a systemic disease



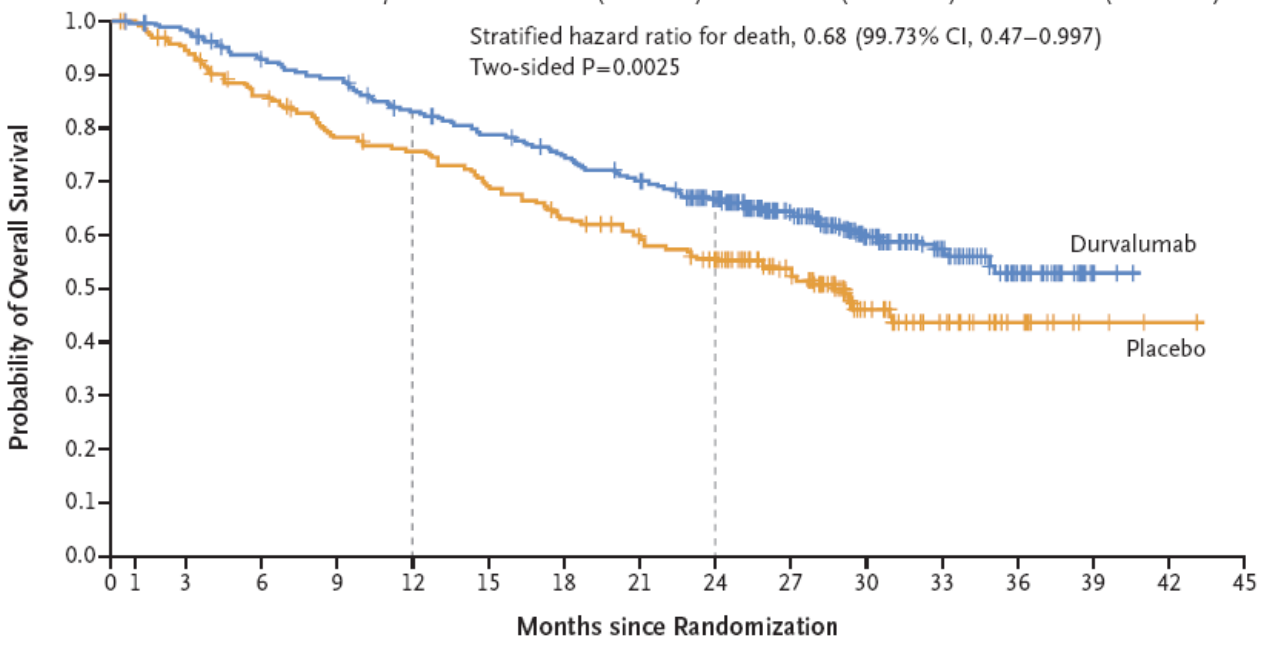
Newell Johnson in Textbook of Oral Cancer 2020



St III NSCLC Adjuvant immuuntherapie na chemoradiotherapie

St III NSCLC Adjuvant immuuntherapie na chemoradiotherapie

	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



No. at Risk															
Durvalumab	476	464	431	415	385	364	343	319	274	210	115	57	23	2	0	0
Placebo	237	220	198	178	170	155	141	130	117	78	42	21	9	3	1	0

Antonia NEJM 2018

De boodschap:

ADJUVANTE IMMUUNTHERAPIE

BIJ STADIUM III NSCLC

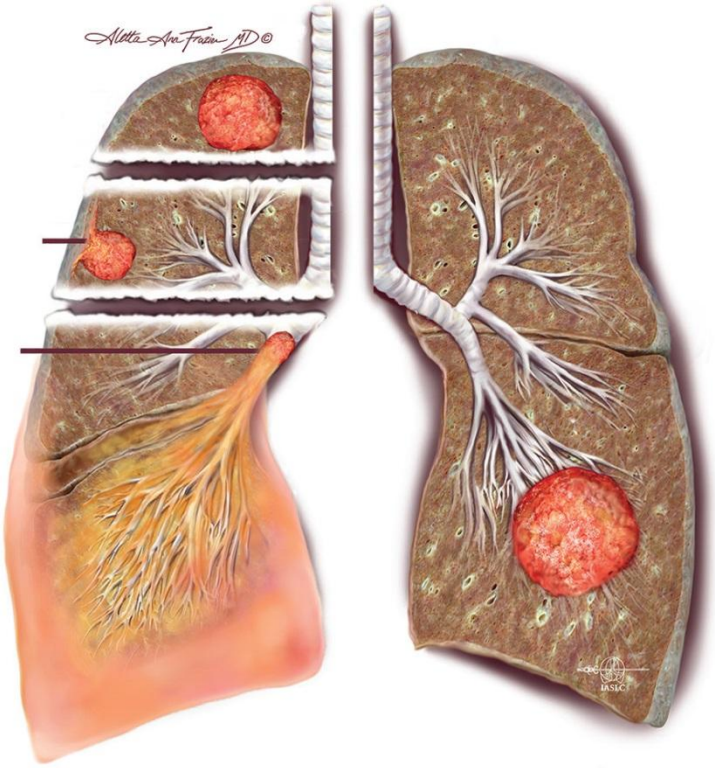
NA CHEMORADIOTHERAPIE

BEREIKT EEN RELEVANTE

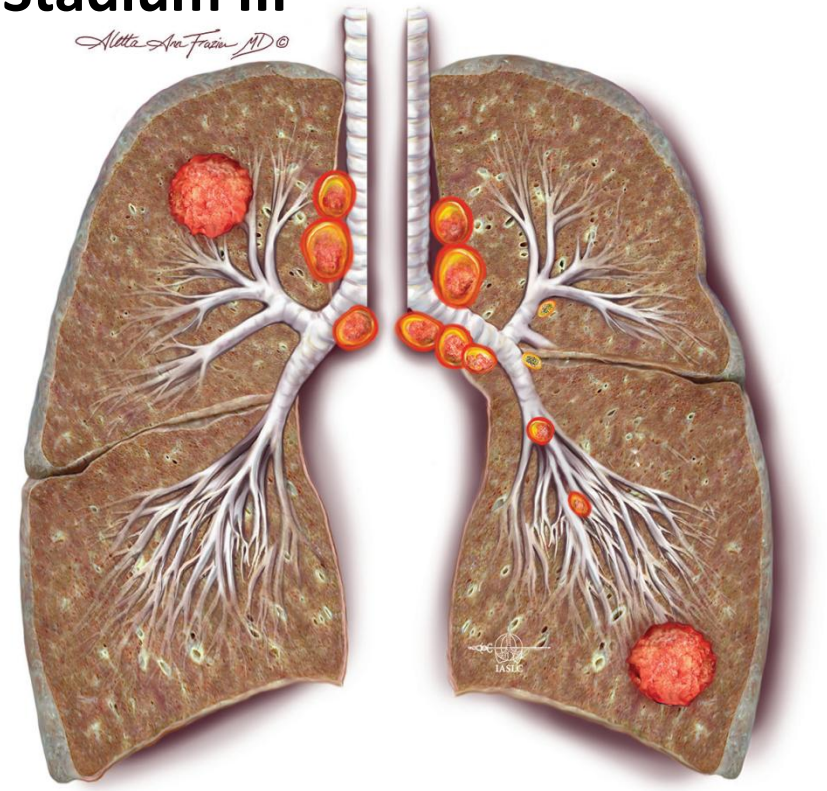
OVERLEVINGSWINST

Chirurgie bij stadium II-III NSCLC? En dan?

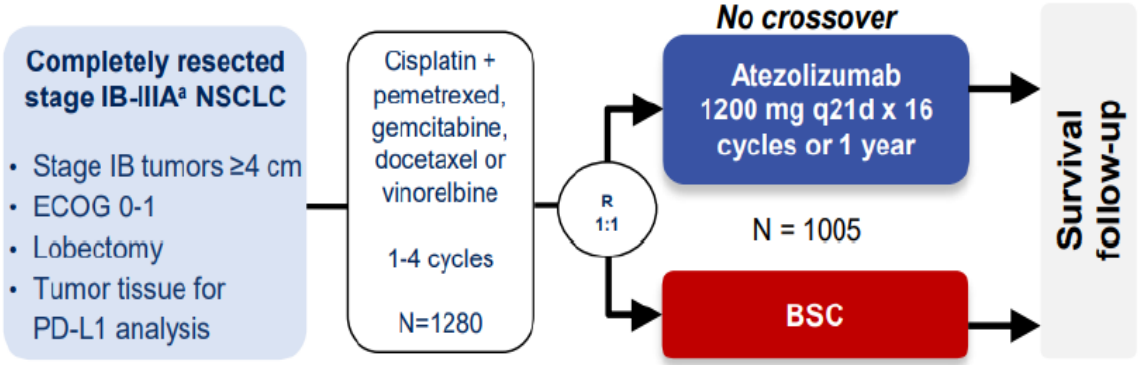
Stadium II



Stadium III



IMpower010: Phase III randomised trial of atezolizumab vs BSC in early-stage NSCLC

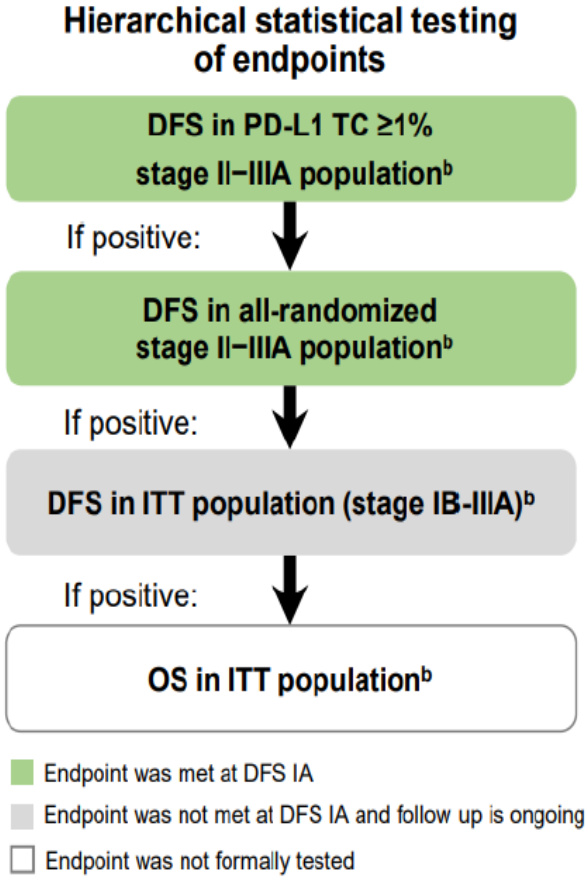


Stratification factors
- Sex | Stage | Histology | PD-L1 status

Primary endpoint
- Investigator-assessed DFS tested hierarchically

Key secondary endpoints
- OS in ITT | DFS in PD-L1 TC ≥50% | 3-yr and 5-year DFS

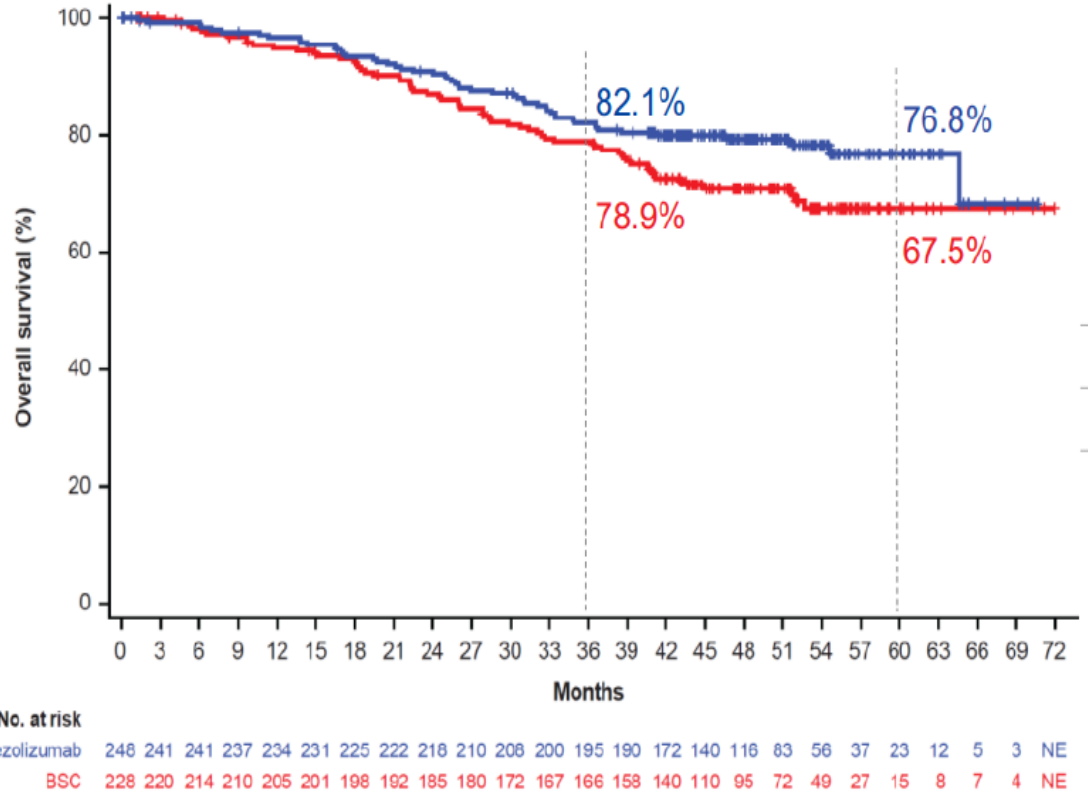
Key exploratory endpoints
- OS biomarker analyses



Clinical cutoff: 18 April 2022. Both arms included observation and regular scans for disease recurrence on the same schedule. ECOG, Eastern Cooperative Oncology Group, q21d, every 21 days.
[a] Per UICC/AJCC staging system, 7th edition. [b] Two-sided α=0.05.

Results of OS IA: PD-L1 TC ≥1%[a] (stage II-IIIA)

(data cutoff: 18 Apr '22, median follow-up: 46 months)

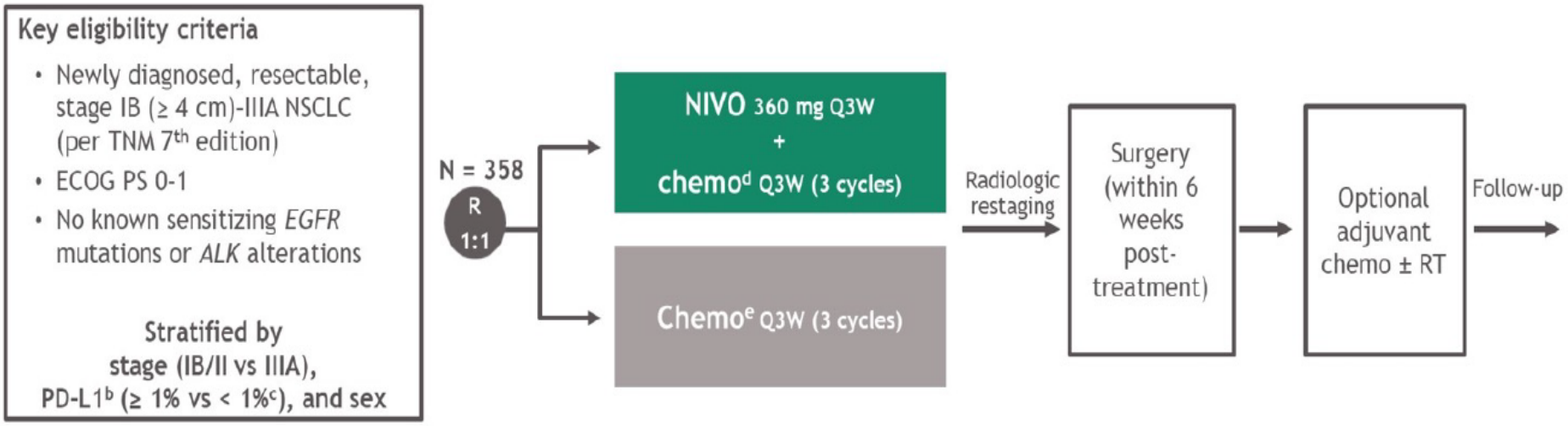


	Atezo (n=248)	BSC (n=228)
Events, n (%)	52 (21.0%)	64 (28.1%)
mOS (95% CI), mo	NR	NR
HR (95% CI)[b]	0.71 (0.49, 1.03)	

mOS, median overall survival; NR, not reached. [a]By SP263 assay. [b]Stratified.

NEO-ADJUVANT
Chemo-immuuntherapie voor de OK

CheckMate 816 study design[a,1]



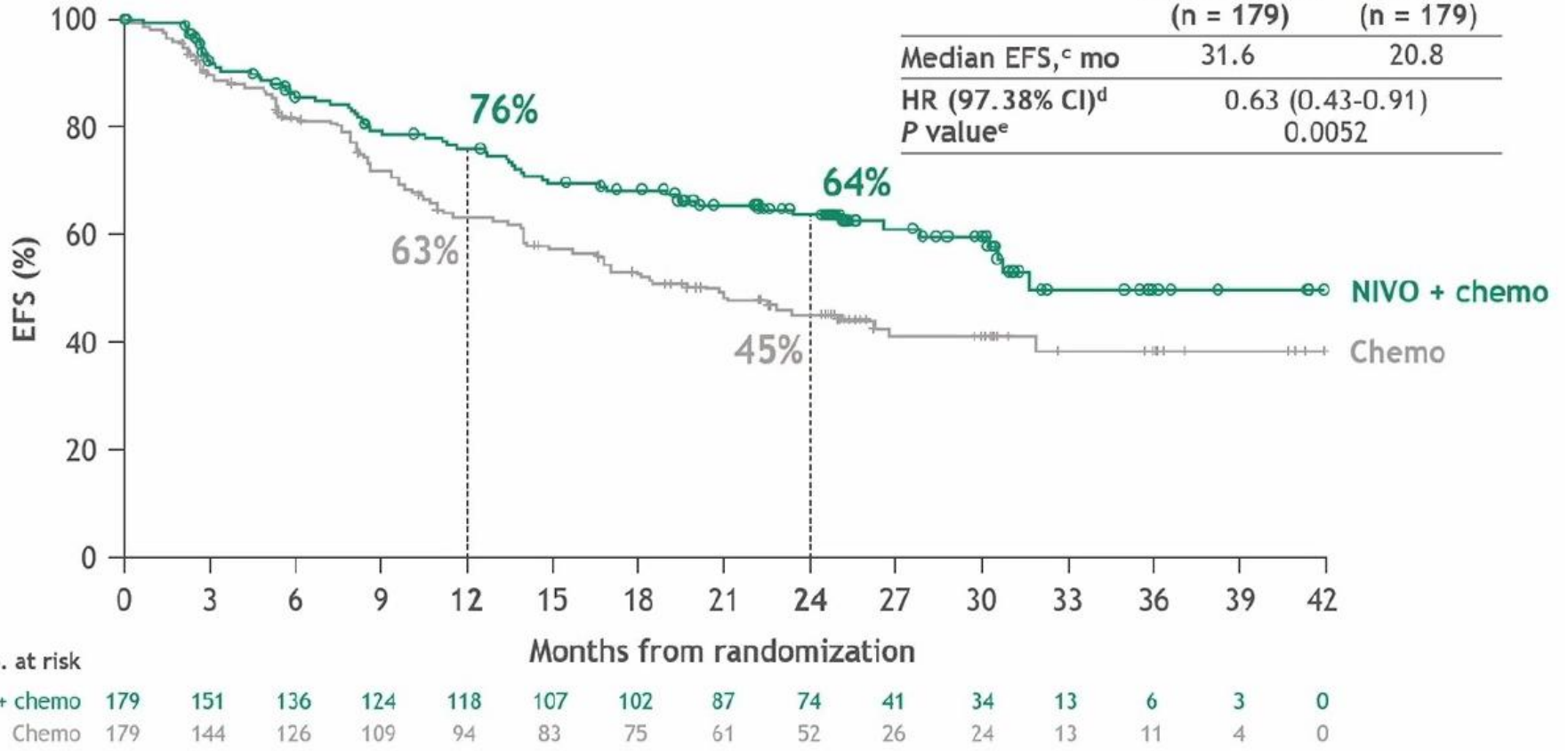
Primary endpoints
- pCR by BIPR
- EFS by BICR

Key secondary endpoints
- MPR by BIPR
- OS
- Time to death or distant metastases

Key exploratory endpoints included
- ORR by BICR
- Feasibility of surgery; peri- and post-operative surgery-related AEs

Immuno voor operatie geeft voordeel

Primary endpoint: EFS[a,b] with neoadjuvant NIVO + chemo vs chemo



Minimum follow-up: 21 months; median follow-up, 29.5 months.

[a]Per BICR; [b]EFS defined as the time from randomization to any progression of disease precluding surgery, progression or recurrence of disease after surgery, progression for patients without surgery, or death due to any cause; patients with subsequent therapy were censored at the last evaluable tumor assessment on or prior to the date of subsequent therapy; [c]95% CI = 30.2-NR (NIVO + chemo) and 14.0-26.7 (chemo); [d]95% CI = 0.45-0.87; [e]The significance boundary at this interim analysis was 0.0262.

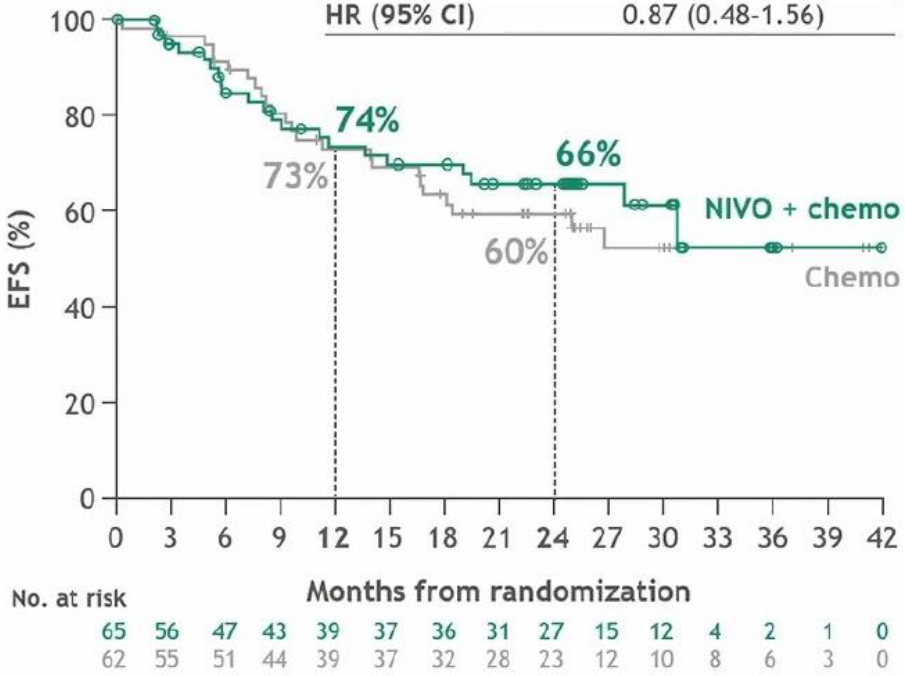
Meeste winst bij hogere stadia

CheckMate 816: EFS with neoadjuvant NIVO + chemo in resectable NSCLC

EFS by baseline stage of disease

Stage IB-II

	NIVO + chemo (n = 65)	Chemo (n = 62)
Median EFS,[a] mo	NR	NR
HR (95% CI)	0.87 (0.48-1.56)	

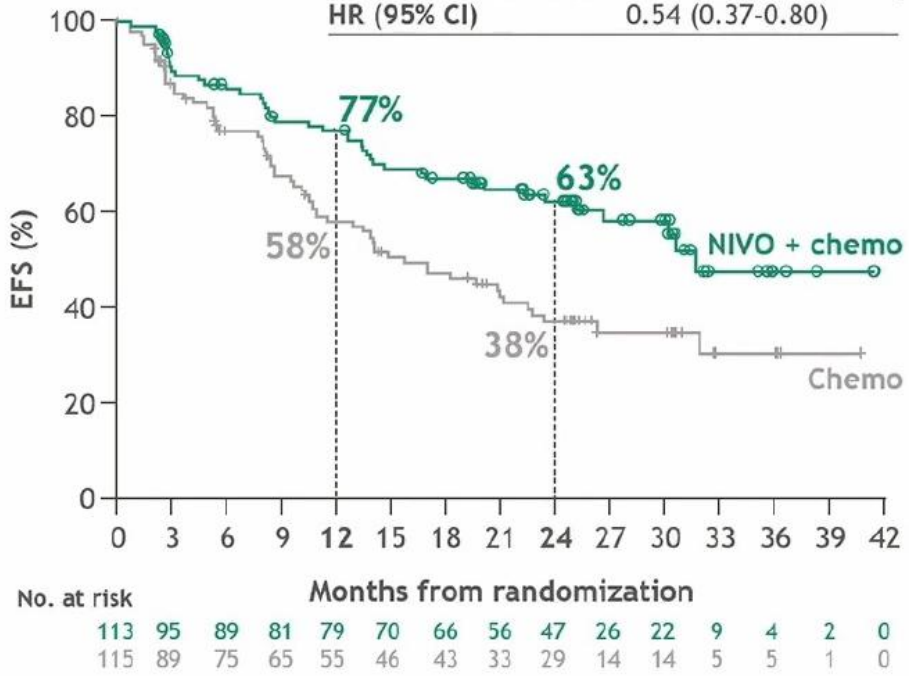


No. at risk

65	56	47	43	39	37	36	31	27	15	12	4	2	1	0
62	55	51	44	39	37	32	28	23	12	10	8	6	3	0

Stage IIIA

	NIVO + chemo (n = 113)	Chemo (n = 115)
Median EFS,[b] mo	31.6	15.7
HR (95% CI)	0.54 (0.37-0.80)	



No. at risk

113	95	89	81	79	70	66	56	47	26	22	9	4	2	0
115	89	75	65	55	46	43	33	29	14	14	5	5	1	0

Minimum follow-up: 21 months; median follow-up, 29.5 months.

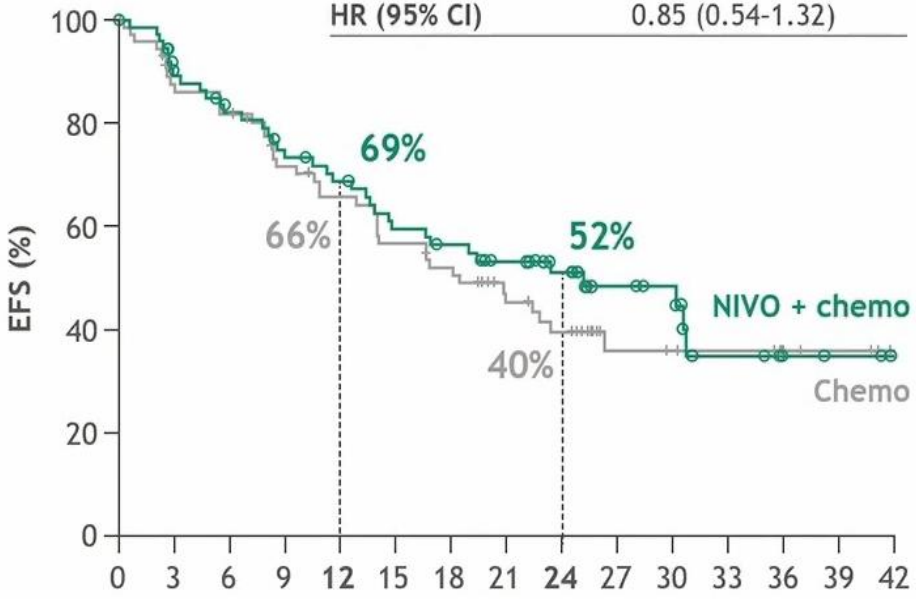
[a]95% CI = 27.8-NR (NIVO + chemo) and 16.8-NR (chemo); [b]95% CI = 26.6-NR (NIVO + chemo) and 10.8-22.7 (chemo).

Winst vooral bij PD-L1 expressie

EFS by tumor PD-L1 expression < 1% or ≥ 1%

PD-L1 < 1%

	NIVO + chemo (n = 78)	Chemo (n = 77)
Median EFS,[a] mo	25.1	18.4
HR (95% CI)	0.85 (0.54-1.32)	

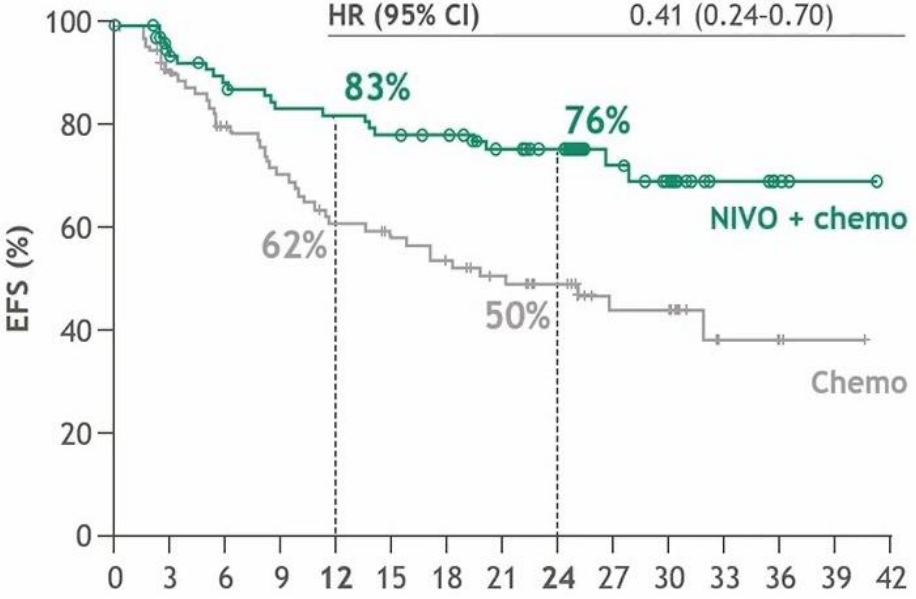


No. at risk

78	65	57	51	46	39	36	30	24	15	13	6	3	2	0
77	62	58	49	44	38	34	25	21	10	9	8	6	3	0

PD-L1 ≥ 1%

	NIVO + chemo (n = 89)	Chemo (n = 89)
Median EFS,[b] mo	NR	21.1
HR (95% CI)	0.41 (0.24-0.70)	



No. at risk

89	76	69	66	65	62	60	53	47	24	19	7	3	1	0
89	71	60	53	45	41	37	32	27	16	15	5	5	1	0

Minimum follow-up: 21 months; median follow-up, 29.5 months.

[a]95% CI = 14.6-NR (NIVO + chemo) and 13.9-26.2 (chemo); [b]95% CI = NR-NR (NIVO + chemo) and 11.5-NR (chemo).

De boodschap:

NEO-ADJUVANTE CHEMOIMMUUNTHERAPIE

is een geregistreerde behandeling

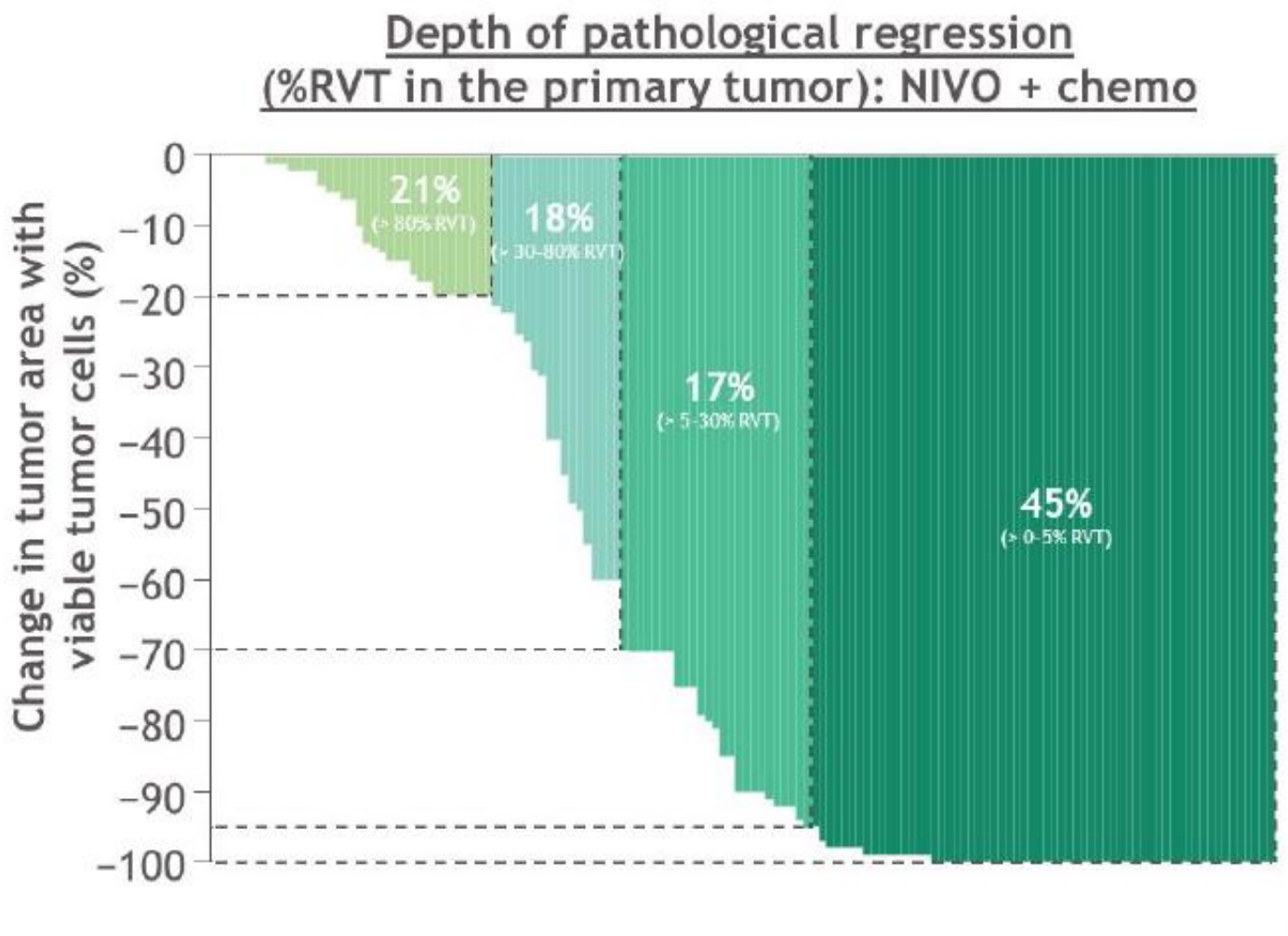
bij PD-L1 + stadium II-IIIa NSCLC

BEREIKT EEN RELEVANTE

WINST

Forde NEJM 2022

PA na de chemo-immuno:



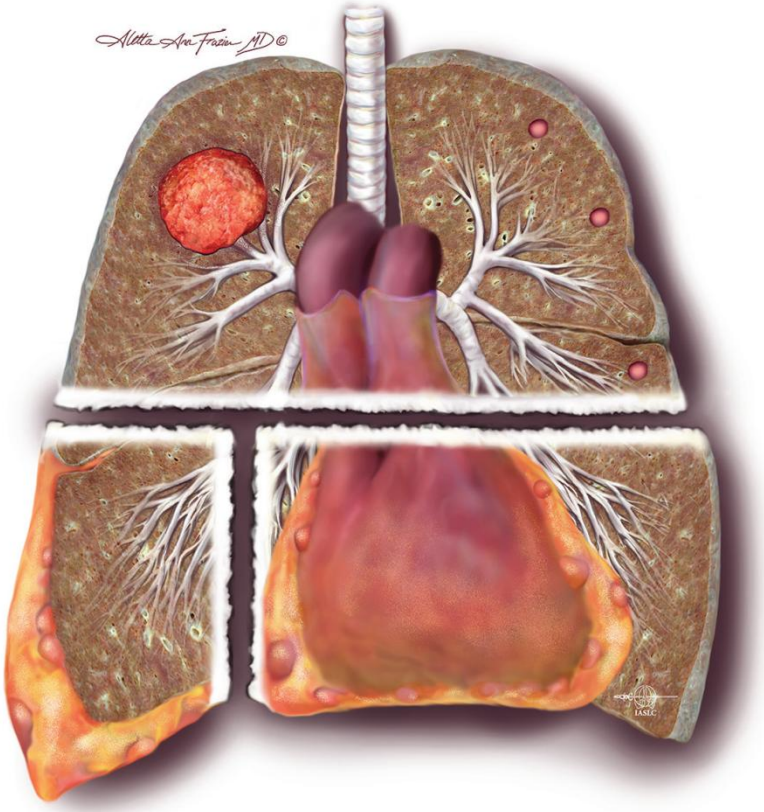
Minimum follow-up: 21 months; median follow-up: 29.5 months.

[a]Path-evaluable patient population.

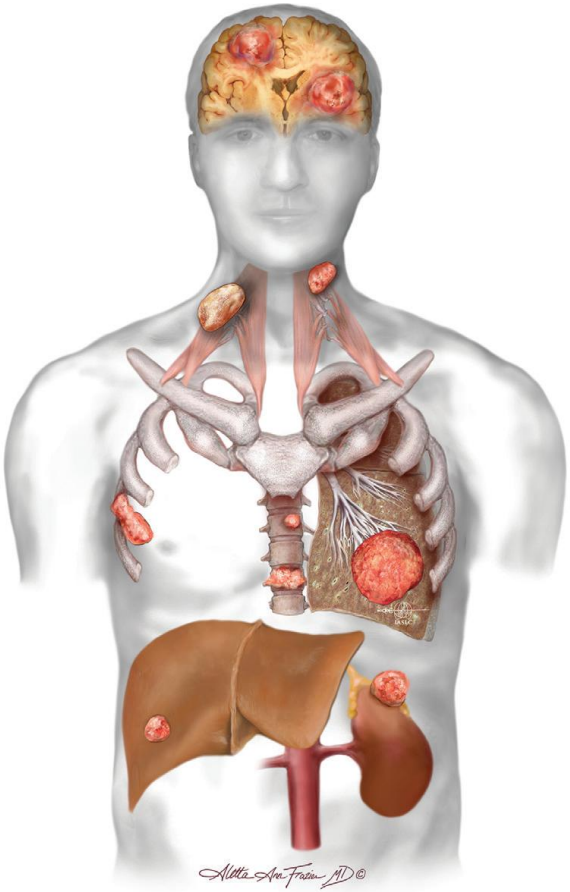
En nu?

- Neo-adjuvant?
- Adjuvant?
- Beide?
- Wie doe je tekort? Wie overbehandel je?

Stadium IV NSCLC

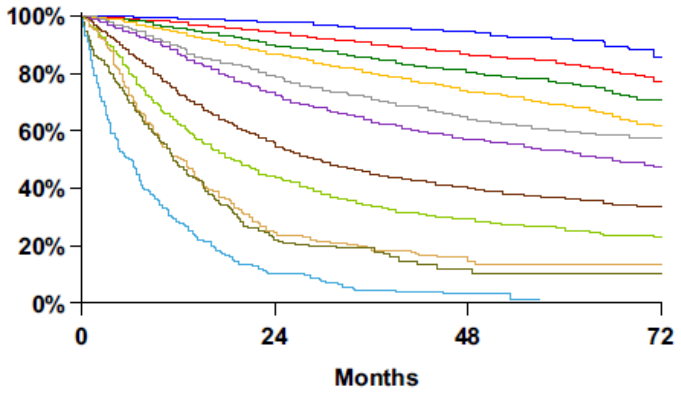


M1a

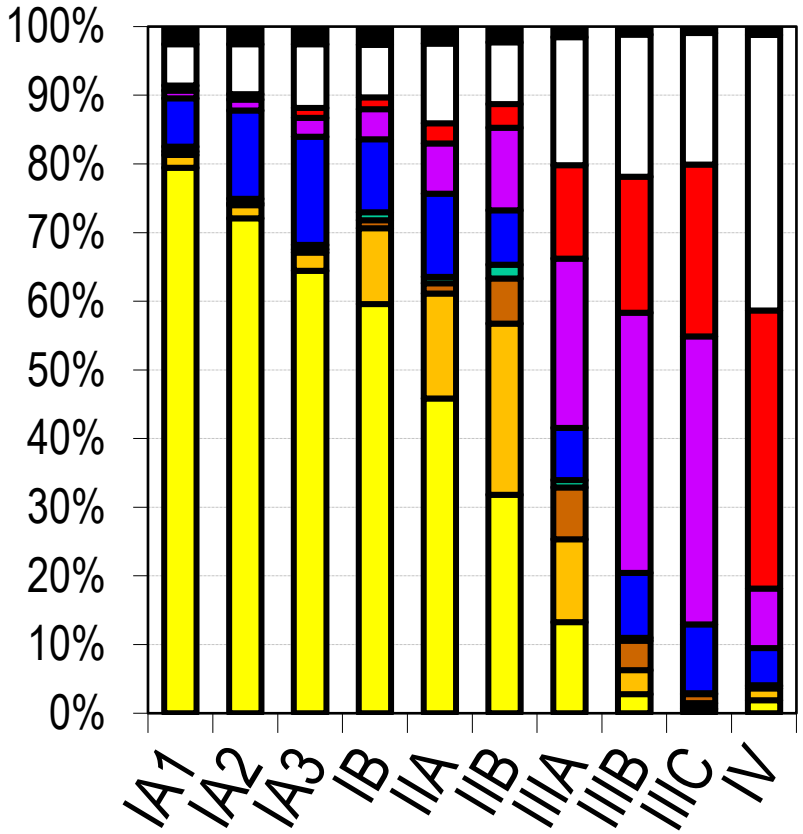


M1c

Stadium IV NSCLC



Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%



Nieuwe patient
met gemetastaseerd NSCLC

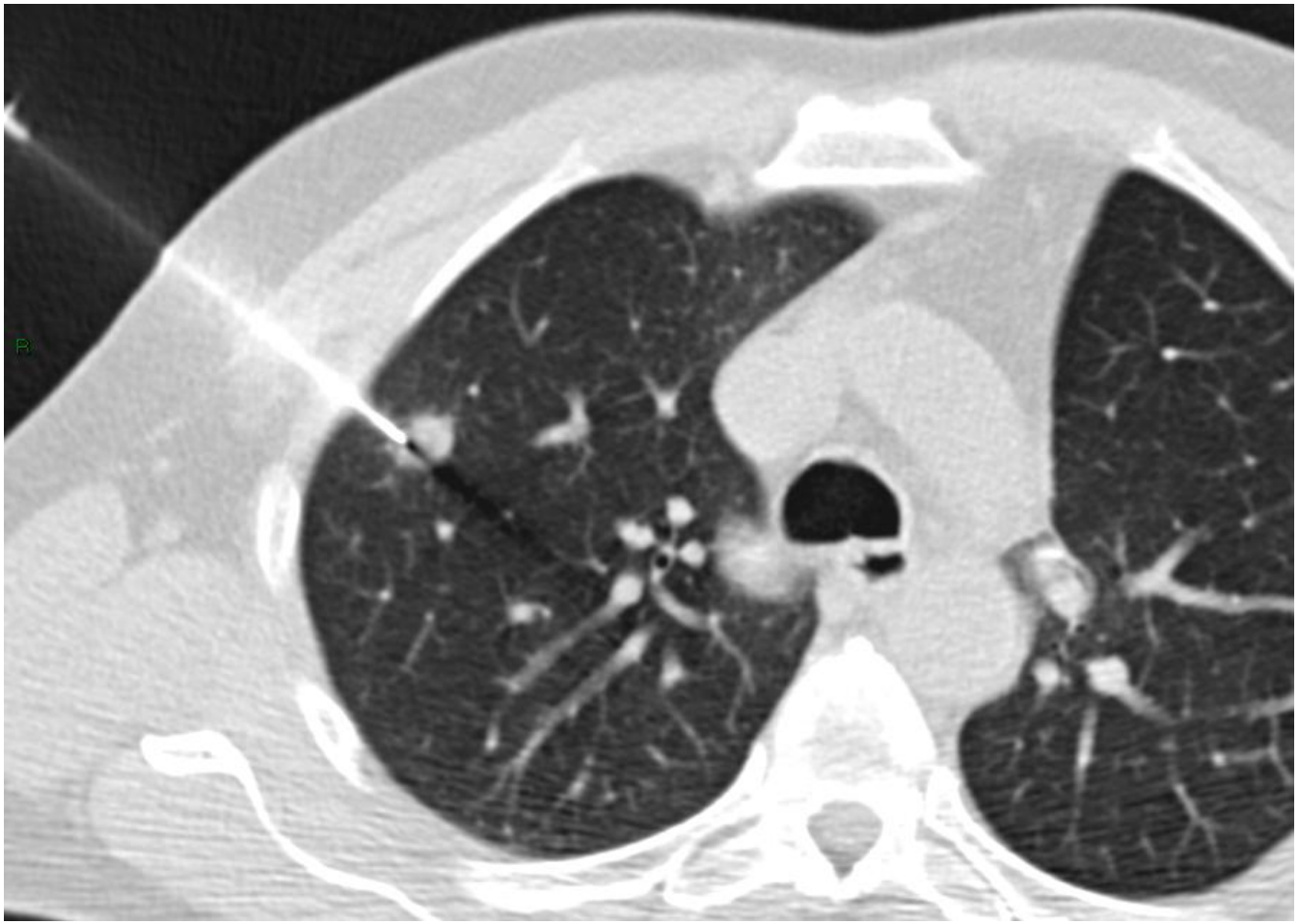
- Wat is het (bijna) eerste dat je wil weten?

PD-L1
en mutaties

- Bepalen de behandeling
- Bepalen de prognose

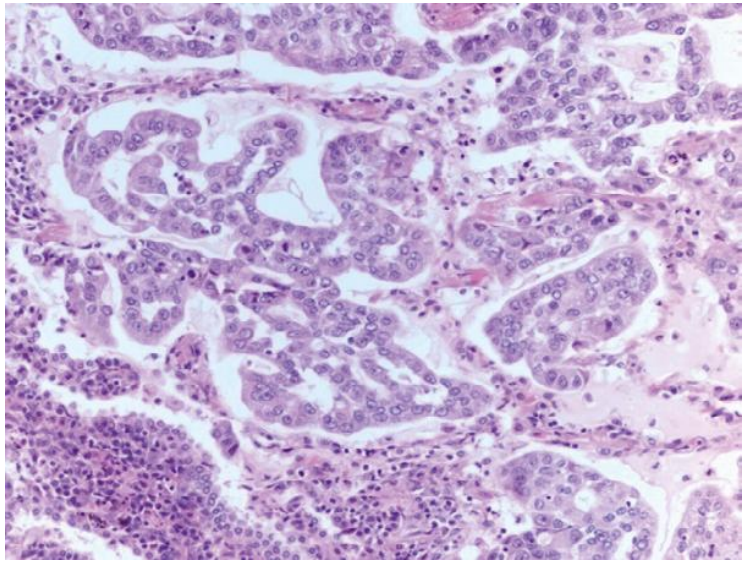
Mutaties:
De molecular tumor board

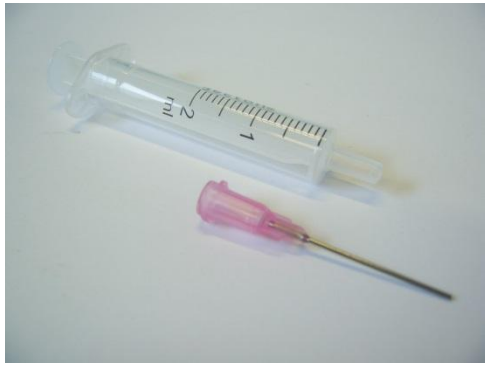
punctie

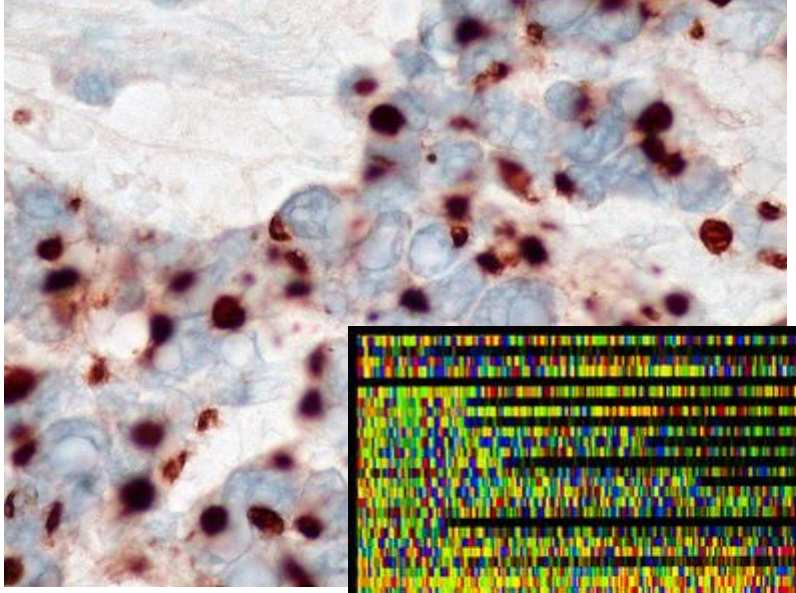


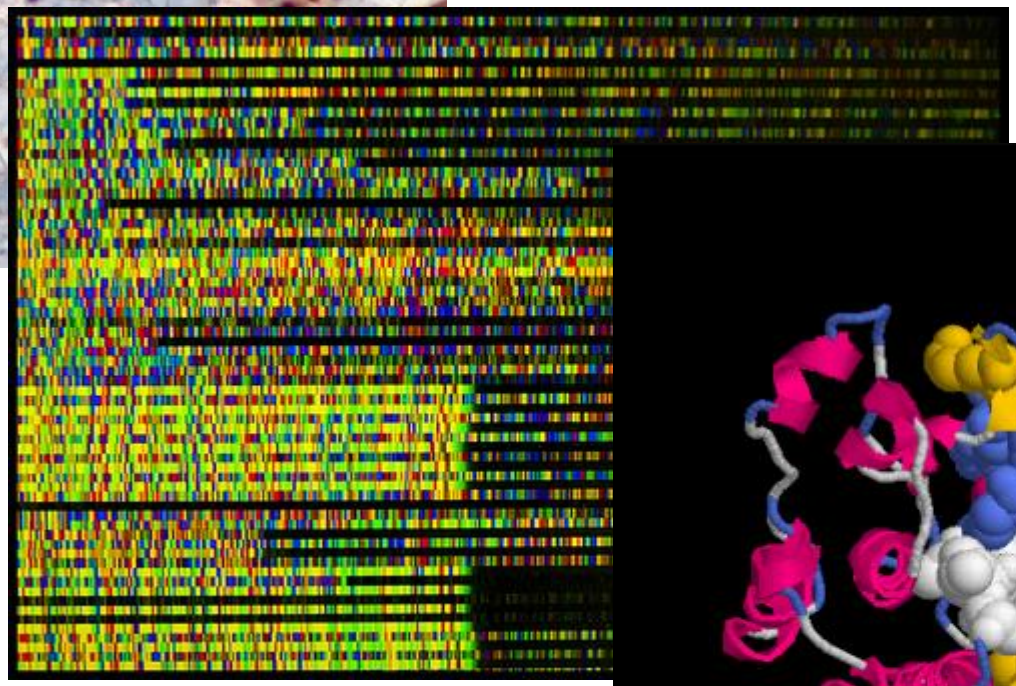
Materiaal verzamelen!

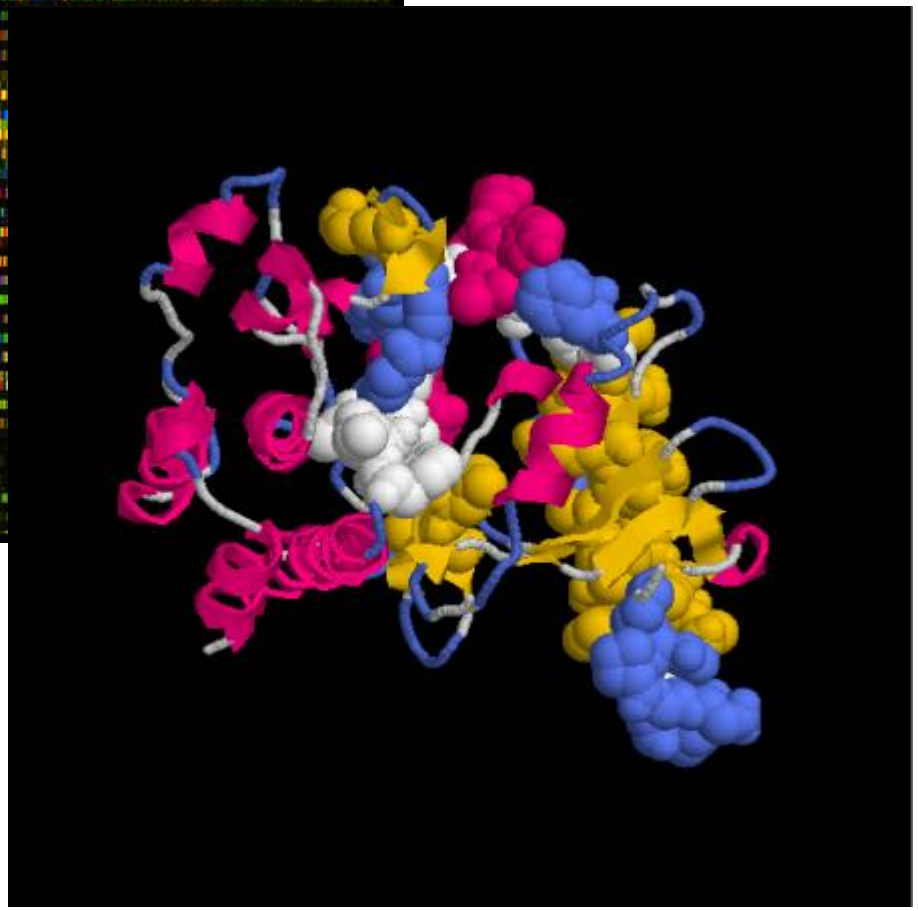
- bronchoscopie
- punctie van de long
- punctie van andere verdachte plekken
- operatie











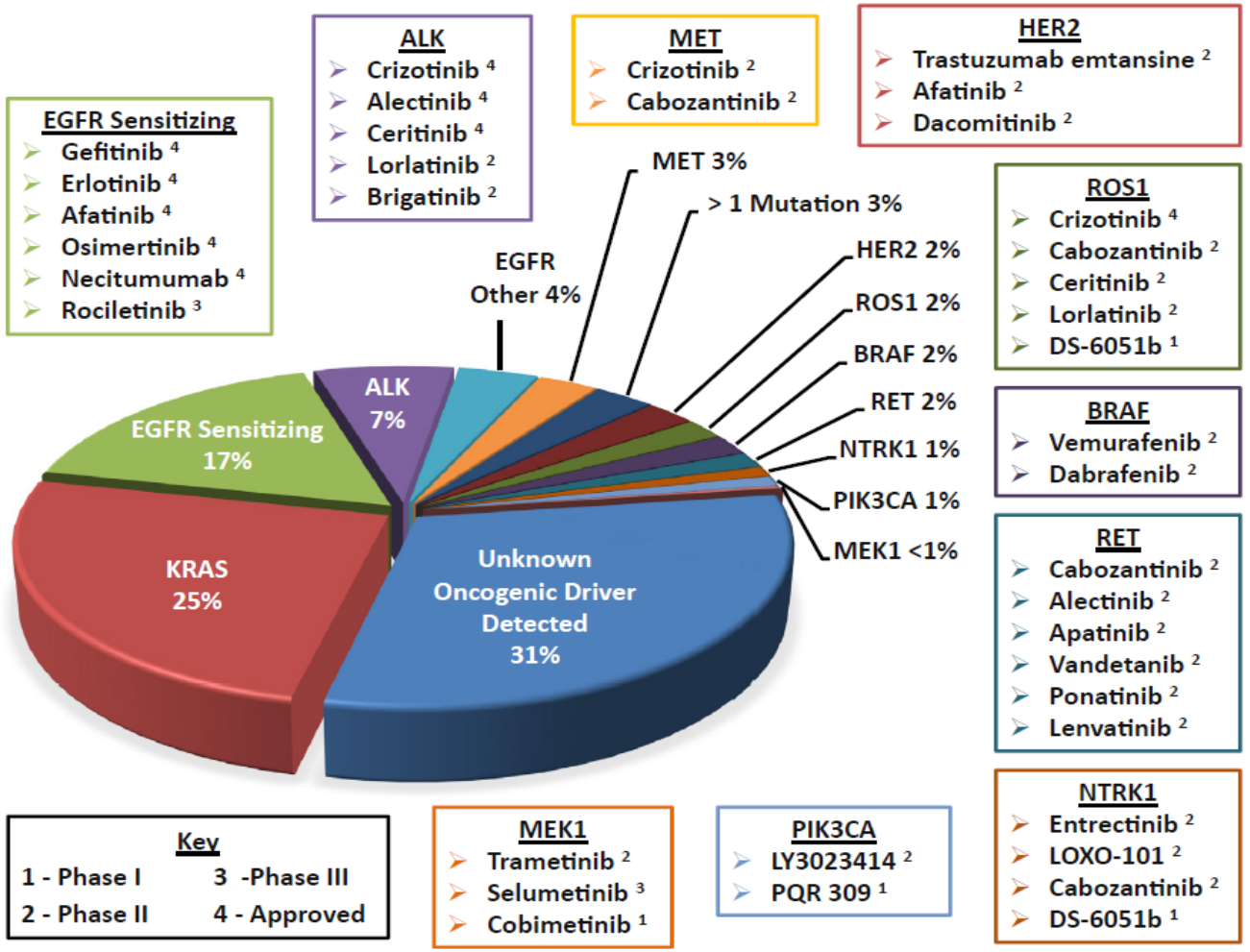
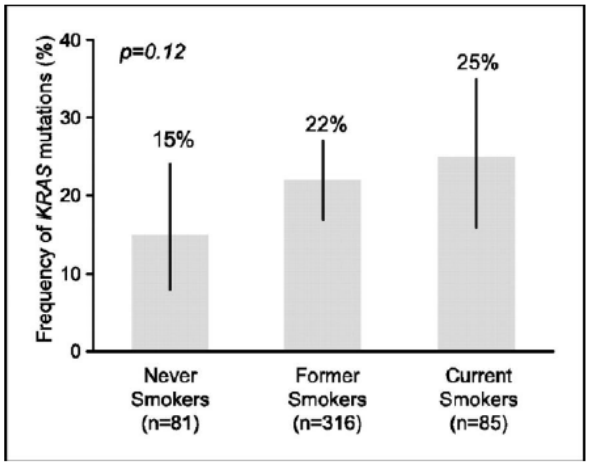
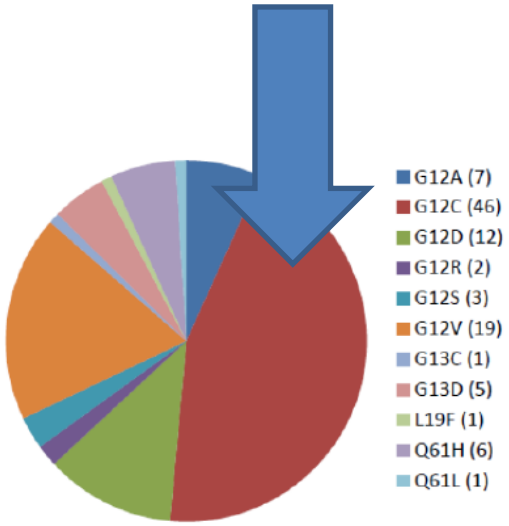


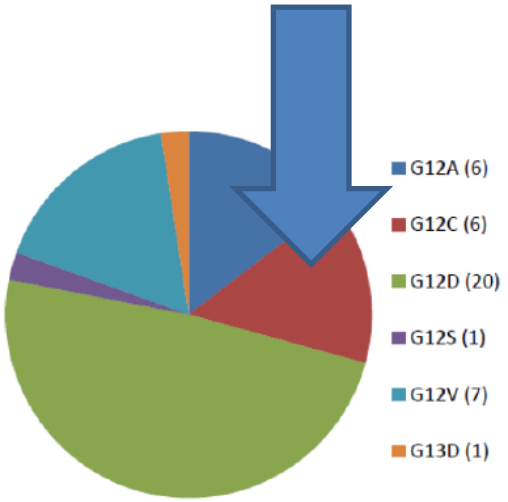
Figure 2. Frequency of molecular aberrations in various driver oncogenes in lung adenocarcinomas and current available drugs against these oncogenic proteins. These frequencies are a combination of data from the Lung Cancer Mutation Consortium and frequencies listed in Shea et al.[81] Shown in the boxes are the available drugs in addition to their developmental phase. EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma receptor tyrosine kinase; MET, mesenchymal-to-epithelial transition factor; HER2, erb-b2 receptor tyrosine kinase 2; ROS1, ROS proto-oncogene 1, receptor tyrosine kinase; BRAF, B-Raf proto-oncogene, serine/threonine kinase; RET, ret proto-oncogene; NTRK1, neurotrophic tyrosine kinase receptor type 1; PIK3A, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; MEK1, mitogen-activate protein kinase kinase 1; KRAS, Kirsten rat sarcoma viral oncogene homolog.

KRAS mutaties?
Bij wie en welke?





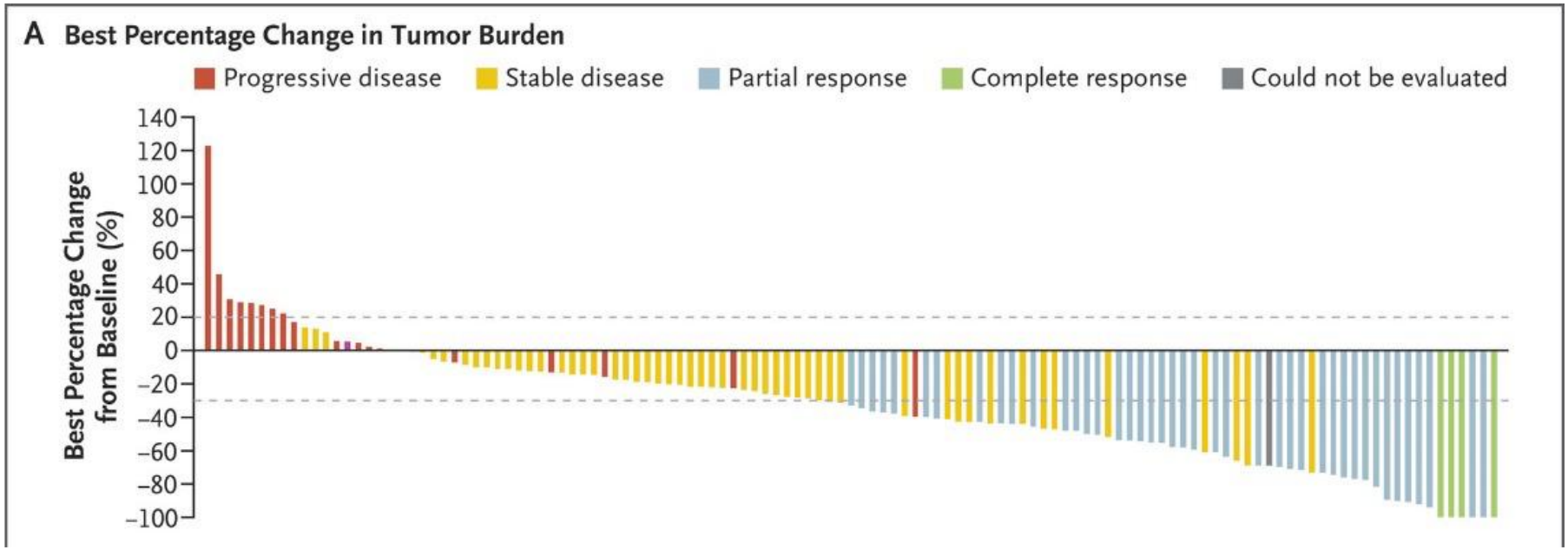
Current/Former Smokers



Never Smokers

Biernacka *Cancer Genet.* 2016;209:195-1; Neumann *Pathol Res Pract.* 2009;205:858-2; Zhou *Med Oncol.* 2016;33:32, Riely, G. et al. CCR 2008; Rediget al. ASCO 2016

CodeBreak100: Sotorasib



Skoulidis et al NEJM 2021; 384

CodeBreak200: PFS

Key eligibility criteria

- Locally advanced/unresectable or metastatic *KRAS G12C*-mutated NSCLC
- **≥ 1 prior treatment including platinum-based chemotherapy and checkpoint inhibitor***
- **No active brain metastases**
- ECOG performance status ≤ 1

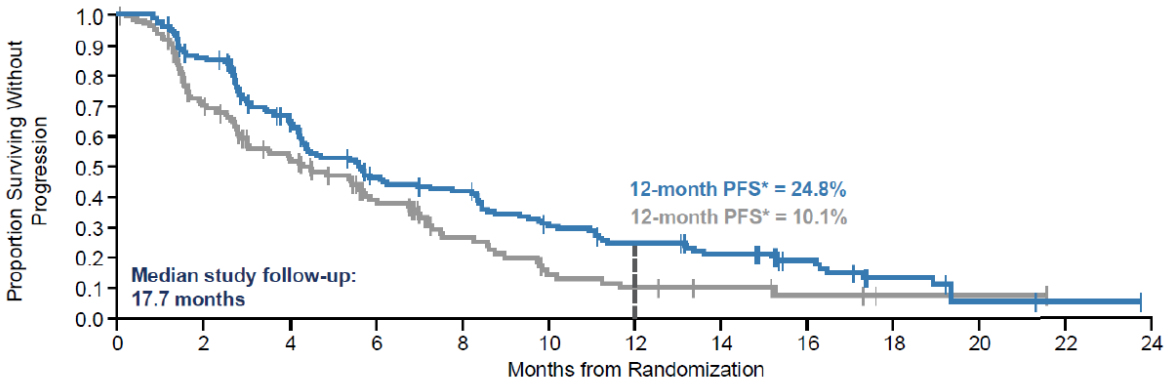
Stratification factors

- Prior lines of therapy (1 vs 2 vs > 2)
- Race (Asian vs non-Asian)
- History of CNS involvement (yes vs no)

Randomisation 1:1 (N = 345)

- **Sotorasib 960 mg oral daily N = 171**
- **Docetaxel 75 mg/m² IV Q3W N = 174**

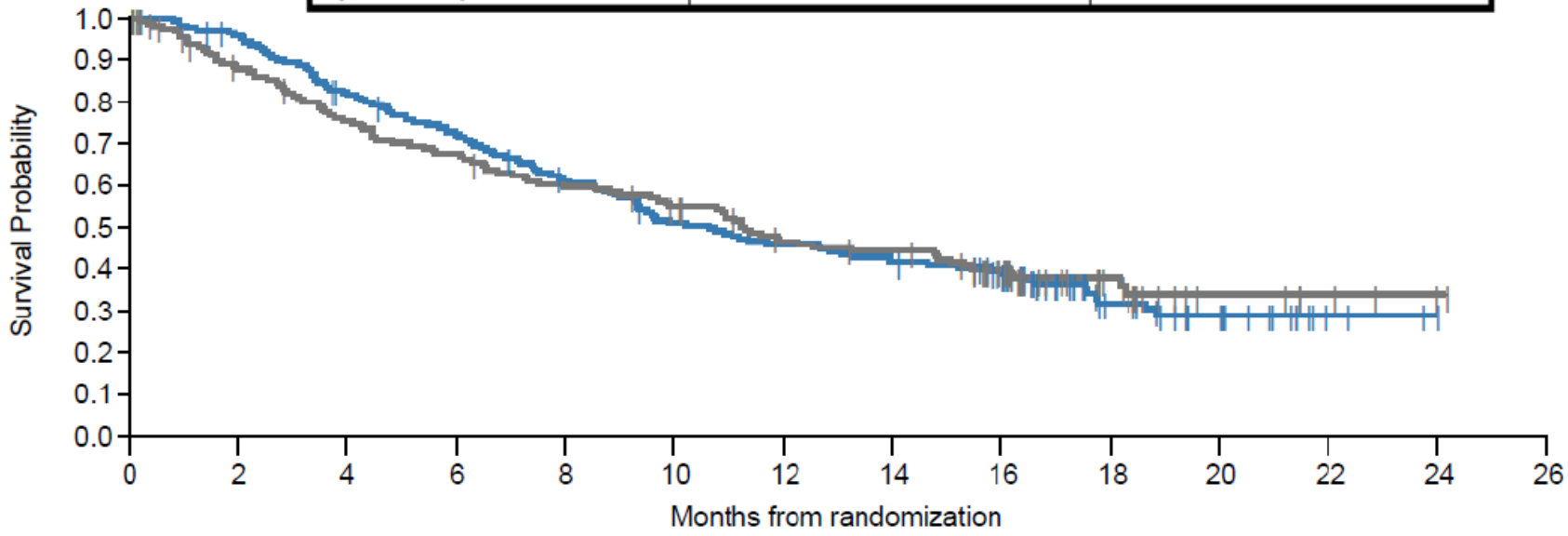
	Sotorasib 960 mg oral daily (N = 171)	Docetaxel 75 mg/m² IV Q3W (N = 174)
HR (95% CI)†	**0.66 (0.51, 0.86)**	
***P*-value (1-sided)**	***P* = 0.002**	
Median PFS, months (95% CI)‡	5.6 (4.3, 7.8)	4.5 (3.0, 5.7)



Johnson et al, ESMO 2022

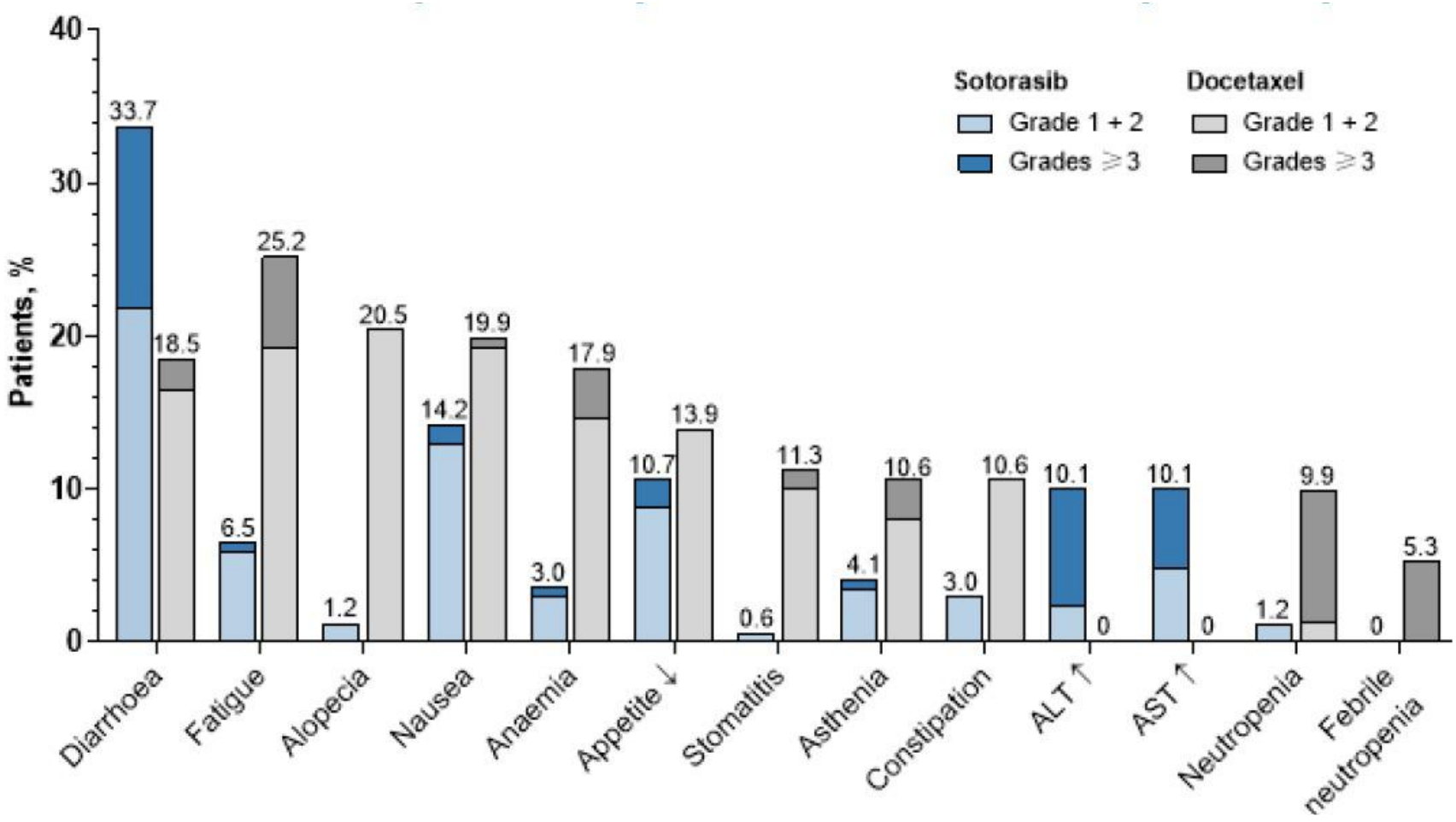
CodeBreak 200: Overleving

	Sotorasib 960 mg oral daily (N = 171)	Docetaxel 75 mg/m² IV Q3W (N = 174)
Deaths, n (%)	109 (63.7)	94 (54)
HR (95% CI)†	**1.01 (0.77, 1.33)**	
***P*-value (1-sided)**	***P* = 0.53**	
Median OS, months (95% CI)‡	10.6 (8.9, 14.0)	11.3 (9.0, 14.9)



Johnson et al, ESMO 2022

Sotorasib Bijwerkingen



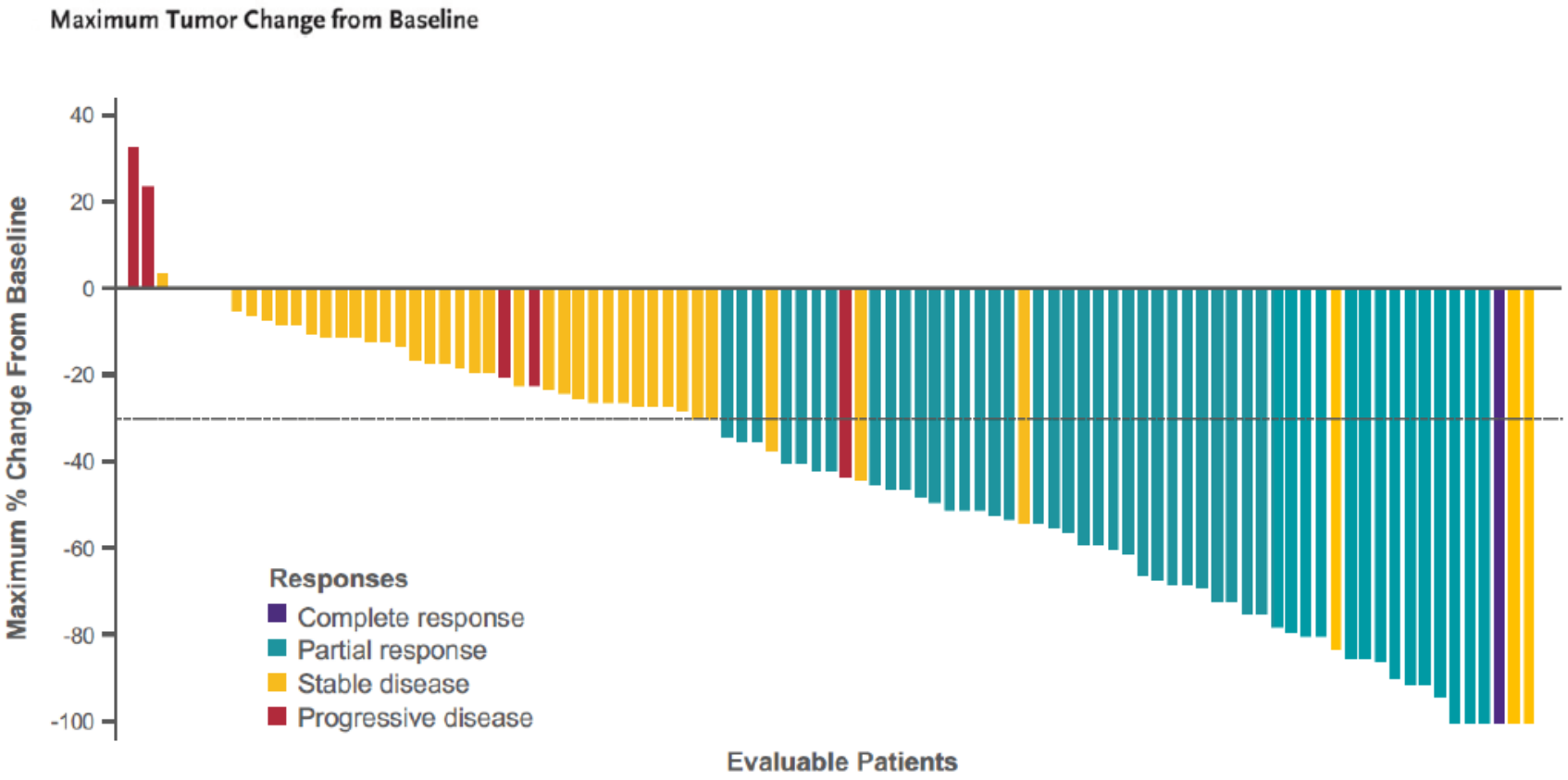
Johnson et al, ESMO 2022

2023 : Niet vergoed

- “Sotorasib voldoet niet aan de Paskwil-2023-criteria”

Rondschrijven van AMGEN

Nieuwere KRAS remmer: Adagrasib



Janne et al, NEJM 2022

Doelgerichte middelen

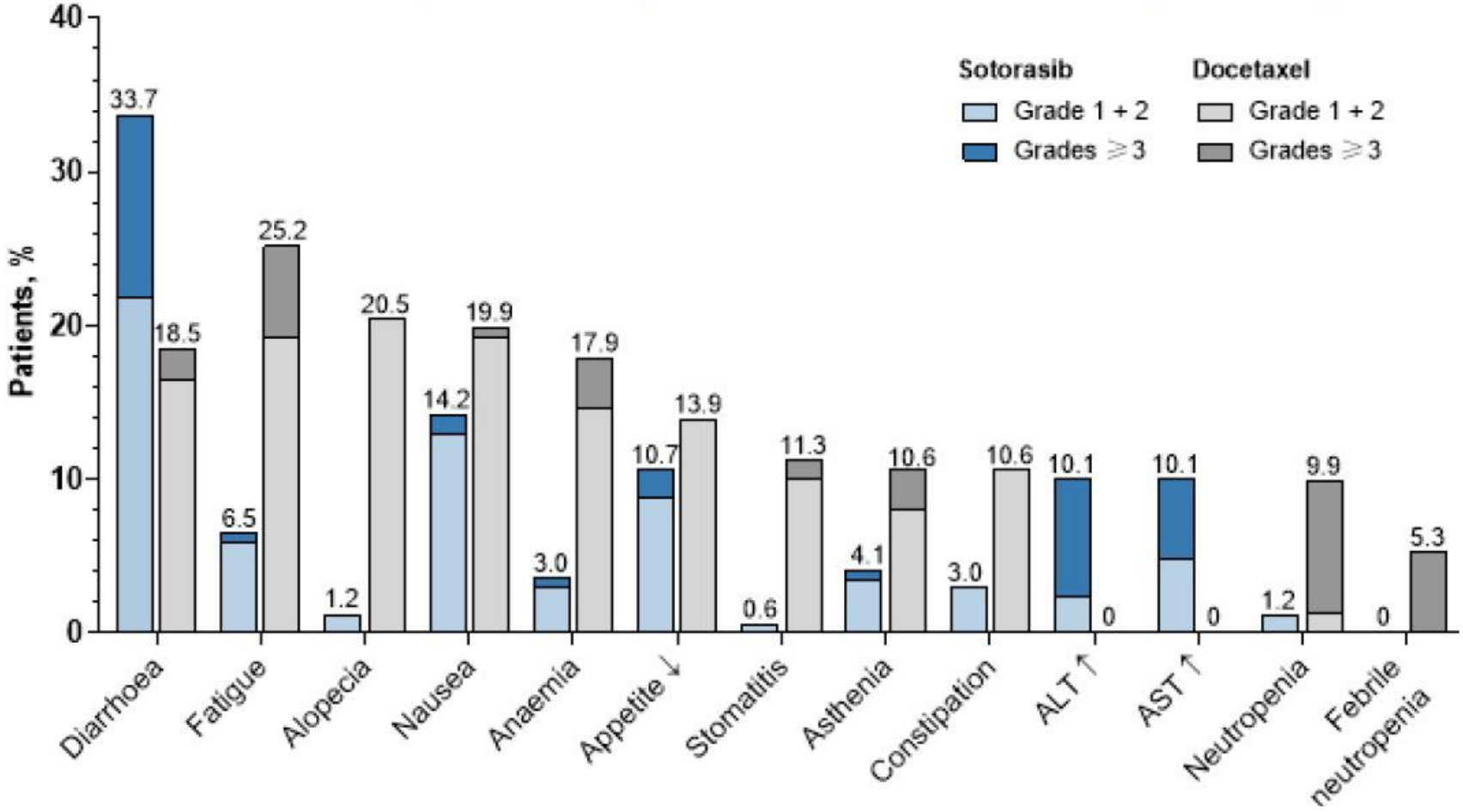
- Regulier te verkrijgen
  - Gefitinib-erlotinib-afatinib-crizotinib-ceritinib-osimertinib-dabrafenib – trametinib- …….
- In centra op comp use/regulier/in studies te verkrijgen
  - alectinib – ~~sotorasib~~ - amivantamab - e.v.a.

Verpleegkundige / VS-er – nieuwe middelen

- Nieuwe toxiciteit
  - Eigen maken
  - Patienten begeleiden
- Zorgpaden starten - volgen
  - Hoe kom je aan de medicatie?
  - Hoe begeleid je de patient?

(Sotorasib-) Bijwerkingen

Neemt alleen maar toe bij de nieuwe TKI-immunotherapie combinaties



Johnson et al, ESMO 2022

De boodschap:

ZOEK NAAR

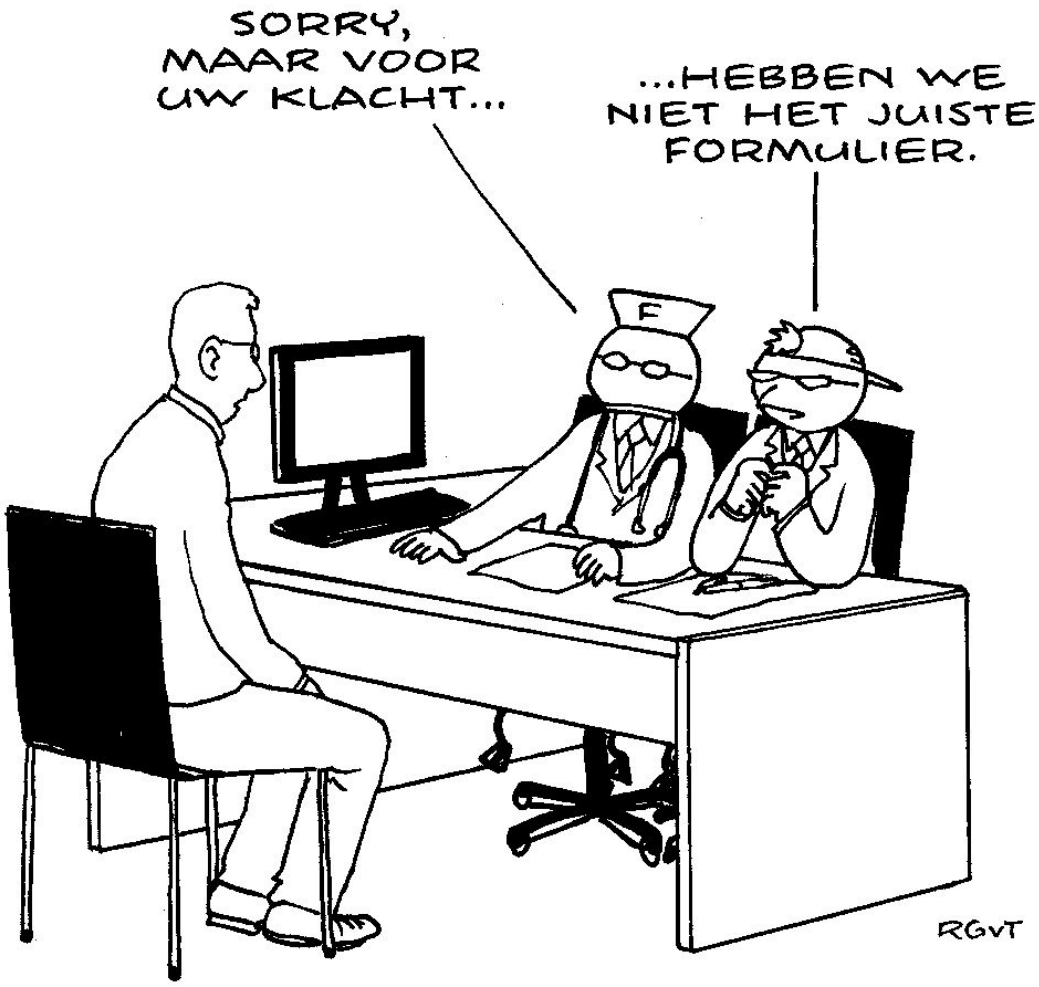
BEHANDELBARE MUTATIES

BIJ ZIEKTEPRESENTATIE

EN BIJ ZIEKTEPROGRESSIE

FOKKE & SUKKE

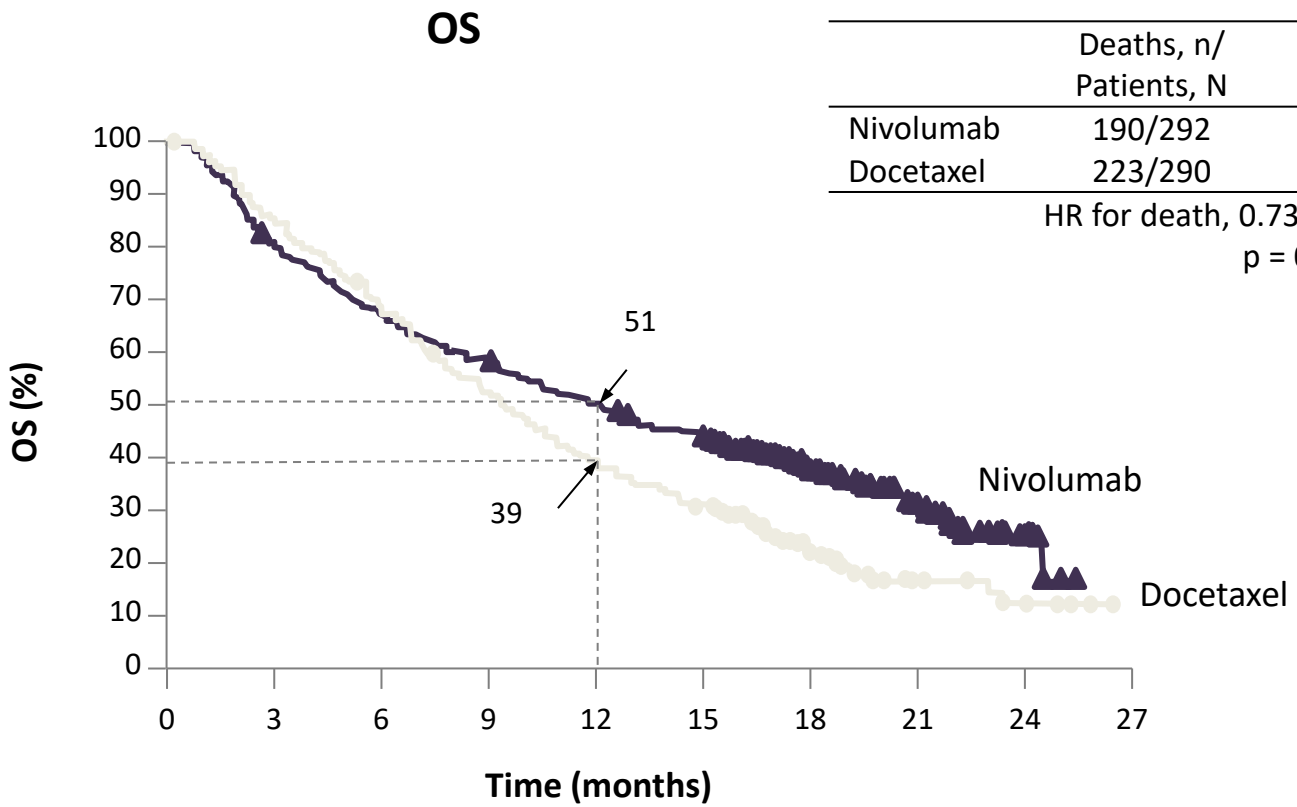
KUNNEN HEM NIET VERDER HELPEN



Immunotherapie

Hoe het begon:

In 2015: Nivolumab Non-squamous, no PD-L1 selection



	Deaths, n/ Patients, N	Median OS (95% CI), mo	1-year OS rate (95% CI), %
Nivolumab	190/292	12.2 (9.7–15.0)	51 (45–56)
Docetaxel	223/290	9.4 (8.1–10.7)	39 (33–45)

HR for death, 0.73 (95% CI 0.59–0.89)
p = 0.002

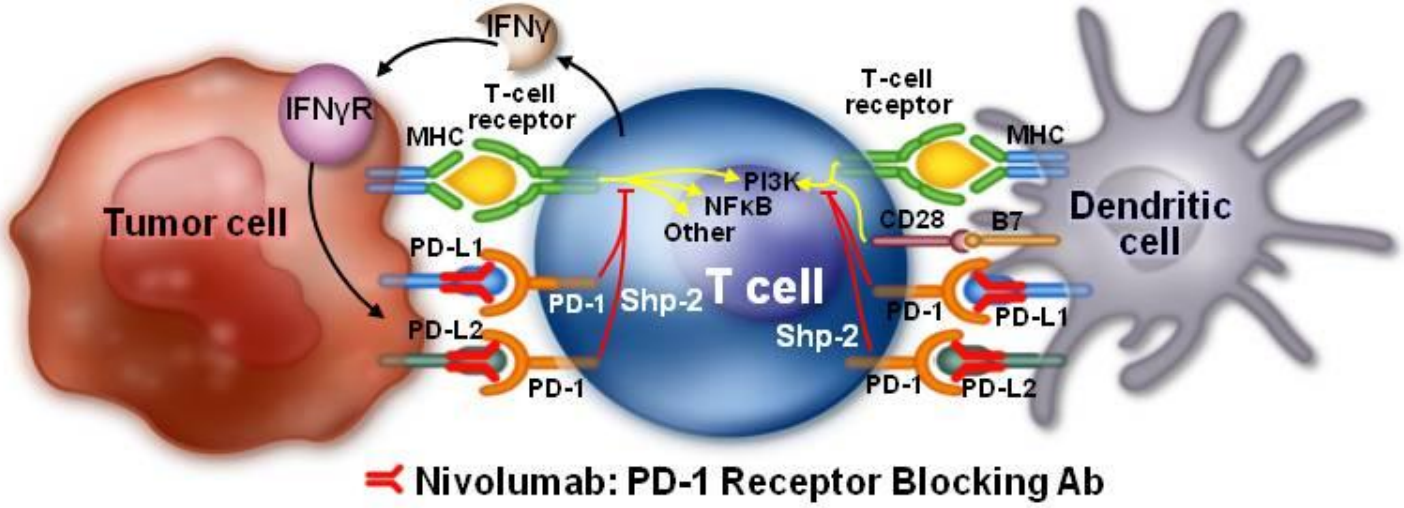
At risk, n

Nivolumab	292	232	194	169	146	123	62	32	9	0
Docetaxel	290	244	194	150	111	88	34	10	5	0

Borghaei H, et al. New Engl J Med. 2015;373:1627-39.

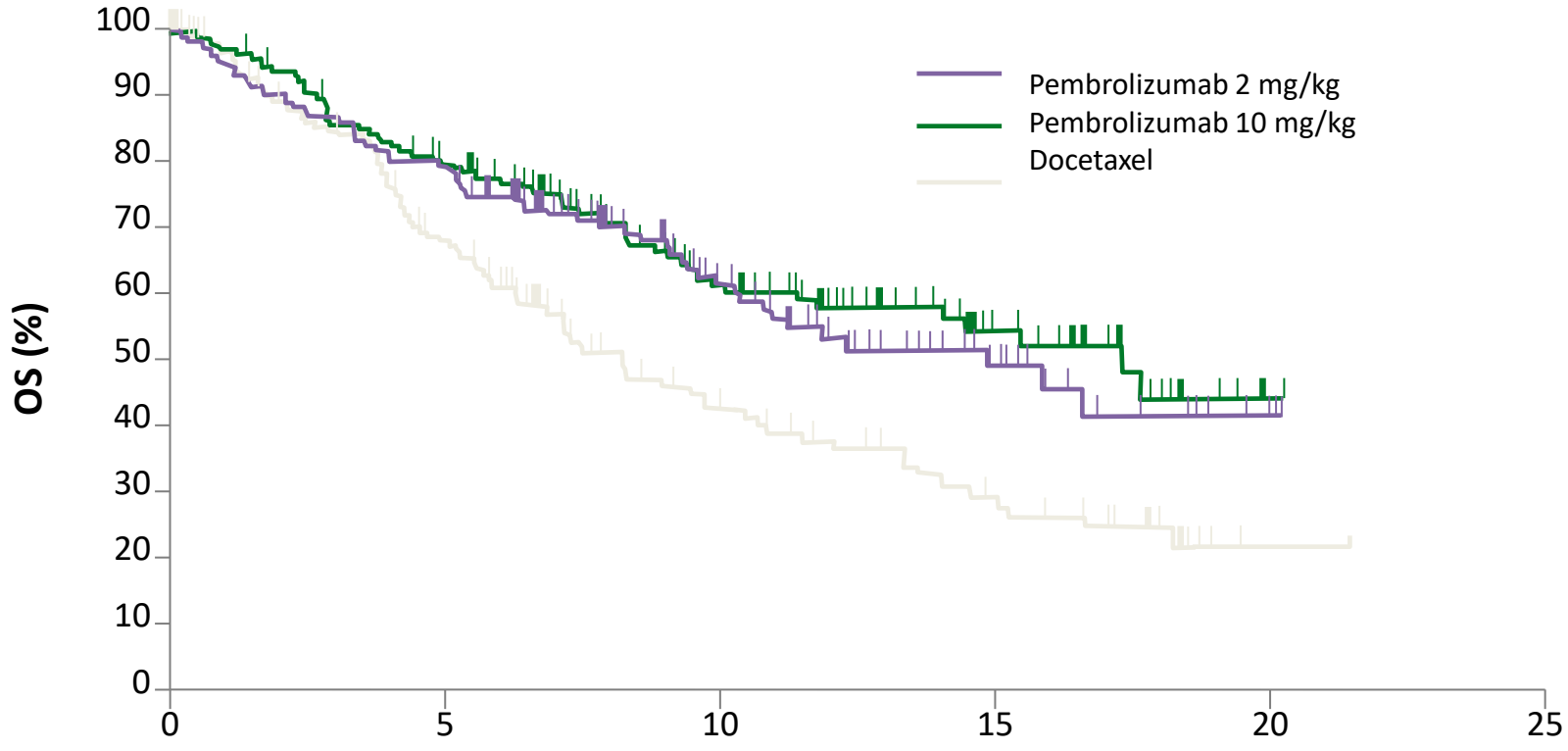
Nivolumab Mechanism of Action

- PD-1 expression on tumor-infiltrating lymphocytes is associated with decreased cytokine production and effector function[10]
- Nivolumab binds PD-1 receptors on T cells and disrupts negative signaling triggered by PD-L1/PD-L2 to restore T-cell antitumor function[11–13]



Wat kwam daarna

Pembrolizumab
All histologies, PD-L1 cut-off > 1%

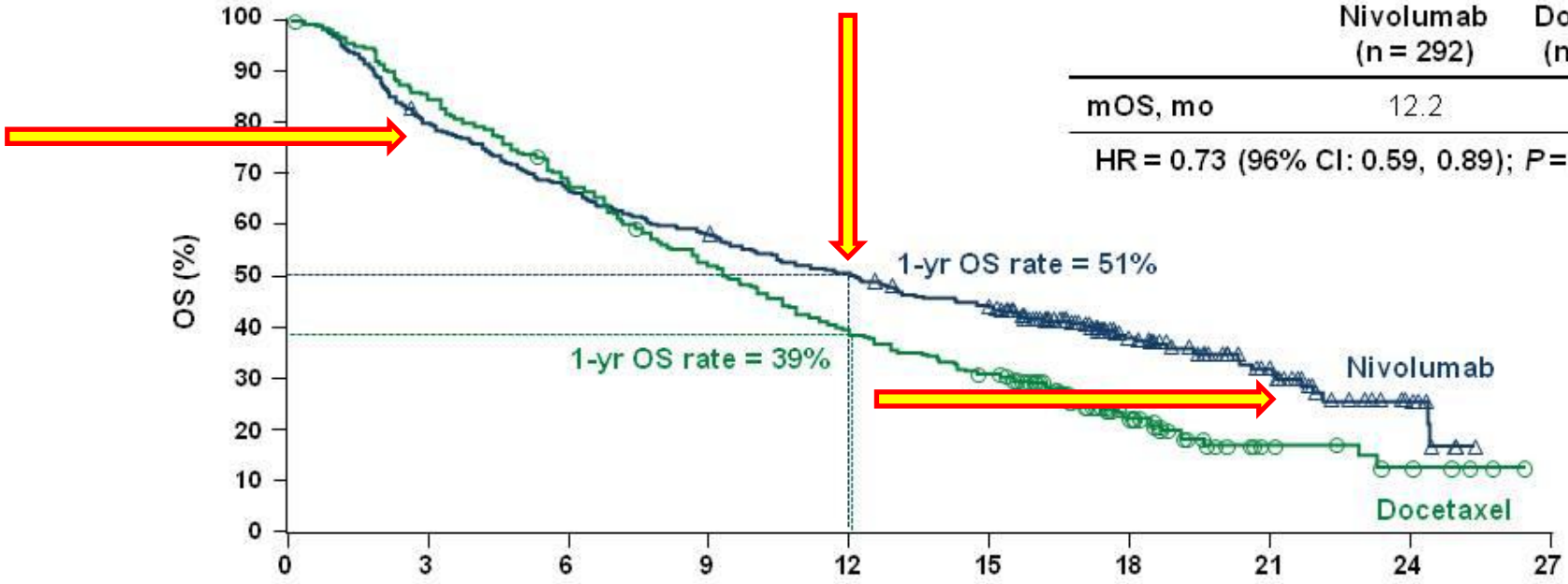


At risk, n						
Pembrolizumab 2 mg/kg	139	110	51	20	3	0
Pembrolizumab 10 mg/kg	151	115	60	25	1	0
Docetaxel	152	90	38	19	1	0

Herbst RS, et al. Lancet. 2016; 387:1540-50.

Bij wie werkt het nu?

Overall Survival



	Nivolumab (n = 292)	Docetaxel (n = 290)
mOS, mo	12.2	9.4

HR = 0.73 (96% CI: 0.59, 0.89); *P* = 0.0015

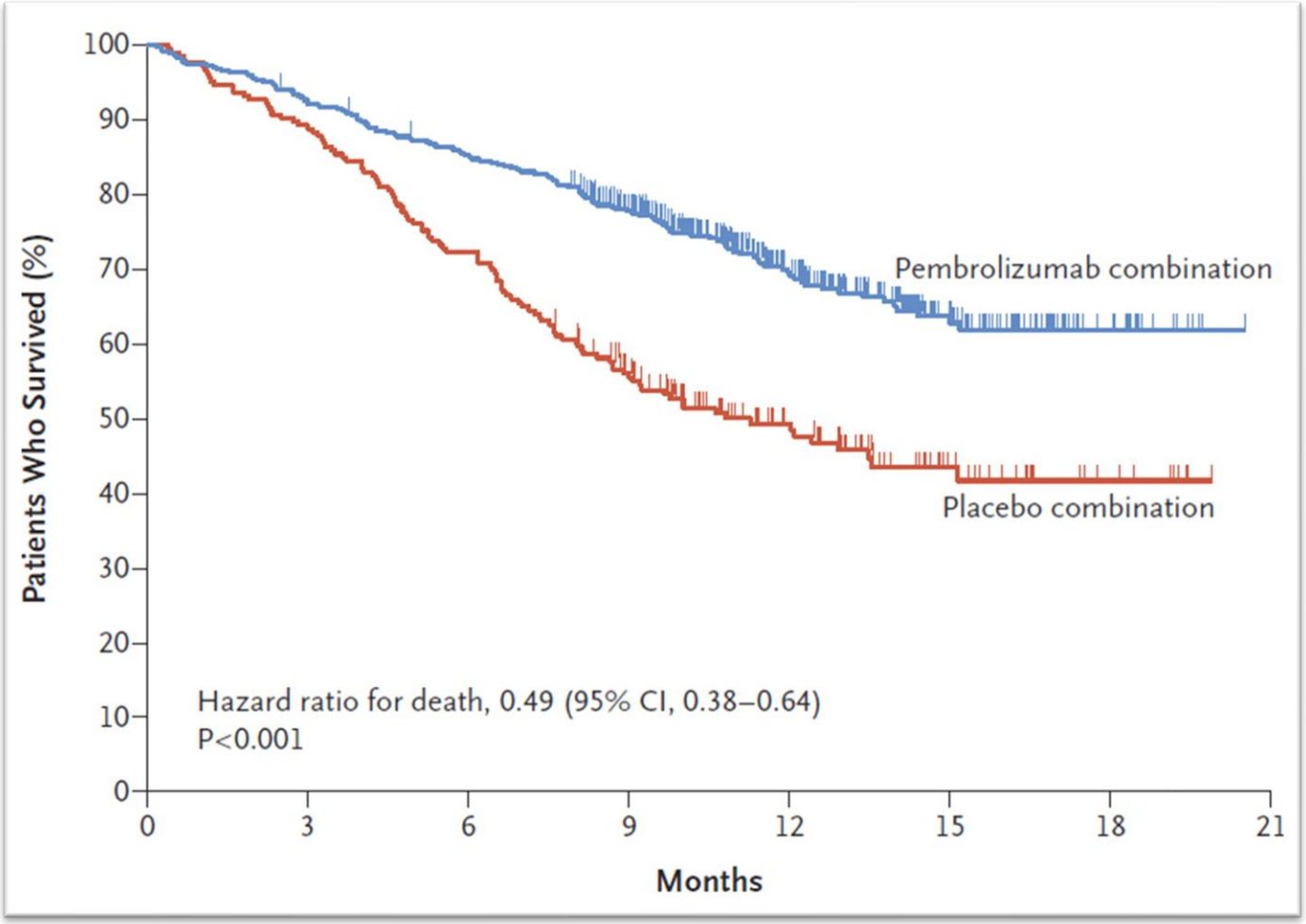
Number of Patients at Risk										
Nivolumab	292	232	194	169	146	123	62	32	9	0
Docetaxel	290	244	194	150	111	88	34	10	5	0

Symbols represent censored observations.

Hoe krijgen we de immuno beter??

- Andere marker voor effectiviteit?
  - Tumor mutational burden
- Combineren met andere behandelingen!

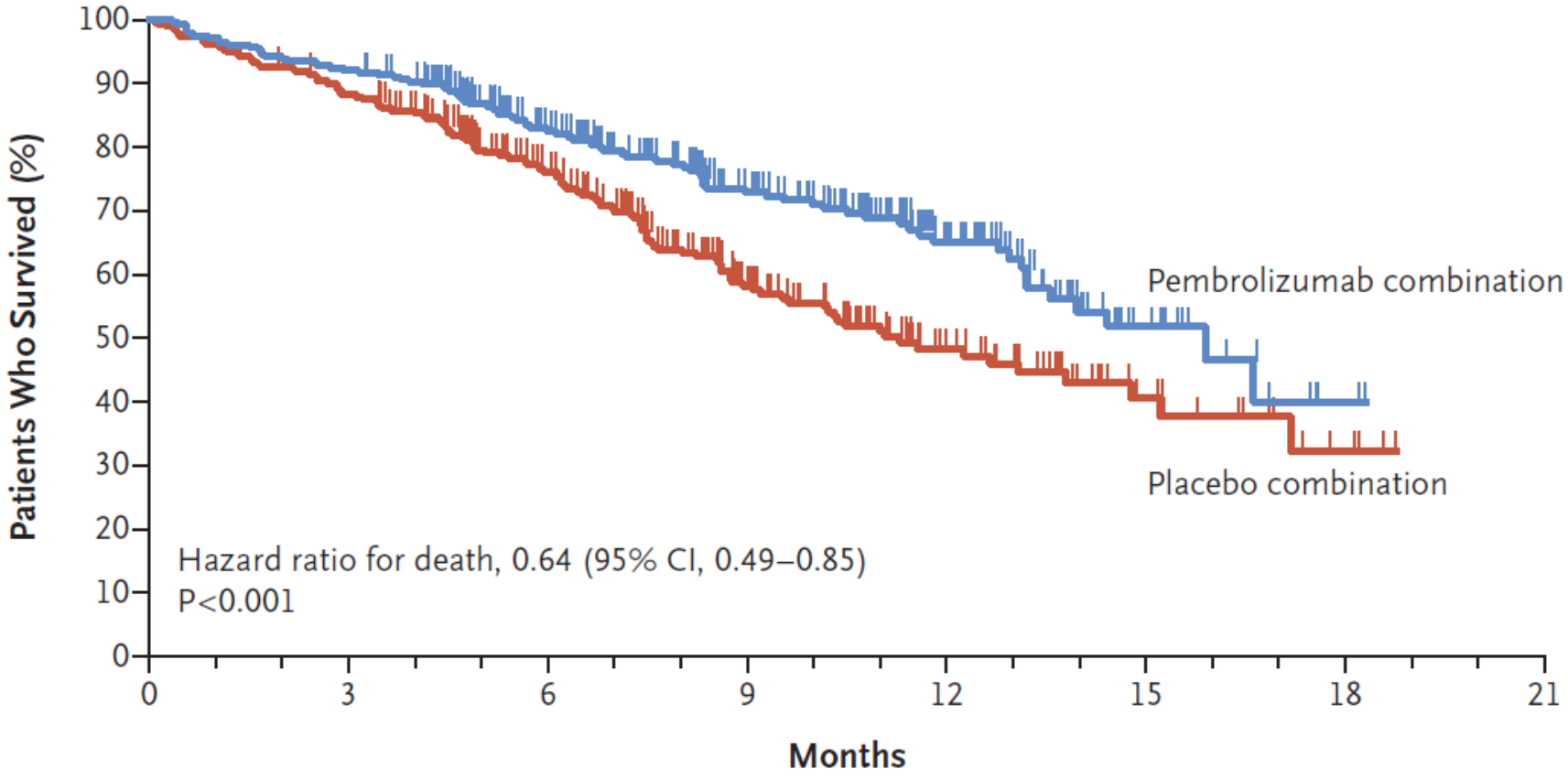
St IV NSCLC **chemo-immuno**-therapie in de eerste lijn!!



Non-squamous NSCLC without EGFR or ALK mutations

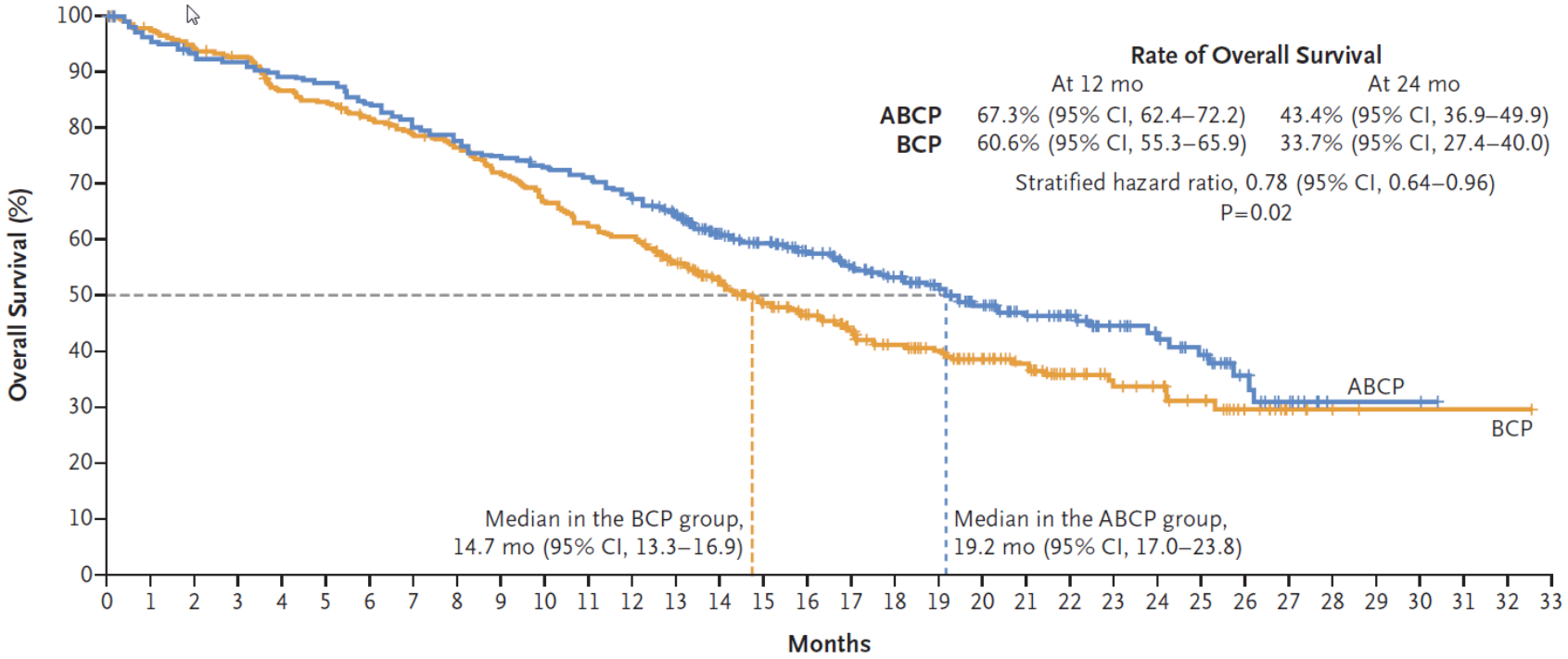
Gandhi NEJM 2018

Pembrolizumab ± chemo for squamous NSCLC st IV



Paz-Ares NEJM 2018

Atezolizumab ± carboplatin-taxol-bevacizumab



Inclusief EGFR en ALK gemuteerd NSCLC

Socinski NEJM 2018

Boodschap

CHEMO-IMMUNOTHERAPIE

is

DE **STANDAARD**BEHANDELING

BIJ STADIUM IV NSCLC

Bij PD-L1 < 50%

Bij PD-L1 > 50% ook mono - immunotherapie

Het vervolg:

- Immuno-doubletten
- Chemo met immuno-doubletten
- Immunotherapie met TKI’s

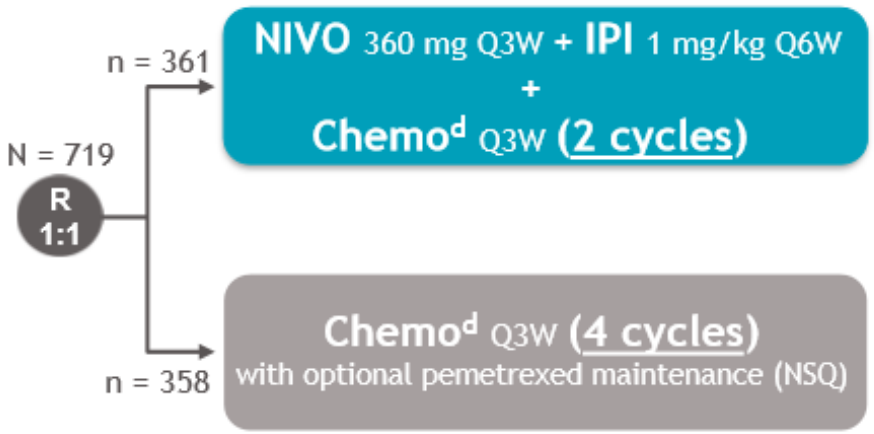
BESCHIKBAAR PER 2023

CheckMate 9LA study design[a]

Key Eligibility Criteria

- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0-1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%), sex, and histology (SQ vs NSQ)



Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint

- OS

Secondary endpoints

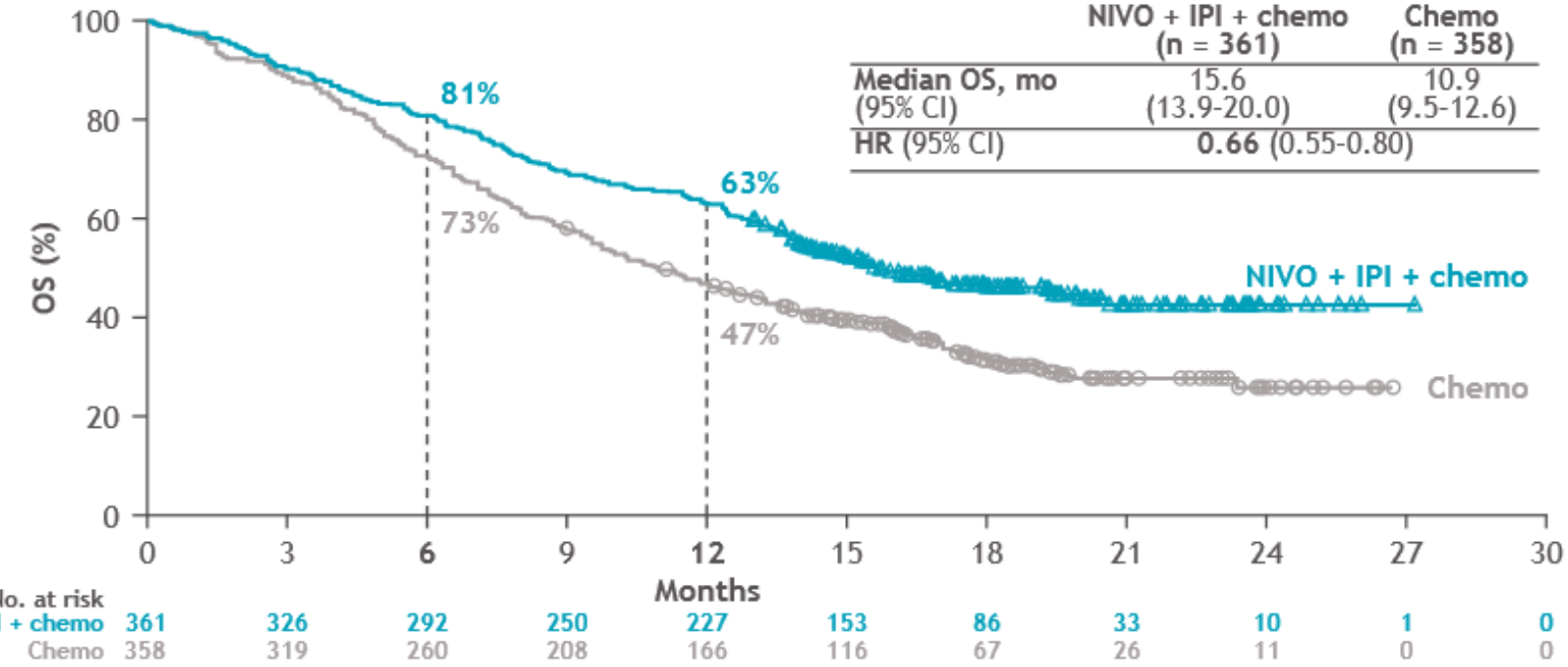
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

Interim database lock: October 3, 2019; minimum follow-up: 8.1 months for OS and 6.5 months for all other endpoints.
Updated database lock: March 9, 2020; minimum follow-up: 12.7 months for OS and 12.2 months for all other endpoints.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

ASCO 2020 M Reck, abstract 9501

Primary endpoint (updated): Overall survival[a]



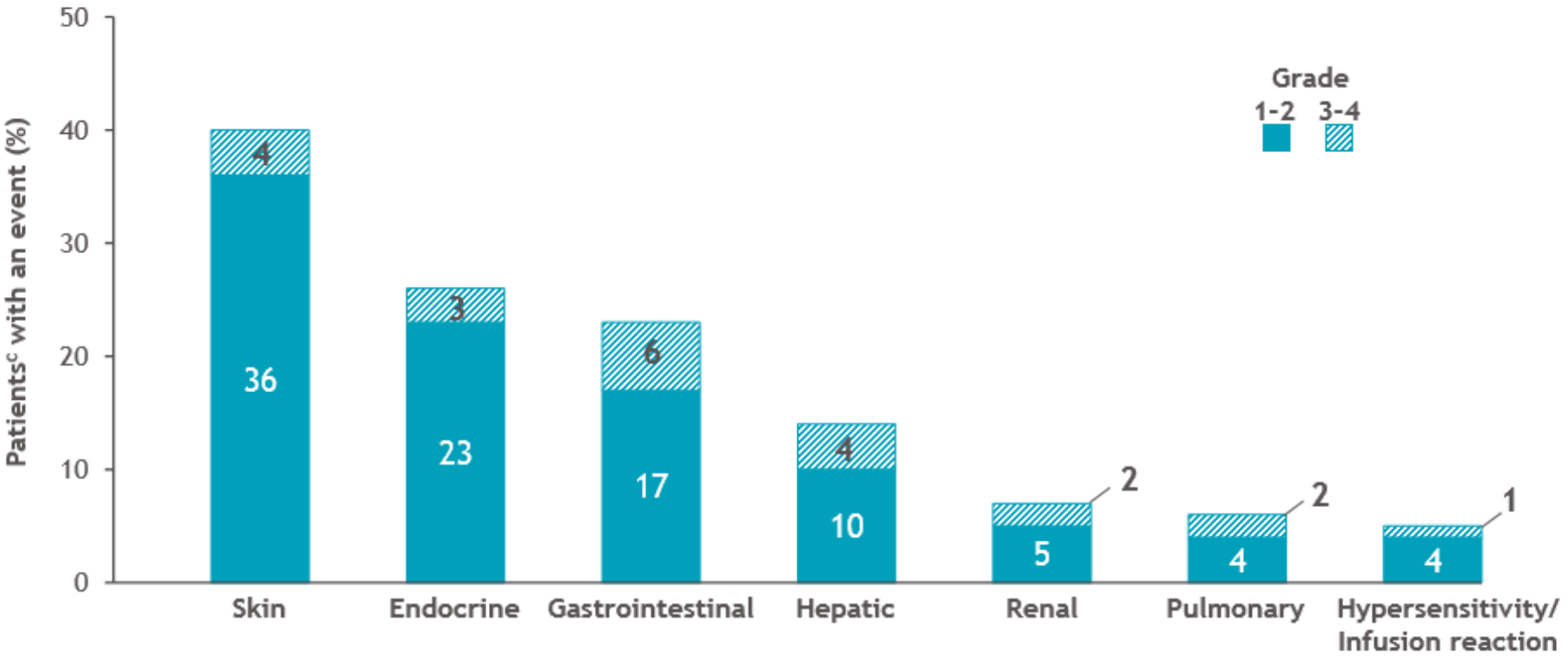
	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS, mo (95% CI)	15.6 (13.9-20.0)	10.9 (9.5-12.6)
HR (95% CI)	**0.66** (0.55-0.80)	

Minimum follow-up: 12.7 months.

[a]Patients remaining in follow-up were censored on the last date they were known to be alive; 47% of patients in the NIVO + IPI + chemo arm and 32% of patients in the chemo arm were censored. Subsequent systemic therapy was received by 31% of patients in the NIVO + IPI + chemo arm and 40% in the chemo arm; subsequent immunotherapy was received by 5% and 30%, and subsequent chemotherapy by 29% and 22%, respectively. Among patients with BICR-confirmed disease progression on study, subsequent systemic therapy was received by 40% in the NIVO + IPI + chemo arm and 44% in the chemo arm; subsequent immunotherapy was received by 7% and 34%, and subsequent chemotherapy by 38% and 24%, respectively

ASCO 2020 M Reck, abstract 9501

Treatment-related select AEs with NIVO + IPI + chemo[a,b]



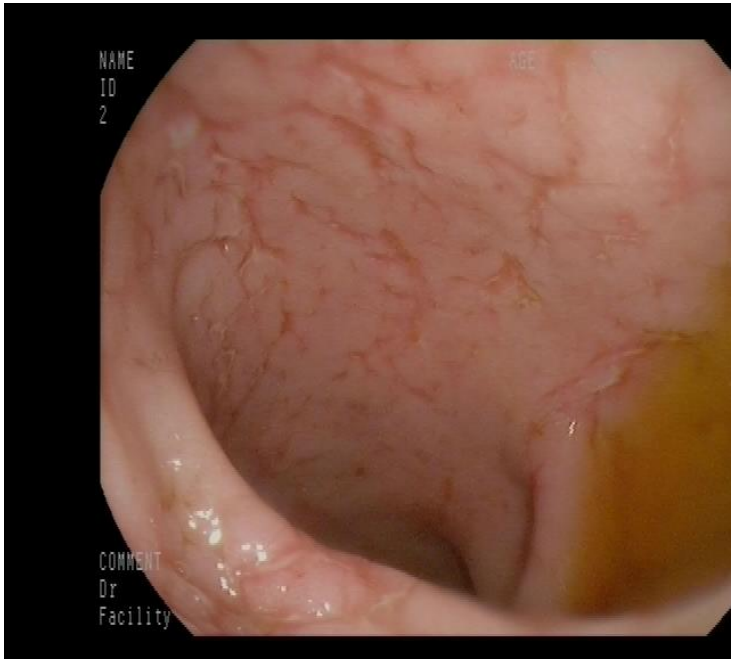
[a]Treatment-related select AEs are those with potential immunologic etiology that require frequent monitoring/intervention; [b]Includes events reported between first dose and 30 days after last dose of study drug; [c]The total number of patients treated with NIVO + IPI + chemo was 358.

ASCO 2020 M Reck, abstract 9501

Meer middelen, meer bijwerkingen

Diarree

- Opname, suppletie en coloscopie
- Scopisch -itis beeld
- Biopten:
  - passend bij nivo effect



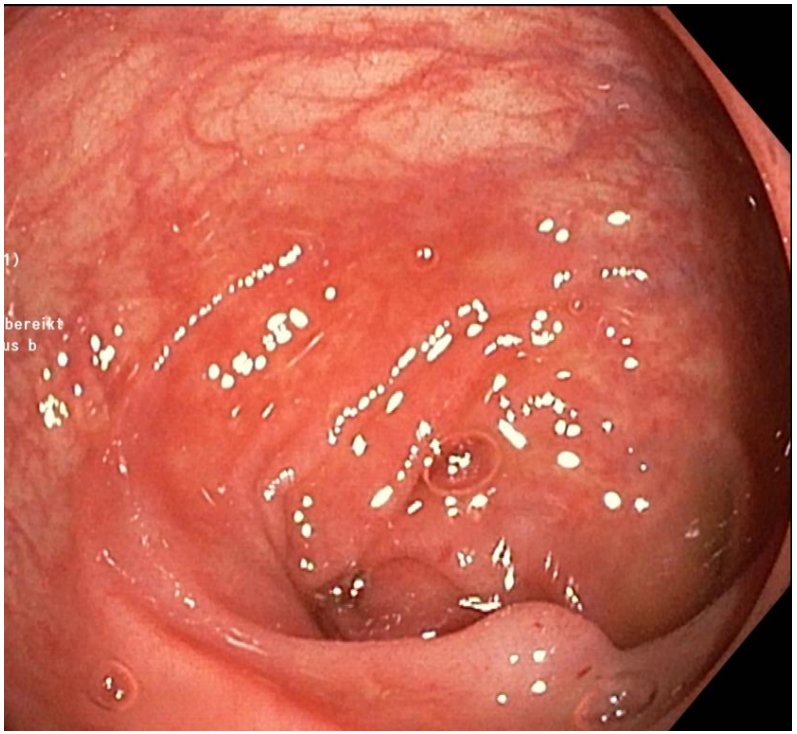
Colitis beschrijven

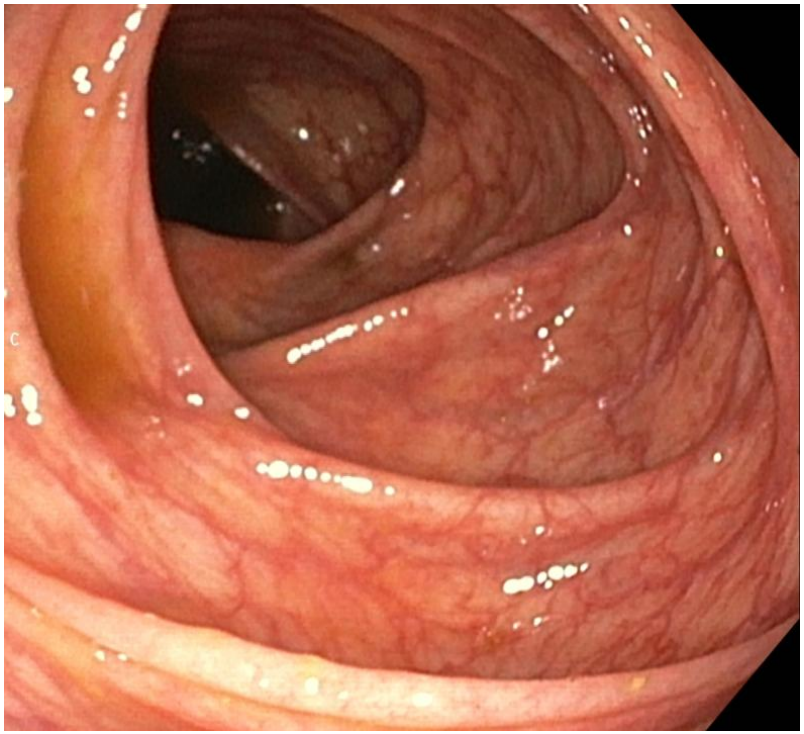
Nivolumab toxiciteitmanagementsrichtijn 1.0

Gastro-intestinale klachten			
Colitis, Diarree	**Graad**	**Management**	**Follow-up**
- Diarree < 4x per dag ten opzichte van baseline - Geen buikpijn - Geen zichtbaar bloedverlies	1	- Continueren van therapie - Symptomatische behandeling *(loperamide)* - Voorlichting van patiënt over contact bij verergering - dieetaanpassing	- Evaluatie van symptomen *(a 1 week)*, - Terugkeer naar baseline
- Diarree 4-6x per dag ten opzichte van baseline - Buikpijn, - Zichtbaar bloedverlies	2	- Onderbreek immuuntherapie - Symptomatische behandeling *(loperamide)* - Controle zouthuishouding, nierfunctie - Bij twijfel over diagnose overweeg coloscopie met biopsie	- Bij verbetering naar graad 1: herstart nivolumab - Bij geen verbetering na 7 dagen of bij verslechtering zie graad 3-4
- Diarree > 7x per dag, - Incontinentie, - Ernstige buikpijn, - Peritoneale weerstanden, - Zichtbaar bloedverlies, - Tekenen van sepsis of perforaties	3-4	- Onderbreek immuuntherapie - Start prednisolon 1 mg /kg/dag - Coloscopie met biopsie - Hydratie - Controle zouthuishouding	- Bij verbetering, continueren van corticosteroïden tot graad 1, dan afbouwen in een maand (oraal equivalent) - Bij aanhoudende klachten (3 dagen) of terugkeer van klachten: toevoegen Inflectra (perforatie of sepsis zijn contraindicatie)

Patient 2

- 2016-11 start nivolumab
- 2017-1 diarree 5 dg tot 20dd. Na bezoek chinees





Prednison 1mg/kg, goede reactie binnen enkele dagen

Treatment-related Select AEs

	Nivolumab (n = 287)		Docetaxel (n = 268)	
	Any Grade	Grade 3–4[a]	Any Grade	Grade 3–4[a]
Endocrine, %				
Hypothyroidism	7	0	0	0
Gastrointestinal, %				
Diarrhea	8	1	23	1
Hepatic, %				
ALT increased	3	0	1	<1
AST increased	3	<1	1	0
Pulmonary, %				
Pneumonitis	3	1	<1	<1
Skin, %				
Rash	9	<1	3	0
Pruritus	8	0	1	0
Erythema	1	0	4	0
Hypersensitivity/Infusion reaction, %				
Infusion-related reaction	3	0	3	<1

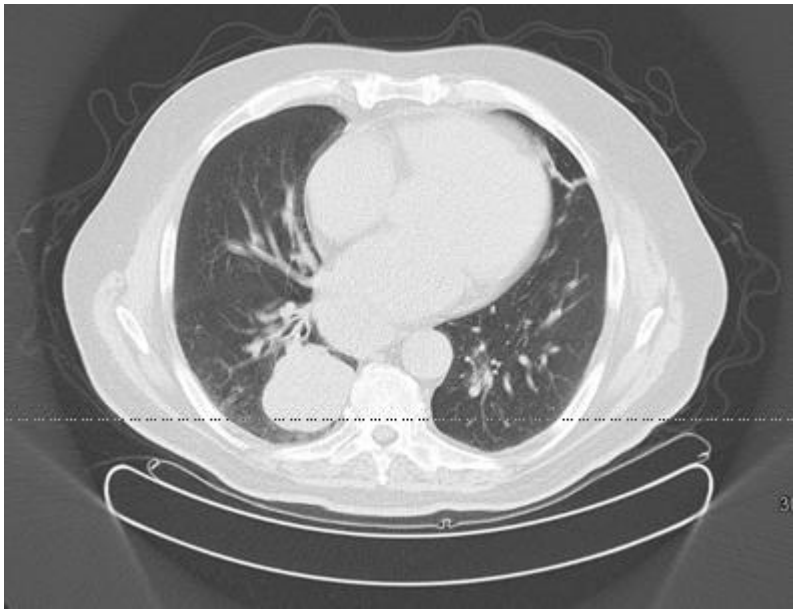
- Select AEs: AEs with potential immunologic etiology that require frequent monitoring/intervention

Includes events reported in ≥2.5% of patients.

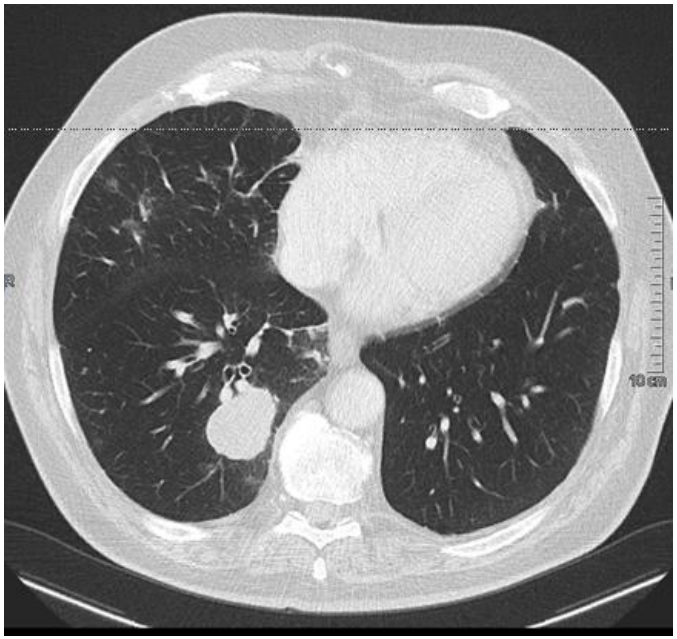
[a]No grade 5 events were reported at DBL;1 grade 5 event for nivolumab was reported post-DBL.

Beloop

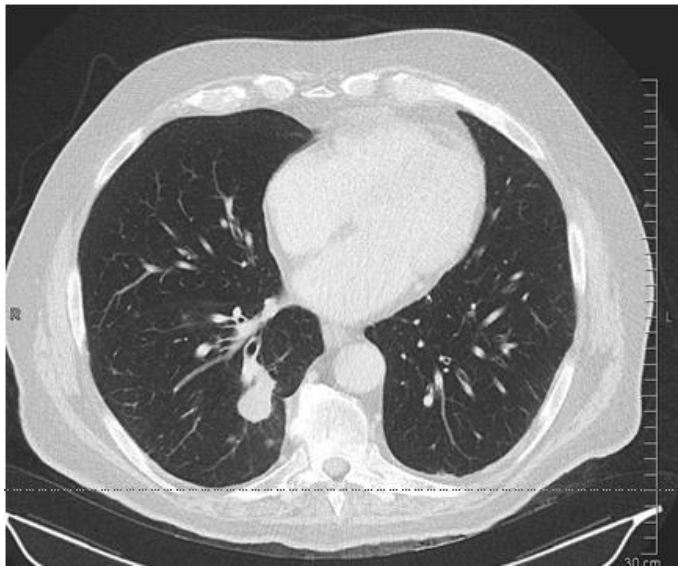
September 2015

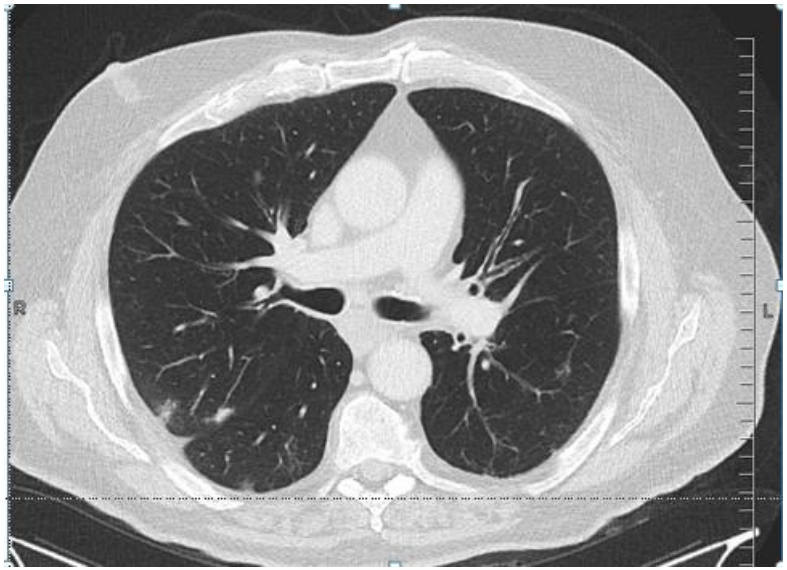


november



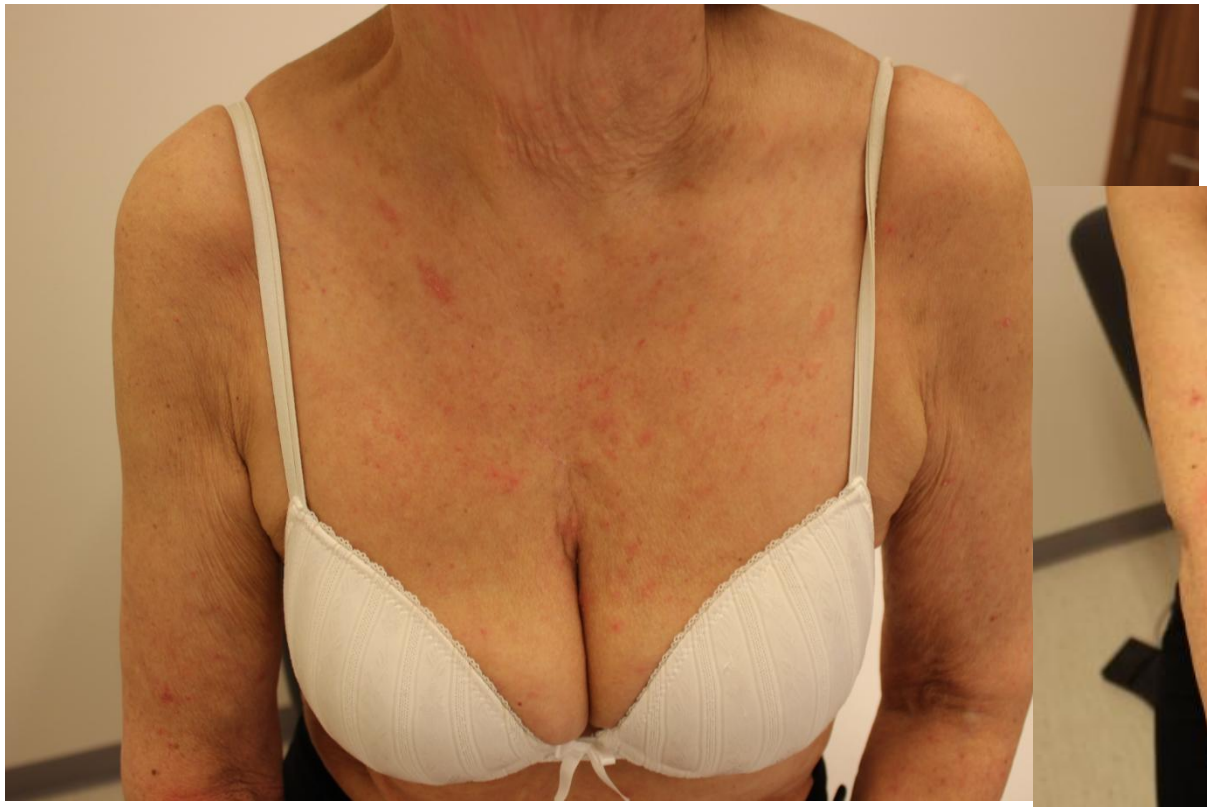
Respons zet door

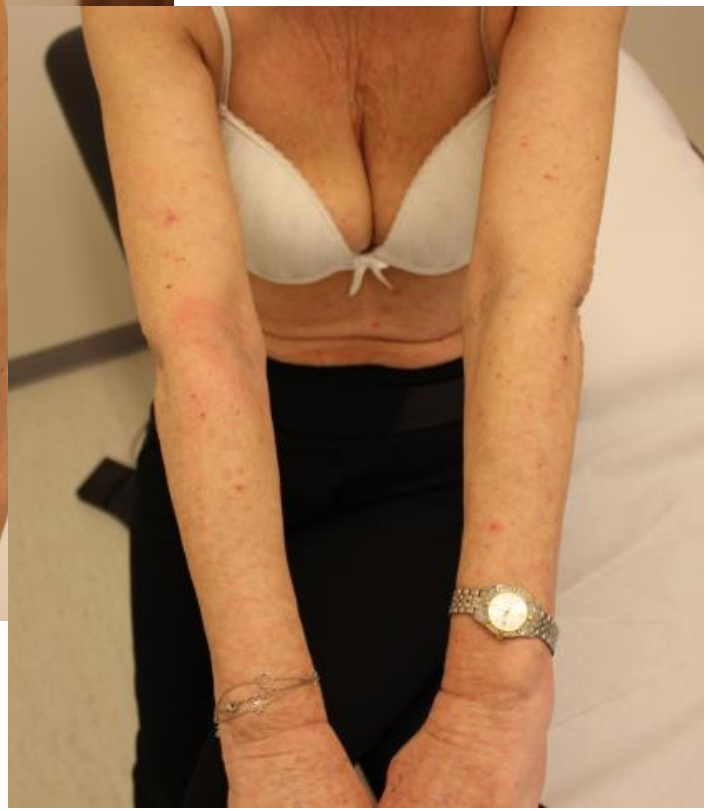




- Dec 2015
  - Fors klachten van jeuk en uitslag onderarmen en romp

Na 4 giften nivolumab : jeuk!





21512522 met toestemming van patiente

schildklierfunctie

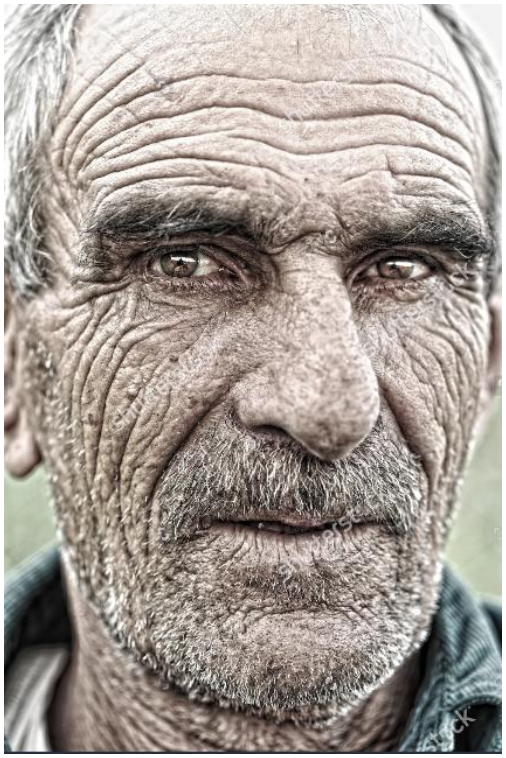
SCHILDKLIER	
TSH	0.283
FT4	11.9
T3	1.3

hormoonstatus

SCHILDKLIER										
TSH	0.283		0.098	0.600						0.339
FT4	11.9		11.2	9.3						9.8
T3	1.3		1.1	1.4						
BIJNIER										
Cortisol										0.37
Cortisol 08:00 uur						<0.03				
ACTH										<5
GONADEN										
LH										3.6
FSH										6.2
GROEI										
IGF-1										6.1 *
ENDOCRINOLOGIE OVERIG										
Prolactine										0.16

Second law of oncology

- The tumor has to shrink faster than the patient



Reclame

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NKI-AVL

- In ‘The history of Oncology” Wagener 2009

In 1886, the French internist Louis Bard (1857–1930) summarized the conclusions of most of his predecessors concerning the genesis of cancer and limited the scope of Virchow's law by rewriting it 'omnis cellula e cellula eiusdem naturae'. This means that as a consequence of cellular specificity, a tissue can only produce a tumor with the same histologic structure as itself. This may be called 'the third law of oncology' or 'Bard's law' (Cabanne et al., 1983).

Niet-kleincellig longkanker

2019: Adjuvante immuuntherapie
bij stadium III NSCLC

2022: Adjuvante immuuntherapie
Bij stadium I en II NSCLC

2023: adjuvante osimertinib na resectie
2023: onvoldoende effect KRAS remmers