ONTWIKKELINGEN IN DE SYSTEMISCHE BEHANDELING VAN STADIUM III NSCLC

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Disclosures

None relevant for this presentation

Honoraria: Bristol-Myers Squibb, AstraZeneca, MSD, Novartis, Pfizer, Roche

Advisory Boards: Bristol-Myers Squibb, Amgen, MSD

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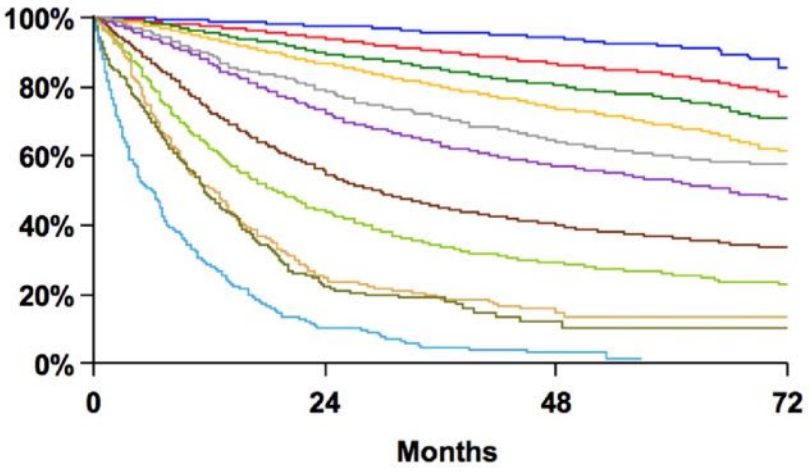
Stadium III NSCLC

Standaard behandeling voor stadium III was voor lange tijd concurrent chemoradiotherapie, met platinumbevattende chemotherapie.[1]

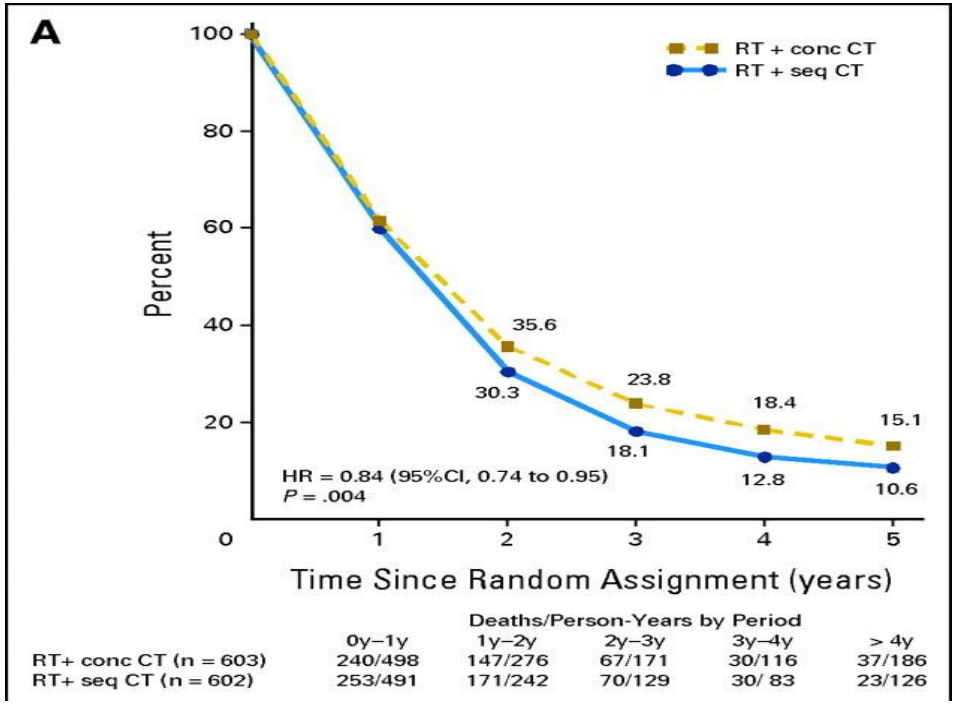
However, outcomes have been poor with ~15% to 30% of patients alive at 5 years[1,2]



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%

1. Yoon SM et al. *World J Clin Oncol.* 2017;8:1-20. **2.** Bradley JD et al. *Int J Radiat Oncol Biol Phys.* 2017;99(Suppl):S105..

Verbeterde overleving met concurrent chemoradiotherapie



Aupérin; *Journal of Clinical Oncology* 2010 282181-2190

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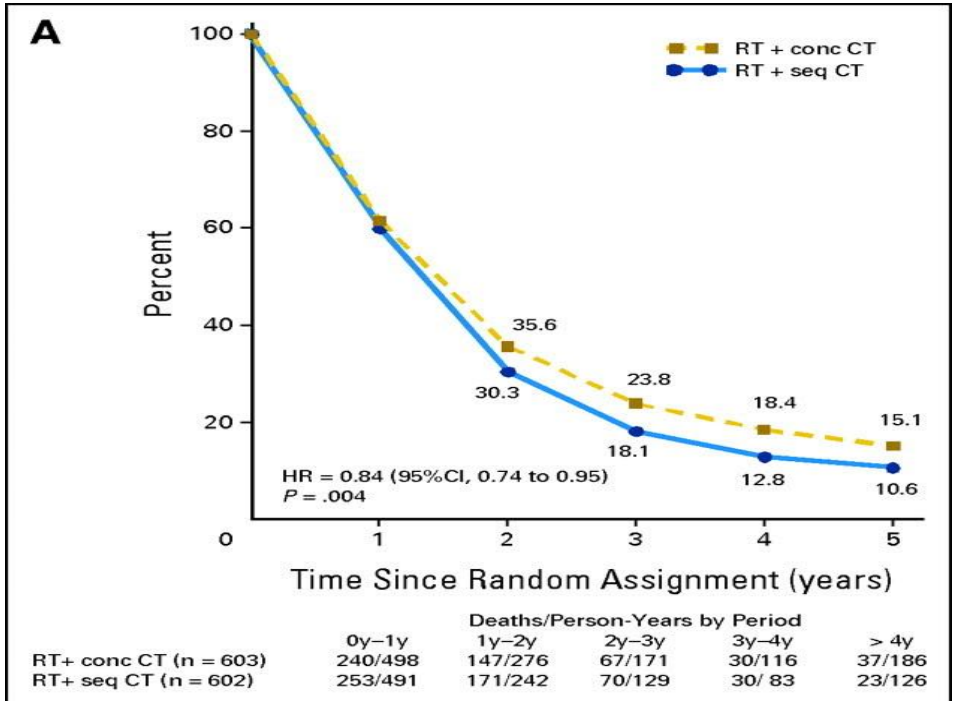
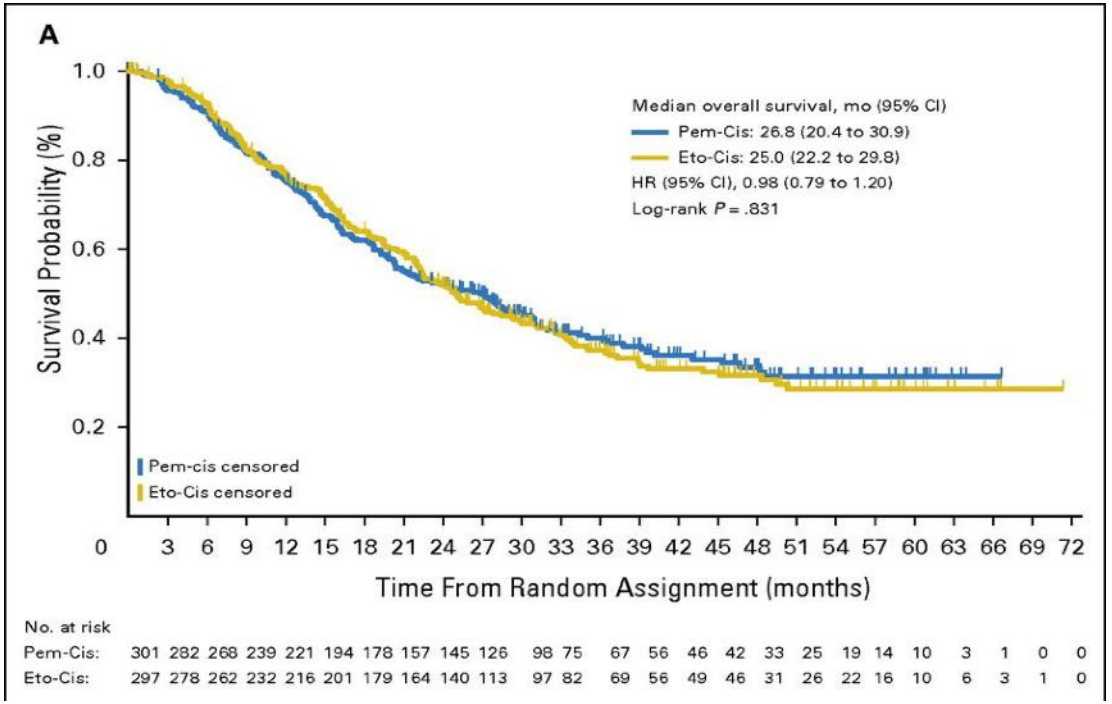
Verbeterde overleving met concurrent chemoradiotherapie





Aupérin; *Journal of Clinical Oncology* 2010 282181-2190

Senan; *Journal of Clinical Oncology* 2016 34953-962

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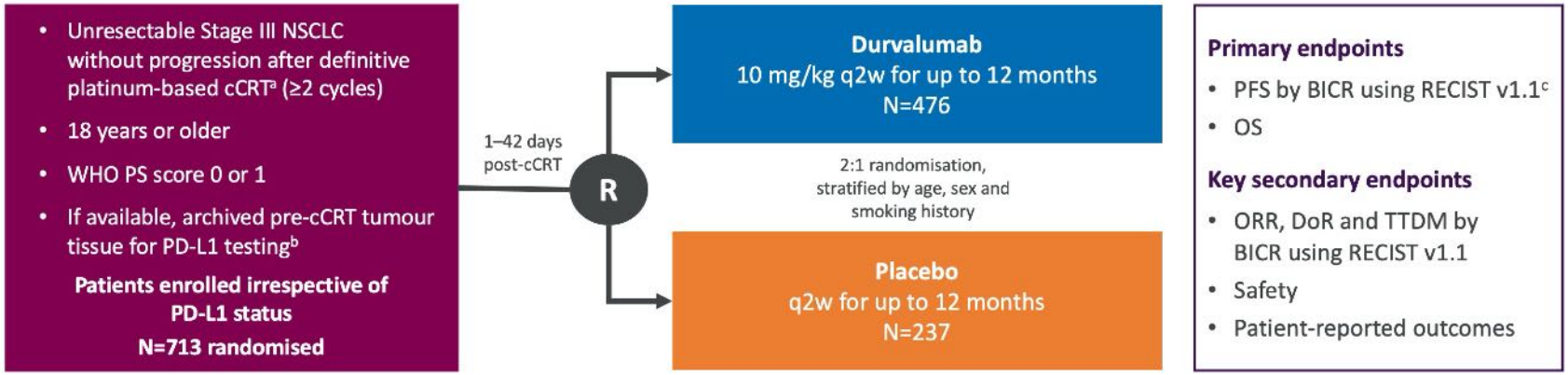
Pacific: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer



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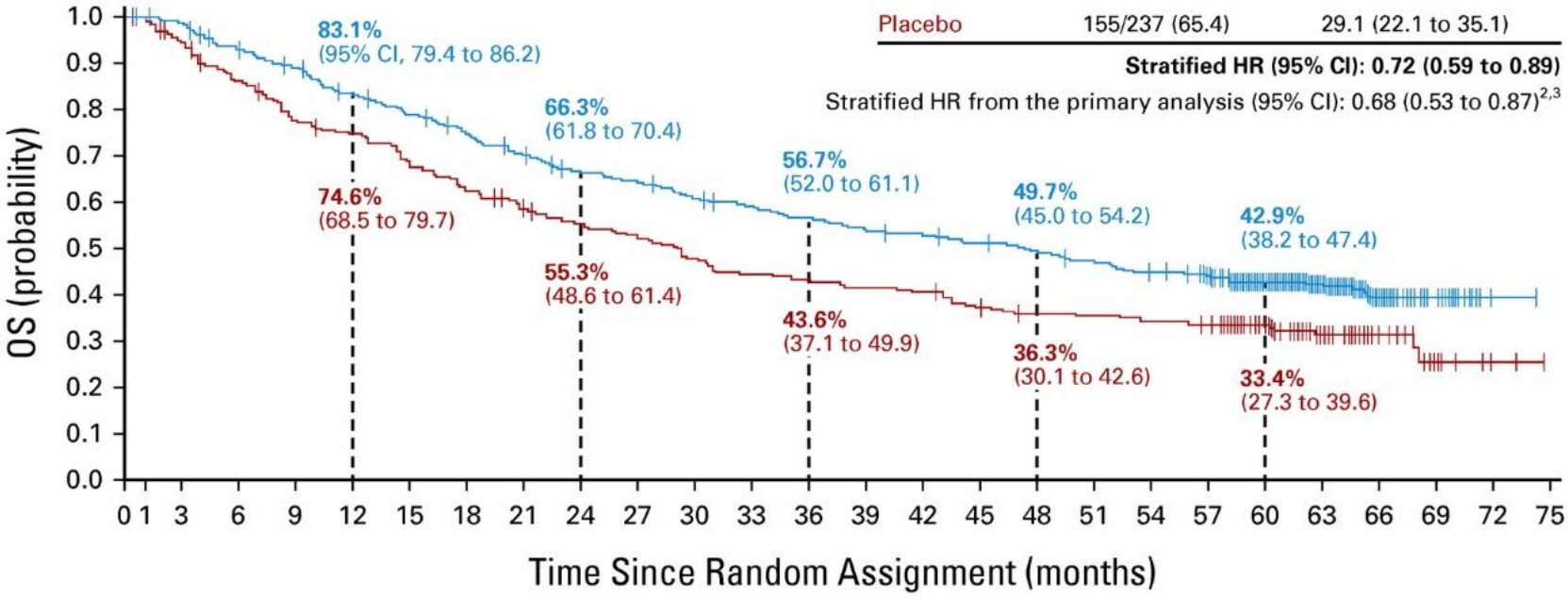
Pacific: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

Stratified HR (95% CI): 0.72 (0.59 to 0.89)

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]



No. at risk:

Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

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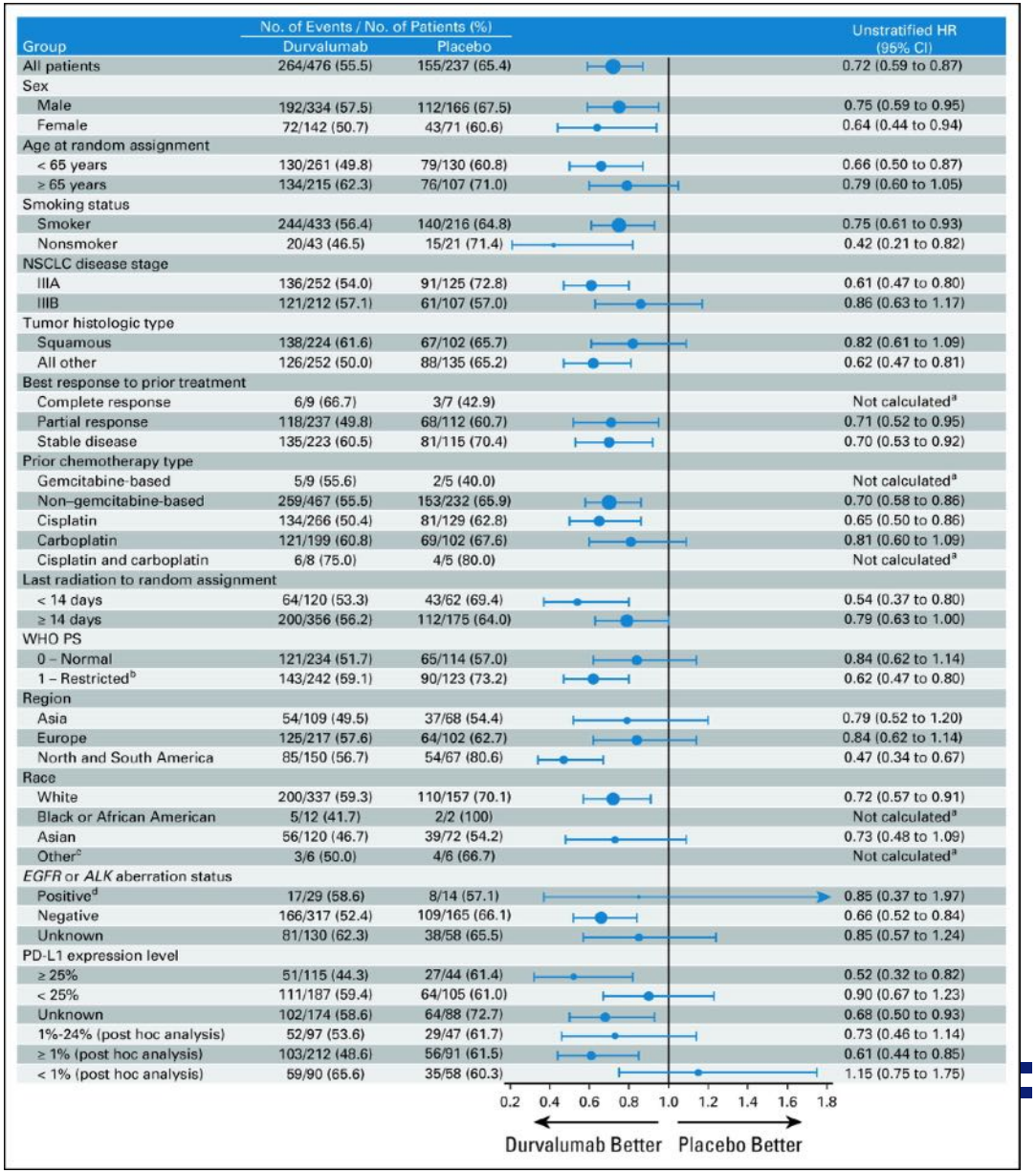
Spigel; *Journal of Clinical Oncology* 2022



Group	No. of Events / No. of Patients (%) Durvalumab	Placebo	Unstratified HR (95% CI)
All patients	264/476 (55.5)	155/237 (65.4)	0.72 (0.59 to 0.87)
Sex			
Male	192/334 (57.5)	112/166 (67.5)	0.75 (0.59 to 0.95)
Female	72/142 (50.7)	43/71 (60.6)	0.64 (0.44 to 0.94)
Age at random assignment			
< 65 years	130/261 (49.8)	79/130 (60.8)	0.66 (0.50 to 0.87)
≥ 65 years	134/215 (62.3)	76/107 (71.0)	0.79 (0.60 to 1.05)
Smoking status			
Smoker	244/433 (56.4)	140/216 (64.8)	0.75 (0.61 to 0.93)
Nonsmoker	20/43 (46.5)	15/21 (71.4)	0.42 (0.21 to 0.82)
NSCLC disease stage			
IIIA	136/252 (54.0)	91/125 (72.8)	0.61 (0.47 to 0.80)
IIIB	121/212 (57.1)	61/107 (57.0)	0.86 (0.63 to 1.17)
Tumor histologic type			
Squamous	138/224 (61.6)	67/102 (65.7)	0.82 (0.61 to 1.09)
All other	126/252 (50.0)	88/135 (65.2)	0.62 (0.47 to 0.81)
Best response to prior treatment			
Complete response	6/9 (66.7)	3/7 (42.9)	Not calculated[a]
Partial response	118/237 (49.8)	68/112 (60.7)	0.71 (0.52 to 0.95)
Stable disease	135/223 (60.5)	81/115 (70.4)	0.70 (0.53 to 0.92)
Prior chemotherapy type			
Gemcitabine-based	5/9 (55.6)	2/5 (40.0)	Not calculated[a]
Non–gemcitabine-based	259/467 (55.5)	153/232 (65.9)	0.70 (0.58 to 0.86)
Cisplatin	134/266 (50.4)	81/129 (62.8)	0.65 (0.50 to 0.86)
Carboplatin	121/199 (60.8)	69/102 (67.6)	0.81 (0.60 to 1.09)
Cisplatin and carboplatin	6/8 (75.0)	4/5 (80.0)	Not calculated[a]
Last radiation to random assignment			
< 14 days	64/120 (53.3)	43/62 (69.4)	0.54 (0.37 to 0.80)
≥ 14 days	200/356 (56.2)	112/175 (64.0)	0.79 (0.63 to 1.00)
WHO PS			
0 – Normal	121/234 (51.7)	65/114 (57.0)	0.84 (0.62 to 1.14)
1 – Restricted[b]	143/242 (59.1)	90/123 (73.2)	0.62 (0.47 to 0.80)
Region			
Asia	54/109 (49.5)	37/68 (54.4)	0.79 (0.52 to 1.20)
Europe	125/217 (57.6)	64/102 (62.7)	0.84 (0.62 to 1.14)
North and South America	85/150 (56.7)	54/67 (80.6)	0.47 (0.34 to 0.67)
Race			
White	200/337 (59.3)	110/157 (70.1)	0.72 (0.57 to 0.91)
Black or African American	5/12 (41.7)	2/2 (100)	Not calculated[a]
Asian	56/120 (46.7)	39/72 (54.2)	0.73 (0.48 to 1.09)
Other[c]	3/6 (50.0)	4/6 (66.7)	Not calculated[a]
EGFR or *ALK* aberration status			
Positive[d]	17/29 (58.6)	8/14 (57.1)	0.85 (0.37 to 1.97)
Negative	166/317 (52.4)	109/165 (66.1)	0.66 (0.52 to 0.84)
Unknown	81/130 (62.3)	38/58 (65.5)	0.85 (0.57 to 1.24)
PD-L1 expression level			
≥ 25%	51/115 (44.3)	27/44 (61.4)	0.52 (0.32 to 0.82)
< 25%	111/187 (59.4)	64/105 (61.0)	0.90 (0.67 to 1.23)
Unknown	102/174 (58.6)	64/88 (72.7)	0.68 (0.50 to 0.93)
1%-24% (post hoc analysis)	52/97 (53.6)	29/47 (61.7)	0.73 (0.46 to 1.14)
≥ 1% (post hoc analysis)	103/212 (48.6)	56/91 (61.5)	0.61 (0.44 to 0.85)
< 1% (post hoc analysis)	59/90 (65.6)	35/58 (60.3)	1.15 (0.75 to 1.75)

Spigel; *Journal of Clinical Oncology* 2022

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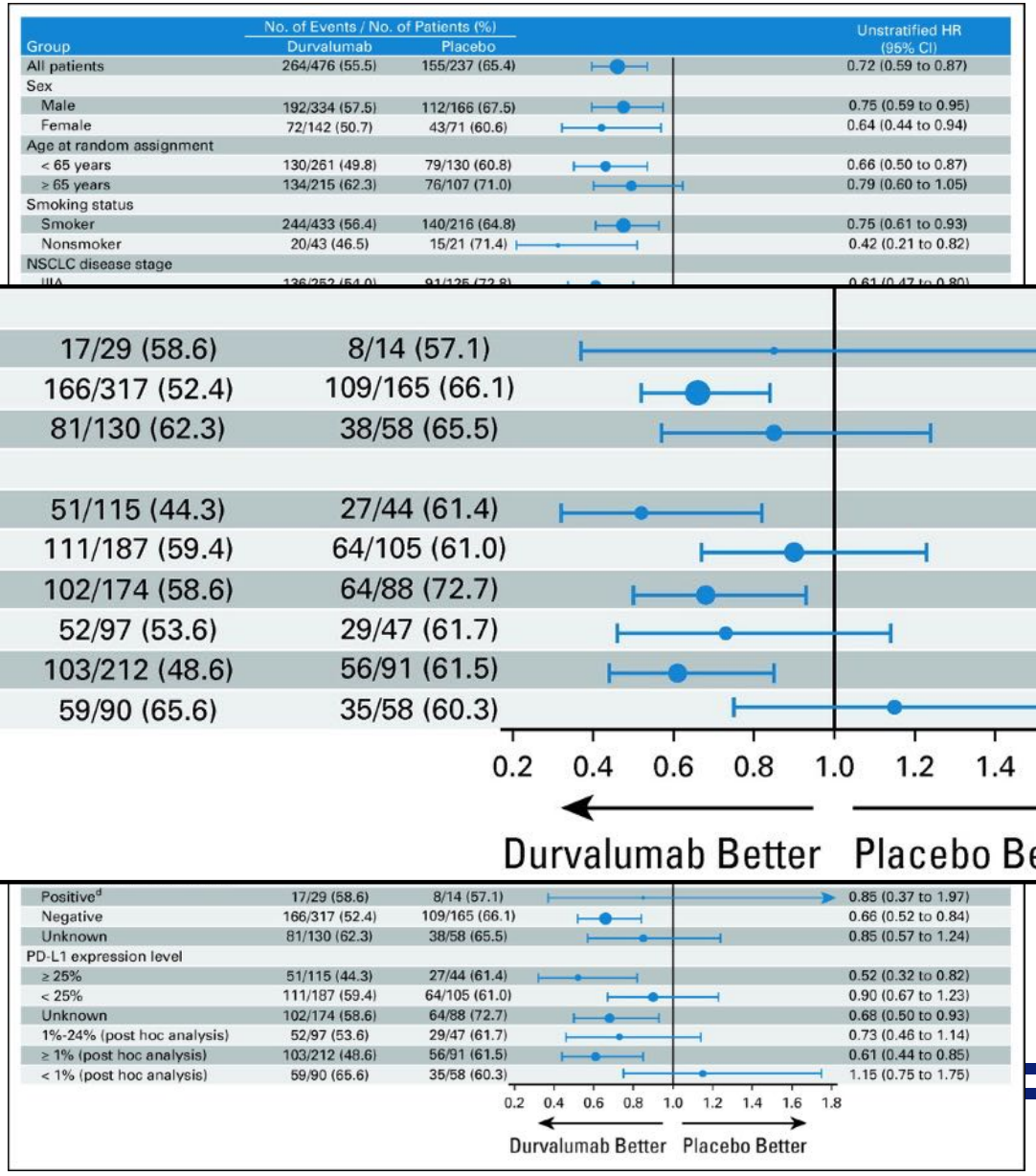

Spigel; *Journal of Clinical Oncology* 2022

1. Effectiviteit van immuuntherapie is verminderd in geval van EGFR/ALK.

2. PDL1 mogelijk voorspellend voor immuuntherapie effect.

1. Oncogene drivers?
2. TKI?
3. Immuuntherapie?
4. Rol chemotherapie?

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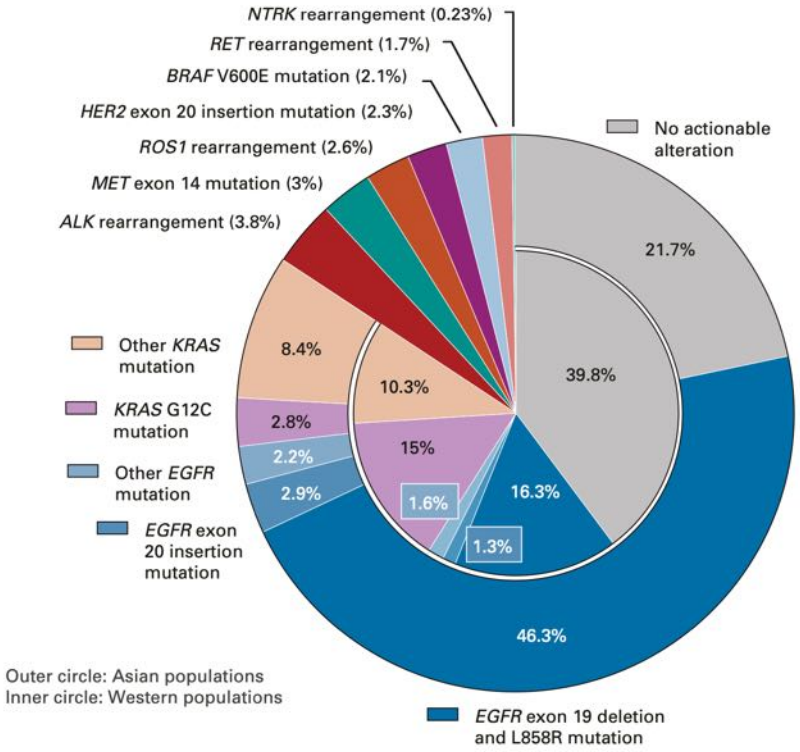
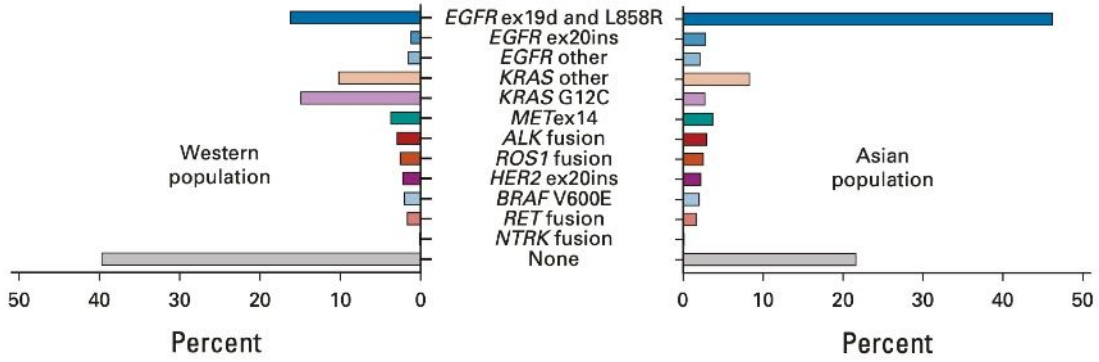
Oncogene drivers are rare *PER* driver, but in total ~15-20%!





Oncogene drivers vaak PDL1 positief

39.3%+	Klassieke EGFR mutaties
86.4%+	Afwijkende EGFR mutaties (G719X, L861Q, S768I, exon 20 inserties)
85.7%+	ALK translocaties

Evans, annals oncolog 2017

Oncogene drivers vaak PDL1 positief

39.3%+ Klassieke EGFR mutaties

86.4%+ Afwijkende EGFR mutaties (G719X, L861Q, S768I, exon 20 inserties)

85.7%+ ALK translocaties

	EGFR	ALK	ROS1	BRAF	KRAS	HER2	MET	RET	NTRK
Targeted therapy	**80%**[a]	**83%**	*77%*	*64%*	*54%*[b]	*55%*	*71%*	*68%*	*75%*
ICI	**11%**	**4%**	**14%**	**24%**	**57%**[c]	**15%**	**23%**	**11%**	**NA**

Calles, Lung Cancer 2020

Evans, annals oncolog 2017

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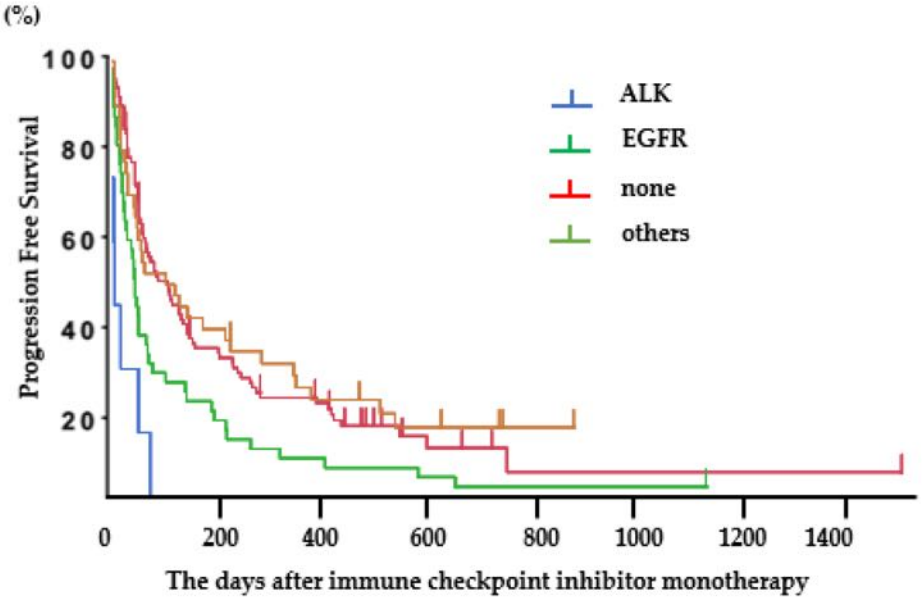
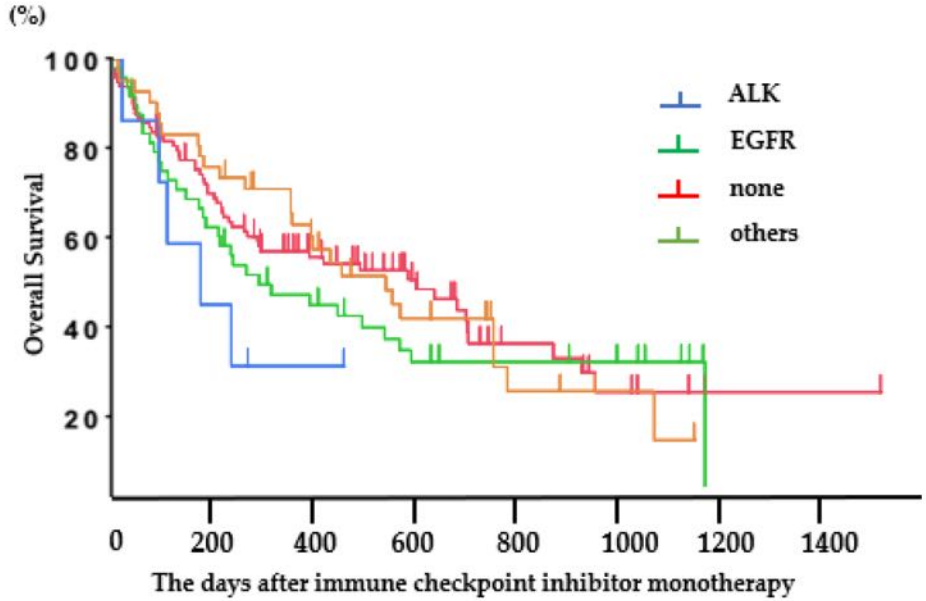
Efficacy of Immune Checkpoint Inhibitor Monotherapy for Advanced NSCLC





Oya, int j mol sci 2020

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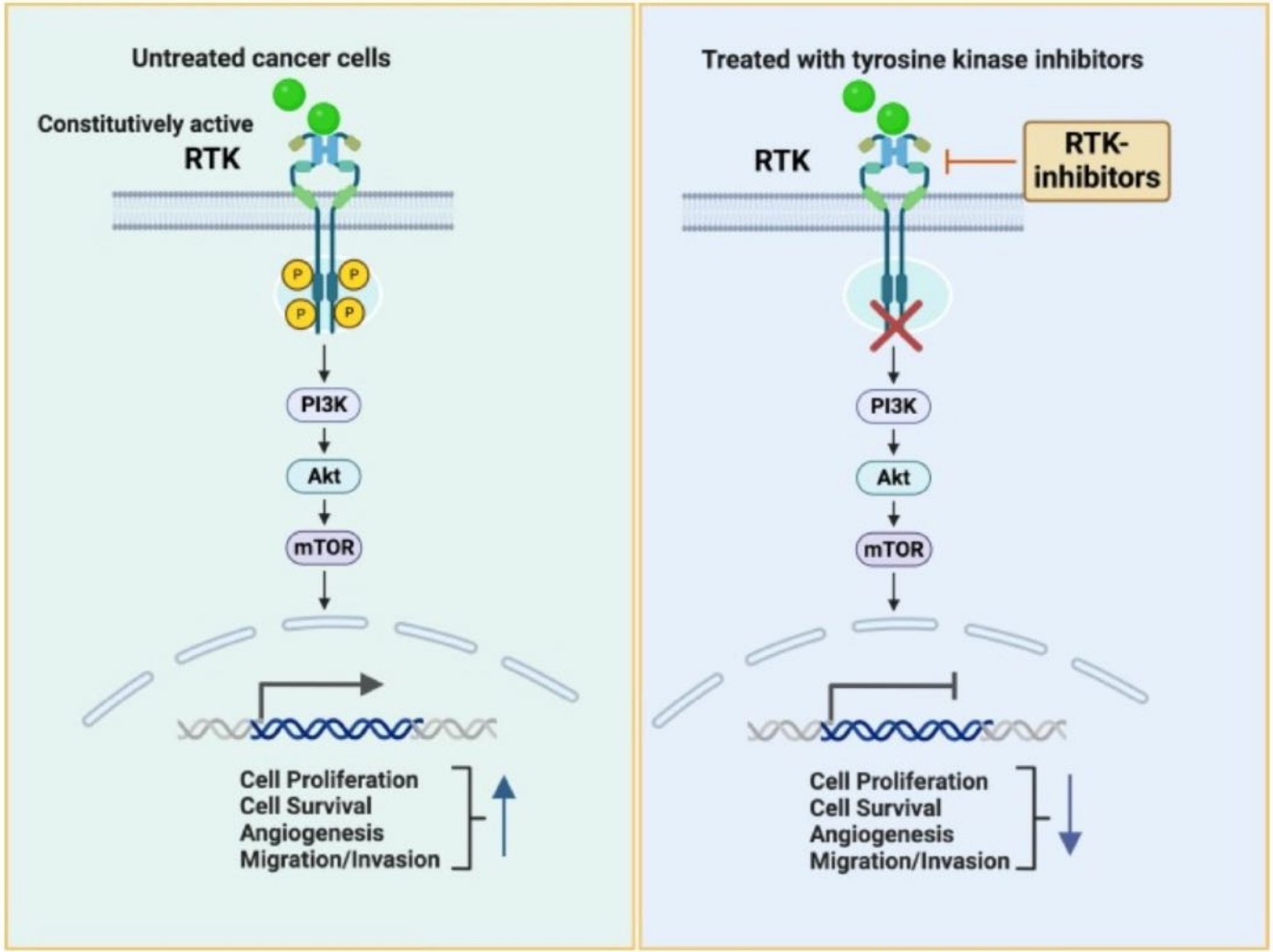
Tyrosine kinase inhibitors (TKI)



Kumar 2024

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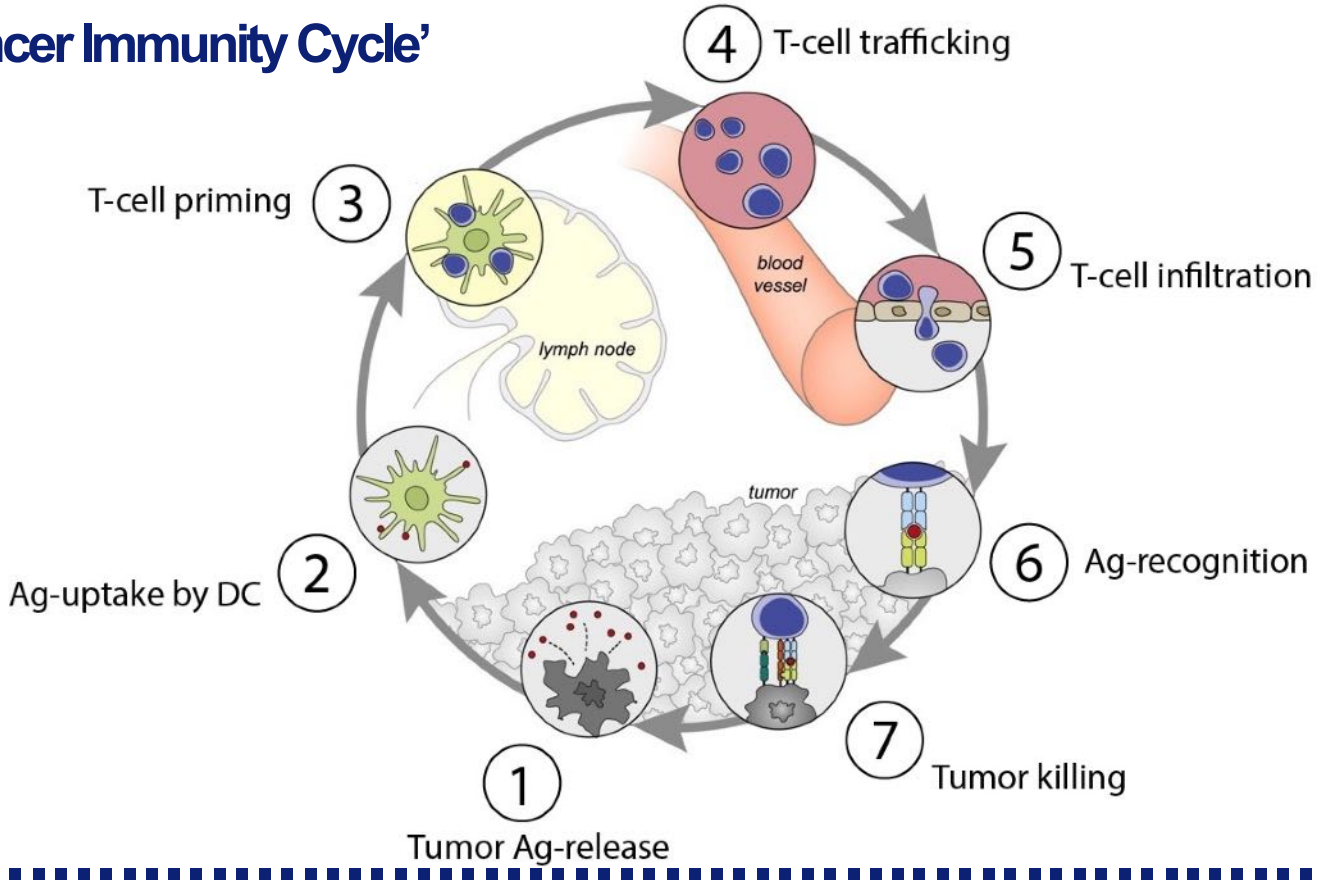
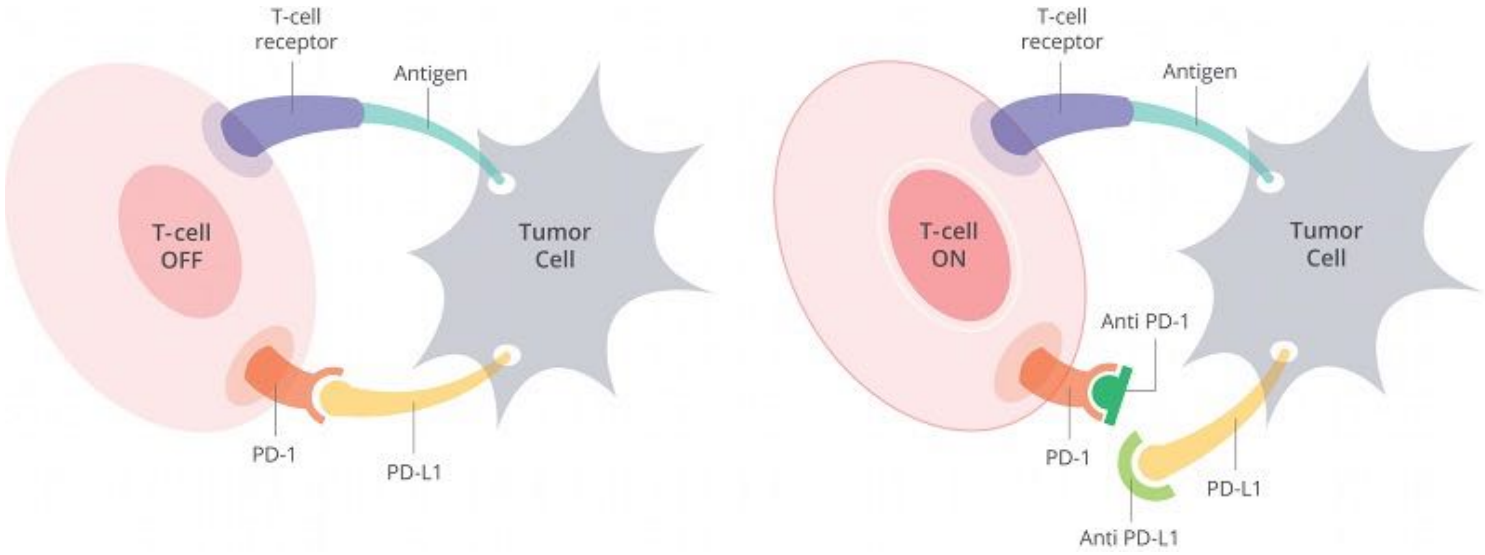
Immuun checkpoint inhibitie

‘Cancer Immunity Cycle’



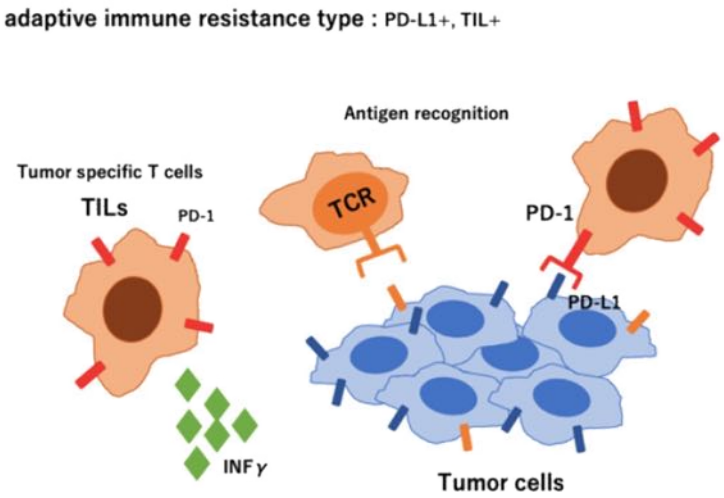
Chen & Mellman et al. Immunity 2013

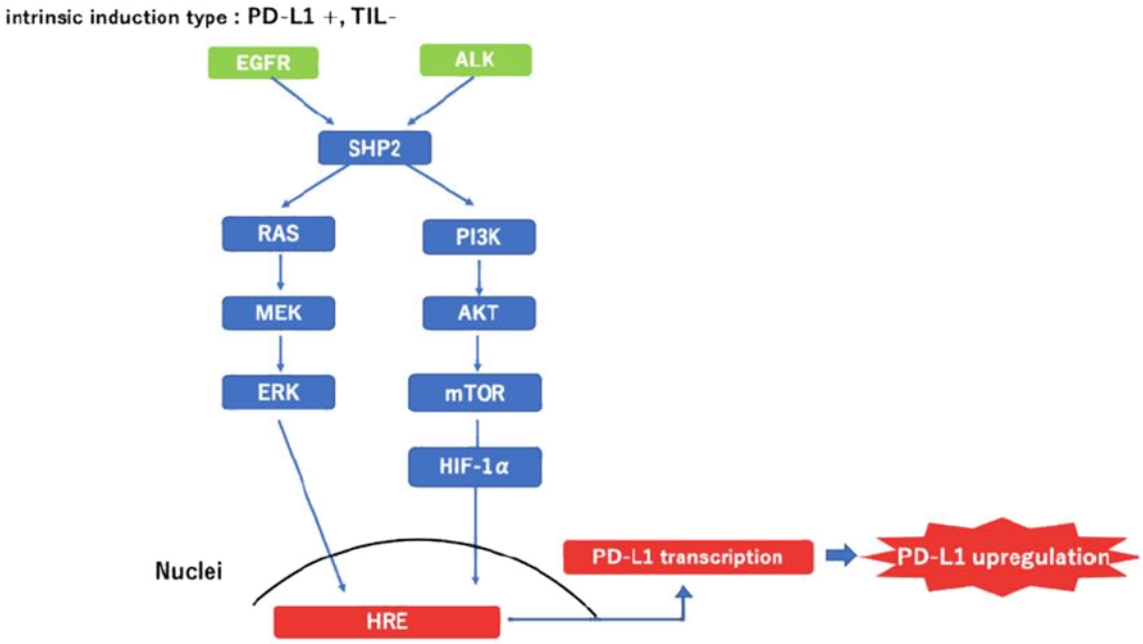
PD(L)1 checkpoint inhibition



https://www.smartpatients.com/targets/pd-1

Upregulation of PD-L-1, not always immune-mediated response





Oya, int j mol sci 2020

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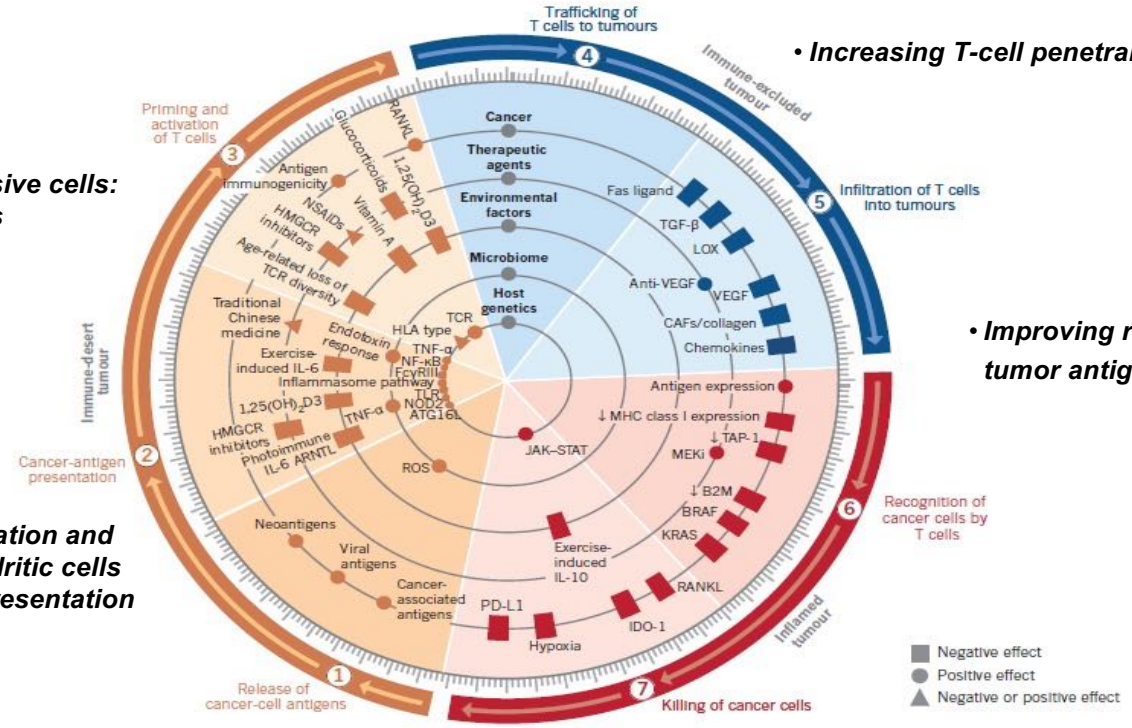
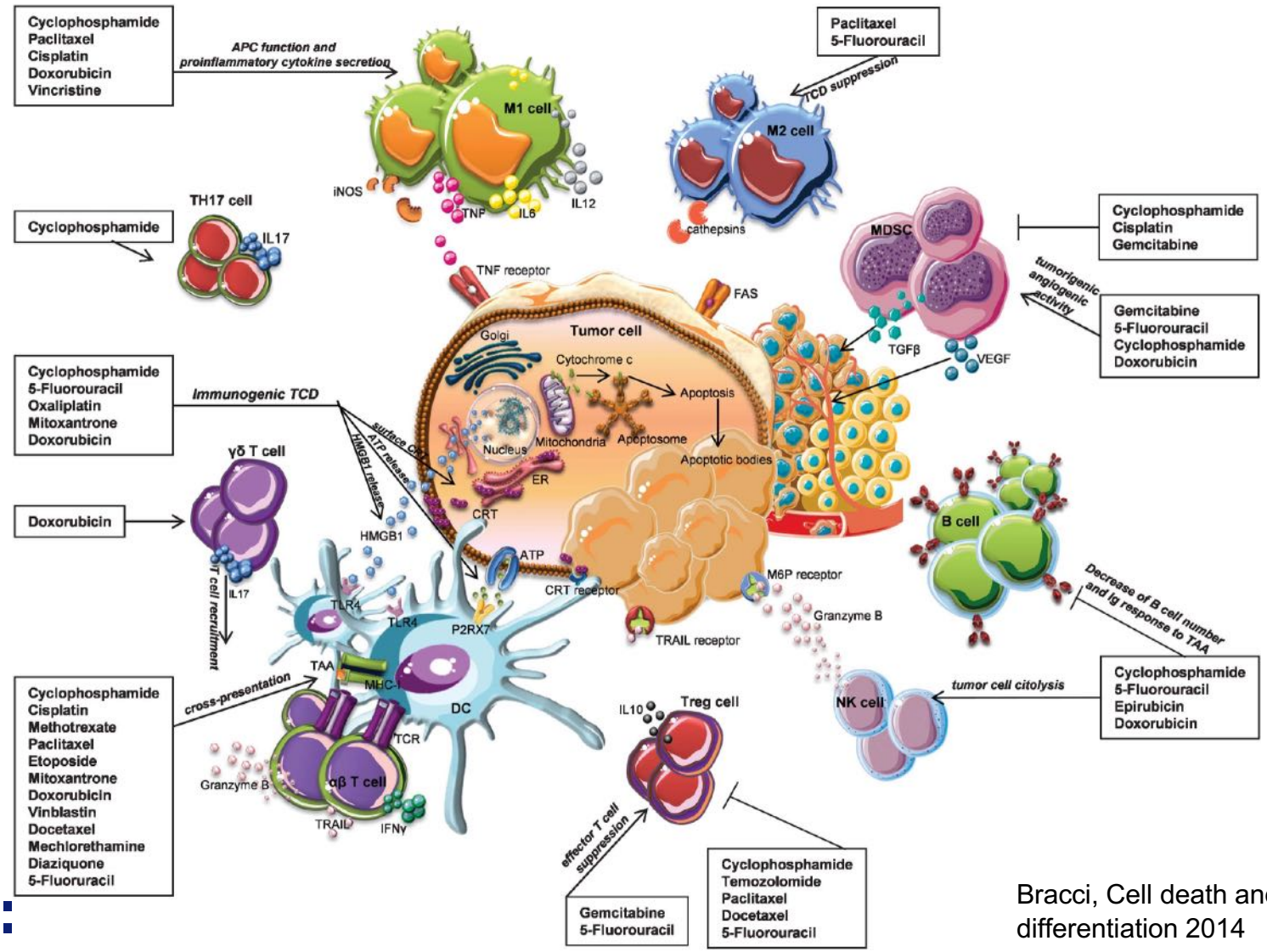
Chemotherapy Enhances Anti-Cancer Immune Response: Rational Partner for Immunotherapy



- ***Increasing T-cell penetrance in the tumor***
- ***Eliminating immunosuppressive cells: T-regulatory cells***
- ***Improving recognition of tumor antigens by T-cell***
- ***Enhancing maturation and activation of dendritic cells toward antigen presentation***
- ***Inducing immunogenic cell death***
- ***Eliminating immunosuppressive cells: T-regs, myeloid-derived suppressor cells, M2 macrophages***

Chen, Nature 2017



Bracci, Cell death and differentiation 2014

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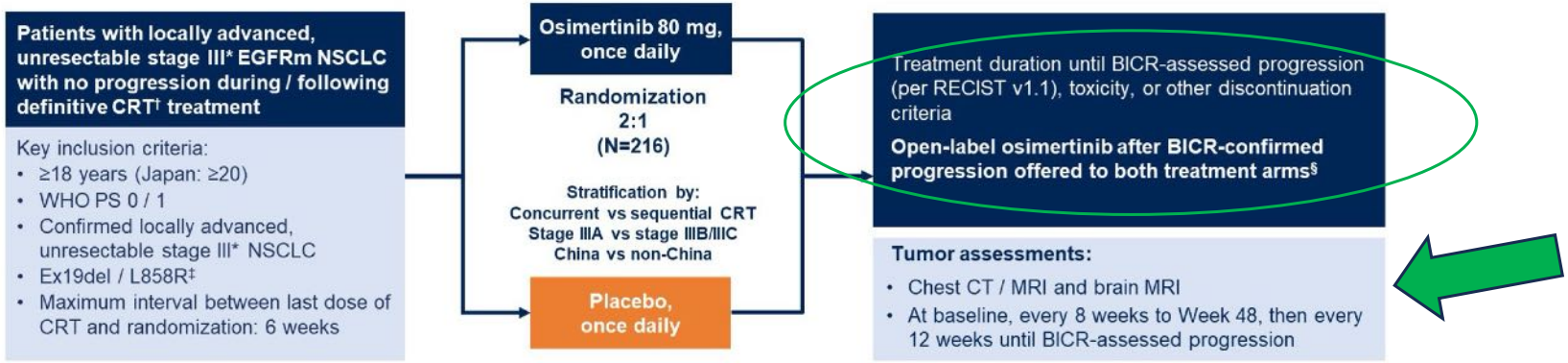
DUS

- Chemotherapie werkt synergistisch met immuuntherapie.
- Oncogene drivers testen
  - Vanwege mogelijkheid TKI
  - Ineffectiviteit immuuntherapie
  - (kosten, toxiciteit, …)

Osimertinib after definitive chemoradiotherapy in patients with unresectable stage III epidermal growth factor receptor-mutated (EGFRm) NSCLC: primary results of the Phase 3 LAURA study



Endpoints

- **Primary endpoint:** PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
- **Secondary endpoints included:** OS, CNS PFS, safety

81% Asian
PET not mandatory
Baseline MRI before randomisation

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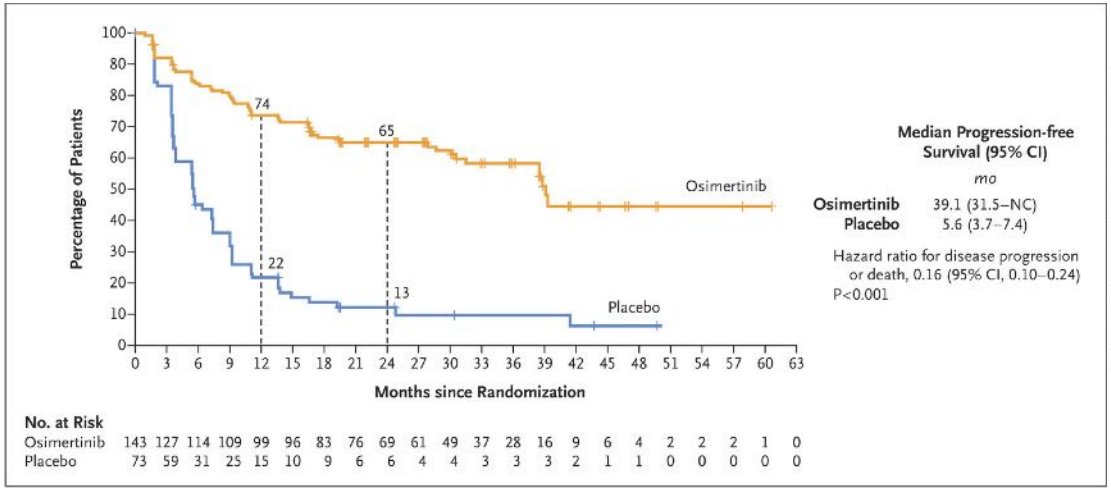
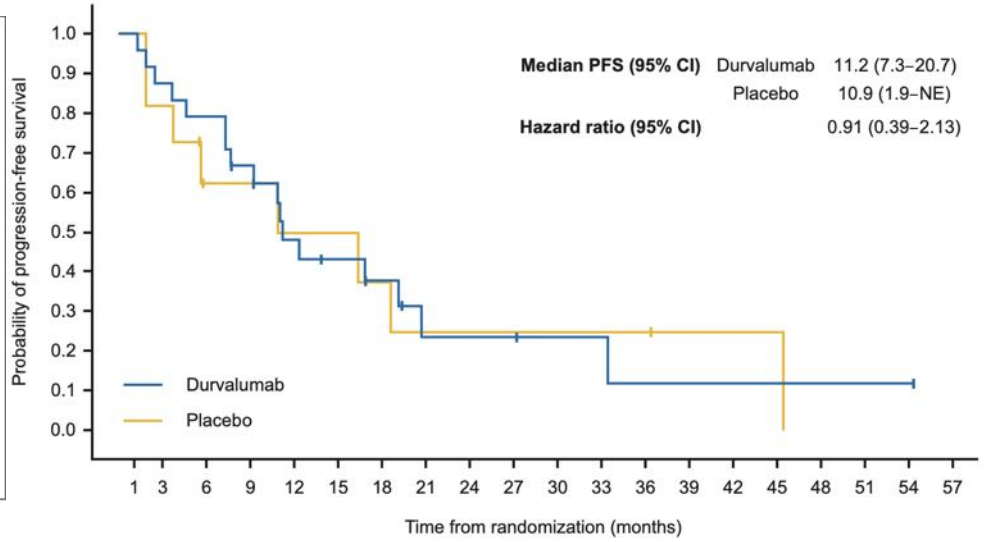
Toename PFS



PACIFIC post-hoc analysis EGFR mutant



Median PFS in placebo groep 5.6m versus 10.9m in pacific?

Shun Lu, NEJM 2024;
Naidoo JTO 2023

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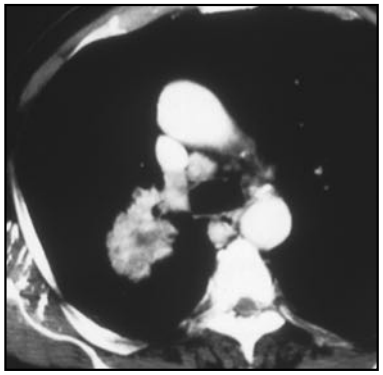
Conclusie:

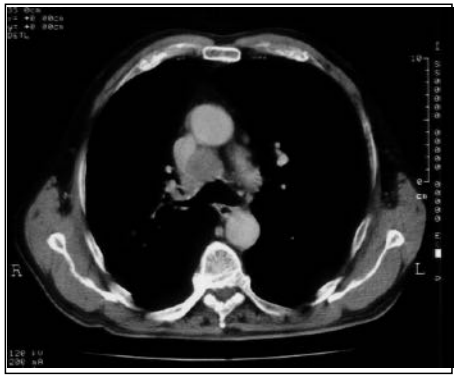
Bij niet resectabel stadium III: concurrent chemoradiotherapie

- gevolgd door durvalumab indien aberraties uitgesloten
- PM gevolgd door osimertinib indien EGFR mutatie?

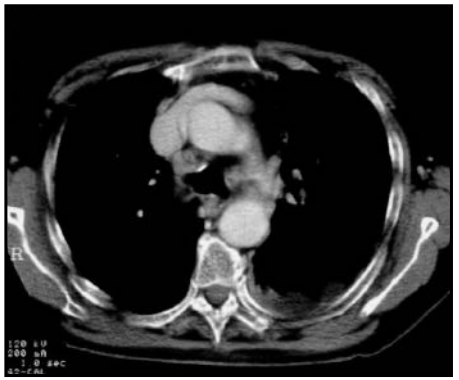
Maar: stadium III niet 1 ziekte



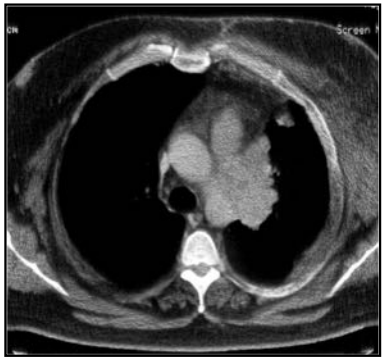
N2 non- bulky (IIIA)



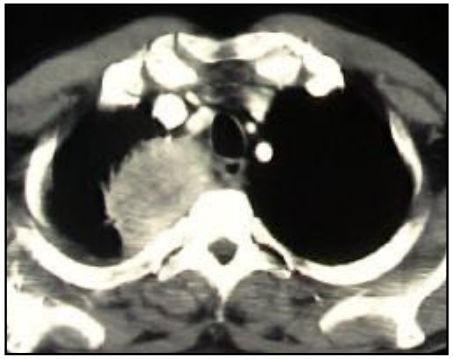
N2 bulky (IIIA)



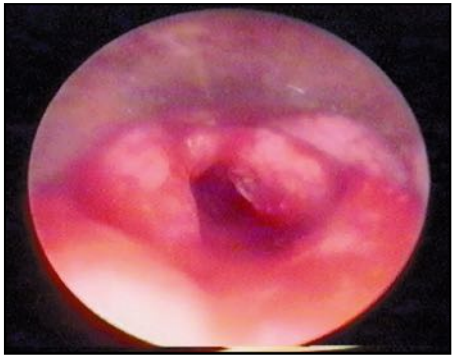
N3 (IIIB)



T4
(mediastinal infiltration)



T4
(Chest Wall infiltration)



T4
(tracheal infiltration)

Dus wat is resectabel?

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What's *resectable* NSCLC?

It's a state of mind!

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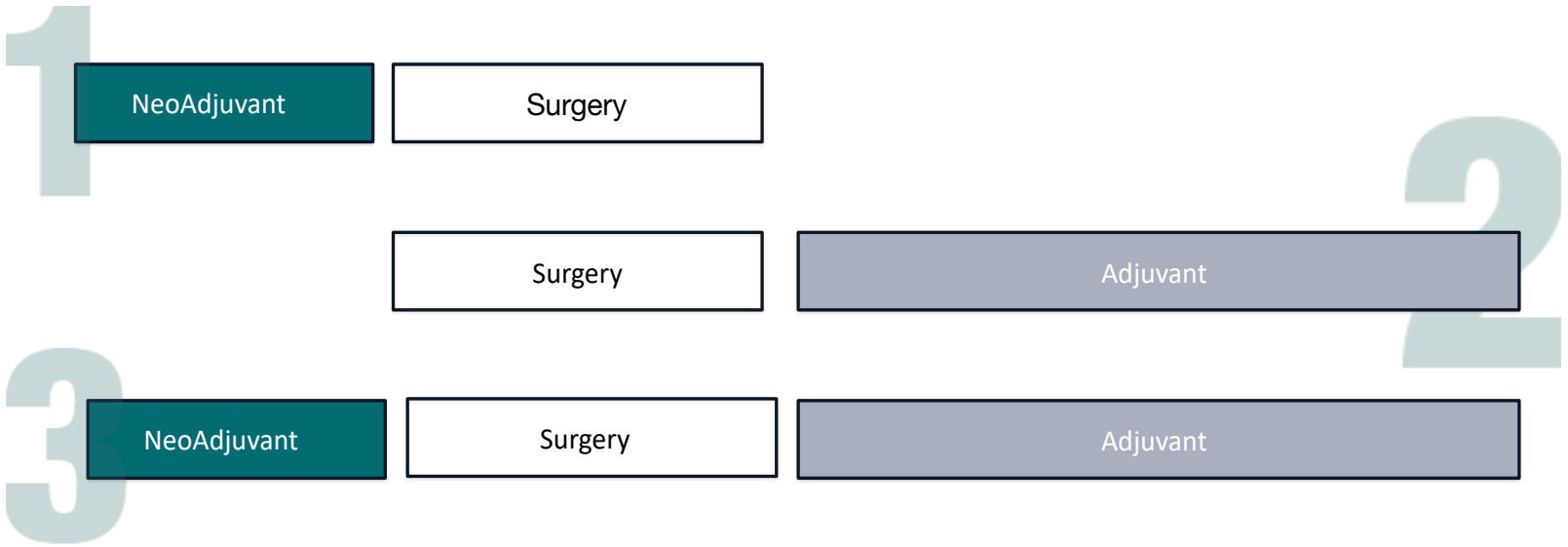
RESECTABEL NSCLC



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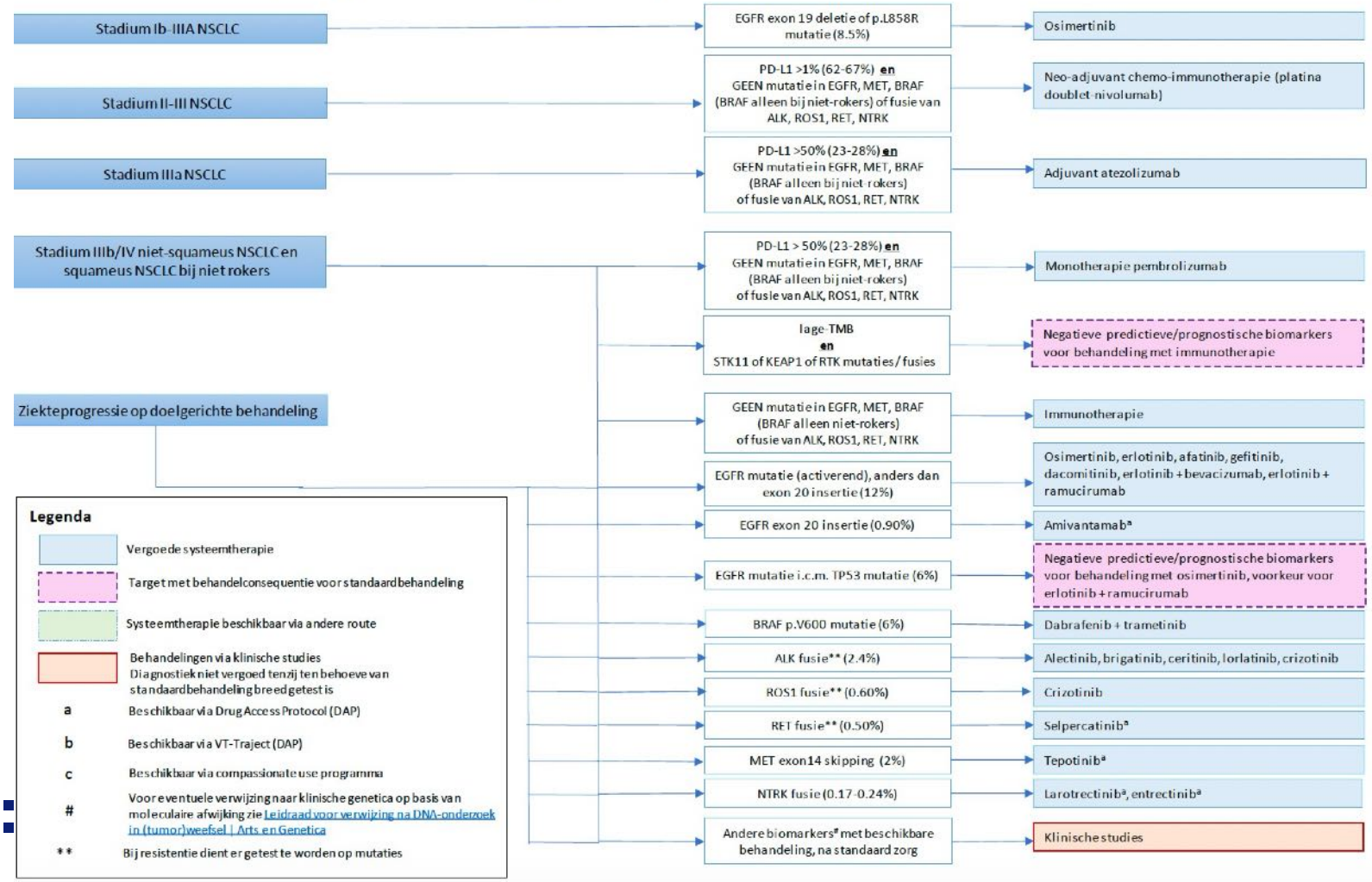
KNT-lijst NSCLC: (Tripartite vastgesteld), versie 2024-2, d.d. 08/01/2024

Versie 1 is op te vragen bij wvlug@nvalt.nl

Niet-kleincellig longcarcinoom (NSCLC)



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Versie 1 is op te vragen bij wvlug@nvalt.nl

Niet-kleincellig longcarcinoom (NSCLC)

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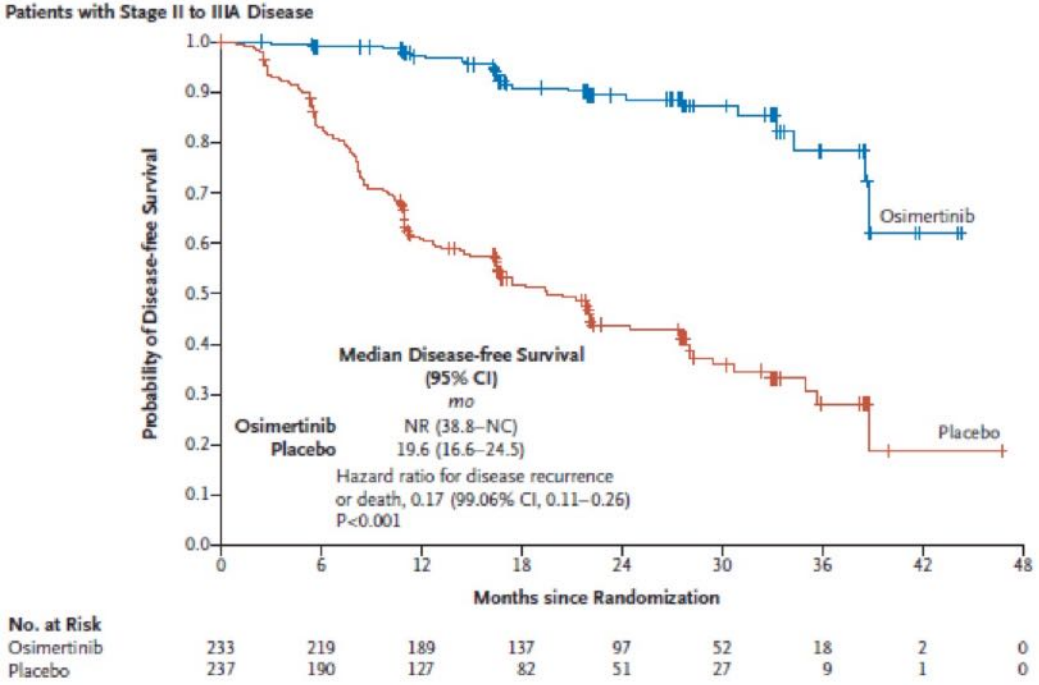
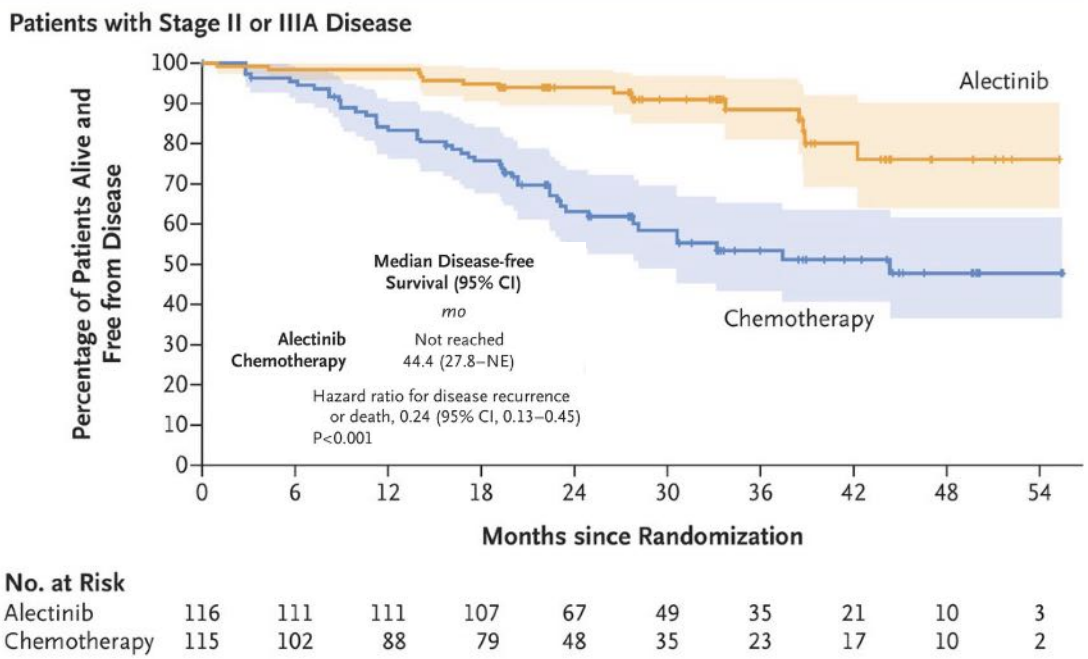
Adjuvante doelgerichte behandeling na resectie

ADAURA STUDY (EGFR)



ALINA STUDY (ALK)



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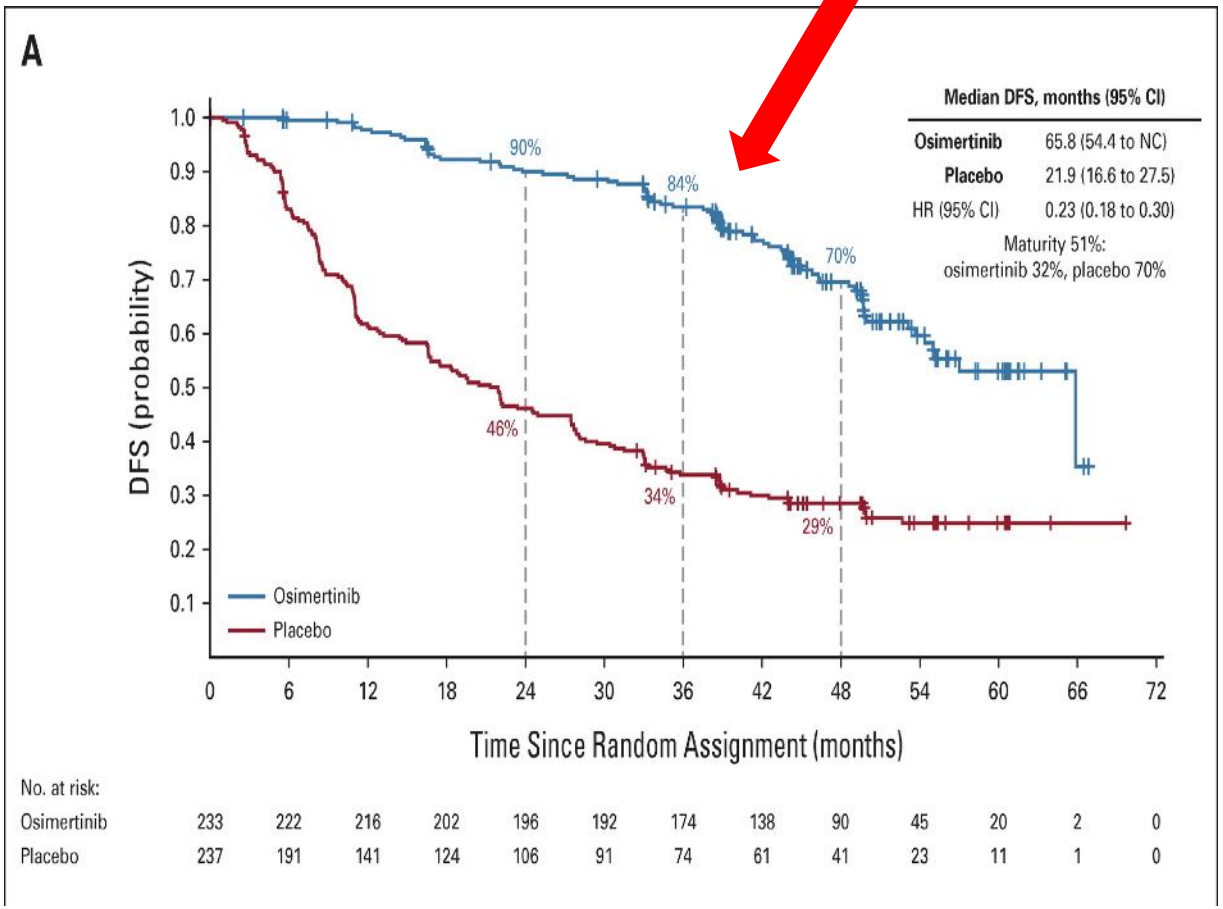
Osimertinib: na resectie
3 years osimertinib vs placebo

St II-IIIA



OSIMERTINIB TOT PROGRESSIE?

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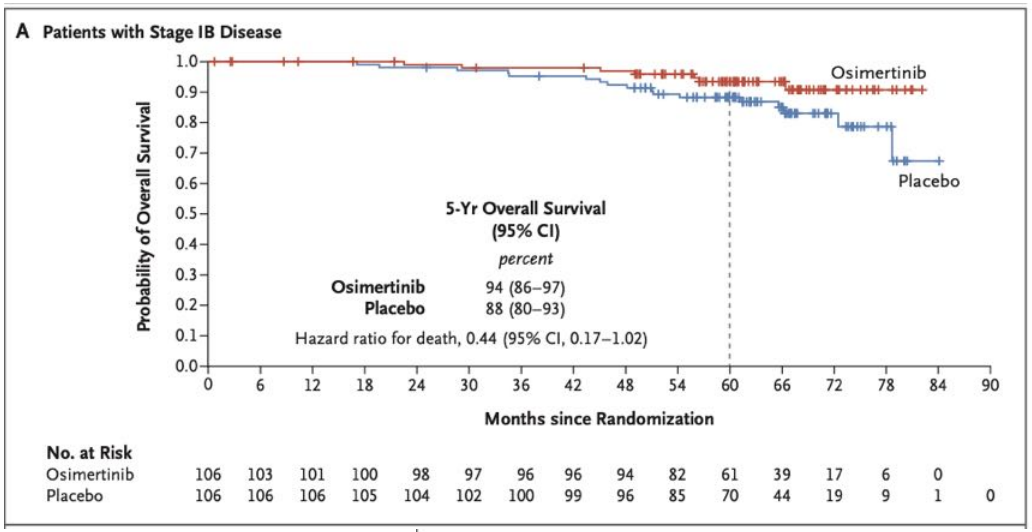
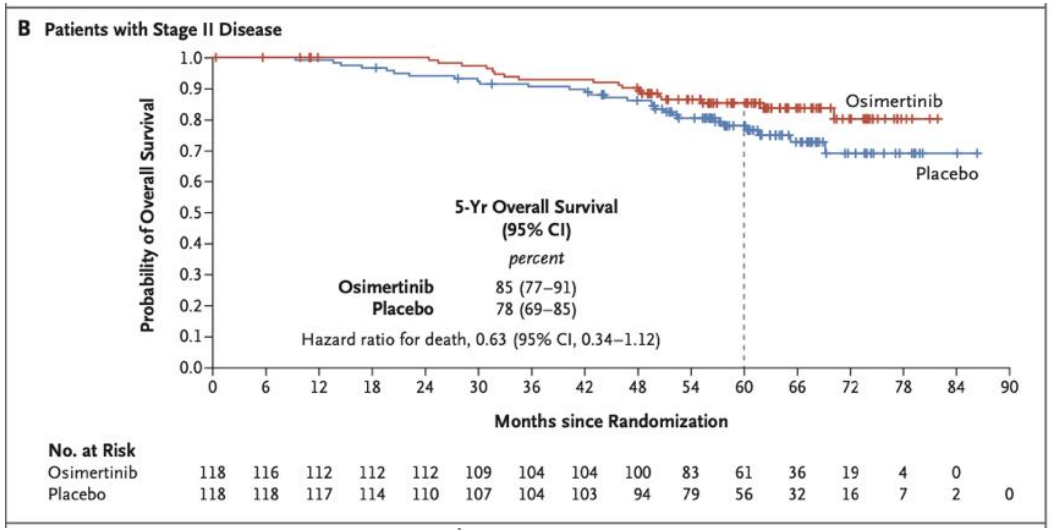
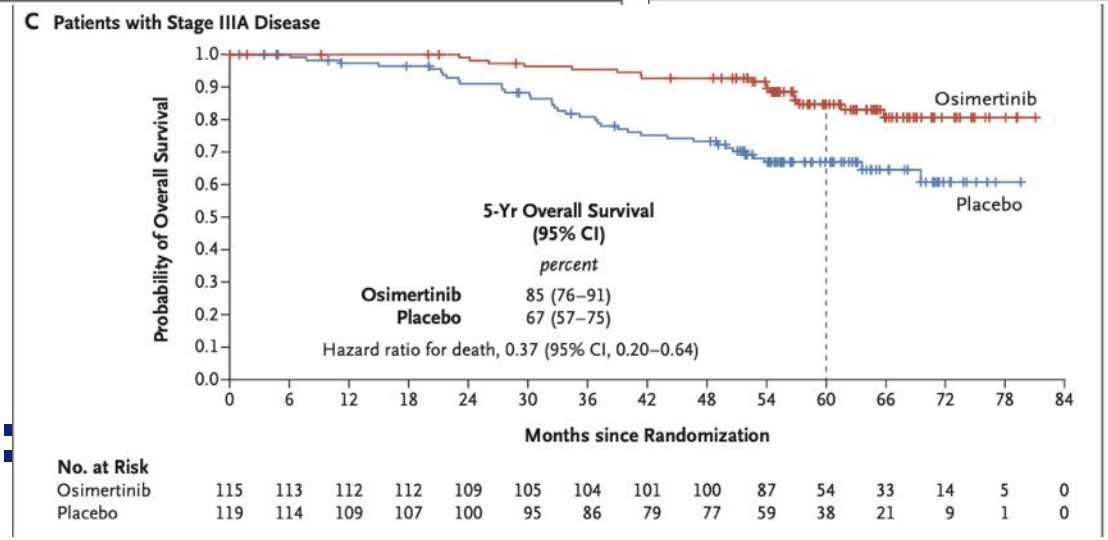
OS advantage driven by higher stage?



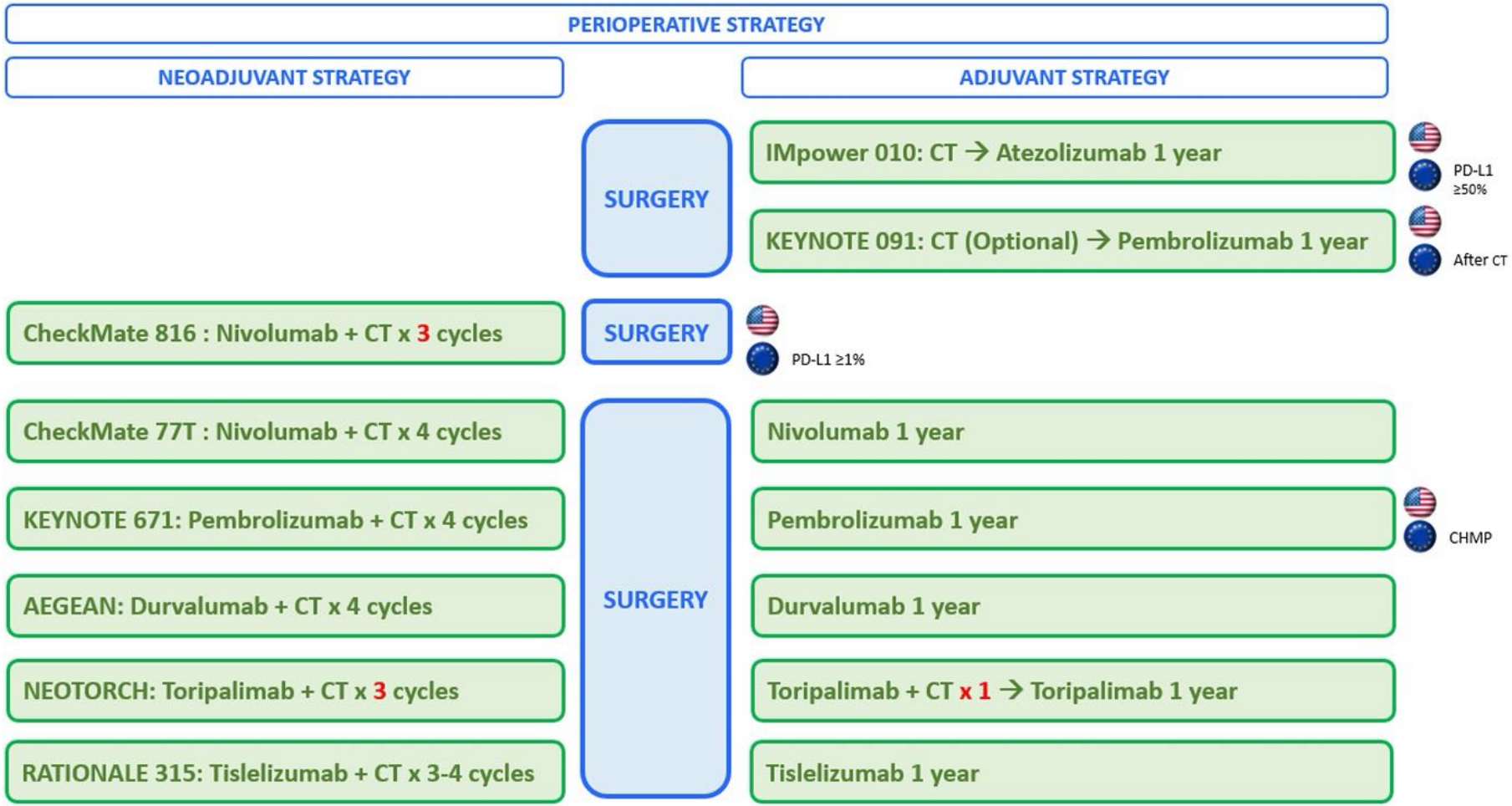




Tsuboi et al *NEJM; 2023: 389:137-47*

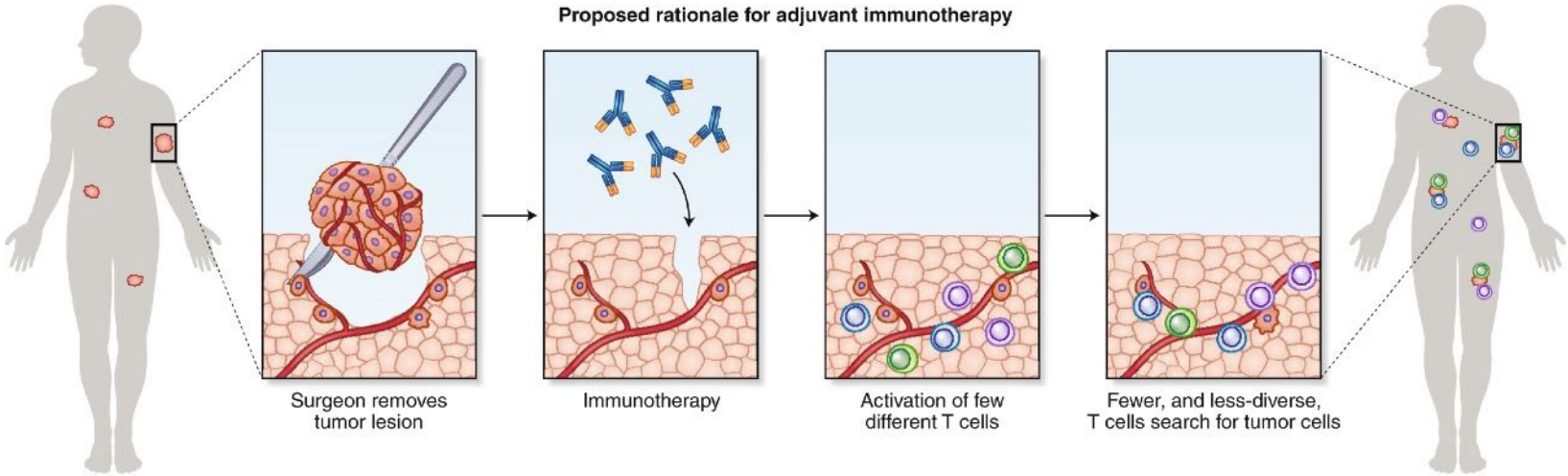
Erasmus MC

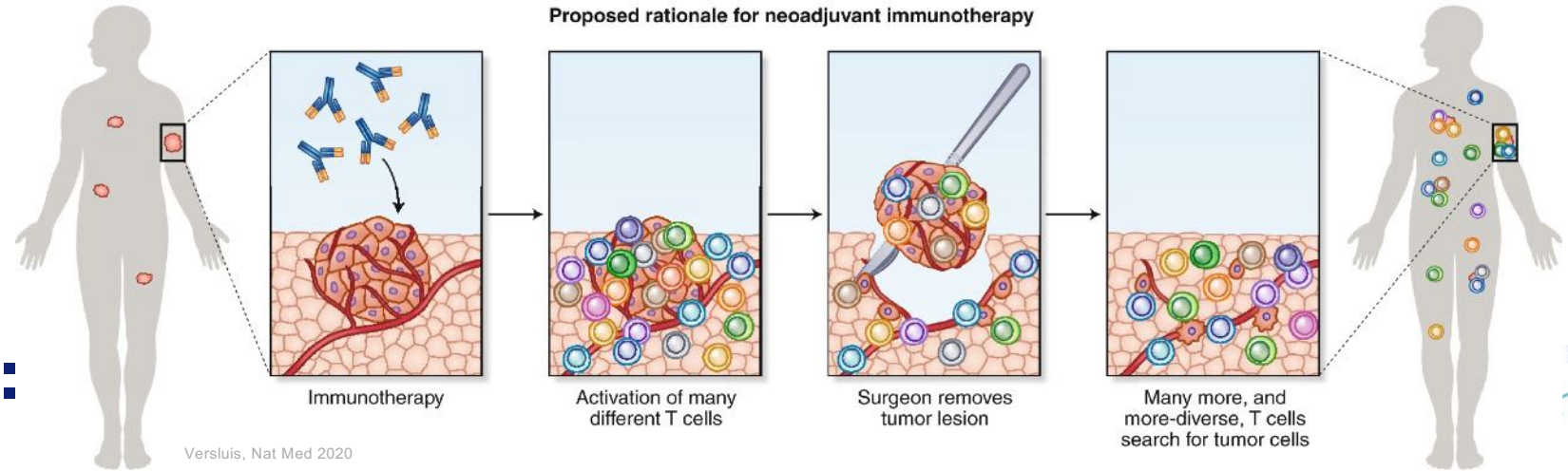
(Neo-)adjuvante immuuntherapie



Lavaud, Cancers 2024

Adjuvant of neoadjuvante behandeling?

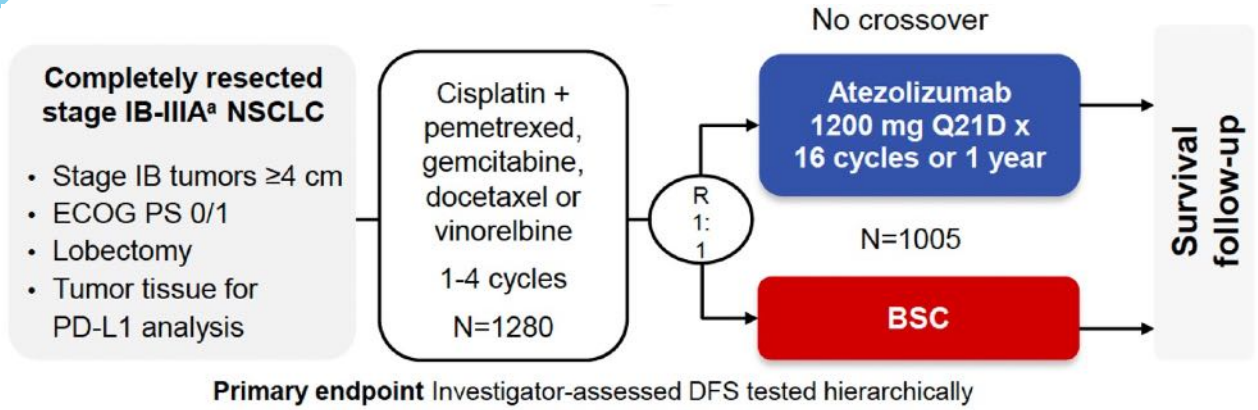




Versluis, Nat Med 2020

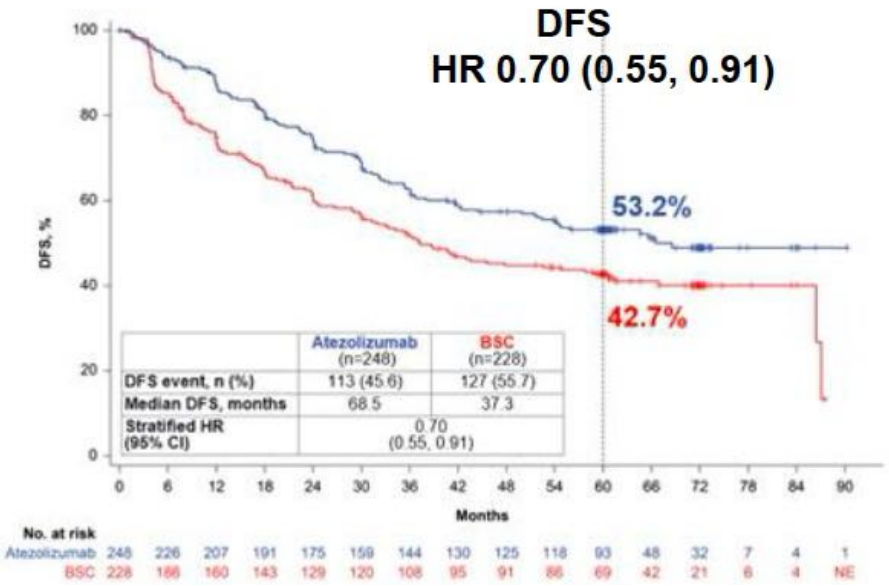
Erasmus MC

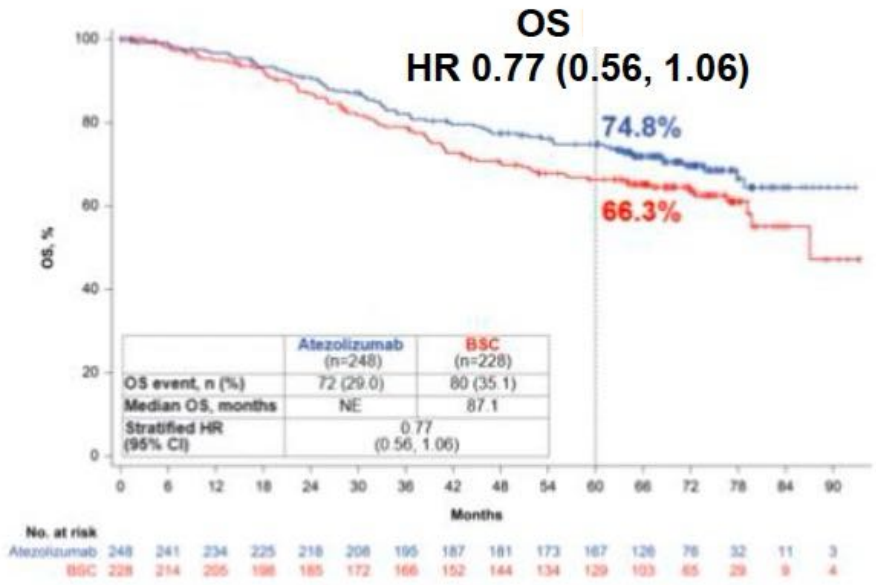
Adjuvant immuuntherapie



Primary endpoint Investigator-assessed DFS tested hierarchically

Efficacy in stage II-IIIA PD-L1 ≥1%





CCTG BR.31 Trial Design

Study population:
- Stage IB (≥4 cm)–IIIA NSCLC (AJCC 7th ed.)
- Complete resection
- ECOG PS 0–1
- EGFRm/ALK+ pts eligible

Surgery → randomization ≥3 weeks

Platinum doublet
(Chemo ineligible, chemo intolerant, patients who refuse chemo may also be included)

N=1415 (all comers)
N=1219 EGFR−/ALK−

R[1] 2:1

Durvalumab
20 mg/kg Q4W x 12 months

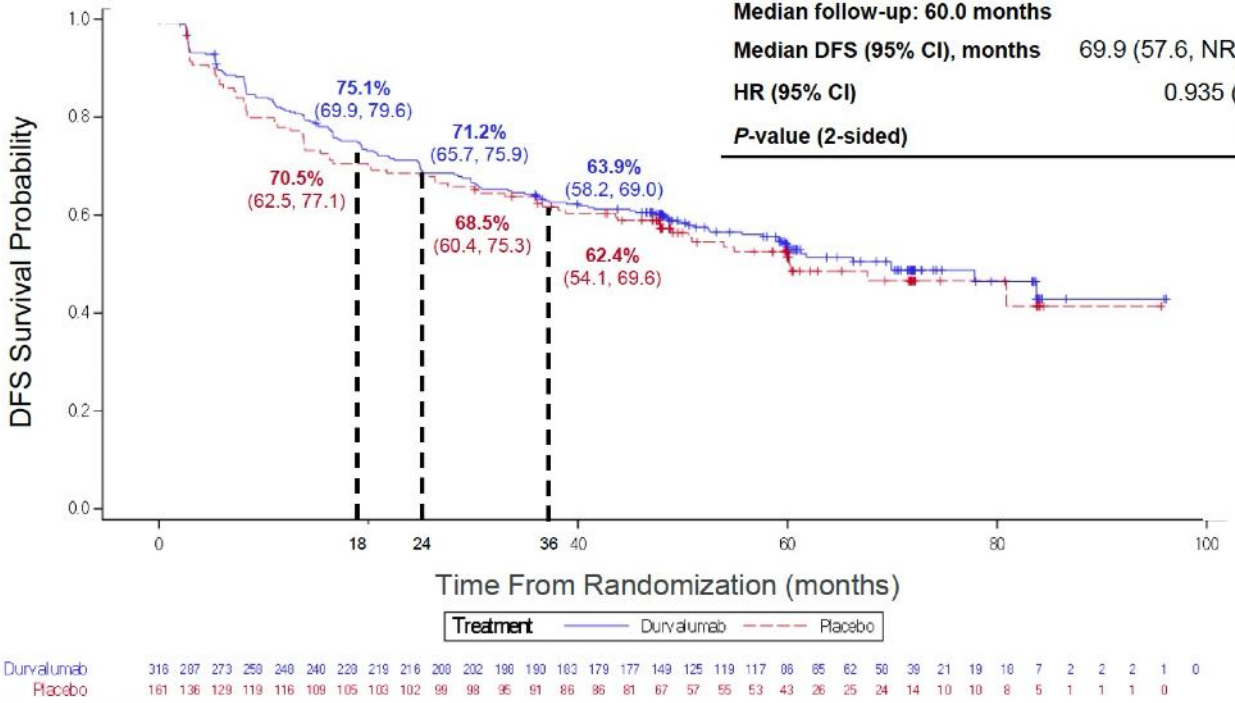
Stratification
- Stage IB (≥4 cm) *vs* II *vs* IIIA
- PD-L1 status (0 *vs* 1–24% *vs* 25–49% *vs* ≥50%)[2]
- Adjuvant platinum-based chemotherapy (≥300 mg/m² cisplatin/equiv *vs* <300 mg/m² vs no chemotherapy)
- Accruing center
- Nodal dissection according to ESTS[3] (yes *vs* no)

Placebo
20 mg/kg Q4W x 12 months

Primary endpoint
- DFS[4] (Investigator Assessed) in patients with PD-L1 TC ≥25% and EGFR−/ALK−

DFS in PD-L1≥25% EGFR−/ALK−

	D arm n=316	PBO arm n=161
Median follow-up: 60.0 months		
Median DFS (95% CI), months	69.9 (57.6, NR)	60.2 (47.7, NR)
HR (95% CI)	0.935 (0.706, 1.247)	
***P*-value (2-sided)**	0.642	



PEARLS/KEYNOTE-091 Study Design

Eligibility for Registration
- Confirmed stage IB (T ≥4 cm), II, or IIIA NSCLC per AJCC v7
- Complete surgical resection with negative margins (R0)
- Provision of tumor tissue for PD-L1 testing

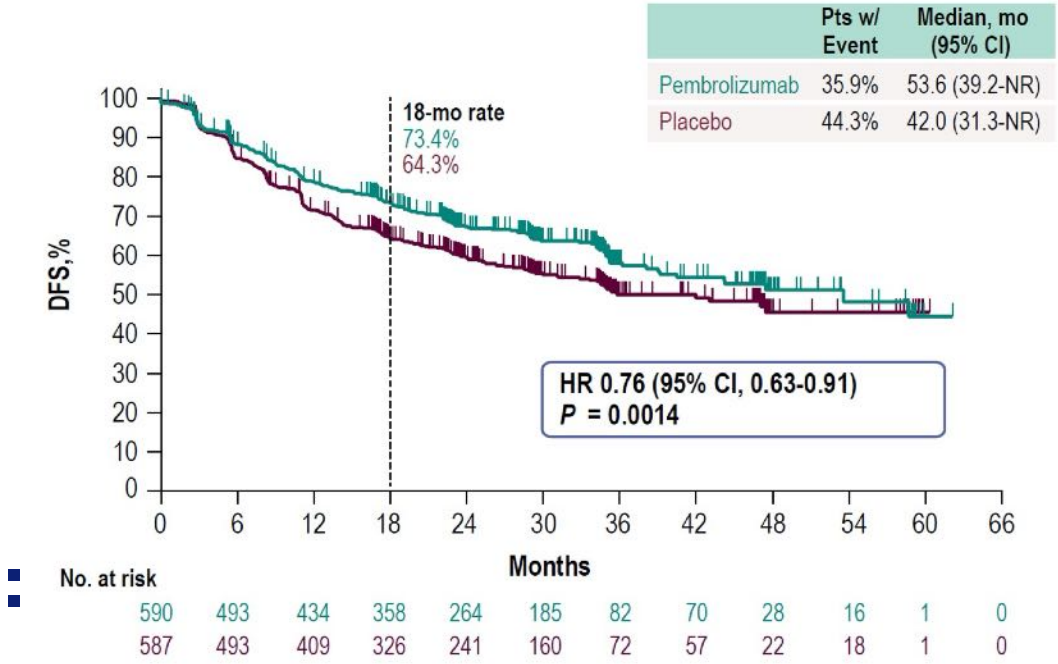
PD-L1 testing
done centrally using PD-L1 IHC 22C3 pharmDx

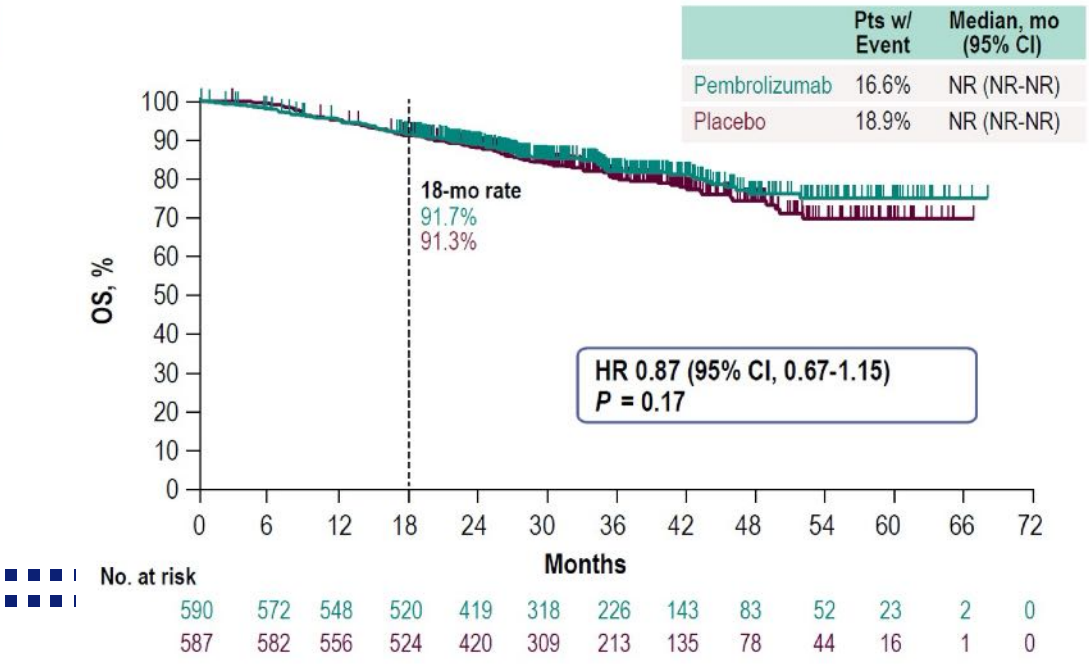
Eligibility for Randomization
- No evidence of disease
- ECOG PS 0 or 1
- Adjuvant chemotherapy
  - Considered for stage IB (T ≥4 cm) disease
  - Strongly recommended for stage II and IIIA disease
  - Limited to ≤4 cycles

R 1:1

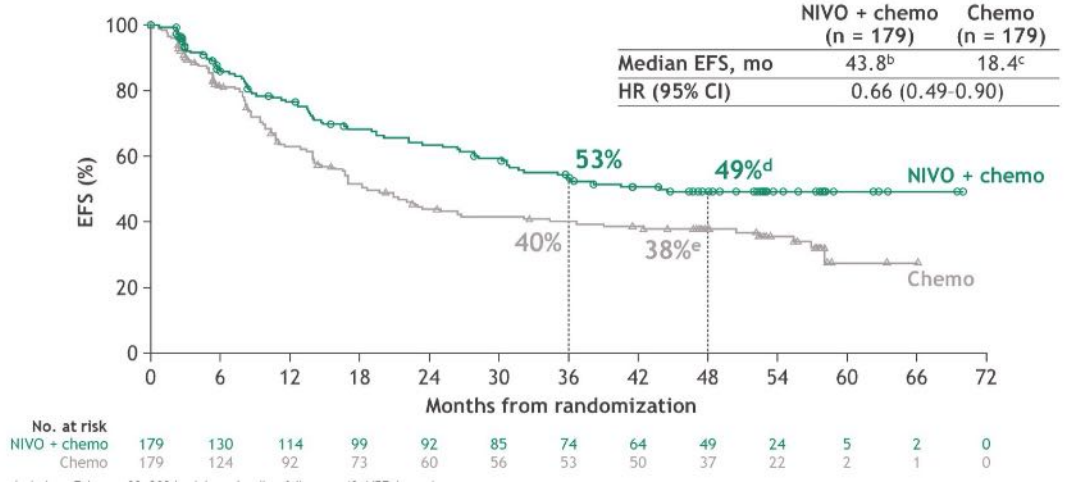
Pembrolizumab 200 mg once every 3 weeks for ≤18 administrations (~1 yr)

Placebo once every 3 weeks for ≤18 administrations (~1 yr)



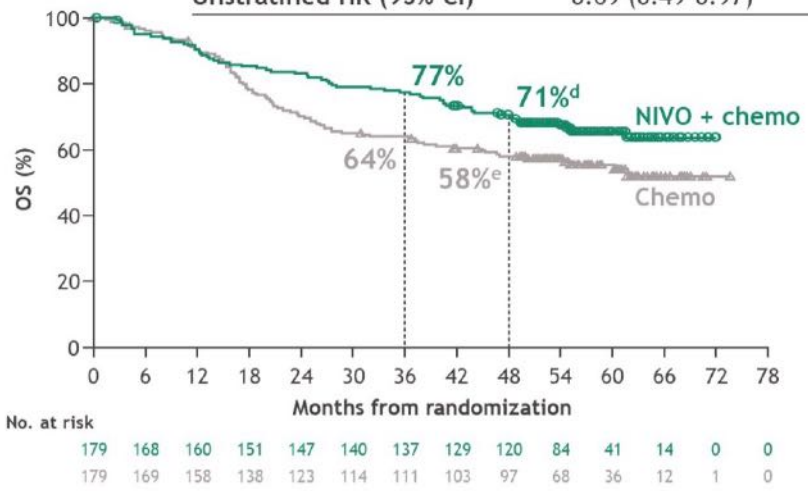


Neoadjuvant nivolumab plus chemotherapy vs chemotherapy in patients with resectable NSCLC: 4-year update from CheckMate 816



	NIVO + chemo (n = 179)	Chemo (n = 179)
Median EFS, mo	43.8[b]	18.4[c]
HR (95% CI)	0.66 (0.49-0.90)	

42/101 (42%) of pts in control arm with EFS event received subsequent immunotherapy



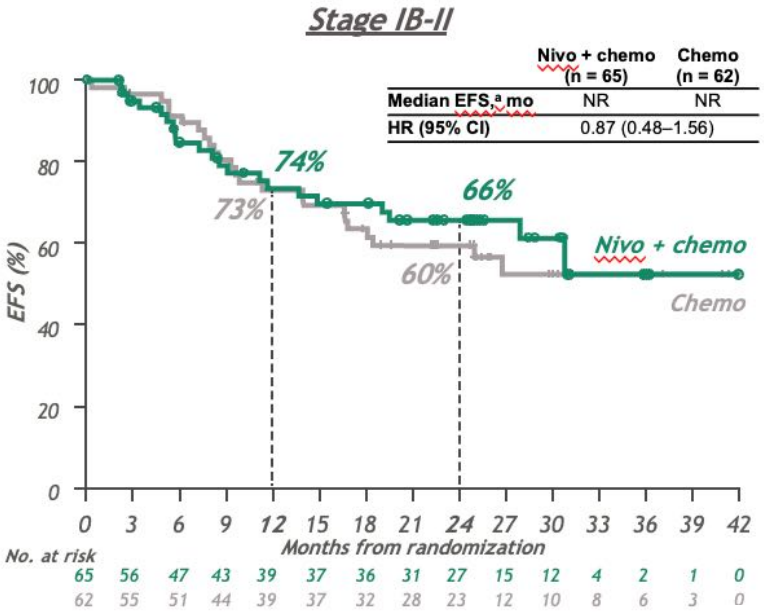
	NIVO + chemo (n = 179)	Chemo (n = 179)
Median OS,[a] mo	NR	NR[c]
HR (98.36% CI); *P* value	0.71 (0.47-1.07); 0.0451[b]	
Unstratified HR (95% CI)	0.69 (0.49-0.97)	

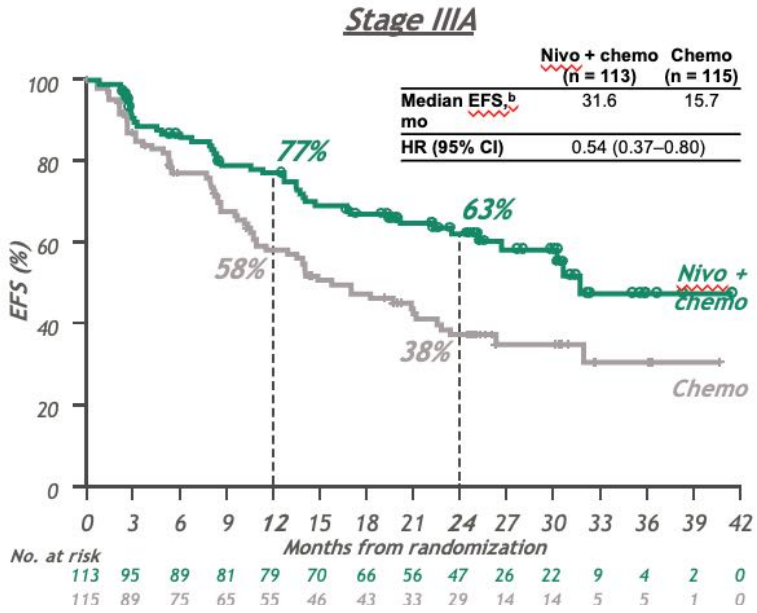
- Patients in the NIVO + chemo arm who had pCR continued to have improved OS vs those who did not (HR [95% CI], 0.08 [0.02-0.34]; **4-year OS rates, 95% vs 63%**)

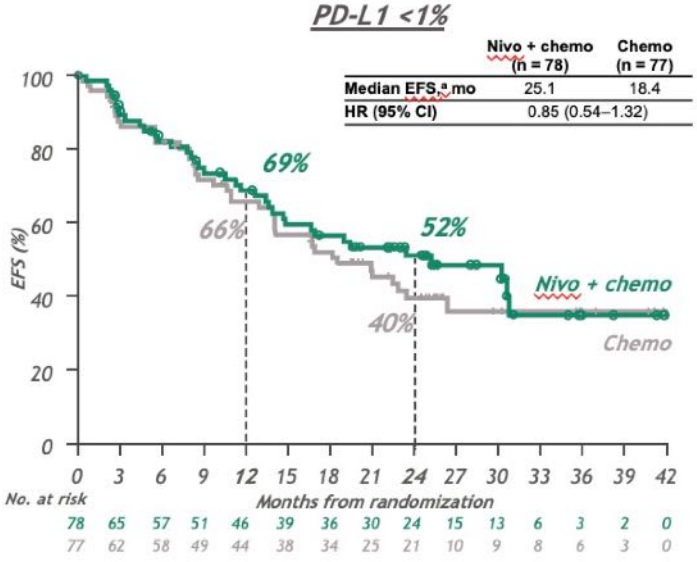
Erasmus MC

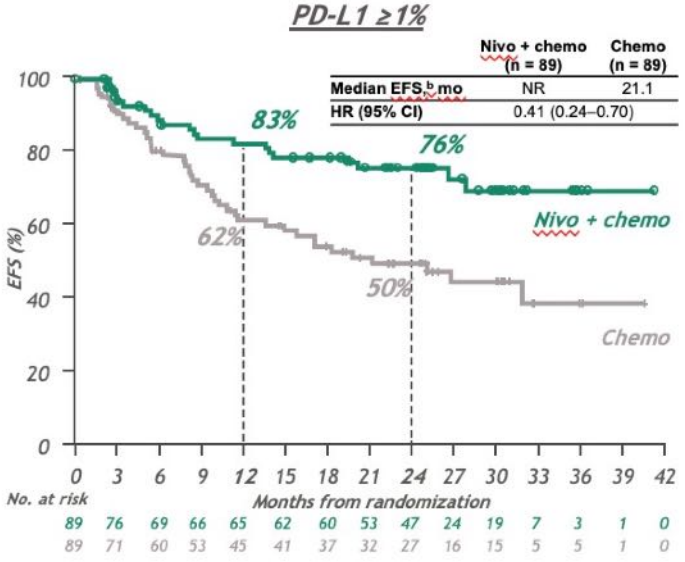
Spicer, ASCO 2024

EFS naar stadium en PDL1



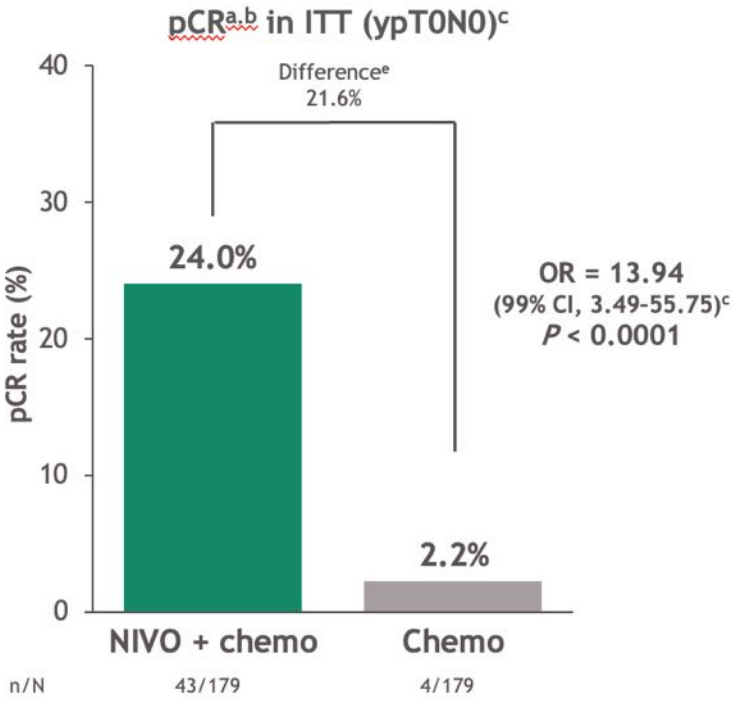


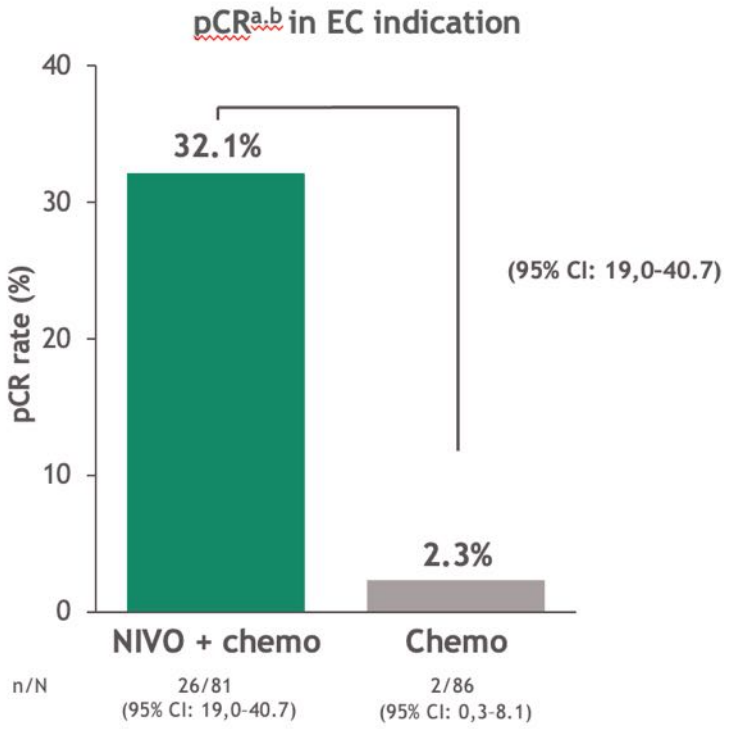




Forde PM, et al. N Engl J Med 2022;386:1973-85.

Pathologisch complete respons



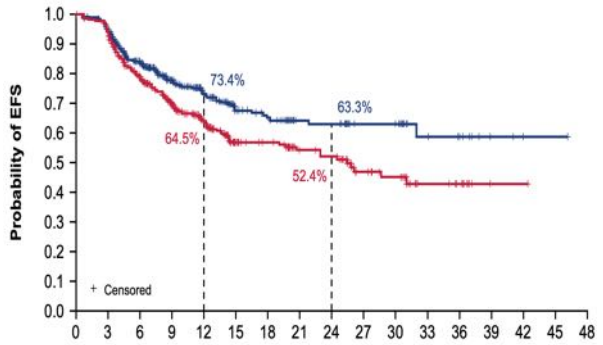


Forde PM, et al. N Engl J Med 2022;386:1973-85.

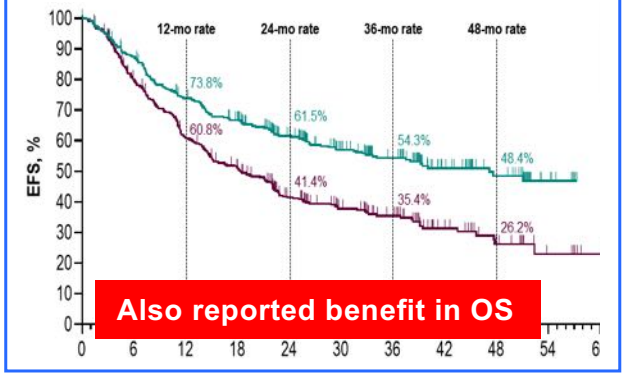
Erasmus MC

Neoadjuvant ICB increases pCR and prolongs EFS

AEGEAN: Perioperative Durvalumab

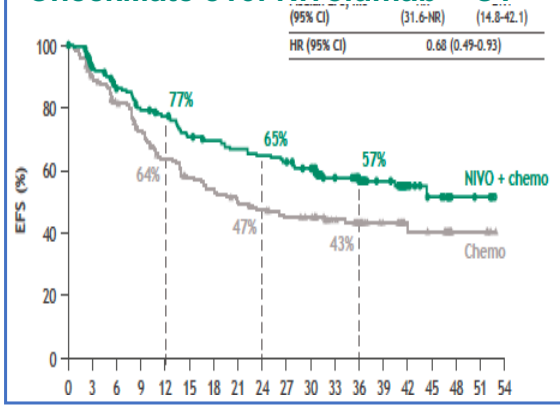


KEYNOTE 671: Pembrolizumab + CT

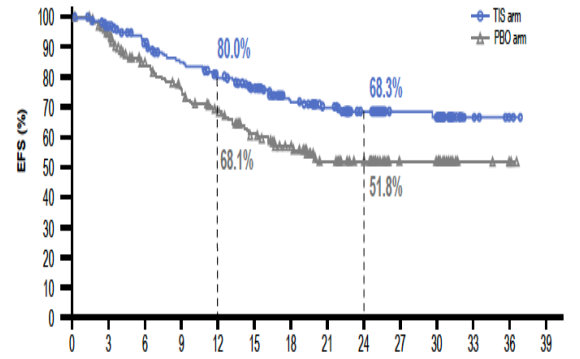


Also reported benefit in OS

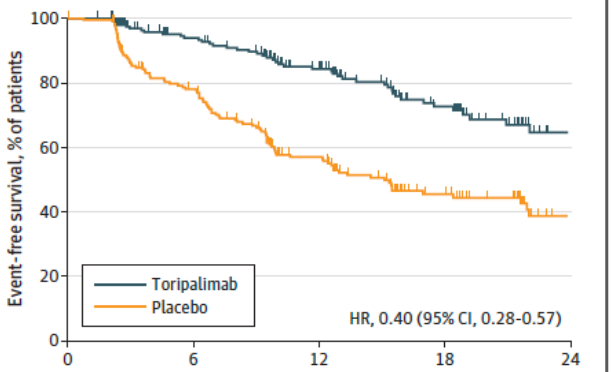
CheckMate 816: Nivolumab + CT



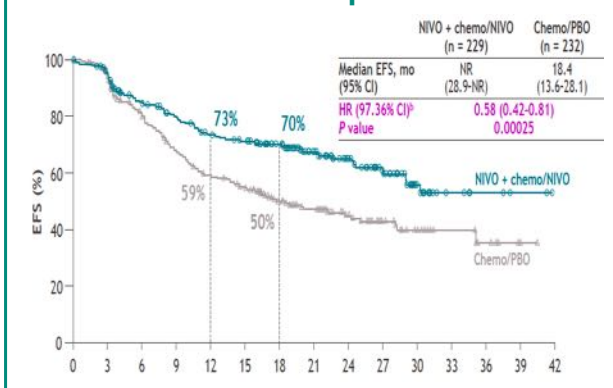
RATIONALE 315: Tislelizumab + C



NEOTORCH: Toripalimab+CT



CheckMate 77T: Perioperative Nivolumab

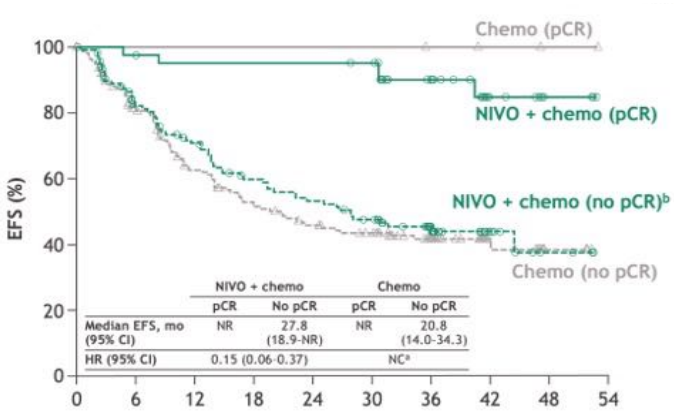


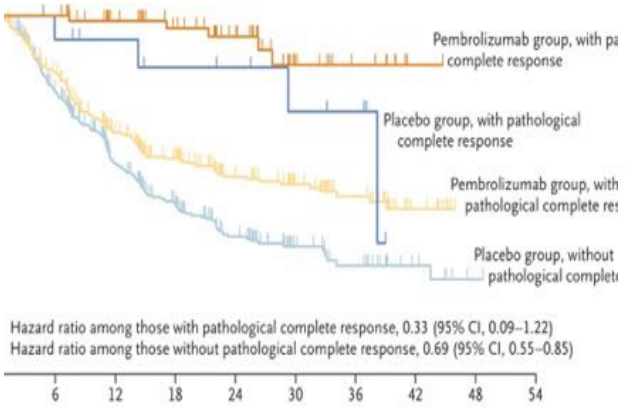
Erasmus MC

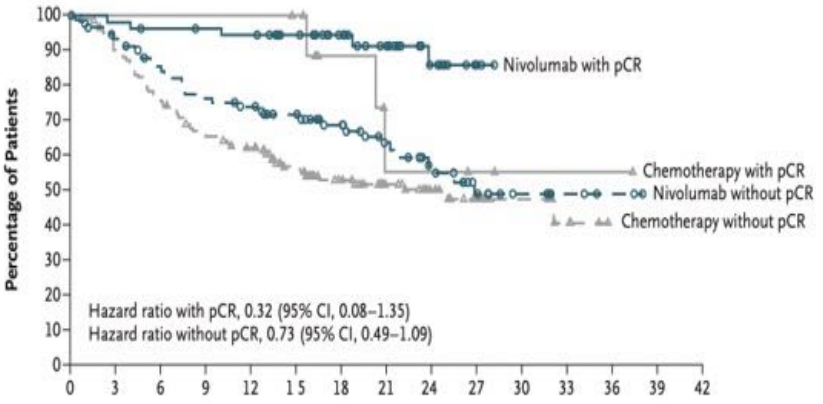
Heymach NEJM 2023 ; Wakelee NEJM 2023; Spicer ESMO 2023; Forde NEJM 2022; Yue ESMO Virtual 2024; Yue ELCC 2024; Lu JAMA 2024; Cascone NEJM 2024

EFS is driven by pCR

CheckMate 816	KEYNOTE 671	CheckMate 77T
3 cycles chemo-nivolumab	4 cycles chemo-pembrolizumab	4 cycles chemo-nivolumab
pCR: 24% MPR: 37%	pCR: 18% MPR: 30%	pCR: 25.3% MPR: 35.4%





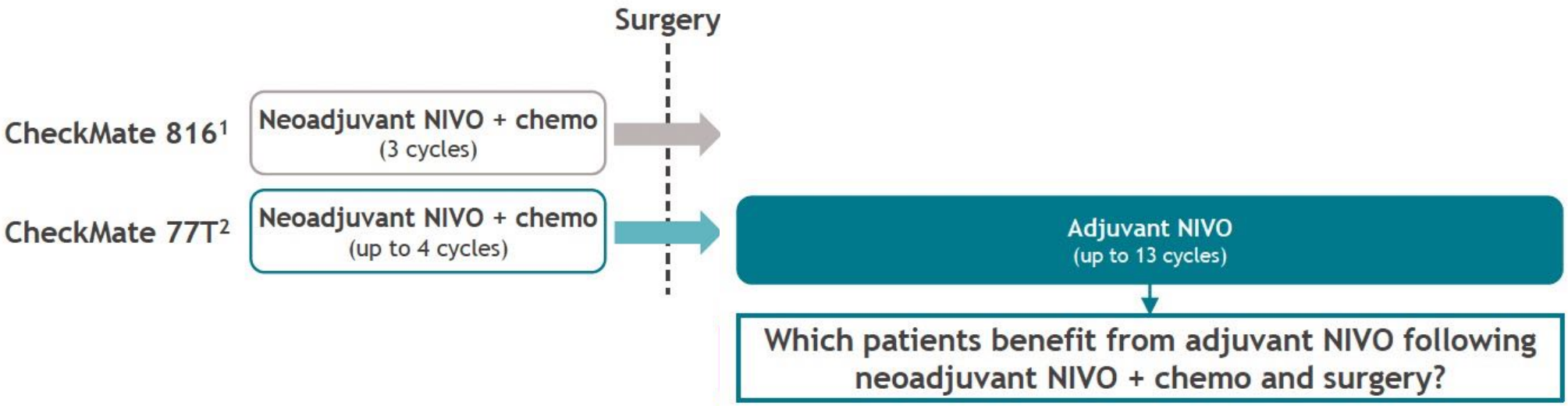


pCR not increased with additional pre-op cycle IO

Forde NEJM 2022, Wakelee NEJM 2023
Cascone NEJM 2024

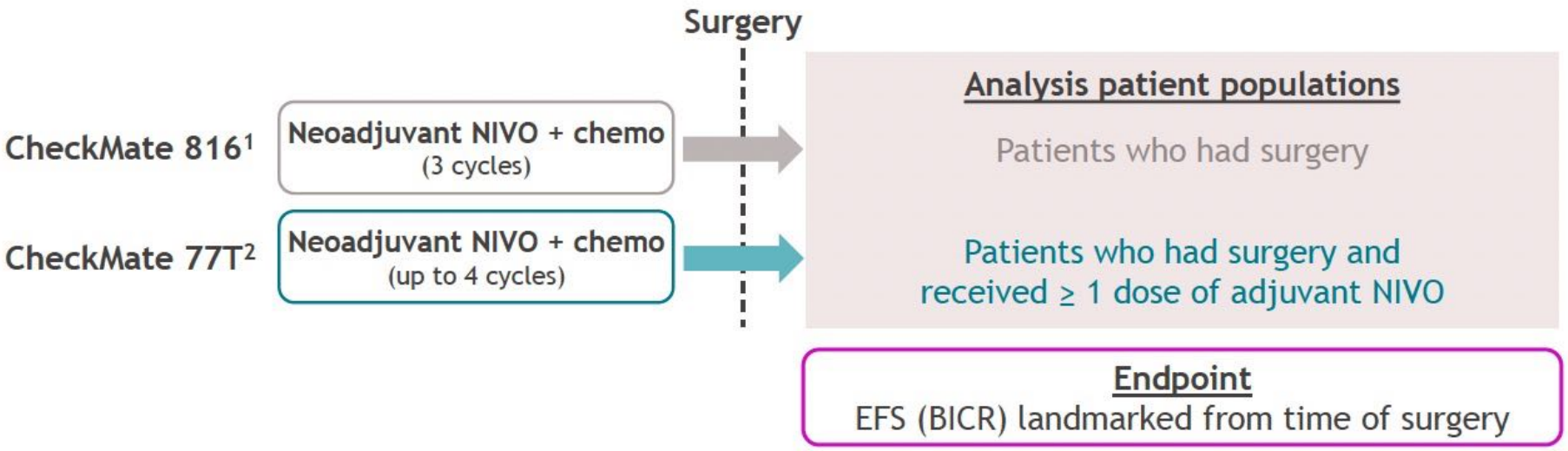
Erasmus MC

Neo-adjuvant of peri-operatief IO?



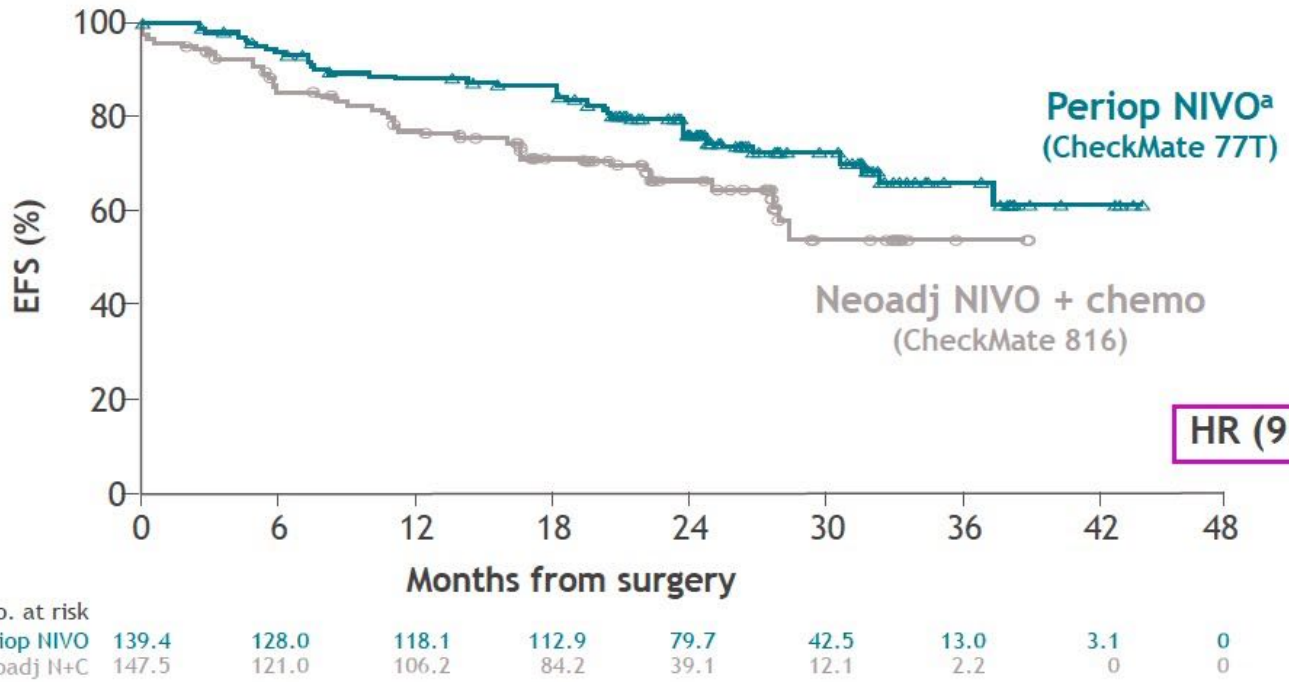
Forde, WCLC 2024

Neo-adjuvant of peri-operatief IO?



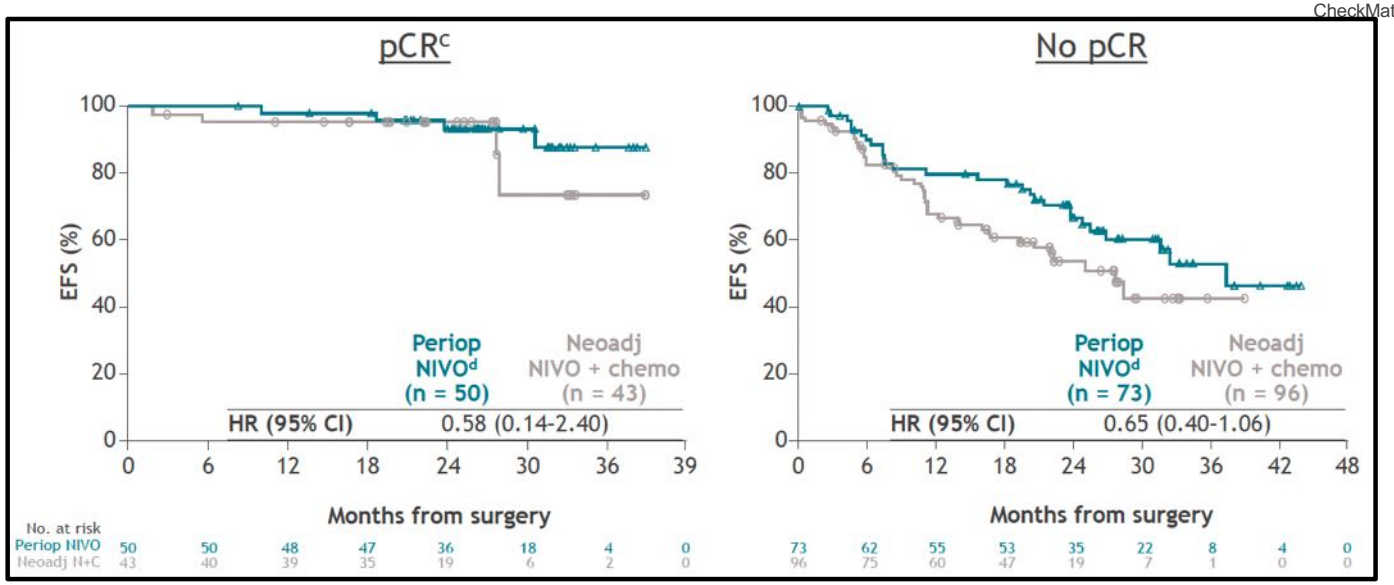
Forde, WCLC 2024

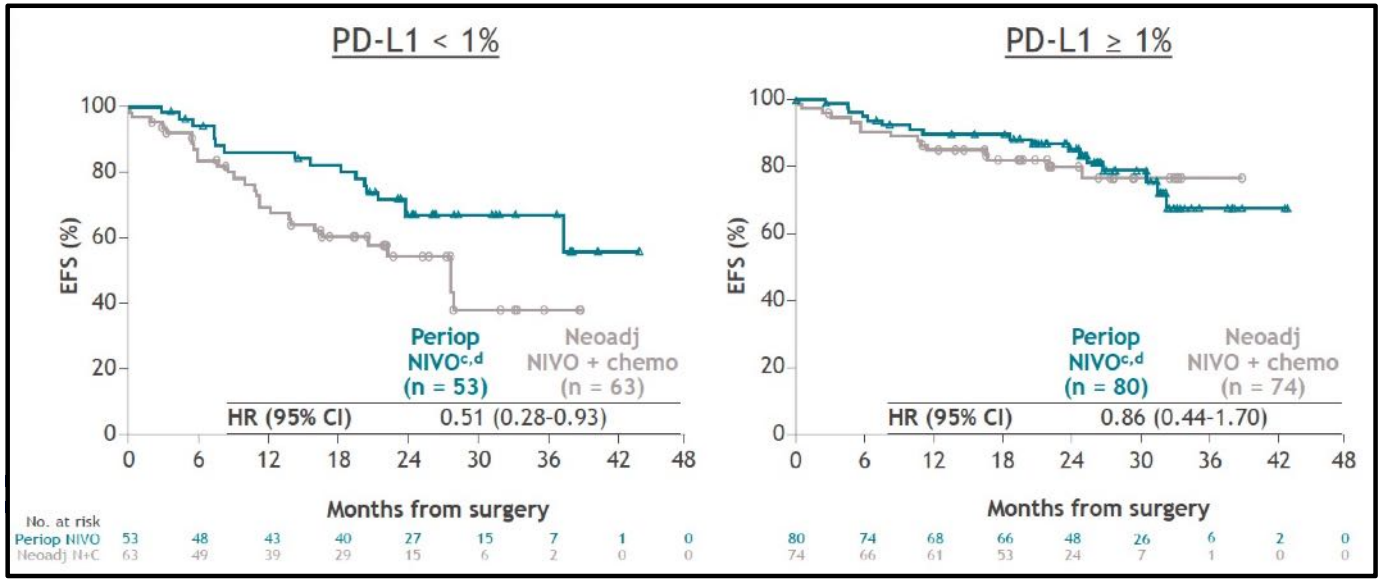
Neo-adjuvant of peri-operatief IO?



	Weighted (ATE)[b]	
	Periop NIVO[a] (n = 139.4[c])	Neoadj NIVO + chemo (n = 147.5[c])
HR (95% CI)	0.61 (0.39-0.97)	

Forde, WCLC 2024





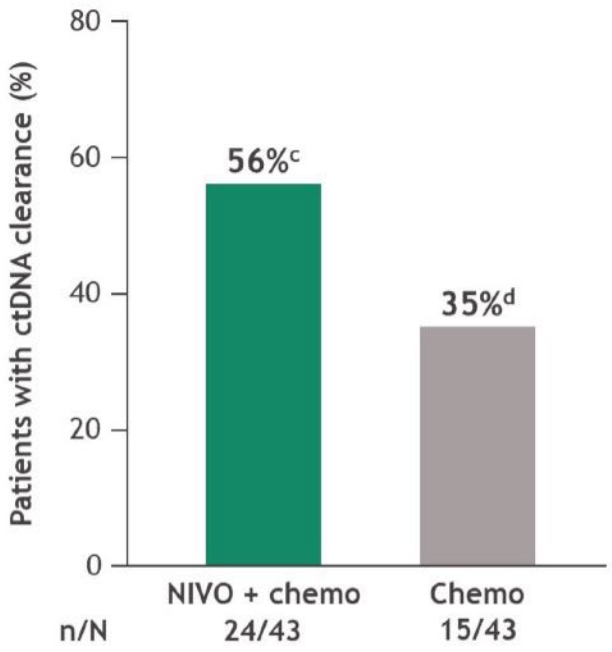
Forde, WCLC 2024

Erasmus MC

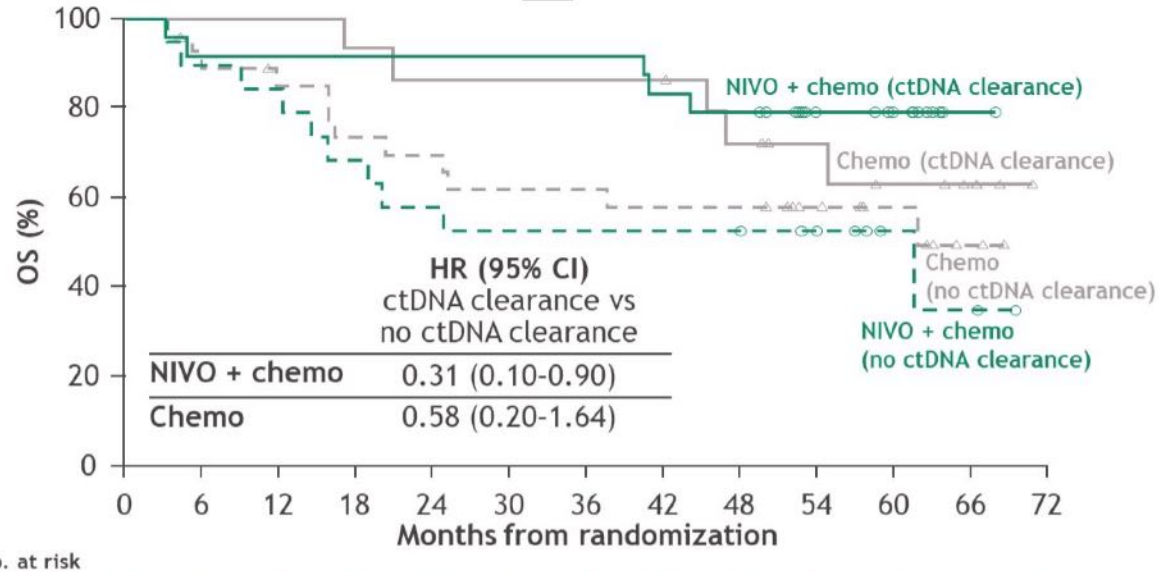
ctDNA clearance rate and OS by ctDNA clearance

- Among concurrently randomized patients, 89 (25%) had evaluable ctDNA levels, and 86 (24%) had detectable ctDNA levels at baseline[1,a]

ctDNA clearance rate[1,b]



OS



No. at risk													
ctDNA clearance	24	22	22	22	22	22	22	20	19	12	9	2	0
ctDNA clearance	15	15	15	14	13	13	13	13	10	8	6	4	0
No ctDNA clearance	19	17	16	13	11	10	10	10	9	7	3	2	0
No ctDNA clearance	28	24	22	19	18	16	16	15	15	11	7	2	0

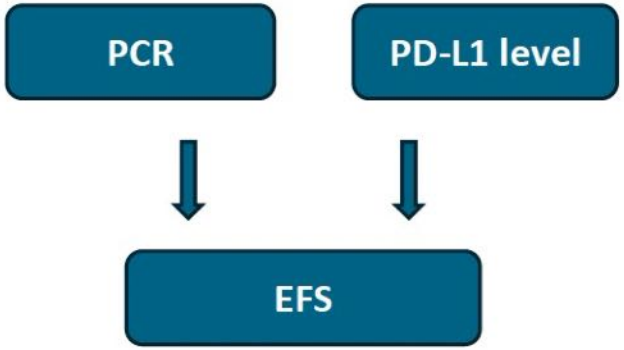
Minimum/median follow-up, 49.1/57.6 months.

[a]The main reasons for sample attrition were lack of tissue for WES and lack of quality control pass for tissue and plasma. [b]ctDNA clearance was defined as pre-surgical change from detectable ctDNA levels before cycle 1 to undetectable ctDNA levels before cycle 3. Analysis was performed using a WES tumor-guided personalized ctDNA panel (ArcherDX Personalized Cancer Monitoring). [c,d]95% CI: [c]40-71; [d]21-51. 1. Forde PM, et al. *N Engl J Med* 2022;386:1973-1985.

pCR and PD-L1 level influence the survival benefit from neoadj/periop chemoimmunotherapy

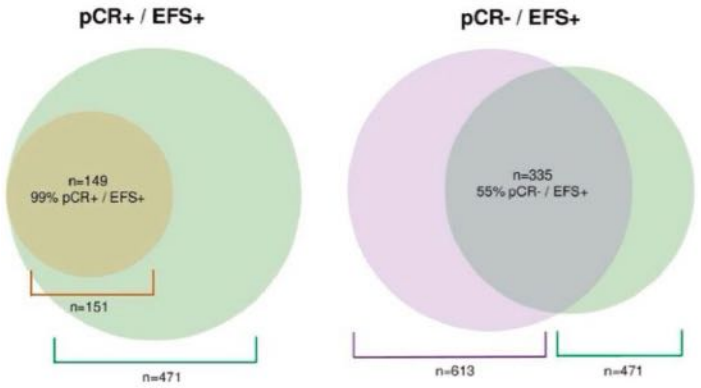
EFS/PFS by PCR

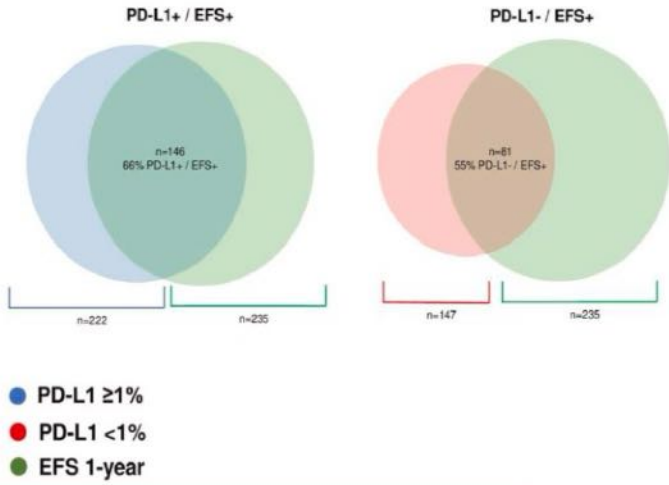
	HR	95%CI
PCR	0.17	0.09-0.33
Non-PCR	0.73	0.62-0.88



DFS/PFS by PD-L1 TPS

PD-L1	HR	95%CI
<1%	0.76	0.62-0.94
1-49%	0.52	0.37-0.72
≥ 50%	0.41	0.29-0.57





Need to answer: Which one would be a better prognostic marker for both treatment approaches?

Nuccio A, et al. Eur J Cancer 2023; 195: 113404

Erasmus MC

Conclusie

Definitie resectabel longkanker schuift op.

Niet resectabel longkanker: chemoradiotherapie gevolgd door IO, danwel TKI

Volledige moleculaire diagnostiek dient dus ook ingezet te worden in vroeg stadium NSCLC.

- PD-L1
- EGFR, MET, BRAF
- ALK, ROS1, RET, NTRK

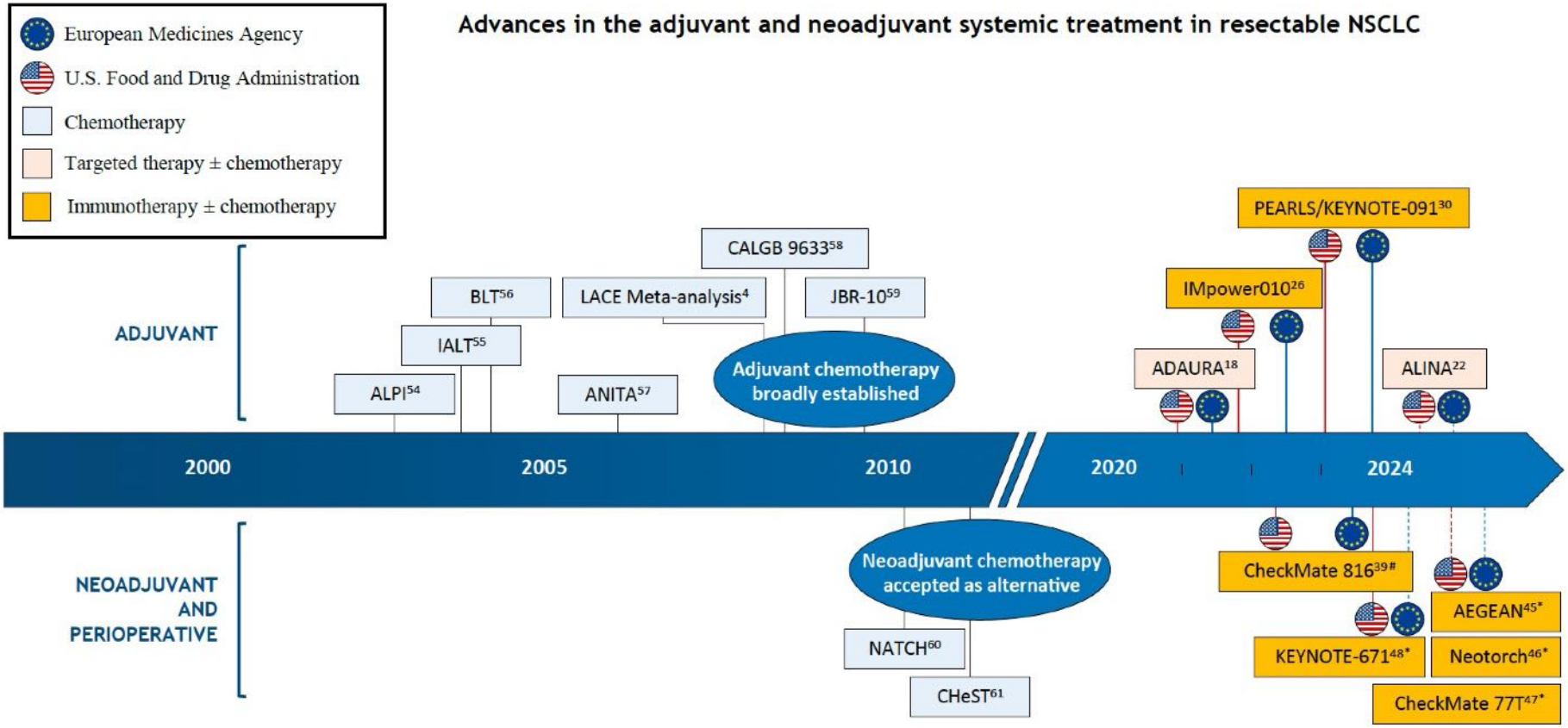
Resectabel longkanker:

- Adjuvante doelgerichte behandeling geeft evidente verbetering van EFS; echter mogelijke vroege stadium IV behandeling.
- Immuuntherapie heeft een rol neo-adjuvant, ook adjuvant? Selectie mogelijk obv PDL1, pCR, ctDNA?

Erasmus MC

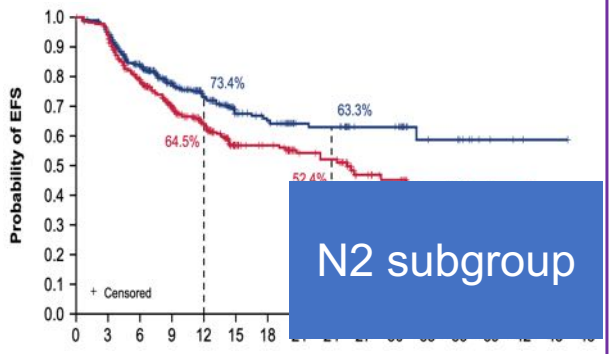
Dank voor de aandacht

d.dumoulin@erasmusmc.nl

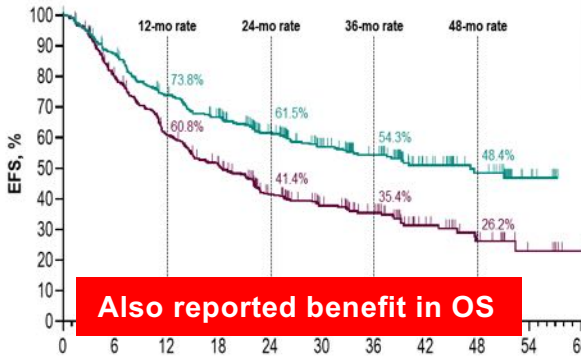

Advances in the adjuvant and neoadjuvant systemic treatment in resectable NSCLC
European Medicines Agency
U.S. Food and Drug Administration
Chemotherapy
Targeted therapy ± chemotherapy
Immunotherapy ± chemotherapy
ADJUVANT
NEOADJUVANT AND PERIOPERATIVE
ALPI[54]
IALT[55]
BLT[56]
ANITA[57]
LACE Meta-analysis[4]
CALGB 9633[58]
JBR-10[59]
Adjuvant chemotherapy broadly established
NATCH[60]
CHeST[61]
Neoadjuvant chemotherapy accepted as alternative
ADAURA[18]
IMpower010[26]
PEARLS/KEYNOTE-091[30]
ALINA[22]
CheckMate 816[39#]
KEYNOTE-671[48*]
AEGEAN[45*]
Neotorch[46*]
CheckMate 77T[47*]
2000
2005
2010
2020
2024

Neoadjuvant ICB increases pCR and prolongs EFS

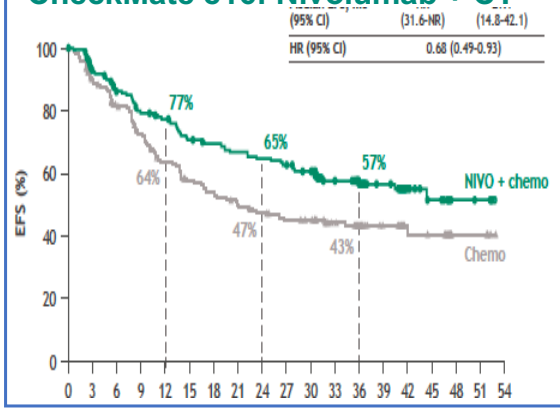
AEGEAN: Perioperative Durvalumab



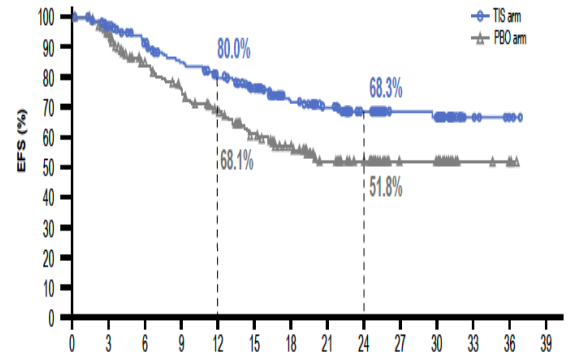
KEYNOTE 671: Pembrolizumab + CT

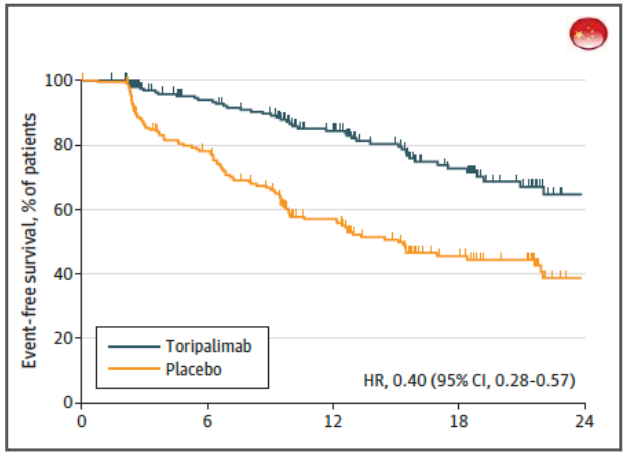


CheckMate 816: Nivolumab + CT

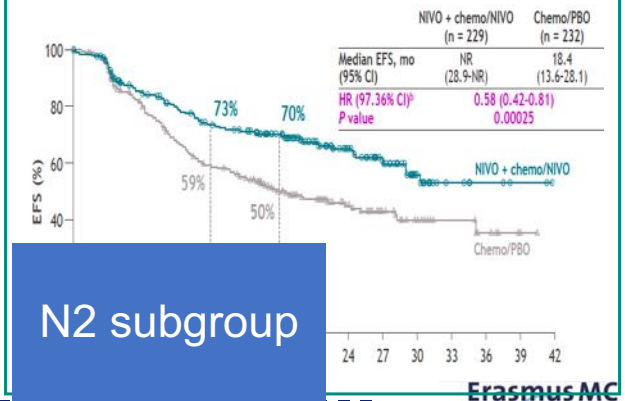


RATIONALE 315: Tislelizumab + C





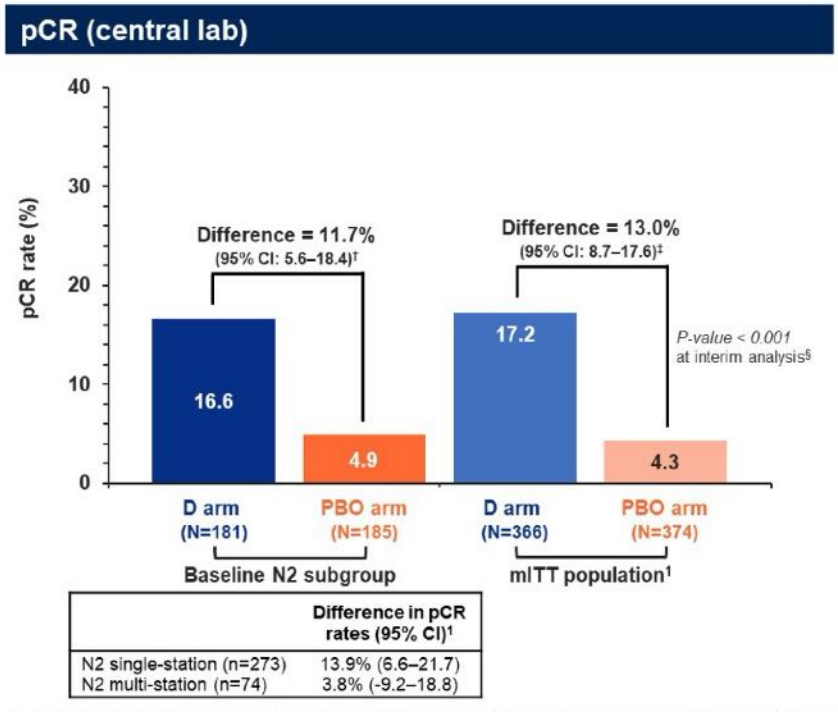
CheckMate 77T: Perioperative Nivolumab



Erasmus MC

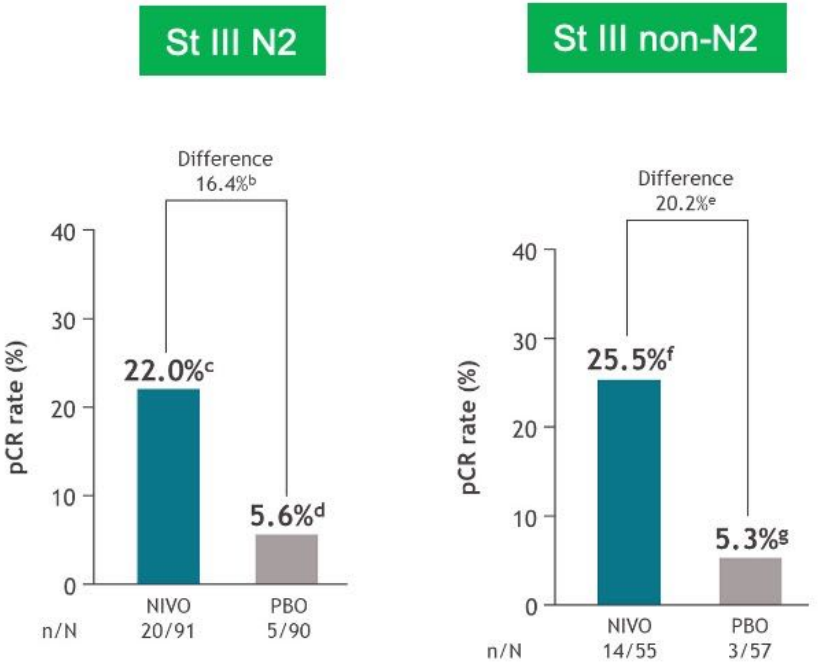
pCR in N2 disease comparable to non-N2

AEGEAN: subgroep N2



	Difference in pCR rates (95% CI)¹
N2 single-station (n=273)	13.9% (6.6–21.7)
N2 multi-station (n=74)	3.8% (-9.2–18.8)

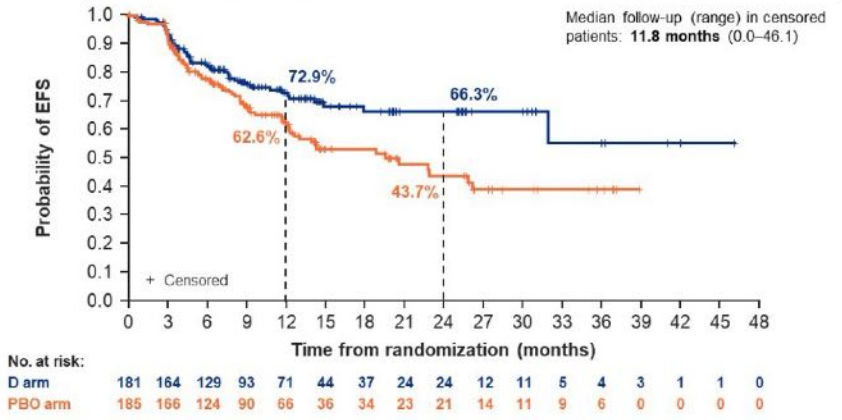
CM 77T: subgroep N2



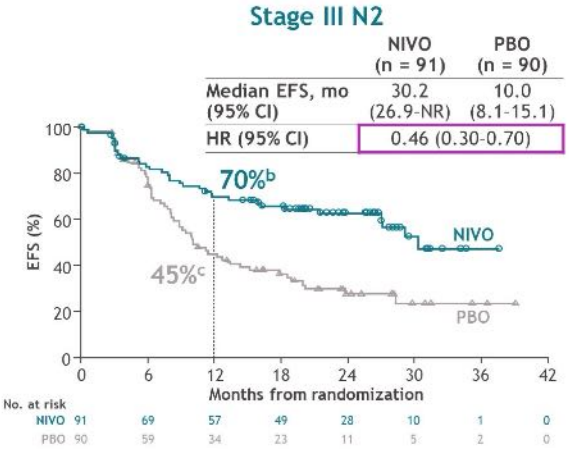
EFS in N2

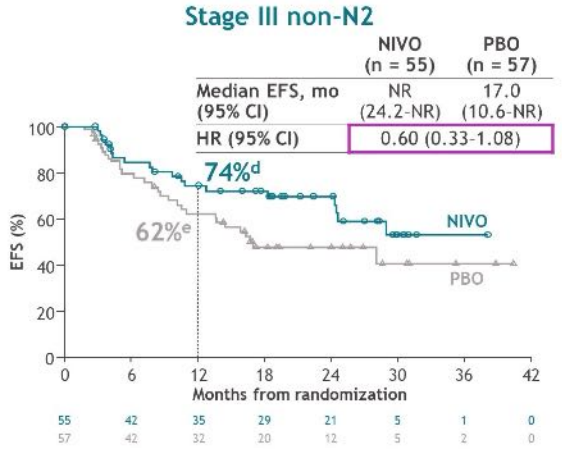
AEGEAN: subgroep N2

Baseline N2 subgroup	D arm	PBO arm
No. events / no. patients (%)	48/181 (26.5)	75/185 (40.5)
mEFS, months (95% CI)	NR (31.9, NR)	19.5 (12.6, 26.2)
Unstratified HR† (95% CI)	**0.63 (0.43, 0.90)**	



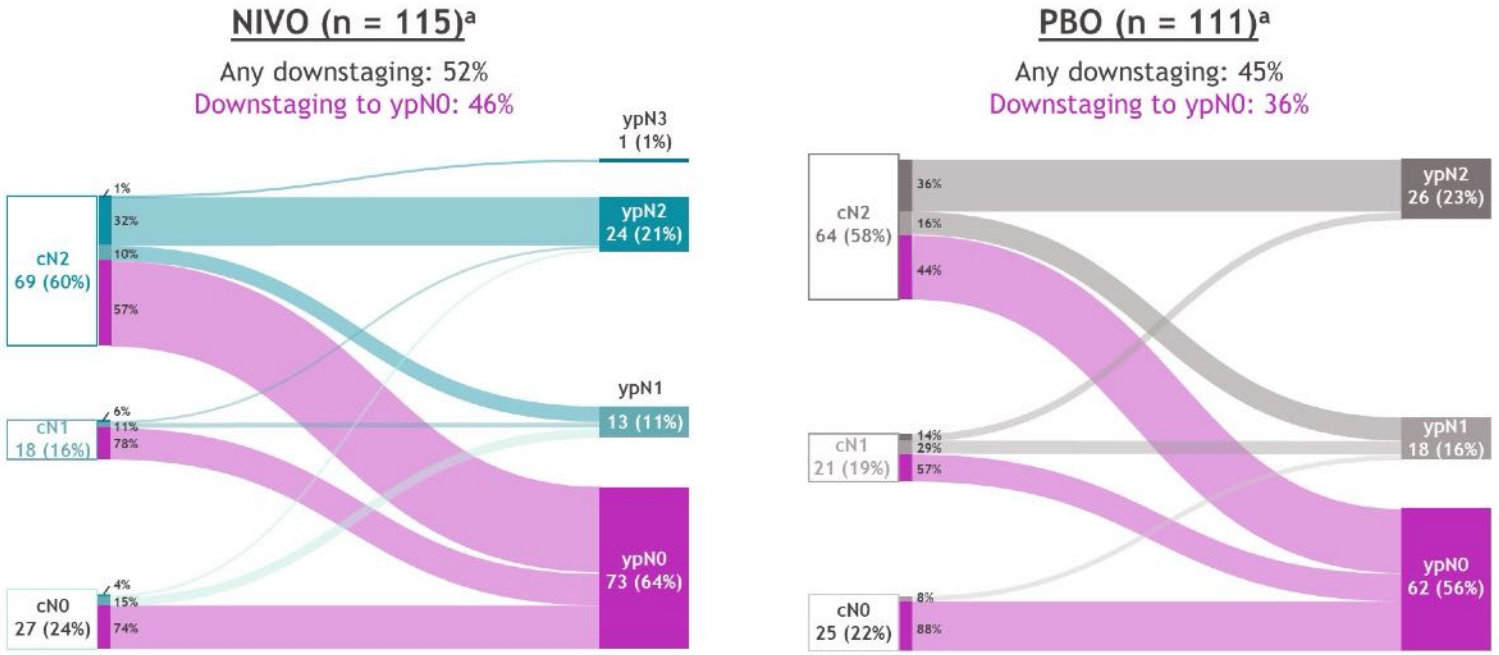
CM 77T: subgroep N2





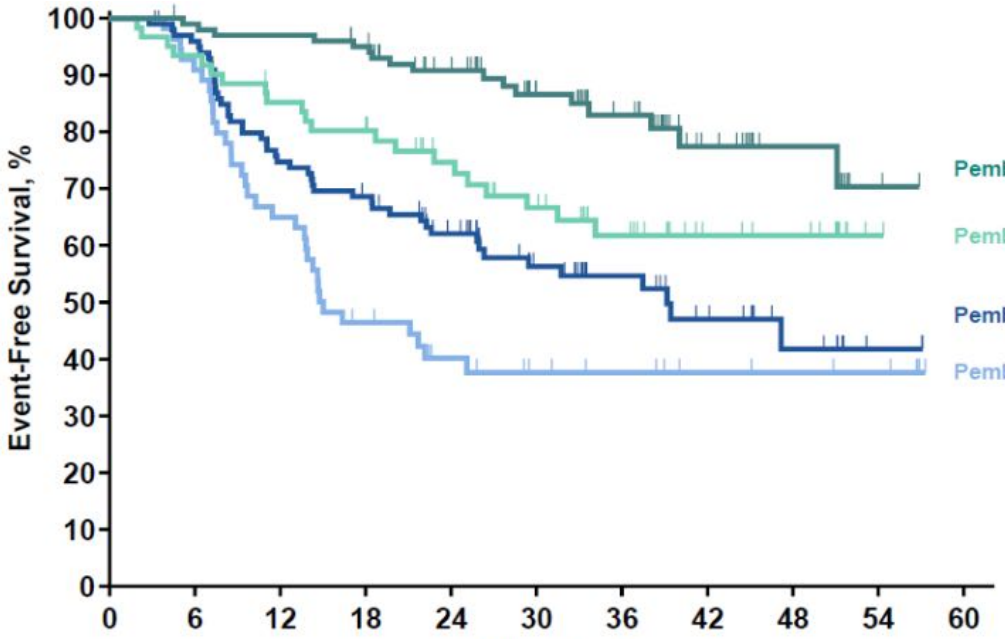
EFS HRs from randomization: 0.49[f] (single-station N2) and 0.43[g] (multi-station N2)[h]

Baseline and post-surgical N stage in stage III



Percentages located inside of each individual ribbon are based on baseline N stage. [a]1 (1%) patient in the NIVO arm and 1 (1%) patient in the PBO arm with not reported or cNX stage at baseline were excluded. Post-surgical N stage was missing for 3 (3%) patients in the NIVO arm and 4 (4%) patients in the PBO arm.

RVT vs. pCR/MPR



No. at risk

%RVT 0%–≤5%	102	100	98	94	77	54	39	21	11	2	0
%RVT >5%–≤30%	61	57	51	48	38	32	23	13	11	1	0
%RVT >30%–≤60%	101	95	73	66	52	34	24	16	8	2	0
%RVT >60%	56	50	35	24	16	12	10	7	6	5	0

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Association of Pathologic Regression With Event-Free Survival in the KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

David R. Jones,[1] Heather Wakelee,[2] Jonathan D. Spicer,[3] Moishe Liberman,[4] Terufumi Kato,[5] Masahiro Tsuboi,[6] Se-Hoon Lee,[7] Wenxiang Wang,[8] Haiquan Chen,[9] Christophe Dooms,[10] Margarita Majem,[11] Ekkehard Eigendorff,[12] Gaston L. Martinengo,[13] Olivier Bylicki,[14] Hsu-Ching Huang,[15] Silvia Novello,[16] Erin Jensen,[17] Steven M. Keller,[17] Ayman Samkari,[17] Neda Kalhor[18]

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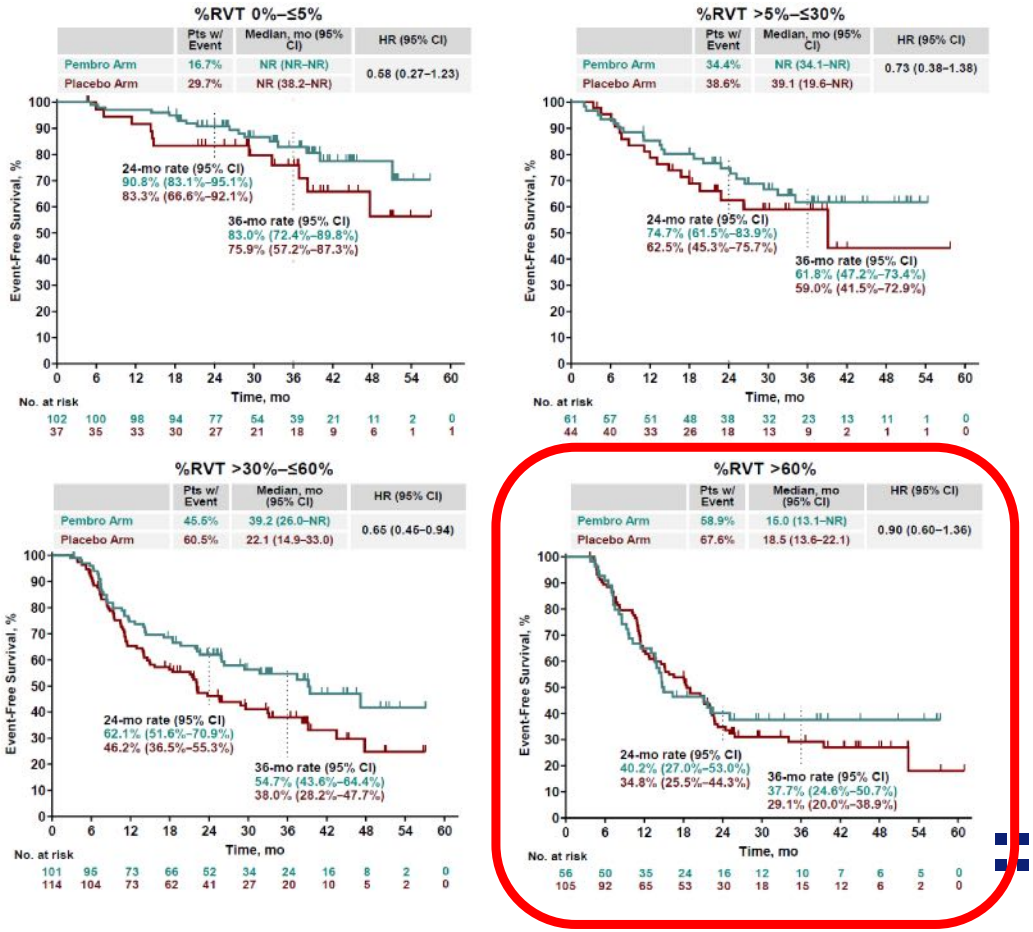

=> Post-operatieve therapie switch noodzakelijk?

Erasmus MC