

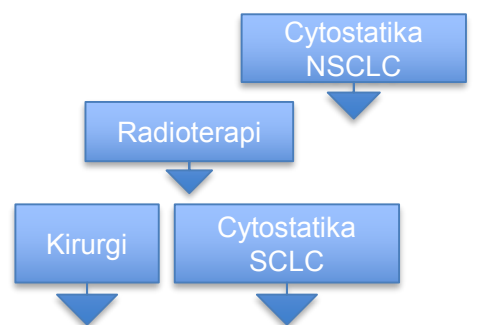


Systemisk behandling av lungekreft

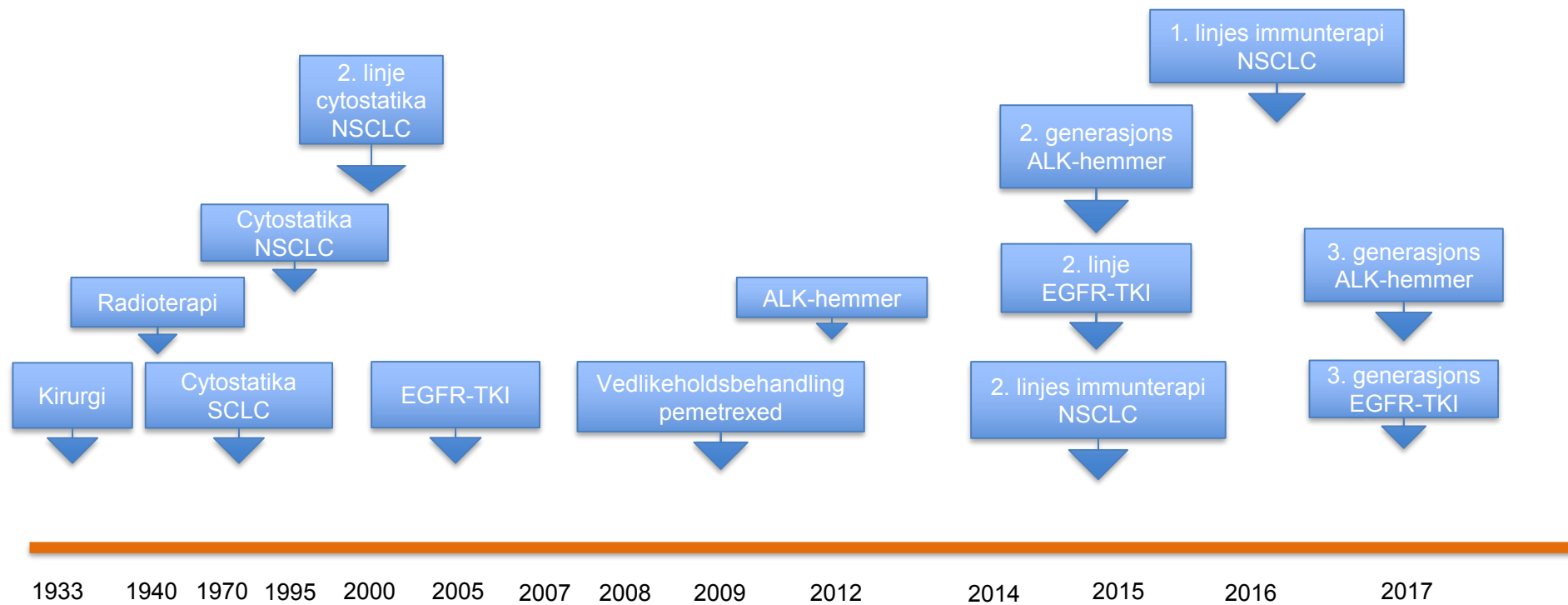
Bjørn H. Grønberg

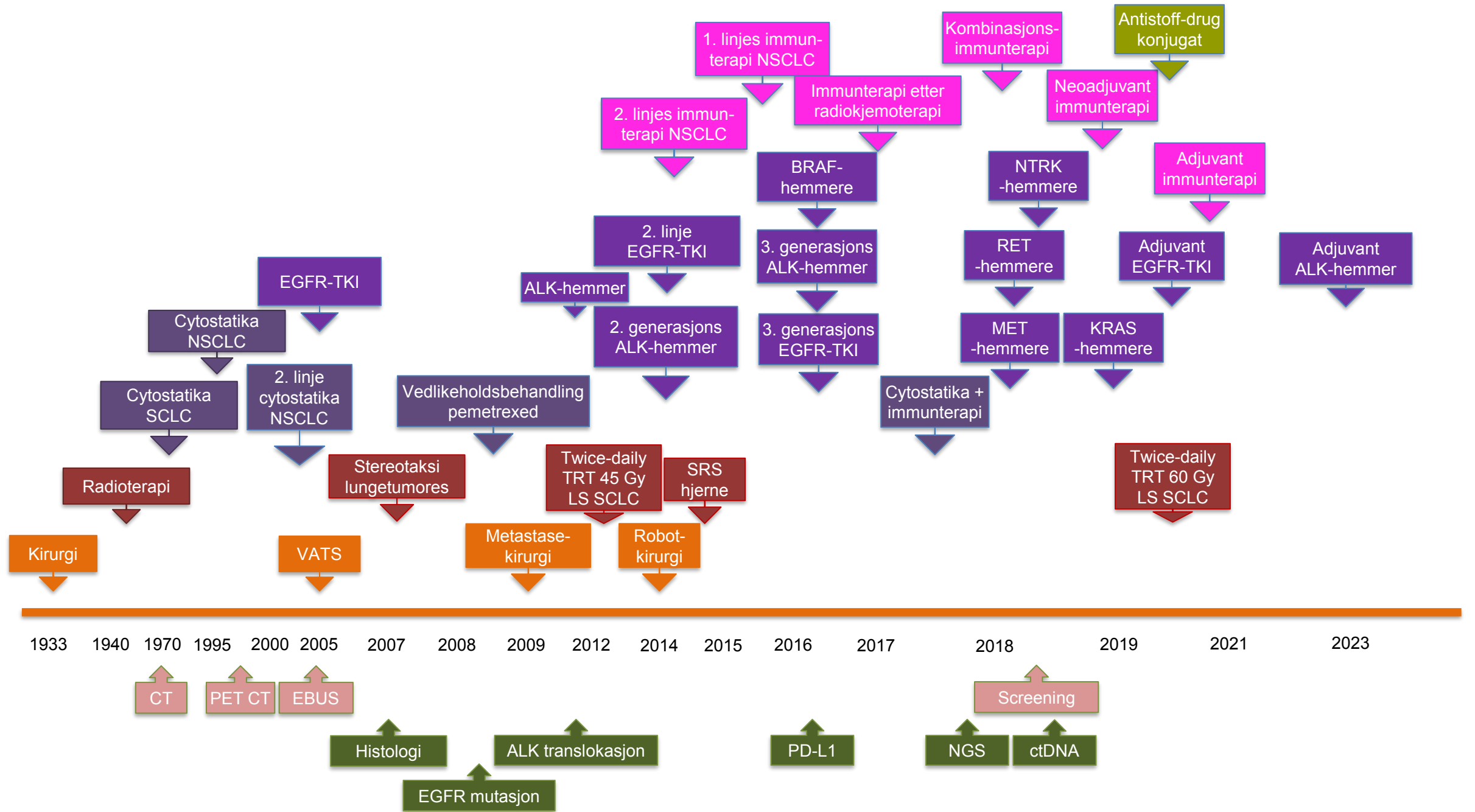
Professor, Institutt for klinisk og molekylær medisin, NTNU
Overlege, Kreftklinikken, St. Olavs Hospital

bjorn.h.gronberg@ntnu.no

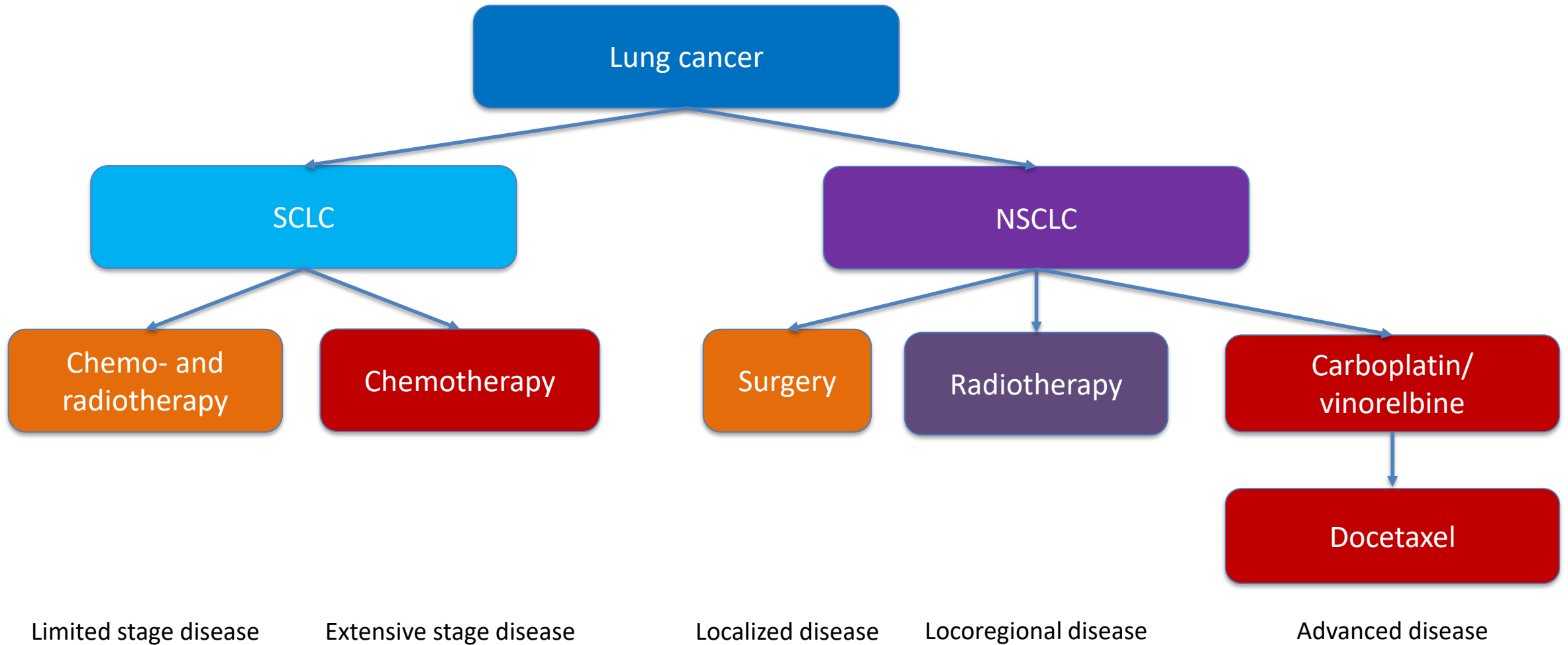


1933 1940 1970 1995 2000



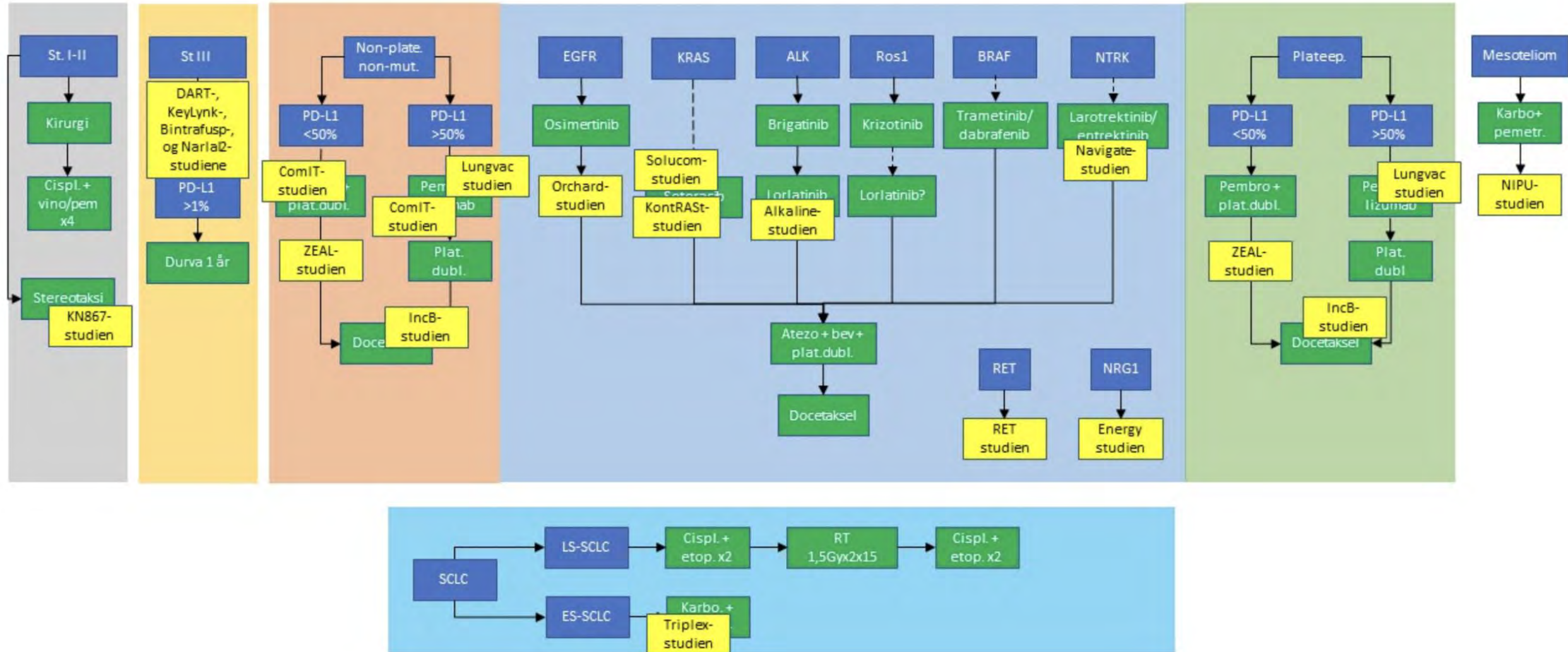


Treatment algorithm until 2008





Behandlingsskjema med studiemuligheter for lungekreft/mesoteliom



Small-cell lung cancer (SCLC)

14 %

Rapid growth, early metastases

All receive same treatment

High sensitivity for chemotherapy and radiotherapy

Chemoradiotherapy most important curative treatment

No targeted therapies established

Immunotherapy established in ES SCLC

Non-small-cell lung cancer (NSCLC)

>80 %

Large variation in growth rate

Treated according to biomarkers

Medium sensitivity for chemotherapy and radiotherapy

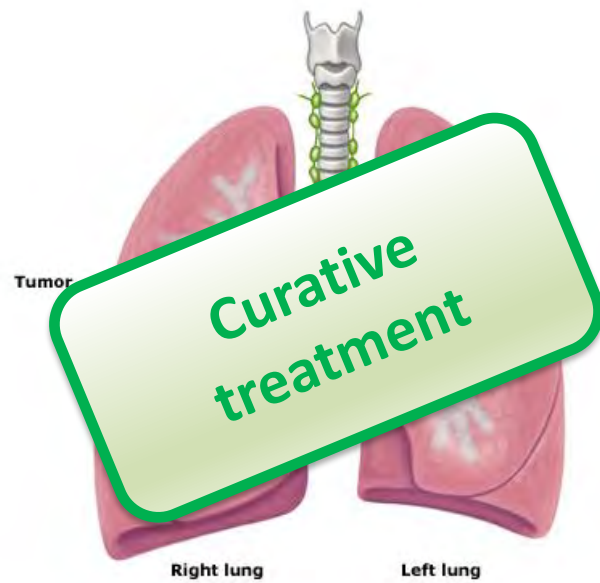
Surgery and SBRT most important curative treatments

Targeted therapies available for many patients

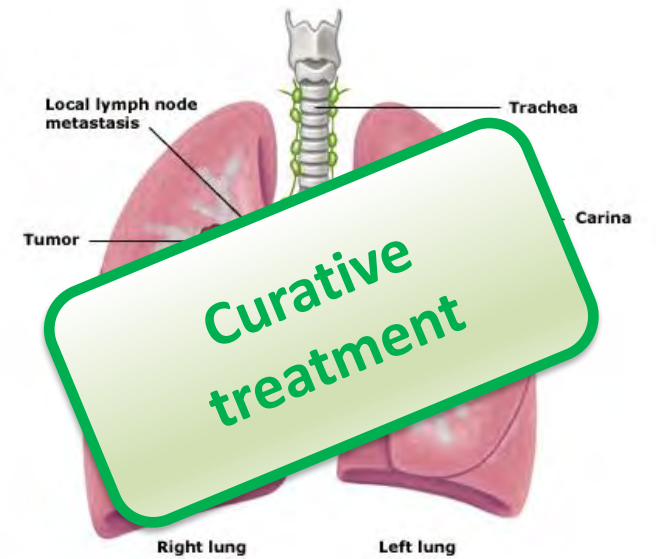
Immunotherapy backbone of systemic therapy for NSCLC without driver alterations

Stages of disease

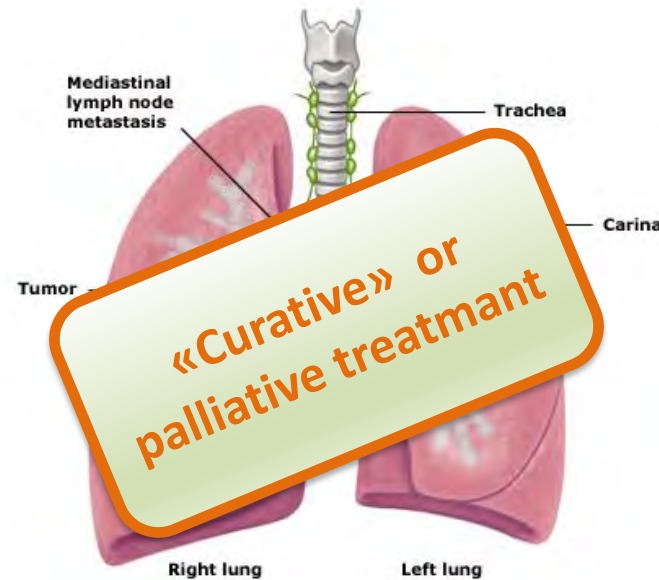
I



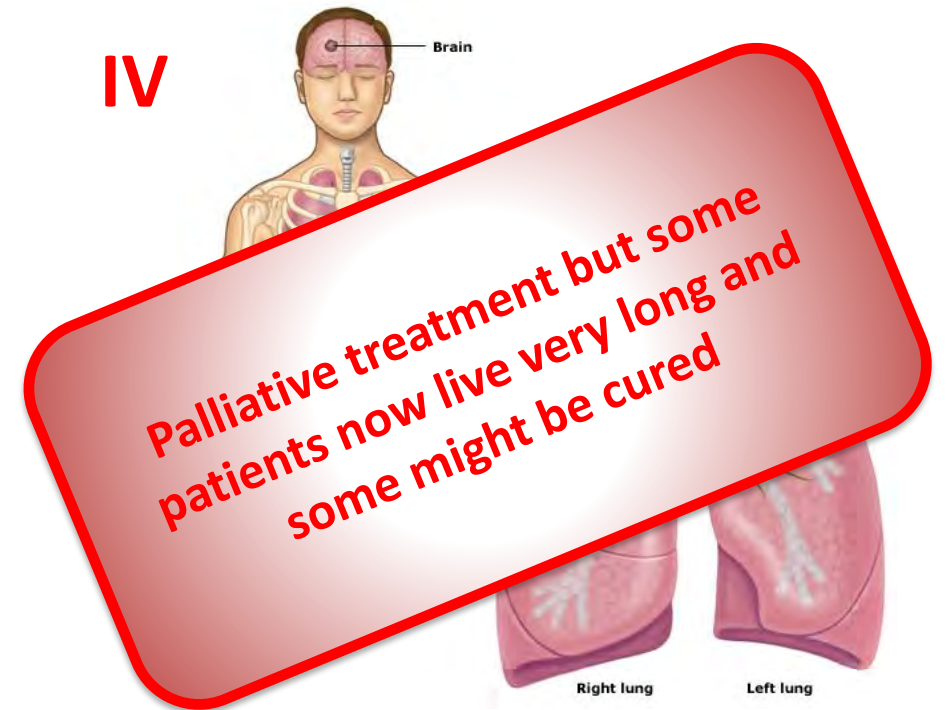
II



III



IV



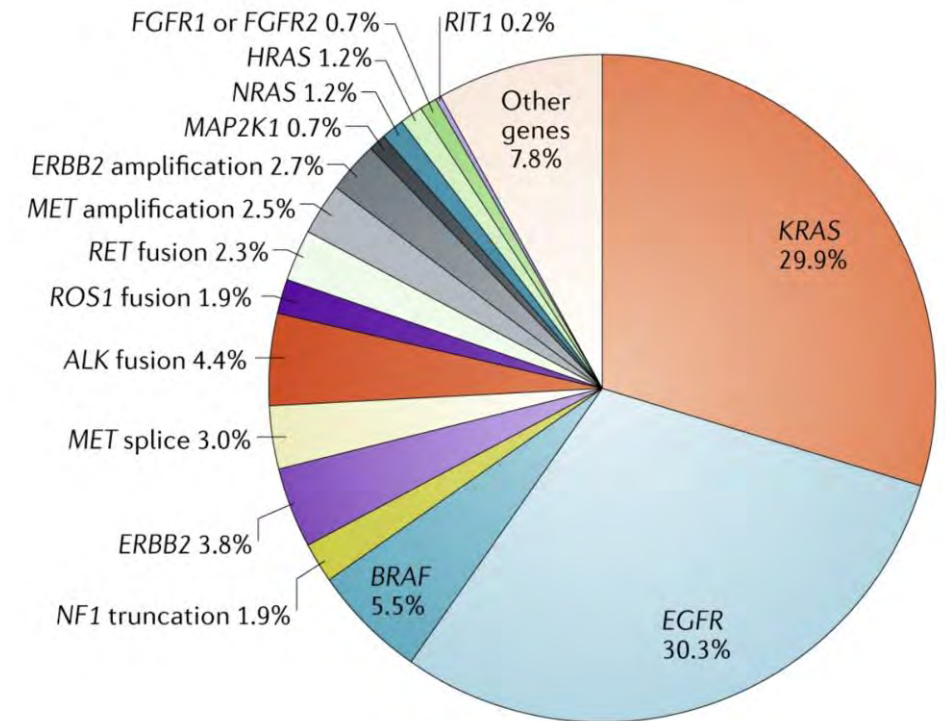
Performance status

PS	Definition
0	Asymptomatic - fully active
1	Symptomatic but completely ambulatory – restricted physical activity
2	Symptomatic, < 50% in bed during the day
3	Symptomatic, > 50% in bed, but not bedbound
4	Bedbound
5	Dead

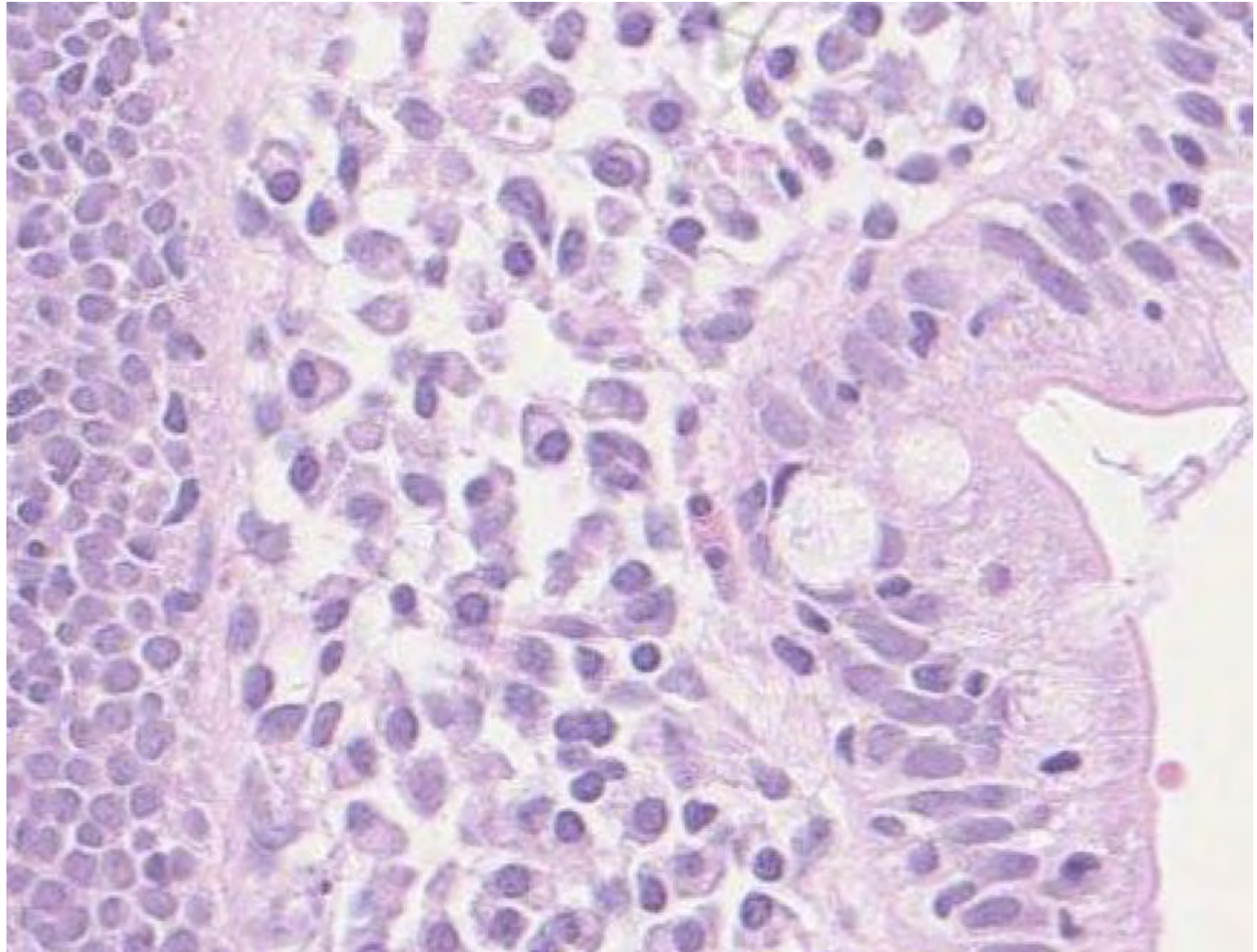
Other prognostic factors

- Sex
- Smoking history
- *LDH?*
- *Glasgow Prognostic Score?*
- *Weight loss, appetite loss*
- *Age?*
- *Comorbidity?*

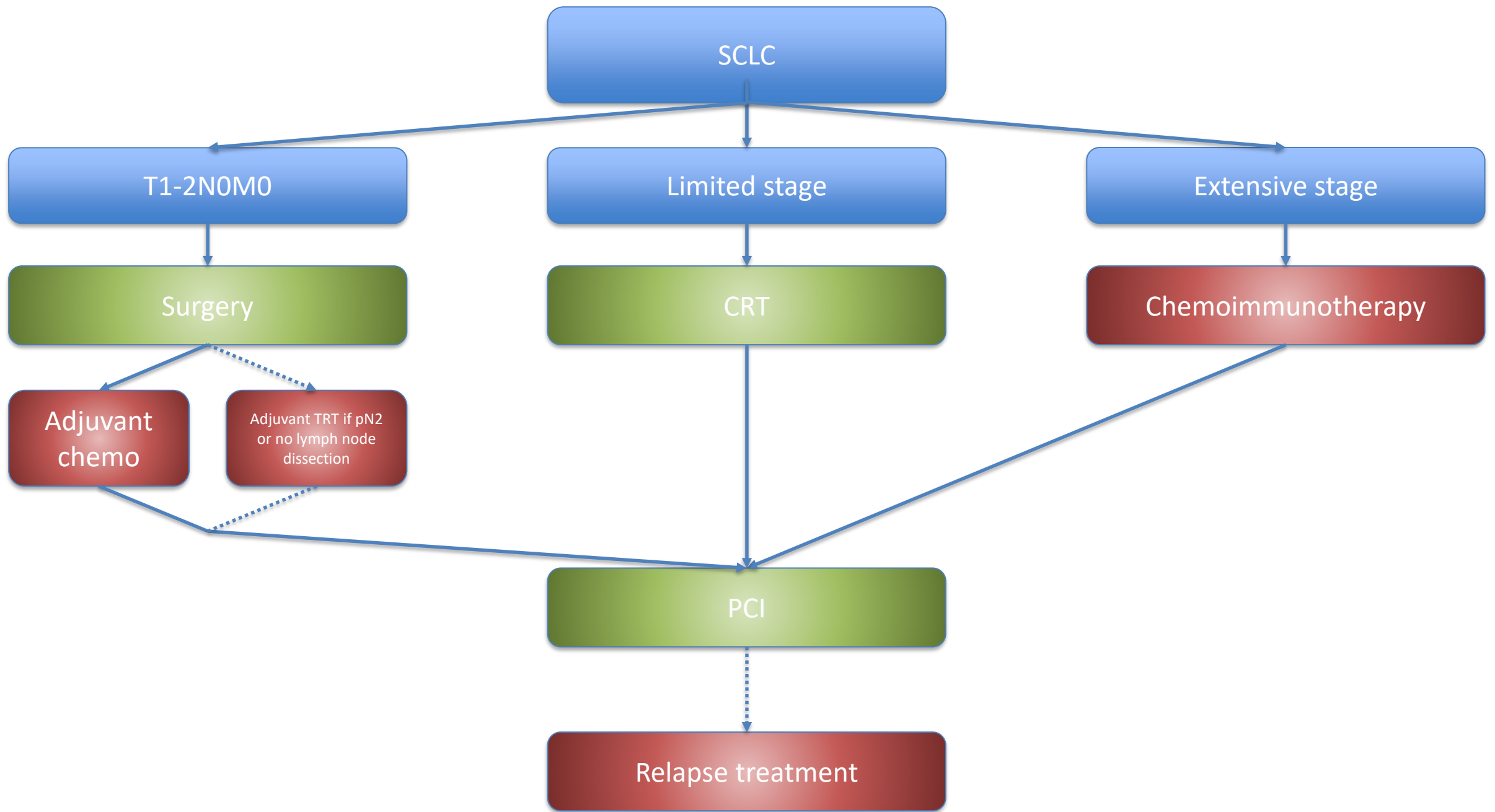
A lot of prognostic factors have been identified, but they are not necessarily applicable when selecting treatment for individual patients



Småcellet lungekreft

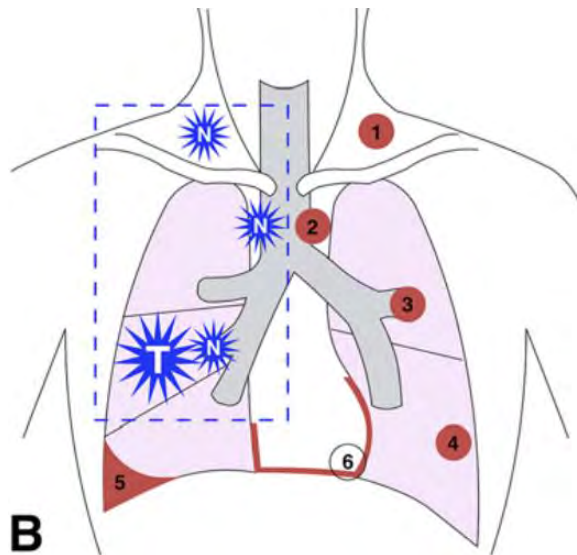




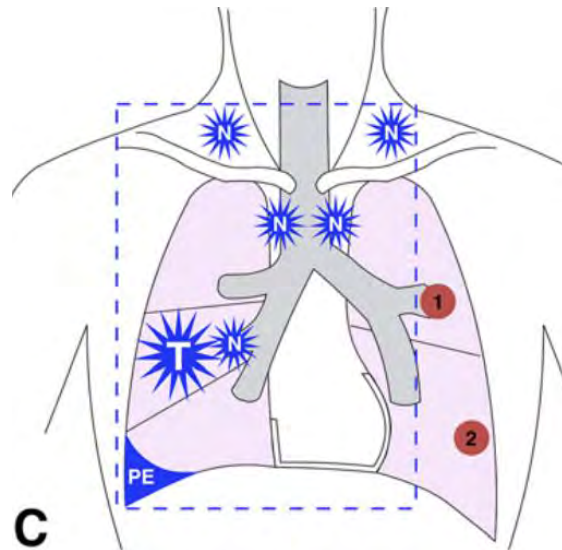


Definitions of limited stage disease (LS)

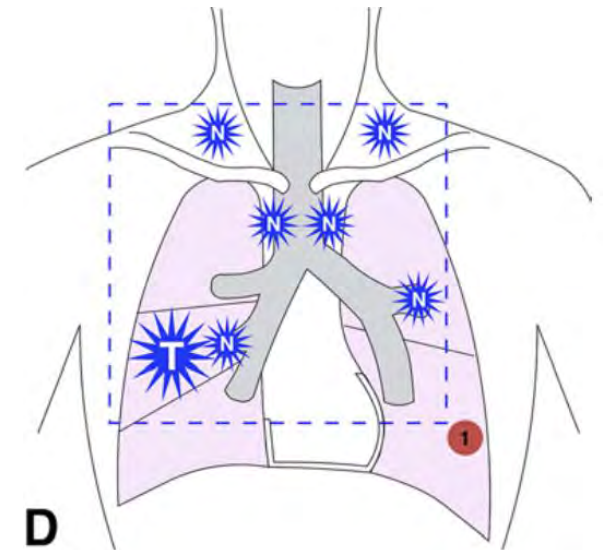
**Veteran Affairs Lung Can Study
Group
1973**

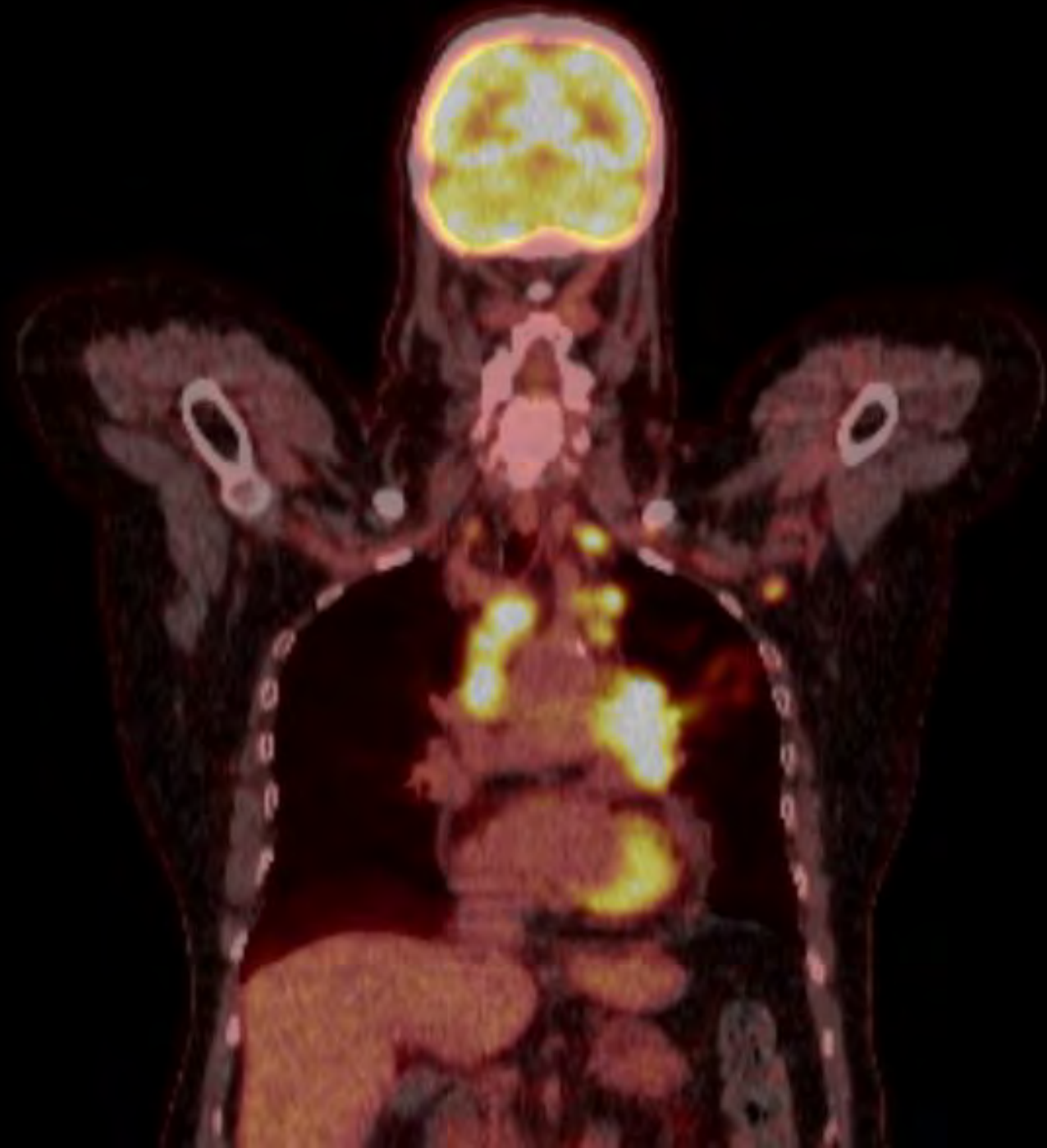


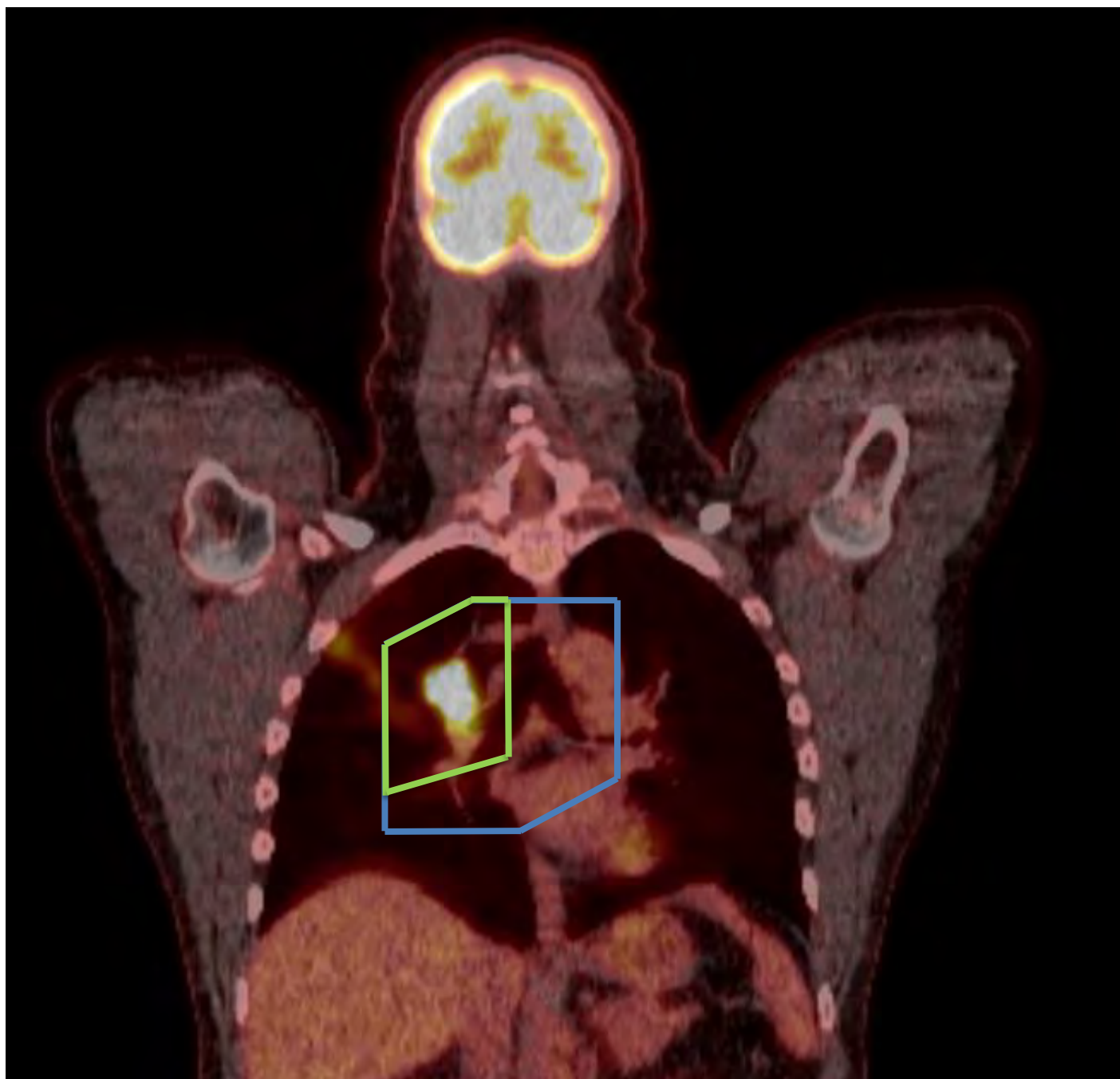
**International Association for the Study of Lung Cancer
1989**



**American Joint Committee on Cancer
2010**







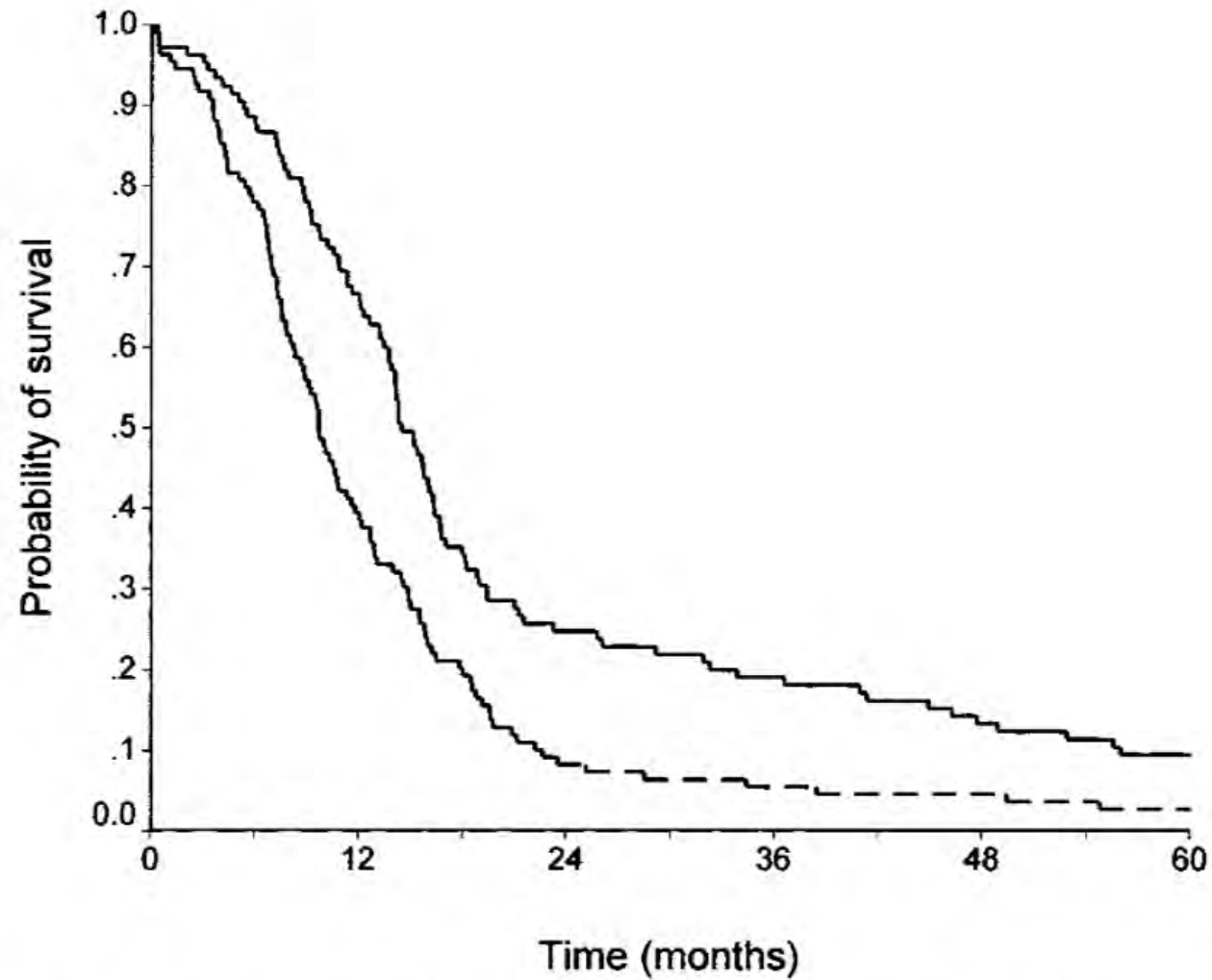


Fig 2. Overall survival of LD-SCLC patients (N = 214) according to treatment arm ($P = .0001$). CEV (dashed line), n = 109; EP (solid line), n = 105.

Patients

3

LS SCLC according to the IASLC definition; ECOG PS 0-2; measurable disease (RECIST 1.1); and adequate bone marrow/liver/kidney function

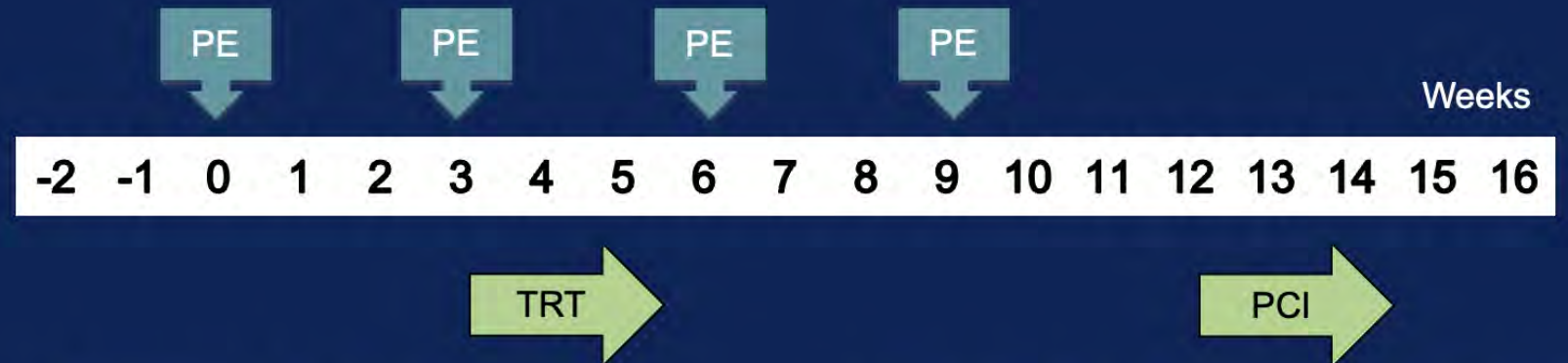
Study treatment

PE:

Cisplatin 75 mg/m² BSA or carboplatin AUC 5-6 IV day 1 *and* etoposide 100 mg/m² BSA IV days 1-3 q3w

TRT:

Commenced 21-28 days after first chemotherapy course, RT fields were limited to PET-CT positive lesions plus margins



Thoracic Radiotherapy:

Arm A: 45 Gy/30 fractions BID

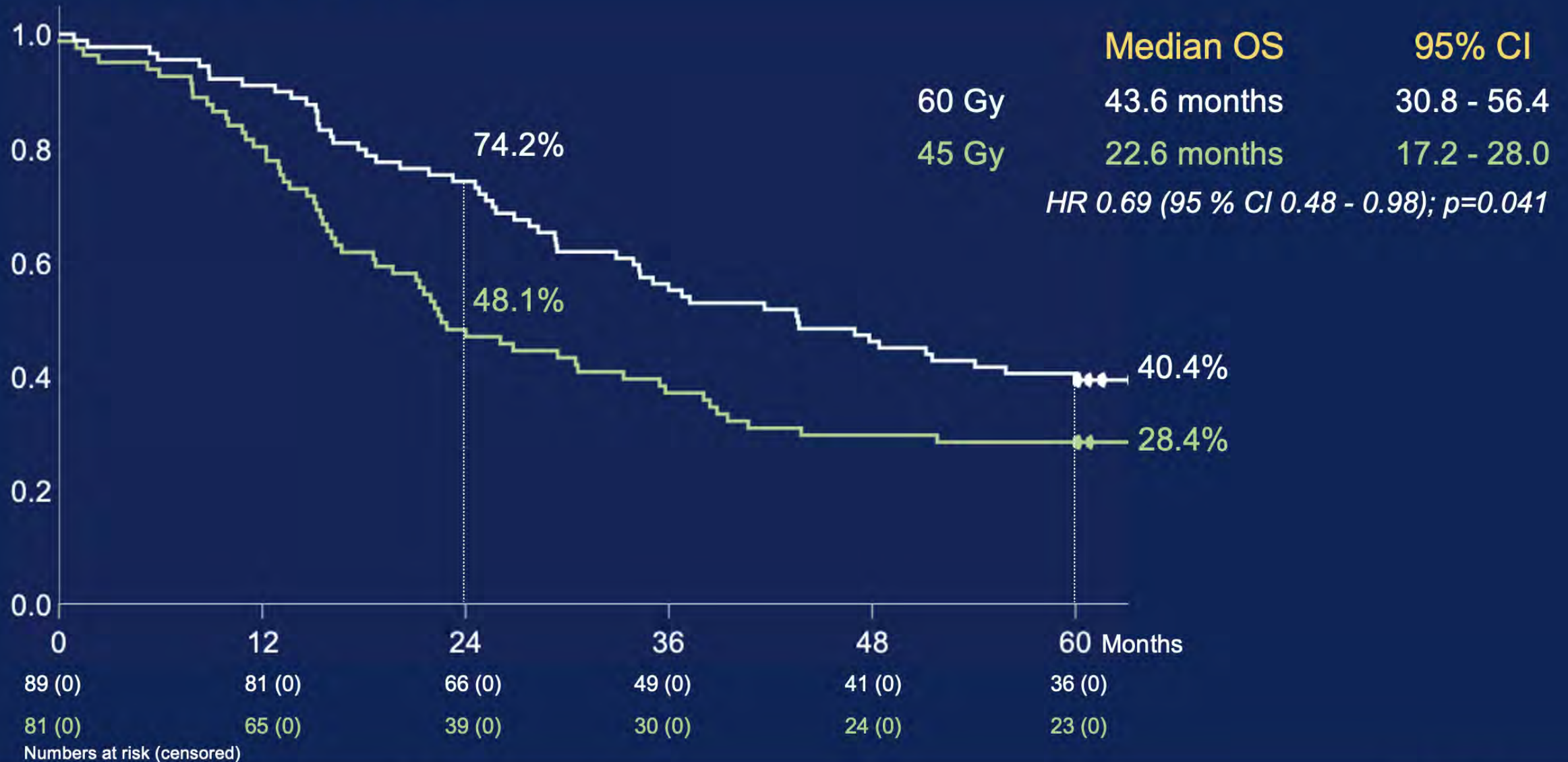
Arm B: 60 Gy/40 fractions BID

Prophylactic Cranial Irradiation:

25 Gy/10 or 30 G/15 fractions QD

Overall survival

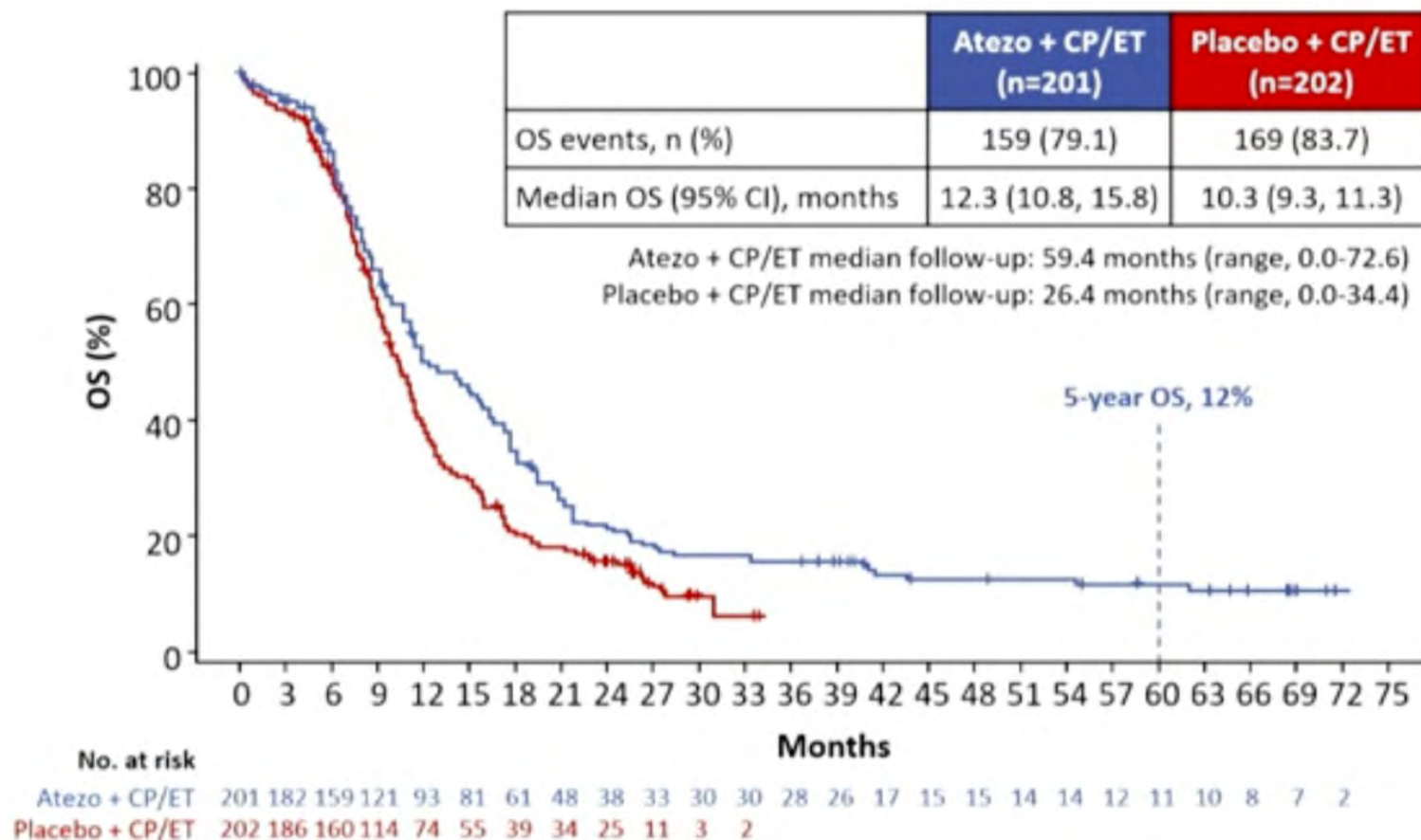
7



Extensive stage disease

- Main treatment is 4 (-6) courses of carboplatin or cisplatin plus etoposide or irinotecan
- Concurrent and maintenance immunotherapy prolongs survival
- The role of PCI is debated
- Consolidation TRT might benefit patients with residual (bulky?) thoracic disease

IMpower133 and IMbrella A: long-term OS

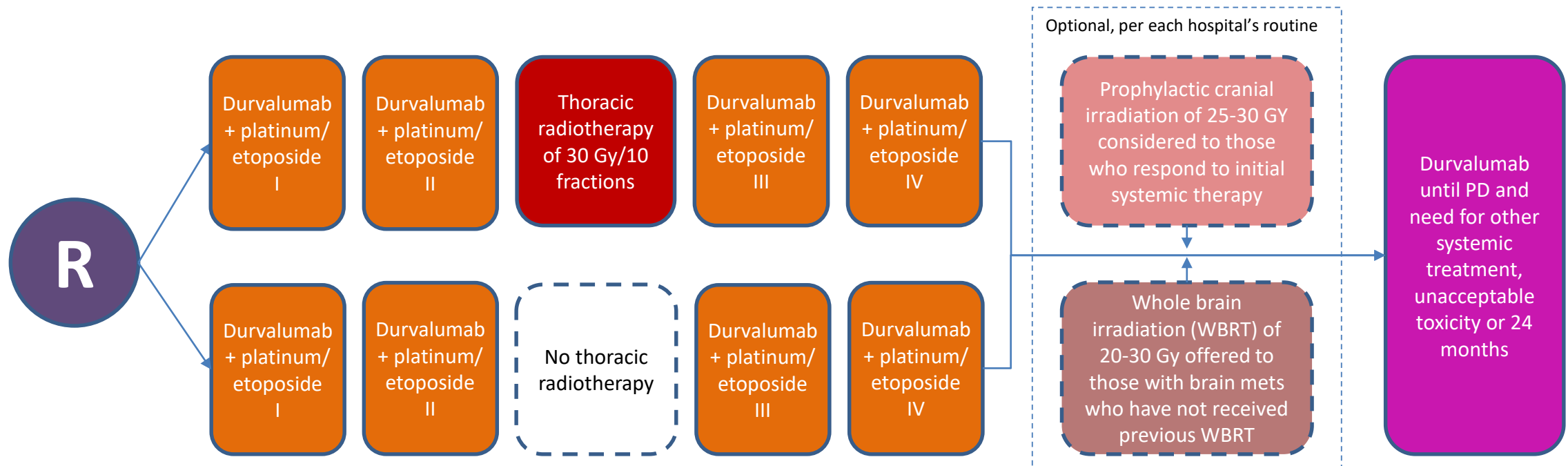


OS rate (95% CI), %	IMpower133 and IMbrella A Atezo + CP/ET (n=201)	IMpower133 only Placebo + CP/ET (n=202)
1-year	52% (45-59)	39% (32-46)
2-year	22% (16-28)	16% (11-21)
3-year	16% (11-21)	NE ^a
4-year	13% (8-18)	NE ^a
5-year	12% (7-17)	NE ^a

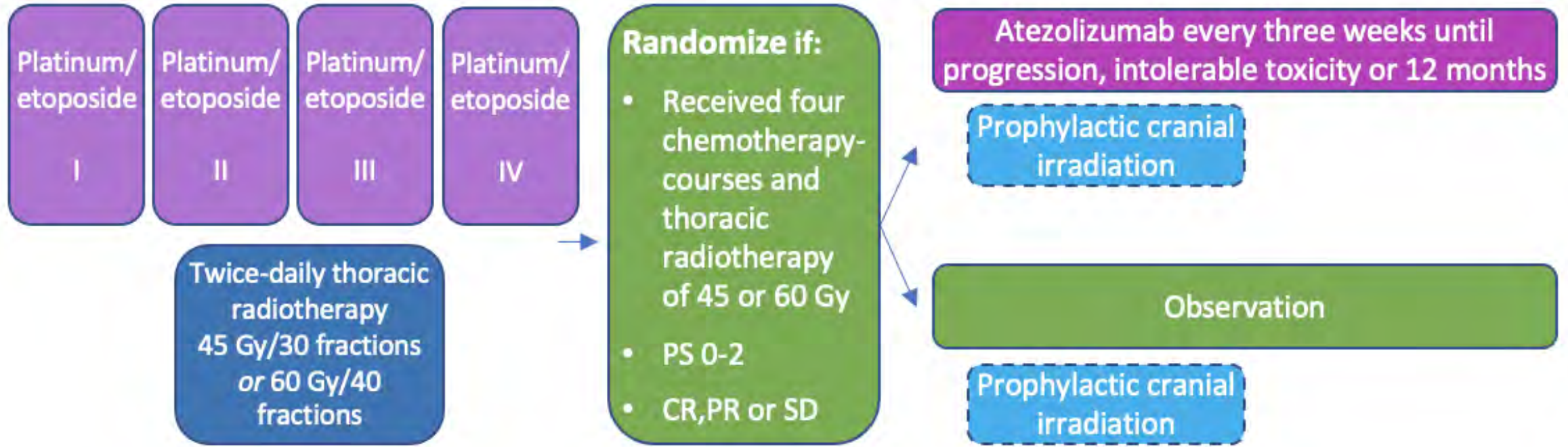
Clinical cutoff date: 16 March 2023. NE, not estimable. ^a OS rates were NE in the control arm as rollover to IMbrella A was not permitted.



Randomisert fase III studie - TRIPLEX



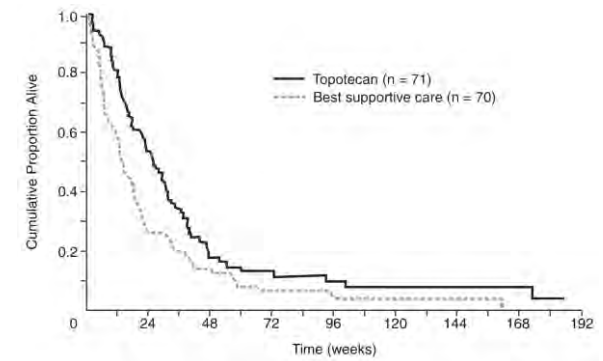
Randomisert fase II studie - ACHILES



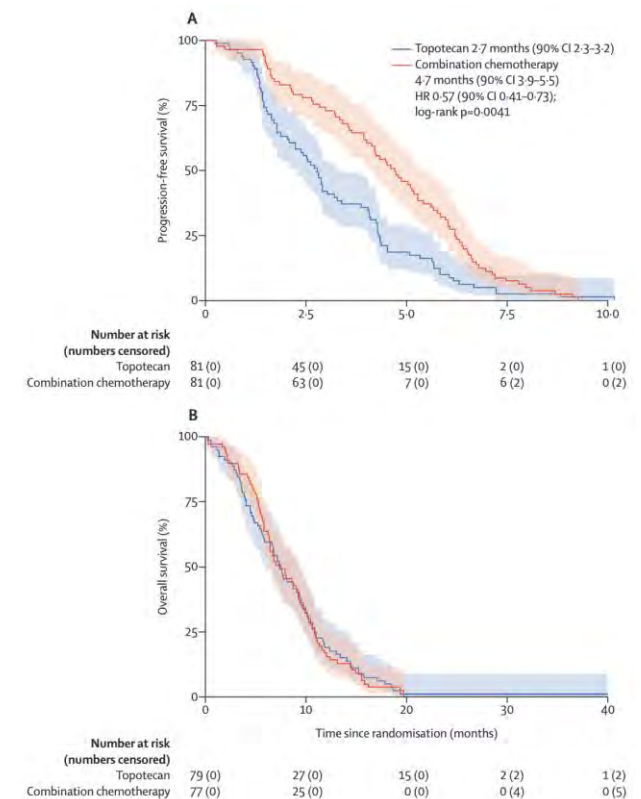
- Inklusjon avsluttet april 2022
- 212 pasienter inkludert Norge, Sverige, Danmark, Litauen, Sveits og Nederland
- Vi håper å presentere første resultat på ESMO 2024

Relapse treatment

- Most effective if relapses occur >3 months after primary treatment
- Re-induction (>3-6 months since primary treatment) or switch to topotecan or CAV
- Palliative radiotherapy for brain mets, painful bone mets, compression of central airways or vessels



O'Brien et al. Phase III trial comparing supportive care alone with supportive care with oral topotecan in patients with relapsed SCLC. *J Clin Oncol* 24, 5441–5447 (2006)



Baize et al. Carboplatin plus etoposide versus topotecan as second-line treatment for patients with sensitive relapsed SCLC: an open-label, multicentre, randomised, phase 3 trial. *Lancet Oncol* 21, 1224–1233 (2020)

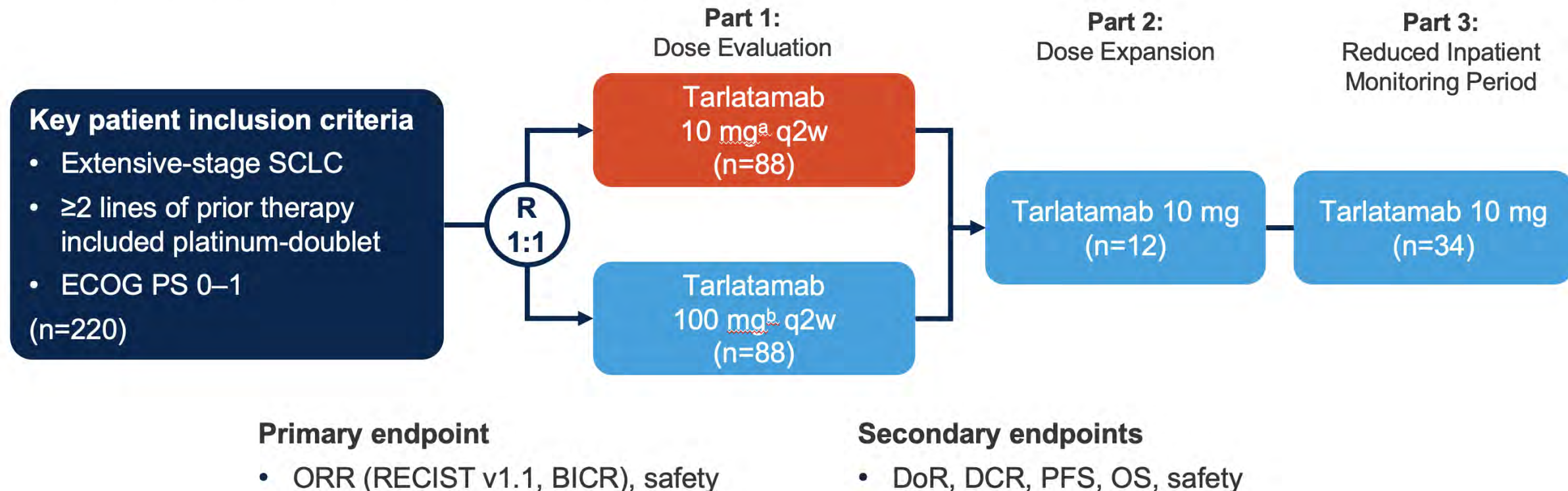


**Hva
kommer?**

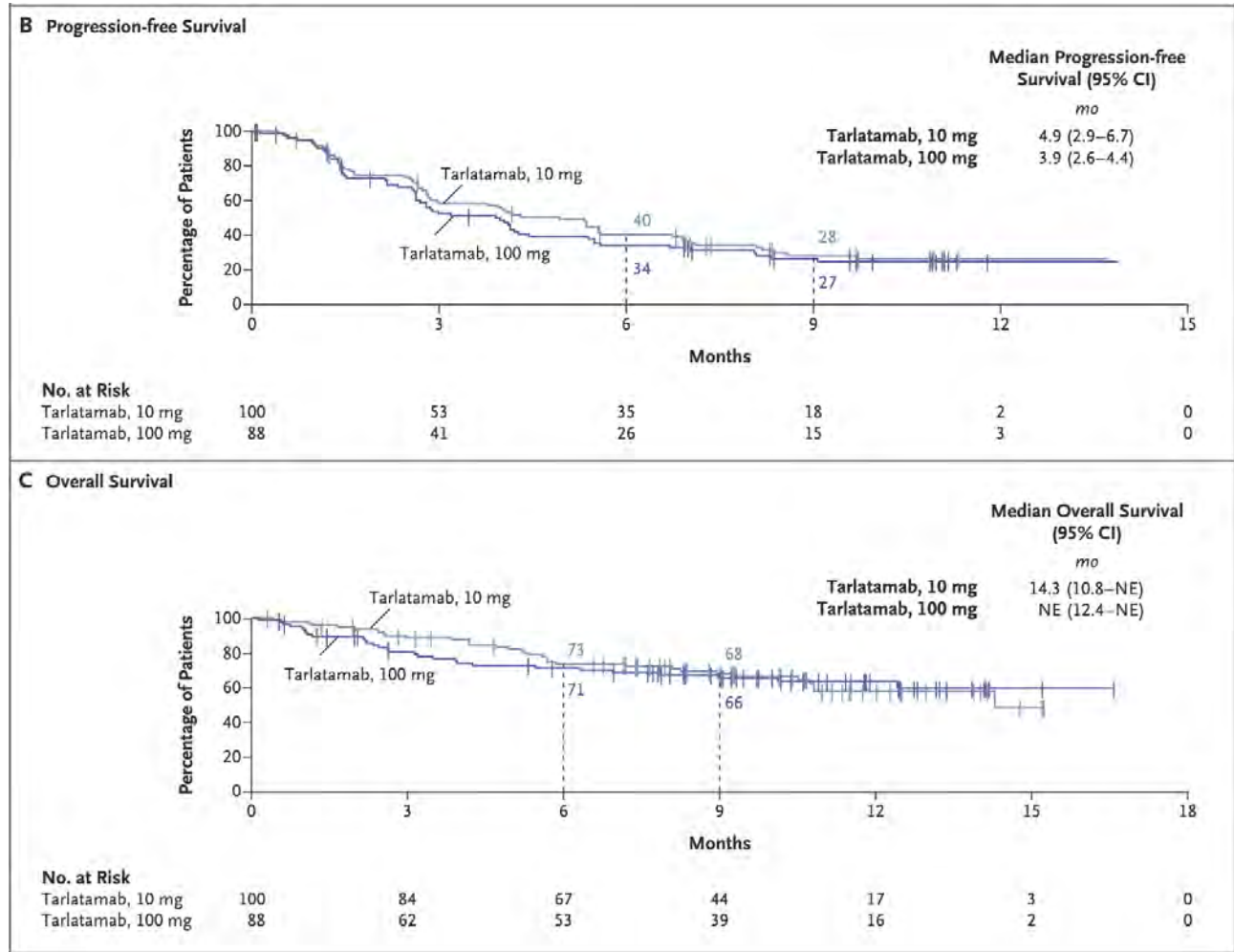
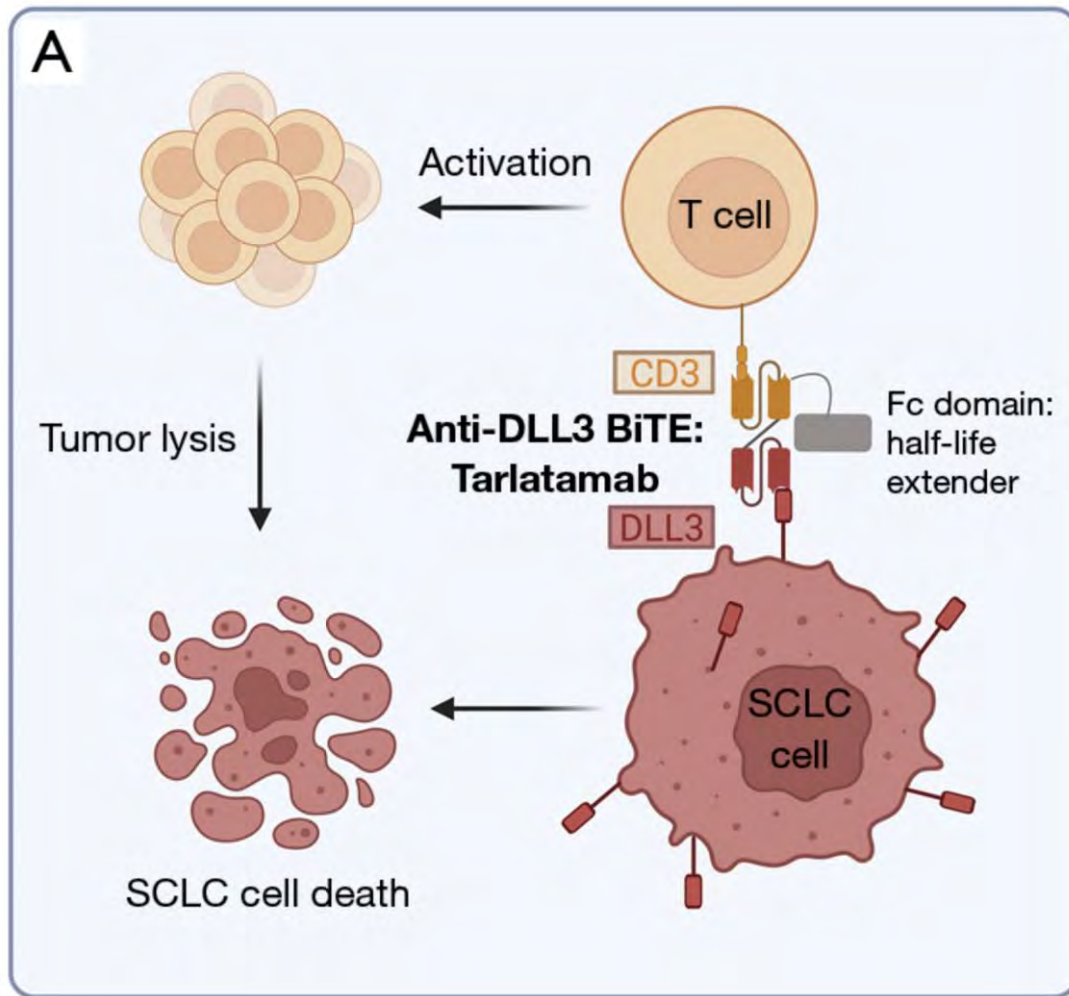
LBA92: Tarlatamab for patients (pts) with previously treated small cell lung cancer (SCLC): Primary analysis of the phase 2 DeLLphi-301 study – Paz-Ares L, et al

- **Study objective**

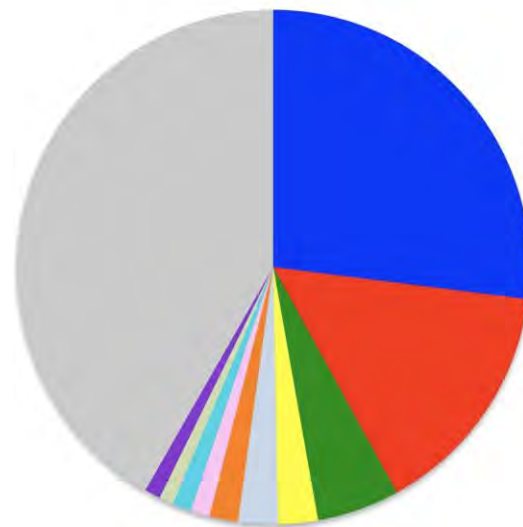
- To evaluate the efficacy and safety of tarlatamab, a bispecific T-cell engager, in previously treated patients with SCLC in the phase 2 DeLLphi-301 study



^a1 mg D1 followed by 10 mg D8, 15 then q2w. ^b1 mg D1 followed by 100 mg D8, 15 then q2w.

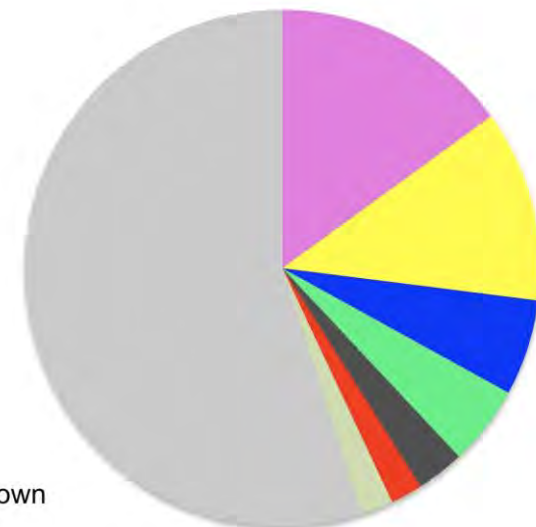


Ikke-småcellet lungekreft



Adenocarcinoma

- KRAS
- EGFR
- ALK
- PIK3CA
- HER2
- BRAF
- ROS
- RET
- NRAS
- MET
- Other/unknown



Squamous cell carcinoma

- FGFR
- PIK3CA
- KRAS
- PDGFR
- DDR2
- EGFR
- NRAS
- Other/unknown

Surgery

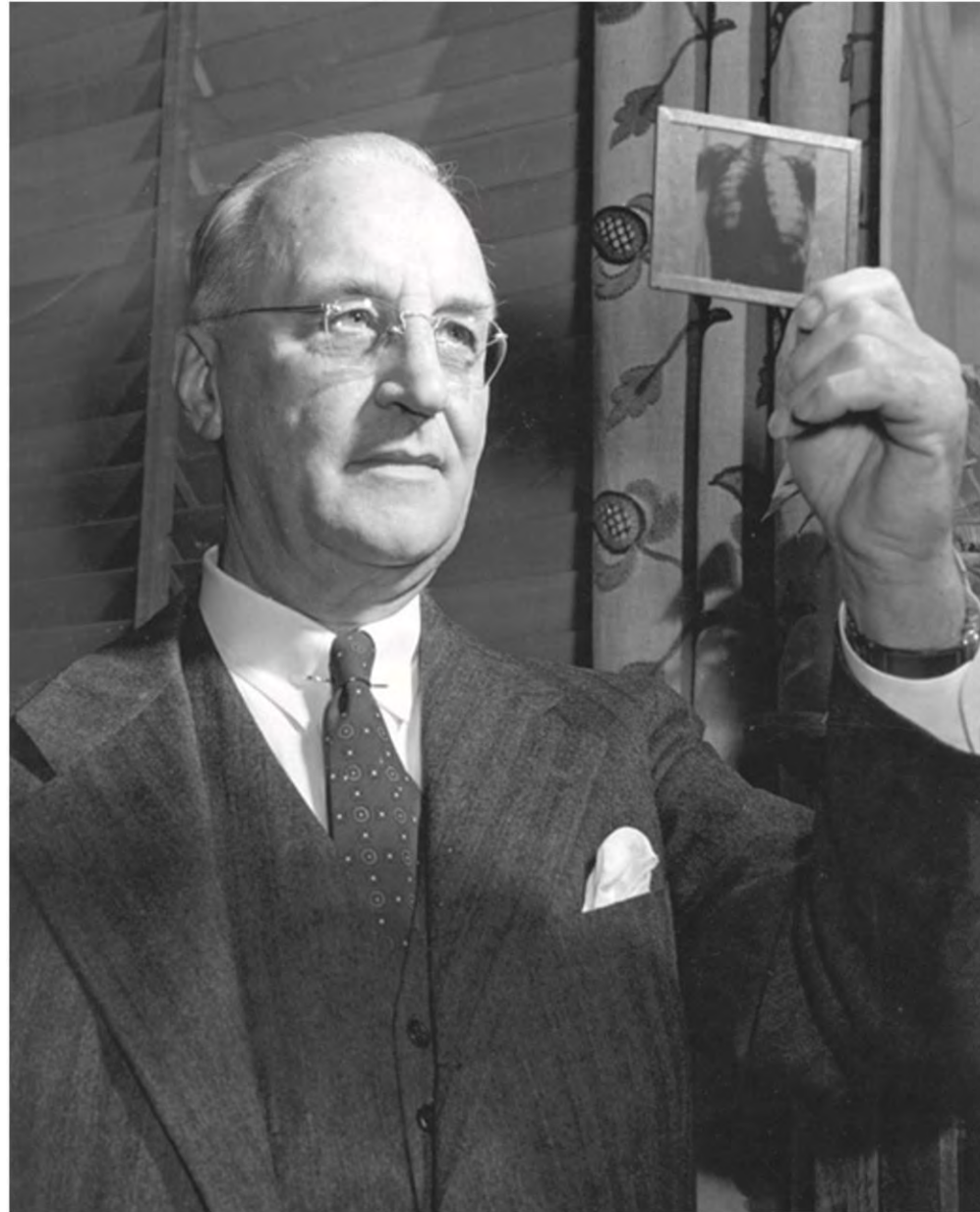
Radiotherapy

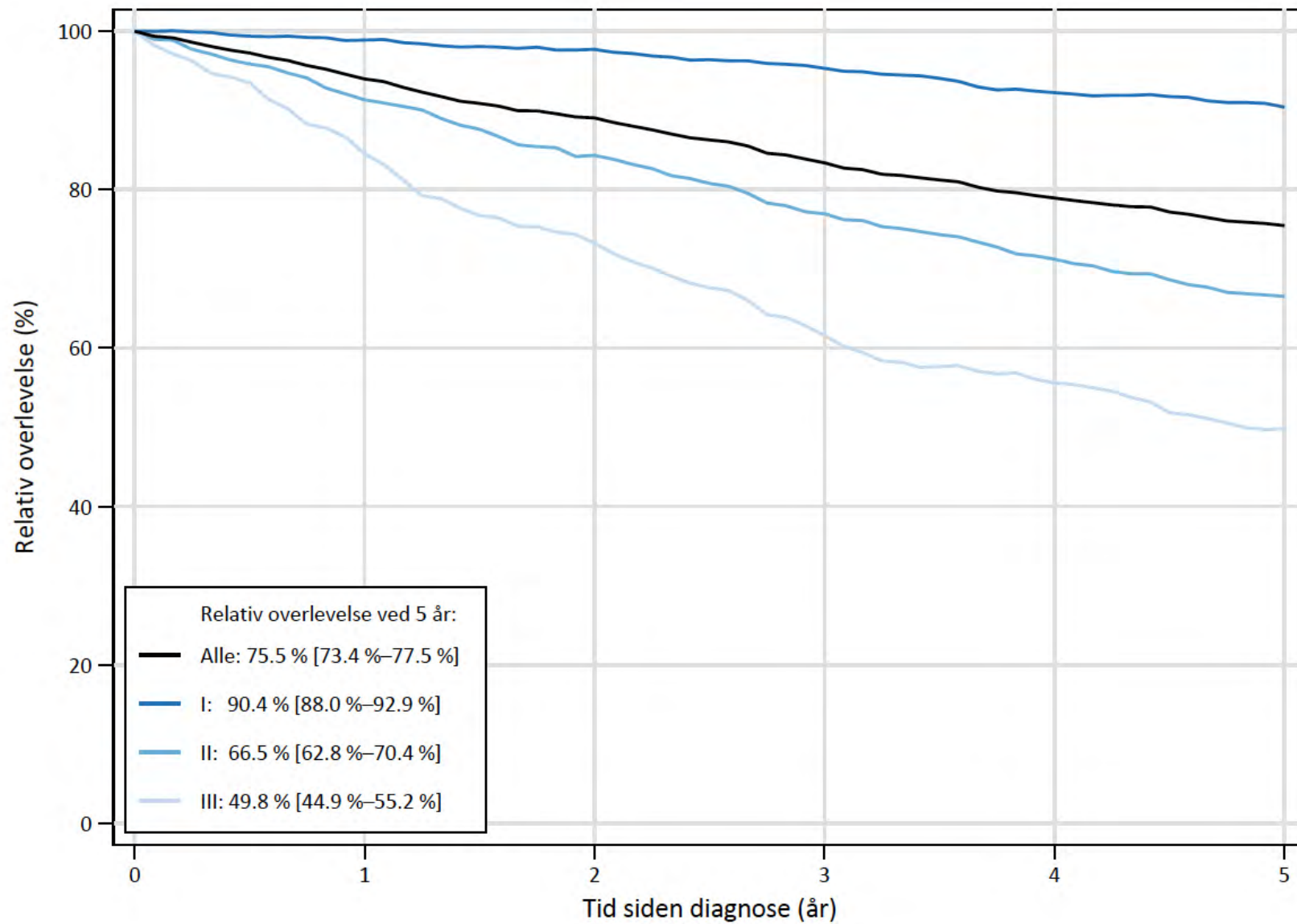
Immunotherapy

Targeted therapy

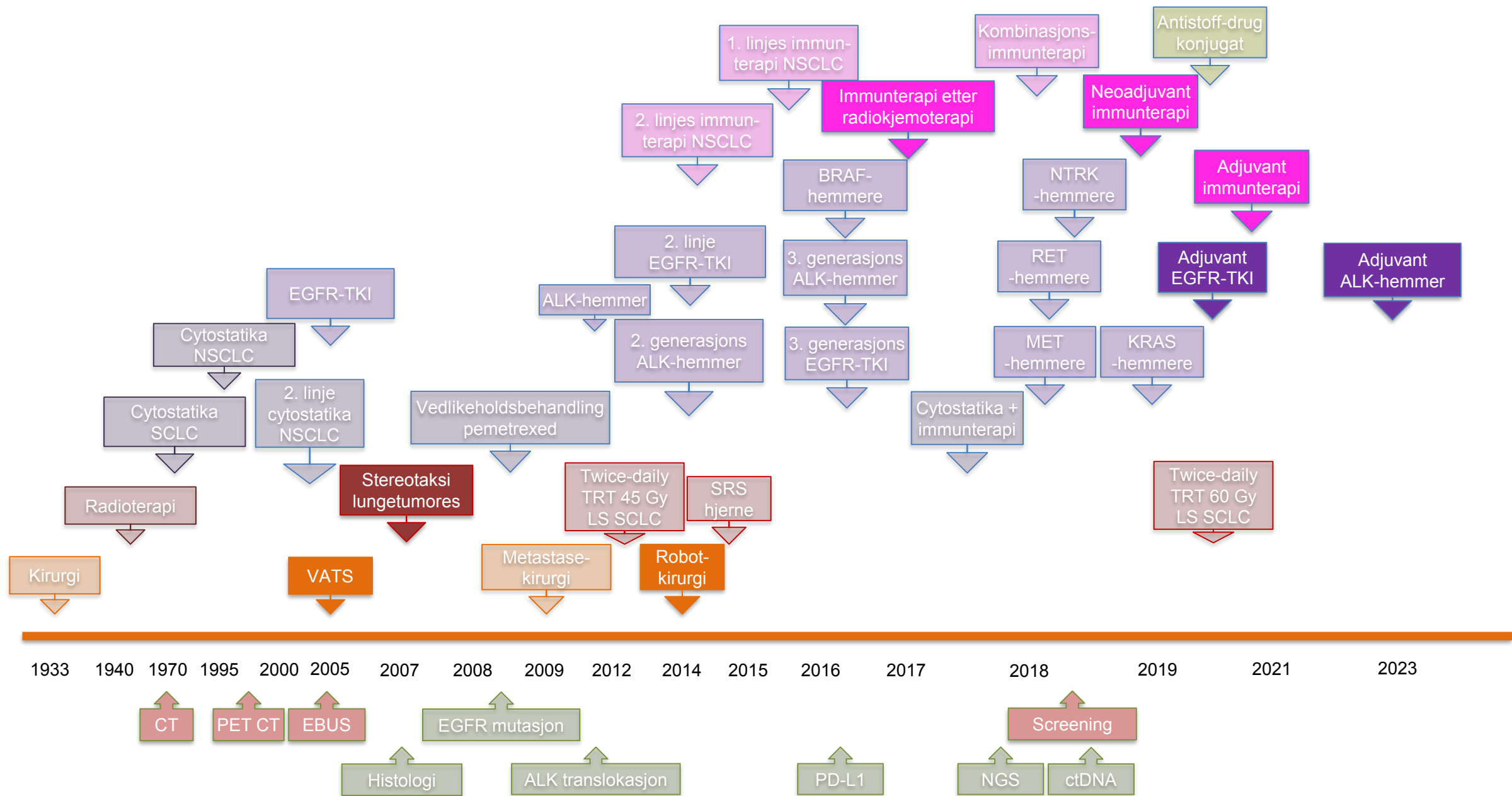
Chemotherapy

Operabel lungekreft





Figur 3.31: Relativ overlevelse opp til fem år etter operasjon for stadiene I-III (pTNM)



Adjuvant chemotherapy

- Provides a small survival benefit
- Should be considered for everybody who has undergone surgery for p-stage II-III

Standard is cisplatin/vinorelbine

Platinum/pemetrexed is less toxic and equally effective

Cisplatin may be replaced with carboplatin

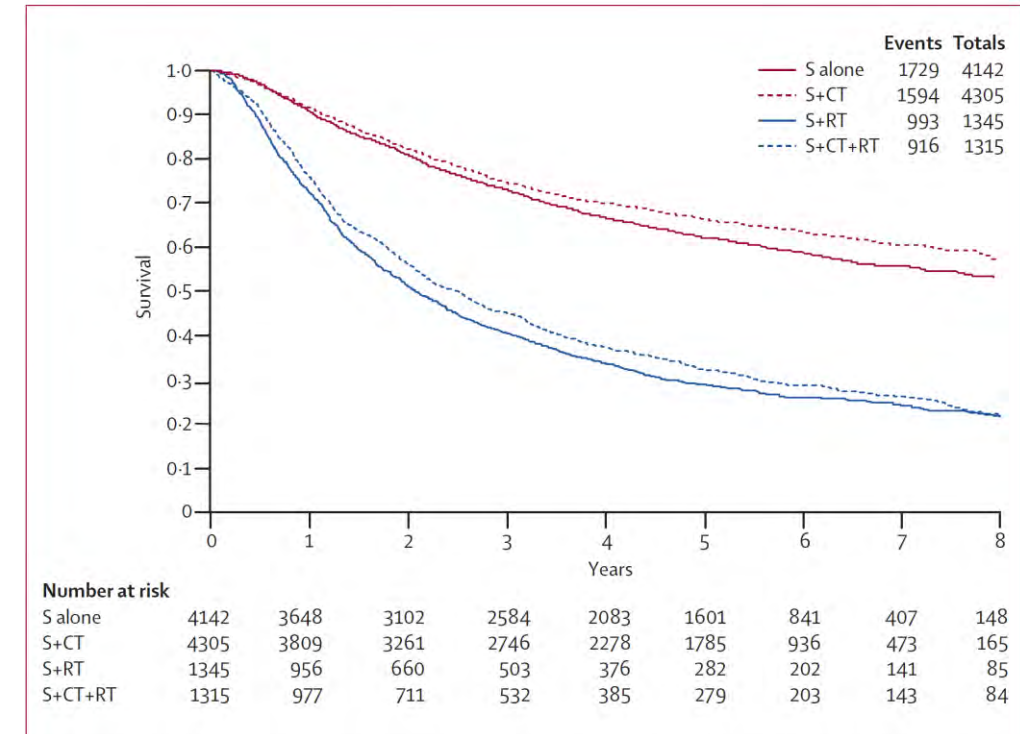


Figure 2: Simple (non-stratified) Kaplan-Meier curves for trials of surgery (S) and chemotherapy (CT) versus surgery alone and for trials of surgery and chemotherapy and radiotherapy (RT) versus surgery and radiotherapy

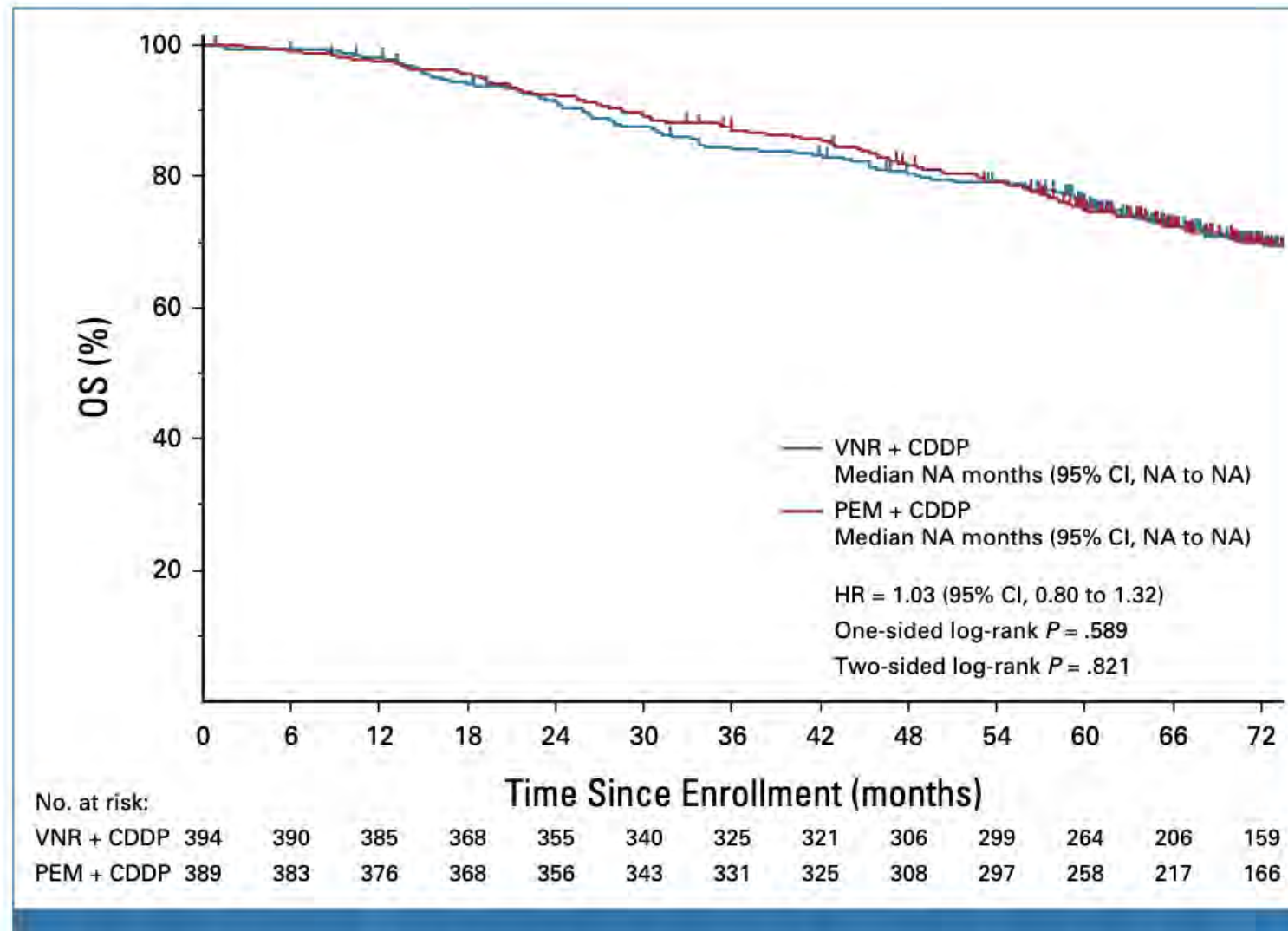
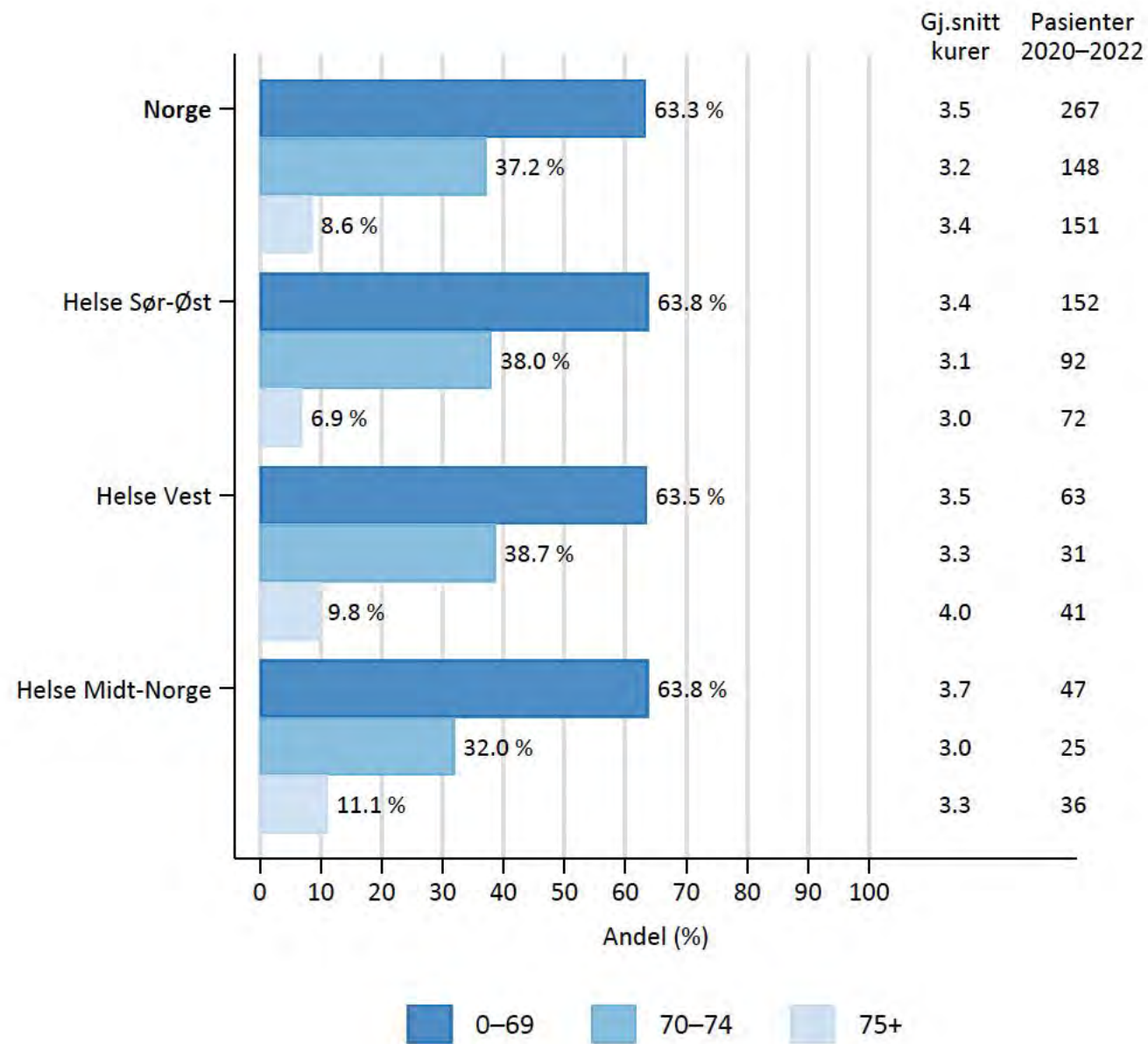
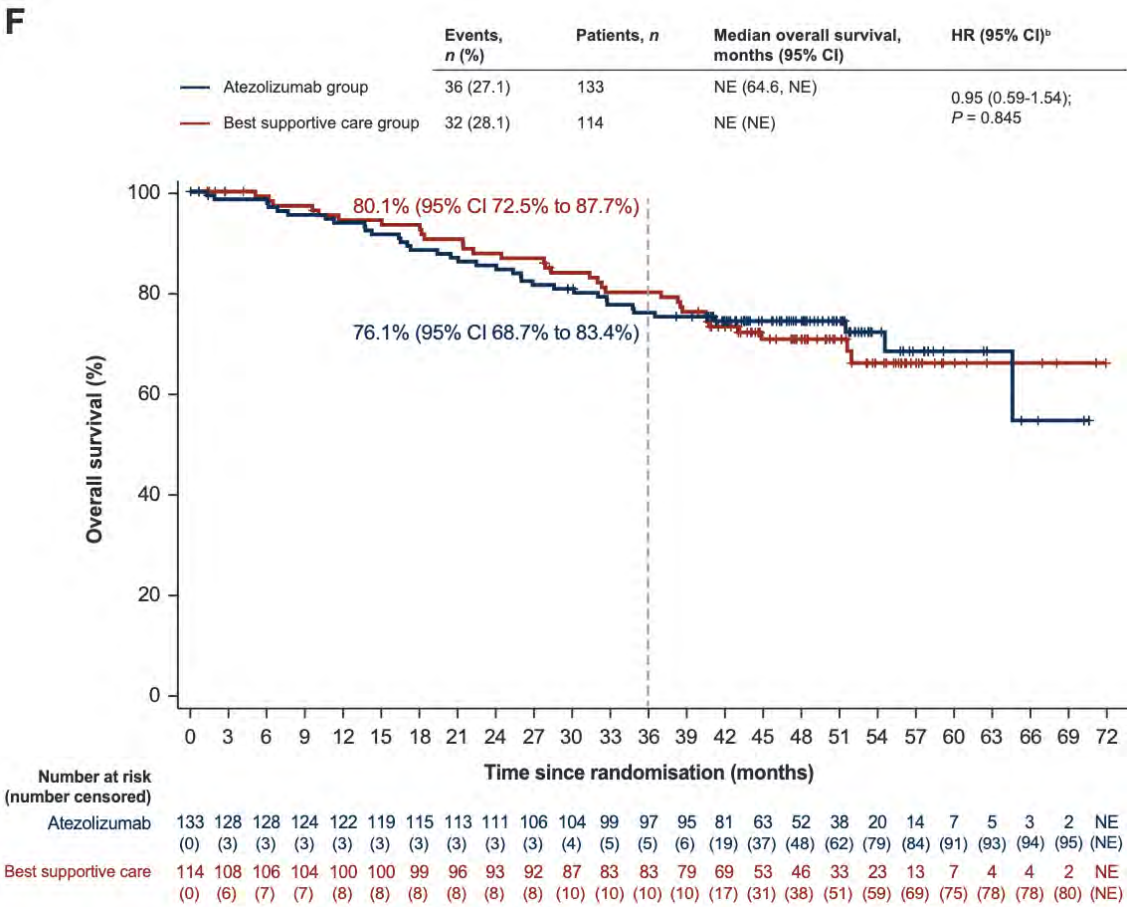


FIG 1. Kaplan-Meier curve for OS in the eligible patients ($n = 783$). CDDP, cisplatin; HR, stratified hazard ratio by the predefined factors (sex, age, pathologic stage, *EGFR* mutation status); NA, not available; OS, overall survival; PEM, pemetrexed; VNR, vinorelbine.

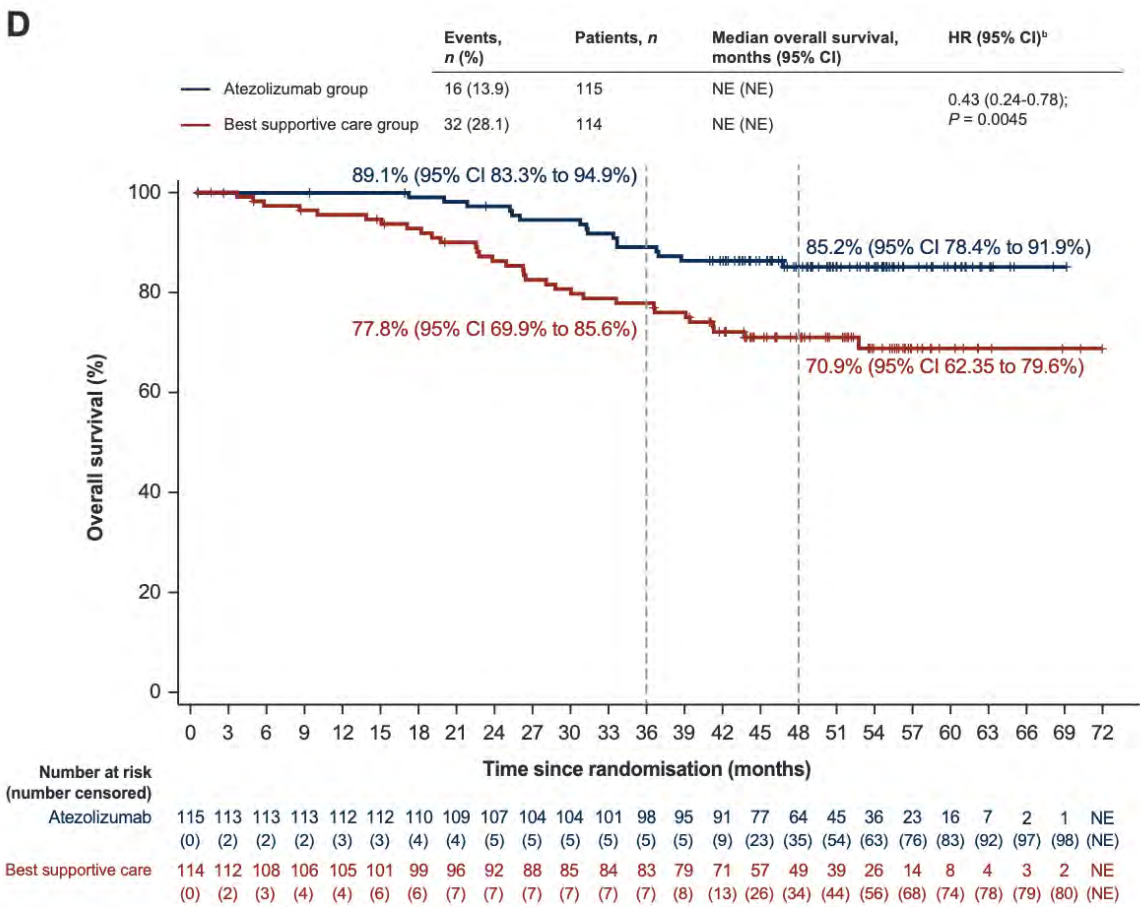


Figur 3.15: Adjuvant behandling etter kirurgi, 2020–2022

PD-L1 1-49%

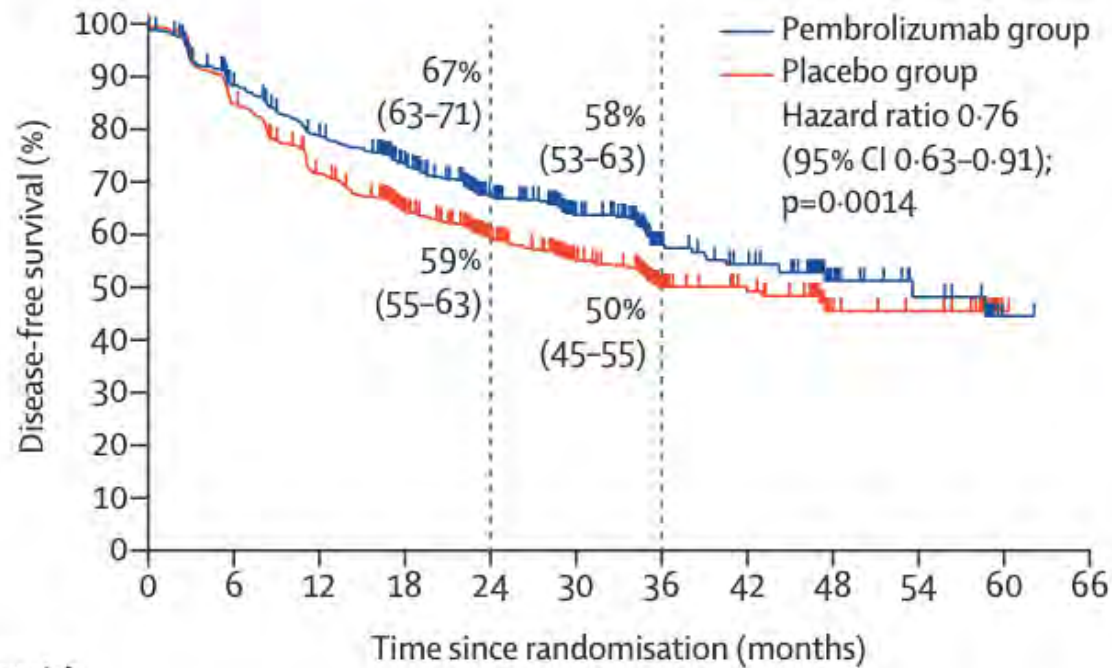


PD-L1 50%+



Felip et al. Overall survival with adjuvant atezolizumab after chemotherapy in resected stage II-IIIa NSCLC (IMpower010): a randomised, multicentre, open-label, phase 3 trial. Ann Oncol (2023)

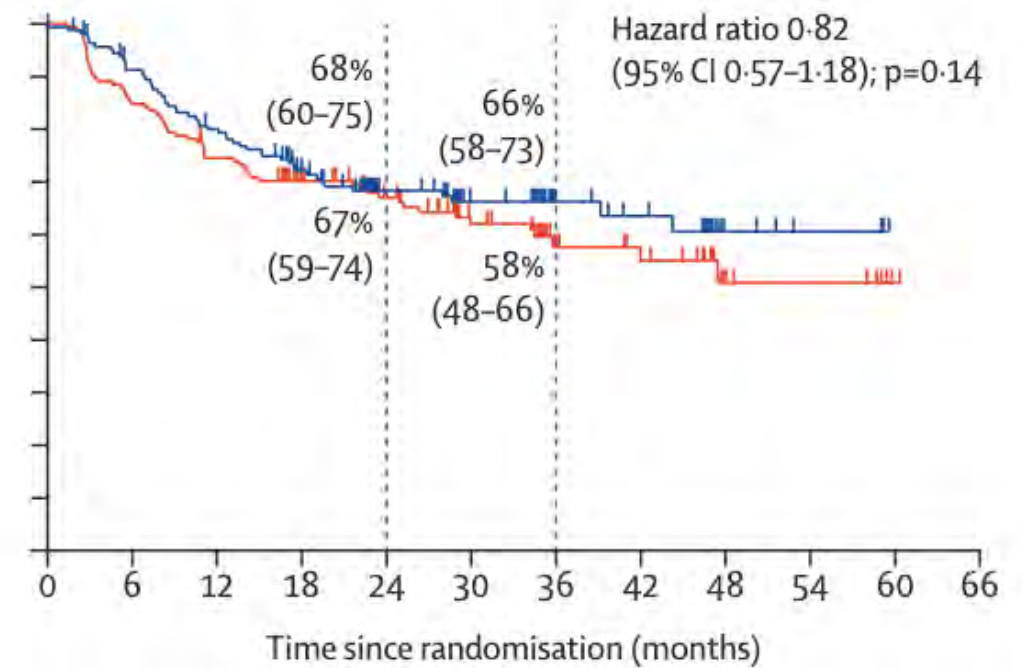
A



Number at risk
(number censored)

Pembrolizumab	590	493	434	358	264	185	82	70	28	16	1	0
	(0)	(30)	(36)	(84)	(150)	(216)	(306)	(313)	(352)	(363)	(377)	(378)
Placebo	587	493	409	326	241	160	72	57	22	18	1	0
	(0)	(5)	(13)	(56)	(118)	(183)	(259)	(273)	(305)	(309)	(326)	(327)

B



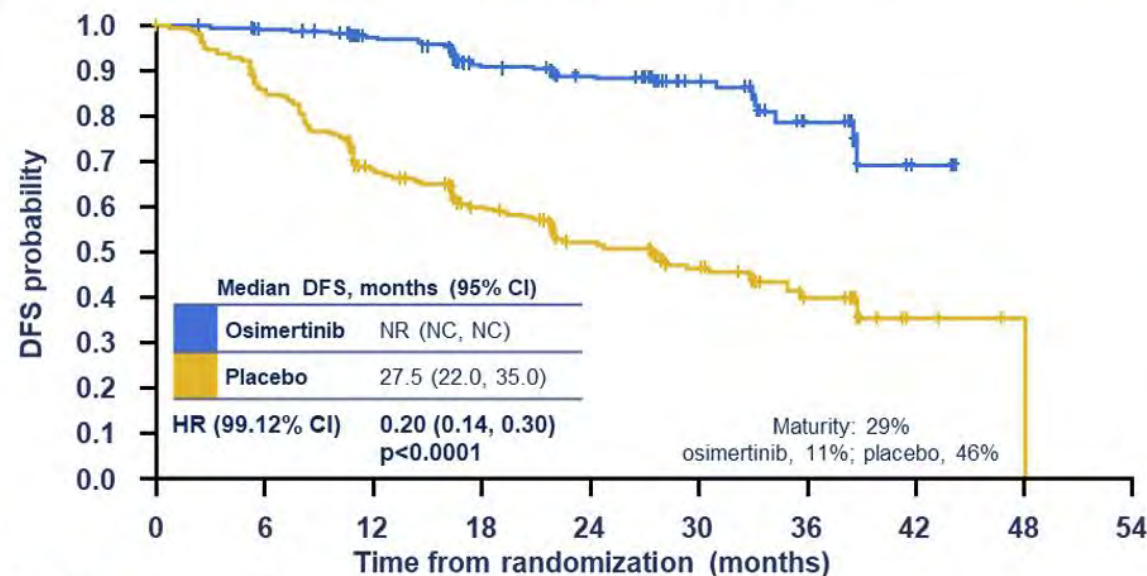
	168	145	126	99	69	50	26	22	7	4	0	0
	(0)	(8)	(9)	(24)	(49)	(66)	(90)	(93)	(107)	(110)	(114)	(114)
	165	140	121	100	75	54	28	22	8	6	1	0
	(0)	(0)	(2)	(16)	(37)	(53)	(76)	(81)	(94)	(96)	(101)	(102)

Adjuvant osimertinib has significantly improved DFS

- Adjuvant osimertinib demonstrated highly statistically significant^{1,2} and clinically meaningful improvement in DFS in completely resected EGFRm NSCLC vs placebo in both the primary (stage IB–IIIA) and overall (IB–IIIA) populations, along with a tolerable safety profile^{1–4}

ADAURA primary DFS analysis^{1,2} (stage IB–IIIA)*

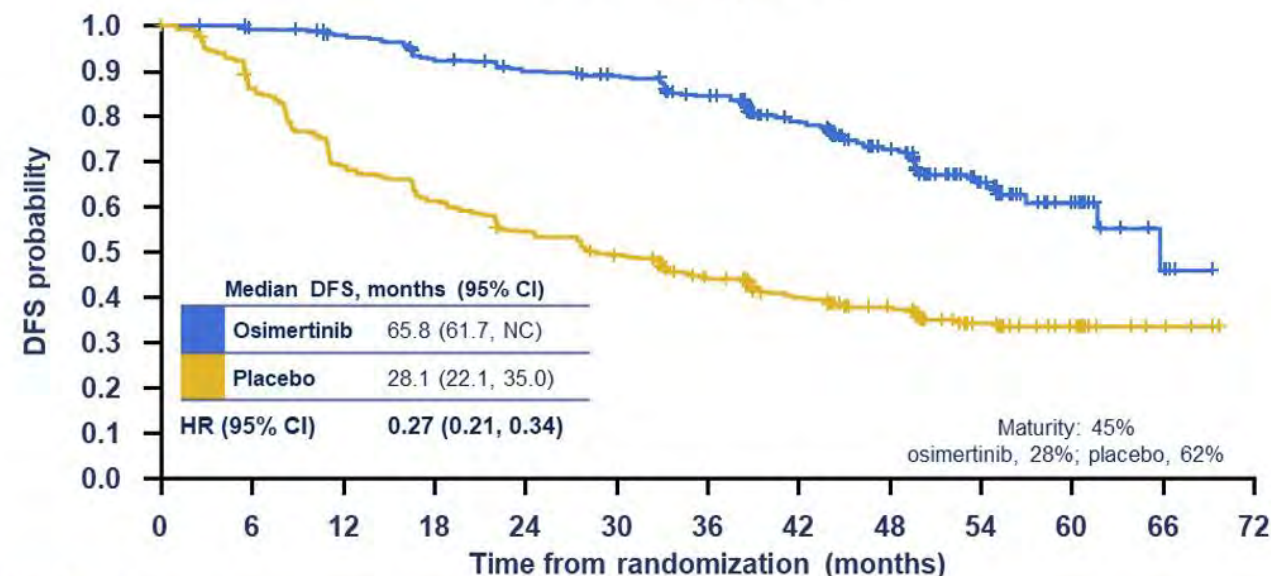
NEJM October 2020



No. at risk										
Osimertinib	339	313	272	208	138	74	27	5	0	-
Placebo	343	287	207	148	88	53	20	3	1	0

ADAURA updated DFS analysis^{3,4} (stage IB–IIIA)†

JCO January 2023



No. at risk														
Osimertinib	339	316	307	289	278	270	249	201	139	73	33	5	0	0
Placebo	343	288	230	205	181	162	137	115	84	48	25	4	0	0

*Data cut-off: January 17, 2020. †Data cut-off: April 11, 2022.
1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2020;38(Suppl 18): abstract/ oral LBA5; 3. Herbst et al. J Clin Oncol 2023;41:1830–1840; 4. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract/ oral LBA47.

Adjuvant osimertinib has significantly improved CNS DFS

- CNS metastases are a poor prognostic factor among patients with NSCLC, and are associated with deterioration in quality of life¹

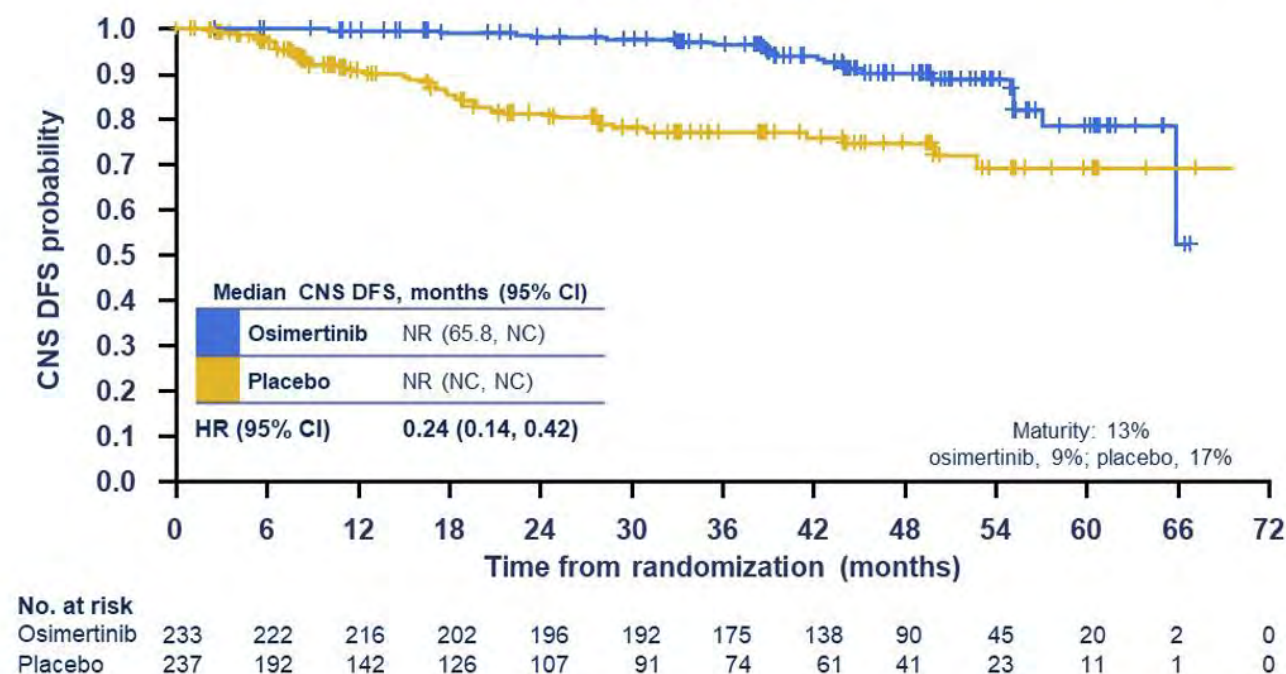
Improved CNS efficacy with osimertinib treatment



- Osimertinib has shown greater penetration of the blood-brain barrier and higher exposure in the brain compared with other EGFR-TKIs²⁻⁴
- Adjuvant osimertinib demonstrated CNS DFS* benefit vs placebo in both the stage II–IIIA and IB–IIIA populations^{5,6}

ADAURA updated CNS DFS analysis^{5,6} (stage II–IIIA)

JCO January 2023

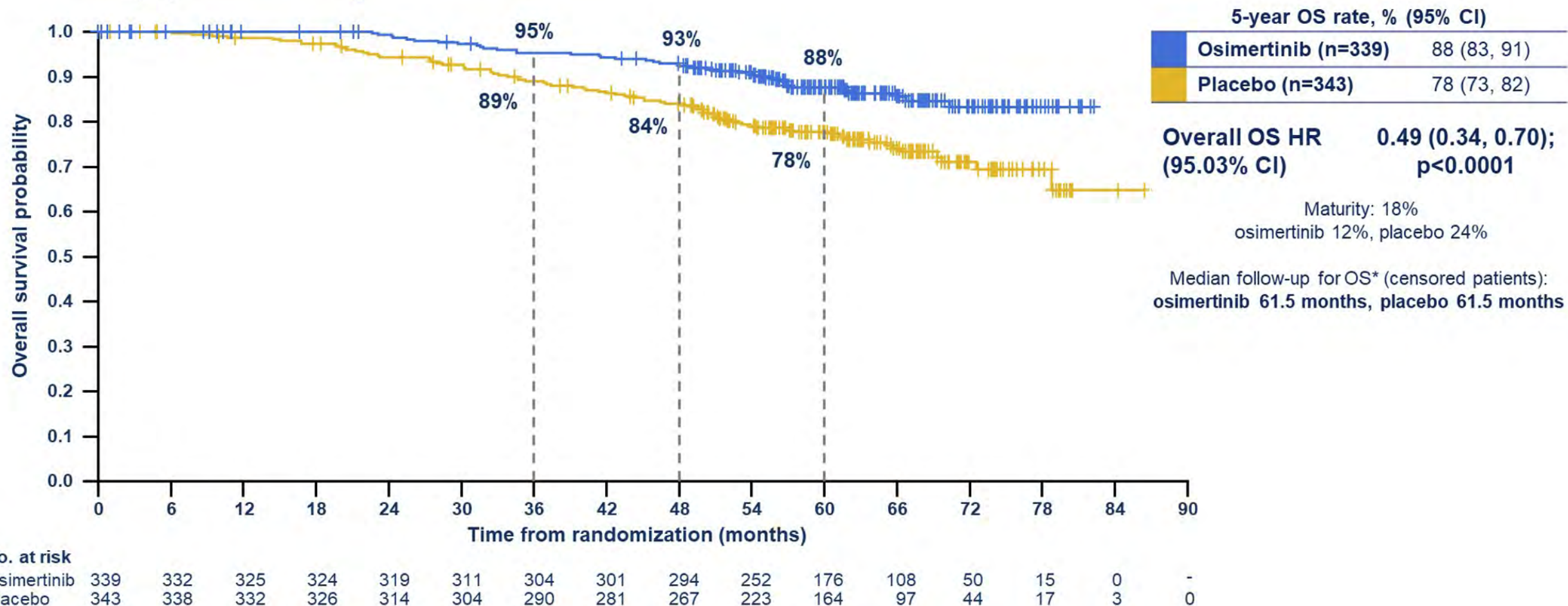


Data cut-off: April 11, 2022.

1. Peters et al. Cancer Treat Rev 2016;45:139–162; 2. Coldclough et al. Eur J Cancer 2016;69:S28; 3. Ballard et al. Clin Cancer Res 2016;22:5130–5140; 4. Vishwanathan et al. Cancer Res 2018;78:CT013; 5. Herbst et al. J Clin Oncol 2023;41:1830–1840; 6. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB—IIIA disease



Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 60.4 months, placebo 59.4 months.

Subsequent treatments

- At data cut-off for this final OS analysis, 76 patients (22%) in the osimertinib arm and 184 patients (54%) in the placebo arm had received any subsequent anti-cancer treatment
- EGFR-TKIs were the most common subsequent anti-cancer treatment received across both arms; most frequently osimertinib

Subsequent treatments, n (%)	Osimertinib (n=339)	Placebo (n=343)
Patients who received subsequent anti-cancer treatment*	76 (22)	184 (54)
EGFR-TKIs	58 (76)	162 (88)
Osimertinib	 31 (41)	79 (43)
Other EGFR-TKIs	28 (37)	114 (62)
Chemotherapy	20 (26)	46 (25)
Radiotherapy	30 (39)	53 (29)
Other anti-cancer treatments	12 (16)	29 (16)

Data cut-off: January 27, 2023.
Percentages of patients by treatment type are calculated from the number of patients who received a subsequent anti-cancer treatment. *Subsequent anti-cancer treatments were identified by medical review and included anti-cancer treatments with a start date on or after the date of discontinuation of study treatment, and before withdrawal from the study. Surgeries and procedures were not included. Patients could have received more than one subsequent anti-cancer treatment.

Preoperative chemotherapy for non-small cell lung cancer: a systematic review and meta-analysis of individual participant data

NSCLC Meta-analysis Collaborative Group*

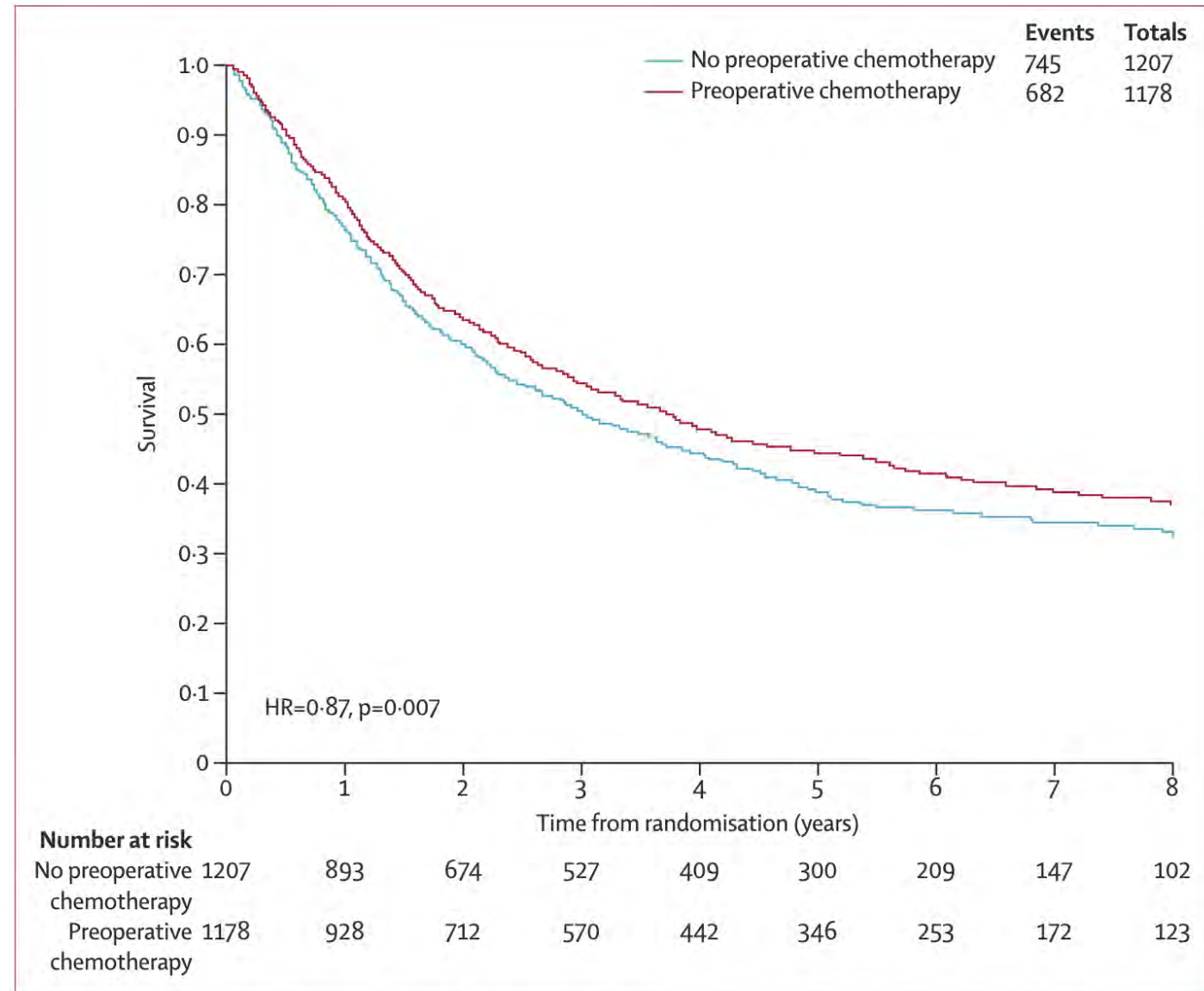
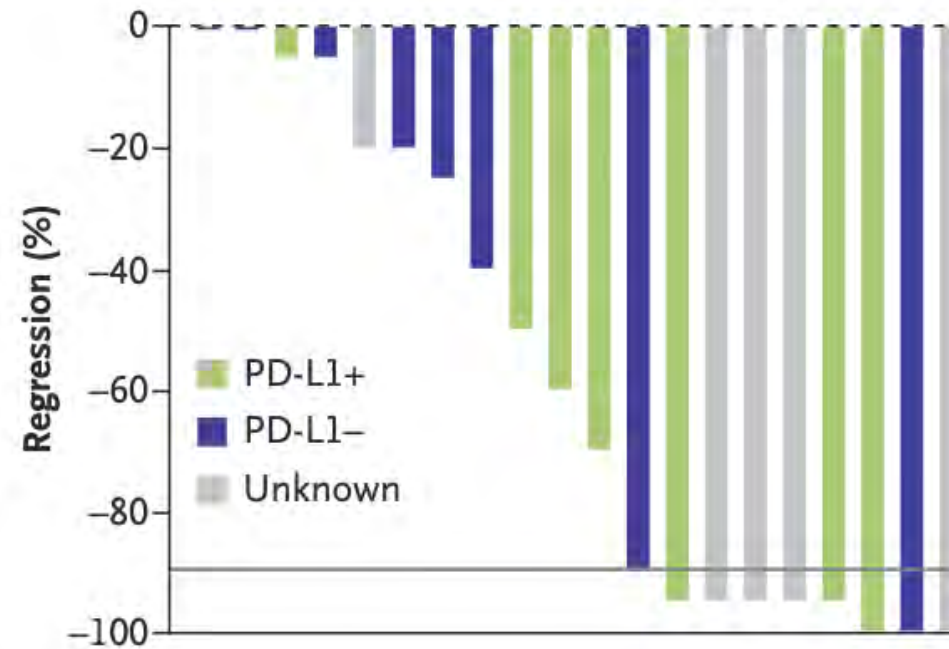
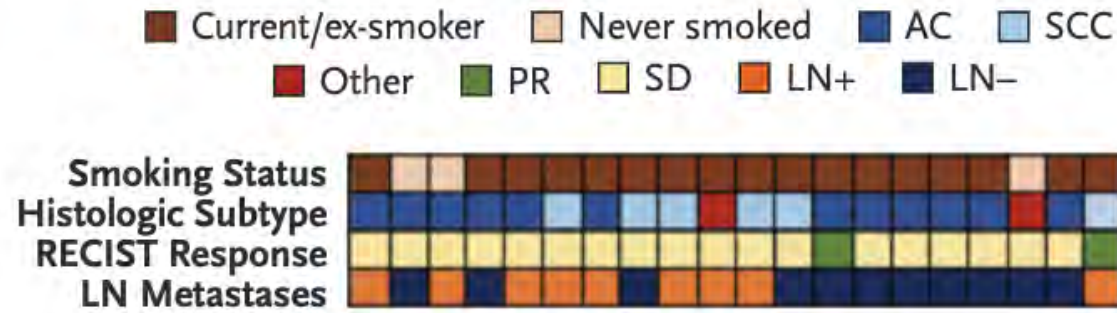


Figure 2: Kaplan-Meier curves (non-stratified) of the effect of preoperative chemotherapy on time to survival

Lancet, 2014

A Percentage of Pathological Regression, According to Subgroup

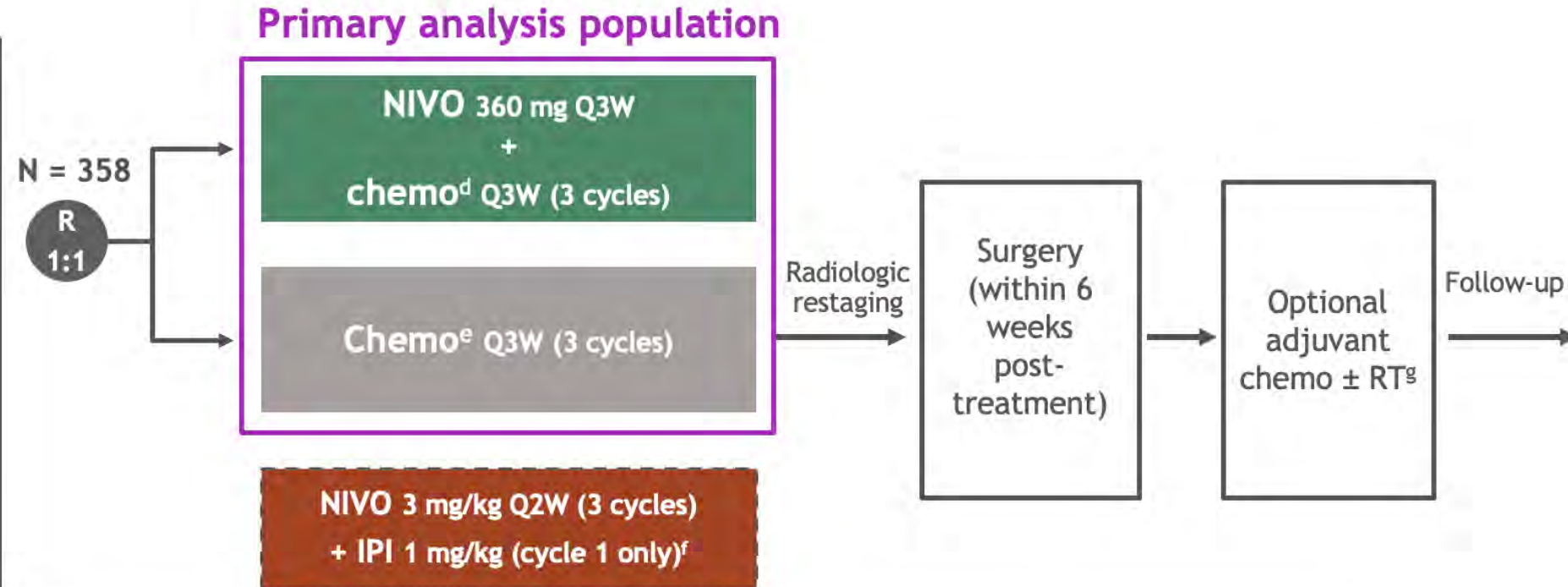


CheckMate 816 study design^a

Key Eligibility Criteria

- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (per TNM 7th edition)
- ECOG performance status 0-1
- No known sensitizing *EGFR* mutations or *ALK* alterations

Stratified by
Stage (IB-II vs IIIA),
PD-L1^b ($\geq 1\%$ vs $< 1\%$ ^c), and sex



Primary endpoints

- pCR by BIPR
- EFS by BICR

Secondary endpoints

- MPR by BIPR
- OS
- Time to death or distant metastases

Exploratory endpoints

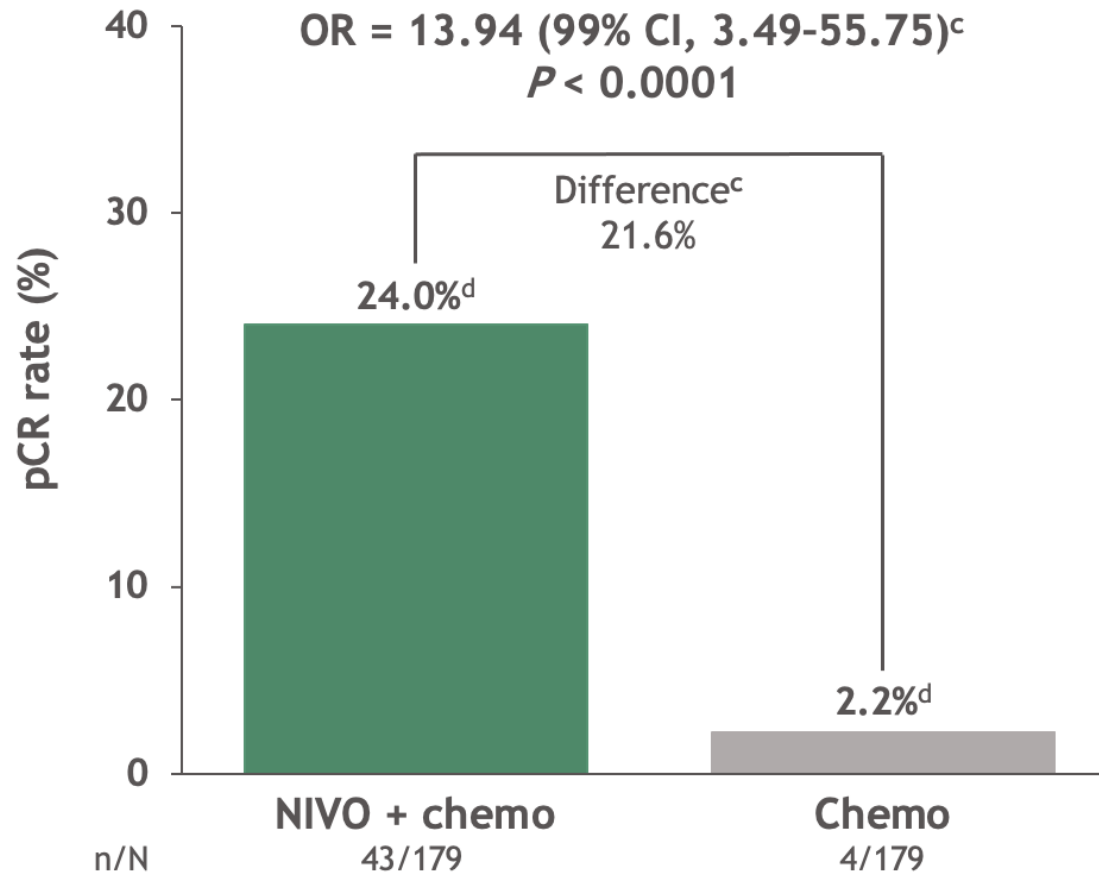
- ORR by BICR
- Predictive biomarkers (PD-L1, TMB, ctDNA^h)

Database lock: September 16, 2020; minimum follow-up: 7.6 months for NIVO + chemo and chemo arms.

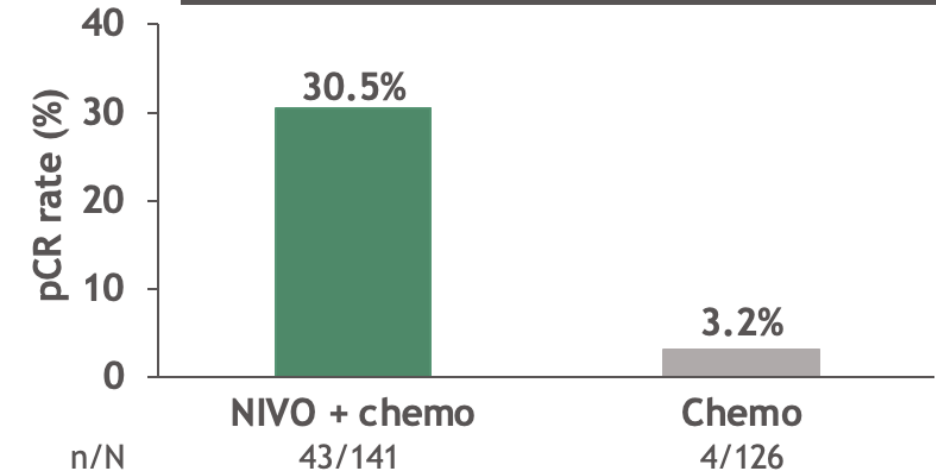
^aNCT02998528; ^bDetermined by the PD-L1 IHC 28-8 pharmDx assay (Dako); ^cIncluded patients with PD-L1 expression status not evaluable and indeterminate; ^dNSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin; ^eVinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin; ^fRandomized exploratory arm (enrollment closed early); ^gPer healthcare professional choice; ^hPerformed using tumor-guided personalized ctDNA panel (ArcherDX Personalized Cancer Monitoring).

Primary endpoint: pCR^a rate with neoadjuvant NIVO + chemo vs chemo

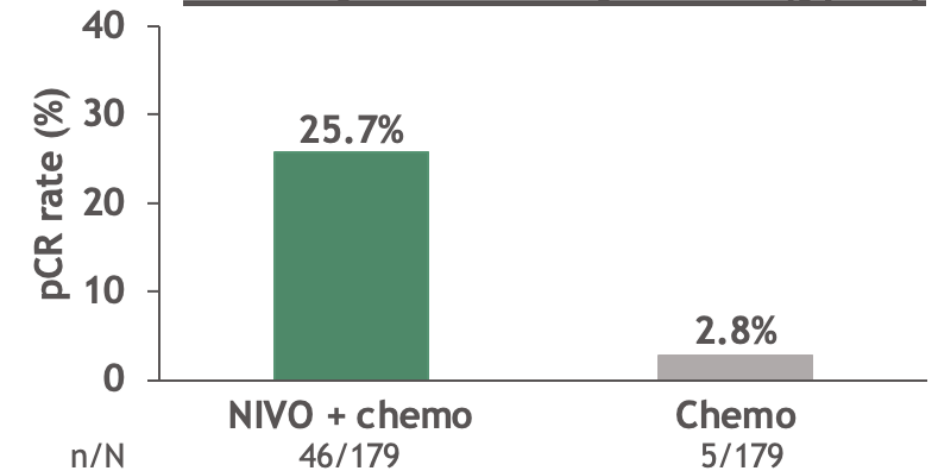
Primary endpoint: ITT (ypT0N0)^b



Patients with resection^e (ypT0N0)



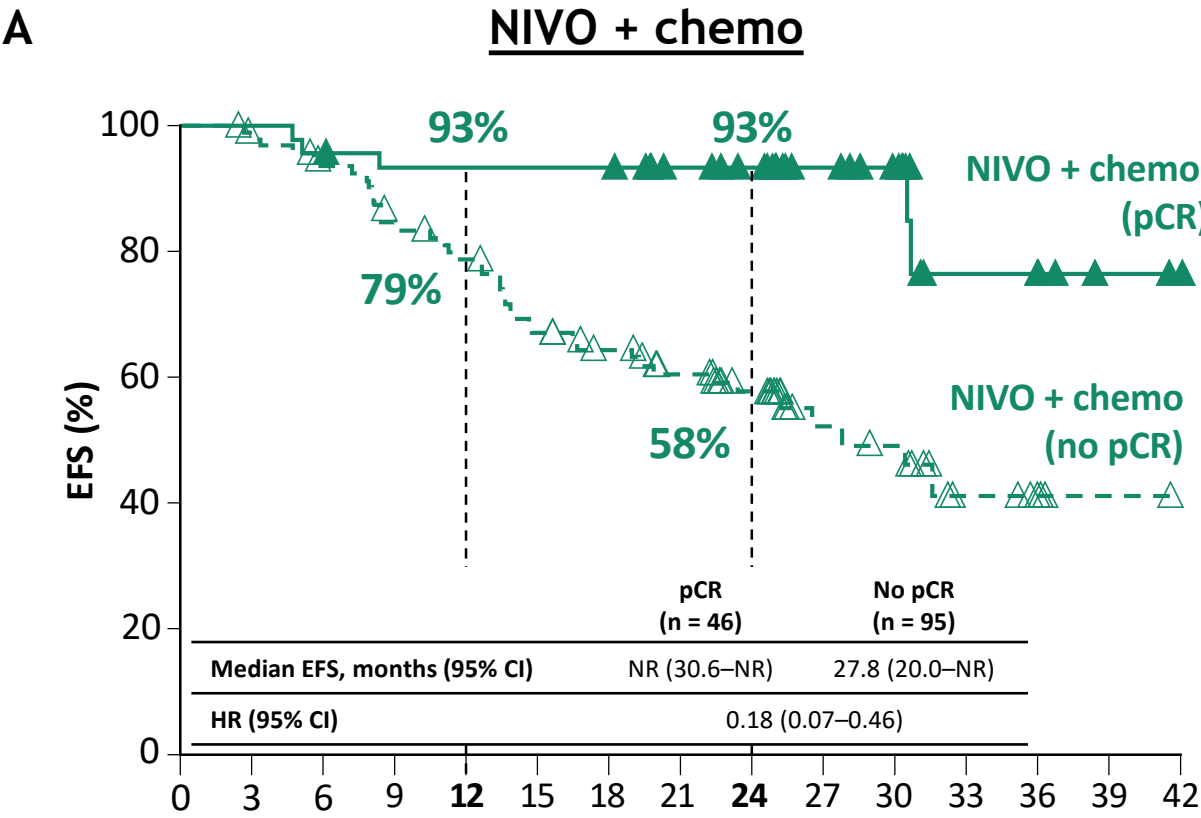
Primary tumor only in ITT (ypT0)



- pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4-29.0)

^aPer BIPR; pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; ^bITT principle: patients who did not undergo surgery counted as non-responders for primary analysis; ^cCalculated by stratified Cochran-Mantel-Haenszel method; ^dpCR rates 95% CI: NIVO + chemo, 18.0-31.0; chemo, 0.6-5.6; ^ePatients who underwent definitive surgery with an evaluable pathology sample for BIPR.

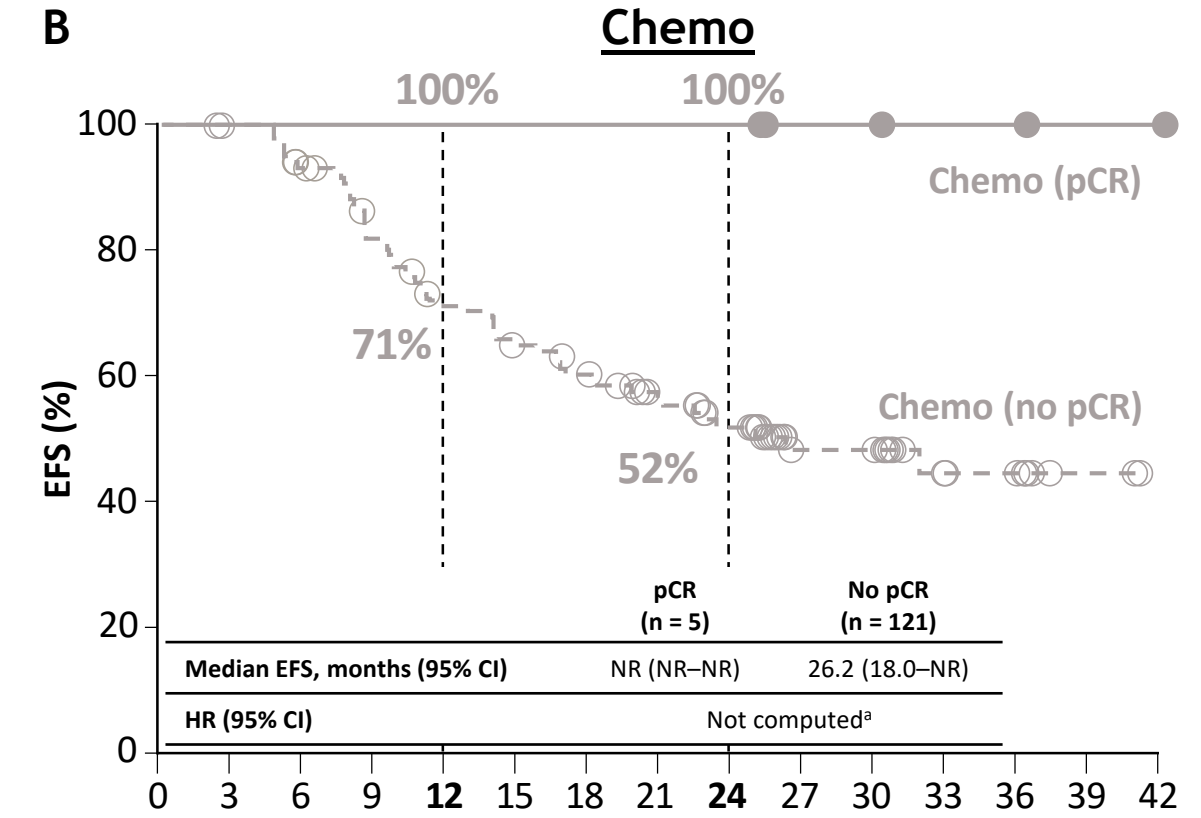
Figure 2. EFS by pCR status (primary tumor) in the path-evaluable patient population



No. at risk

pCR	46	46	43	42	42	42	42	37	34	20	15	7	4	2	0
No pCR	95	92	84	74	68	57	52	45	35	18	16	6	2	1	0

Minimum follow-up: 21 months; median follow-up: 29.5 months.
^aHR was not computed for the chemo arm due to only 5 patients having a pCR.
NR, not reached.

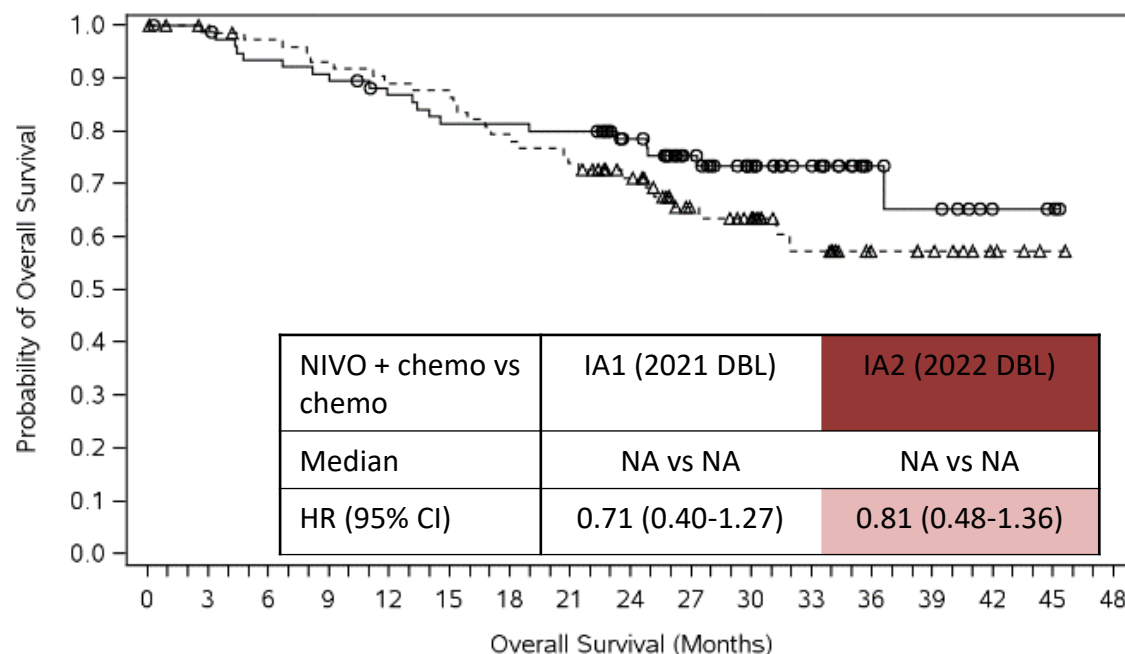


No. at risk

pCR	5	5	5	5	5	5	5	5	5	3	2	2	2	1	0
No pCR	121	119	108	93	79	71	64	53	44	21	20	10	8	2	0

OS by baseline PD-L1 $<1\%$ and $\geq 1\%$ (KM curves are IA1, 2021 DBL)

PD-L1 $<1\%$



Number of Subjects at Risk

Arm C: Nivo + Chemo

78 76 71 69 64 60 60 59 50 39 28 20 10 8 3 2 0

Arm B: Chemo (Conc.)

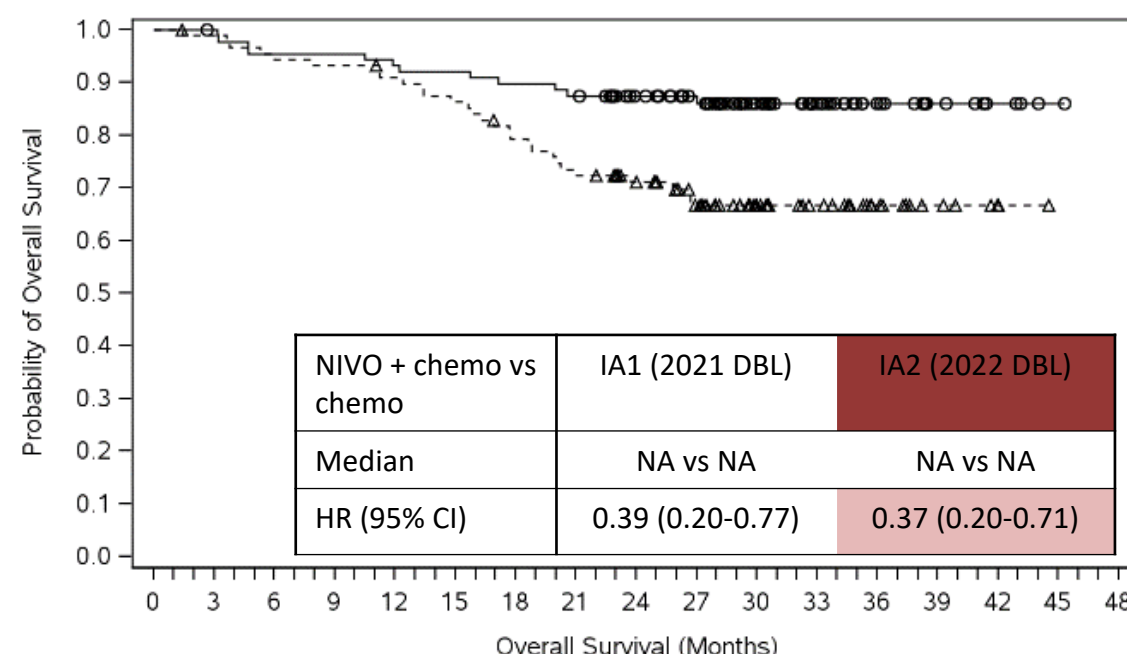
77 74 71 68 65 64 58 54 45 31 26 18 11 9 4 1 0

—○— Arm C: Nivo + Chemo (events: 20/78), median and 95% CI: N.A. (36.60, N.A.)

--△-- Arm B: Chemo (Conc.) (events: 27/77), median and 95% CI: N.A. (31.24, N.A.)

Arm C: Nivo + Chemo vs. Arm B: Chemo (Conc.) HR (95% CI): 0.71 (0.40, 1.27)

PD-L1 $\geq 1\%$



Number of Subjects at Risk

Arm C: Nivo + Chemo

89 88 84 84 82 81 79 77 67 58 40 26 14 8 4 1 0

Arm B: Chemo (Conc.)

89 87 83 82 79 75 68 62 56 44 29 22 12 6 2 0 0

—○— Arm C: Nivo + Chemo (events: 12/89), median and 95% CI: N.A.

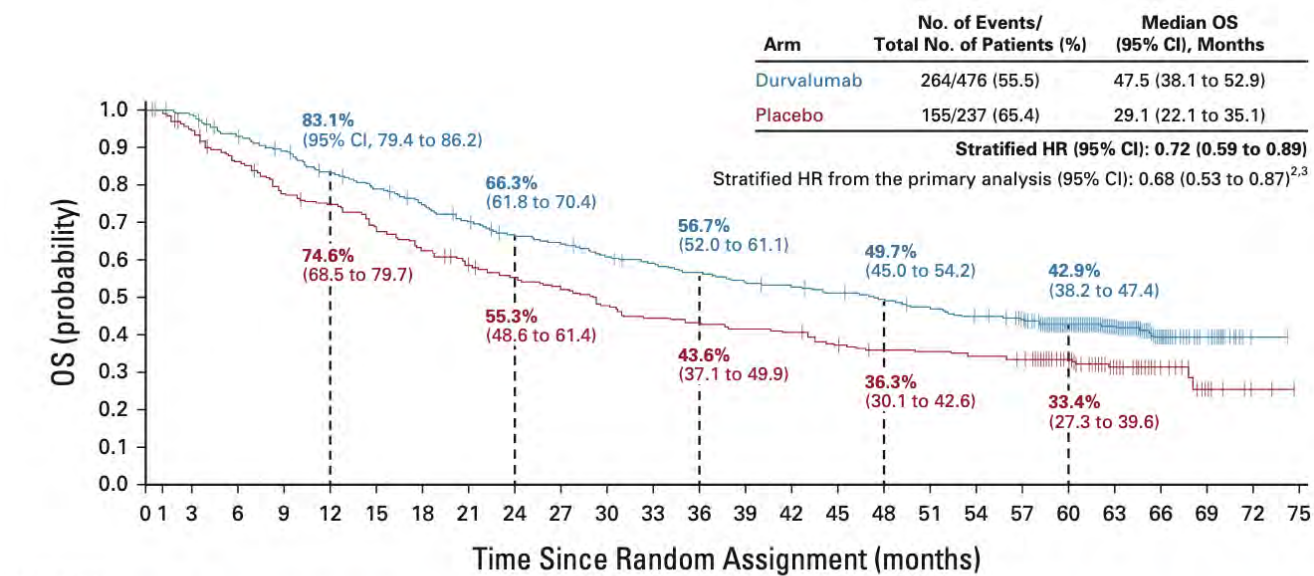
--△-- Arm B: Chemo (Conc.) (events: 28/89), median and 95% CI: N.A.

Arm C: Nivo + Chemo vs. Arm B: Chemo (Conc.) HR (95% CI): 0.39 (0.20, 0.77)

Note: OS KM curves are from IA1 DBL (2021); OS IA2 KM curves are included in the EPAR. Median and HR from IA2 are included in the tables above.

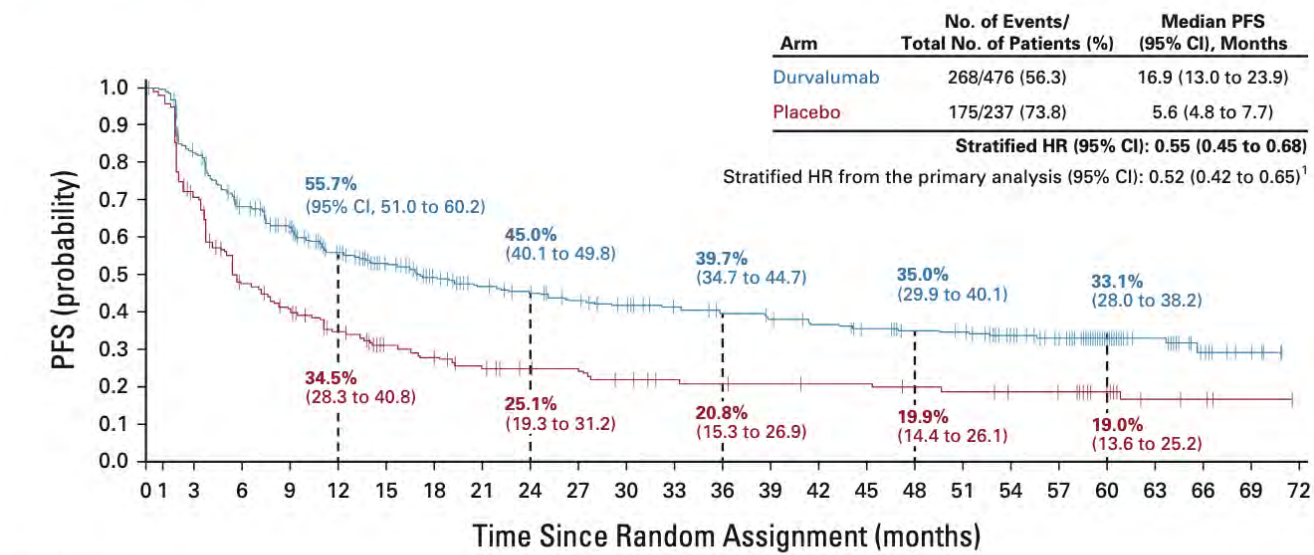
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer

David R. Spigel, MD¹; Corinne Faviere-Finn, MD, PhD²; Jhanelle E. Gray, MD³; David Vicente, MD⁴; David Planchard, MD, PhD⁵; Luis Paz-Ares, MD, PhD⁶; Johan F. Vansteenkiste, MD, PhD⁷; Marina C. Garassino, MD^{8,9}; Rina Hui, PhD¹⁰; Xavier Quantin, MD, PhD¹¹; Andreas Rimner, MD¹²; Yi-Long Wu, MD¹³; Mustafa Özgüroğlu, MD¹⁴; Ki H. Lee, MD¹⁵; Terufumi Kato, MD¹⁶; Maike de Wit, MD, PhD¹⁷; Takayasu Kurata, MD¹⁸; Martin Reck, MD, PhD¹⁹; Byoung C. Cho, MD, PhD²⁰; Suresh Senan, PhD²¹; Jarushka Naidoo, MBBCH, MHS²²; Helen Mann, MSc²³; Michael Newton, PharmD²⁴; Piruntha Thiagarajah, MD²⁵; and Scott J. Antonia, MD, PhD²⁶; on behalf of the PACIFIC Investigators



No. at risk:

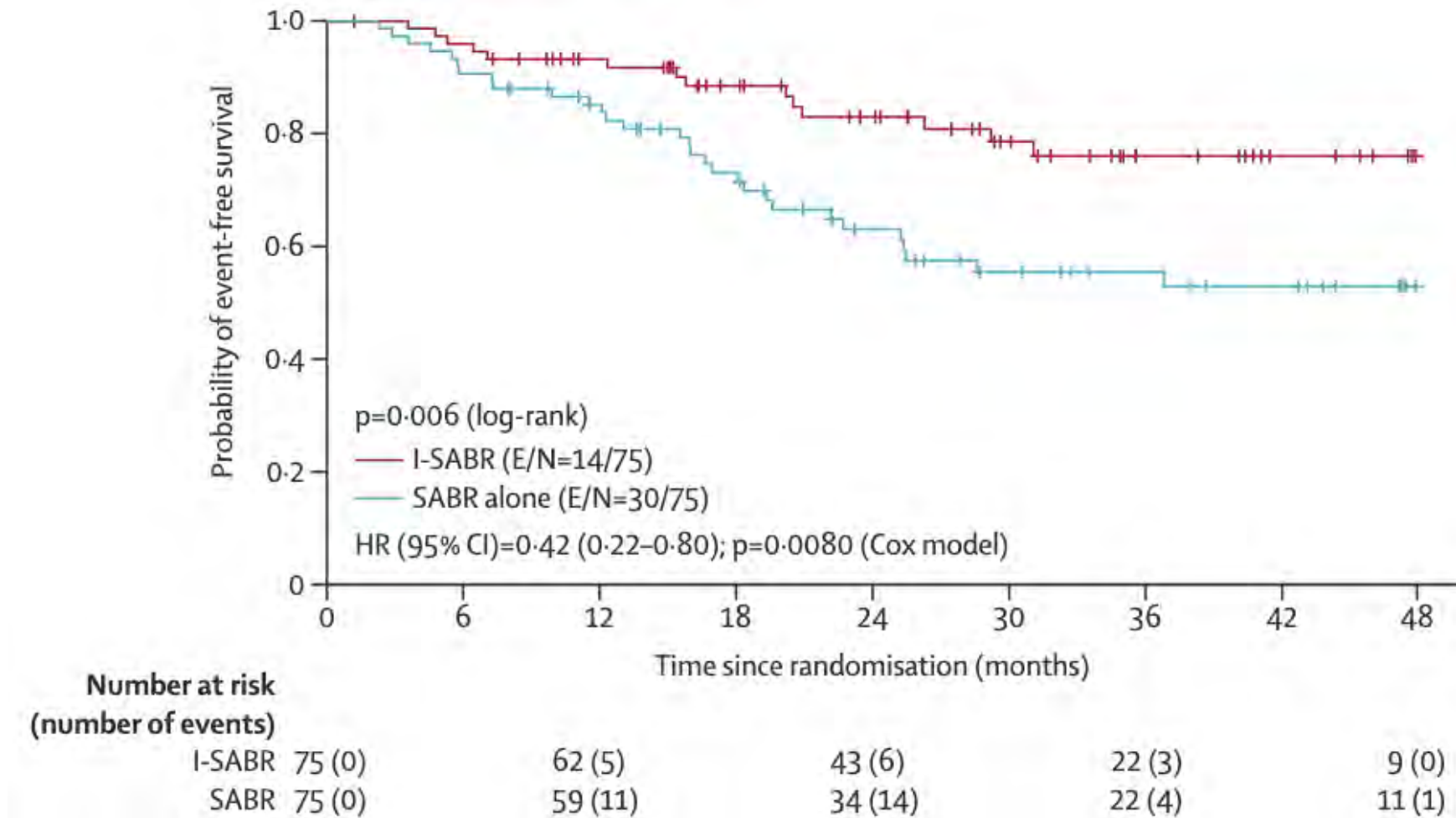
	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0



No. at risk:

	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Durvalumab	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

SBRT +/- nivolumab i 3 måneder



Chang et al. SBRT with or without immunotherapy for early-stage or isolated lung parenchymal recurrent node-negative NSCLC: an open-label, randomised, phase 2 trial. *Lancet* (2023)

**“Palliativ”
systemisk
behandling**



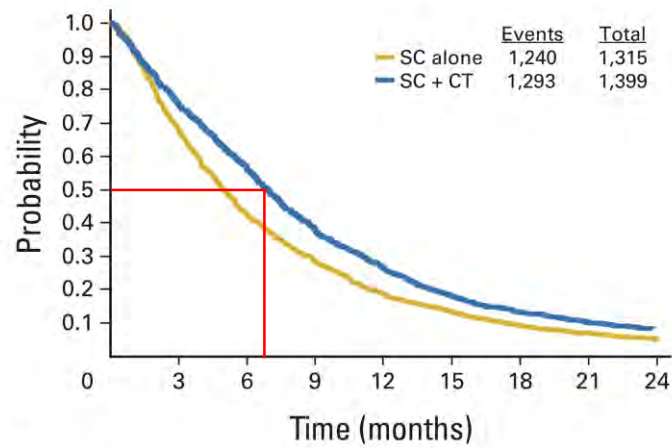
Cytotoxic chemotherapy

- Platinum-doublets are standard
- Cisplatin is preferred for «curative» treatment, carboplatin for «palliative» treatment, but there is probably not much differences
- Pemetrexed is standard for non-squamous NSCLC, maintenance pemetrexed provides a survival benefit of 3-5 months
- Paclitaxel standard for squamous NSCLC in the US, in Europe, gemcitabine was preferred, maintenance therapy not established in this setting
- 2nd line docetaxel monotherapy prolongs survival by 3 months (ORR 10%)

2000

Chemotherapy in Addition to Supportive Care Improves Survival in Advanced Non-Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 16 Randomized Controlled Trials

NSCLC Meta-Analyses Collaborative Group

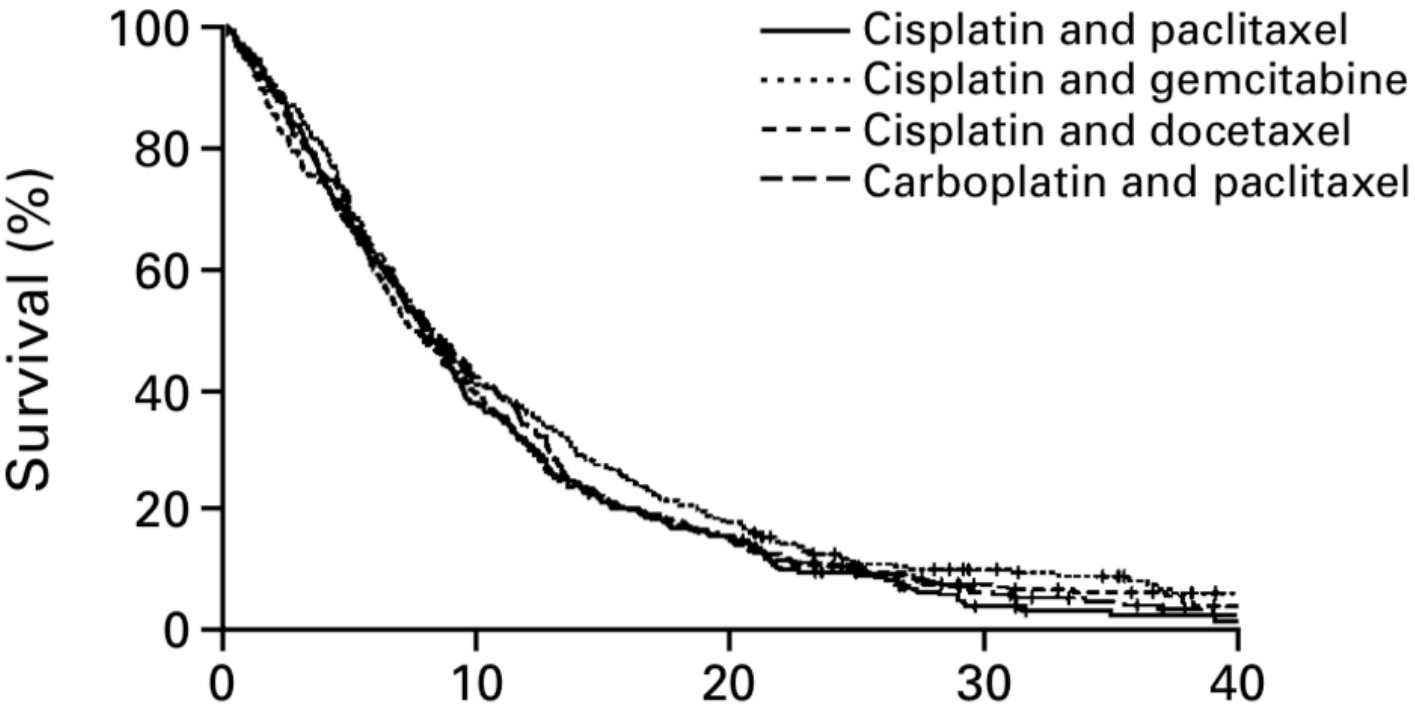


Patients at risk									
SC alone	1,315	884	552	363	231	161	107	77	55
SC + CT	1,399	1,052	779	519	349	233	165	115	91

J Clin Oncol, 2008

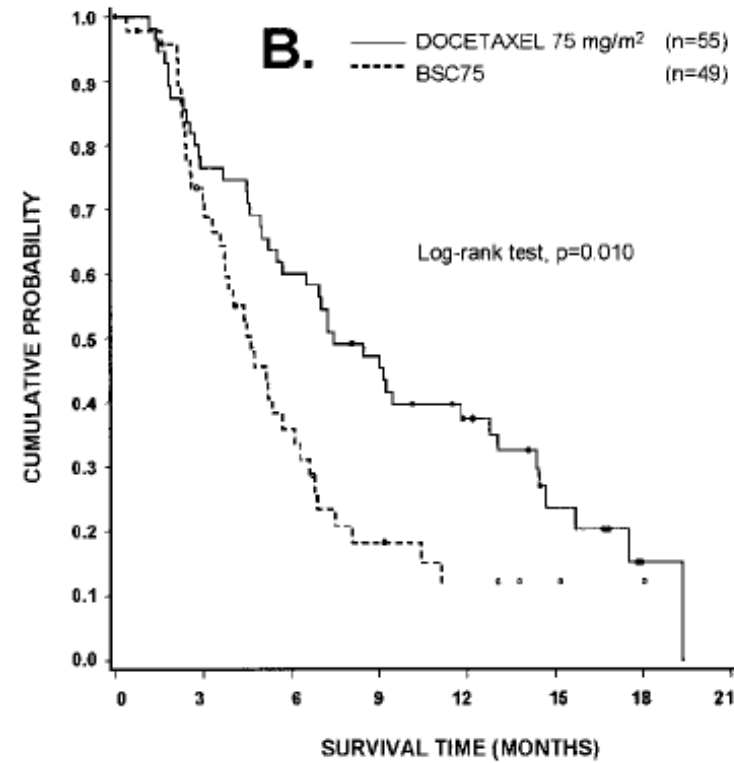
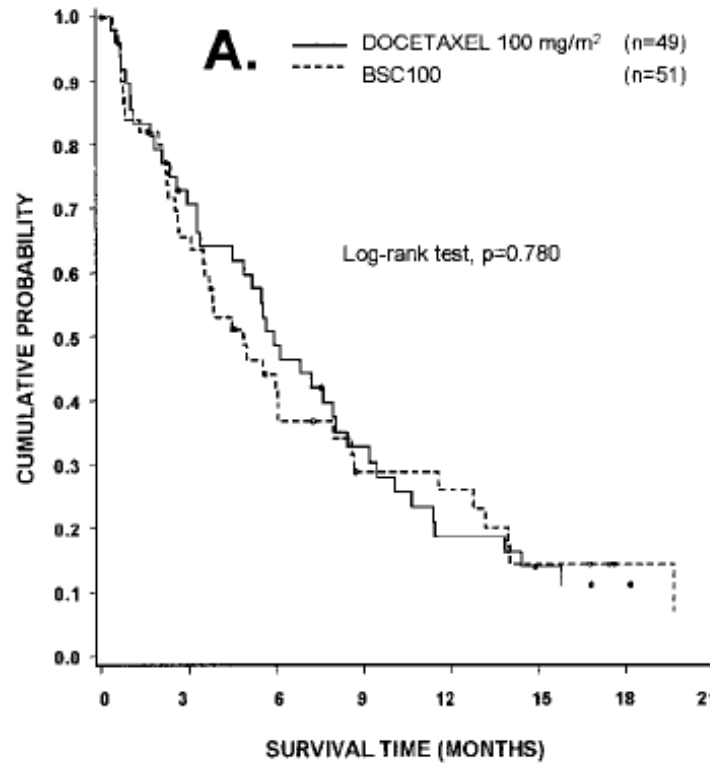
COMPARISON OF FOUR CHEMOTHERAPY REGIMENS FOR ADVANCED
NON-SMALL-CELL LUNG CANCER

JOAN H. SCHILLER, M.D., DAVID HARRINGTON, PH.D., CHANDRA P. BELANI, M.D., COREY LANGER, M.D.,
ALAN SANDLER, M.D., JAMES KROOK, M.D., JUNMING ZHU, PH.D., AND DAVID H. JOHNSON, M.D.,
FOR THE EASTERN COOPERATIVE ONCOLOGY GROUP



Prospective Randomized Trial of Docetaxel Versus Best Supportive Care in Patients With Non-Small-Cell Lung Cancer Previously Treated With Platinum-Based Chemotherapy

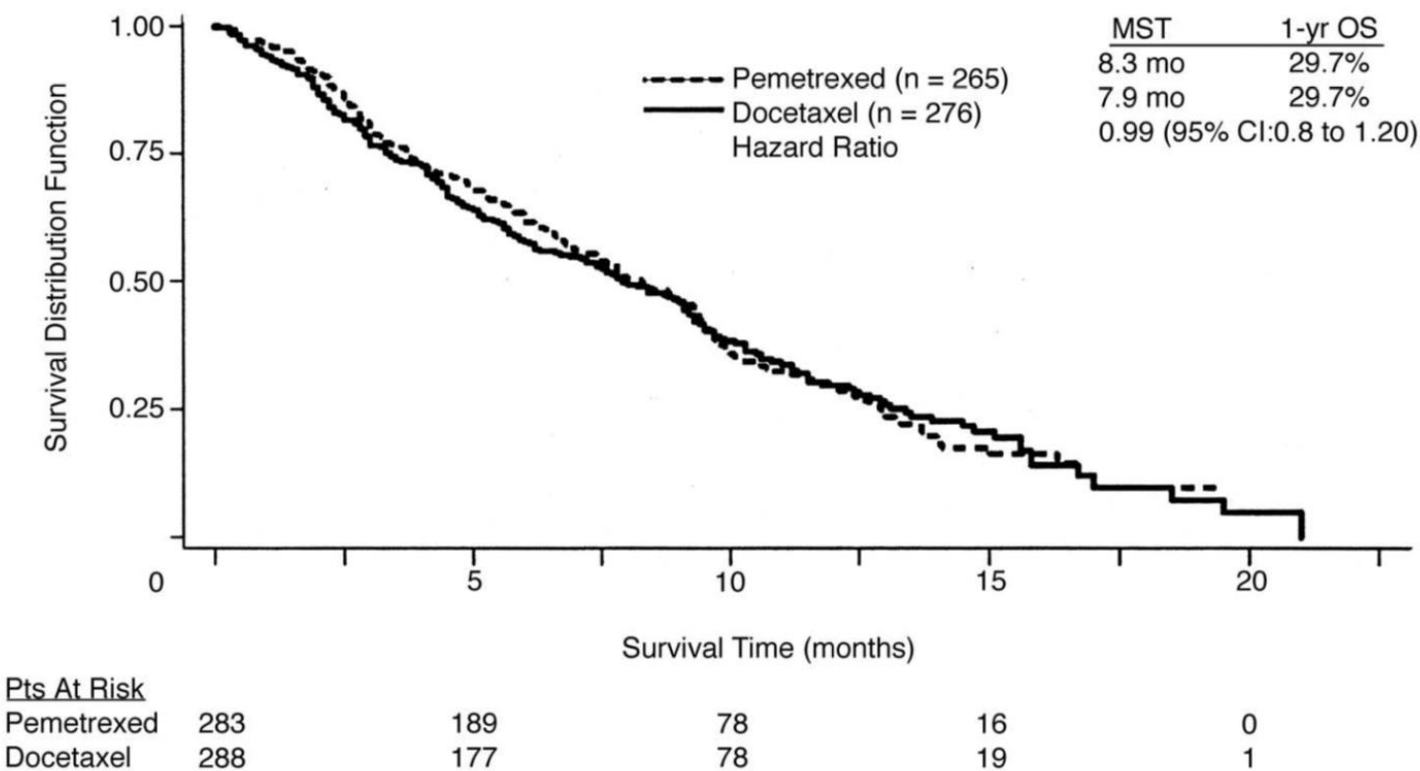
By Frances A. Shepherd, Janet Dancey, Rodryg Ramlau, Karin Mattson, Richard Gralla, Mark O'Rourke, Nathan Levitan, Laurent Gressot, Mark Vincent, Ronald Burkes, Susan Coughlin, Yong Kim, and Jocelyne Berille



NB! Previous taxanes was not allowed in the trial

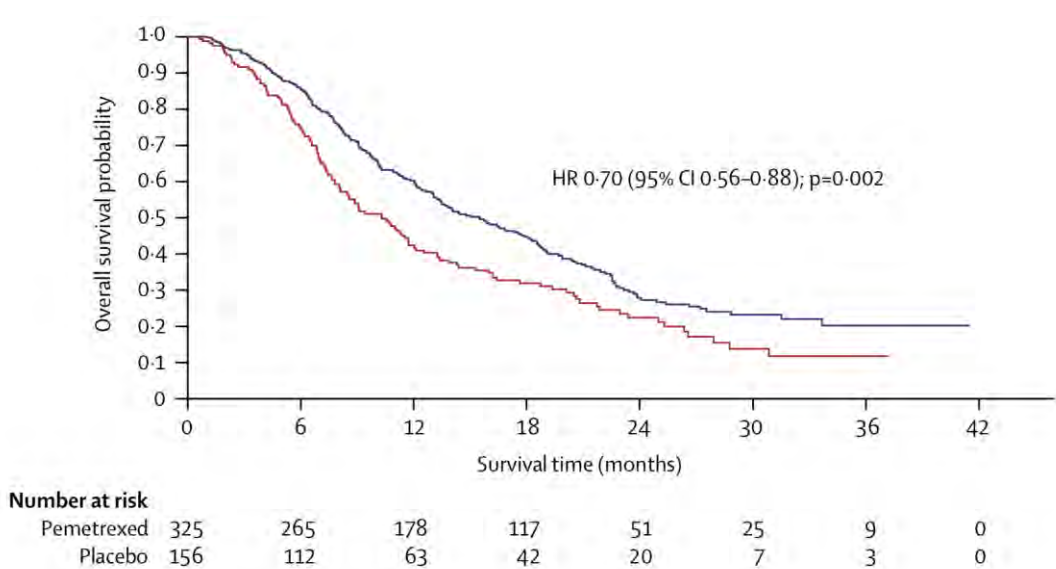
Randomized Phase III Trial of Pemetrexed Versus Docetaxel in Patients With Non–Small-Cell Lung Cancer Previously Treated With Chemotherapy

Nasser Hanna, Frances A. Shepherd, Frank V. Fossella, Jose R. Pereira, Filippo De Marinis, Joachim von Pawel, Ulrich Gatzemeier, Thomas Chang Yao Tsao, Miklos Pless, Thomas Muller, Hong-Liang Lim, Christopher Desch, Klara Szondy, Radj Gervais, Shaharyar, Christian Manegold, Sofia Paul, Paolo Paoletti, Lawrence Einhorn, and Paul A. Bunn Jr.



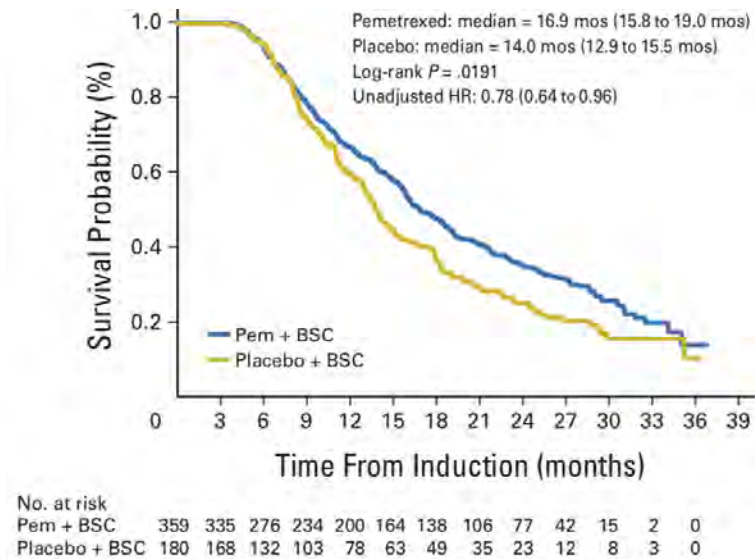
Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: a randomised, double-blind, phase 3 study

Tudor Ciuleanu, Thomas Brodowicz, Christoph Zielinski, Joo Hang Kim, Maciej Krzakowski, Eckart Laack, Yi-Long Wu, Isabel Bover, Stephen Begbie, Valentina Tzekova, Branka Cucevic, Jose Rodrigues Pereira, Sung Hyun Yang, Jayaprakash Madhavan, Katherine P Sugarman, Patrick Peterson, William J John, Kurt Krejcy, Chandra P Belani



PARAMOUNT: Final Overall Survival Results of the Phase III Study of Maintenance Pemetrexed Versus Placebo Immediately After Induction Treatment With Pemetrexed Plus Cisplatin for Advanced Nonsquamous Non–Small-Cell Lung Cancer

Luis G. Paz-Ares, Filippo de Marinis, Mircea Dediu, Michael Thomas, Jean-Louis Pujol, Paolo Bidoli, Olivier Molinier, Tarini Prasad Sahoo, Eckart Laack, Martin Reck, Jesús Corral, Symantha Melemed, William John, Nadia Chouaki, Annamaria H. Zimmermann, Carla Visseren-Gruel, and Cesare Gridelli



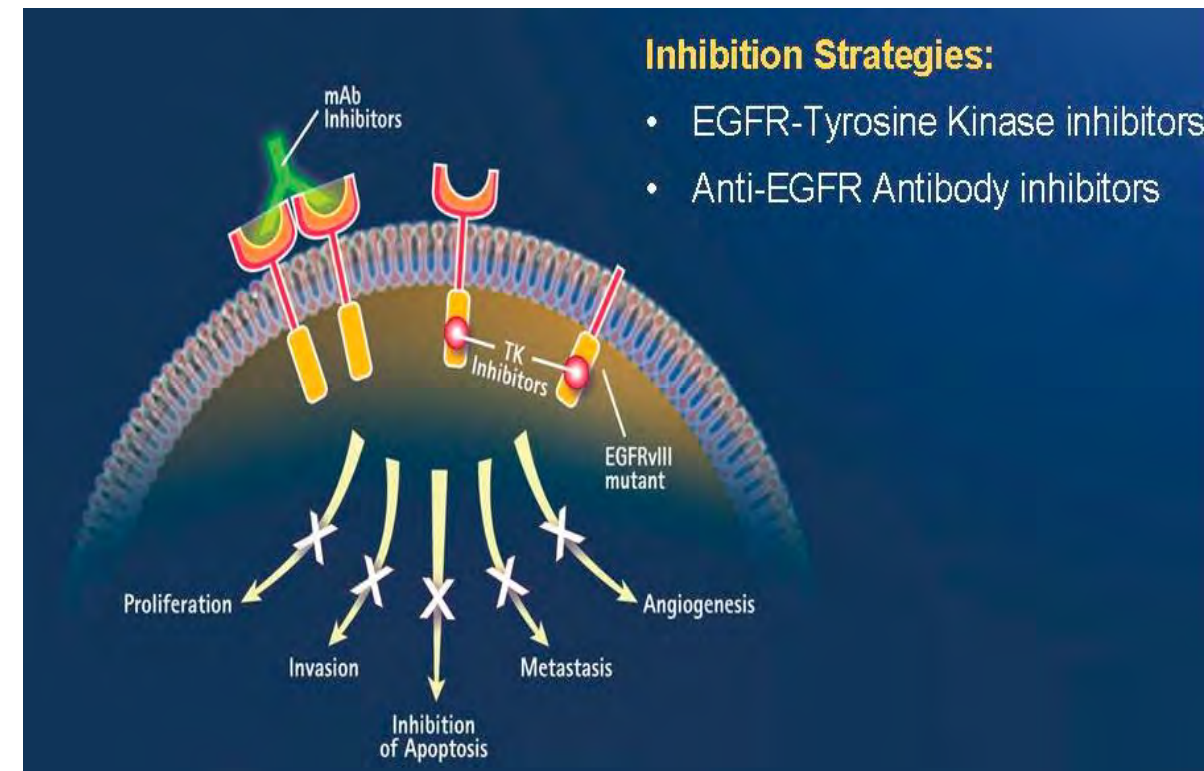
Målrettet behandling





Epidermal Growth Factor Receptor

- EGFR-TKIs blocks the intracellular part of the EGFR
- Ca. 10% of non-squamous NSCLC in the Western world, more common in South-East Asia
- Up to 85% respond



Does it work?

Before treatment



After 3 weeks



- 73 years old man
- Very advanced disease in both lungs and the brain, in need for oxygen supply
- No response to chemotherapy
- Fantastic effect of gefitinib



Frisk med ny kreft-kur

ÅLESUND (VG) For to år siden fikk han dødsdommen: Uhelbredelig lungekreft med spredning til hodet.

Av **FREDDY KONGSBERG**
15. november 2003

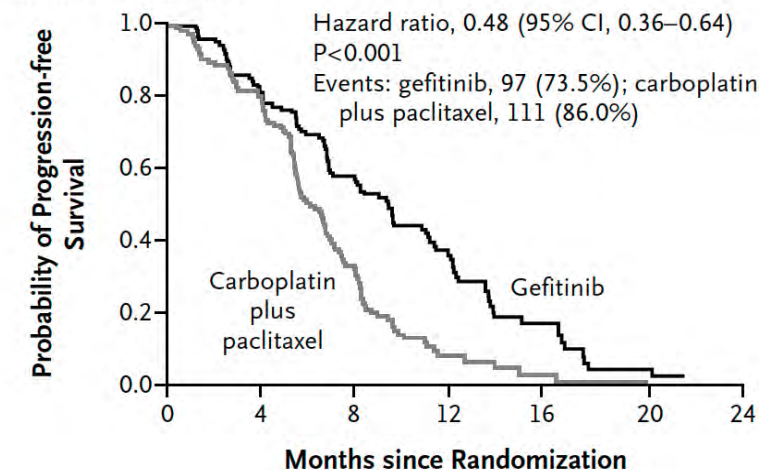


Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma

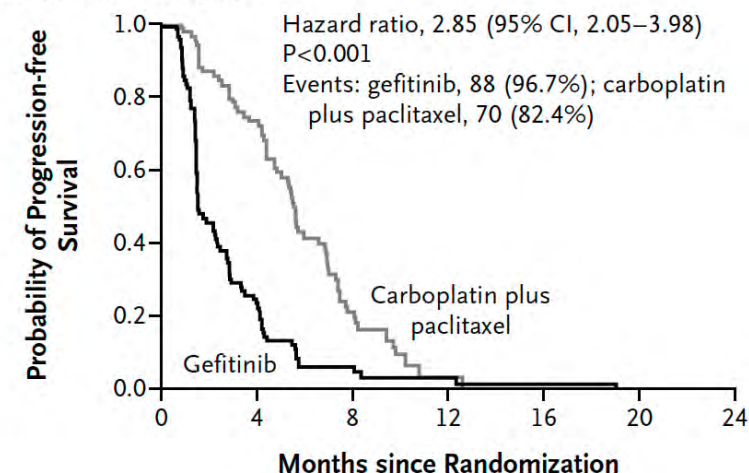
Tony S. Mok, M.D., Yi-Long Wu, M.D., F.A.C.S., Sumitra Thongprasert, M.D., Chih-Hsin Yang, M.D., Ph.D.,
Da-Tong Chu, M.D., Nagahiro Saijo, M.D., Ph.D., Patrapim Sunpaweravong, M.D., Baohui Han, M.D.,
Benjamin Margono, M.D., Ph.D., F.C.C.P., Yukito Ichinose, M.D., Yutaka Nishiwaki, M.D., Ph.D.,
Yuichiro Ohe, M.D., Ph.D., Jin-Ji Yang, M.D., Busyamas Chewaskulyong, M.D., Haiyi Jiang, M.D.,
Emma L. Duffield, M.Sc., Claire L. Watkins, M.Sc., Alison A. Armour, F.R.C.R., and Masahiro Fukuoka, M.D., Ph.D.

- Tidlige studier viste at kvinner, ikke-røykende, sør-øst asiater hadde bedre respons enn andre
- Senere studier viste at det først og fremst er pasienter med EGFR-mutasjoner som responderer
- Nevnte subgrupper har oftere EGFR-mutasjoner
- Alle pasienter med non-squamous histologi testes rutinemessig for EGFR-mutasjoner i Norge
- Tre aktuelle medikament til første-linjes behandling: gefitinib, erlotinib og afatinib

EGFR-Mutation–Positive



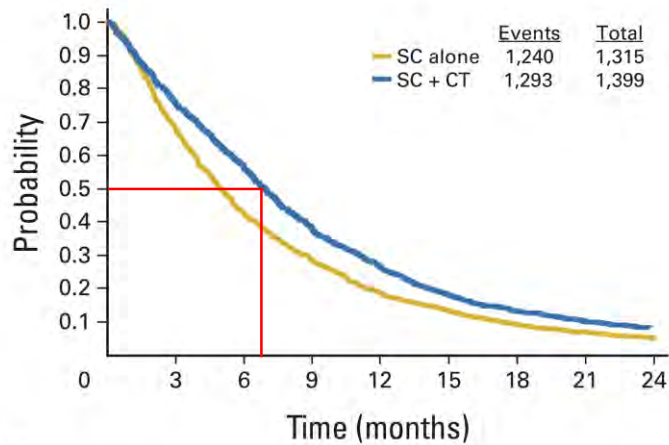
EGFR-Mutation–Negative



2000

Chemotherapy in Addition to Supportive Care Improves Survival in Advanced Non-Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 16 Randomized Controlled Trials

NSCLC Meta-Analyses Collaborative Group



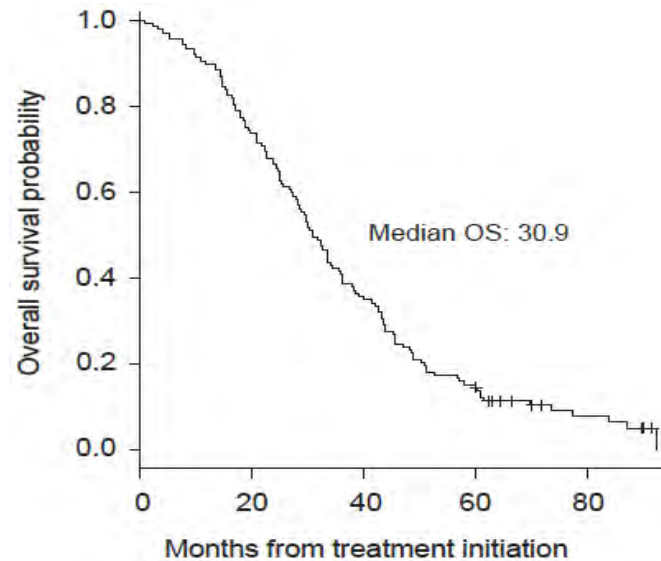
Patients at risk									
SC alone	1,315	884	552	363	231	161	107	77	55
SC + CT	1,399	1,052	779	519	349	233	165	115	91

J Clin Oncol, 2008

2010

Five-Year Survival in *EGFR*-Mutant Metastatic Lung Adenocarcinoma Treated with *EGFR*-TKIs

Jessica J. Lin, MD,^{a,b} Stephanie Cardarella, MD,^{a,c} Christine A. Lydon, BA,^a Suzanne E. Dahlberg, PhD,^d David M. Jackman, MD,^{a,b,e} Pasi A. Jänne, MD, PhD, Bruce E. Johnson, MD^{a,b,e,*}



J Thor Oncol, 2015

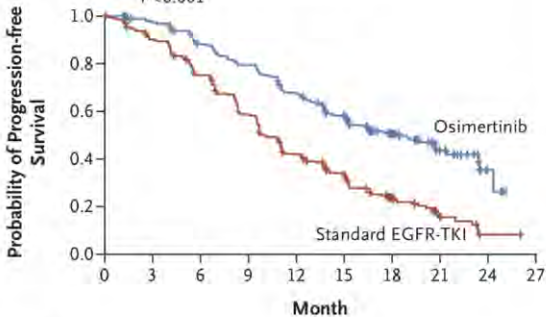
Osimertinib in Untreated EGFR-Mutated Advanced Non-Small-Cell Lung Cancer

J.-C. Soria, Y. Ohe, J. Vansteenkiste, T. Reungwetwattana, B. Chewaskulyong, K.H. Lee, A. Dechaphunkul, F. Imamura, N. Nogami, T. Kurata, I. Okamoto, C. Zhou, B.C. Cho, Y. Cheng, E.K. Cho, P.J. Voon, D. Planchard, W.-C. Su, J.E. Gray, S.-M. Lee, R. Hodge, M. Marotti, Y. Rukazenzov, and S.S. Ramalingam, for the FLAURA Investigators*

A Progression-free Survival in Full Analysis Set

	No. of Patients	Median Progression-free Survival (95% CI) mo
Osimertinib	279	18.9 (15.2–21.4)
Standard EGFR-TKI	277	10.2 (9.6–11.1)

Hazard ratio for disease progression or death, 0.46 (95% CI, 0.37–0.57)
P<0.001

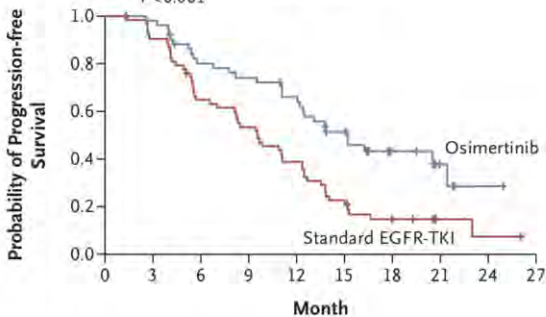


No. at Risk	279	262	233	210	178	139	71	26	4	0
Osimertinib	277	239	197	152	107	78	37	10	2	0
Standard EGFR-TKI										

B Progression-free Survival in Patients with CNS Metastases

	No. of Patients	Median Progression-free Survival (95% CI) mo
Osimertinib	53	15.2 (12.1–21.4)
Standard EGFR-TKI	63	9.6 (7.0–12.4)

Hazard ratio for disease progression or death, 0.47 (95% CI, 0.30–0.74)
P<0.001

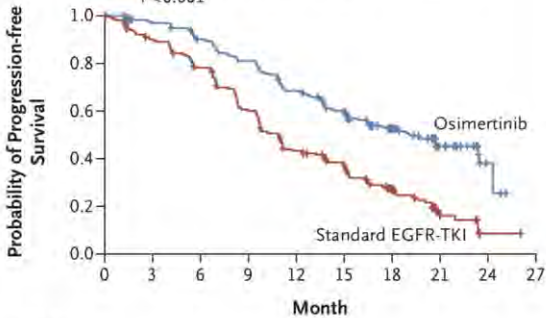


No. at Risk	53	51	40	37	32	22	9	4	1	0
Osimertinib	63	57	40	33	24	13	6	2	1	0
Standard EGFR-TKI										

C Progression-free Survival in Patients without CNS Metastases

	No. of Patients	Median Progression-free Survival (95% CI) mo
Osimertinib	226	19.1 (15.2–23.5)
Standard EGFR-TKI	214	10.9 (9.6–12.3)

Hazard ratio for disease progression or death, 0.46 (95% CI, 0.36–0.59)
P<0.001

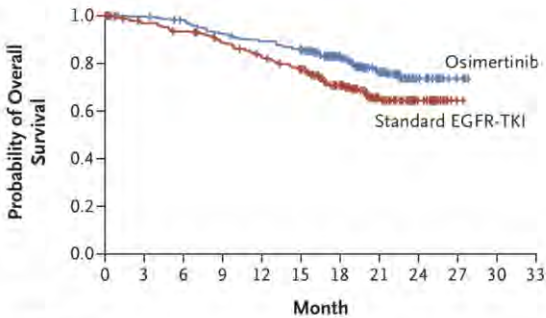


No. at Risk	226	211	193	173	146	117	62	22	3	0
Osimertinib	214	182	157	119	83	65	31	8	1	0
Standard EGFR-TKI										

D Overall Survival

	No. of Patients	Median Overall Survival (95% CI) mo
Osimertinib	279	NC (NC–NC)
Standard EGFR-TKI	277	NC (NC–NC)

Hazard ratio for death, 0.63 (95% CI, 0.45–0.88)
P=0.007

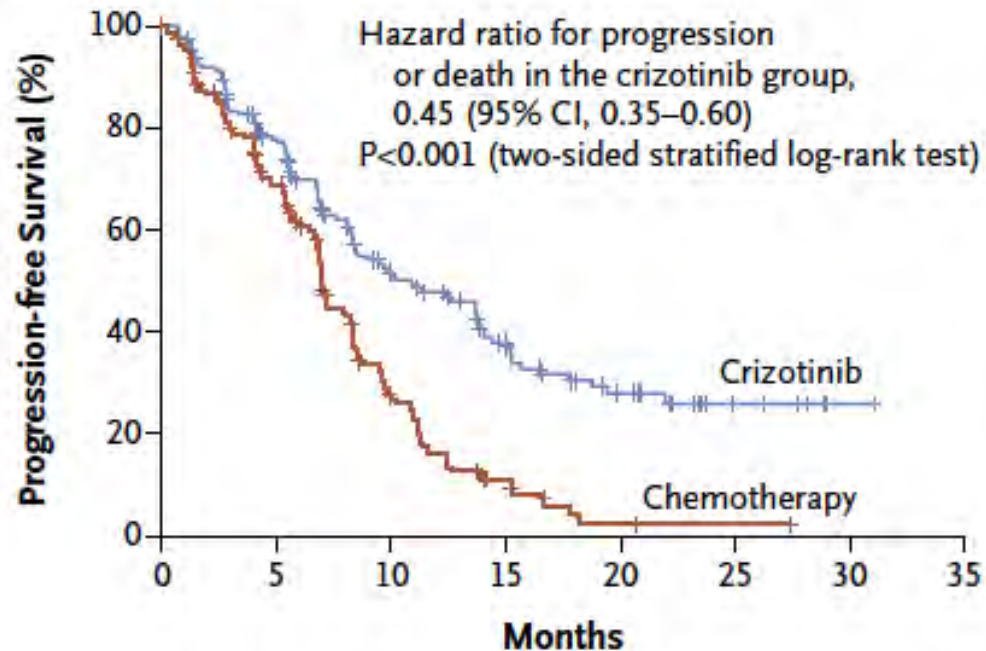


No. at Risk	279	276	269	253	243	232	154	87	29	4	0	0
Osimertinib	277	263	252	237	218	200	126	64	24	1	0	0
Standard EGFR-TKI												

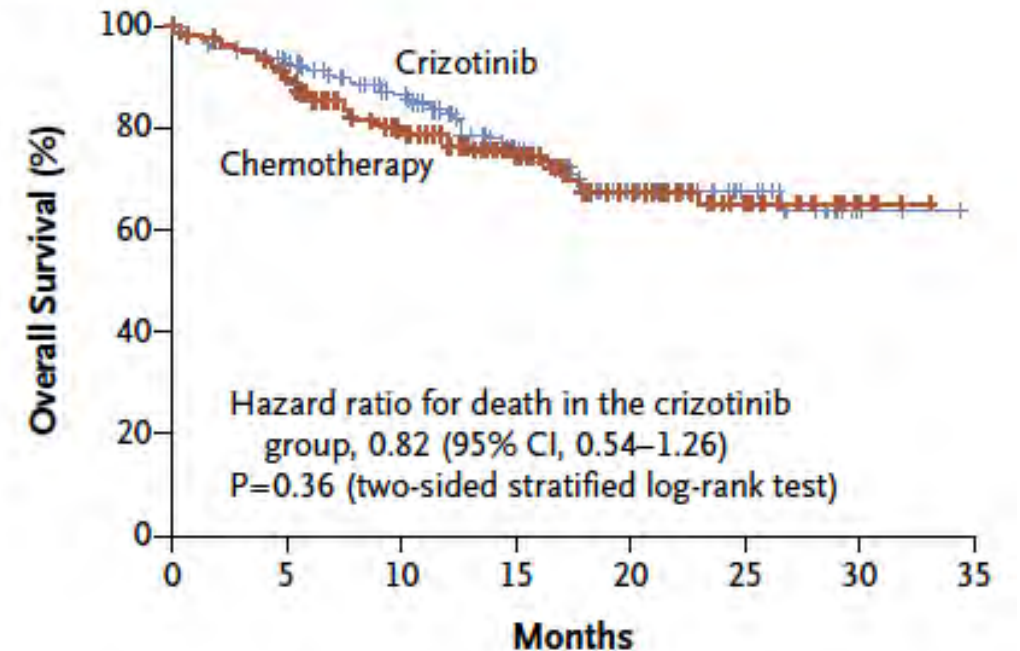
First-Line Crizotinib versus Chemotherapy in ALK-Positive Lung Cancer

Benjamin J. Solomon, M.B., B.S., Ph.D., Tony Mok, M.D.,
Dong-Wan Kim, M.D., Ph.D., Yi-Long Wu, M.D.,
Kazuhiko Nakagawa, M.D., Ph.D., Tarek Mekhail, M.D.,
Enriqueta Felip, M.D., Ph.D., Federico Cappuzzo, M.D., Jolanda Paolini, B.Sc.,
Tiziana Usari, B.Sc., Shrividya Iyer, Ph.D., Arlene Reisman, M.P.H.,
Keith D. Wilner, Ph.D., Jennifer Tursi, M.Sc., and Fiona Blackhall, M.D., Ph.D.,
for the PROFILE 1014 Investigators*

A Progression-free Survival

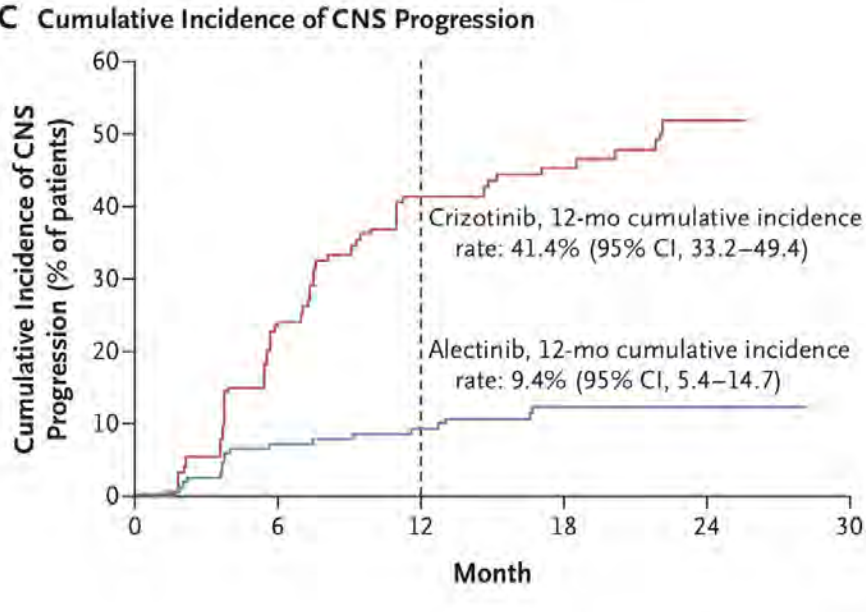


B Overall Survival



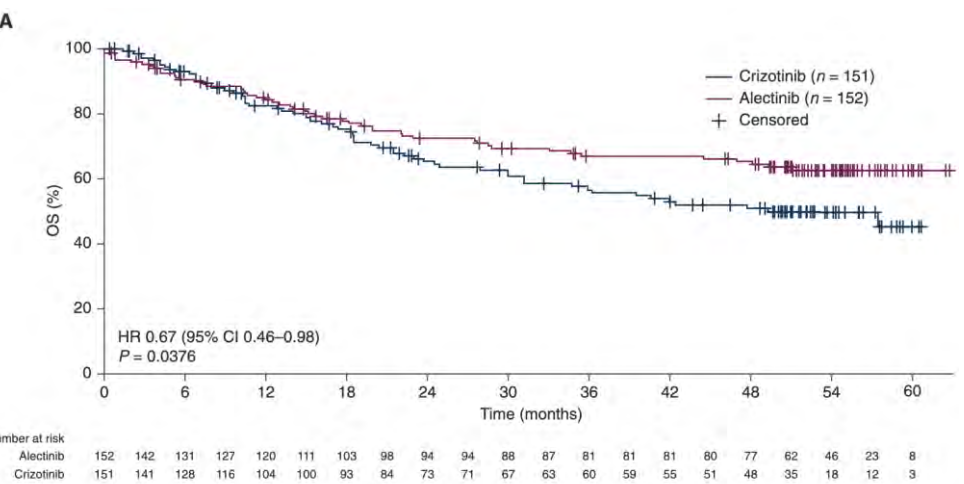
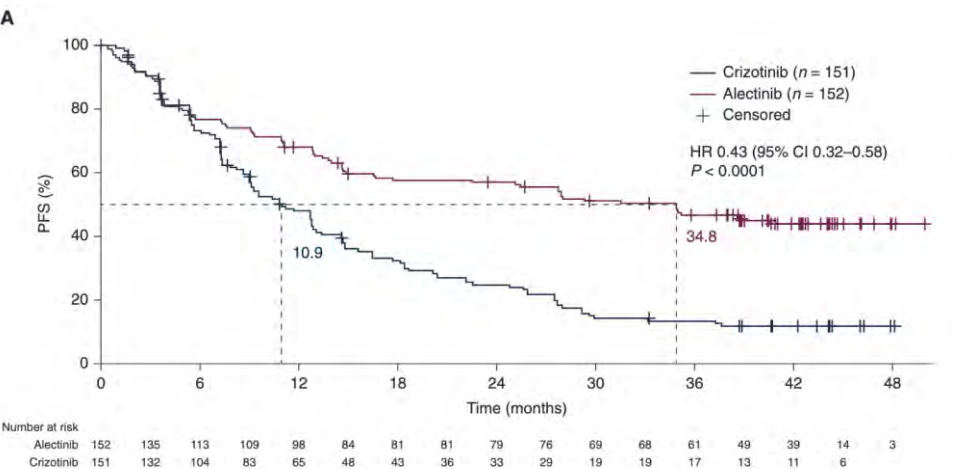
Alectinib versus Crizotinib in Untreated ALK-Positive Non-Small-Cell Lung Cancer

Solange Peters, M.D., Ph.D., D. Ross Camidge, M.D., Ph.D., Alice T. Shaw, M.D., Ph.D., Shirish Gadgeel, M.D., Jin S. Ahn, M.D., Dong-Wan Kim, M.D., Ph.D., Sai-Hong I. Ou, M.D., Ph.D., Maurice Pérol, M.D., Rafal Dziadziuszko, M.D., Rafael Rosell, M.D., Ph.D., Ali Zeaiter, M.D., Emmanuel Mitry, M.D., Ph.D., Sophie Golding, M.Sc., Bogdana Balas, M.D., Johannes Noe, Ph.D., Peter N. Morcos, Pharm.D., and Tony Mok, M.D., for the ALEX Trial Investigators*



Updated overall survival and final progression-free survival data for patients with treatment-naïve advanced ALK-positive non-small-cell lung cancer in the ALEX study

T. Mok¹, D. R. Camidge², S. M. Gadgeel³, R. Rosell⁴, R. Dziadziuszko⁵, D.-W. Kim⁶, M. Pérol⁷, S.-H. I. Ou⁸, J. S. Ahn⁹, A. T. Shaw^{10†}, W. Bordogna¹¹, V. Smoljanovic¹¹, M. Hilton¹¹, T. Ruf¹¹, J. Noé¹¹ & S. Peters^{12*}

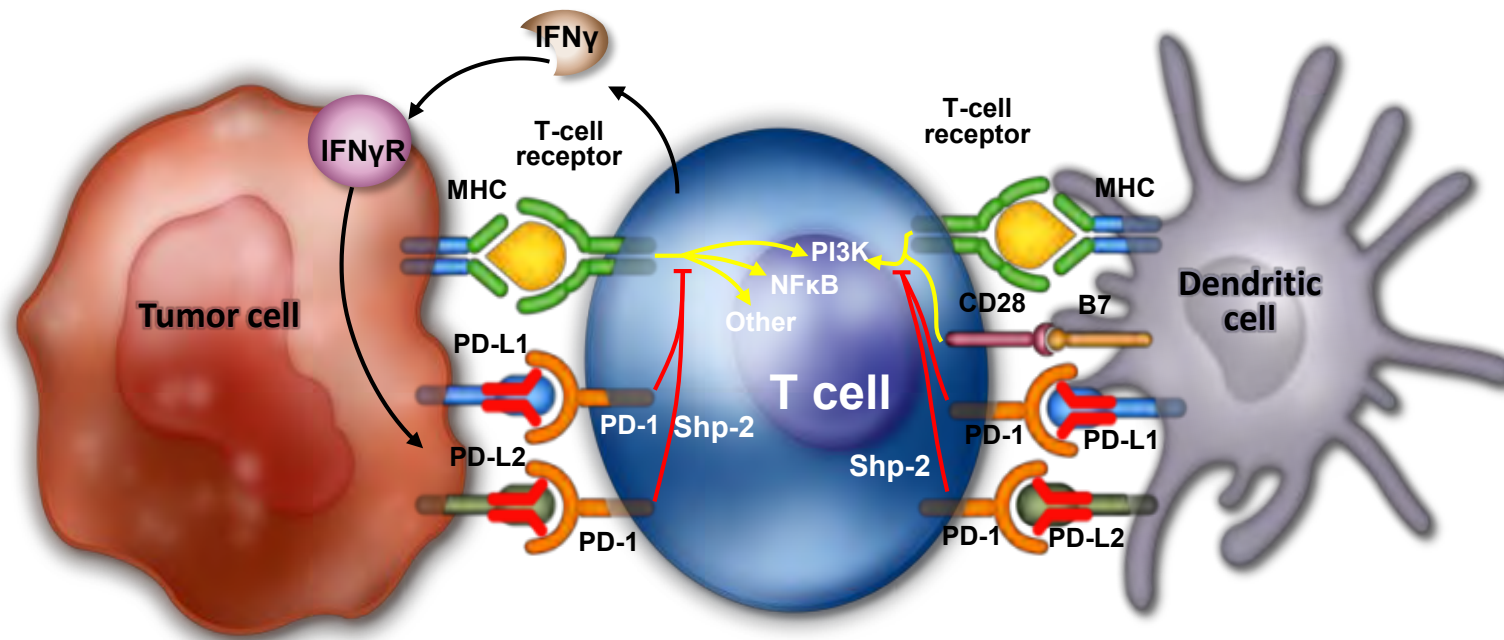


Targeted therapies for NSCLC

Target	Dokumented effect	Approved	Reimbursed in Norway	Available in Norway
EGFR	+	+	+	
EGFR exon 20	+	+	(-)	
ROS1	+	+	+	
ALK	+	+	+	
BRAF	+	+	+	
RET	+	+	+	
MET	+	+	-	+
KRAS G12C	+	+	-	+
NTRK	+	+	+	

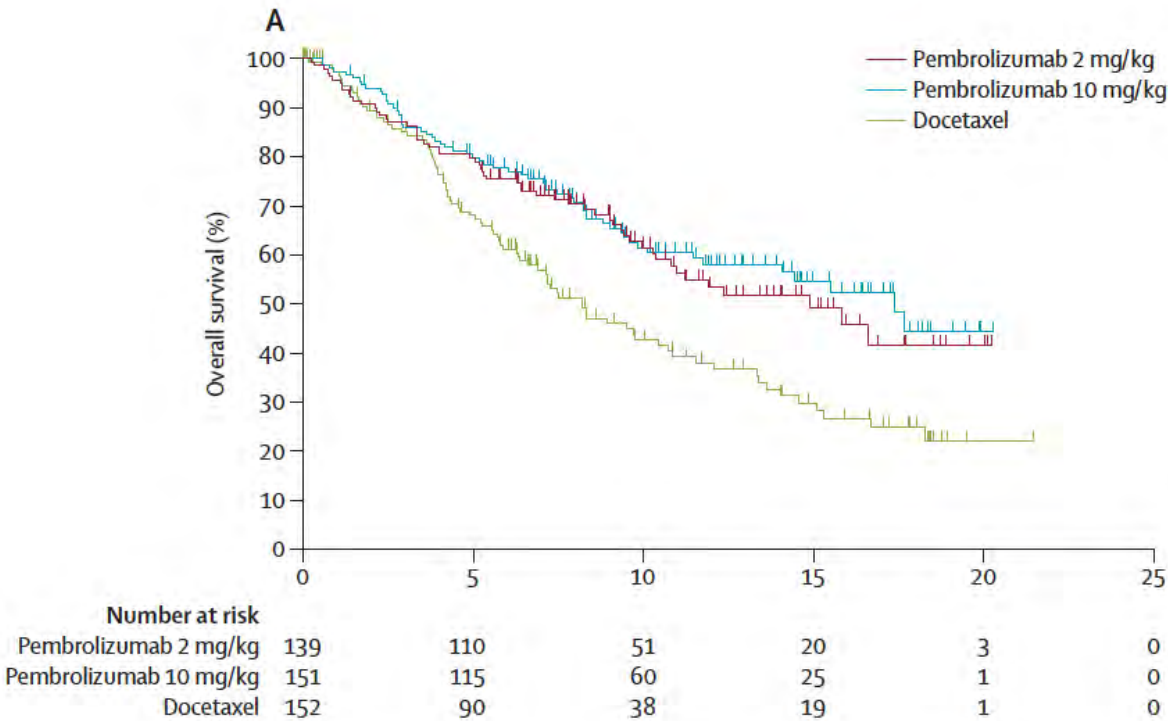
Immunterapi

- PD-1 (Programmed Cell Death-1) is expressed on the surface of T-cells
- PD-L1 is expressed on tumor cells
- PD1/PD-L1 inhibitors bind to PD-1 on T-cells and interrupts inhibitory signal and re-establishes the anti-tumor effect of T-cells

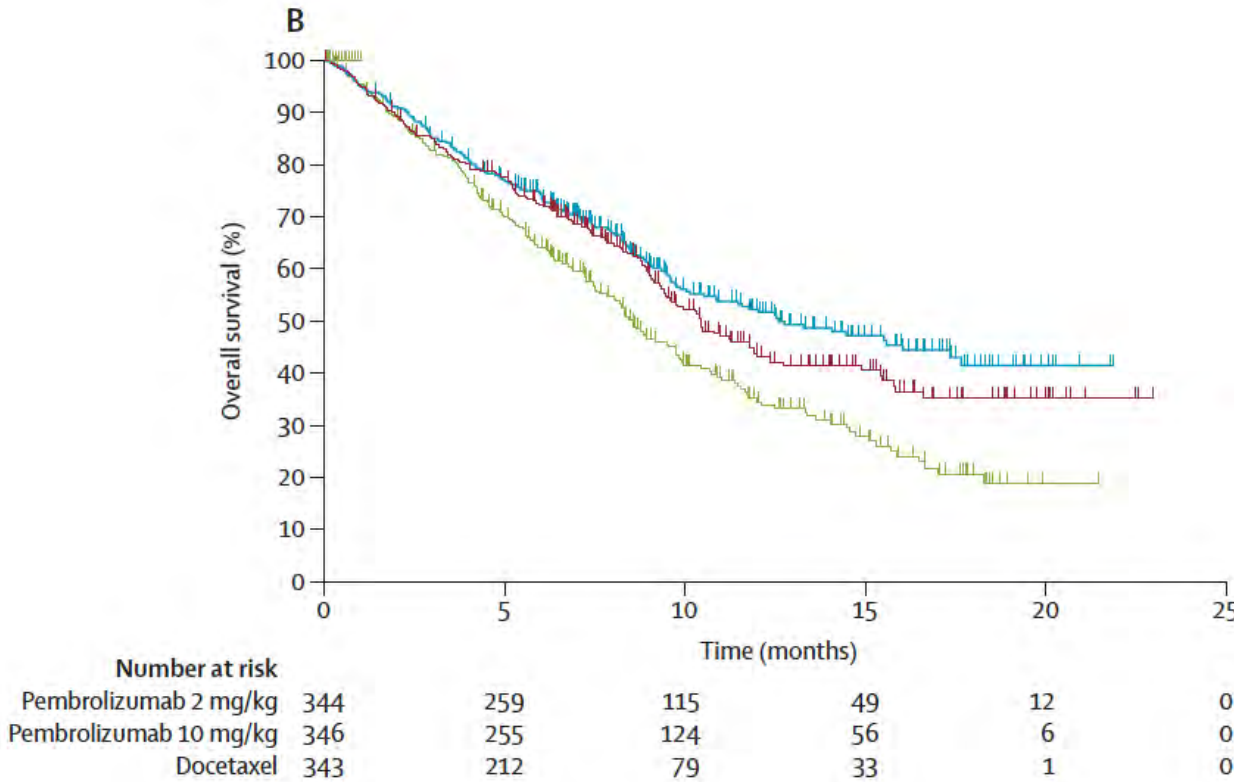


Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial

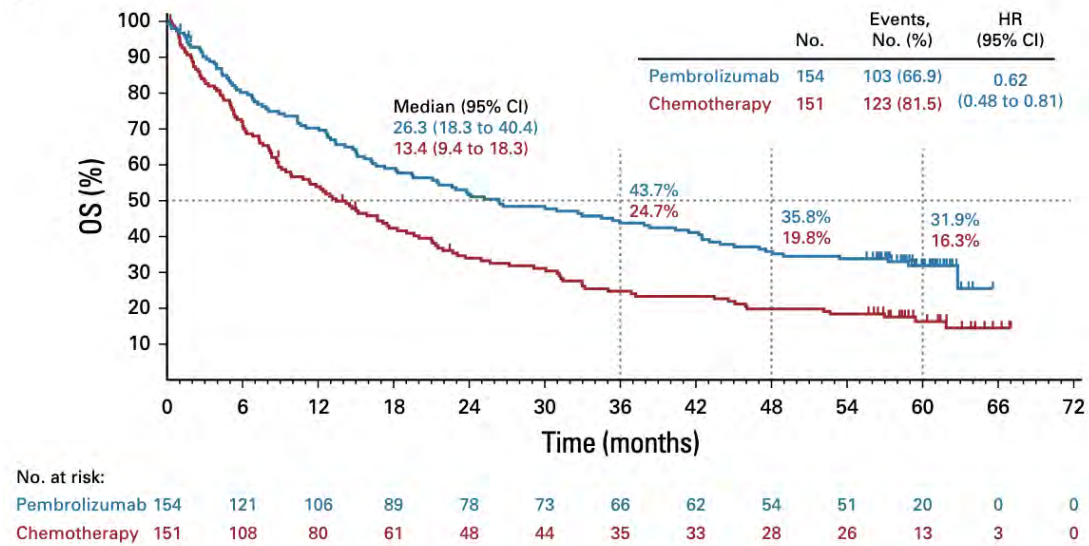
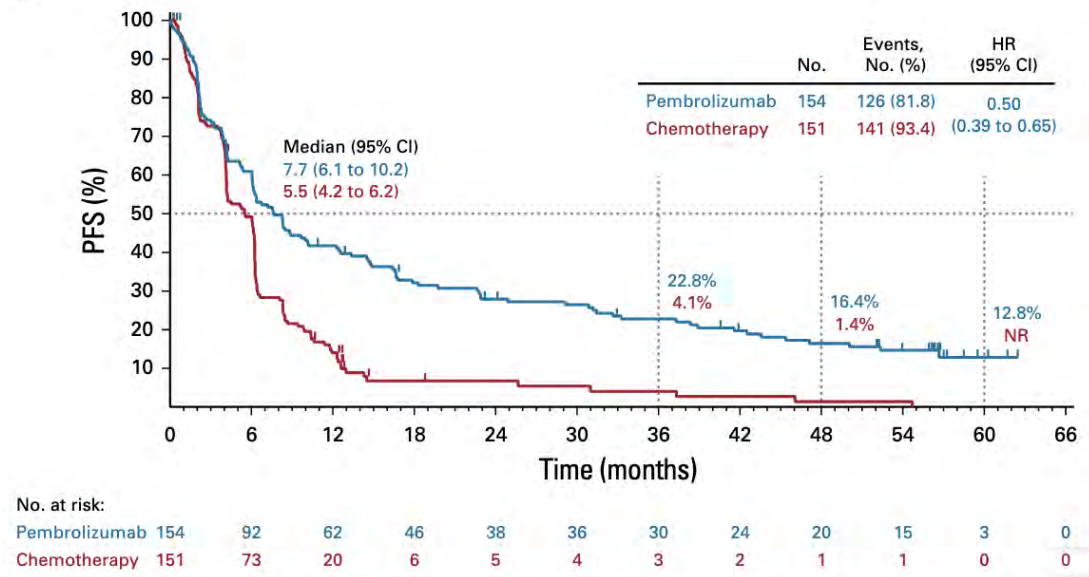
Roy S Herbst, Paul Baas, Dong-Wan Kim, Enriqueta Felip, José L Pérez-Gracia, Ji-Youn Han, Julian Molina, Joo-Hang Kim, Catherine Dubos Arvis, Myung-Ju Ahn, Margarita Majem, Mary J Fidler, Gilberto de Castro Jr, Marcelo Garrido, Gregory M Lubiniecki, Yue Shentu, Ellie Im, Marisa Dollé-Filhart, Edward B Garon



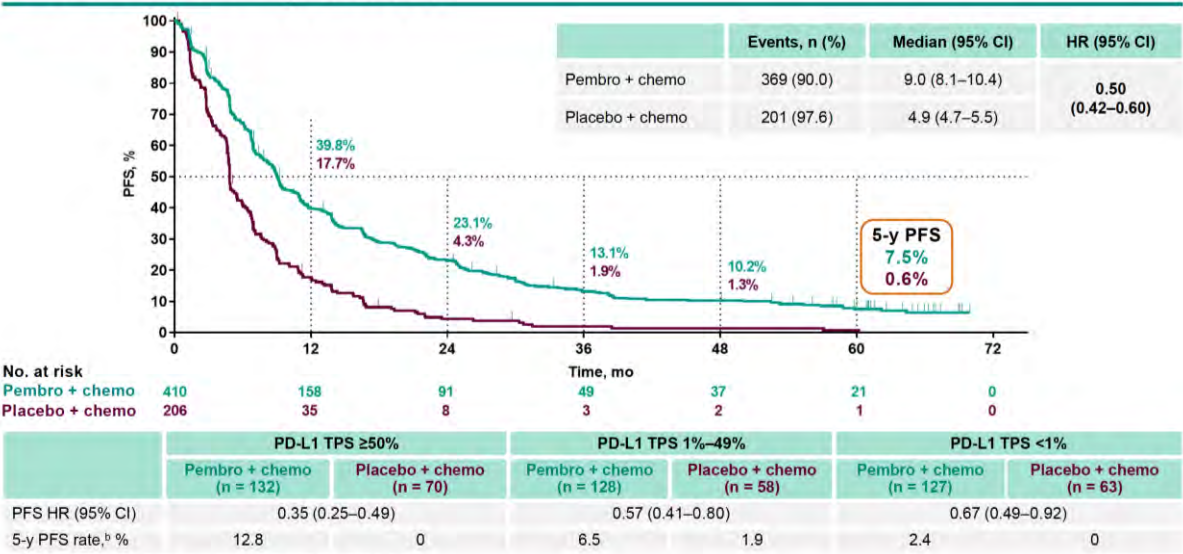
50-100% PD-L1 positive



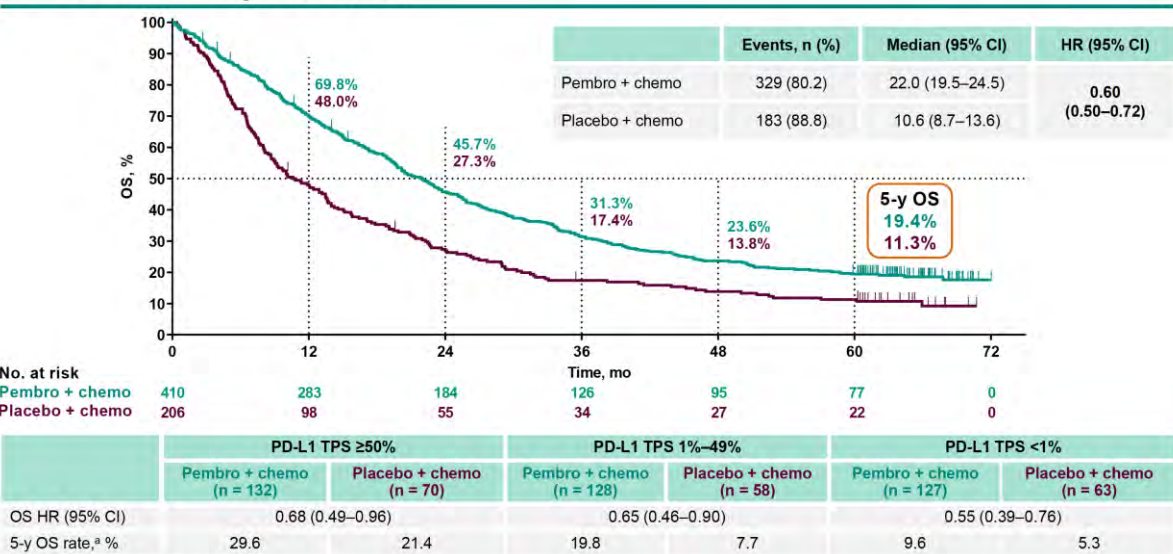
Alle pasienter

A**B**

PFS^a: ITT Population



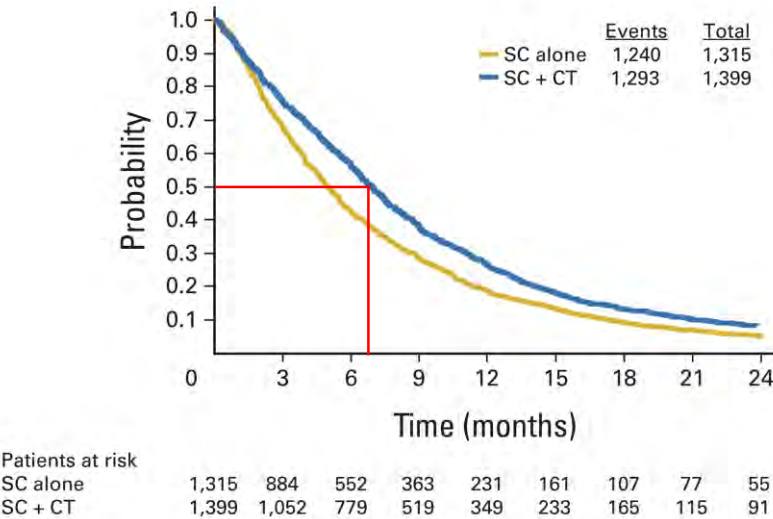
OS: ITT Population



2000

Chemotherapy in Addition to Supportive Care Improves Survival in Advanced Non–Small-Cell Lung Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 16 Randomized Controlled Trials

NSCLC Meta-Analyses Collaborative Group

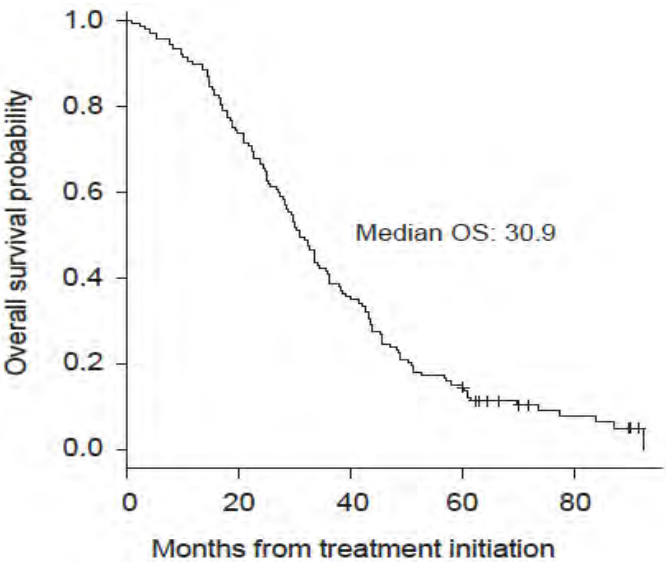


J Clin Oncol, 2008

2010

Five-Year Survival in EGFR-Mutant Metastatic Lung Adenocarcinoma Treated with EGFR-TKIs

Jessica J. Lin, MD,^{a,b} Stephanie Cardarella, MD,^{a,c} Christine A. Lydon, BA,^a Suzanne E. Dahlberg, PhD,^d David M. Jackman, MD,^{a,b,e} Pasi A. Jänne, MD, PhD, Bruce E. Johnson, MD^{a,b,e,*}

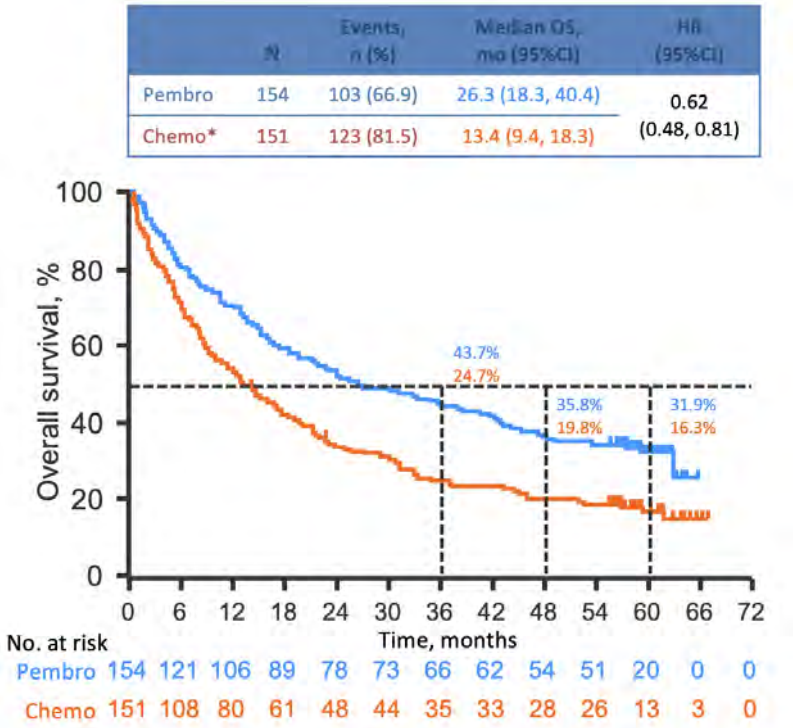


J Thor Oncol, 2015

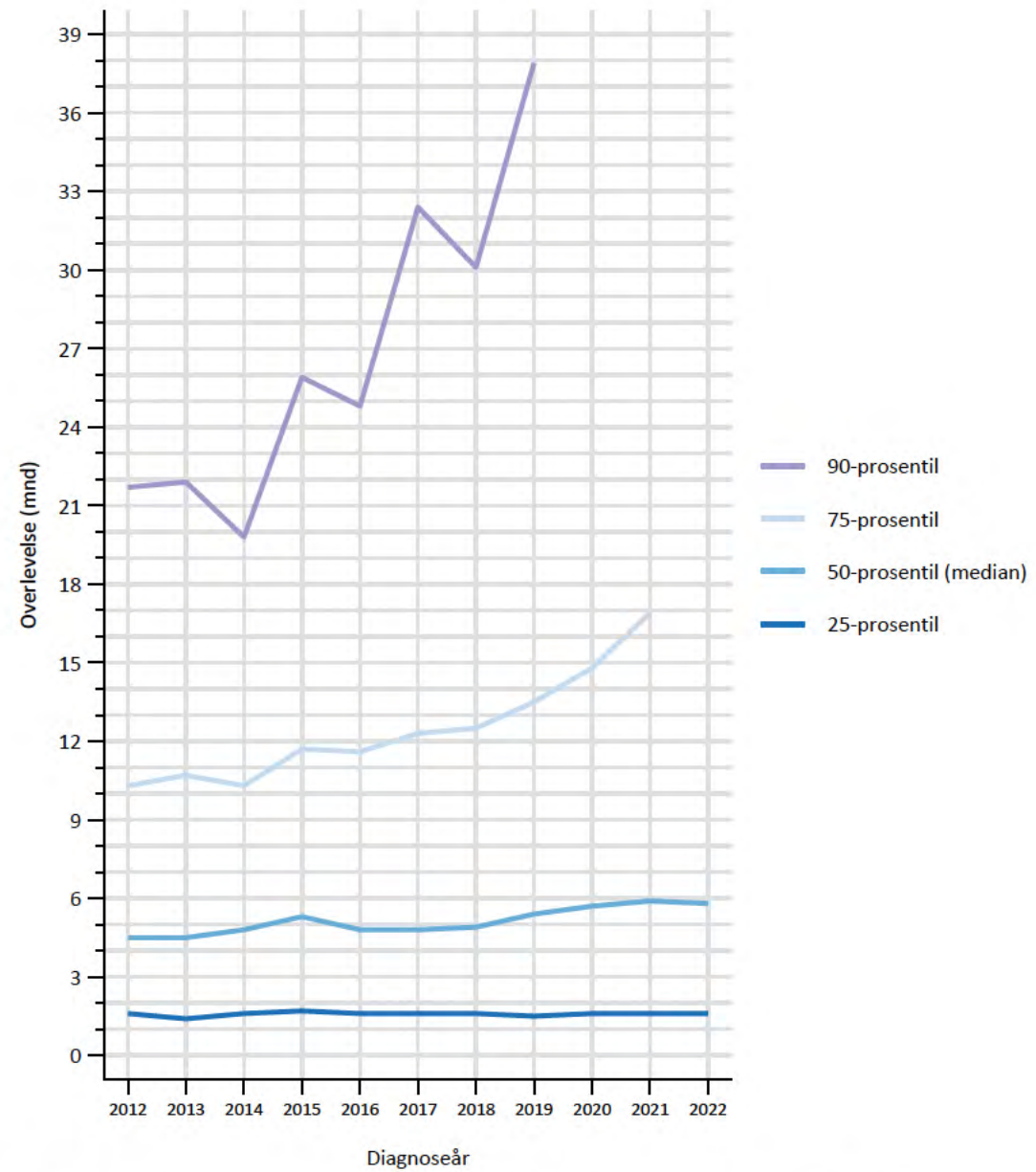
2020

Five-Year Outcomes With Pembrolizumab Versus Chemotherapy for Metastatic Non–Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ≥ 50%

Martin Reck, MD, PhD¹; Delays Rodriguez-Abreu, MD, PhD²; Andrew G. Robinson, MD, MSc³; Rina Hui, MBBS, PhD⁴; Tibor Csösz, MD⁵; Andrea Fülop, MD⁶; Maya Gottfried, MD⁷; Nir Peled, MD, PhD⁸; Ali Tafreshi, MD⁹; Sinead Cuffe, MD¹⁰; Mary O'Brien, MD¹¹; Suman Rao, MD¹²; Katsuyuki Hotta, MD, PhD, MPH¹³; Ticiania A. Leal, MD¹⁴; Jonathan W. Riess, MD, MS¹⁵; Erin Jensen, MS¹⁶; Bin Zhao, MD, PhD¹⁶; M. Catherine Pietanza, MD¹⁶; and Julie R. Brahmer, MD¹⁷

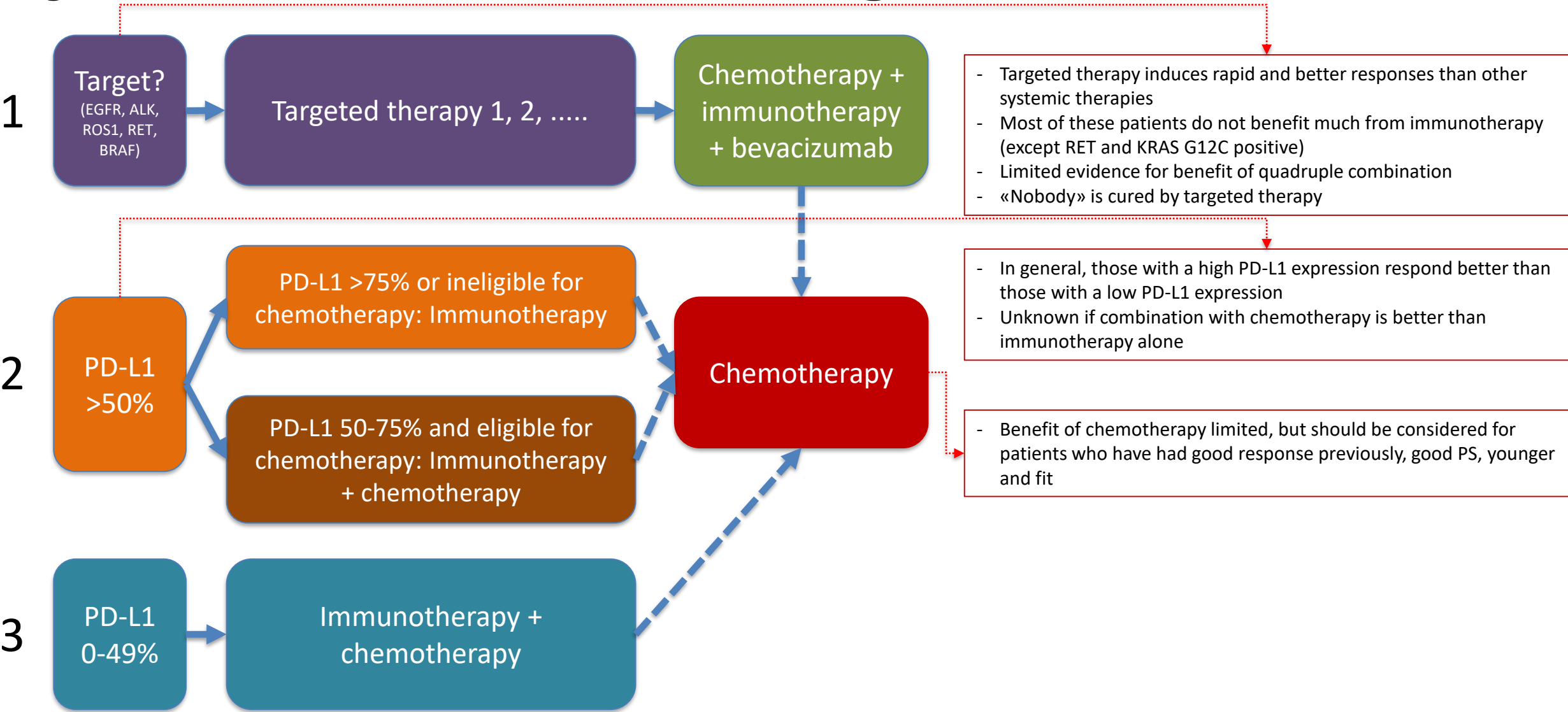


J Clin Oncol, 2021



Figur 3.34: Totaloverlevelse for pasienter med lungekreft i stadium IV, 2012–2022

Systemic treatment for stage IV NSCLC



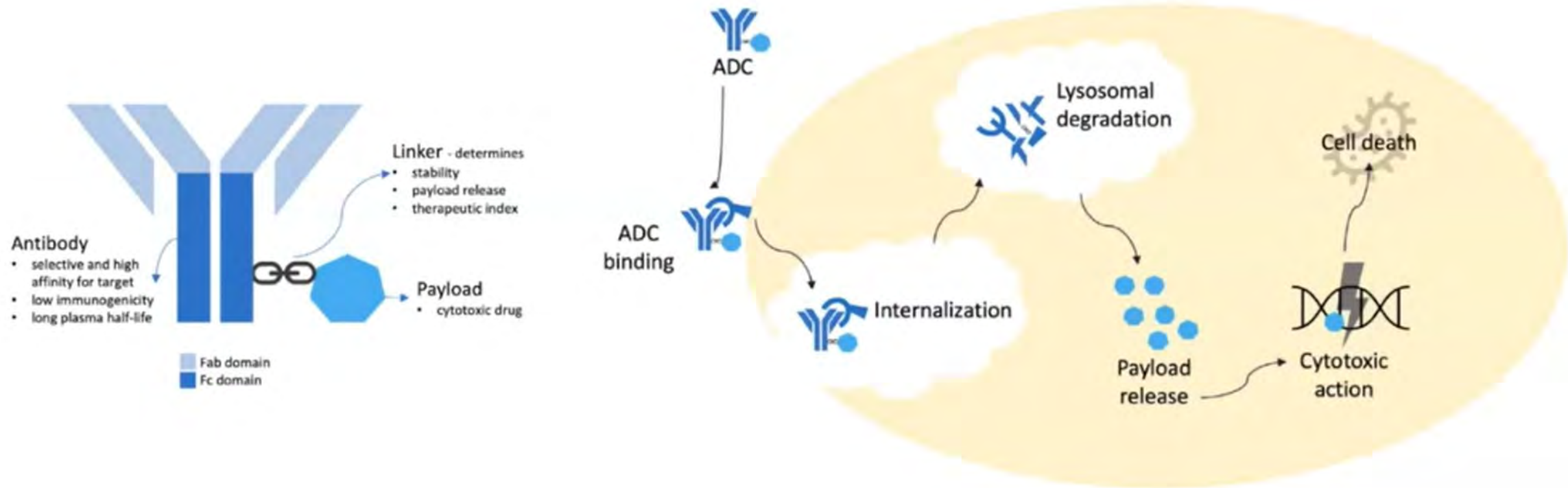
Største udekkede behov

- Hva gir vi etter når all målrettet behandling er uttømt?
- Hva gir vi etter progresjon på immunterapi?
- Hva gir vi de som ikke responderer på målrettet behandling eller immunterapi?



**Hva
kommer?**

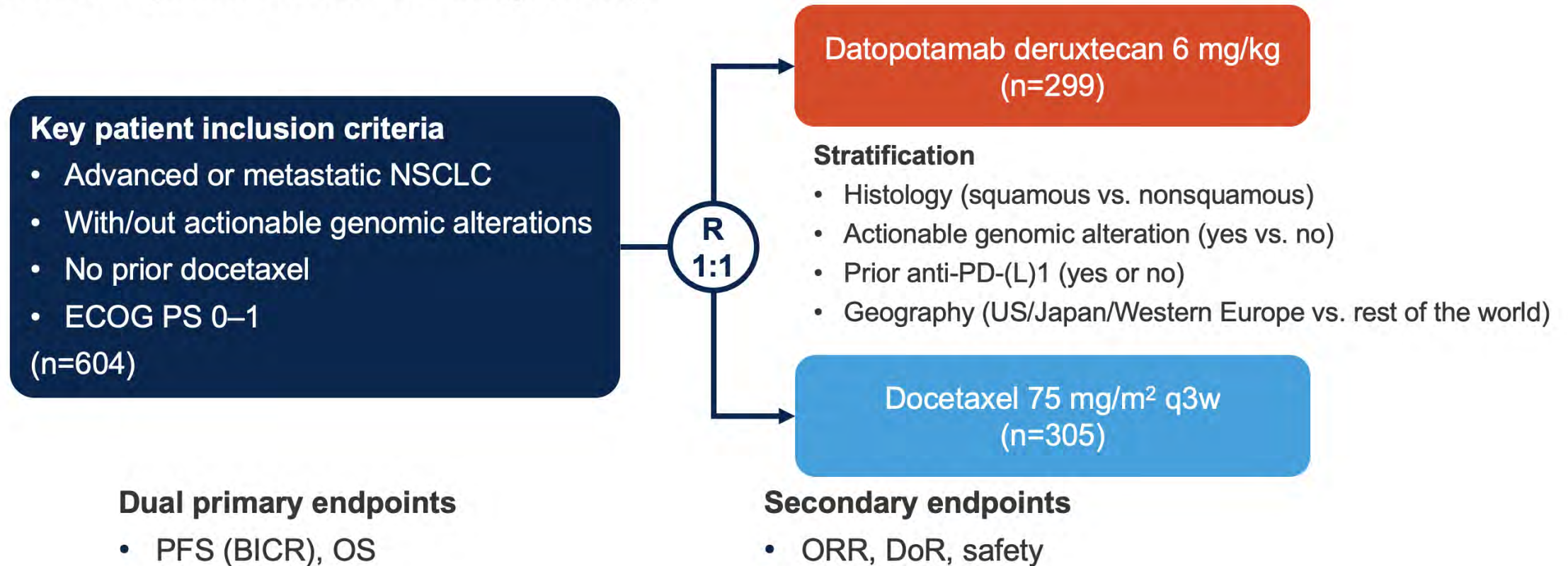
ADC structure and mechanism of action



LBA12: Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): results of the randomized phase 3 study TROPION-Lung01 – Lisberg AE, et al

- **Study objective**

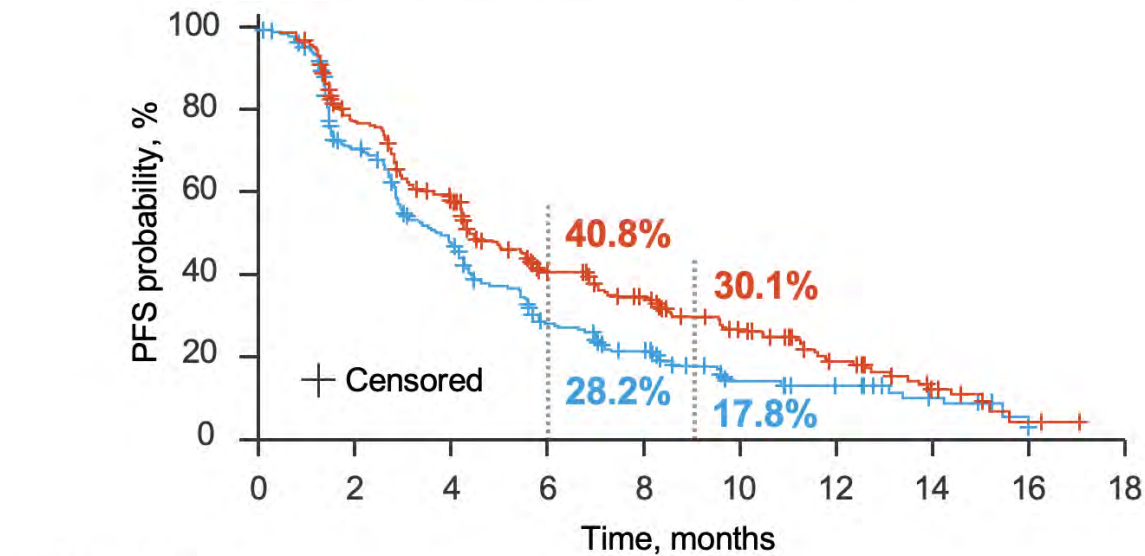
- To evaluate the efficacy and safety of datopotamab deruxtecan in previously treated patients with metastatic NSCLC in the phase 3 TROPION-Lung01 study



LBA12: Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): results of the randomized phase 3 study TROPION-Lung01 – Lisberg AE, et al

- Key results (cont.)

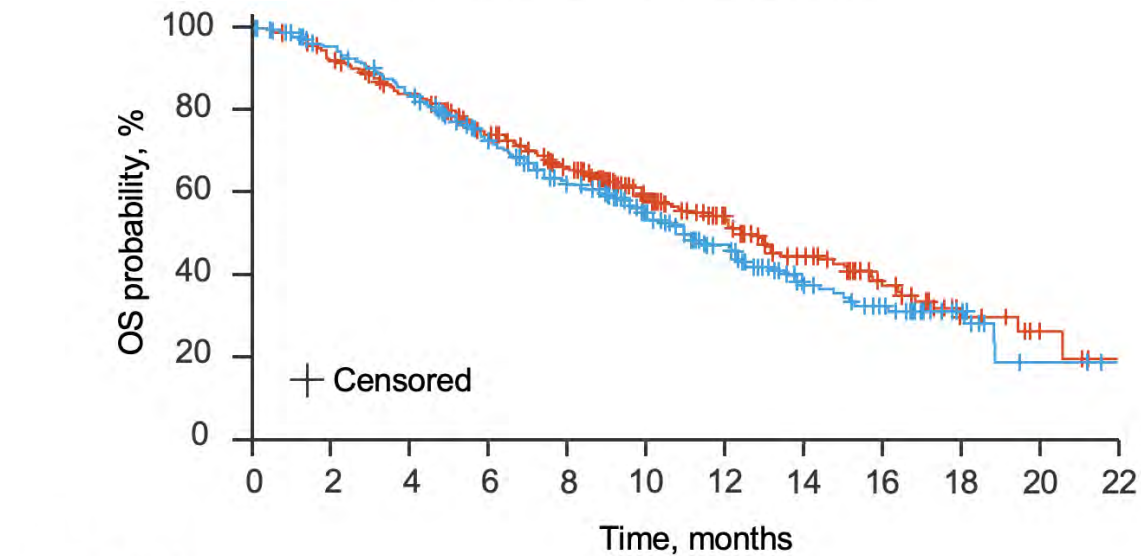
Progression-free survival



No. at risk										
— Dato-DXd	299	216	156	96	74	46	24	10	2	0
— Docetaxel	305	186	120	63	42	19	14	7	0	0

	Dato-DXd	Docetaxel
mPFS, mo (95%CI)	4.4 (4.2, 5.6)	3.7 (2.9, 4.2)
HR (95%CI); p-value	0.75 (0.62, 0.91); 0.004	
Prespecified boundary (2-sided)	0.008	

Interim overall survival



No. at risk													
— Dato-DXd	299	273	243	201	166	121	85	56	33	14	6	1	
— Docetaxel	305	273	239	193	156	115	76	42	29	13	4	1	

	Dato-DXd	Docetaxel
mOS, mo (95%CI)	12.4 (10.8, 14.8)	11.0 (9.8, 12.5)
HR (95%CI)	0.90 (0.72, 1.13)	

LBA12: Datopotamab deruxtecan (Dato-DXd) vs docetaxel in previously treated advanced/metastatic (adv/met) non-small cell lung cancer (NSCLC): results of the randomized phase 3 study TROPION-Lung01 – Lisberg AE, et al

• Key results (cont.)

TRAEs, n (%)	Dato-DXd (n=297)	Docetaxel (n=290)
Any	257 (87)	252 (87)
Grade ≥3	73 (25)	120 (41)
Led to dose reduction	58 (20)	85 (29)
Led to dose delay	49 (17)	31 (11)
Led to discontinuation	23 (8)	34 (12)
Led to death	3 (1)	2 (1)
Serious	30 (10)	36 (12)
Grade ≥3	25 (8)	33 (11)

TRAEs, n (%)		Dato-DXd (n=297)		Docetaxel (n=290)	
		Any grade	Grade ≥3	Any grade	Grade ≥3
Blood and lymphatic system	Anemia	43 (15)	11 (4)	59 (20)	11 (4)
	Neutropenia	12 (4)	2 (1)	76 (26)	68 (23)
Gastrointestinal	Stomatitis	140 (47)	19 (6)	45 (16)	3 (1)
	Nausea	100 (34)	7 (2)	48 (17)	3 (1)
	Vomiting	38 (13)	3 (1)	22 (8)	1 (0.3)
	Constipation	29 (10)	0	30 (10)	0
	Diarrhea	28 (9)	1 (0.3)	55 (19)	4 (1)
	Asthenia	55 (19)	8 (3)	55 (19)	5 (2)
	Fatigue	34 (11)	2 (1)	40 (14)	6 (2)
General					
Metabolism and nutrition	Appetite decreased	68 (23)	1 (0.3)	45 (16)	1 (0.3)
Skin and subcutaneous	Alopecia	95 (32)	0	101 (35)	1 (0.3)
	Rash	36 (12)	0	18 (6)	0
	Pruritus	30 (10)	0	12 (4)	0

• Conclusions

- In patients with metastatic NSCLC, datopotamab deruxtecan demonstrated a statistically significant improvement in PFS over docetaxel, which was primarily driven by patients with nonsquamous histology. OS remains immature and although there were no new safety signals observed, the specific tolerability profiles require close monitoring



Nyheter

Retningslinjer

Studier

Publikasjoner

Aktiviteter og referater

Lenker

Om NLCG

Norsk lungekreftgruppe

Nasjonalt handlingsprogram

Publikasjoner

Studier

Møtekalender

Meld deg inn i NLCG

Nyheter

- **HORIZON-01:** 12.01.24

OUS har åpnet en ny studie for pasienter med ALK positiv, stadium III, NSCLC , som er kandidater for kjemoradioterapi. Ta kontakt med Maria Bjaanæs ved spørsmål eller aktuelle pasienter.

- **Herthena studien stengt for inklusjon** 26.11.23

Herthena studien har inkludert veldig raskt, og ble denne uken lukket for inklusjon av nye pasienter. Men sjekk ut om dine pasienter kan være aktuell for andre lungekreftstudier i studieappen ([Lungekreftstudier \(icgi.net\)](https://icgi.net)) eller på NLCG sine nettsider

- **Compassionate use avtale -MET ekson 14-skiping mutasjon** 06.10.23

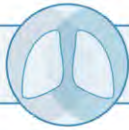
Det er laget en compassionate use avtale for medikamentet Savolitinib til pasienter med lokalavansert eller metastatisk NSCLC med aktiverende MET ekson 14-skiping mutasjoner som har progrediert på standardbehandling. Avtalen om inklusjon av nye pasienter gjelder frem til 31.12.23.

- **Adjuvant immunterapi med Atezolizumab etter kirurgi** 25.09.23

I dag ble det besluttet at Atezolizumab (Tecentriq) blir innføres som adjuvant behandling etter fullstendig reseksjon og platina-basert kjemoterapi til voksne pasienter med ikke-småcellet lungekreft (NSCLC) med høy risiko for tilbakefall der tumor har PD-L1- ekspresjon i $\geq 50\%$ av tumorcellene (TC) og som ikke har påvist EGFR-mutasjon eller ALK-translokasjon. Behandlingstid i 1 år. Revidert handlingsprogram er lagt ut på hjemmesiden.

Dette gjelder fra i dag.

NLCG



NORSK LUNGE CANCER GRUPPE



Norsk lungekreftgruppe

54 liker · 63 følgere



Opprett med avatar

Rediger forsidebilde

InnleggOmOmtalerAnmeldelserFølgereBilderFlere

Presentasjon

Fagmedisinsk nasjonal interessegruppe for å fremme norsk lungekreftomsorg

Rediger biografi

Side · Helse og medisin

nlcg.no

Promoter nettsted

Ikke vurdert ennå (0 anmeldelser)

Rediger detaljer

Legg til hobbyer

Legg til fremhevet innhold

Bilder

Se alle bilder



Hva tenker du på?

Direktesendt videoBilde/videoReels-video

Fremhevet

Norsk lungekreftgruppe

12. september kl. 16:01 ·



HEALTHTALK.NO

Kombinasjonsmedisin bremser forverring av lungekreft - men...

Norsk lungekreftgruppe

11. september kl. 21:23 ·



Norsk lungekreftgruppe, en fagmedisinsk interesseorganisasjon for lungekreftinteresserte leger, er nå på...

NLCG.NO

Norsk lungekreftgruppe

Innlegg

FiltreAdministrer innlegg

ListevisningRutenettvisning

21:29

NORSKLUNGEKREFTGRUPPE

Innlegg

norsklungekreftgruppe

1/2



Likt av marianneaanerud og 20 andre

norsklungekreftgruppe I disse dager har Lungekreftforeningen lanseringsturne for «Hver dag teller - lungekreftboka». I dag var det bokslipp i... mer

20. november 2023 · Se oversettelse

HomeSearchAddPostActivity

82

NU



NASJONALT ORGAN FOR RÅDGIVING VED ALVORLIG
LIVSFORKORTENDE SYKDOM

Ekspertpanelet

Ekspertpanelet er en nasjonal ordning som gir pasienter med alvorlig livsforkortende sykdom mulighet for en ny vurdering. En viktig hensikt er at pasienter og pårørende skal kjenne seg sikre på at all relevant behandling er vurdert.

Panelet vurderer sykdommen og behandlingen som er gitt. Vi kan gi råd om ytterligere godkjent behandling, vi leter etter studier i Norge og utlandet og vi kan gi råd om behandling som ennå ikke er godkjent i Norge.



Retningslinje for bruk av nye legemidler før markedsføringstillatelse (compassionate use)

For nye legemidler uten markedsføringstillatelse (MT) som er oppført på nasjonal liste skal det inngås en nasjonal standardavtale før behandlingsstart.

RHF-ene har ansvar for den nasjonale listen som oppdateres ca. en gang per måned:

[Siste versjon av Nasjonal liste over legemidler uten markedsføringstillatelse \(MT\) som det skal det inngås en nasjonal standardavtale for før behandlingsstart \(pdf\) \(18.12.2023\)](#)

[Oversikt over inngåtte avtaler mellom legemiddelleverandør og RHF \(pdf.\) \(09.11.2023\)](#)

Nye vilkår for legemidler med kort forventet behandlingsvarighet ble godkjent av Beslutningsforum 21. juni 2021.

Det foreligger derfor to standardavtaler:

- en ny for standardavtale legemidler med kort forventet behandlingsvarighet (normalt inntil 6 mnd.), og
- eksisterende standardavtale for legemidler som ikke er aktuelle for ny standardavtale med kort forventet behandlingsvarighet.



Takk for oppmerksomheten!