State of the art radiotherapy for Lung Cancer

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Erasmus MC Cancer

Conflict of Interest

Institutional financial interests (no personal financial interests):

- Research grant/ support: Bristol-Myers Squibb, AstraZeneca, Beigene, Philips, Olink
- Advisory board: Bristol-Myers Squibb, AstraZeneca, Philips

Small cell lung cancer

Simple to treat for a doctor; hard to cure

- Stage I-III
  - Concurrent cisplatin-etoposide and 45 Gy BID chest RT
  - PCI in fit patients without PD after CCRT

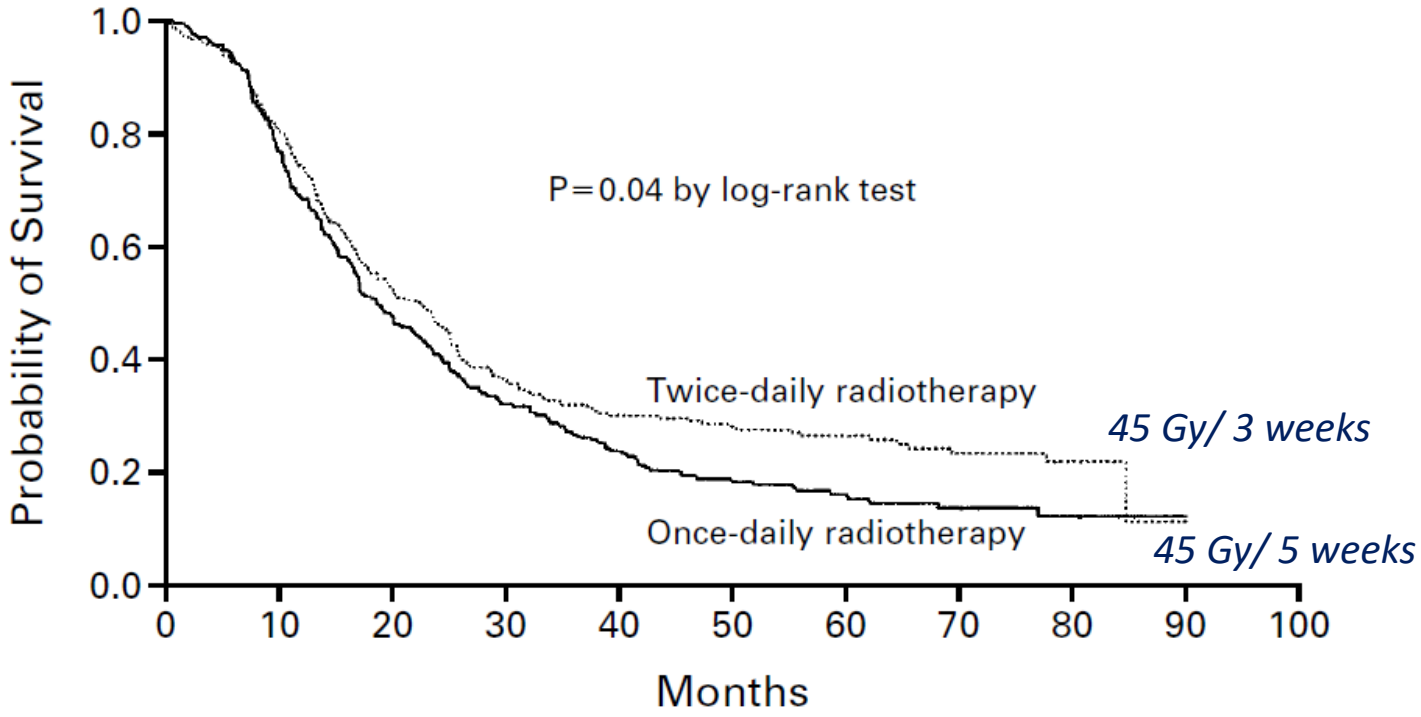
  ➔ On average 25 % 5-y OS

- Stage IV
  - Carboplatin-etoposide x 4/ IO ➔ PCI or MRI brain surveillance
  - Thoracic RT to be considered

  ➔ On average less than 5 % 5-y OS

Dingemans et al. Ann Oncol 2021

Intensification of thoracic radiotherapy



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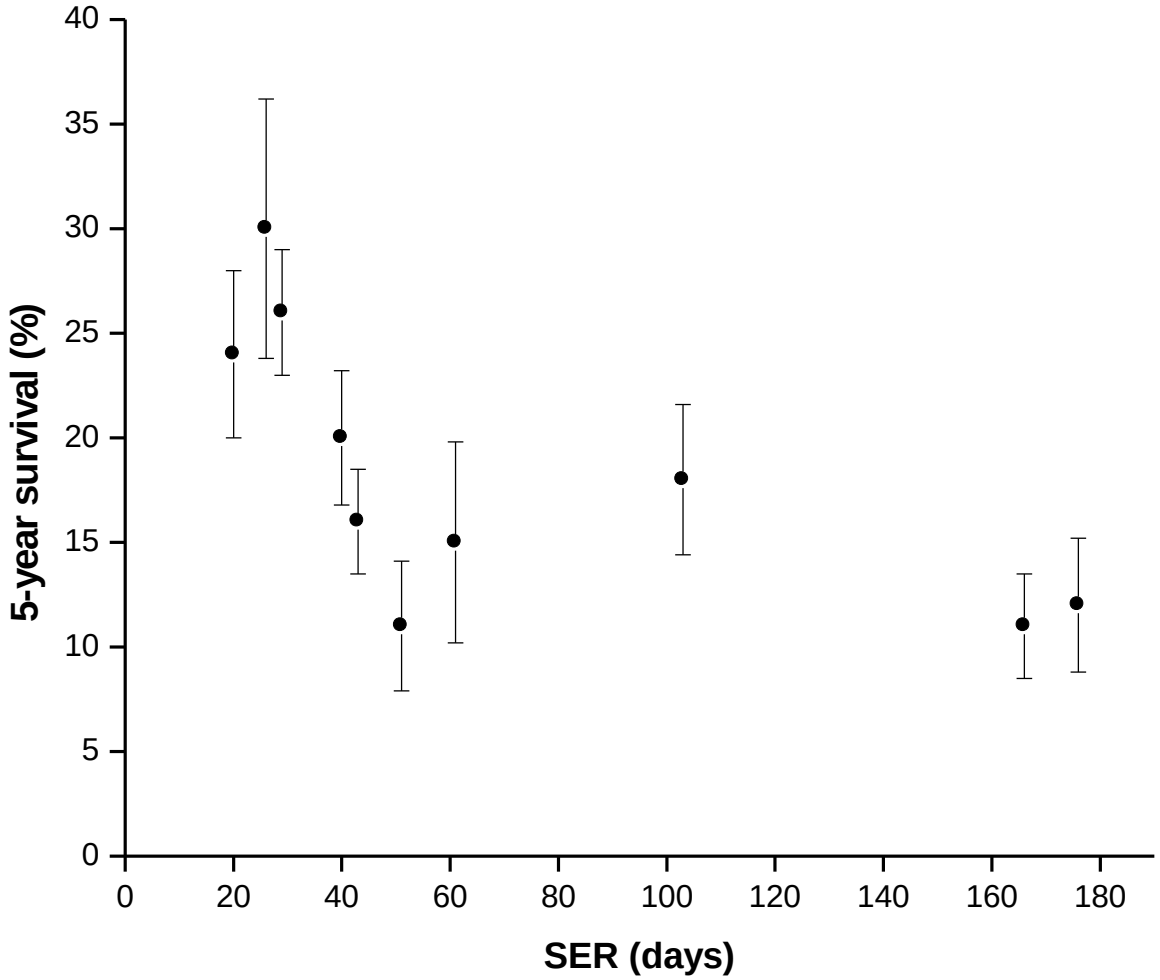
Turrisi et al. New Engl J Med 1999

Time is important



De Ruysscher et al. J Clin Oncol 2005

Van Meerbeeck, Fenell, De Ruysscher. Lancet 2011

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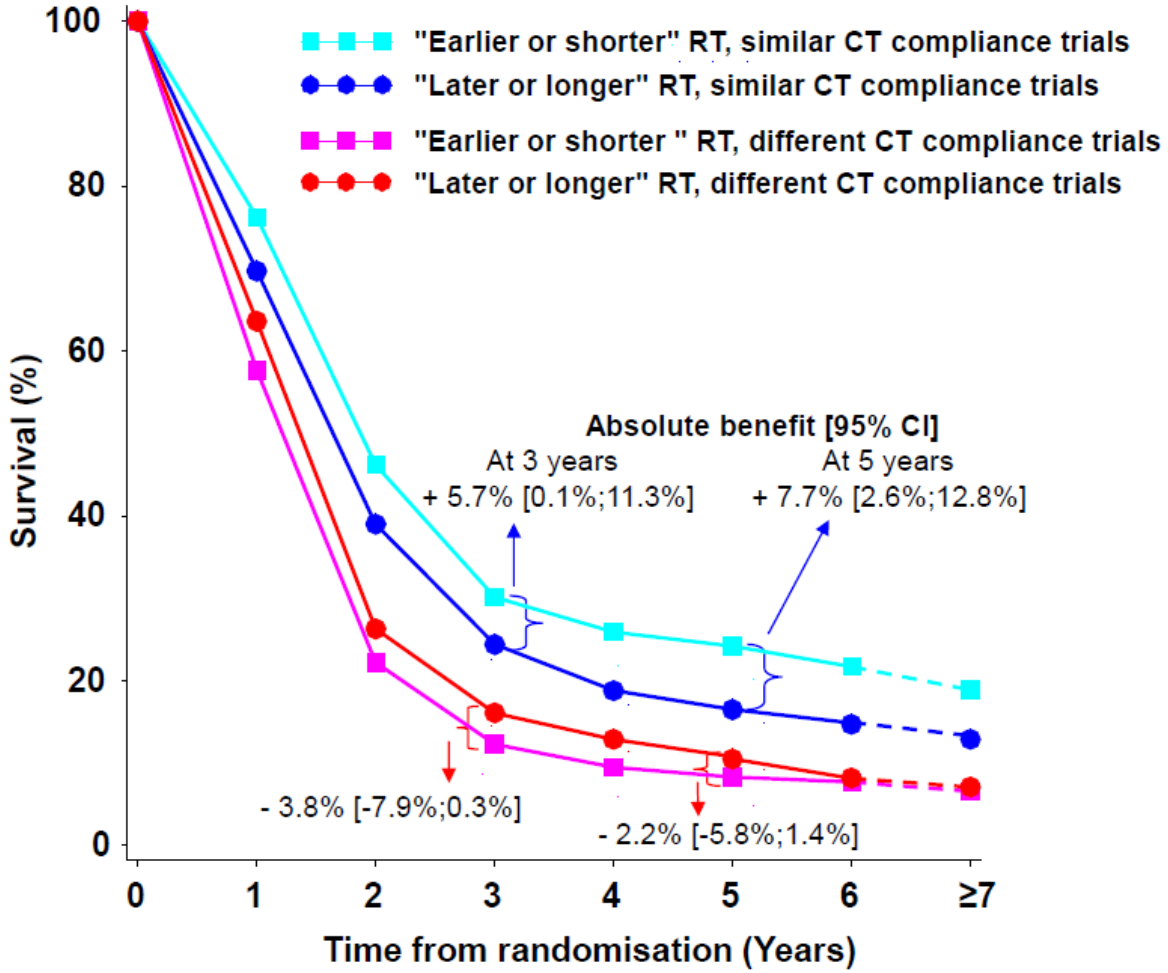
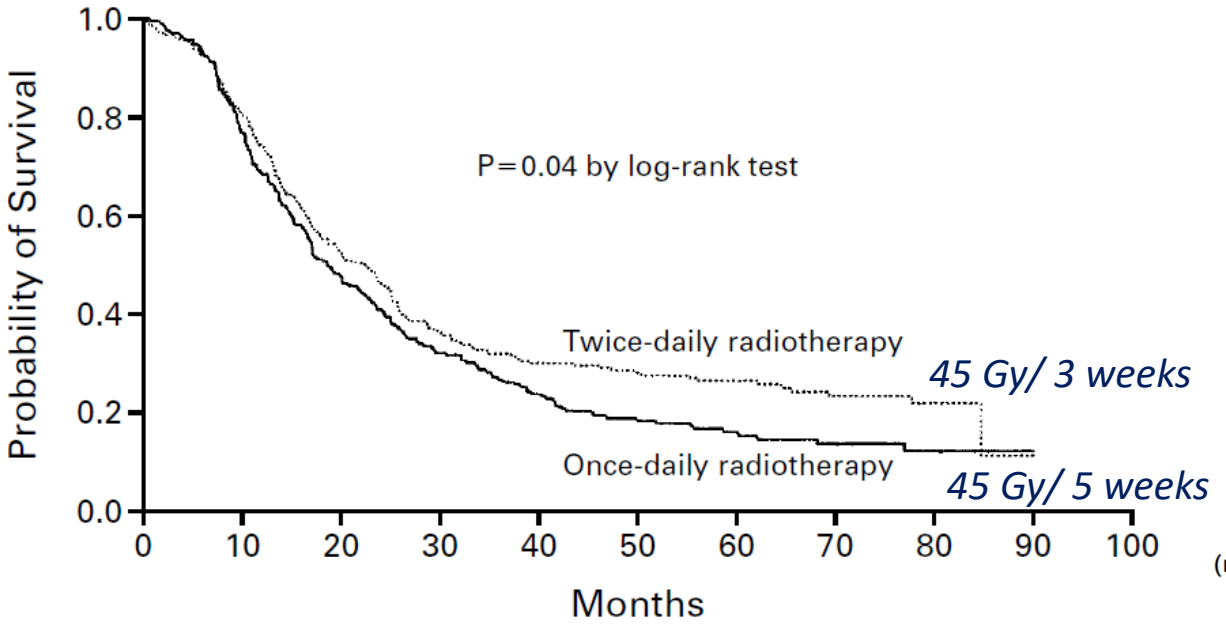
Effect of early, accelerated radiotherapy as a function of chemotherapy compliance

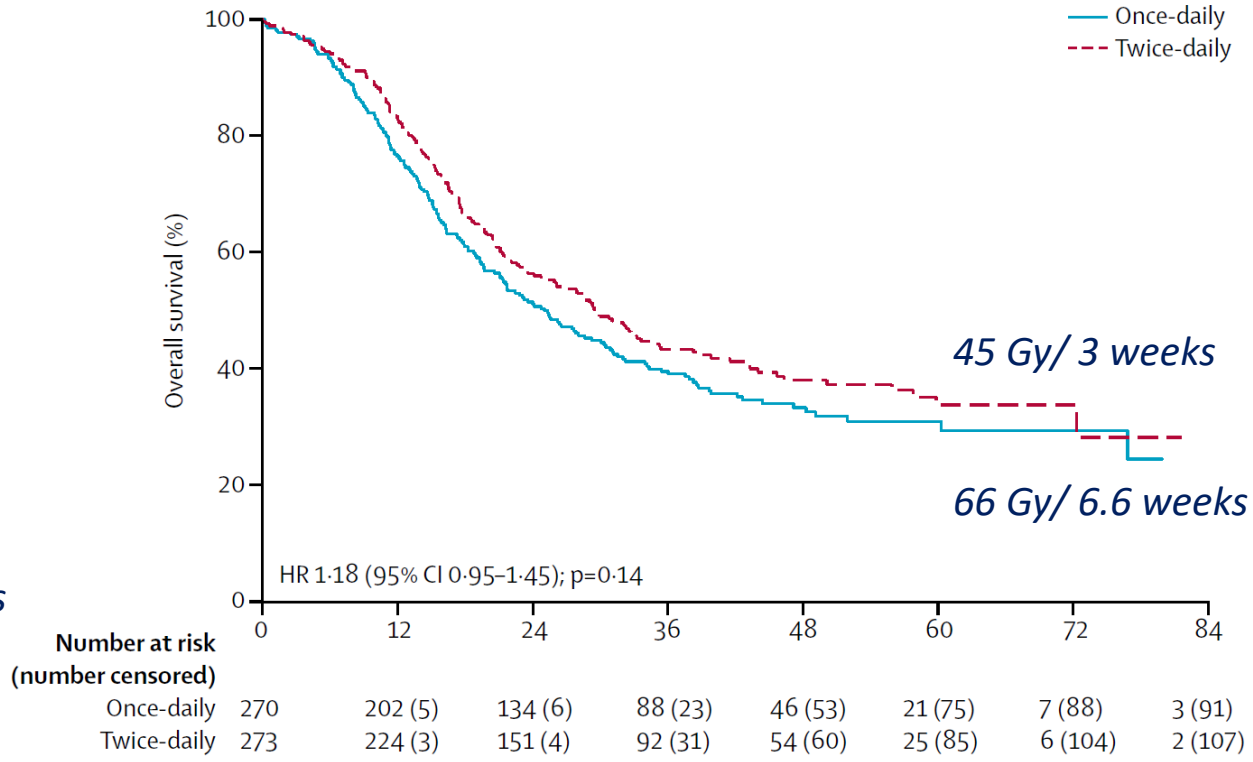


De Ruysscher et al. Ann Oncol 2016

Fractionation studies: Phase III



Turrisi et al. New Engl J Med 1999



Faivre-Finn et al. Lancet Oncol 2016

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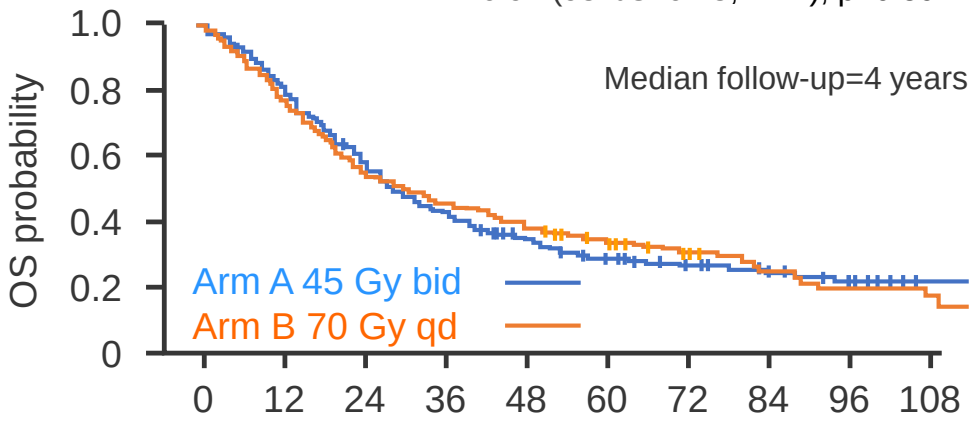
CALGB 30610 (Alliance)/RTOG 0538

Overall survival

	mOS, mo (95%CI)	2-years OS, % (95%CI)	5-years OS, % (95%CI)
45 Gy bid	28.5 (25.4, 35.5)	58 (53, 64)	29 (23, 35)
70 Gy qd	30.5 (25.4, 41.1)	56 (51, 62)	34 (23, 35)

HR 0.94 (95%CI 0.75, 1.17); p=0.591

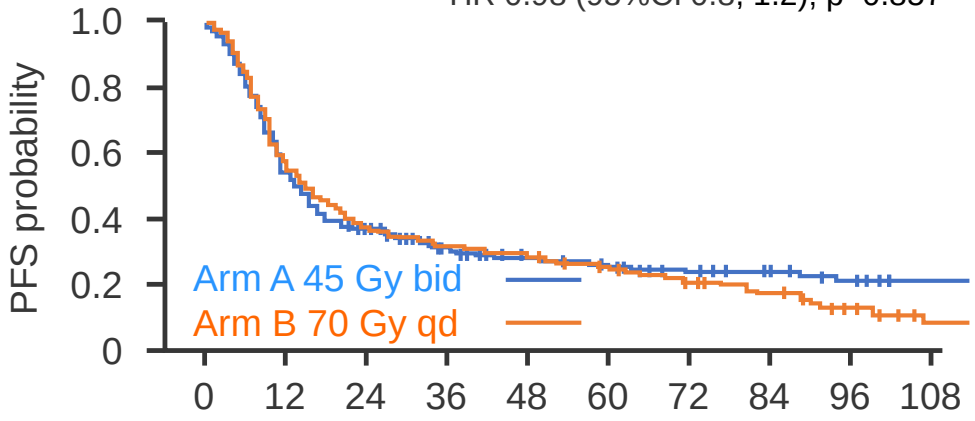


No. at risk										
45 Gy bid	313	239	150	99	66	44	30	23	16	9
70 Gy qd	325	238	158	111	82	58	45	24	13	6

Progression-free survival

	mPFS, mo (95%CI)	2-years PFS, % (95%CI)	5-years PFS, % (95%CI)
45 Gy bid	13.5 (11.7, 15.8)	36 (31, 42)	25 (20, 31)
70 Gy qd	14.2 (11.9, 17.7)	36 (31, 42)	24 (20, 30)

HR 0.98 (95%CI 0.8, 1.2); p=0.857



No. at risk										
45 Gy bid	313	158	96	67	51	36	28	21	14	8
70 Gy qd	325	168	104	81	64	47	32	15	7	2

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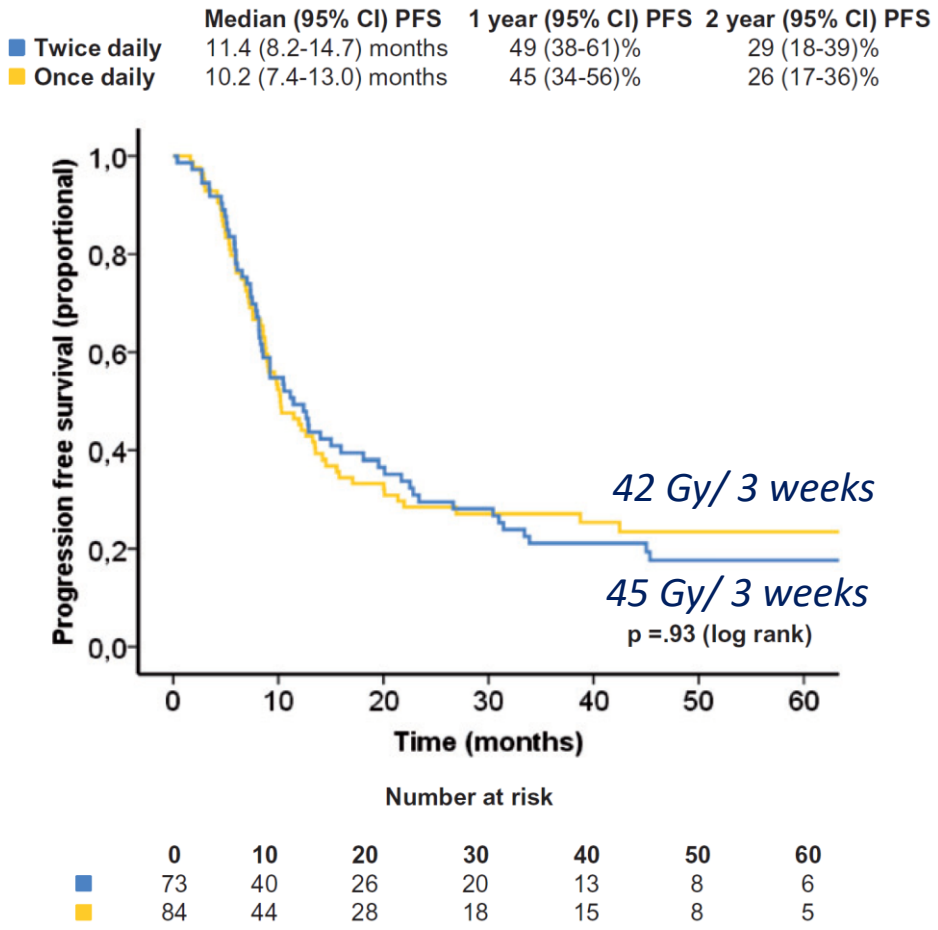
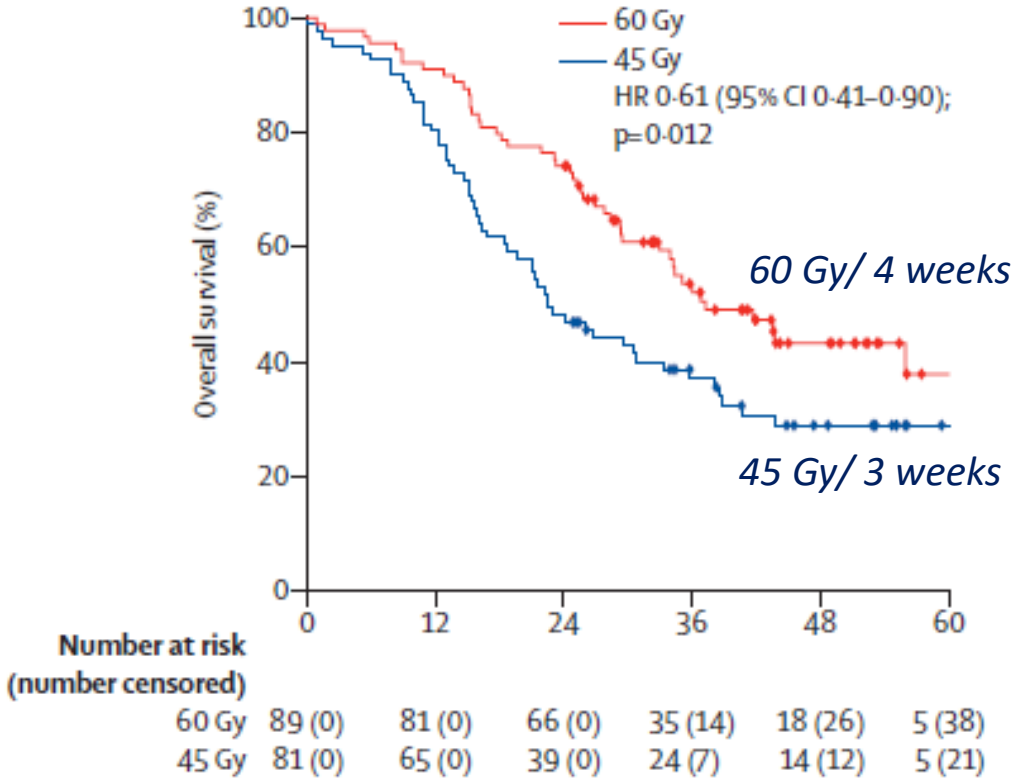
Bogart et al. J Clin Oncol 2023

Fractionation studies: Phase II



Grønberg et al. Acta Oncol 2016



Grønberg et al. Lancet Oncol 2021

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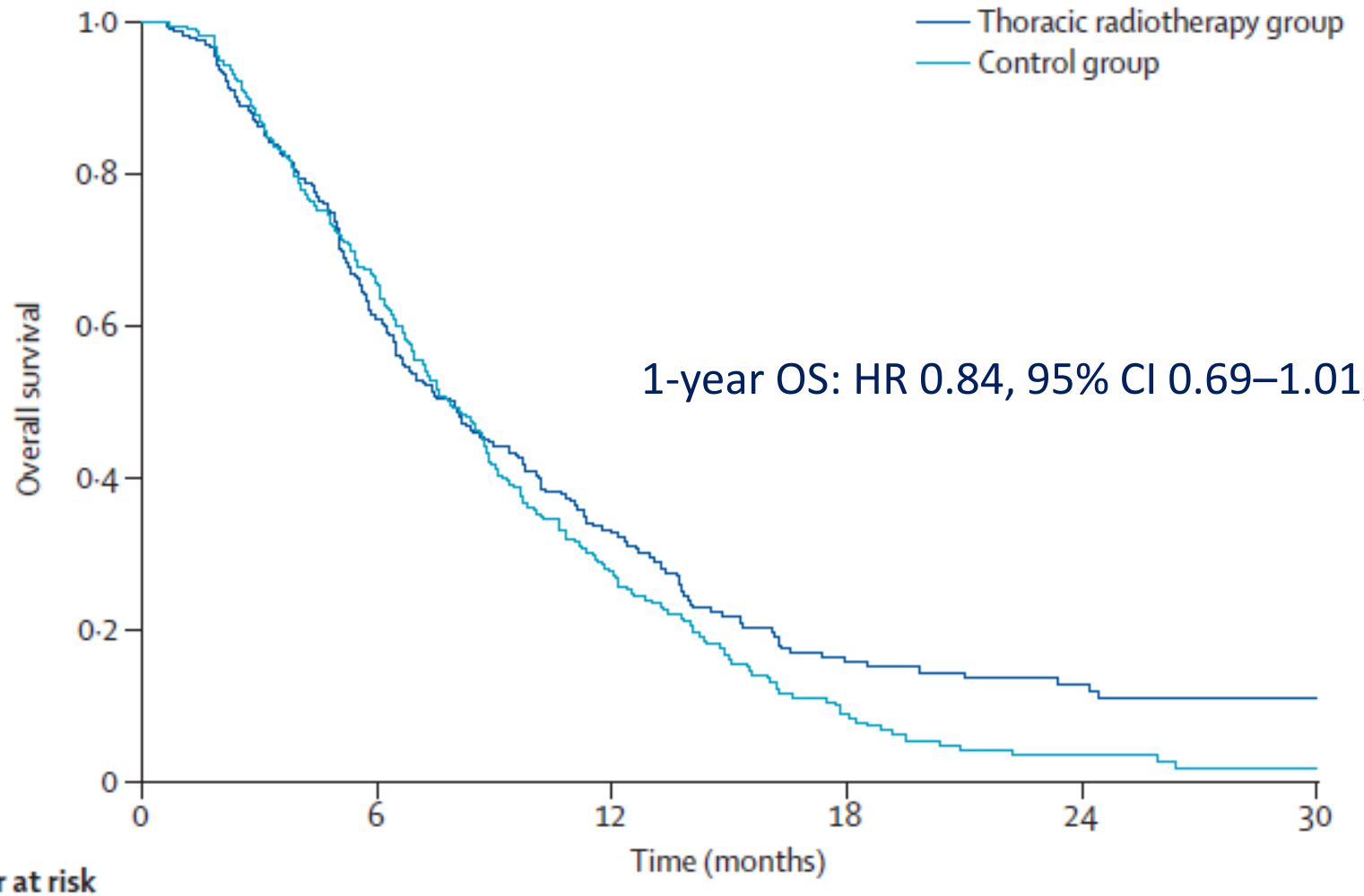
CREST



1-year OS: HR 0.84, 95% CI 0.69–1.01; p=0.066

Number at risk						
Thoracic radiotherapy group	247	147	67	26	14	7
Control group	248	160	61	17	5	1

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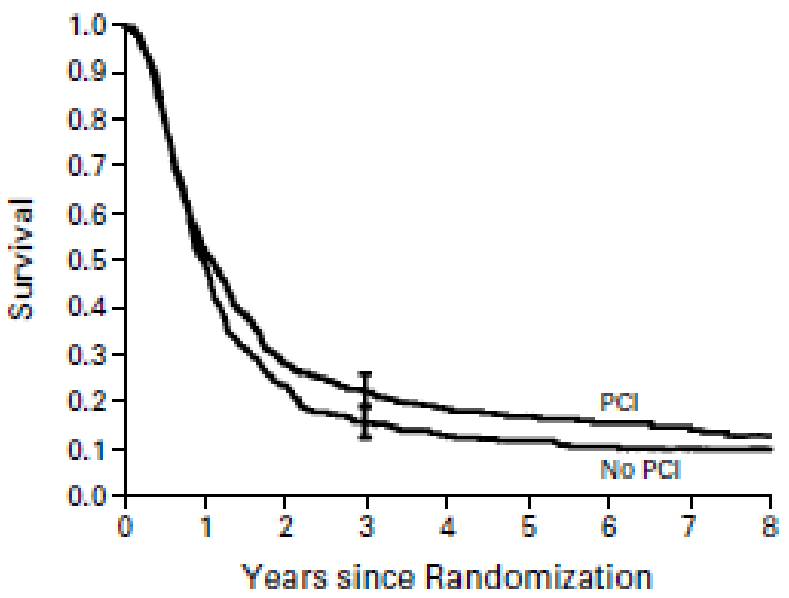
Slotman et al. Lancet 2015

Prophylactic Cranial Irradiation in small cell lung cancer

«Limited disease» small cell lung cancer

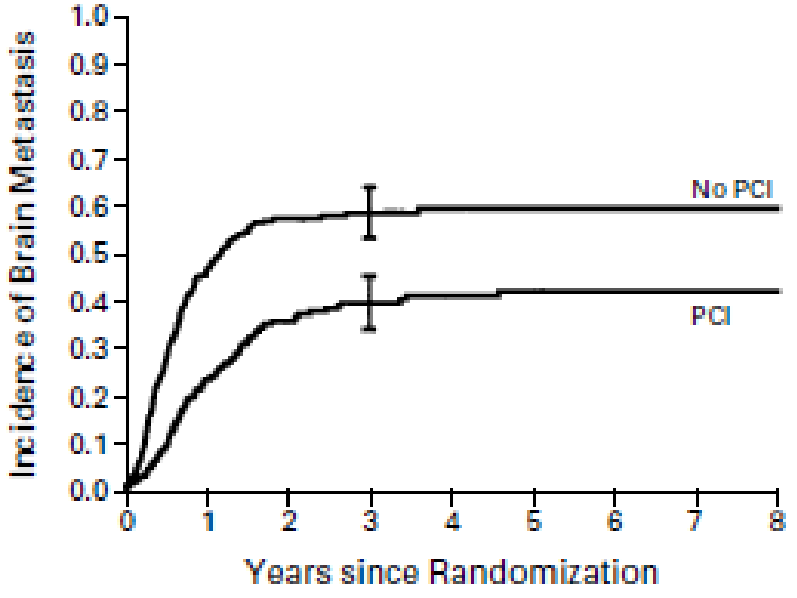
Aupérin et al. NEJM 1999; 341:476-484

PROPHYLACTIC CRANIAL IRRADIATION FOR PATIENTS WITH SMALL-CELL LUNG CANCER IN COMPLETE REMISSION



No. at Risk

No PCI	461	224	103	61	44	34	23	19	15
PCI	526	276	139	101	66	52	40	29	17



No. at Risk

No PCI	457	171	88	57	41	32	21	18	14
PCI	524	248	133	96	66	52	40	29	17

Increased overal survival and less BM in patients with a CR **on chest X-ray**

No concurrent chemo-radiotherapy

No high quality CT (no MRI) of the brain

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PCI: «Extensive disease» SCLC

(Slotman et al. NEJM 2007;357:664-72)

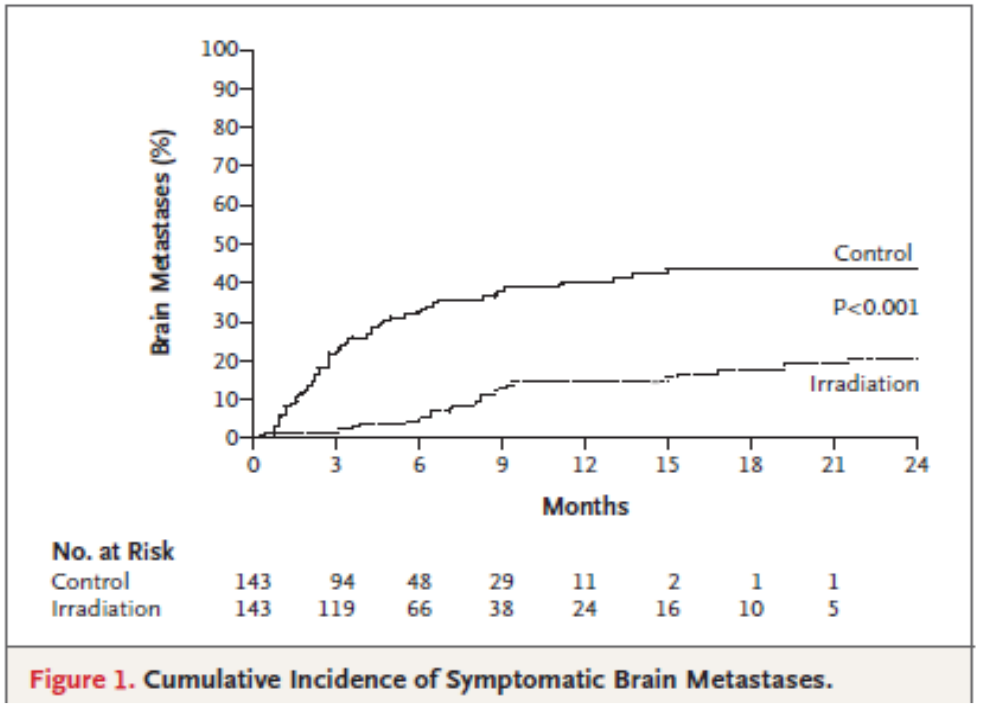


Figure 1. Cumulative Incidence of Symptomatic Brain Metastases.

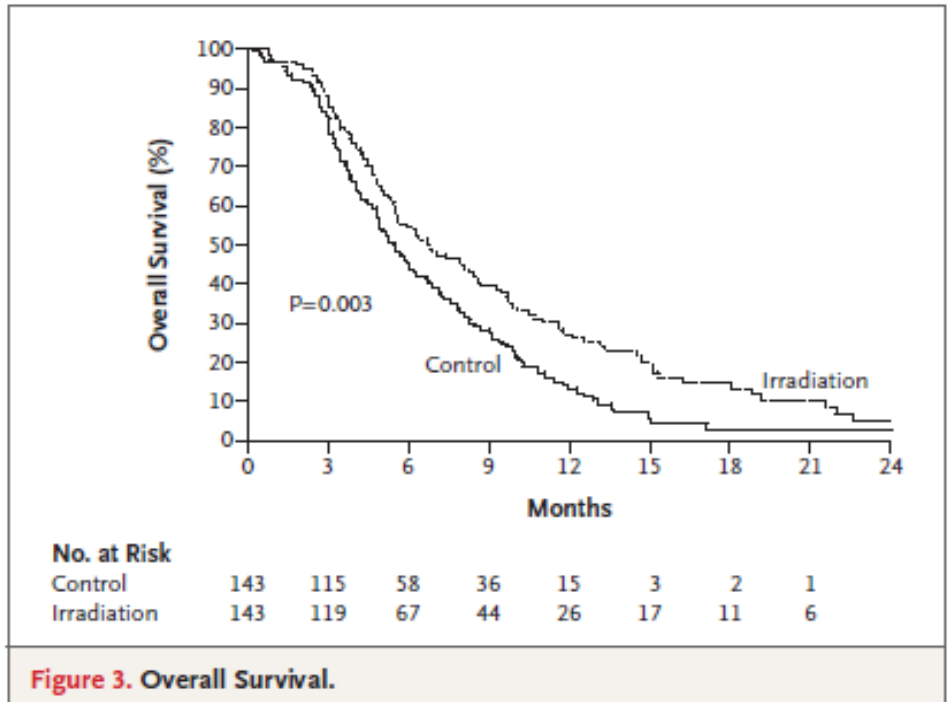


Figure 3. Overall Survival.

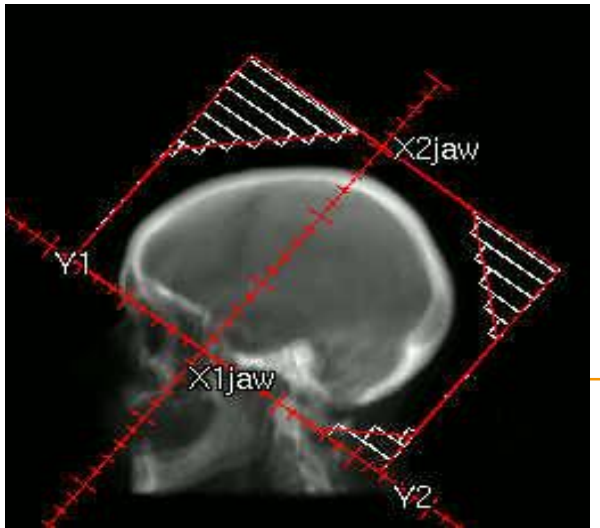
Hippocampus Avoidance PCI
A randomized phase III trial (NCT01780675)

SCLC (LD and ED)

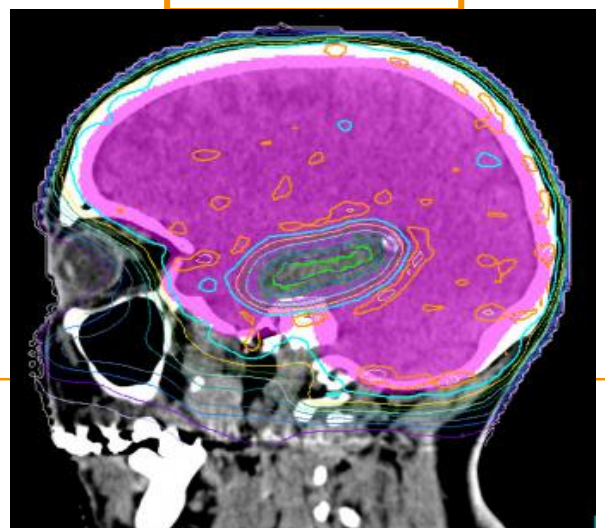
PCI

R

standard PCI



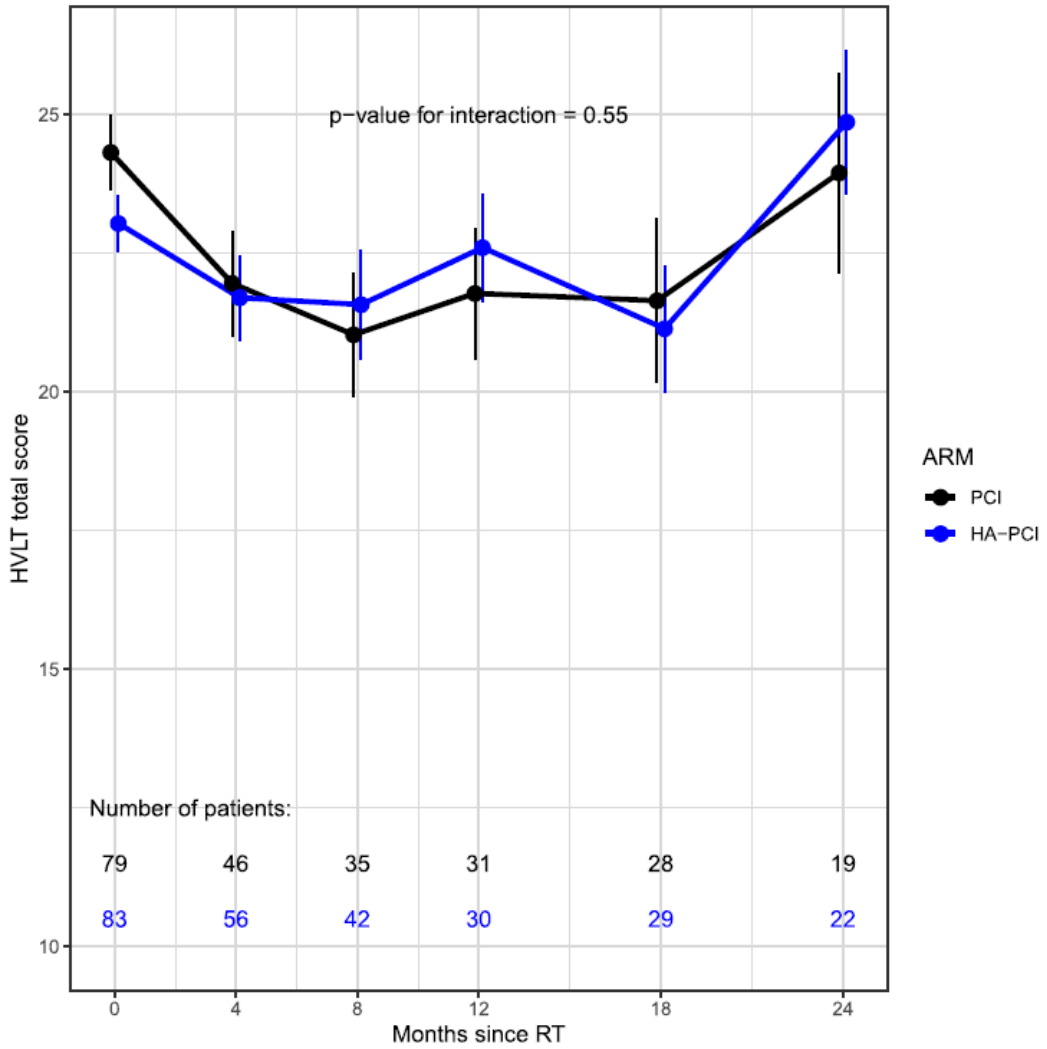
HA-PCI



- Prescription dose 25 Gy/10 fx
- Neurocognitive test battery baseline and 4 /8 /12 /18/ 24 mths
- MRI baseline, 4 mths and 1 year

Belderbos et al. J Thorac Oncol 2021

Primary endpoint: HVLT-R



Belderbos et al. J Thorac Oncol 2021

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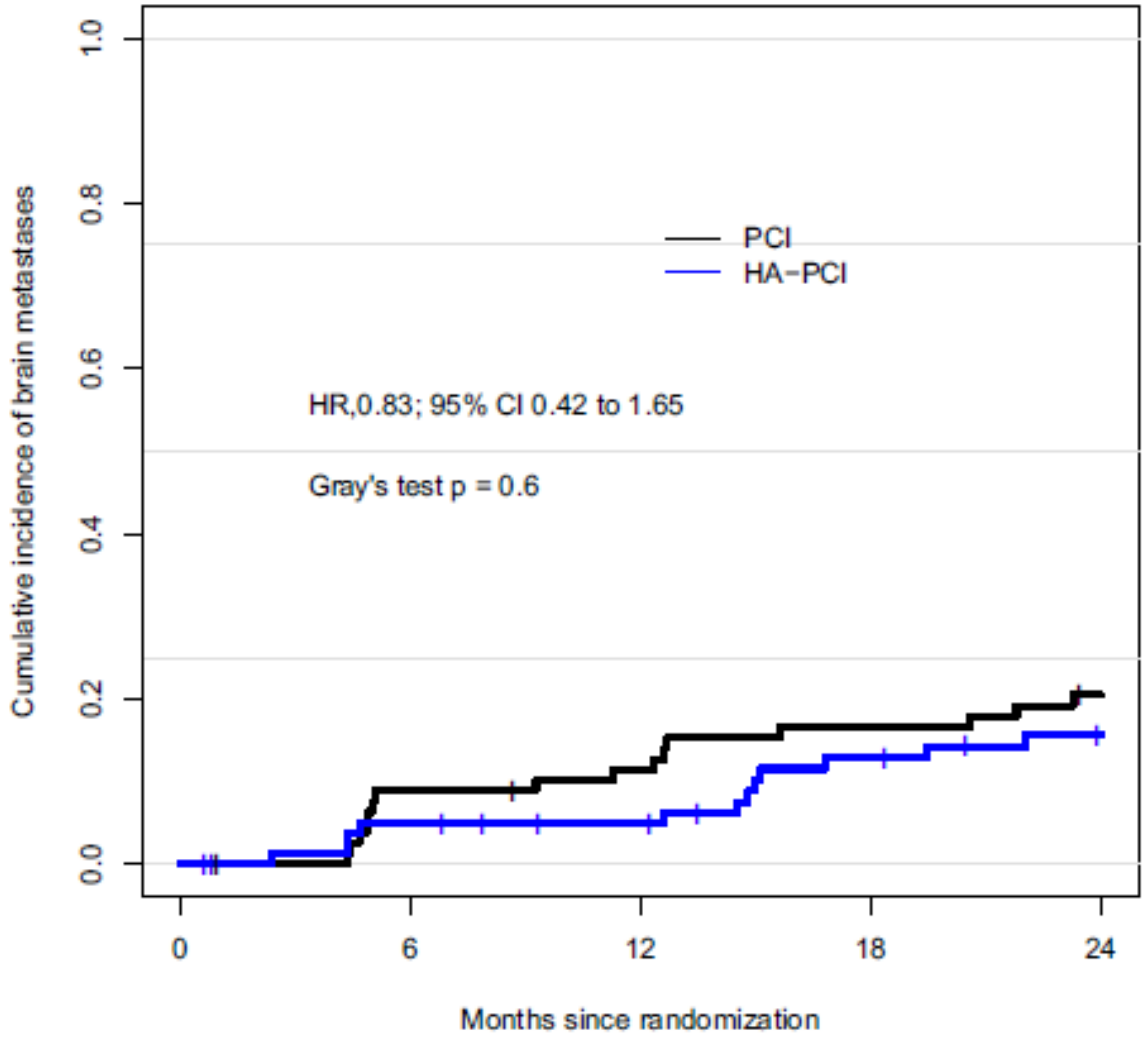
Incidence of brain metastases



Belderbos et al. J Thorac Oncol 2021

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IMpower 133: PROM

Table 5. CNS-related AEs in all patients and in patients who received PCI

CNS-related AEs, *n* (%)	Atezolizumab + CP/ET			Placebo + CP/ET		
	All patients (*n* = 198)	Patients with PCI (*n* = 23)		All patients (*n* = 196)	Patients with PCI (*n* = 21)	
		AEs at any time	AEs after PCI[a]		AEs at any time	AEs after PCI[a]
Headache	24 (12)	8 (35)	6 (26)	23 (12)	3 (14)	3 (14)
Asthenia	25 (12)	5 (22)	1 (4)	20 (10)	2 (10)	0
Dizziness	19 (10)	2 (9)	0	11 (6)	0	0
Insomnia	15 (8)	3 (13)	1 (4)	13 (7)	1 (5)	1 (5)
Fall	8 (4)	2 (9)	1 (4)	4 (2)	1 (5)	1 (5)
Balance disorder	2 (1)	1 (4)	1 (4)	0	0	0
Lethargy	2 (1)	1 (4)	1 (4)	1 (<1)	0	0
Syncope	5 (3)	1 (4)	0	1 (<1)	0	0
Agitation	1 (<1)	0	0	1 (<1)	1 (5)	1 (5)
Confusional state	3 (2)	0	0	3 (2)	1 (5)	1 (5)

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Mansfield et al. Ann Oncol 2020

Conclusions fractionation stage I-III small cell lung cancer

- “Small cell lung cancer is a chemo- and radiosensitive disease” is a myth. We were fooled by their immediate effects.
- Optimize chemotherapy, then optimizing radiotherapy improves OS.
- *Concurrent chemo-RT:* 45 Gy/ 1.5 Gy BID/ 3 weeks (70 Gy/ 2 Gy QD/ 7 weeks)
- *[Sequential chemo-RT:* only one phase III trial: 45 Gy BID*]*

Conclusions PCI

- PCI remains SoC in localized small cell lung cancer when no progressive disease is found after concurrent chemo-radiotherapy and the performance status is 0-2
- PCI in metastatic disease should be considered as well as MRI follow-up
- Hippocampus sparing is of no use
- The neuro-cognitive side effects of PD-(L)1 antibodies and especially combined with PCI should be investigated further

Conclusions chest irradiation in stage IV disease

- Chest irradiation (30 Gy/ 10 fractions) in metastatic disease after a response to chemotherapy and a performance status of 0-2 should be considered
- Chest irradiation can be combined safely with PD-(L)-1 antibodies

Non-Small Cell Lung Cancer

Early stage NSCLC: Stereotactic Radiotherapy

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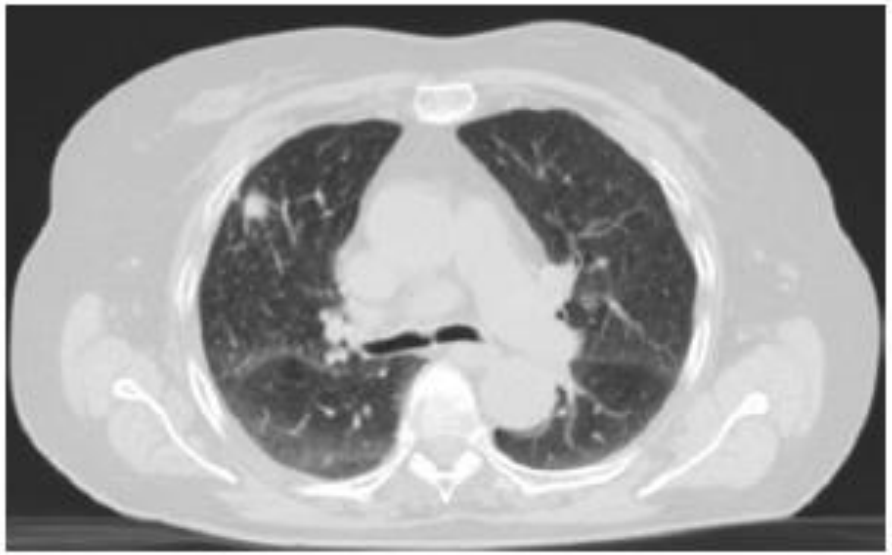
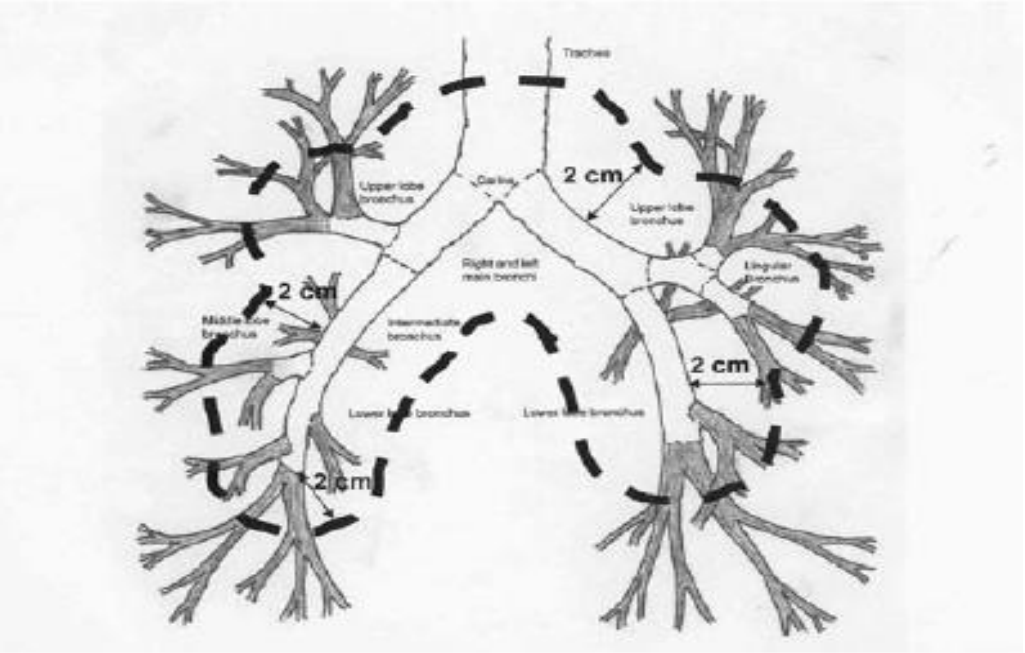
Inclusion



Exclusion



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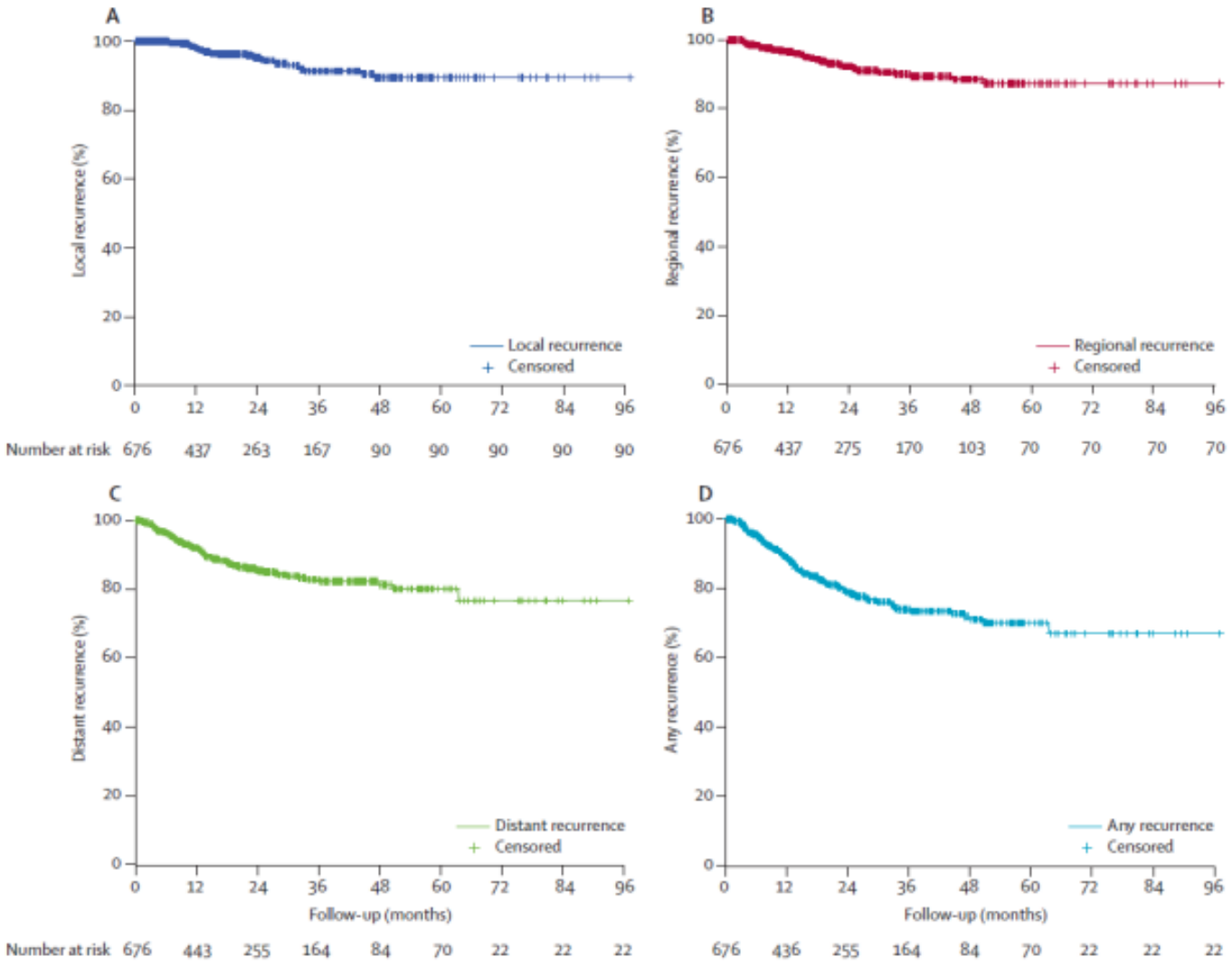
Retrospective series



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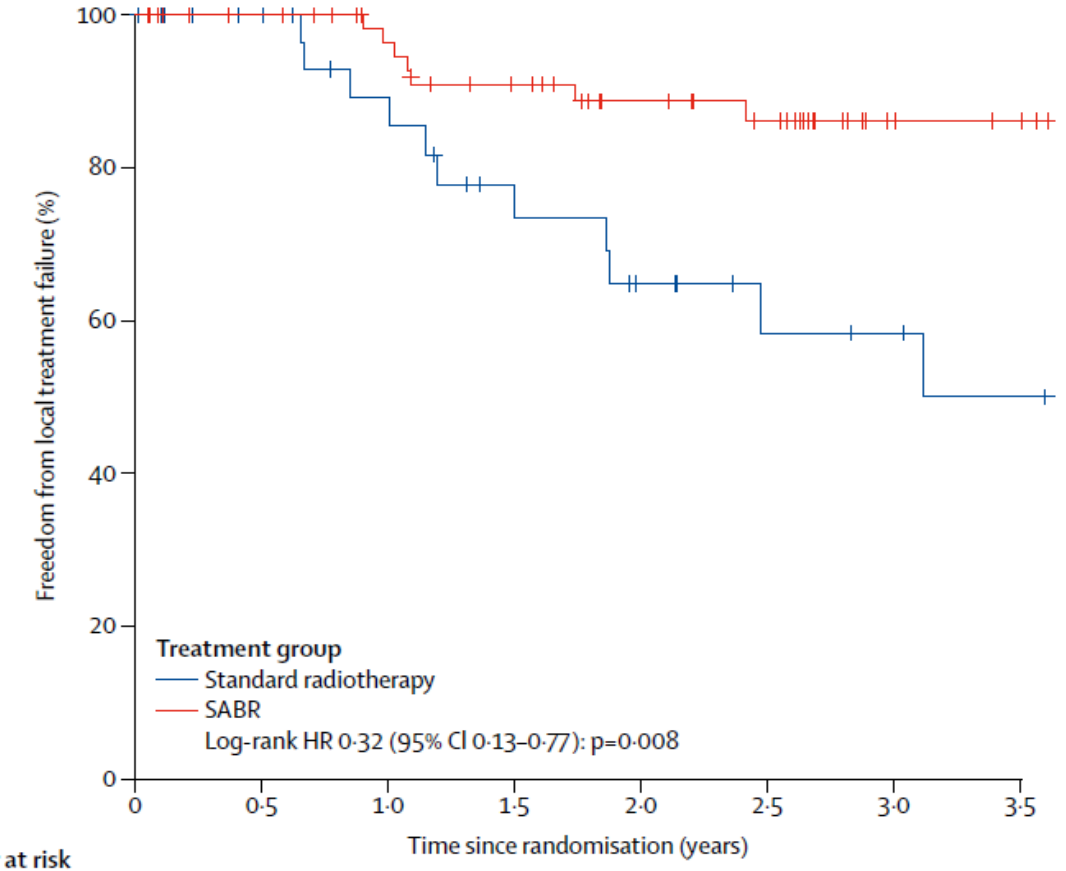
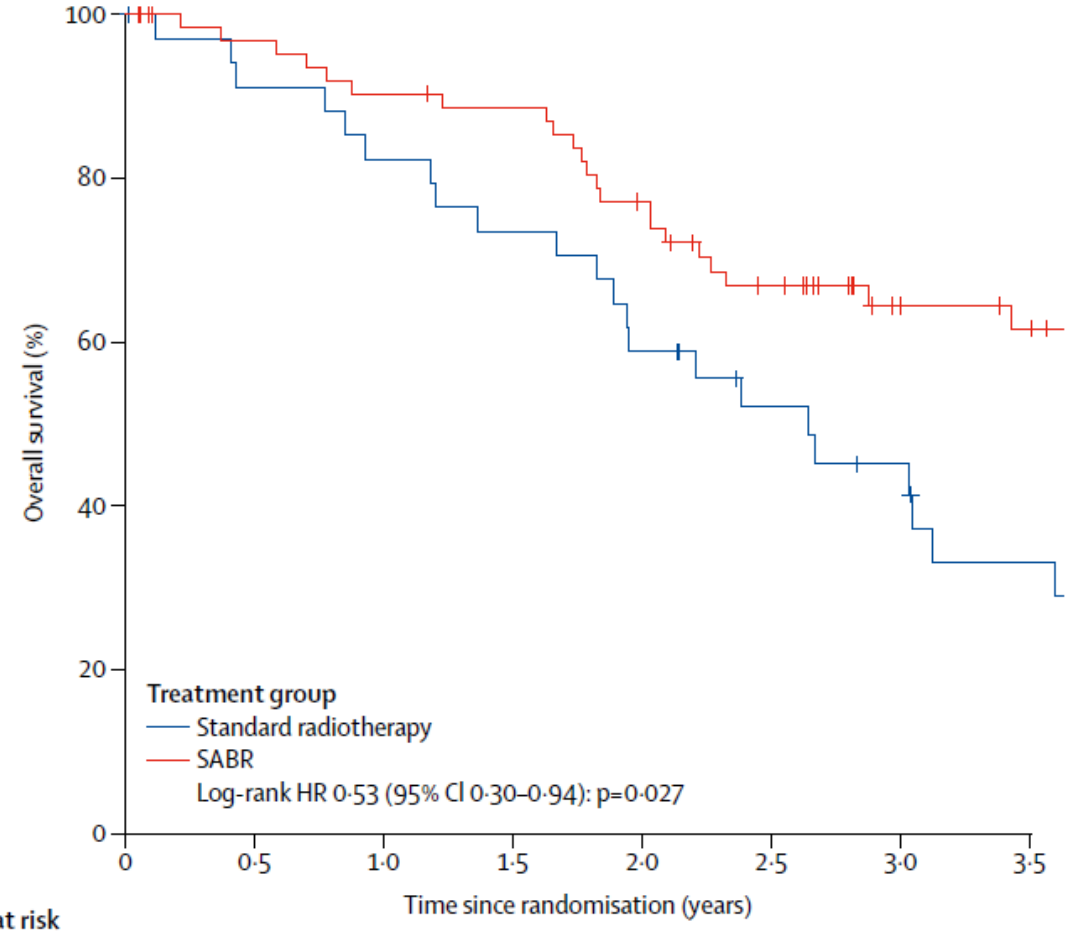
Senthi et al. Lancet Oncol 2012

CHISEL RCT



Number at risk (number censored)								
Standard radiotherapy	35 (0)	30 (5)	24 (8)	17 (11)	13 (13)	9 (16)	8 (17)	6 (18)
SABR	66 (0)	60 (6)	53 (11)	46 (15)	37 (23)	32 (27)	19 (40)	17 (42)



Number at risk (number censored)								
Standard radiotherapy	35 (0)	31 (1)	28 (1)	25 (1)	20 (1)	15 (4)	12 (5)	8 (6)
SABR	66 (0)	60 (4)	56 (4)	54 (5)	46 (6)	37 (9)	25 (20)	22 (22)

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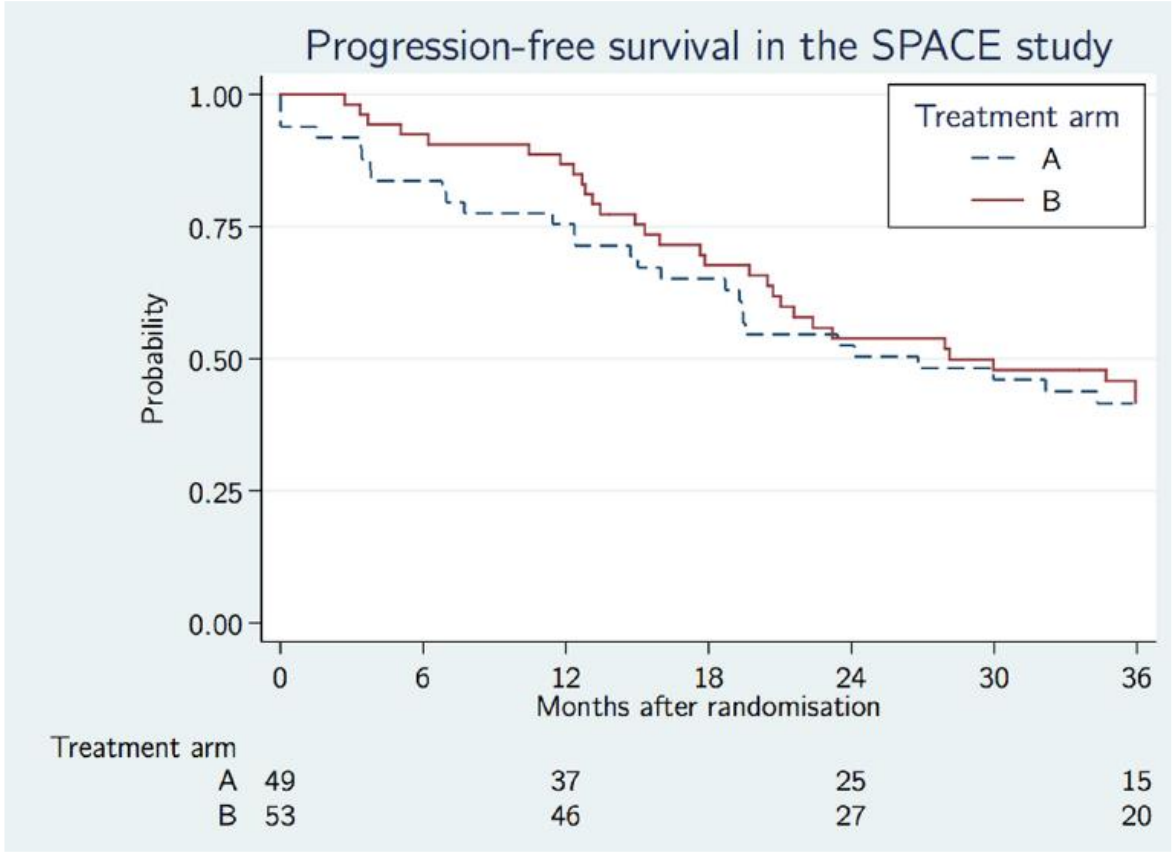
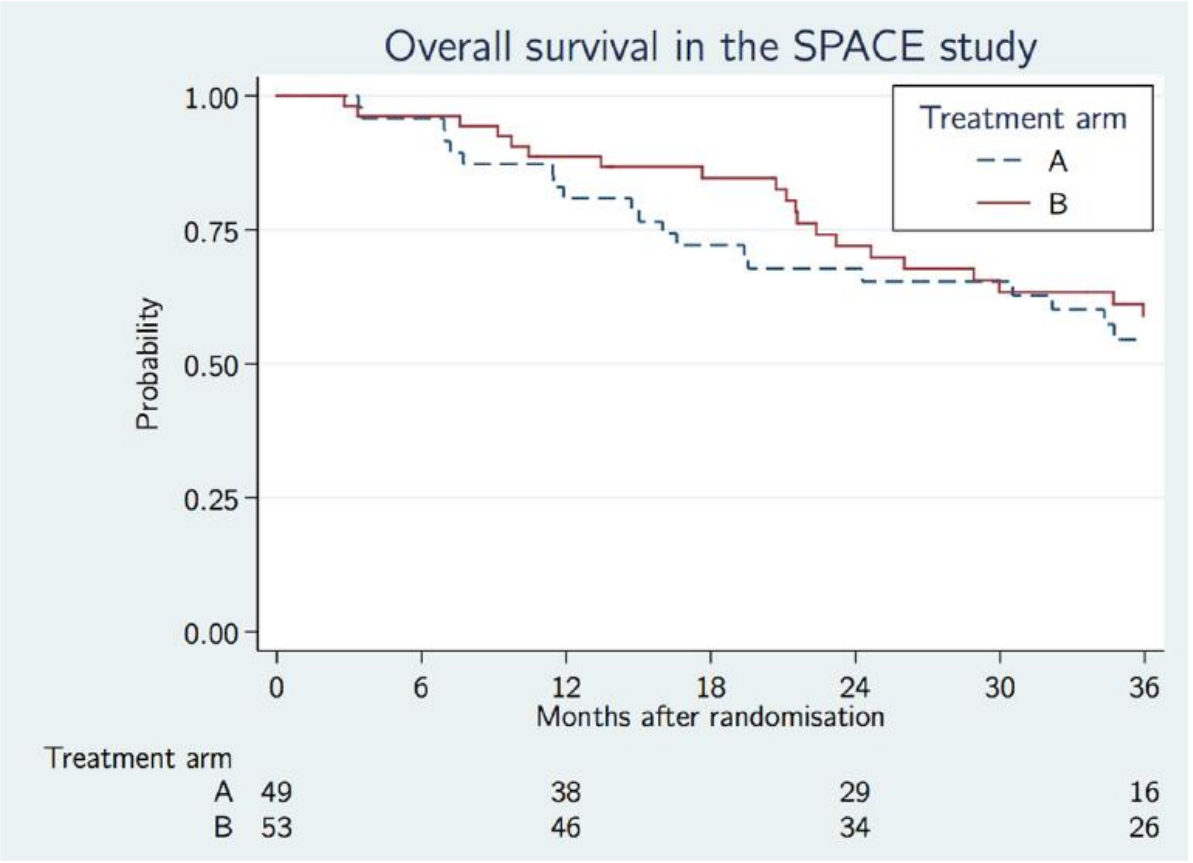
Ball et al. Lancet Oncol 2019

SPACE RCT

A=SBRT; B=3DCRT





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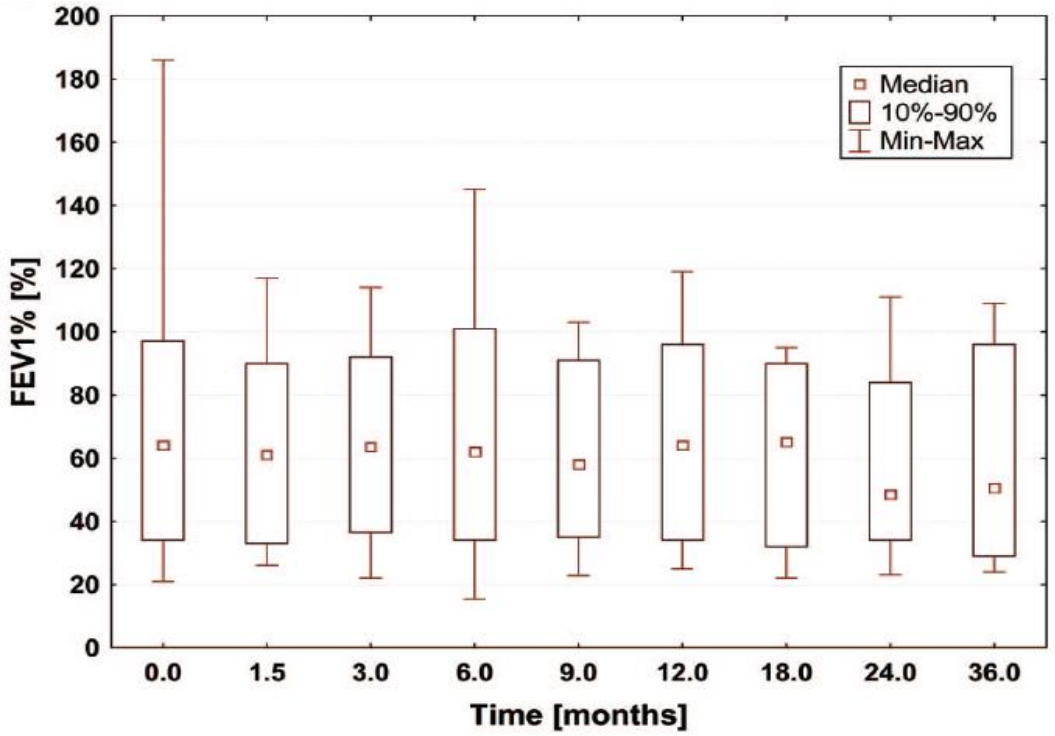
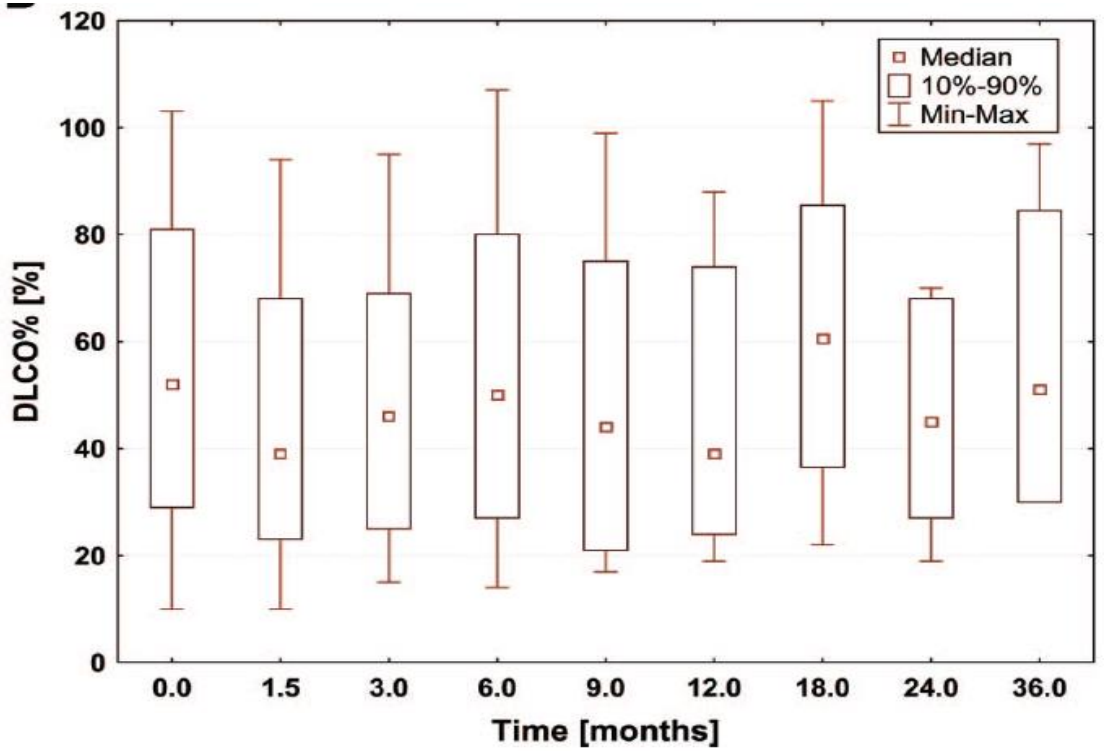
Nyman et al. Radiother Oncol 2016

SBRT: No change of FeV1 or DLCO over time





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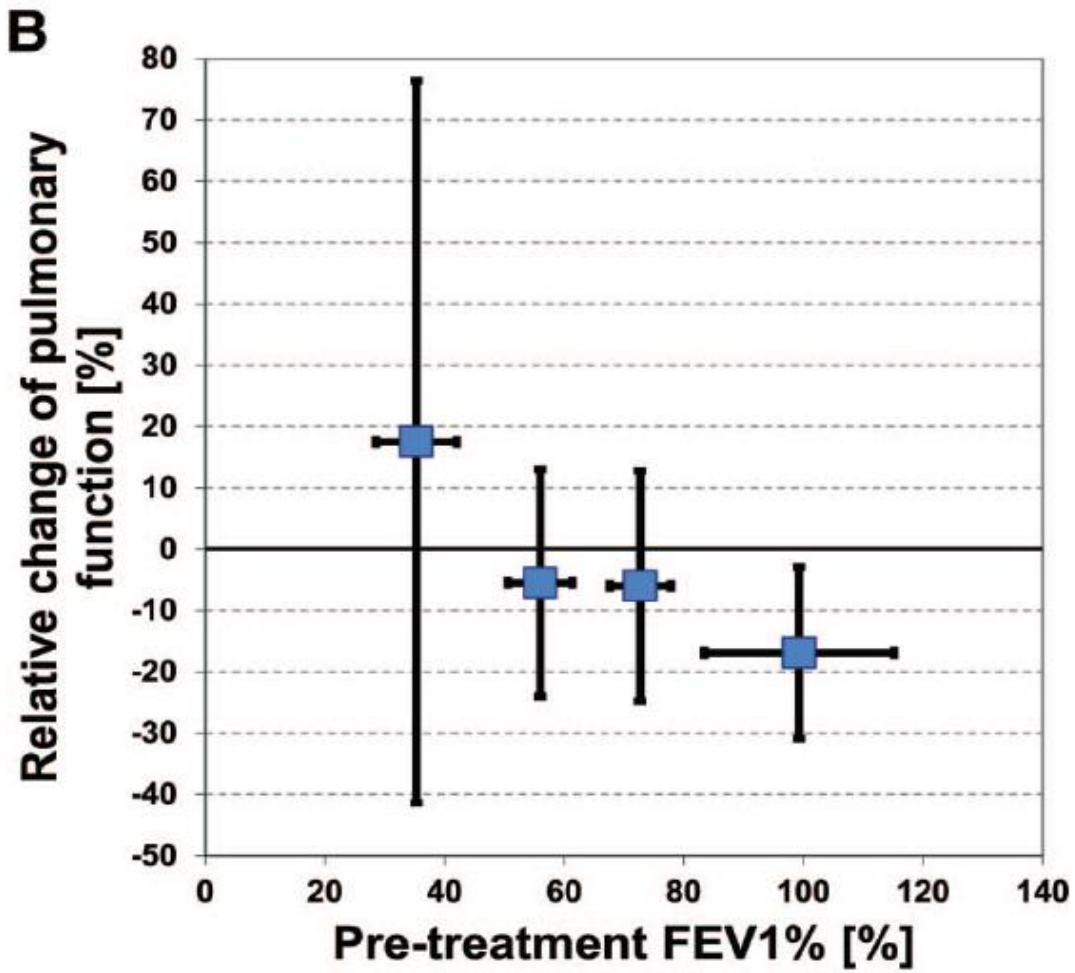
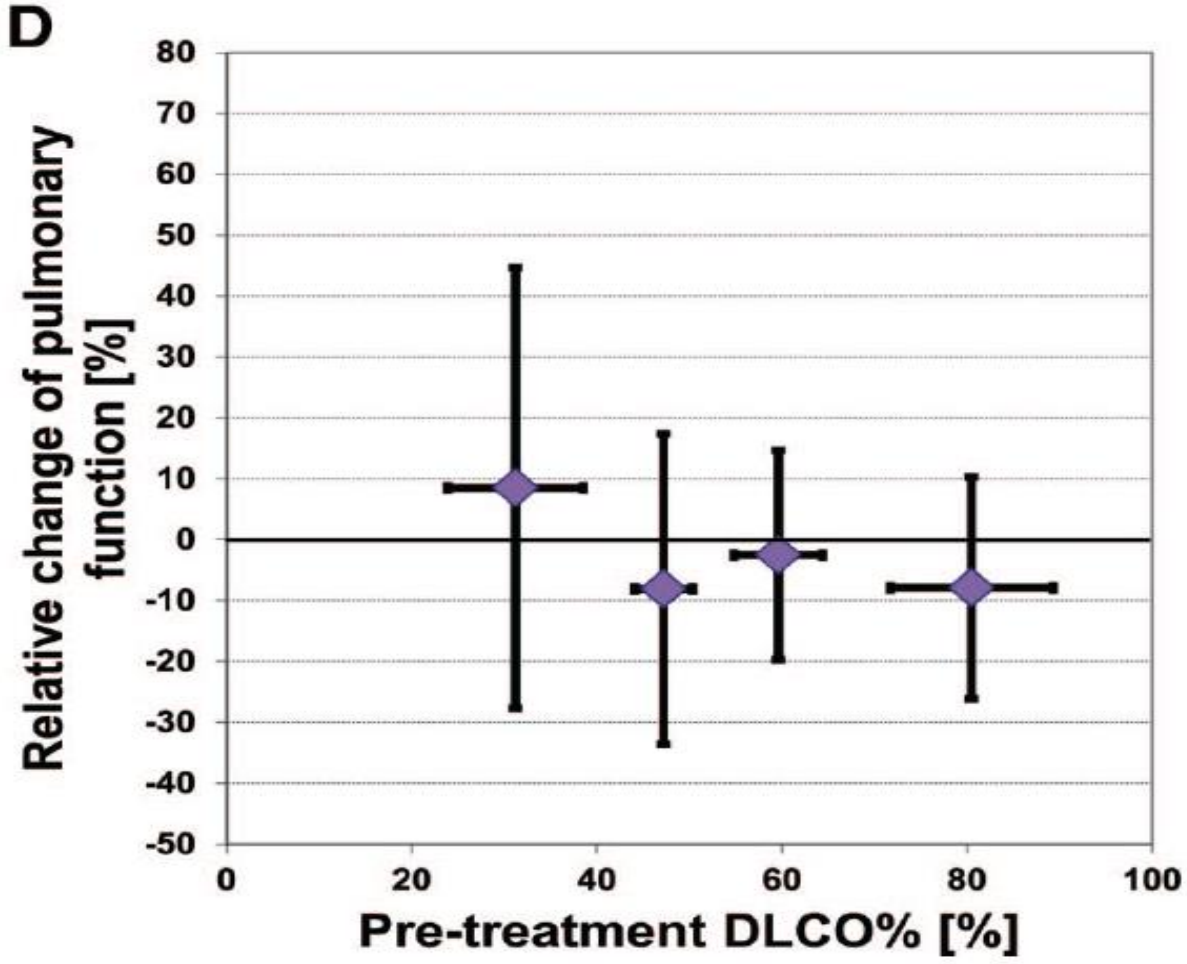
Guckenberger et al. J Thor Oncol 2012

SBRT: No decline in FeV1 or DLCO in patients with poor pulmonary function





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Guckenberger et al. J Thor Oncol 2012

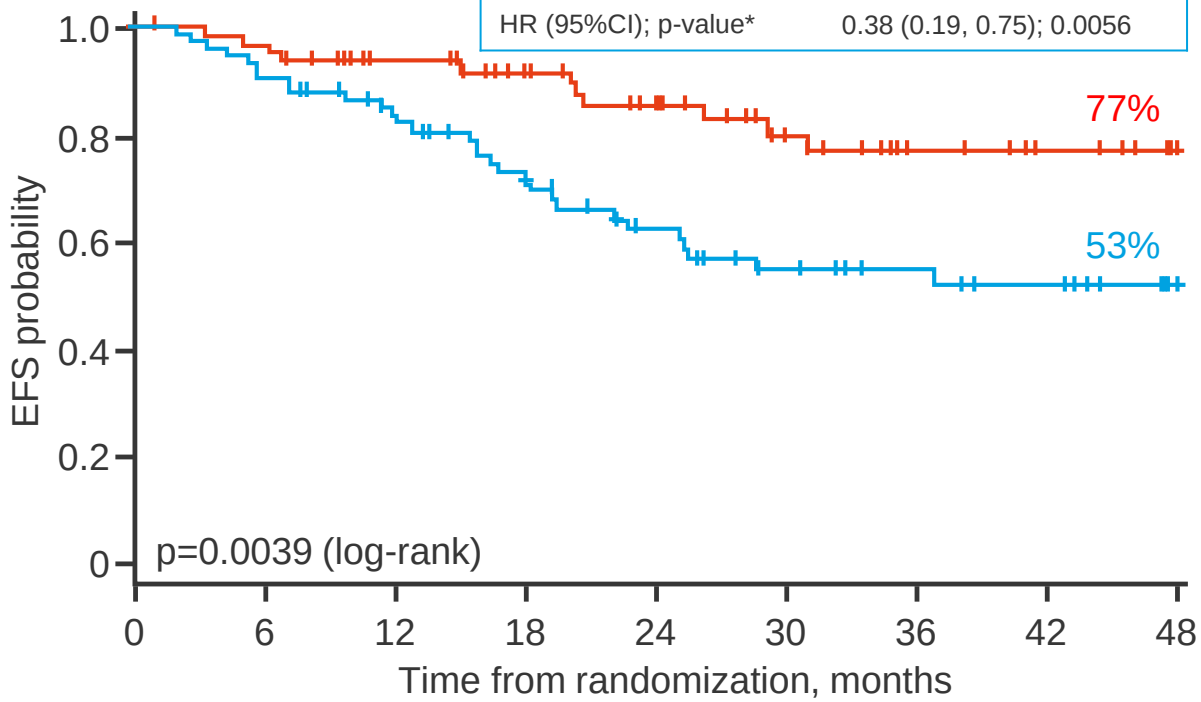
OA12.04: Nivolumab After Stereotactic Ablative Radiotherapy for Early-Stage Non-Small Cell Lung Cancer: Randomized I-SABR Trial – Chang JY, et al

- **Key results**

Event-free survival

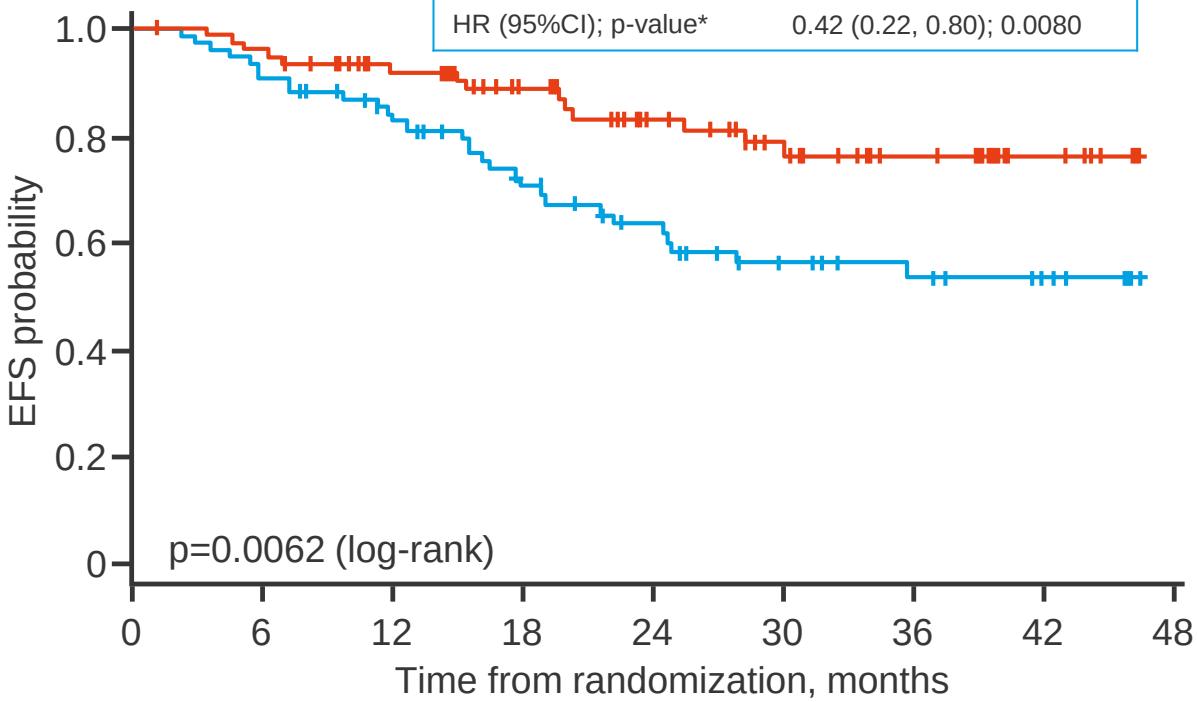
Per protocol

	I-SABR (n=66)	SABR (n=75)
Events, n	11	30
HR (95%CI); p-value*	0.38 (0.19, 0.75); 0.0056	



ITT

	I-SABR (n=75)	SABR (n=75)
Events, n	14	30
HR (95%CI); p-value*	0.42 (0.22, 0.80); 0.0080	



No. at risk (events)

I-SABR	66 (0)	54 (4)	38 (4)	18 (3)	7 (0)	75 (0)	62 (5)	43 (6)	22 (3)
SABR	75 (0)	59 (11)	34 (14)	22 (4)	11 (1)	75 (0)	59 (11)	34 (14)	22 (4)

*Cox model.

Chang JY et al. Lancet 2023

Chang JY, et al. J Thorac Oncol 2023;18(suppl 9):Abstr OA12.04

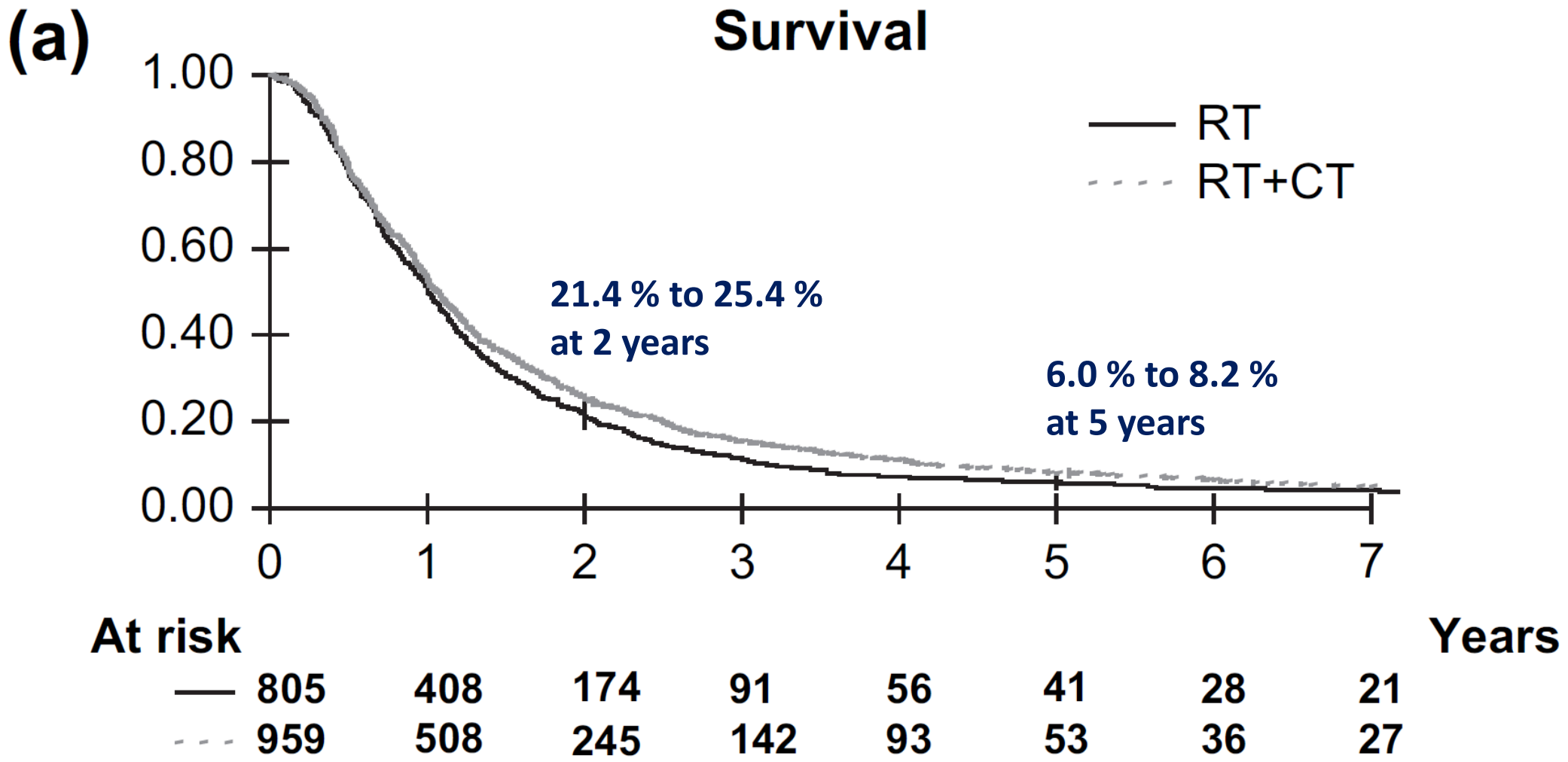
Conclusion: SBRT for inoperable patients

- Local tumour control at 5 years > 90 %
- Regional tumour control 80 %, Distant metastases: 30-40 %
- Severe toxicity < 5 %
- No decline in pulmonary function
- Safe in patients with severely impaired lung function
- **IPF is the major risk factor**
- (Ultra)- central tumors: in case of doubt: protracted schedule

De Ruysscher et al. J Clin Oncol 2010, Radiother Oncol 2017

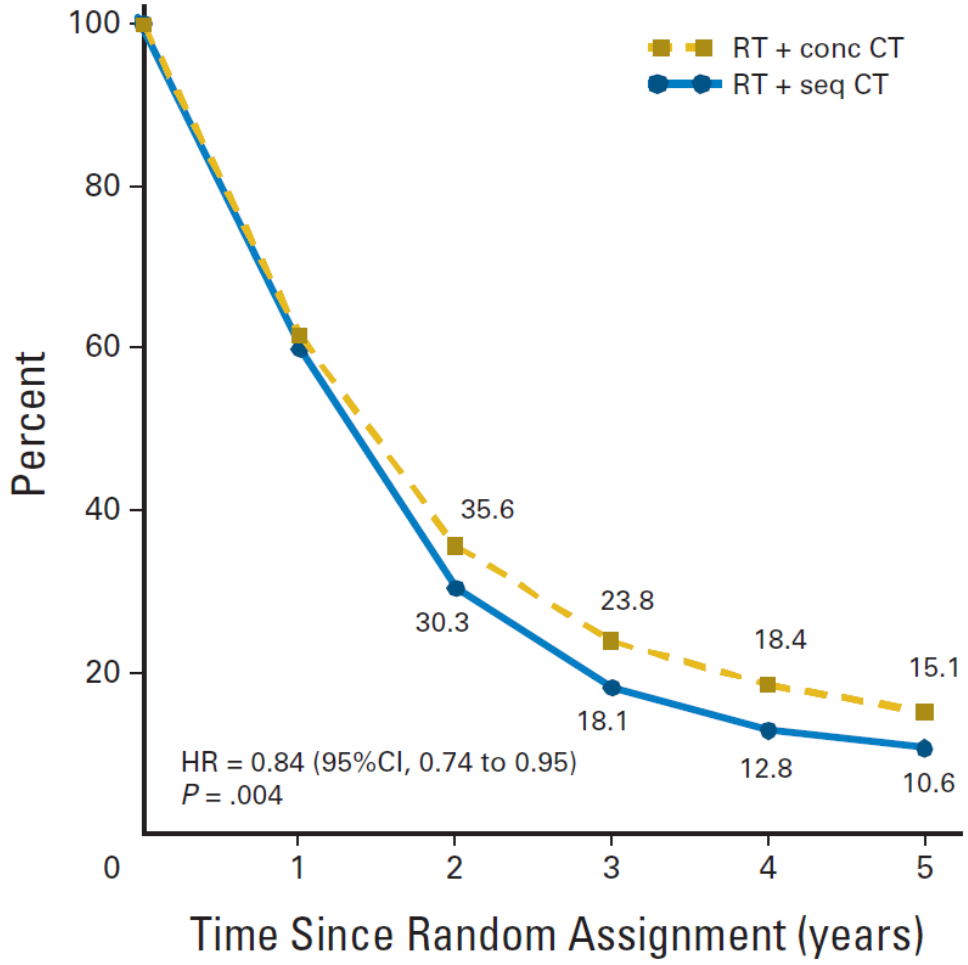
Locally advanced NSCLC

Sequential chemo-radiotherapy



Aupérin et al. Ann Oncol 2006

Concurrent chemo-radiotherapy



	Deaths/Person-Years by Period				
	0y–1y	1y–2y	2y–3y	3y–4y	> 4y
RT+ conc CT (n = 603)	240/498	147/276	67/171	30/116	37/186
RT+ seq CT (n = 602)	253/491	171/242	70/129	30/ 83	23/126

Aupérin et al. J Clin Oncol 2010

Integration of FDG-PET-CT in radiation planning

Mean esophageal dose decreased from 30.7 Gy to 17.2 Gy (p=0.004):

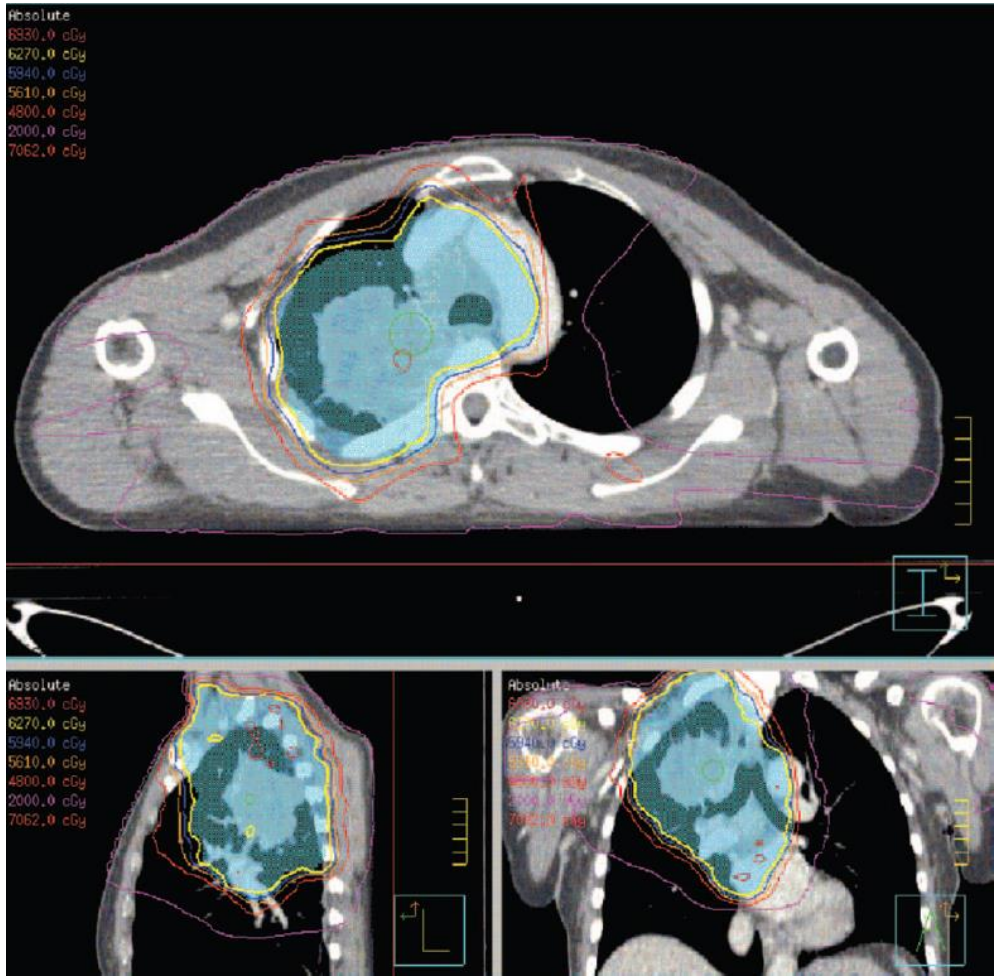
G3 esophagitis from 30 % to 18 %

Table 2. Patterns of recurrence

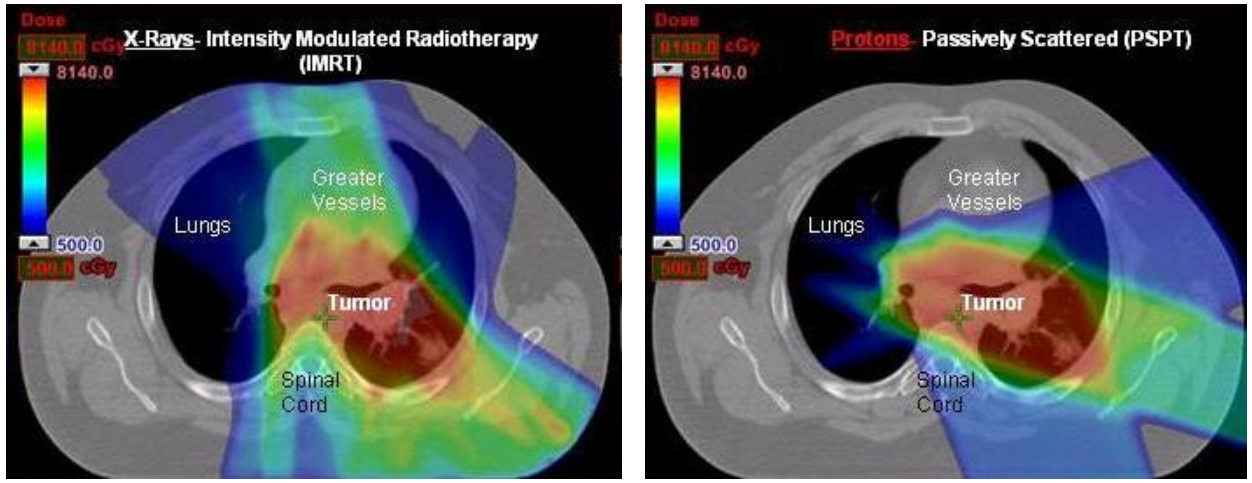
Recurrences	No. of patients (%)
None	26 (59)
In-field	10 (23)
Exclusively in-field	5
In-field and distant	5
Isolated nodal	1 (2)
Nodal (outside of CTV) along with local or distant failure	2 (4.5)
Distant only	7 (16)
Brain only	1

Abbreviation: CTV = clinical target volume.

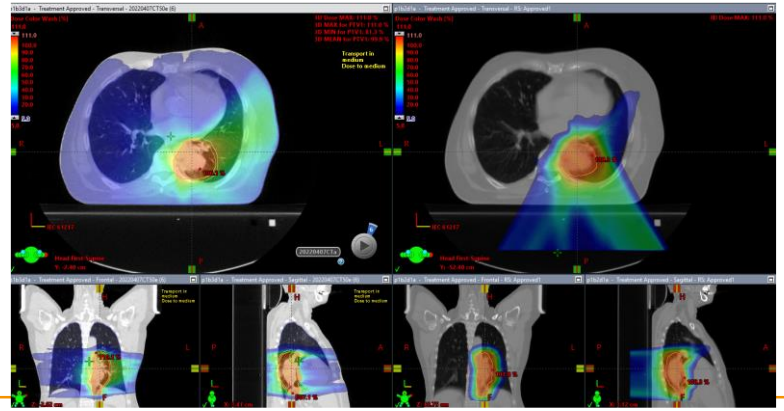
IMRT/ VMAT: very conformal for high-dose regions



Proton Therapy to reduce low-dose volumes



De Ruysscher D, Chang JY Sem Radiat Oncol 2014



IMPT

Mean Lung Dose
16 Gy ➔ 8 Gy
Mean Heart Dose
25 Gy ➔ 6 Gy

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Chan et al. J Thorac Oncol 2014

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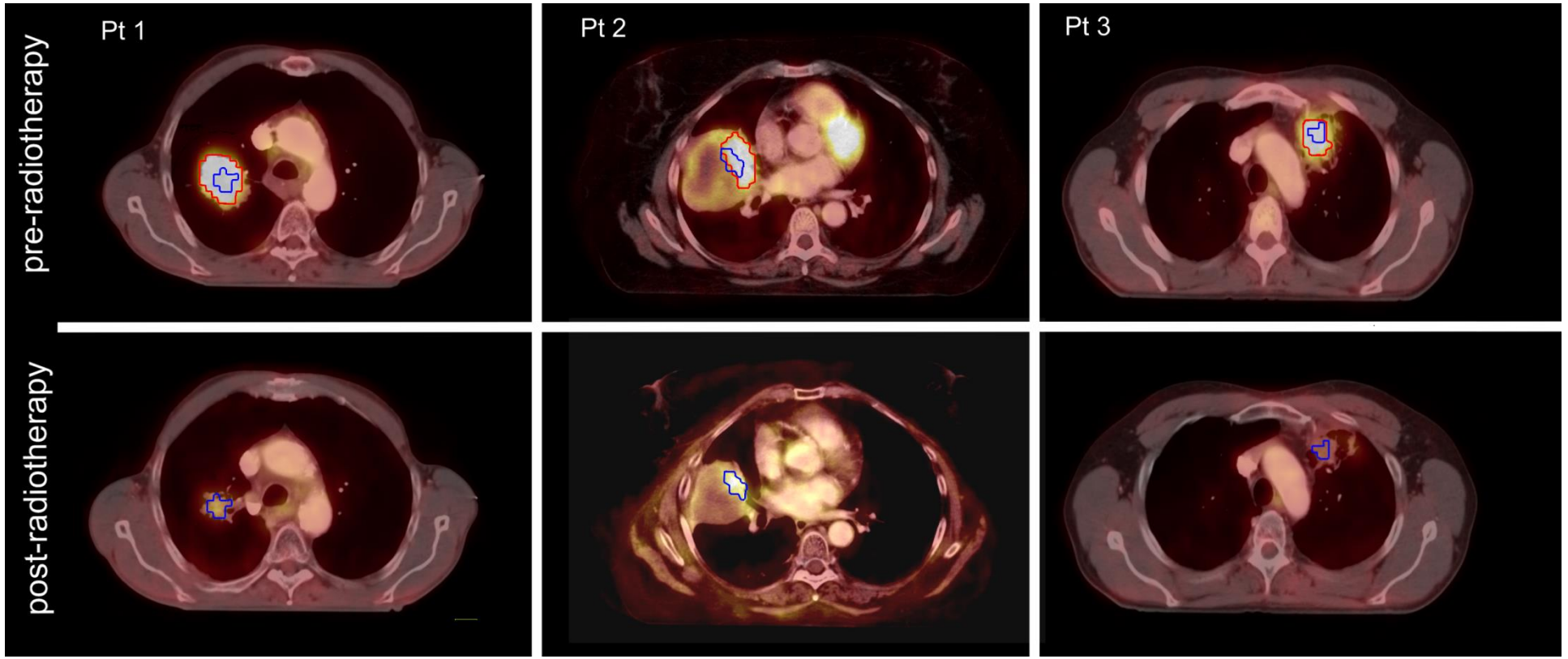
Tackling intra-tumor heterogeneity? PET-boost failed



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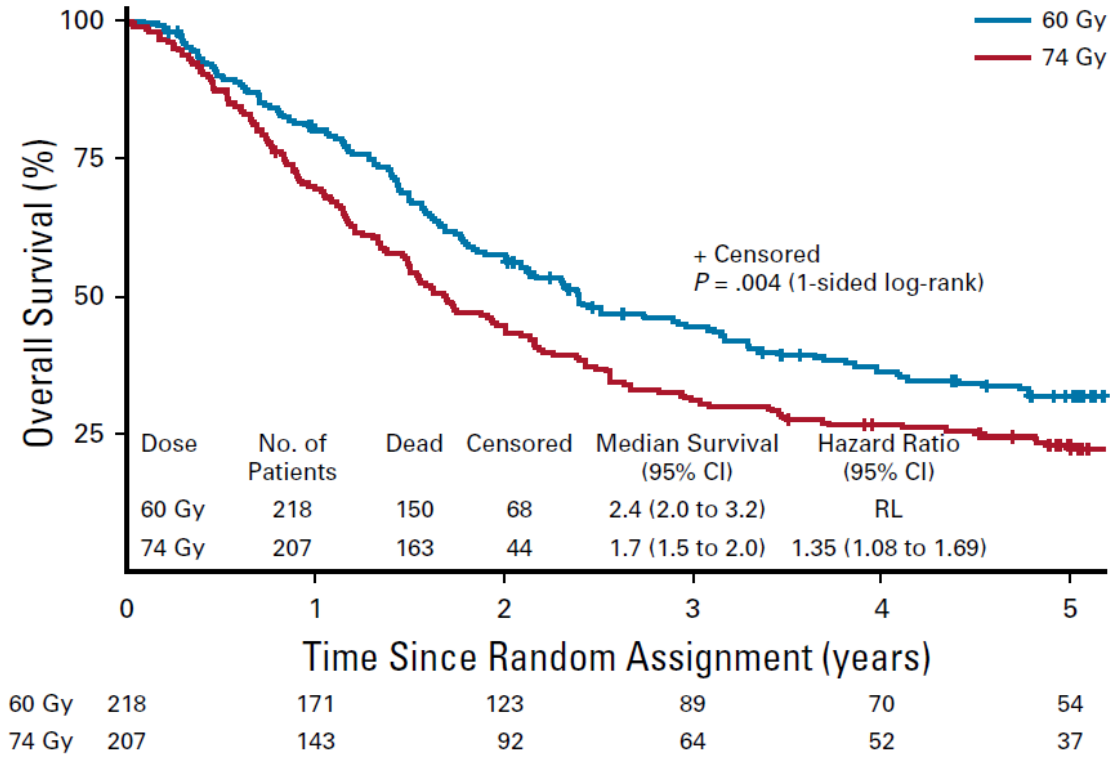
Aerts et al. Radiother Oncol 2009
van Diessen et al. Radiother Oncol 2019

Cooke et al. Radiother Oncol 2023

Erasmus MC Cancer Institute

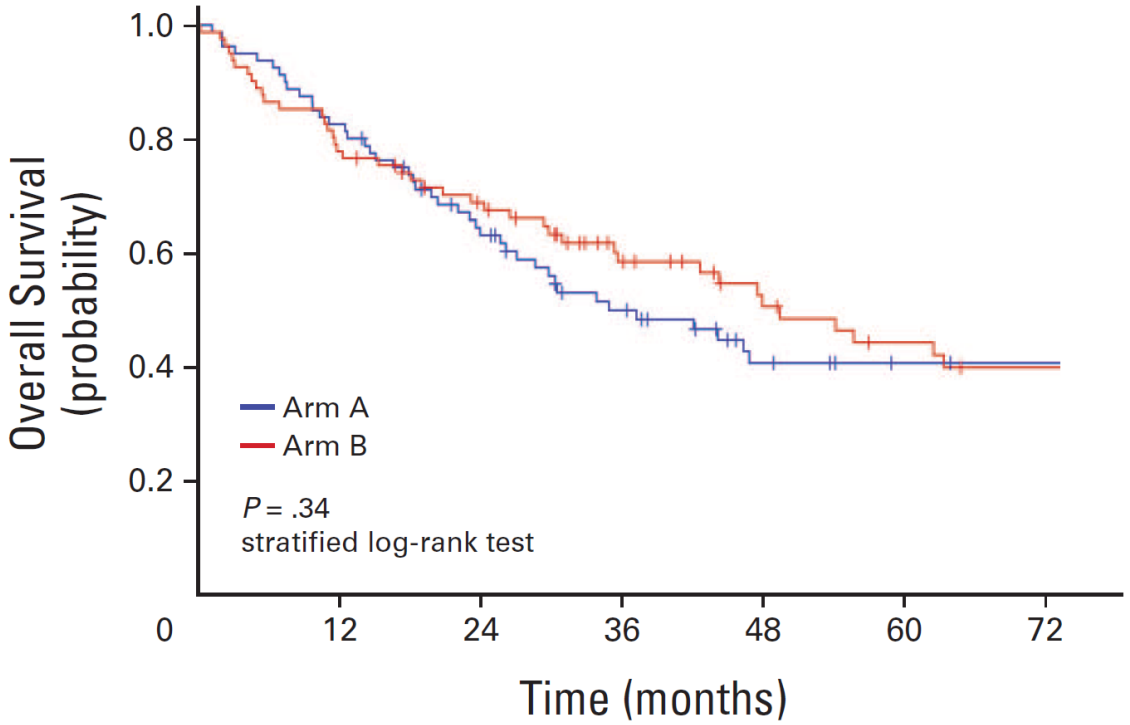
Dose-escalation in concurrent chemo-RT: RTOG 0617: Failed



	Standard Dose (60 Gy)		High Dose (74 Gy)		
Failure Pattern	**Failed, % (95% CI)**	**No. at Risk**	**Failed, % (95% CI)**	**No. at Risk**	***P***
Local	38.2 (31.7 to 44.8)	40	45.7 (38.7 to 52.4)	27	.07
Regional	35.7 (29.3 to 42.2)	37	38.4 (31.7 to 45.0)	27	.54
Locoregional	49.7 (42.8 to 56.3)	34	55.4 (48.3 to 61.9)	25	.17
Distant	52.3 (45.3 to 58.8)	36	57.6 (50.4 to 64.1)	24	.32

Bradley et al. J Clin Oncol 2019

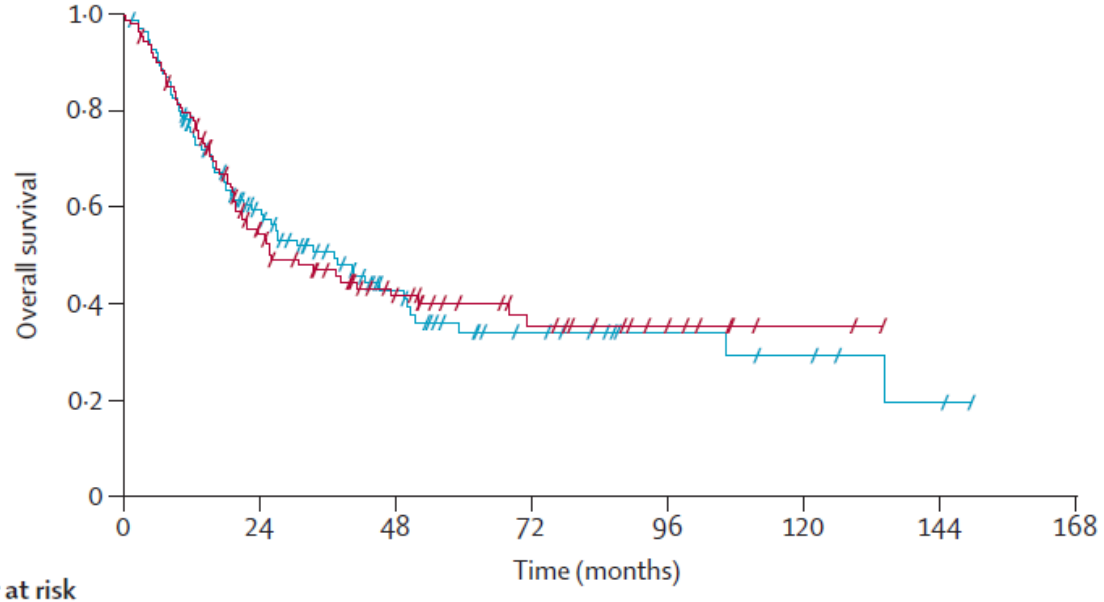
Addition of surgery: Failed



No. at risk

Arm A	80	66	47	32	20	16	15
Arm B	81	63	51	35	25	20	17

Eberhardt et al. J Clin Oncol 2015



Number at risk

Chemoradiotherapy group	117	57	27	13	7	5	2	0
Chemotherapy group	115	53	28	15	7	2	0	0

Pless et al. Lancet 2015

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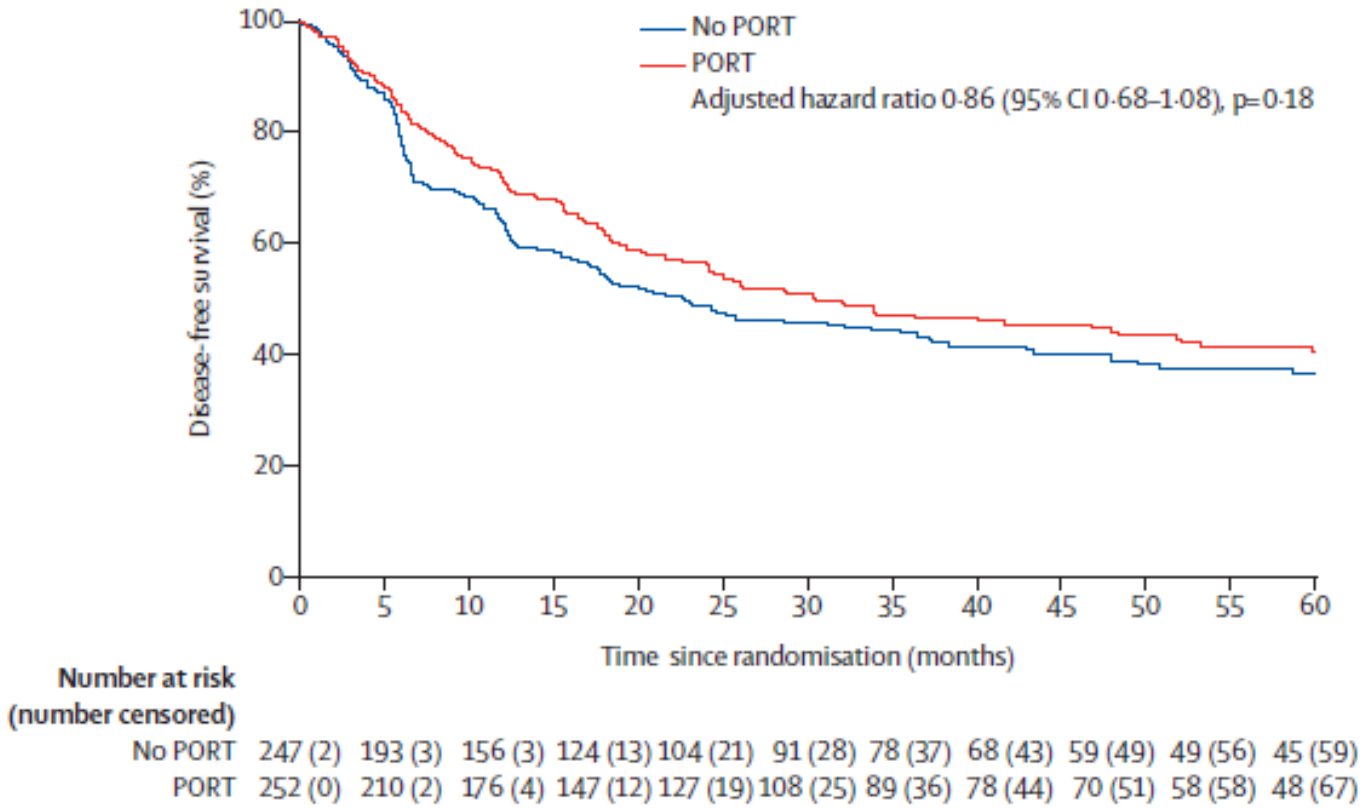
PORT reduces loco-regional relapses after complete resection: Lung-ART trial

	PORT group (n=252)	Control group (n=249)
All disease-free survival events	144	152
Relapses and metastases	123 (85%)	144 (95%)
Mediastinal relapse	36 (25%)	70 (46%)
	36/252 (14 %)	*70/249 (28 %)*
Death	21 (15%)	8 (5%)
Causes of death		
Cardiopulmonary	11 (8%)	0
	11/252 (4 %)	
Progression	1 (1%)	0
Second primary cancer	4 (3%)	2 (1%)
Vascular	0	1 (1%)
Unknown	3 (2%)	4 (3%)

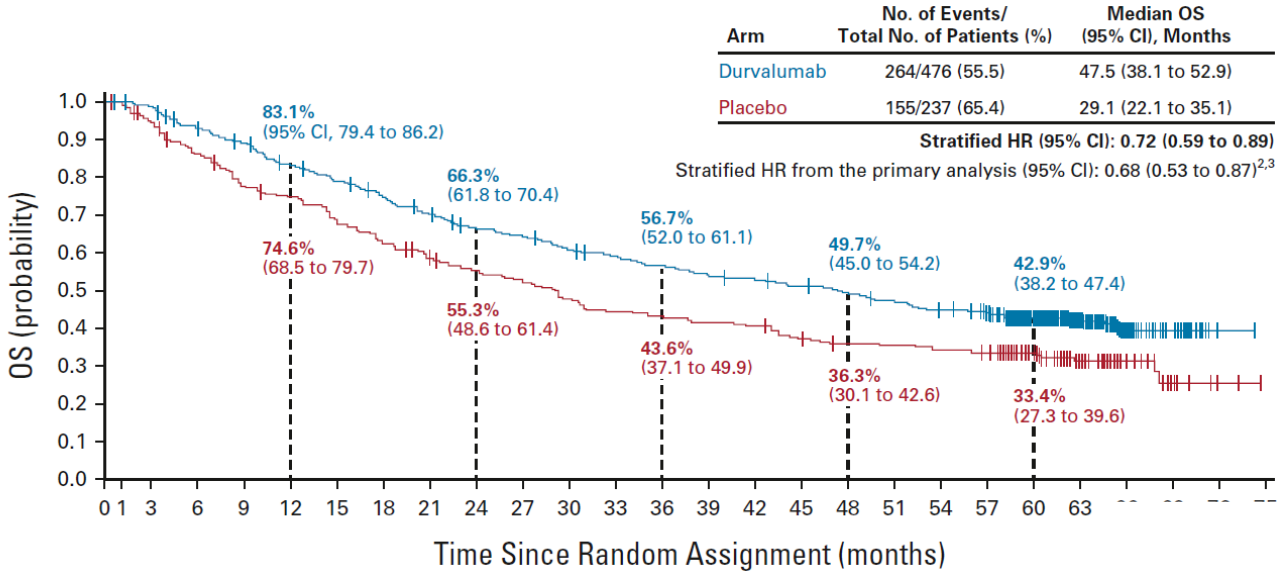
Data are n (%), regarding the number of patients with event. Patients can have several different events at the same time. PORT=postoperative radiotherapy.

Table 3: **Disease-free survival events**



Le Pechoux et al. Lancet Oncol 2022

PACIFIC: stage III NSCLC: concurrent chemo-RT → durvalumab



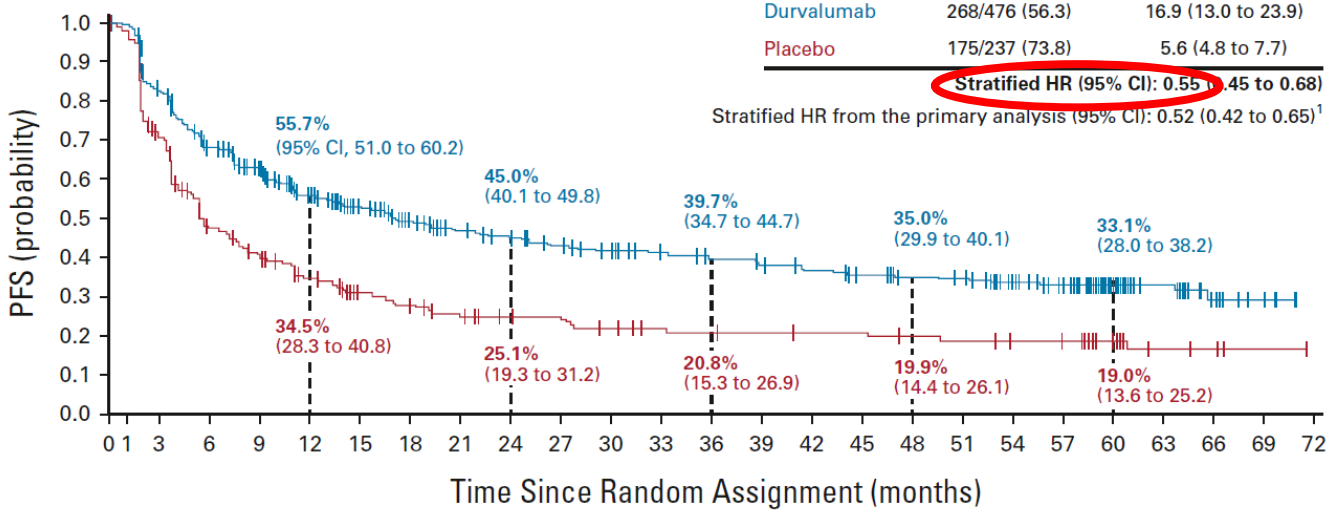
Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

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
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33



Arm	No. of Events/ Total No. of Patients (%)	Median PFS (95% CI), Months
Durvalumab	268/476 (56.3)	16.9 (13.0 to 23.9)
Placebo	175/237 (73.8)	5.6 (4.8 to 7.7)

Stratified HR (95% CI): 0.55 (0.45 to 0.68)

Stratified HR from the primary analysis (95% CI): 0.52 (0.42 to 0.65)[1]

No. at risk:

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

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Spigel et al. J Clin Oncol 2022

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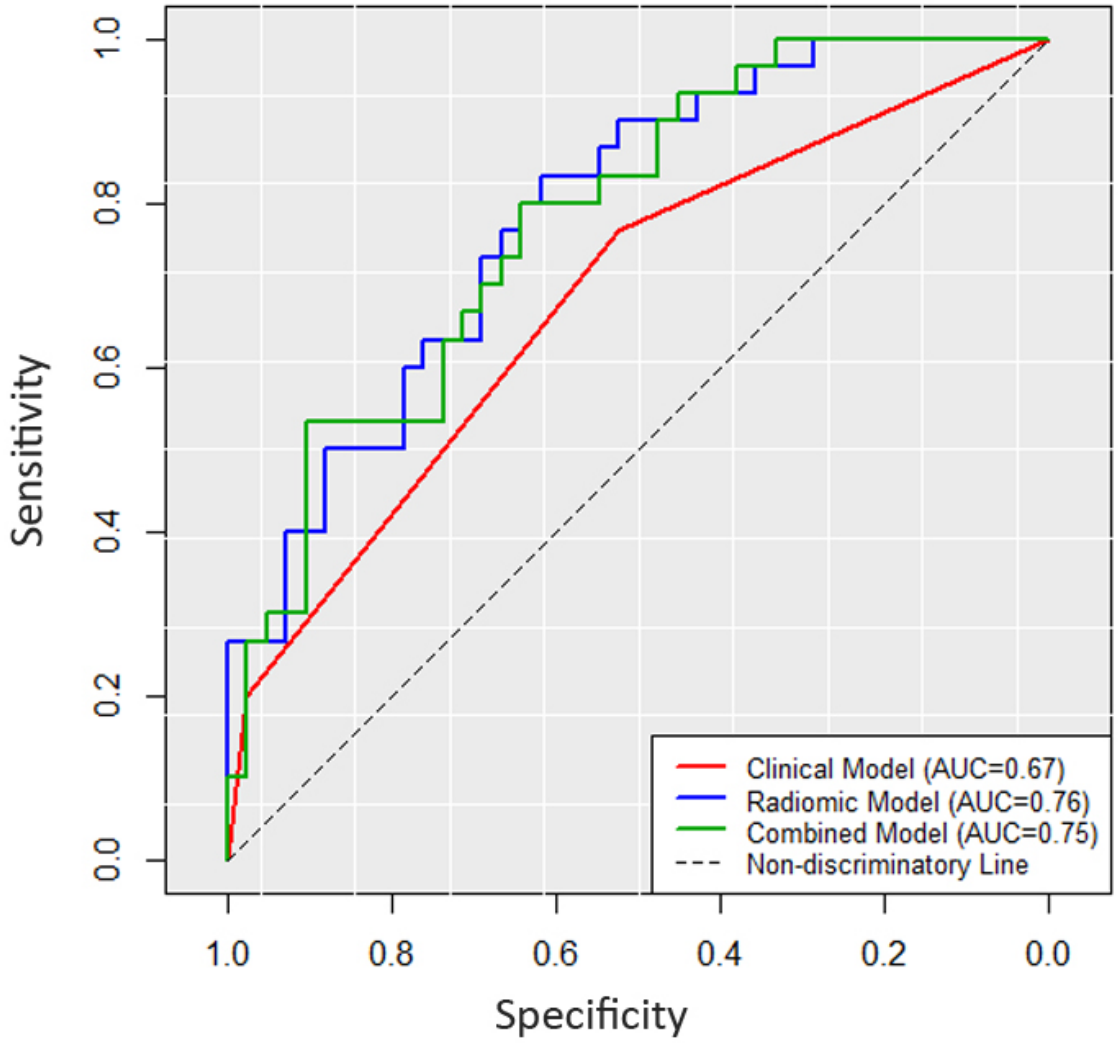
What is the cause of pneumonitis? Deep learning



		Clinical model		Radiomic model		Combined model	
		IIP	OTP	IIP	OTP	IIP	OTP
Observed outcome	IIP	23	7	25	5	24	6
	OTP	20	22	16	26	15	27
Sensitivity (%)		77		83		80	
Specificity (%)		52		62		64	
PPV (%)		53		61		62	
NPV (%)		76		84		82	
Accuracy (%)		62		71		71	
AUC (95% CI)[a]		0.67 (0.56 to 0.79)		0.76 (0.68 to 0.88)		0.75 (0.67 to 0.88)	
Brier score (95% CI)		0.21 (0.14 to 0.23)		0.19 (0.11 to 0.21)		0.19 (0.11 to 0.21)	

Abbreviations: AUC, Area under the ROC Curve; CI, Confidence Interval; IIP, Immunotherapy-Induced Pneumonitis; NPV, Negative Predictive Value; OTP, Other Types of Pneumonitis; PPV, Positive Predictive Value.

[a] Comparison of AUCs using n=1000 bootstrap samples:

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Tohidinezhad et al. Eur J Cancer 2023

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Conclusion: Stage III NSCLC

- Most fit patients qualify for concurrent chemo-radiotherapy followed by durvalumab immunotherapy
- Recurrences remain a major problem
- Optimal local treatment remains debatable
- Many questions remain

Oligometastatic NSCLC

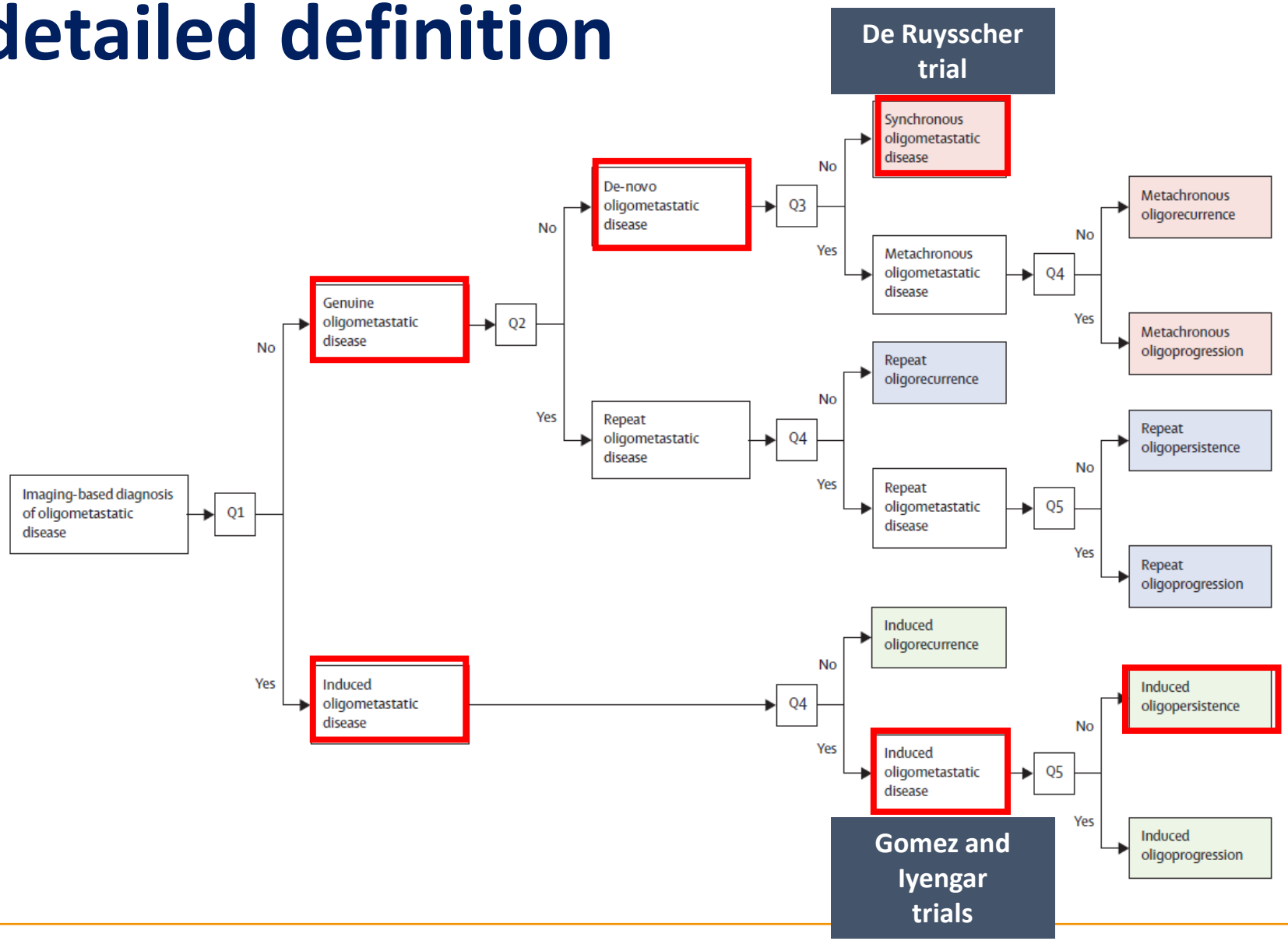
Oligometastatic definitions

synchronous	Time of initial diagnosis
oligopersistent	Persistent disease in limited number of sites after/on systemic disease
oligoprogressive	Progression in limited number of metastasis
oligorecurrent	Recurrence after control of localized primary tumor

EORTC: Maximum of five metastases and three organs
Mediastinal lymph node involvement is not counted as a metastatic site

Dingemans AC et al. J Thorac Oncol 2019

More detailed definition



Guckenberger et al. Lancet Oncol 2020

Actual series/trial inclusion vs criteria

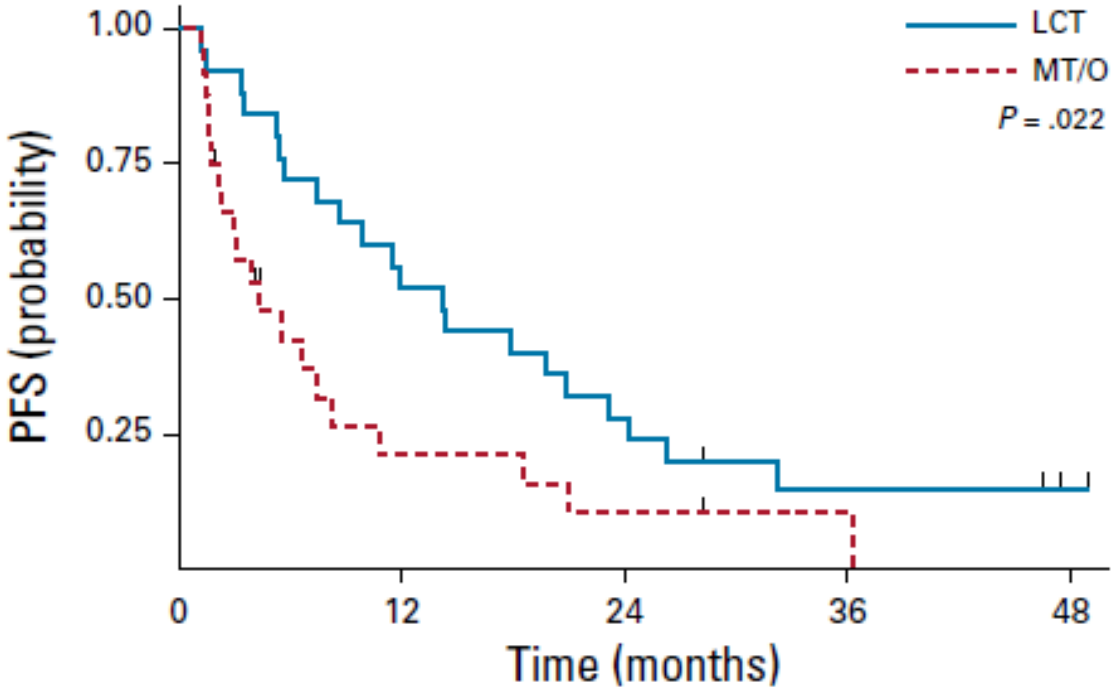
Articles	Number of patients	Maximal number metastases defined	Maximal number of metastases treated	Patients with ≤ 2 metastases treated (%)
Downey R. 2002	23	1	1	100%
Khan A. 2006	23	2	2	100%
Inoue St et al. 2010	25	5	5	N.A.
Cheruvu P. 2011	38	8	8	N.A
Collaud S. 2012	29	1	1	100%
Congedo M. 2012	53	2	2	100%
De Ruysscher D. 2012	40	5	3	97.4%
Lopez Guerra J. 2012	78	4	4	91%
Griffioen G. 2013	61	3	3	96.7%
Nieder C.S. 2014	23	3	2	100%
Parikh R. 2014	186	5	5	74%
Sheu T. 2014	90	3	3	88%
Plones T. 2015	56	5	4	99%
Su Ss. 2015	198	3	3	56%*
Xanthopoulos E. et al. 2015	25	4	4	84%
Fleckenstein J. 2016	39	5	5	90%
Johnson K. 2016	37	5	N.A.	N.A.
Sakai Ks.2016	18	5	N.A.	N.A.
Su Ss. 2016	91	4	N.A.	N.A.
Iyengar P. 2017	29	5	3	93%**
Gomez D. 2019	49	3	3	98%
Bauml JM. 2019 [3]	51	4	4	94%
Arrieta O. 2019 [4]	37	5	N.A.	65%

Most: 3-5

Included: ≤2

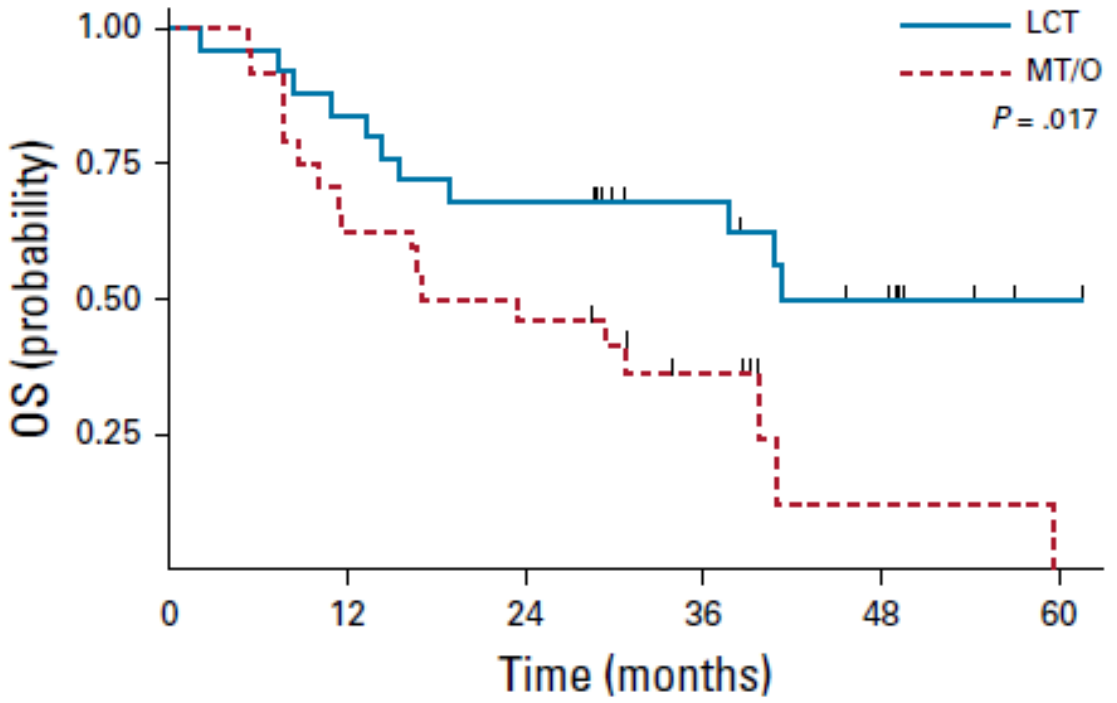
Giaj Levra N et al. Lung Cancer 2019

Randomized study after response on chemotherapy/ TKI



No. at risk

LCT:	25	13	7	3	1
MT/O:	24	4	2	1	0



No. at risk

LCT:	25	21	17	12	7	1
MT/O:	24	15	11	6	1	0

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Gomez et al. J Clin Oncol 2019

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SABR-COMET: *Controlled* primary tumor; metachronous

Characteristic	Arm, No. (%) Control (n = 33)	SABR (n = 66)
Median age, years (IQR)	69 (64-75)	67 (59-74)
Sex		
Male	19 (58)	40 (61)
Female	14 (42)	26 (39)
Site of original primary tumor		
Breast	5 (15)	13 (20)
Colorectal	9 (27)	9 (14)
Lung	6 (18)	12 (18)
Prostate	2 (6)	14 (21)
Other	11 (33)	18 (27)
Median time from diagnosis of primary tumor to random assignment, years (IQR)	2.3 (1.3-4.5)	2.4 (1.6-5.3)

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Palma et al. J Clin Oncol 2020

Erasmus MC Cancer

Radiation Therapy for Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline

Developed in collaboration with the European Society for Radiotherapy and Oncology

Endorsed by the Canadian Society of Radiation Oncology and the Royal Australian and New Zealand College of Radiologists

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Iyengar et al. Pract Radiat Oncol 2023

Conclusion: Oligometastatic NSCLC

- A small group of these patients will experience a long PFS and OS by adding a local treatment to all metastatic sites to systemic therapy
- Probably the best is to begin with the best available systemic treatment, in case of a response or clinical improvement, add local therapy
- Many questions unanswered

What you may optimize now: Supportive care

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

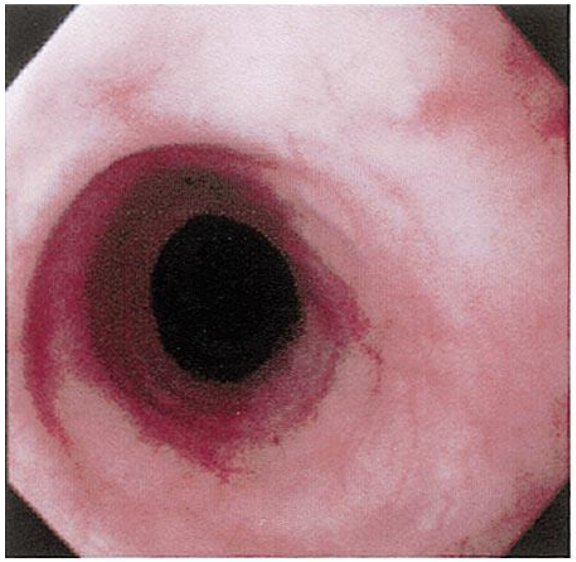
REVIEW

Recommendation for supportive care in patients receiving concurrent chemotherapy and radiotherapy for lung cancer☆

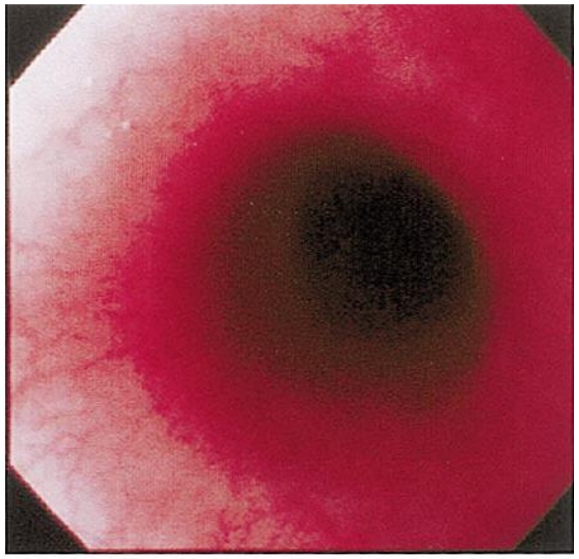
D. De Ruysscher[1*], C. Faivre-Finn[2], K. Nackaerts[3], K. Jordan[4], J. Arends[5], J. Y. Douillard[6], U. Ricardi[7] & S. Peters[8]

Endoscopic findings of radiation-induced esophagitis

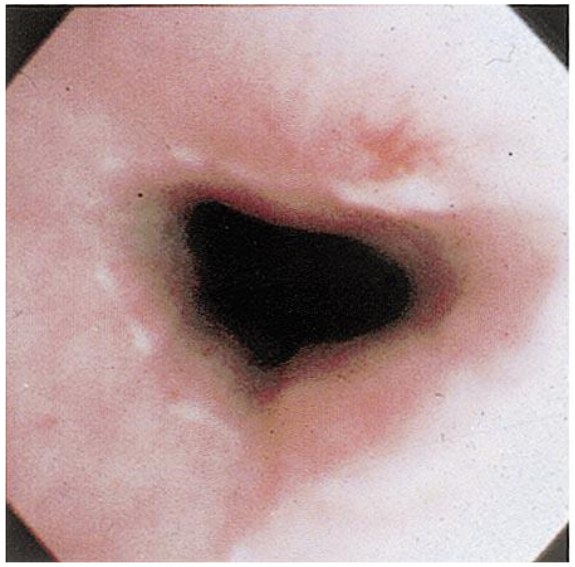
Normal



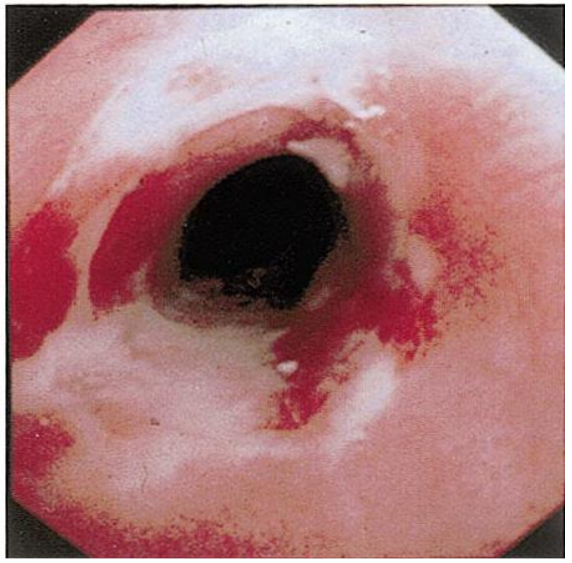
Grade 1



Grade 2



Grade 3



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Hirota et al. Radiother Oncol 2001

Conclusions

- Because of the increased esophageal transit time and the healing time of esophagitis, the administration of a proton pump inhibitor at a daily dose of 40 mg, up to three months after the end of radiotherapy is recommended (level V, grade B).
- Because esophageal candidiasis frequently occurs, patients with grade 2 or more esophagitis may be given appropriate anti-fungal drugs (level V, grade B.
- Symptomatic care, such as the administration of local anaesthetics (e.g. lidocaine), systemic analgesics including opioids, and appropriate feeding, incl. naso-gastric tube, is essential (level V, grade A).

Practical recommendations

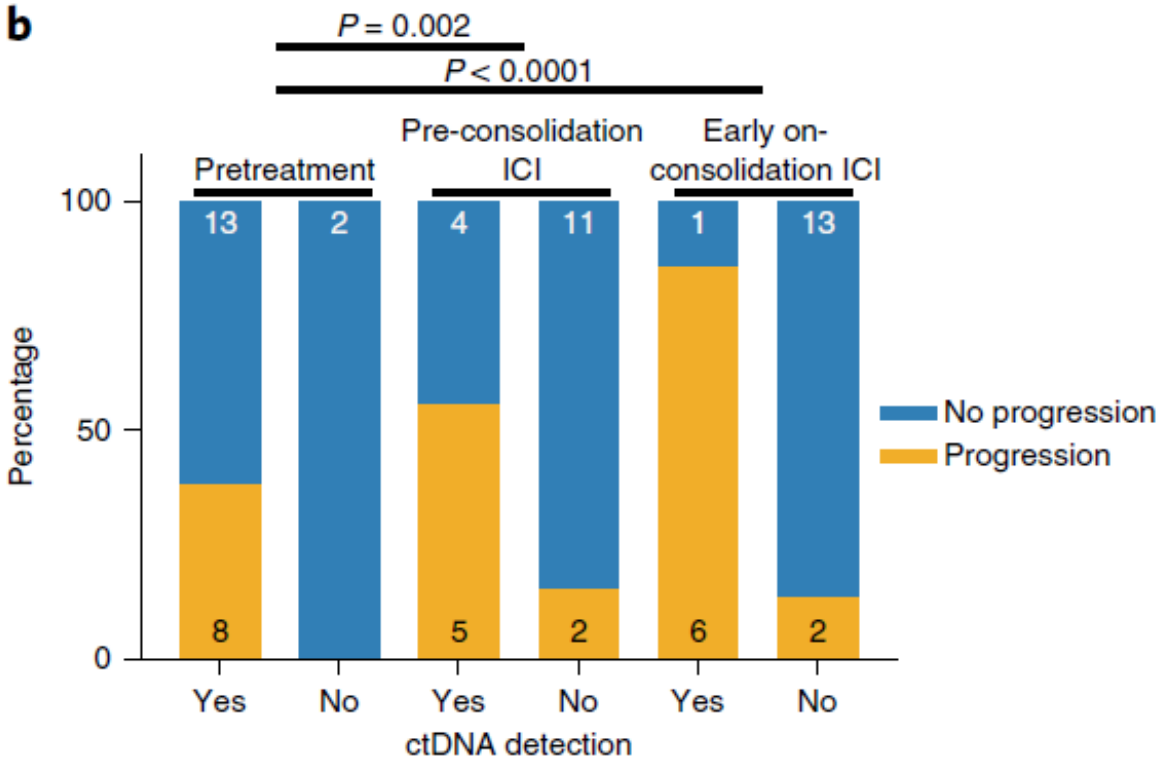
Screen for	malnutrition	NRS, Nutrition Risk Screening 2002
	sarcopenia	SARC-F
	systemic inflammation	mGPS, modified Glasgow Prognostic Score
	fatigue	FSI, Fatigue Symptom Inventory
	depression	PHQ-2, Public Health Questionnaire

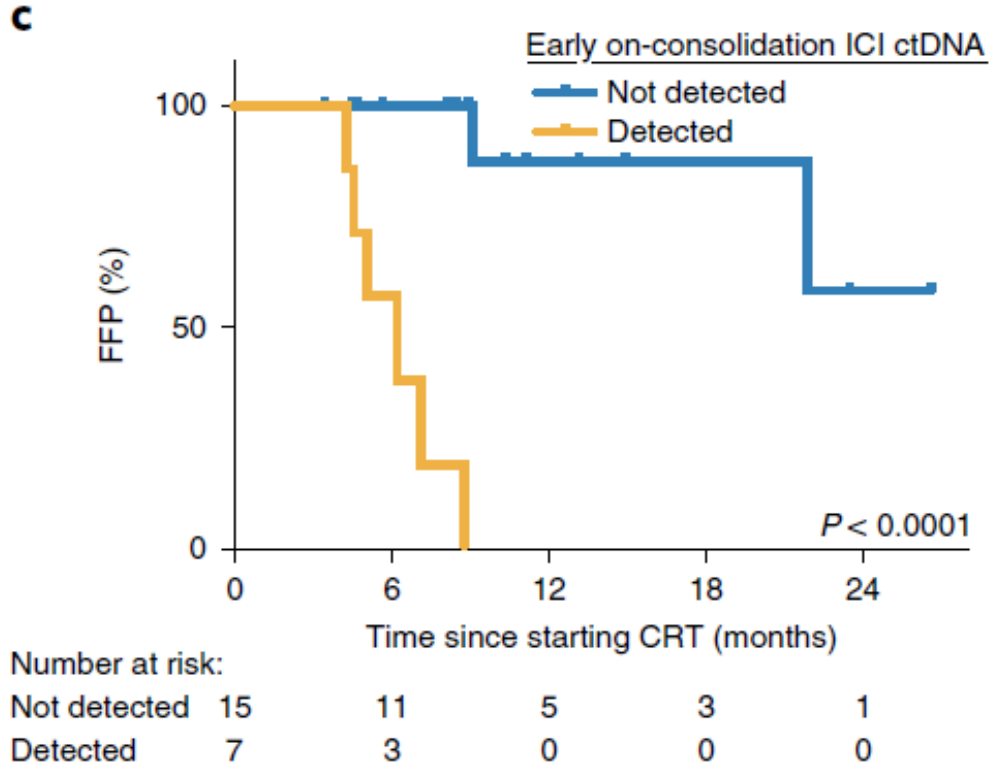
Practical recommendations

Aim for	**energy**	25-35 kcal/kg body weight
	protein	1.0- 1.5 g/kg
	micronutrients	RDA
Artificial nutrition	**ONS**, oral nutritional supplements	
	add **parenteral nutrition** if oral inadequate	

The future

cf tumor DNA: Who needs durvalumab?





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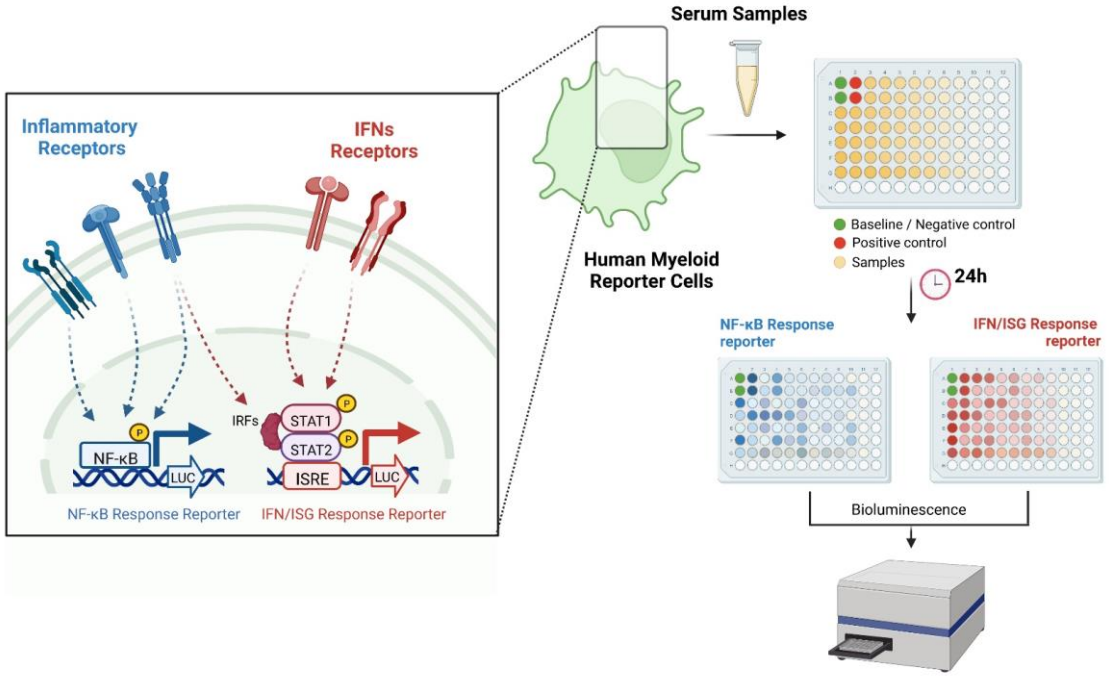
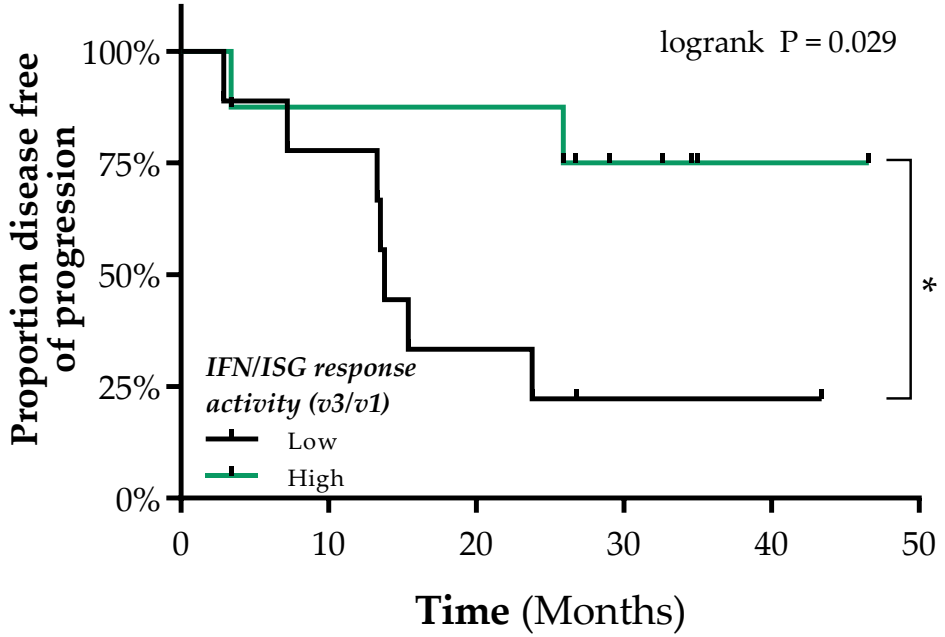
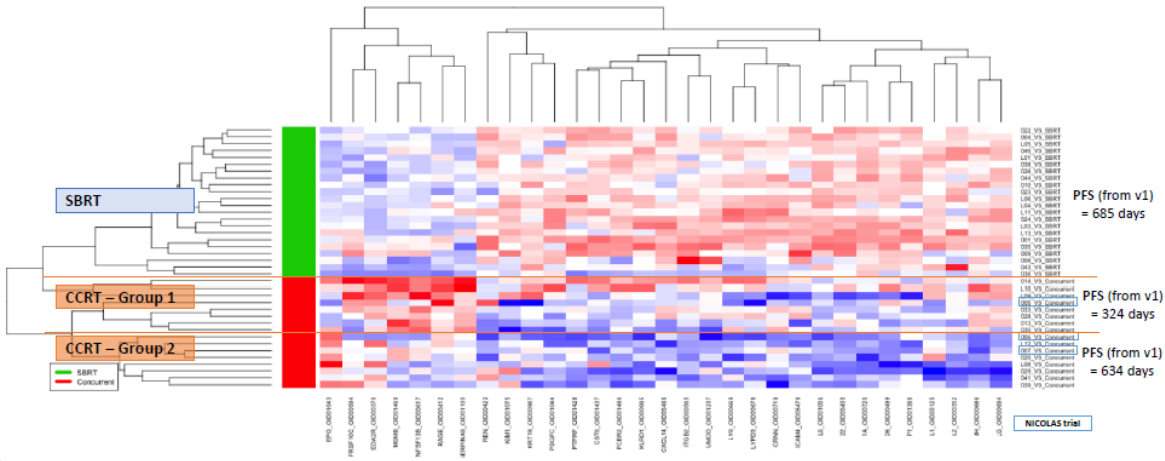
Moding et al. Nature Cancer 2020

Erasmus MC Cancer

Identify prognostic and predictive biomarkers in the blood







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Sprooten et al. J Immunother Cancer 2021

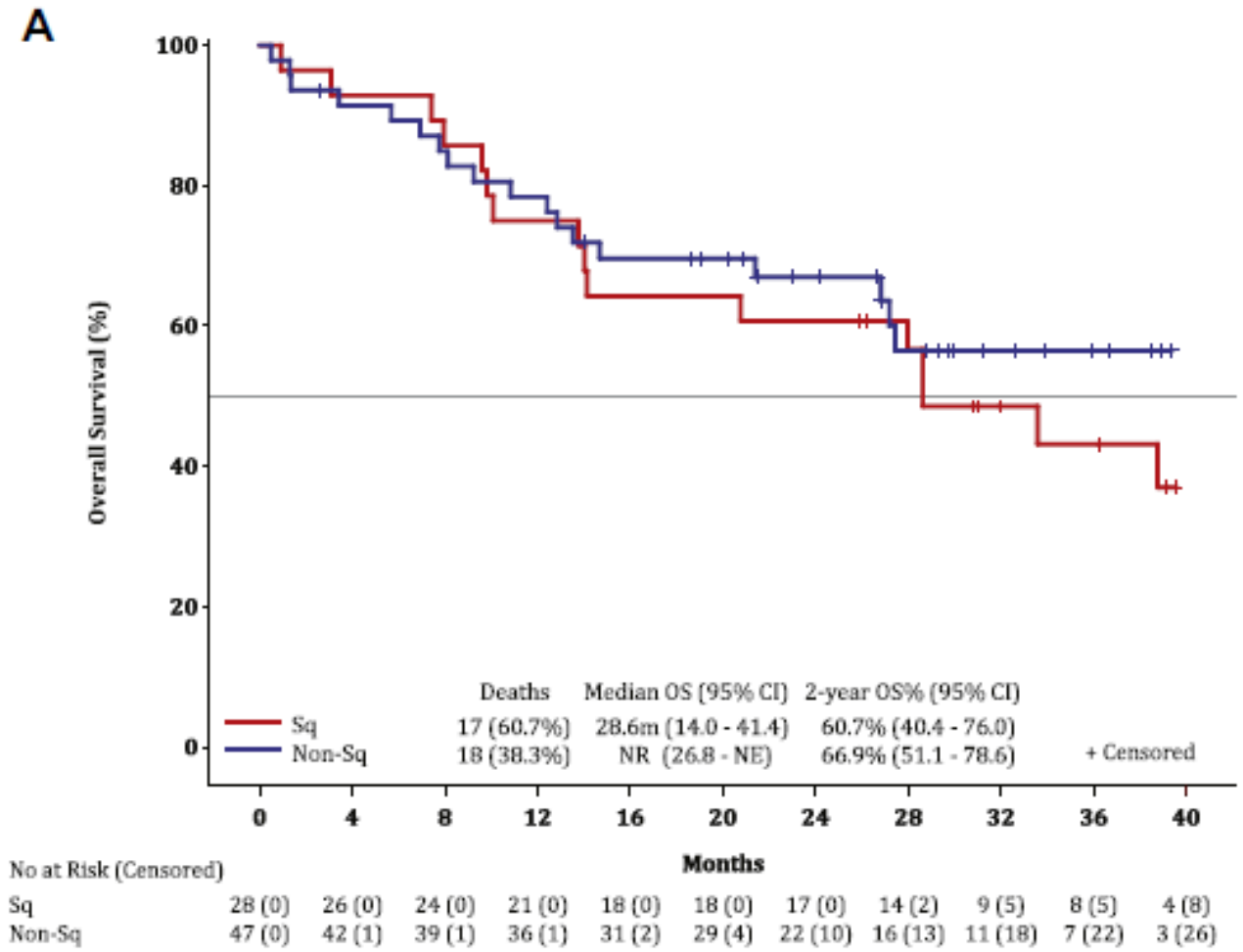
Vaes et al. Cancers 2021

Erasmus MC Cancer

Add concurrent immunotherapy to CCRT?

Progression-Free and Overall Survival for Concurrent Nivolumab With Standard Concurrent Chemoradiotherapy in Locally Advanced Stage IIIA-B NSCLC: Results From the European Thoracic Oncology Platform NICOLAS Phase II Trial (European Thoracic Oncology Platform 6-14)

Solange Peters, MD, PhD,[a] Enriqueta Felip, MD, PhD,[b] Urania Dafni, ScD,[c,d] Amanda Tufman, MD,[e,f] Matthias Guckenberger, MD,[g] Ruth Álvarez, MD,[h] Ernest Nadal, MD, PhD,[i] Annemarie Becker, MD, PhD,[j] Hansjörg Vees, MD,[k] Miklos Pless, MD,[l] Alex Martinez-Marti, MD,[b] Maarten Lambrecht, MD, PhD,[m] Nicolaus Andratschke, MD,[g] Zoi Tsourti, PhD,[c] Anne-Christine Piguet, PhD,[n] Heidi Roschitzki-Voser, PhD,[n] Adrian Gasca-Ruchti, MD,[n] Johan Vansteenkiste, MD, PhD,[o] Rolf A. Stahel, MD,[n,*] Dirk De Ruysscher, MD, PhD[p]



Peters et al. J Thorac Oncol 2020

Go beyond checkpoint inhibitors: e.g. IL2 immunocytokines

Strong pre-clinical effects. Radiation to a tumor before IL2 necessary.

NHS-IL2

- Untreated stage IV NSCLC
- 5x4 Gy to primary tumor
- NHS-IL2

- 2/13 patients > 3 year PFS

van den Heuvel et al. J Transl Med 2015

L19-IL2

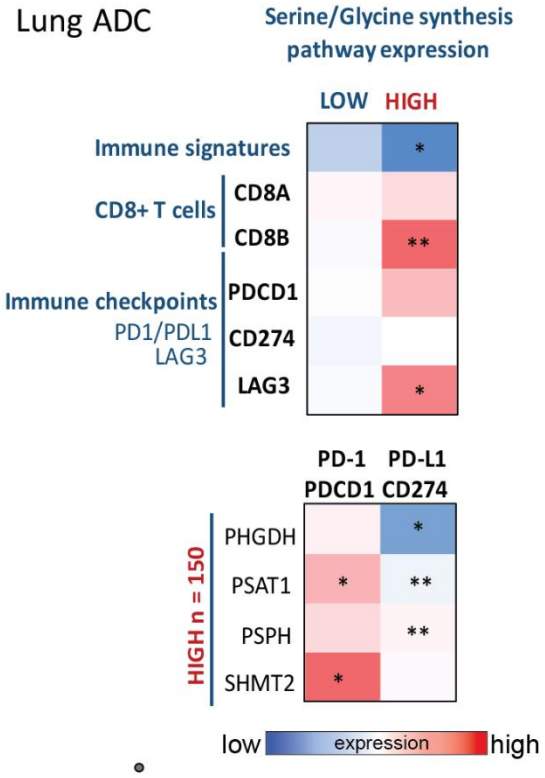
- Untreated stage IV NSCLC
- 3x8 Gy to a metastasis
- L19-IL2

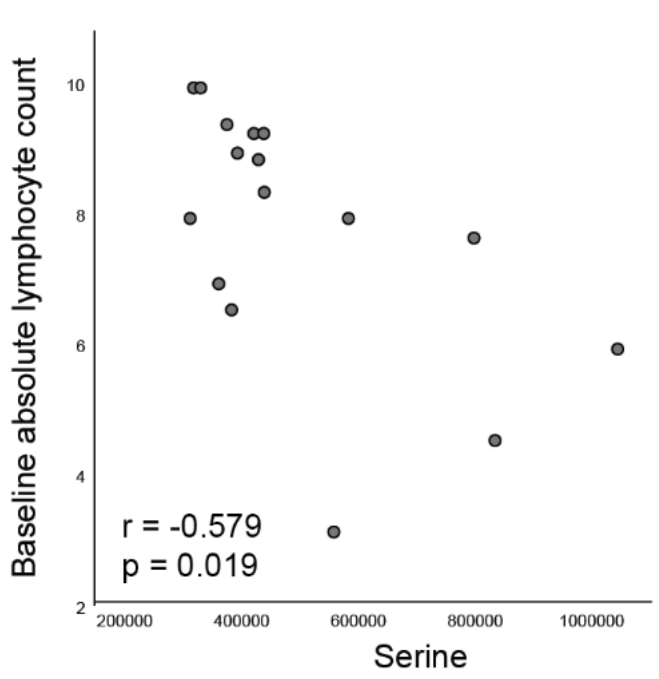
- 2/6 patients > 3 year PFS

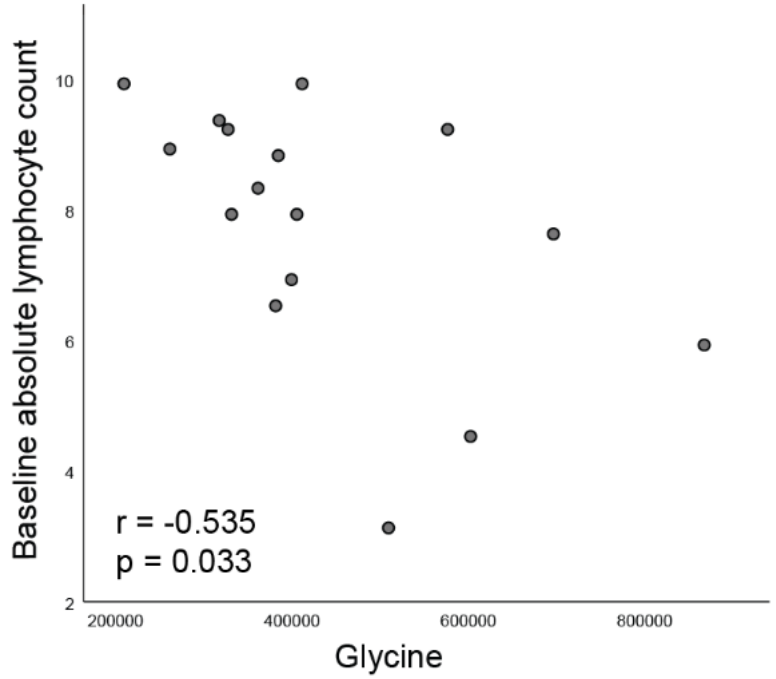
Van Limbergen et al. Int J Radiat Oncol Biol Phys 2021

Work on the TME and metabolism

Serine/glycine pathway activation associates with an immunosuppressive signature in lung cancer patients







Geeraerts et al. Nature Metabolism 2021

Geeraerts et al. Mol Cancer Therap 2021

Sánchez-Castillo et al. Cancers 2021

Vaes et al. Cancers 2021