

IV SESSIONE

SCLC: dalla pratica clinica attuale alle prospettive future

Il ruolo della radioterapia

Niccolò Giaj Levra

Radiation Oncology, MD PhD

Advanced Radiation Oncology Department

IRCCS Sacro Cuore Don Calabria, Negrar di Valpolicella, Italy

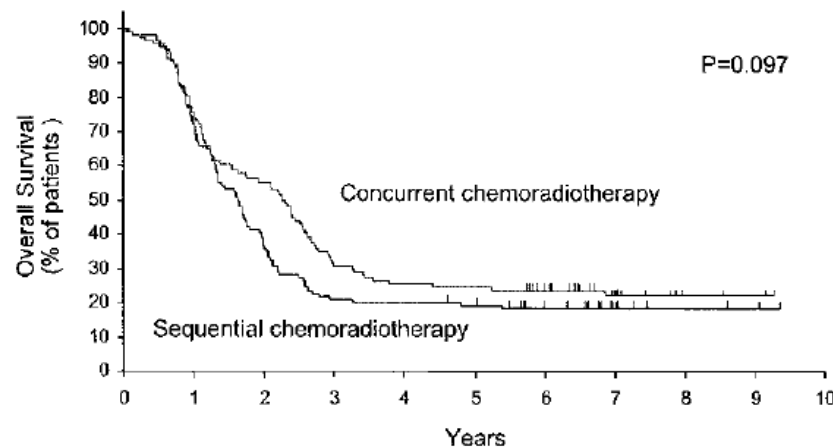


- Role of radiotherapy in SCLC limited disease
 - Timing and sequencing with chemotherapy
 - Dose prescription
- Role of radiotherapy in SCLC extensive disease
- Prophylactic brain irradiation
 - LD SCLC
 - ED SCLC

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TIMING AND SEQUENCING WITH CHEMOTHERAPY

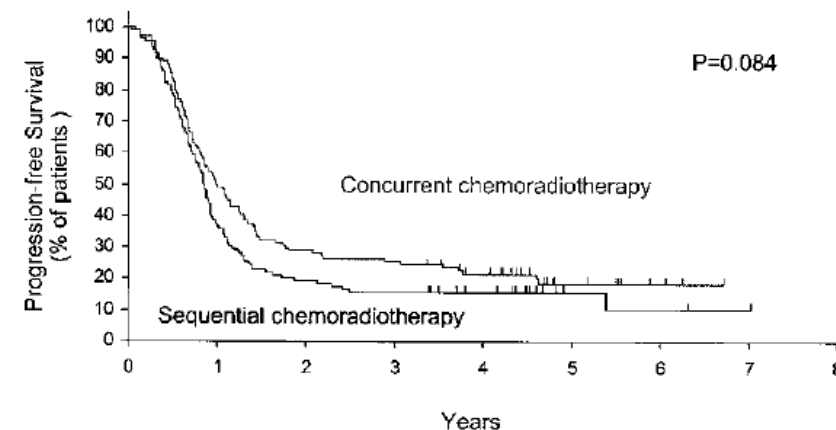
JCOG-9104 phase III trial



No. at Risk	0	1	2	3	4	5	6	7	8	9	10
Sequential chemoradiotherapy	114	83	41	24	23	21	14	7	3	2	
Concurrent chemoradiotherapy	114	86	63	34	29	28	21	12	3	2	

Overall survival

Median OS: 27 months (concurrent) vs. 19.7 months (sequential)
p= 0.08



No. at Risk	0	1	2	3	4	5	6	7	8
Sequential chemoradiotherapy	114	43	22	18	13	3	2	1	
Concurrent chemoradiotherapy	114	57	33	29	21	9	4		

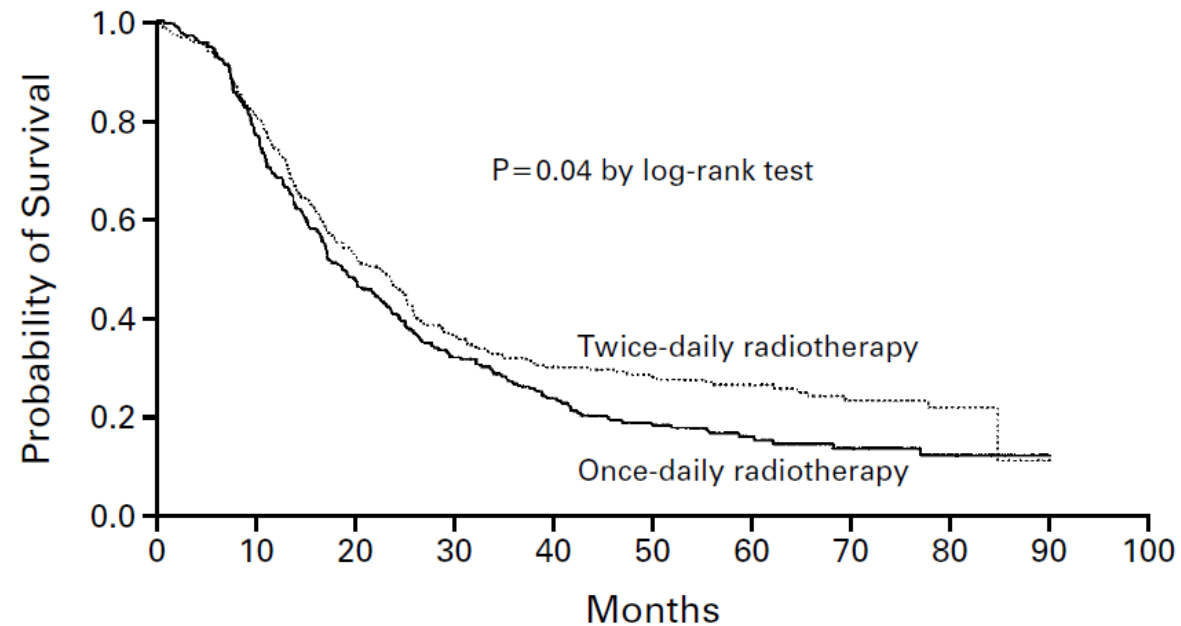
Progression Free survival

TIMING AND SEQUENCING WITH CHEMOTHERAPY

Trial	Years	N	Chemotherapy	TRT	TRT Duration (weeks)	TRT Start	SER (days)	Med OS (months)
INT-0096 ¹⁷	1989-1992	417	PE	45 Gy once daily	5	Cycle 1	33 ^a	19
				45 Gy twice a day	3	Cycle 1	19 ^a	23
NCCTG ¹⁸	1990-1996	262	PE	50.4 Gy once daily	5.5	Cycle 4	101	21.9 ^b
				48 Gy twice a day split	5	Cycle 4	93	19.9 ^b
CALGB 9235 ¹⁹	1993-1999	307	PE	50 Gy once daily	5	Cycle 4	96	20.6
			TamPE	50 Gy once daily	5	Cycle 4		18.4
RTOG 9609 ²⁰	1996-1998	55	PET	45 Gy twice a day	3	Cycle 1	19	24.7
ECOG 2596 ²¹	1997-1998	61	PET	63 Gy	7	Cycle 3	89	15.7
SWOG 9713 ²²	1998-1999	87	PE—TC	61 Gy	6.5	Cycle 1	45	17
CALGB 39808 ²³	1999-2000	75	TTpo—CE	70 Gy	7	Cycle 3	89	22.4
SWOG 0222 ²⁴	2003-2006	68	TpzPE—PE	61 Gy	6.5	Cycle 1	45	21
CALGB 30002 ²⁵	2001-2003	65	TETpo—CE	70 Gy	7	Cycle 3	89	20
RTOG 0239 ²⁶	2003-2006	72	PE	61.2 Gy CB	5	Cycle 1	33	19
CONVERT ⁸	2008-2013	547	PE	45 Gy twice a day	3	Cycle 2	40	30
				66 Gy once daily	6.5		66	25
Scandinavian ²⁷	2014-2018	170	PE ^c	45 Gy twice a day	3	Cycle 2	40	22.6
				60 Gy twice a day	4		47	37.2
CALGB 30610 RTOG 0538 ⁷	2008-2019	638	PE (81%)	45 Gy twice a day	3	Cycle 1 or 2	19-40	28.5
			CE (19%)	70 Gy once daily	7		47-68	30.5

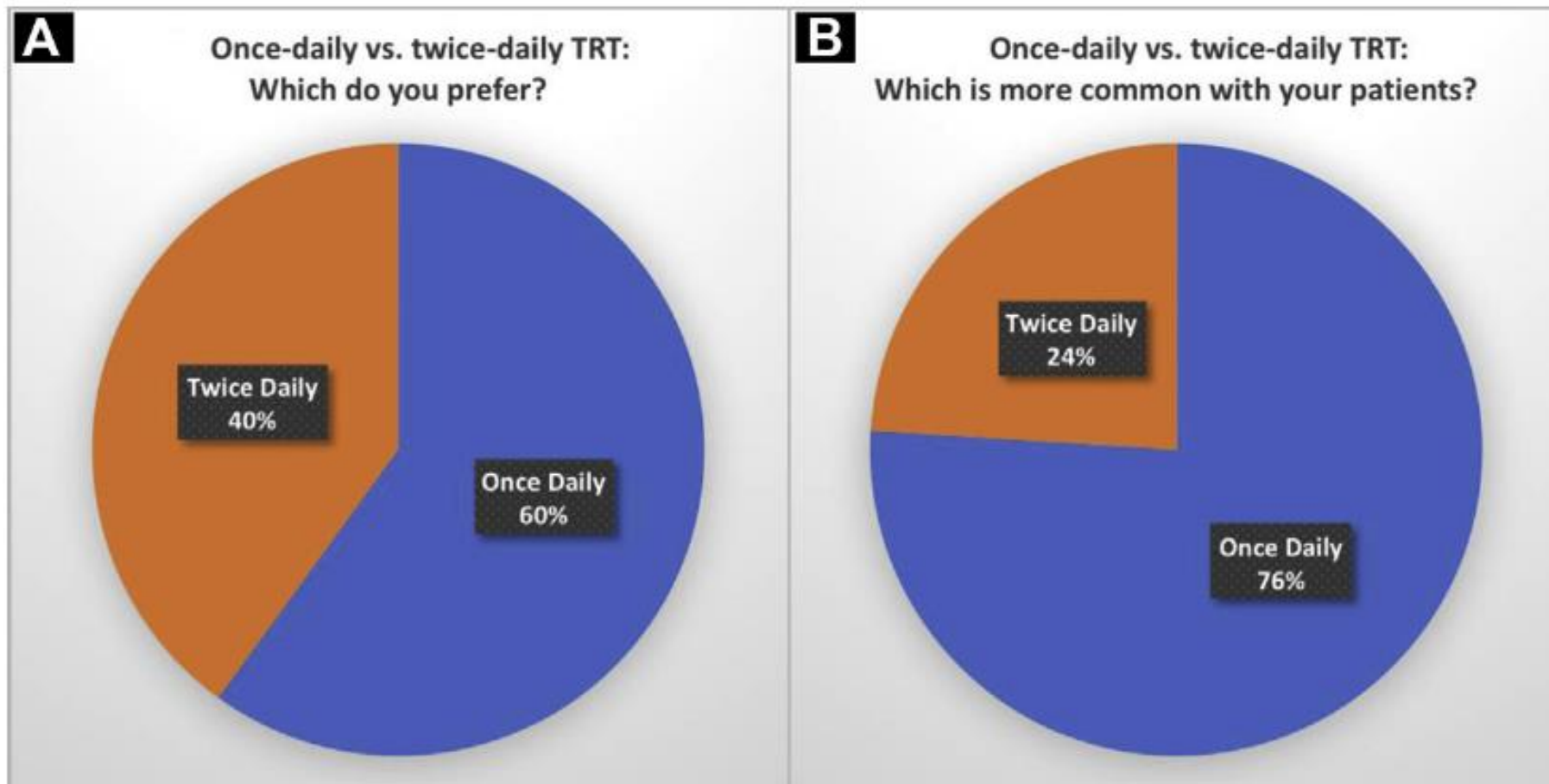
DOSE AND FRACTIONATION

INT-0096 trial



TREATMENT GROUP	0–20 Mo	20–40 Mo	40–60 Mo	60–80 Mo	80–100 Mo
	no. of deaths/no. at risk				
Once daily	108/206	48/96	15/47	4/21	0/5
Twice daily	100/211	47/109	7/62	5/42	1/14

DOSE AND FRACTIONATION



CONVERT phase III trial

Study design

multinational, phase III randomised study

RTP after randomisation
RT started on D22 cycle 1

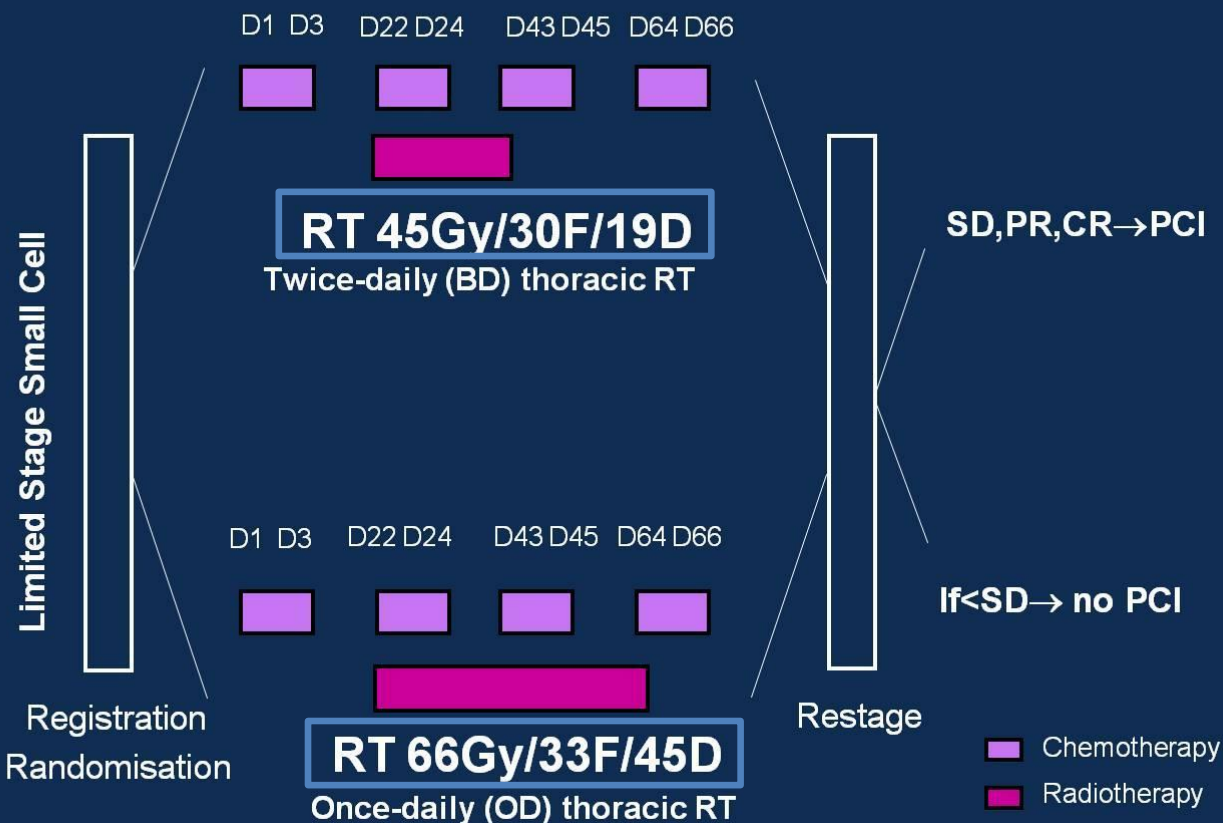
- 3DCRT or IMRT
- No ENI
- QA programme

Chemotherapy
4 to 6 cycles

- Cisplatin 25mg/m² D1-3 or 75mg/m² D1
- Etoposide 100mg/m² D1-3

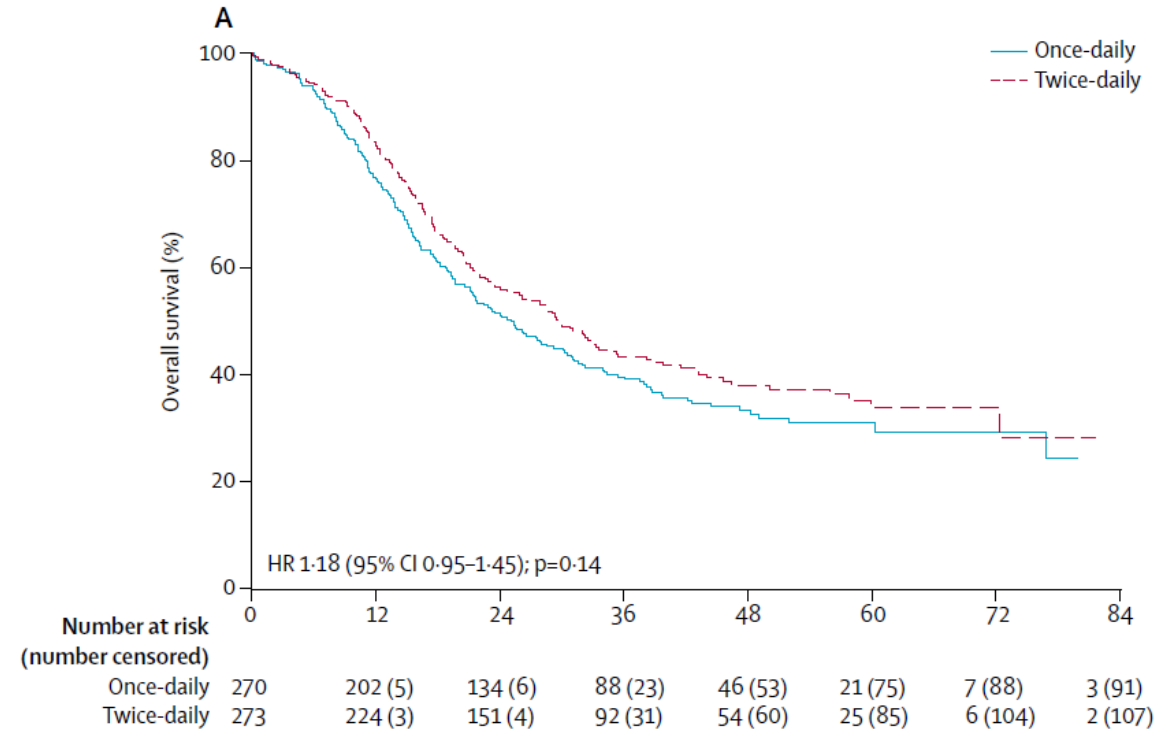
Stratification factors

- Centre
- No. of cycles chemo: 4 vs.6
- PS: 0,1 vs. 2



DOSE AND FRACTIONATION

CONVERT phase III trial



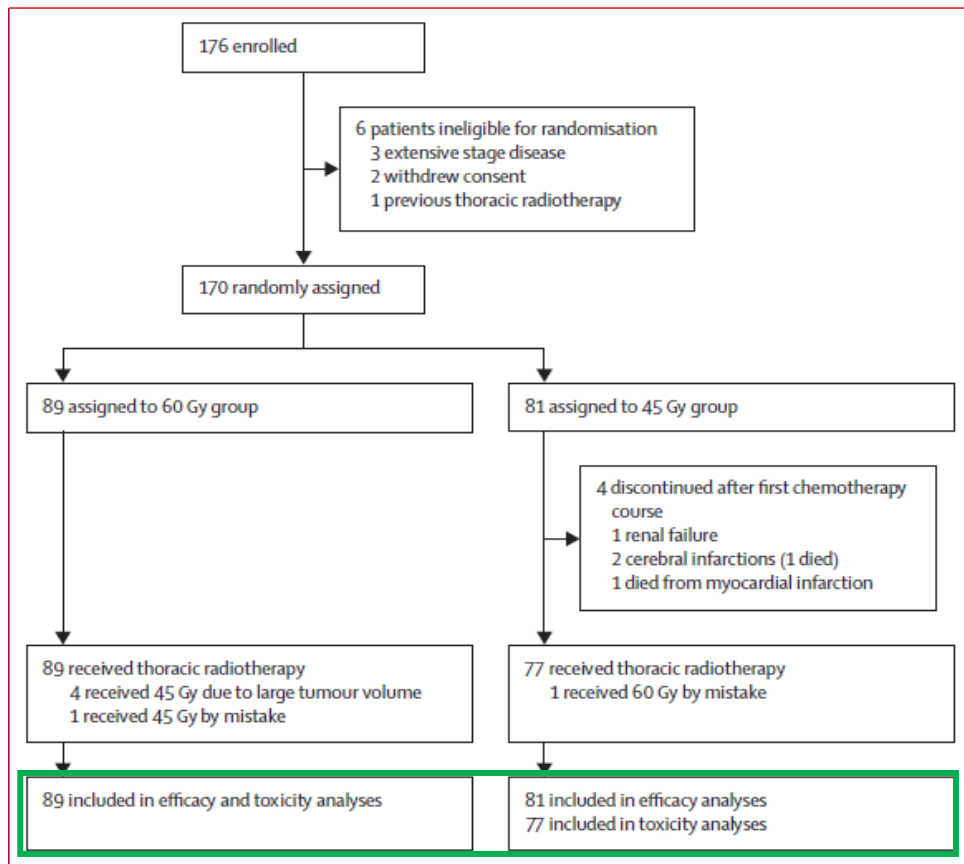
Overall survival

Superiority trial: 45 Gy in 30 fractions twice vs. 66 Gy in 33 fractions

High-dose versus standard-dose twice-daily thoracic radiotherapy for patients with limited stage small-cell lung cancer: an open-label, randomised, phase 2 trial

2021

Bjørn Henning Grønberg, Kristin Toftaker Killingberg, Øystein Fløtten, Odd Terje Brustugun, Kjersti Hornslien, Tesfaye Madebo, Seppo Wang Langer, Tine Schytte, Jan Nyman, Signe Risum, Georgios Tsakonas, Jens Engleson, Tarje Onsøien Halvorsen



First randomised trial comparing high-dose, twice-daily thoracic RT **60Gy/40#** with the established schedule **45 Gy/30#**

CHEMOTHERAPY → → PLATINUM + ETOPOSIDE_{x4}

ENI was not allowed

Primary endpoint



2-year overall survival (Δ 25%)

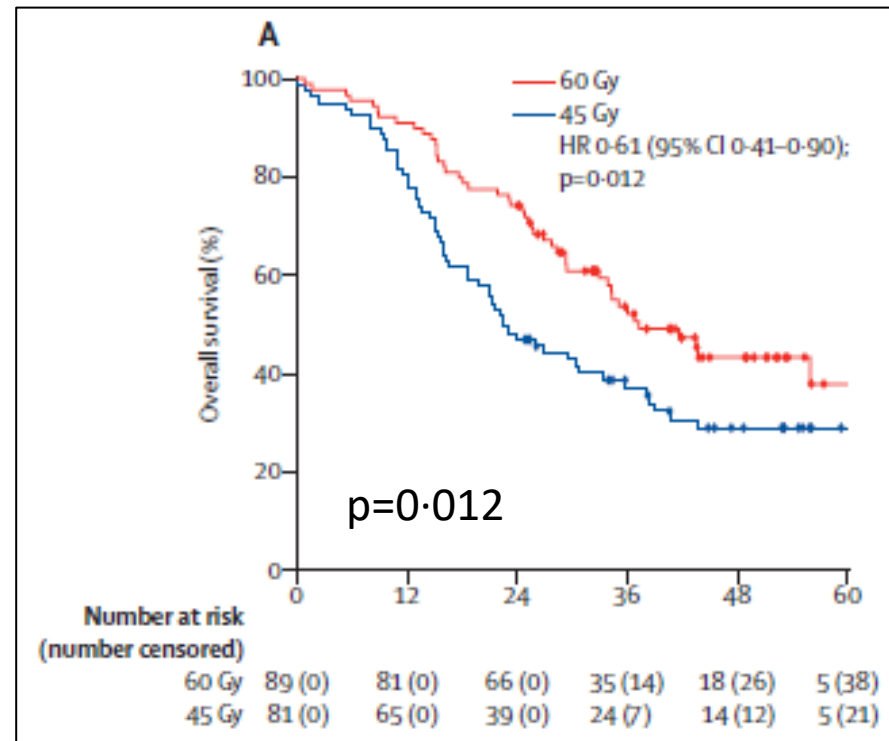
High-dose versus standard-dose twice-daily thoracic radiotherapy for patients with limited stage small-cell lung cancer: an open-label, randomised, phase 2 trial

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Median follow-up 49 months

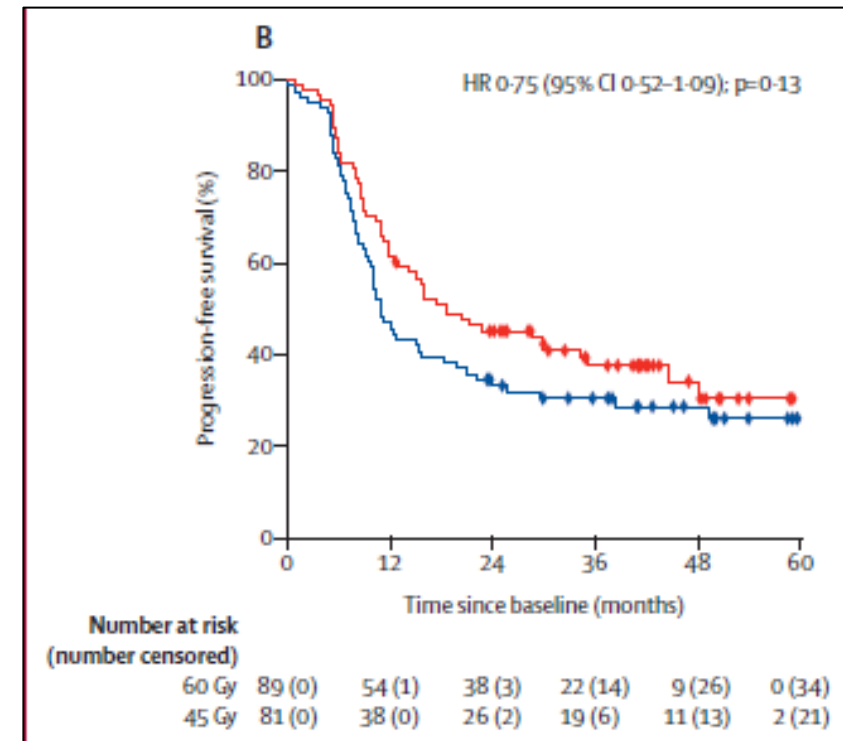
Median OS was significantly longer in 60 Gy group
37.2 months vs 22.6 months

Median PFS was longer in 60 Gy group
18.6 months vs 10.2 months



OS @ 2yrs

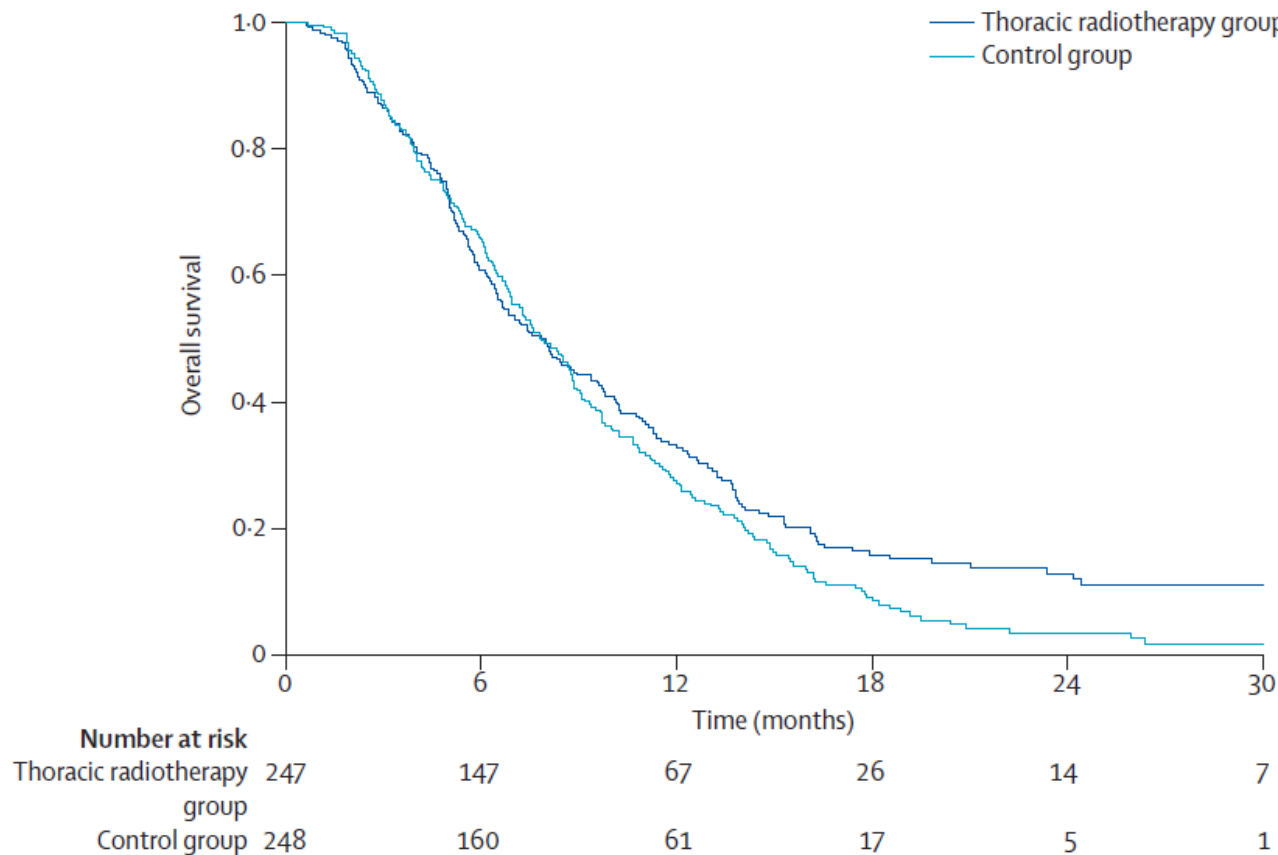
74,2%
Vs
48,1%



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CREST- phase III trial

PCI in all patients



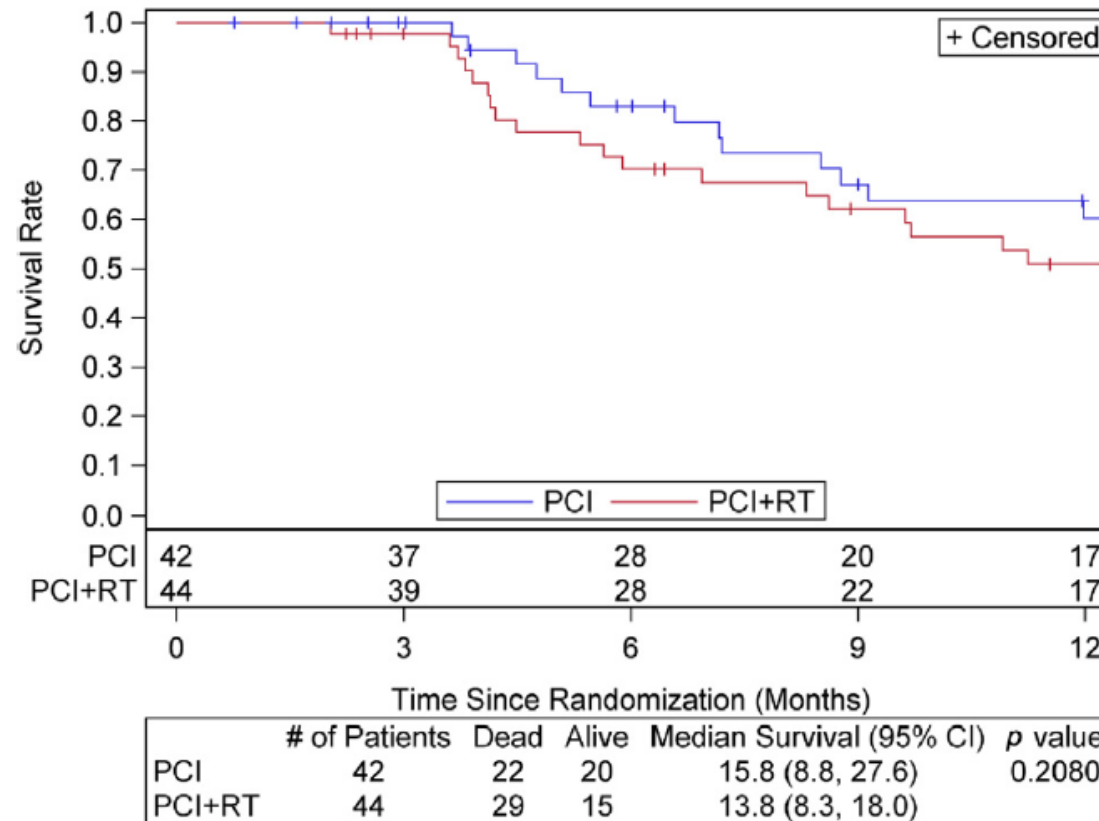
OS @ 2 years
13% (95% CI 9–19)
versus
3% (95% CI 2–8; p=0.004)

Radiation dose prescription: 30 Gy in 10 fractions

Slotman BJ et al. Lancet. 2014

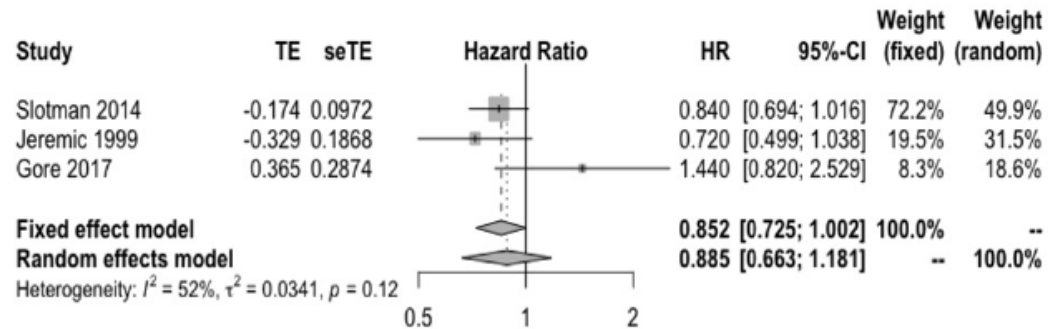
RTOG 0937- phase III trial

4 or fewer metastatic sites

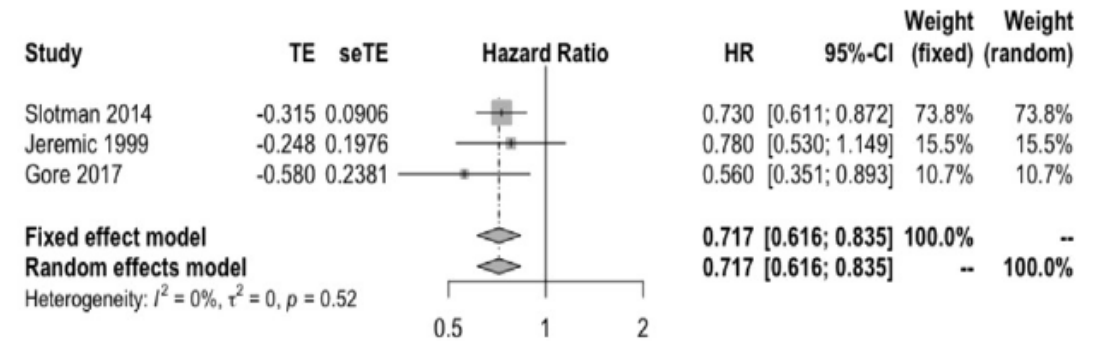


Radiation dose prescription: 45 Gy in 15 fractions

Meta-analysis – Thoracic radiotherapy in ED SCLC



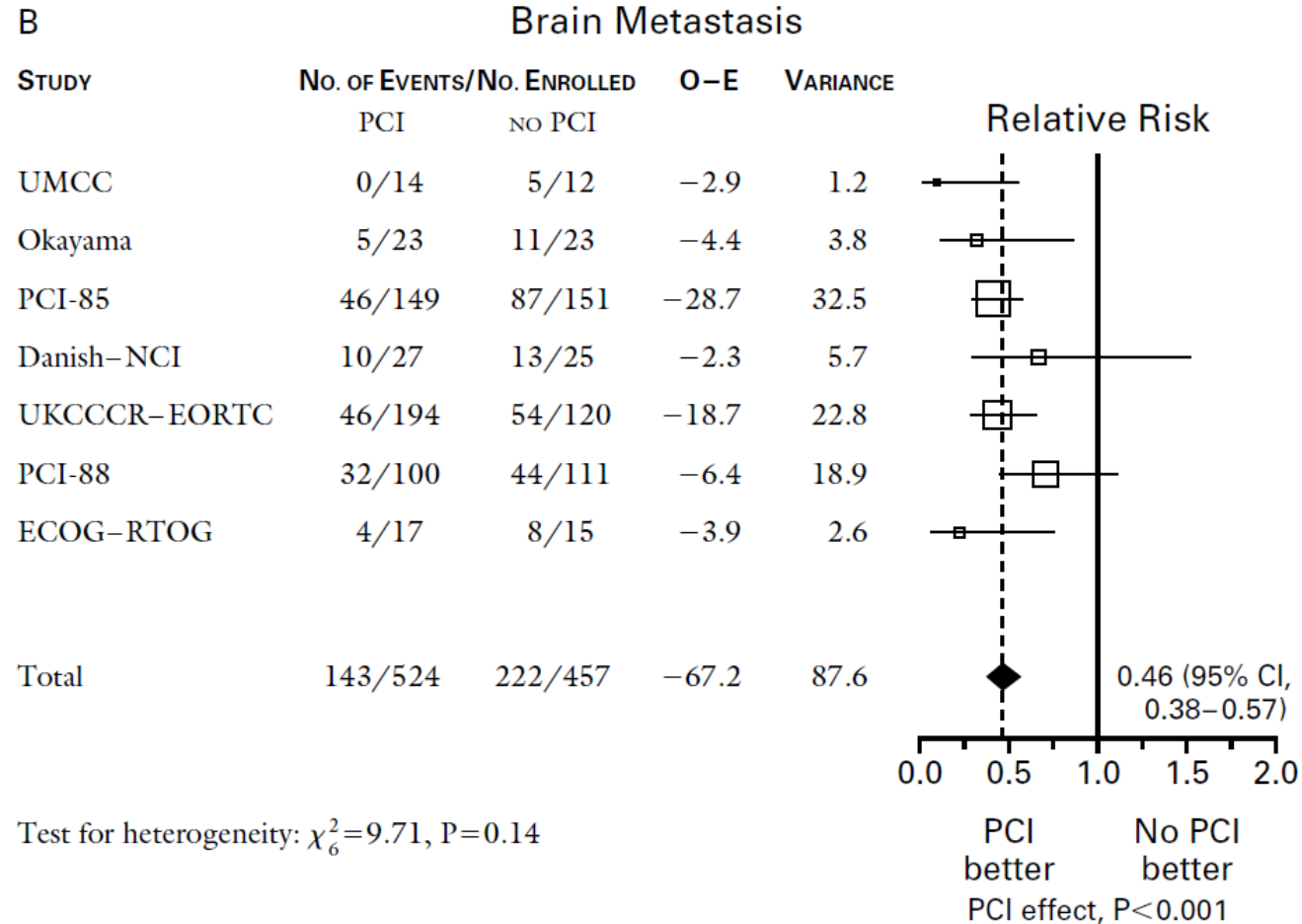
Overall survival



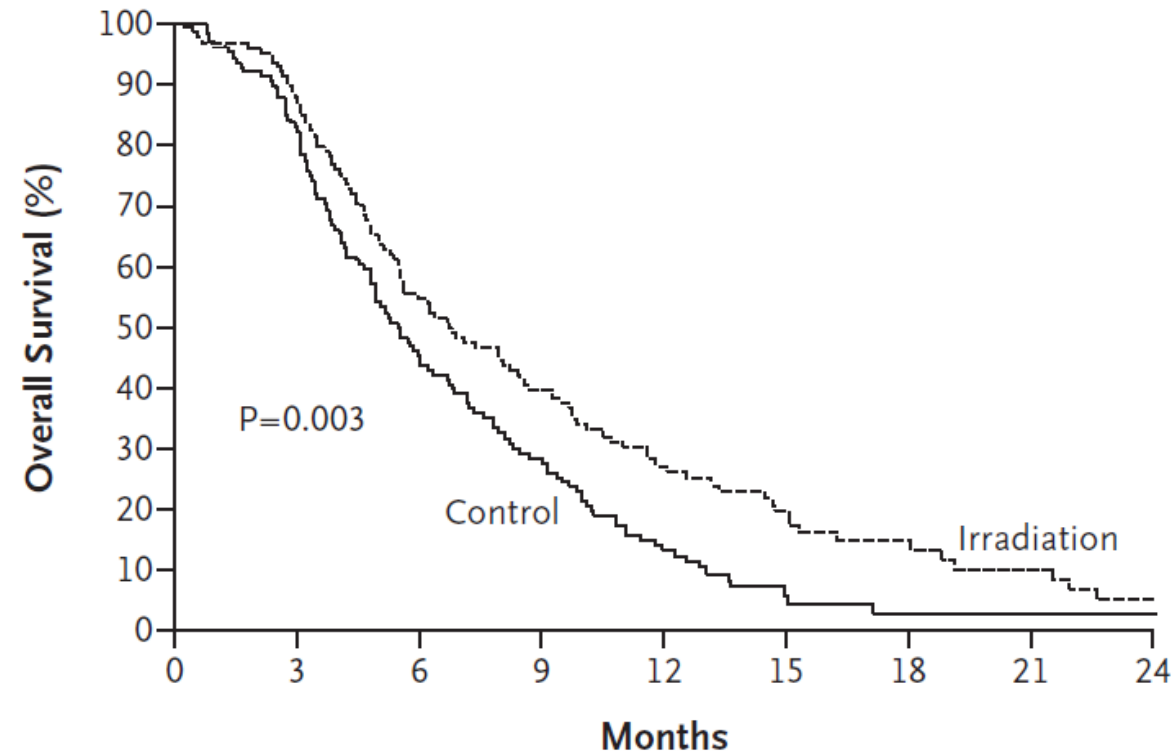
Progression Free survival

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Meta-analysis – PCI in LD



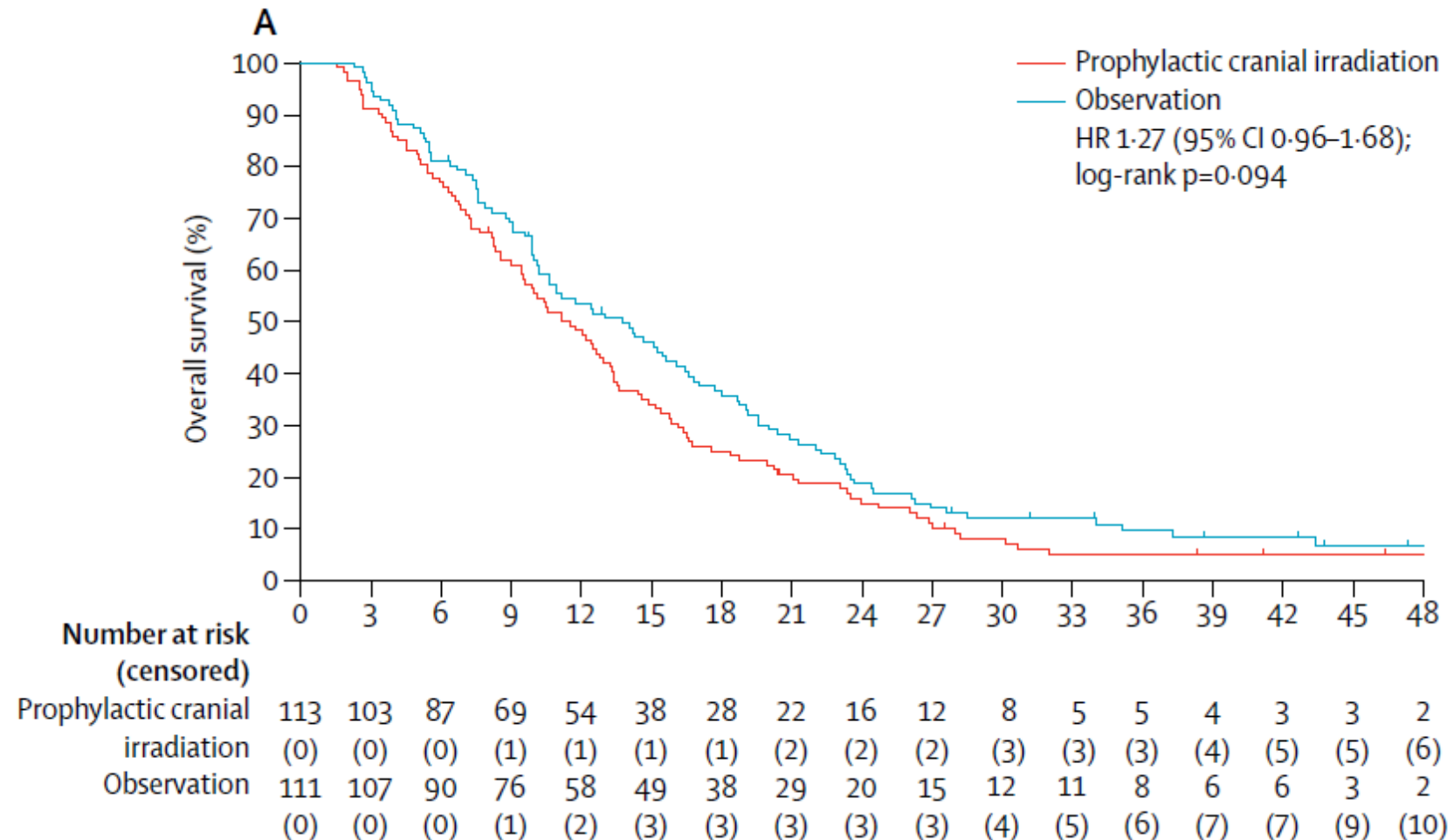
PCI in ED



No. at Risk

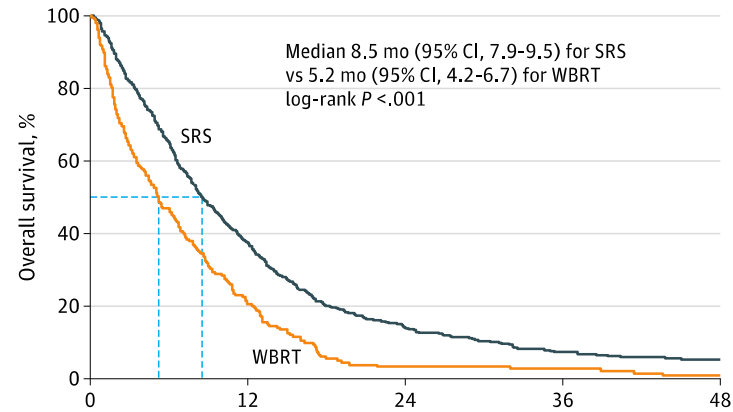
Control	143	115	58	36	15	3	2	1
Irradiation	143	119	67	44	26	17	11	6

PCI in ED – Phase III trial

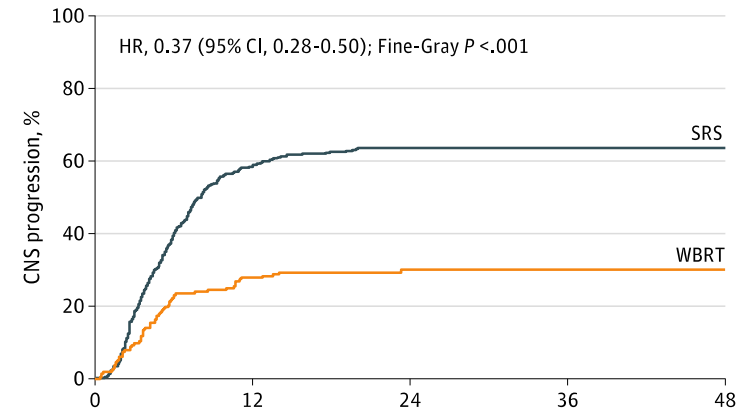


BRAIN METASTASES AND SCLC

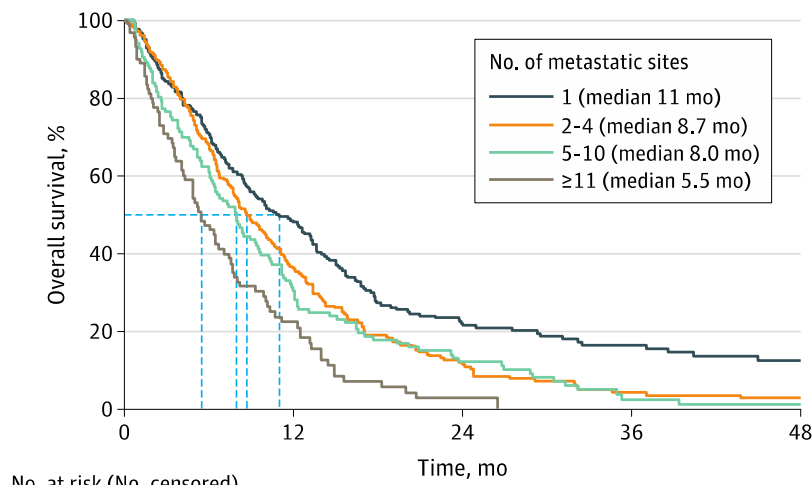
A OS for the total SRS and WBRT cohorts



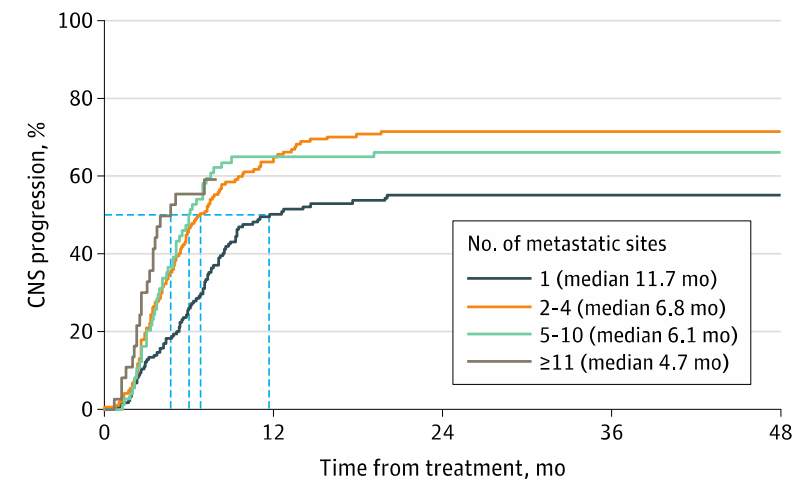
B Cumulative incidence for TTCP for the total cohort with available data on CNS control



C OS stratified by 1, 2-4, 5-10, and ≥ 11 brain metastases



D Cumulative incidence for TTCP stratified by 1, 2-4, 5-10, and ≥ 11 brain metastases



CONCLUSIONS

- Concurrent chemo-radiotherapy is the standard of care for SCLC LD
- Twice daily twice-daily hyperfractionated regimens is still considered appropriate, despite conventional fractionation is feasible
- More evidence are coming for the use of consolidative radiotherapy in SCLC ED with benefit in terms of OS and PFS
- PCI in SCLC LD is strongly recommended
- PCI in SCLC ED should be discussed for each patient and MRI surveillance could be considered as an alternative
- Combination of IO and thoracic radiotherapy is under investigation