EUROPEAN LUNG CANCER
CONFERENCE 2016

PRIMARY RADIOCHEMOTHERAPY

Radiation Oncology in NSCLC
– Current developments and state-of-the-art

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DISCLOSURE SLIDE

Nothing to declare

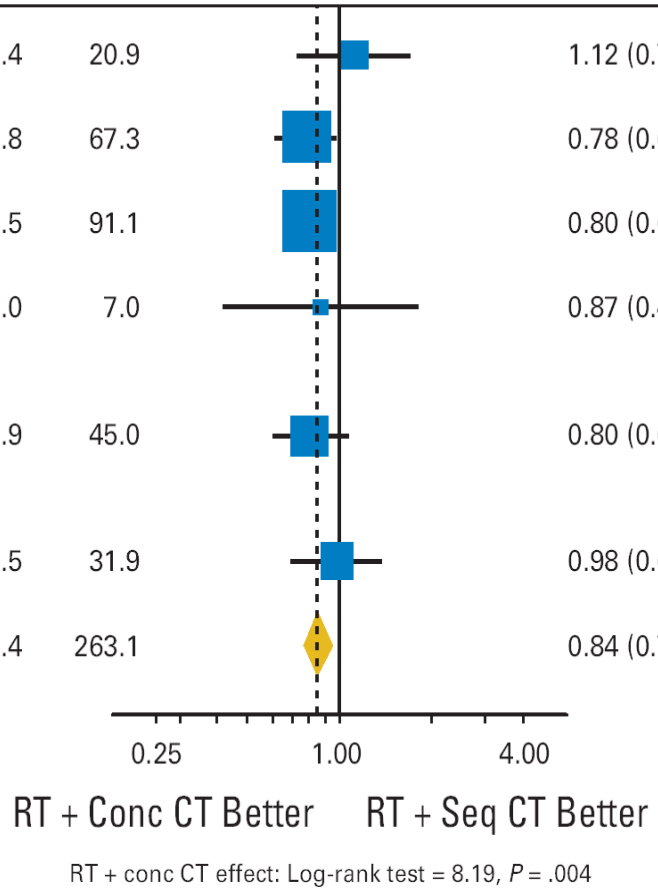
Current radiochemotherapy standards in stage III NSCLC

CONCURRENT VS. SEQUENTIAL CHEMORADIATION: METAANALYSIS OF SURVIVAL

A

Trial	No. Deaths / No. Entered RT + Conc CT	RT + Seq CT	O-E	Variance	Hazard Ratio	HR (95% CI)
CALGB 8831	45/46	39/45	2.4	20.9		1.12 (0.73 to 1.72)
WJLCG	131/156	142/158	-16.8	67.3		0.78 (0.61 to 0.99)
RTOG 9410	180/204	189/203	-20.5	91.1		0.80 (0.65 to 0.98)
GMMA Ankara 95	15/15	15/15	-1.0	7.0		0.87 (0.41 to 1.82)
GLOT-GFPC NPC	87/102	96/103	-9.9	45.0		0.80 (0.60 to 1.07)
EORTC 08972	63/80	66/78	-0.5	31.9		0.98 (0.69 to 1.39)
Total	521/603	547/602	-46.4	263.1		0.84 (0.74 to 0.95)

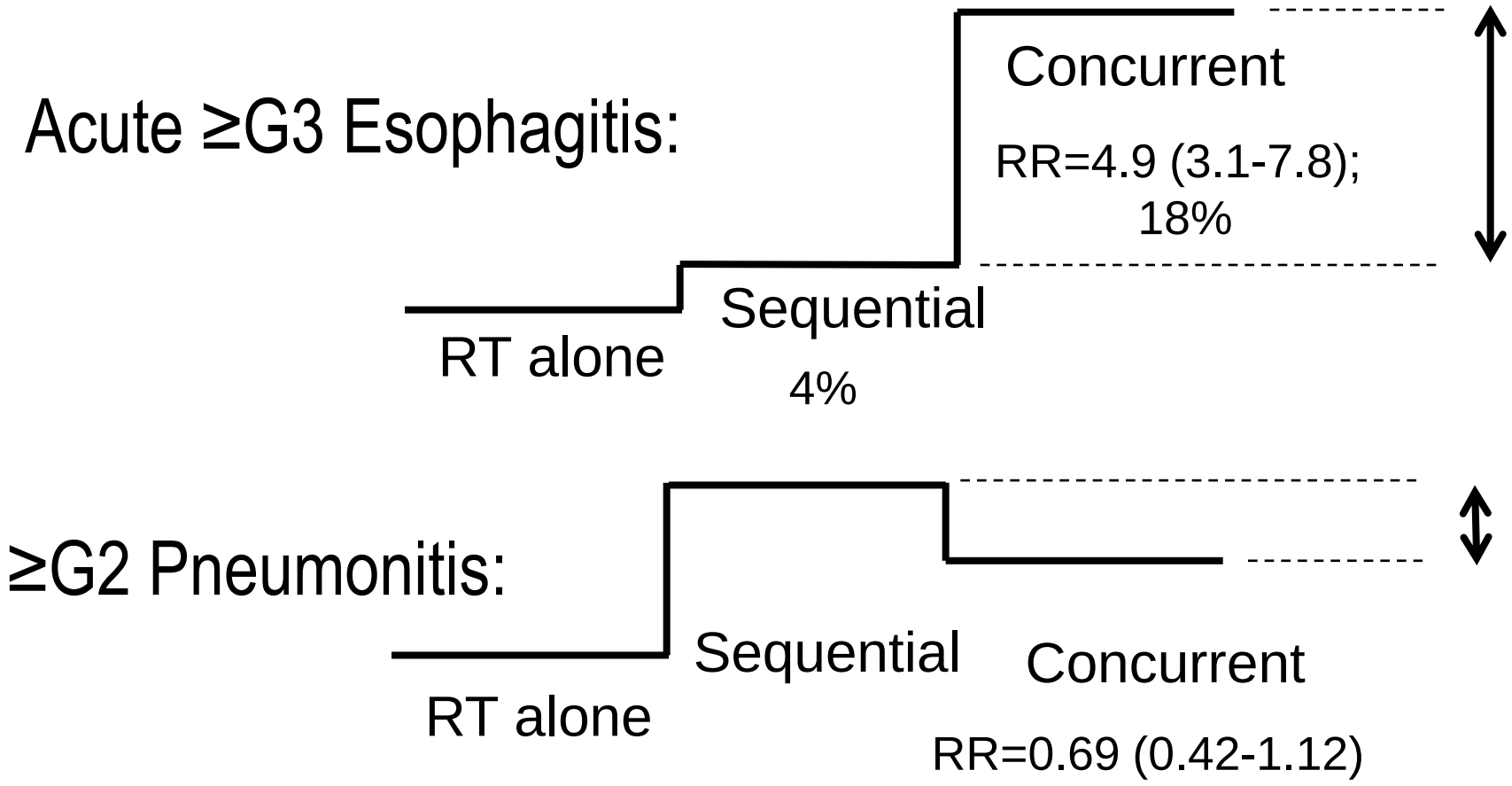
Test for heterogeneity:
$\chi^2_5 = 3.24$, $P = .66$, $I^2 = 0\%$



RT + conc CT effect: Log-rank test = 8.19, $P = .004$

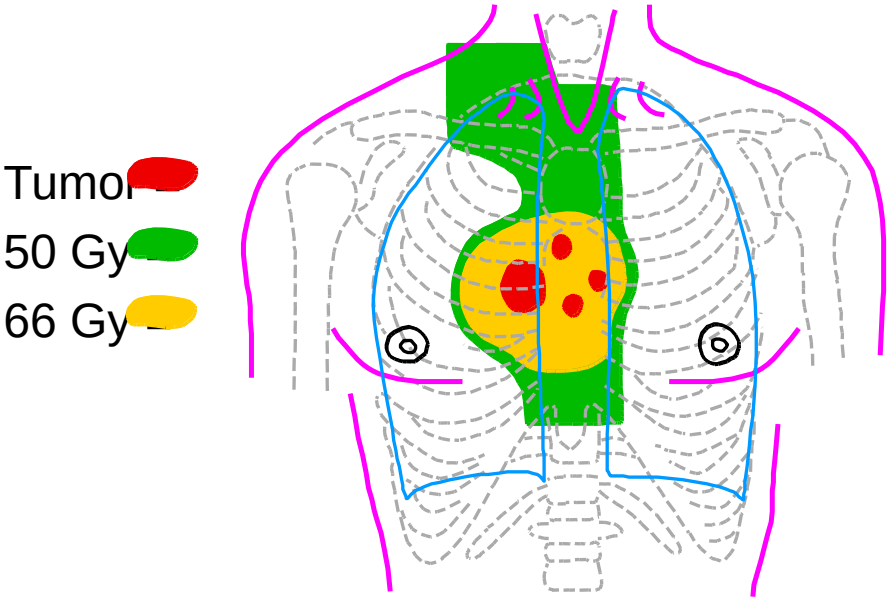
Aupérin A. et al.
J. Clin. Oncol. 2010; 28:2181

Chemoradiation in stage III NSCLC : RT alone vs. Sequential vs. Concurrent - Toxicity

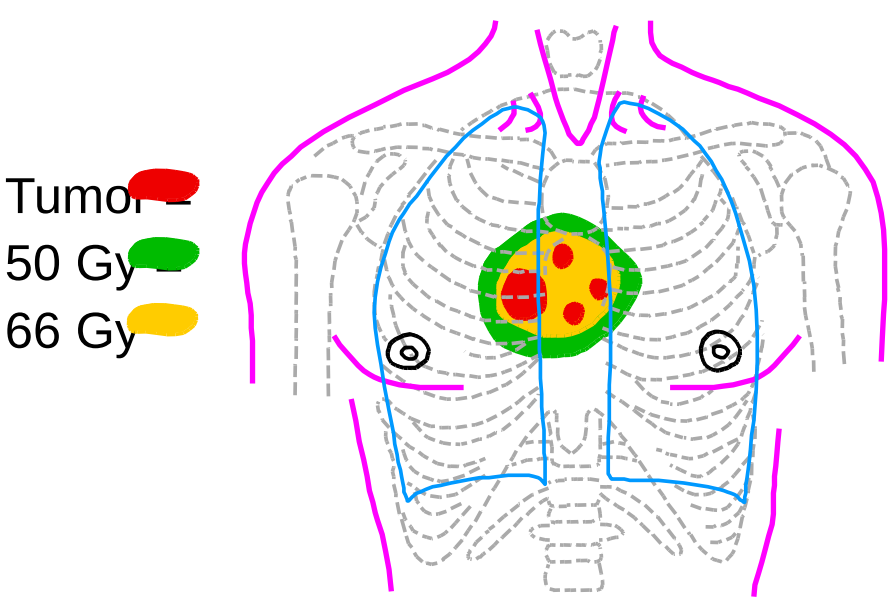


Aupérin A. et al.
J. Clin. Oncol. 2010; 28:2181

Chemoradiation for stage III NSCLC: Optimal radiation volume

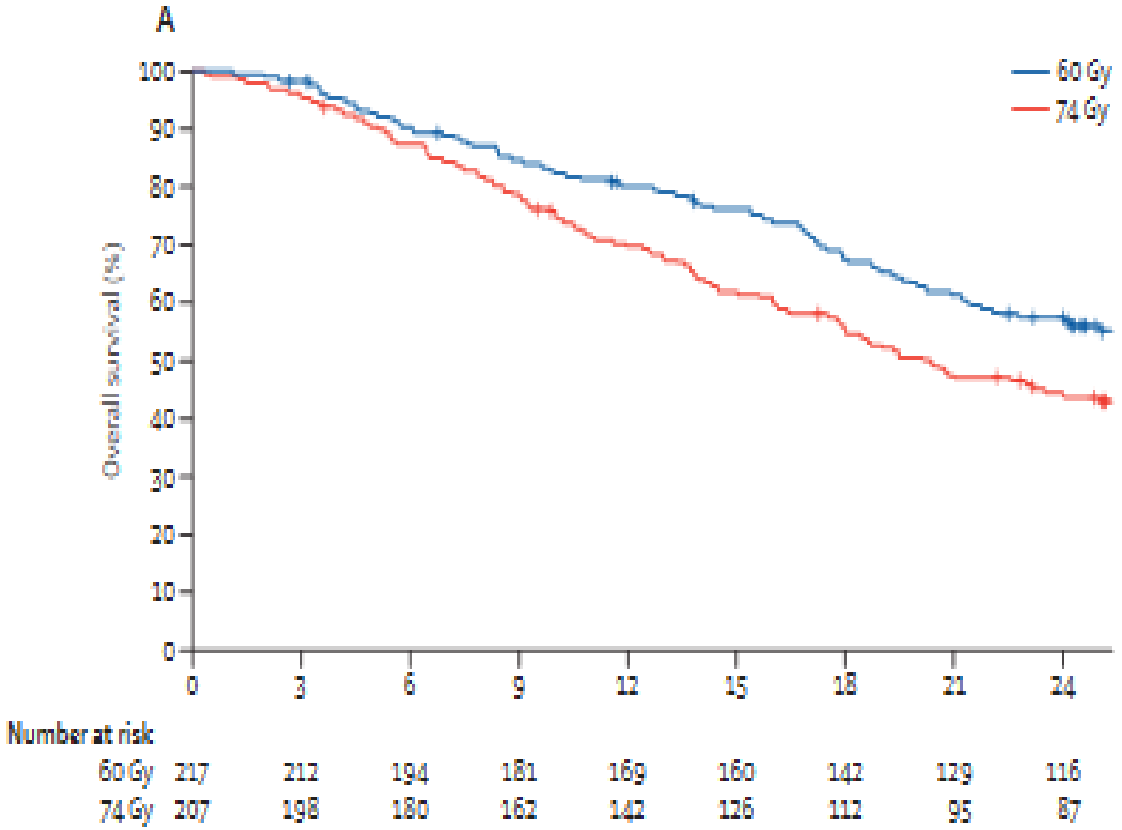


Extended Field RT



Involved Field RT

Chemoradiation for stage III NSCLC: Optimal radiation dose – RTOG 0617 results



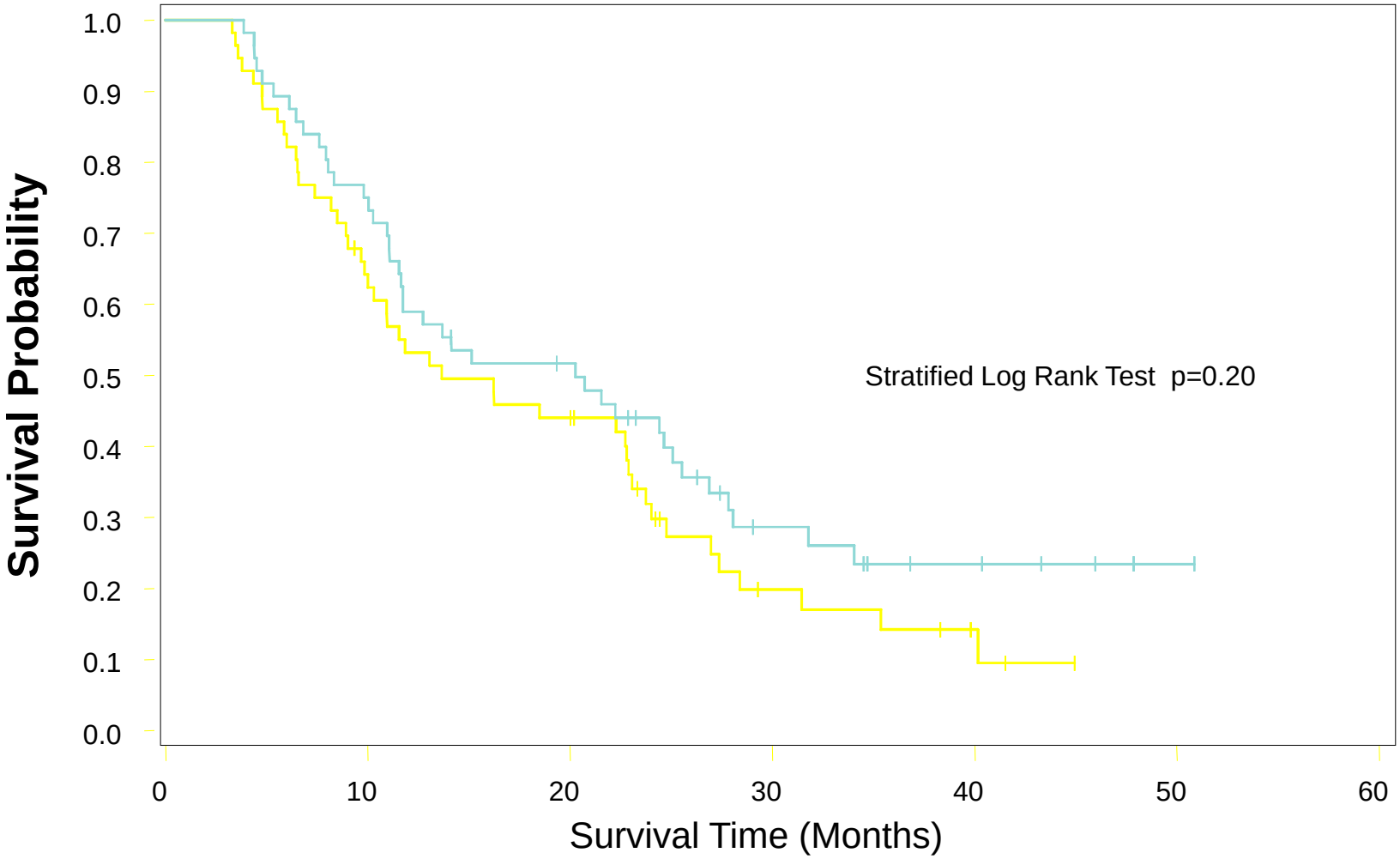
Bradley J. et al.,
Lancet Oncol 2015; 16:187-199

Radiochemotherapy of stage III NSCLC: Unresolved issues

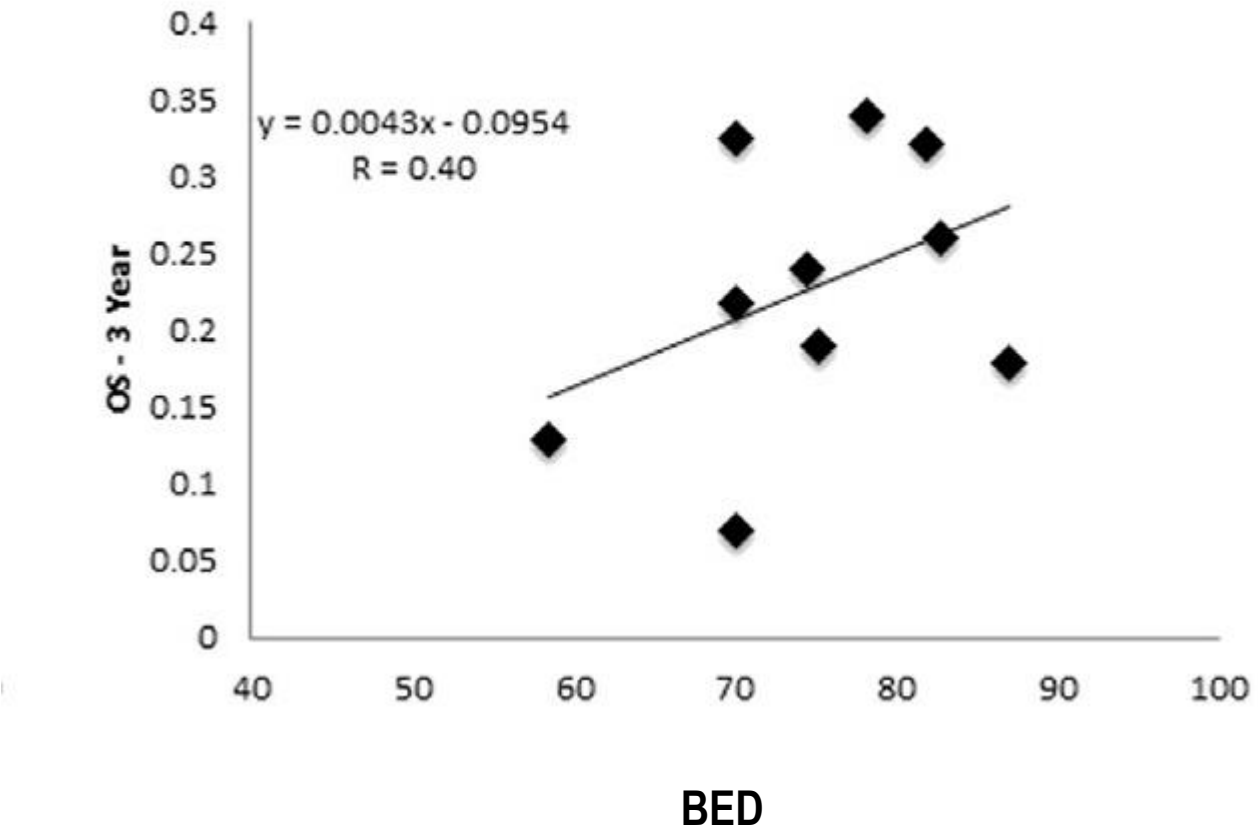
- Altered fractionation and treatment acceleration
- Value of proton and carbon ion therapy
- Optimal cytotoxic drugs and schedules
- Investigational systemic therapies

Altered fractionation and treatment acceleration

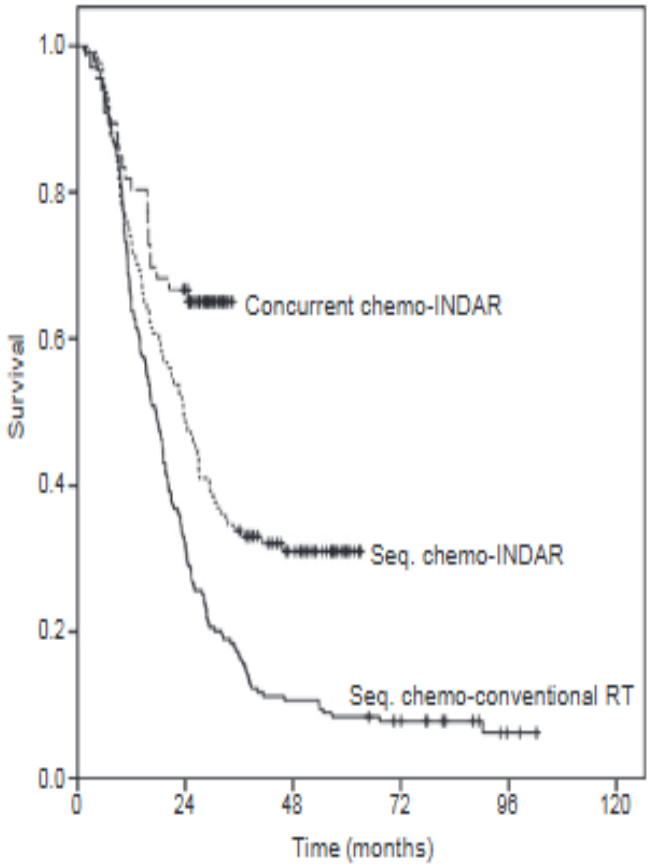
Induction chemotherapy followed by accelerated hyperfractionation: ECOG HART Trial (N=112)



Systematic analysis of trials with hypofractionated definitive radio(chemo)therapy

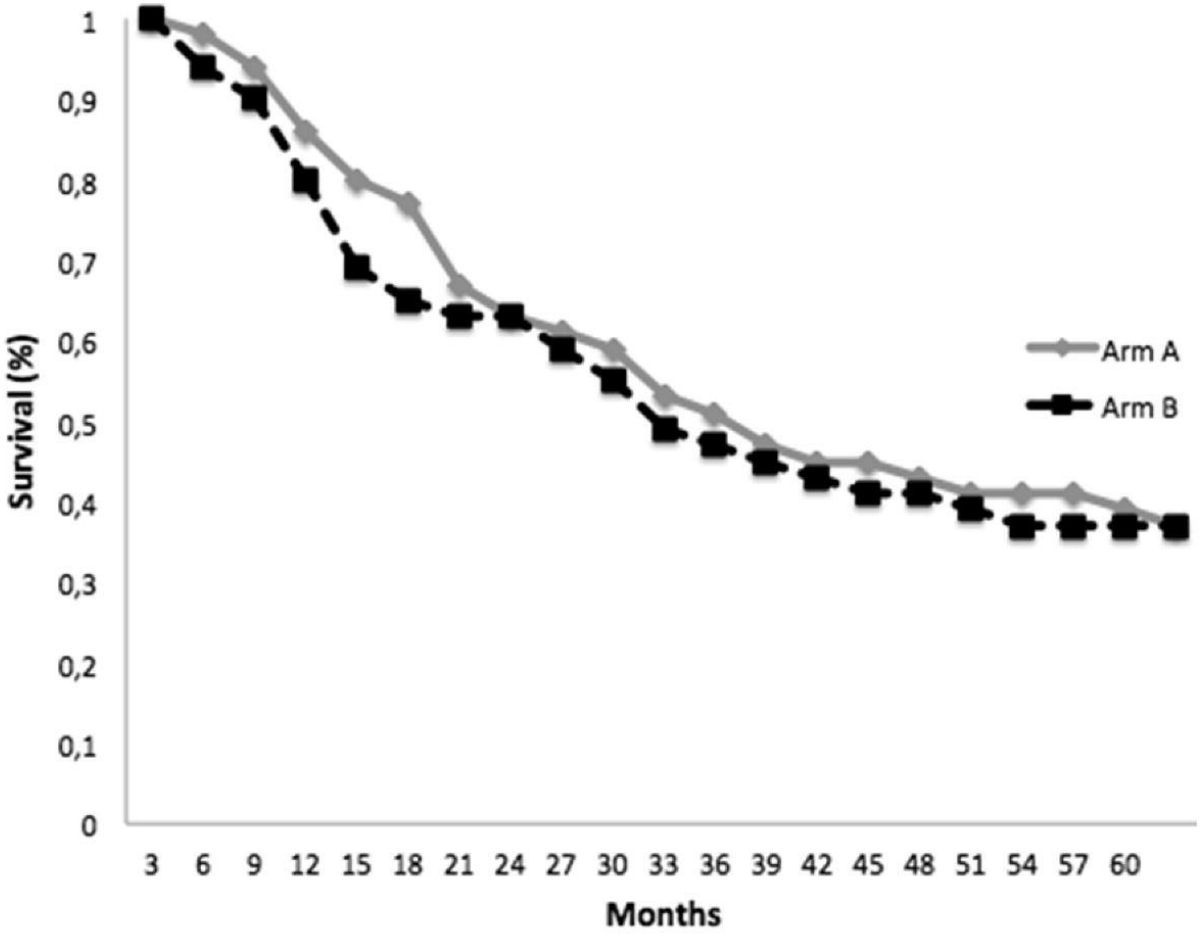


Sequential vs. concurrent individualized <u>isotoxic</u> accelerated radiotherapy (INDAR) and chemotherapy



De Ruysscher D. et al., Radiother Oncol 2012

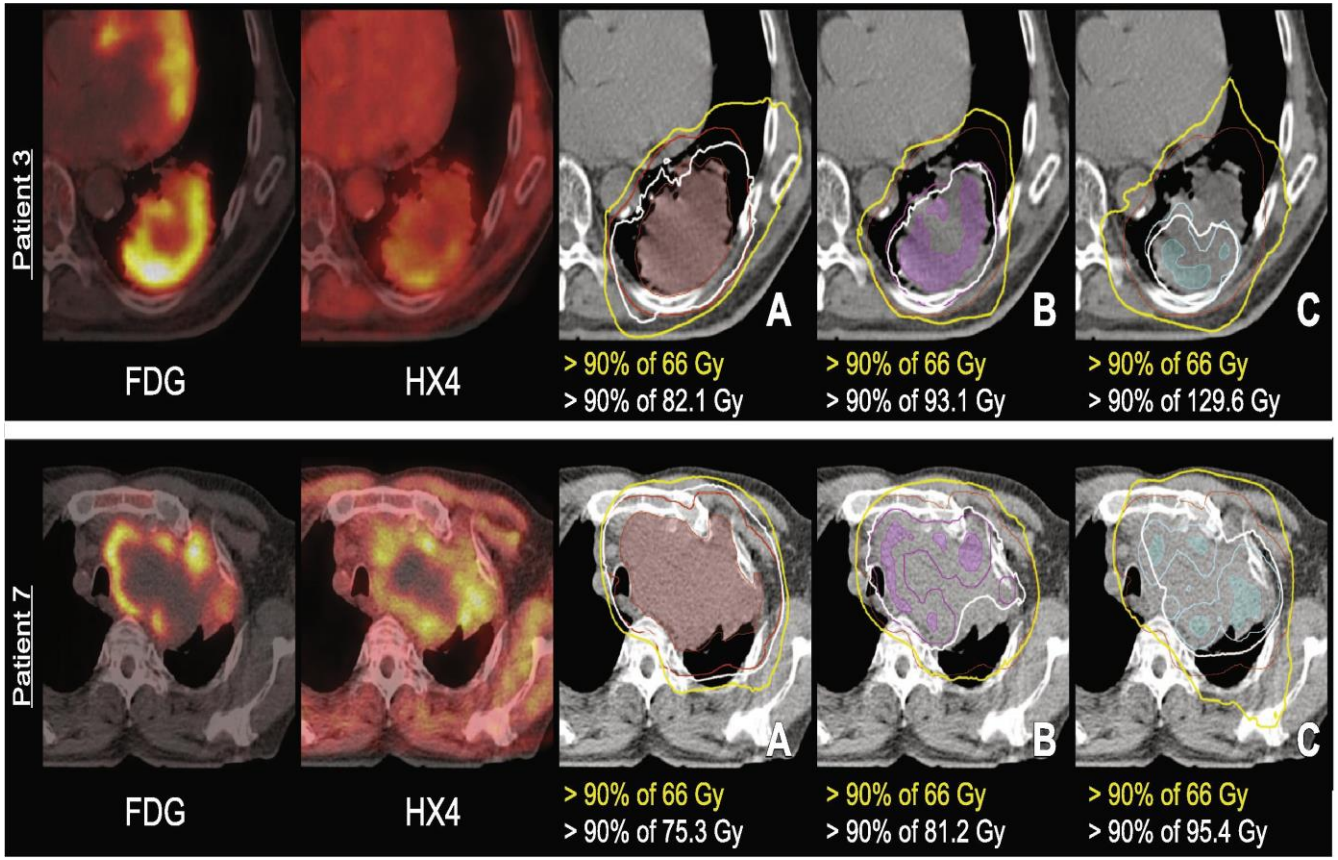
Hypofractionated definitive radiotherapy with daily cisplatin +/- cetuximab: NKI data



Arm A	51	50	48	44	41	39	34	32	31	30	27	26	24	23	23	22	21	21	21	20
Arm B	51	48	46	41	35	33	32	32	30	28	25	24	23	22	21	21	20	19	19	19

Walraven I et al., Radiother Oncol 2016

Homogenous vs. FDG-PET vs. HX4-PET boost - modeling study



Even AJG et al.,
Radiother Oncol 2015

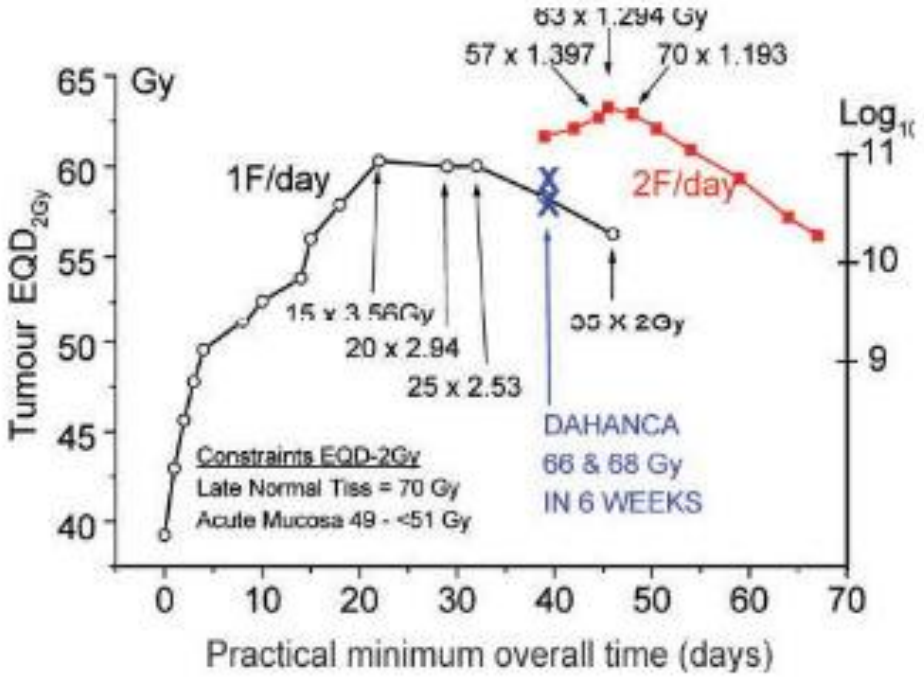
Radiobiological basis of hypofractionated radiotherapy

The British Journal of Radiology, 83 (2010), 554–568

REVIEW ARTICLE

21 years of Biologically Effective Dose

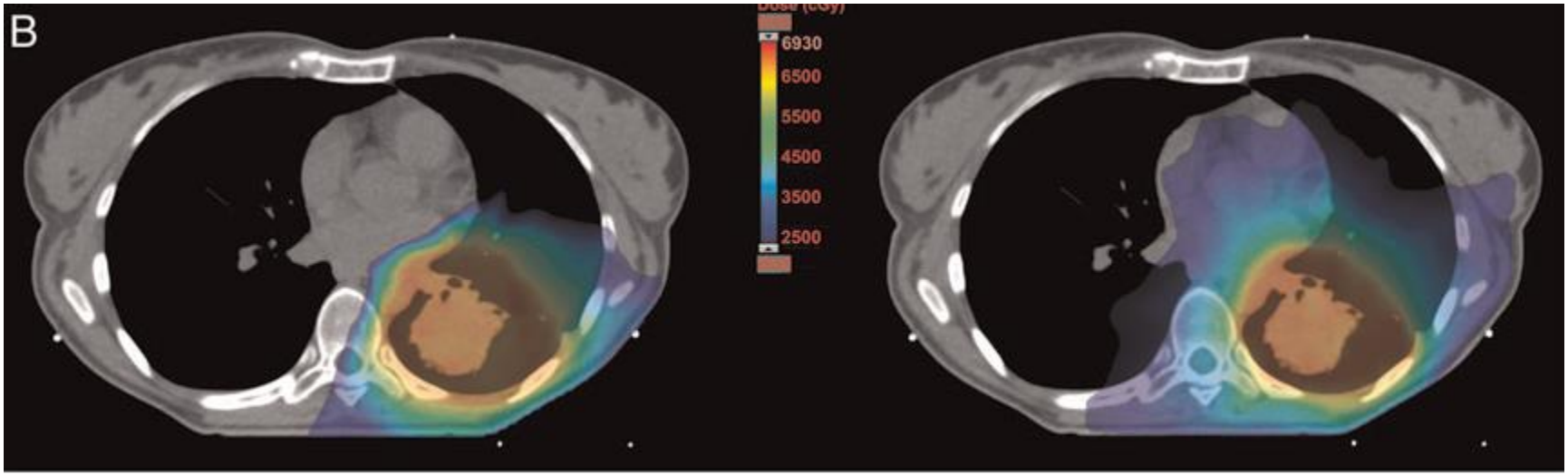
J F FOWLER, DSc, PhD, FInsTP



Fowler JF, Br J Radiol 2010

Proton and carbon-ion Radiochemotherapy for lung cancer

Proton and carbon-ion radiochemotherapy



Proton and carbon-ion radiochemotherapy

- Results of a phase II randomized trial suggest small OS advantage for protons (median OS 24 vs. 17 months)
- Phase III clinical trial is currently ongoing (RTOG -1308)

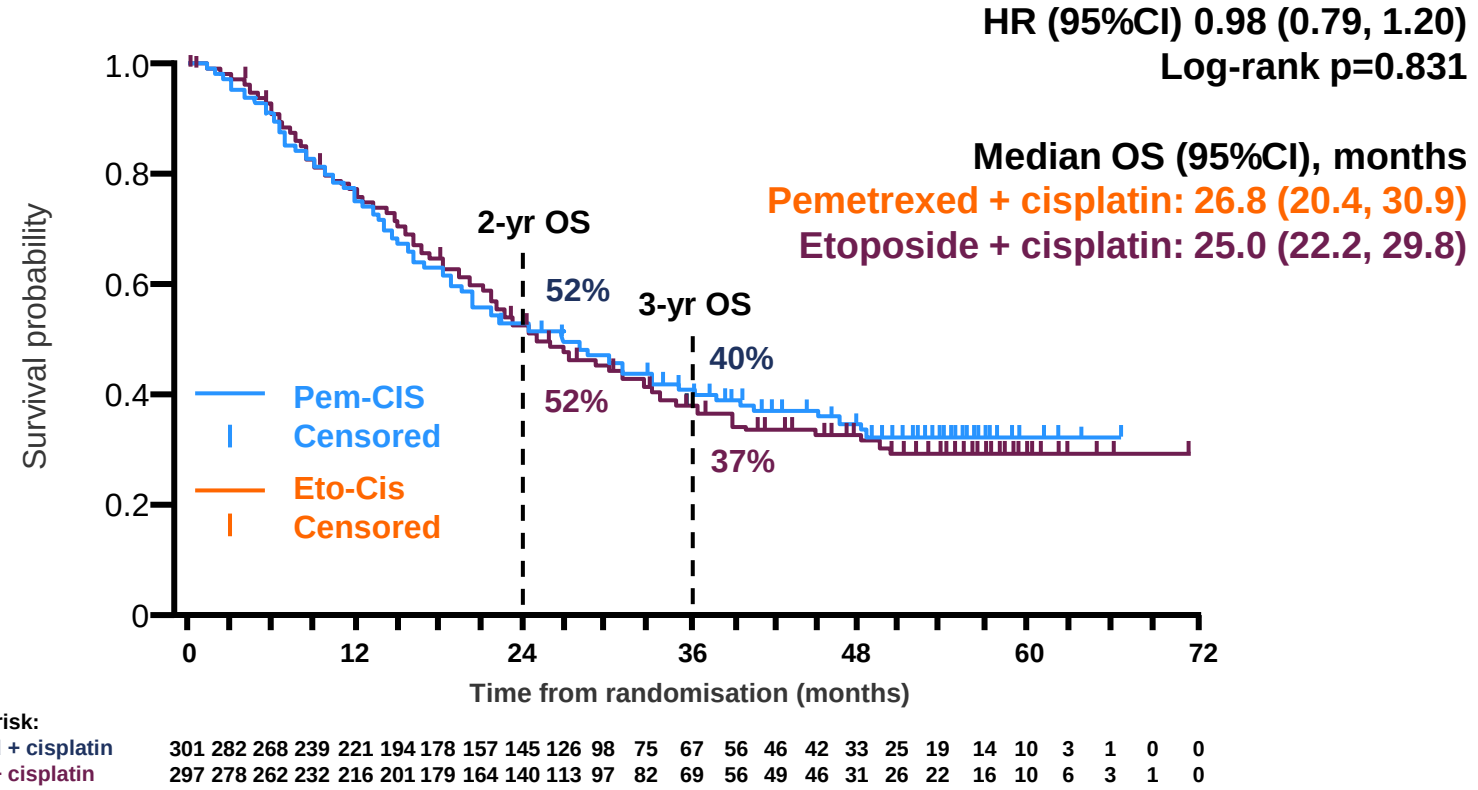
Optimal chemotherapy

Chemoradiation in stage III NSCLC: Drugs and schedules

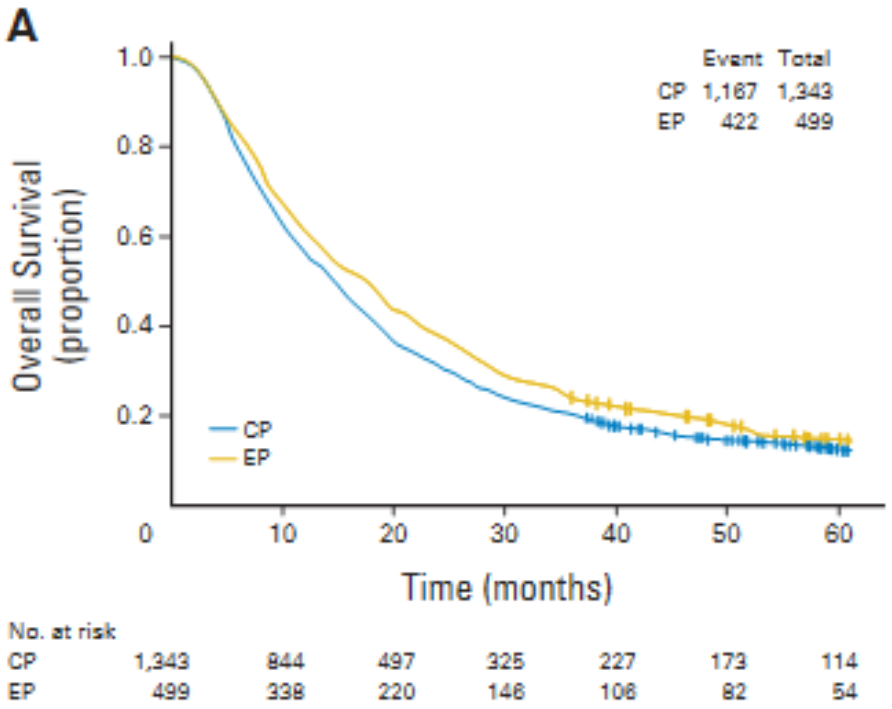
- Cisplatin - etoposide
- Cisplatin - vinorelbine
- Cisplatin - pemetrexed
- Carboplatin - paclitaxel (more common in the US)
- Cisplatin daily (NKI, Netherlands)

PROCLAIM TRIAL: PEM/CIS vs. ETOPOSIDE/CIS in chemoradiation of stage III NSCLC

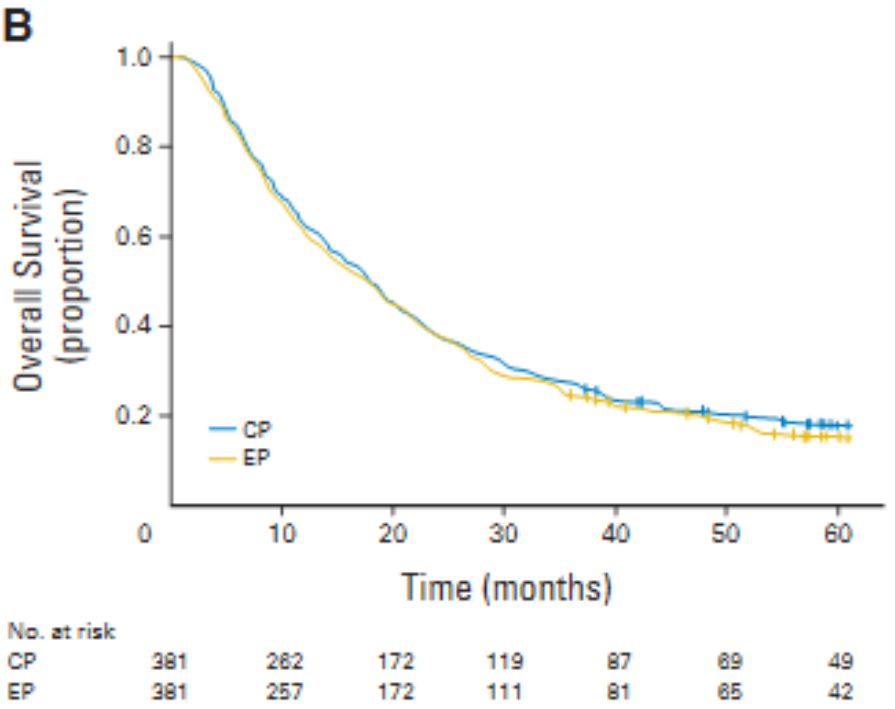
Senan S. et al., ASCO 2015; #7506



Chemoradiation with ETOPOSIDE/CIS vs. weekly CARBO/PACLITAXEL
Retrospective VA database comparison



Before propensity score matching

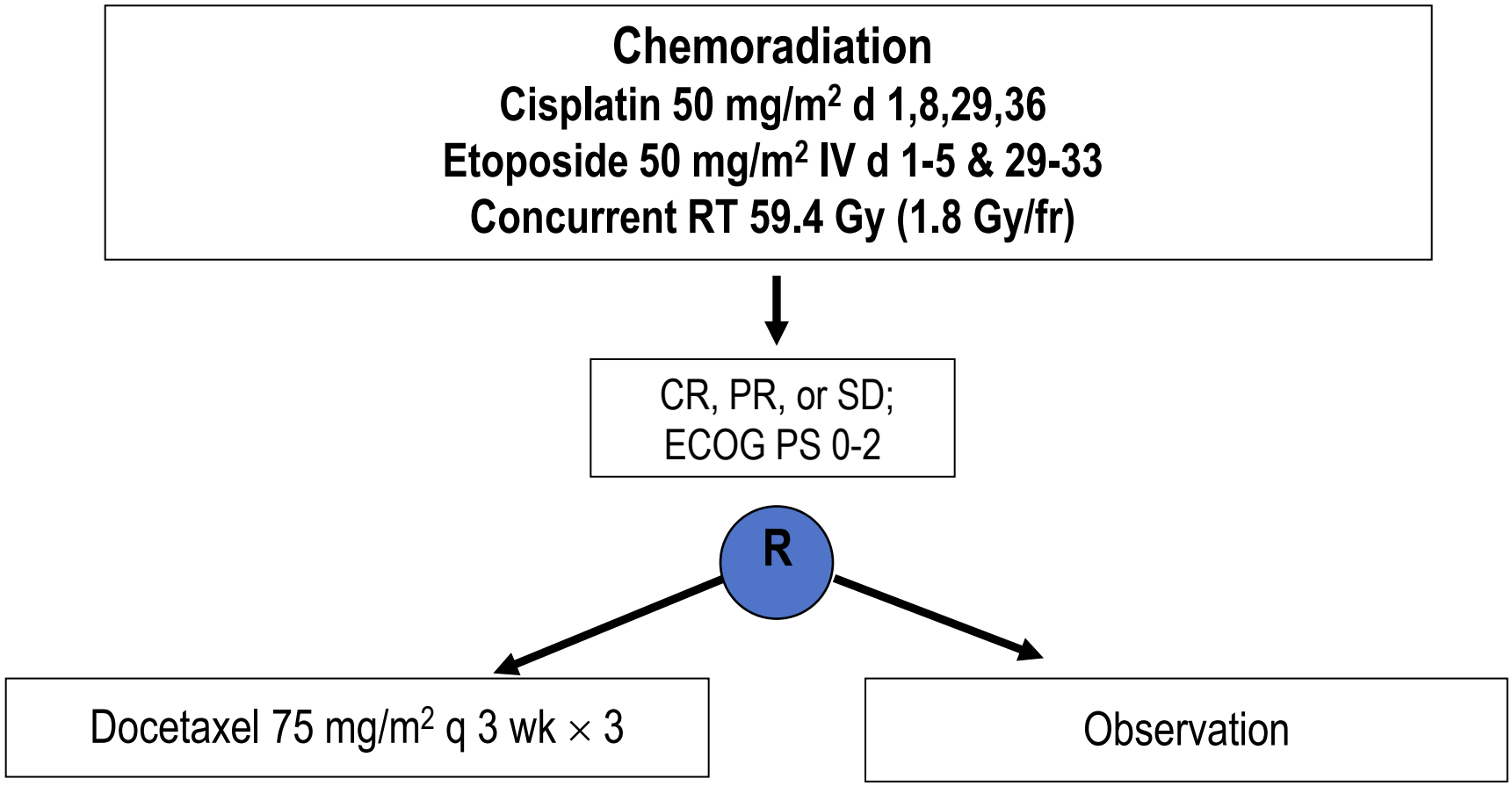


After propensity score matching

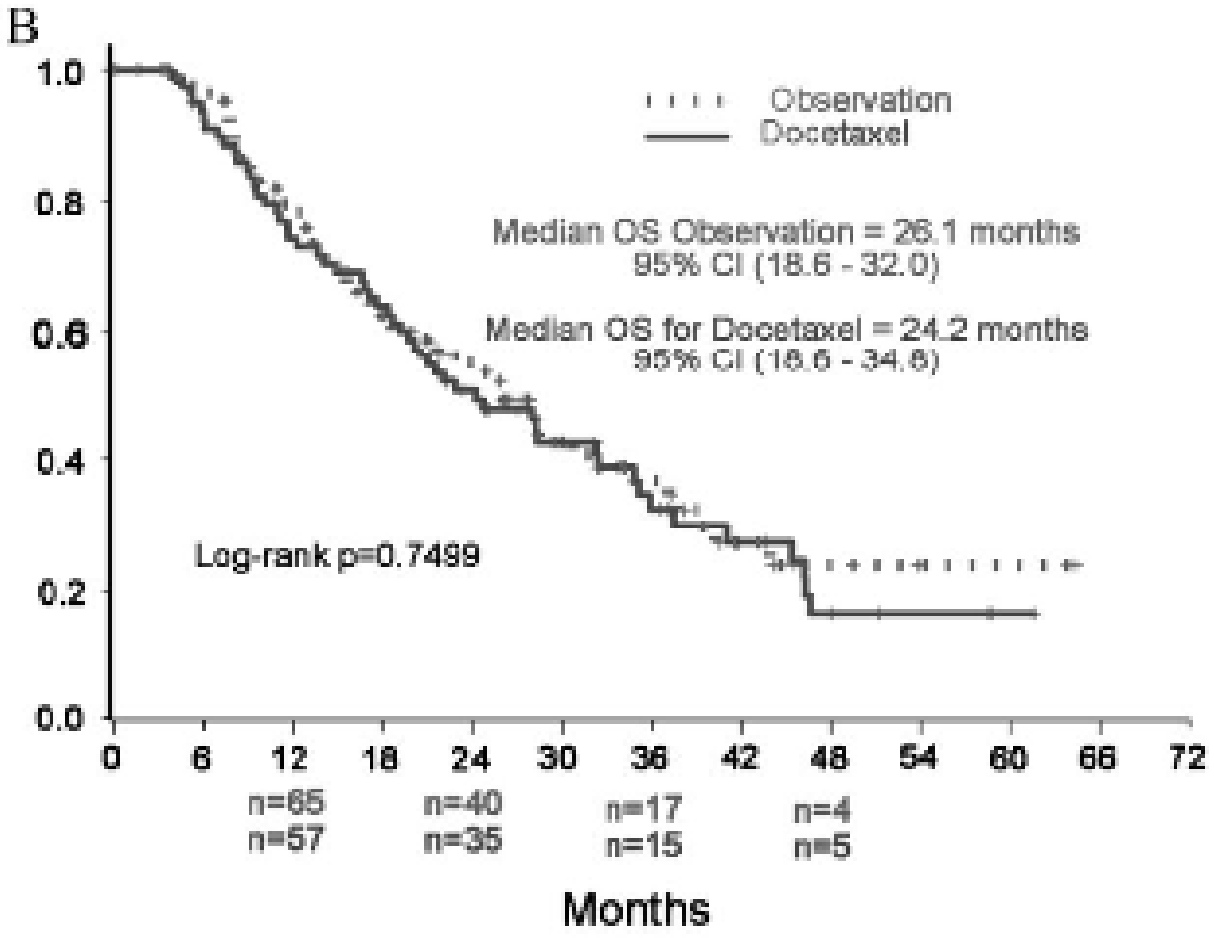
elcc

Santana-Davila et al., J Clin Oncol 33:567-574

Consolidation after chemoradiation
Phase III Hoosier Oncology Group Trial



Consolidation after chemoradiation
Phase III Hoosier Oncology Group Trial



Jalal SI et al., Ann Oncol 2011

Investigational systemic therapies

Investigational systemic therapies

- Targeted therapies in oncogene-addicted stage III NSCLCs (RTOG 1306 phase II; EGFR and ALK cohorts)
- PARP inhibitors (SWOG S1206 phase I – II)
- Immune checkpoint inhibitors (PACIFIC durvalumab phase III)
- Metformin (randomized phase II NRG-LU001)

Conclusions

- Therapeutic plateau reached with regard to chemotherapy schedules combined with concurrent RT with ~ 30-35% 5-year OS
- Dose escalation with conventional fractionation – no value (RTOG 0617)
- Number of phase II trials with altered fractionation and acceleration ongoing with good outcomes (BUT no phase III evidence)
- Identification of patients likely to show early dissemination may be key to focus on systemic treatment
  (~ 20 – 30% of patients die within 12 months!)
- More effective systemic therapies urgently needed
  – several trials currently ongoing