

6th ELCC, 2016.13 April

SCLC: Advances & state of the art

**Advances in systemic treatment of
SCLC excluding immunotherapy**

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Disclosure

Honoraria: Eli-Lily, Taiho, Chugai

SCLC: State of the art in 1983

	LD	ED	Total
CR+PR (%)	80	75	75
CR (%)	50	25	35
Median Survival (mo)	14	7	12
3-year Survival (%)	15-20	0	5-10

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Meta-Analysis: Cisplatin or Not in SCLC

Trials/#patients	19/4054
Eligibility	No prior chemotherapy
Survival	20% reduction in mortality at 1 year with CDDP regimen ($P=.002$)
Response	Better in CDDP (9% relative increase, $P<.05$)
Mortality	No difference

JCOG 9511: CPT-11 + CDDP vs. Etoposide + CDDP

ESCLC
PS 0-2
Age 70≥

R

Irinotecan+ CDDP (IP) (n=77)

Cisplatin 60mg/m² day 1

Irinotecan 60mg/m² days 1, 8, 15

4 cycles every 4 weeks

ETOP + CDDP (EP) (n=77)

Cisplatin 80mg/m² day 1

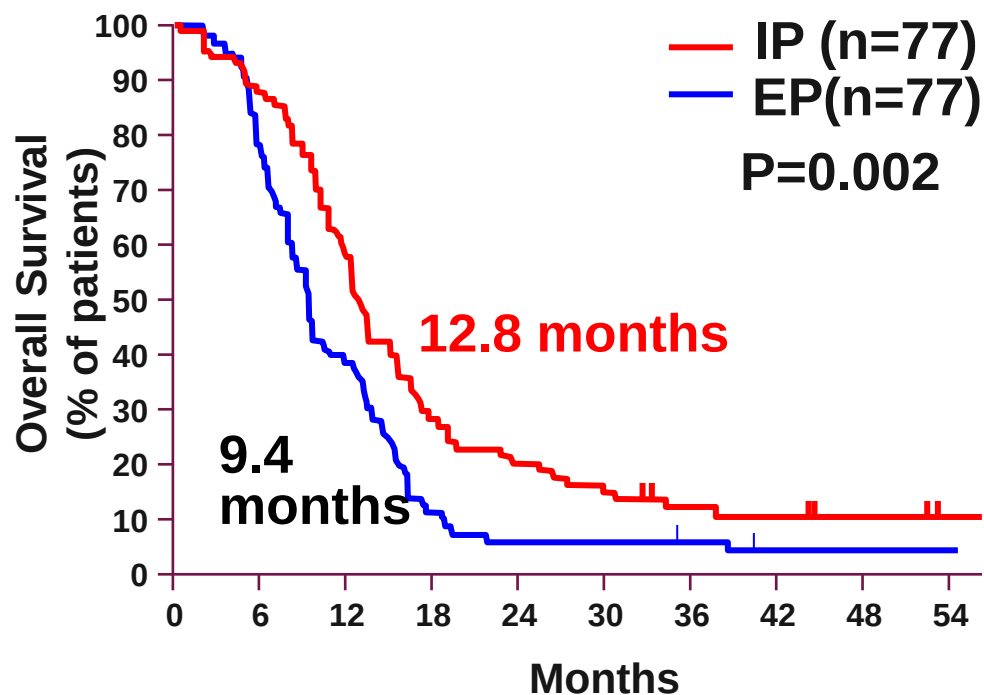
Etoposide 100mg/m² days 1-3

4 cycles every 3 weeks

ED-SCLC: CDDP+CPT-11 vs CDDP+ETP

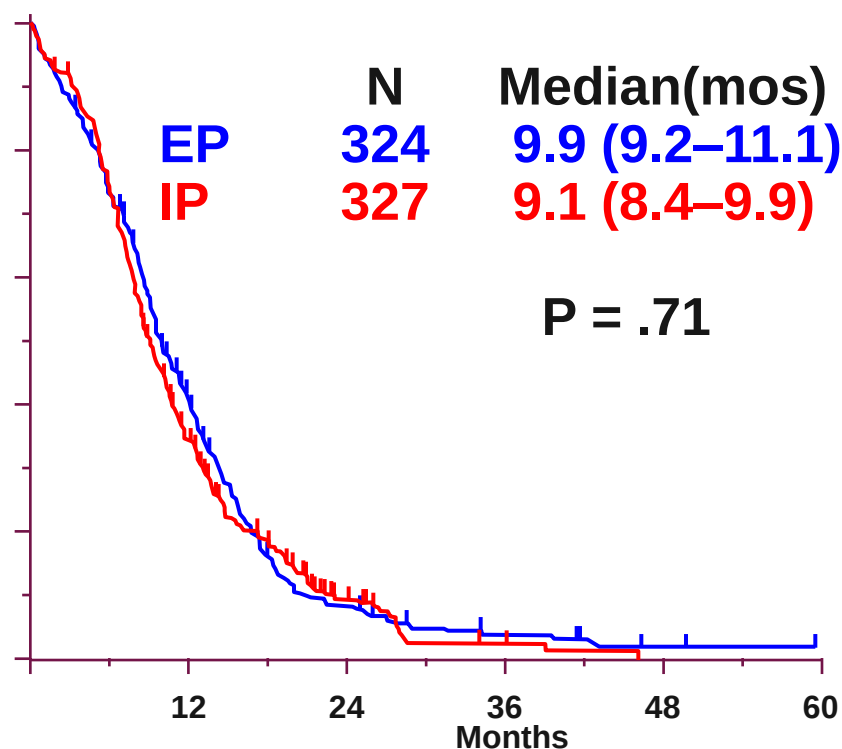
OS

JCOG9511



Noda K. N. Engl J Med 346:85-91, 2002

SWOG0124

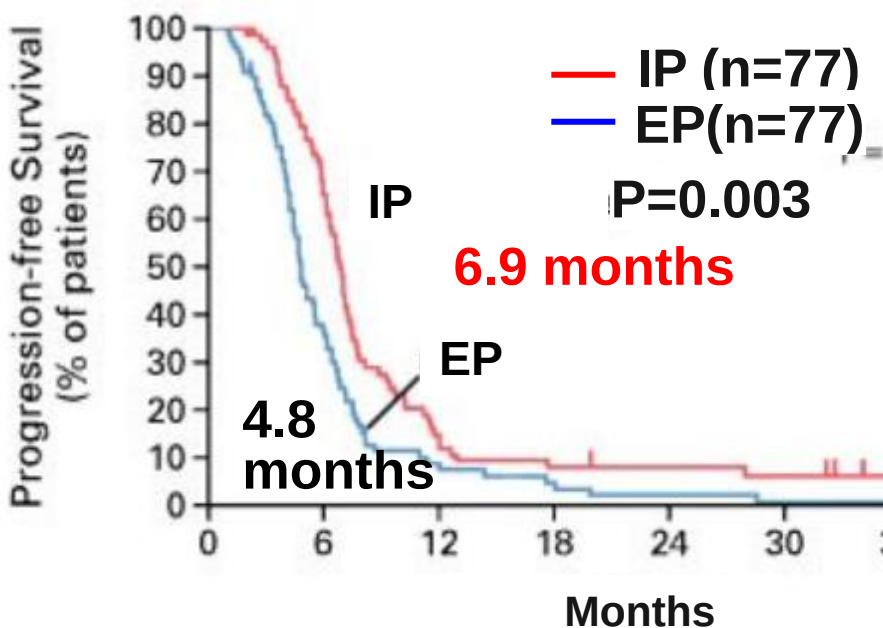


Lara PN. J Clin Oncol 27:2530-5, 2009

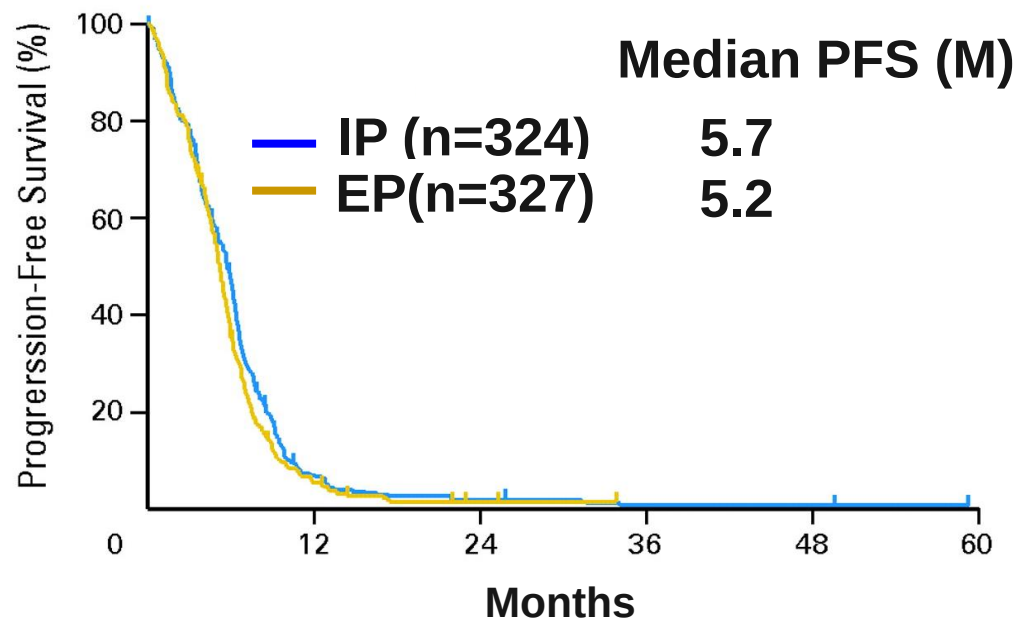
ED-SCLC: CDDP+CPT-11 vs CDDP+ETP

PFS

JCOG9511



SWOG0124



Meta-analyses: Irinotecan or Etoposide in ED-SCLC

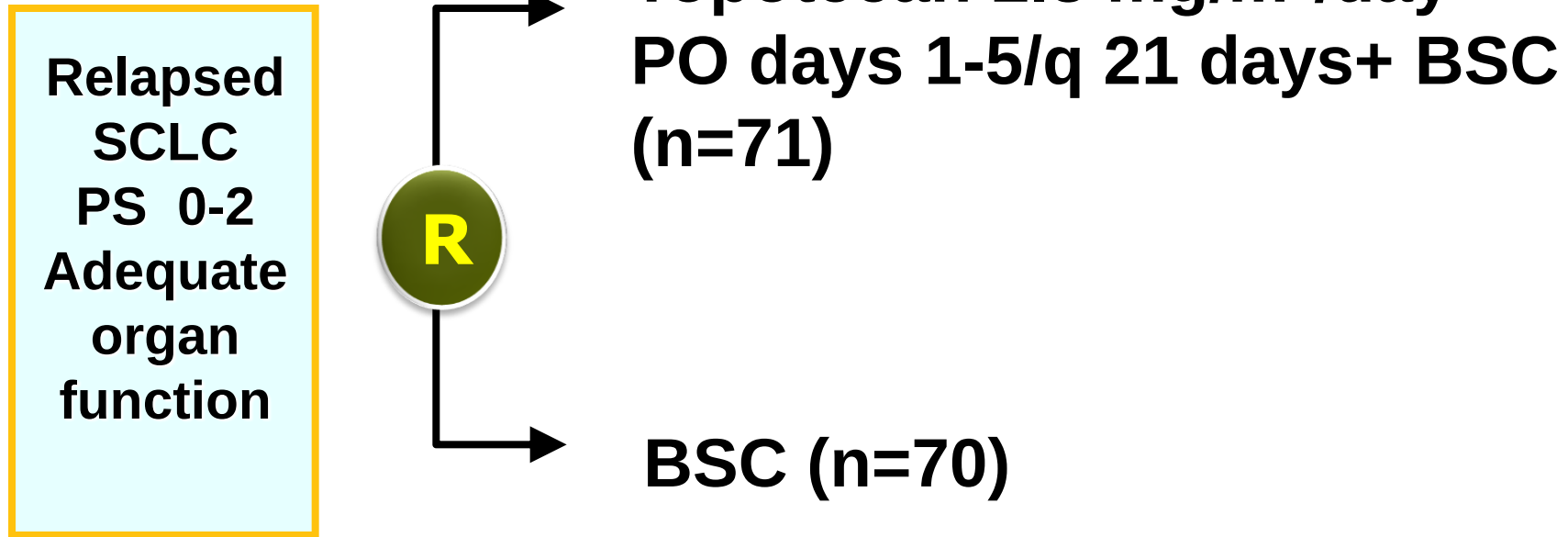
- **Irinotecan/platinum vs Etoposide/platinum:
6 trials 1476 pts. OS: IP>EP HR 0.81 95%CI: 0.66-0.99
P=0.044**

Jian J et al. J Thorac Oncol 5: 867, 2010

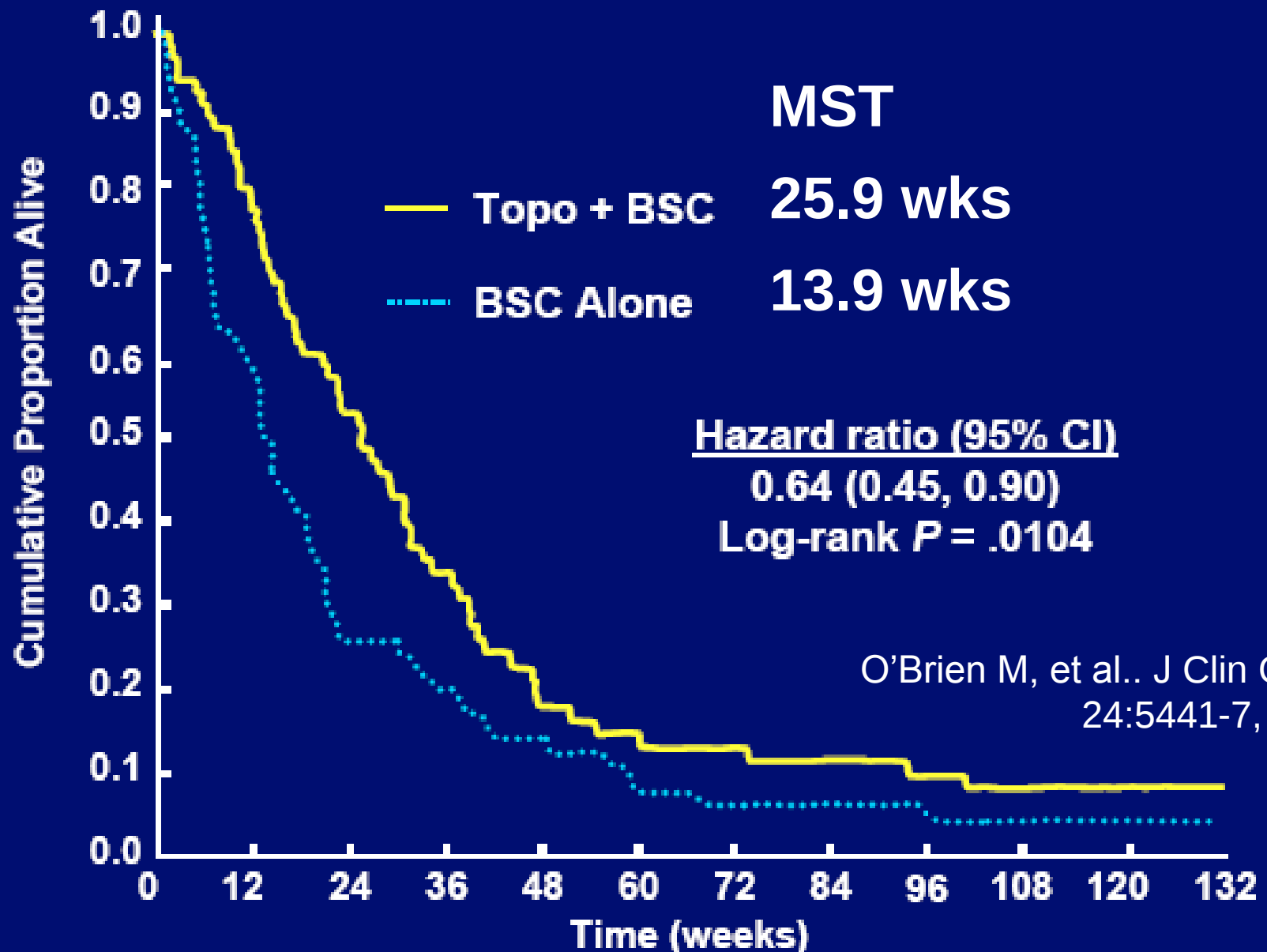
- **Irinotecan/platinum vs Etoposide/platinum:
4 western trials 1407 pts. OS: IP>EP
HR 0.87 95%CI: 0.78-0.97 P=0.02**

Lima J et al. J Thorac Oncol 5: 1986, 2010

Phase III trial of Oral Topotecan vs. BSC for Previously Treated ED-SCLC



Overall Survival (ITT)



Activity of Anti-Cancer Agents for SCLC

agent	Previous treatment	#report	#pts	response (%)	MST (mo)
Irinotecan	no	1	8	50	-
	yes	4	118	25	4.2~8.2
Topotecan	no	3	92	33	8.7~10
	yes	7	435	23	4.7~8.7
Amrubicin	no	1	33	76	11.7
	yes	2	94	52	9.2~11.2

JCOG0509: Study Design

ED-SCLC
20-70 yrs
PS 0-1

Stratification

- PS
- institution
- sex

Sample size

N=282

(n=141 per Arm)

**R
A
N
D
O
M
I
Z
E**

IP

irinotecan 60mg/m² D1,8,15
cisplatin 60mg/m² D1
Q4 weeks x 4 cycles

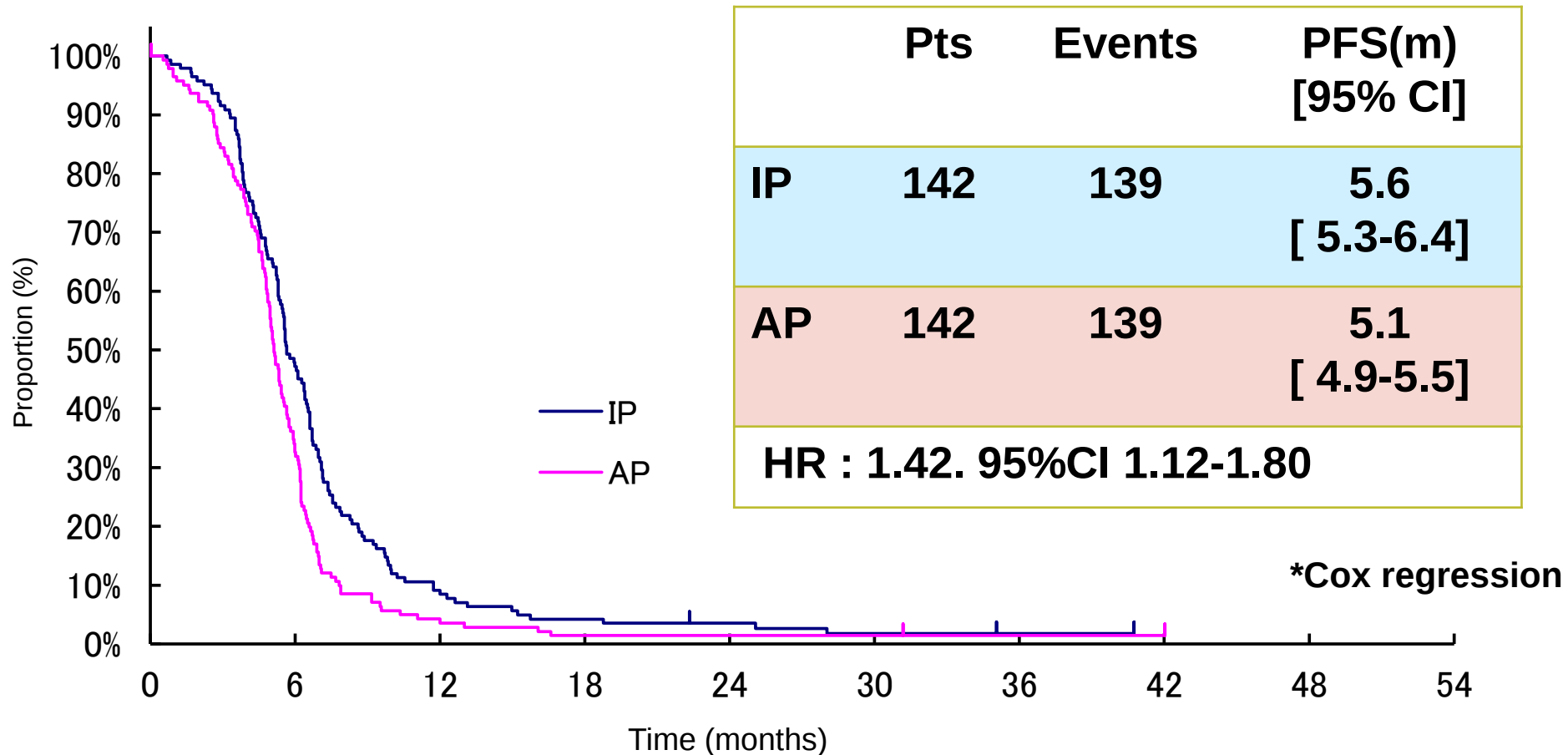
PCI
for CR
cases

2.5Gy
10 Fr

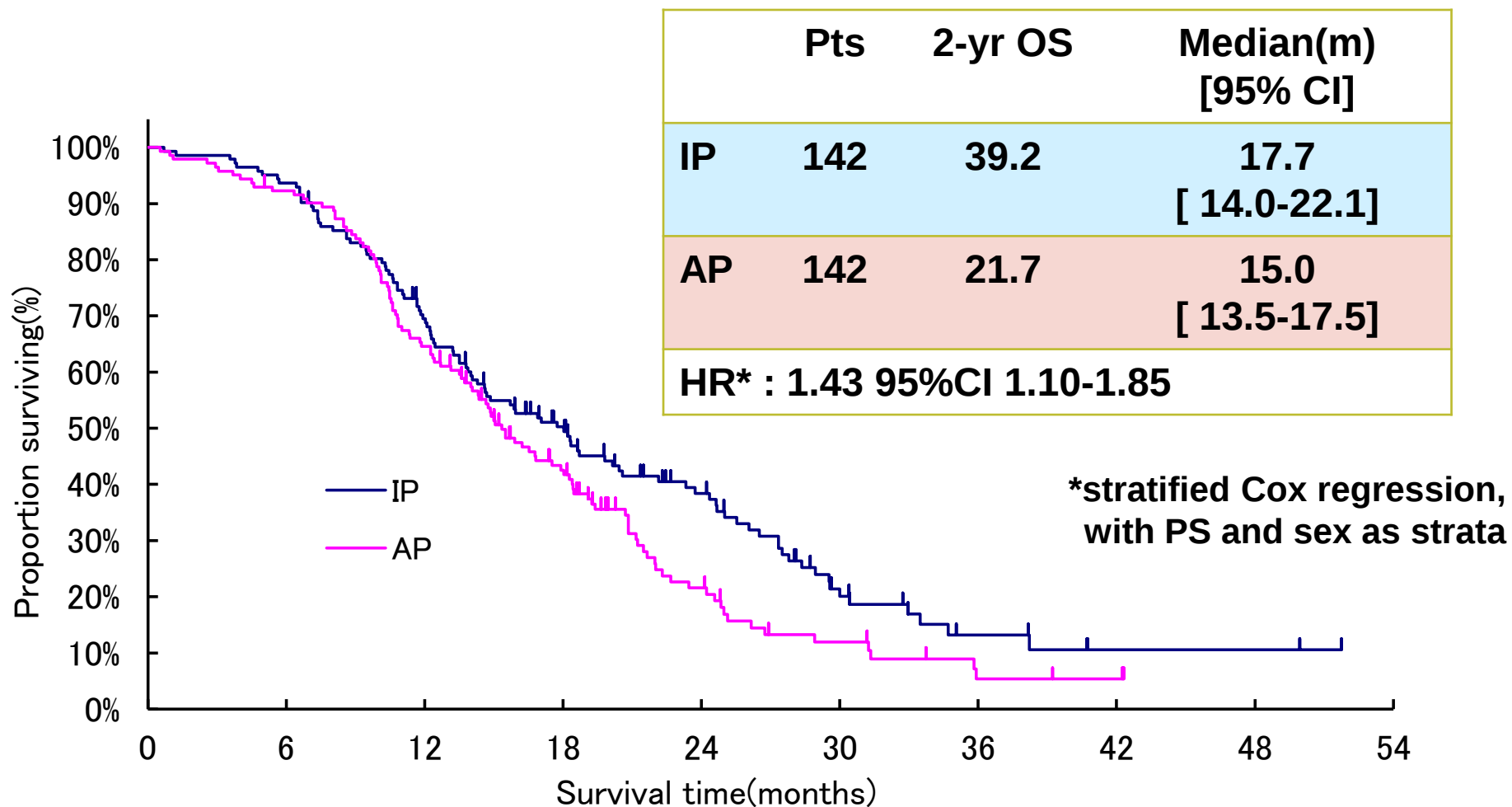
Amrubicin 40→35mg/m² D1-3
cisplatin 60mg/m² D1
Q3 weeks x 4 cycles

AP

Progression-free Survival



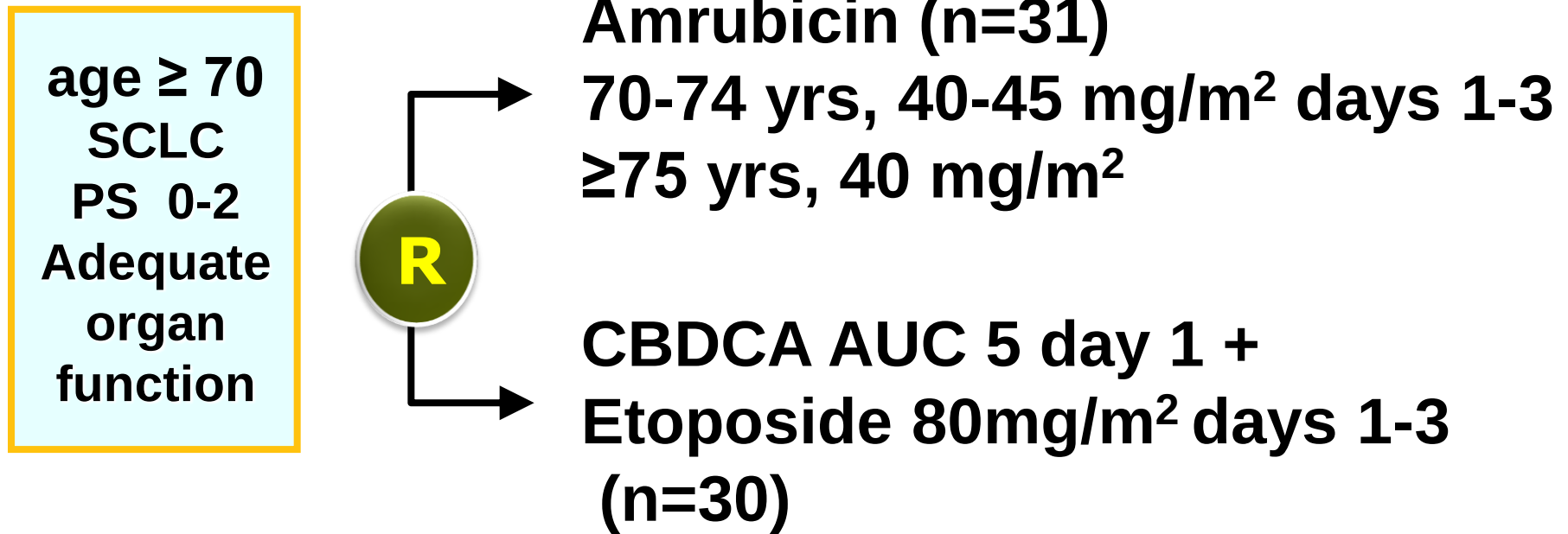
Overall Survival



JCOG0509: Post-Study Therapy

Chemotherapy	Second Line		Third Line	
	IP (n=127)	AP (n=122)	IP (n=84)	AP (n=87)
Irinotecan	3	24	7	19
Amrubicin	61	2	34	12
CBDCA+Etoposide	22	29	25	24
Topotecan	12	23	6	5
other	29	44	12	27

A Randomized Phase III Study of Single-Agent Amrubicin Vs. Carboplatin/Etoposide in Elderly Patients With ED SCLC



Target # of pts: 130

A Randomized Phase II Study of Single-Agent Amrubicin Vs. Carboplatin/Etoposide in Elderly Patients With ED SCLC

	RR (%)	TTP (month)	OS (month)	FN (%)	G3 ILD (%)	TRD (%)
AMR (N=31)	74	4.7	10.9	34.4	12.5	9.7
CBDCA +ETP (N=30)	60	4.3	11.3	3.3	0	0

**Conclusion: Amrubicin monotherapy at 40 to 45 mg/m²
is toxic and intolerable in elderly Japanese patients with
ED-SCLC**

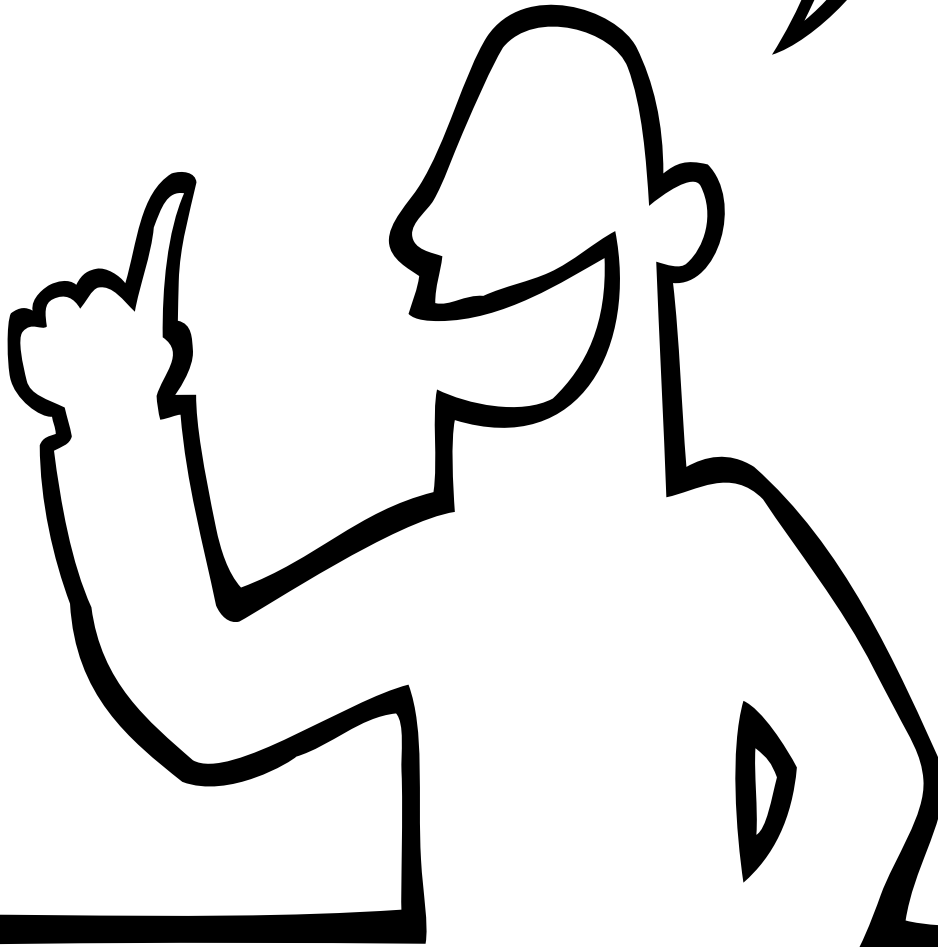
Amrubicin: Clinical Practice in Japan

Elderly Patients: 30-35mg/m², days 1-3

Younger Patients: 35-40mg/m², days 1-3

**More is not always
better**

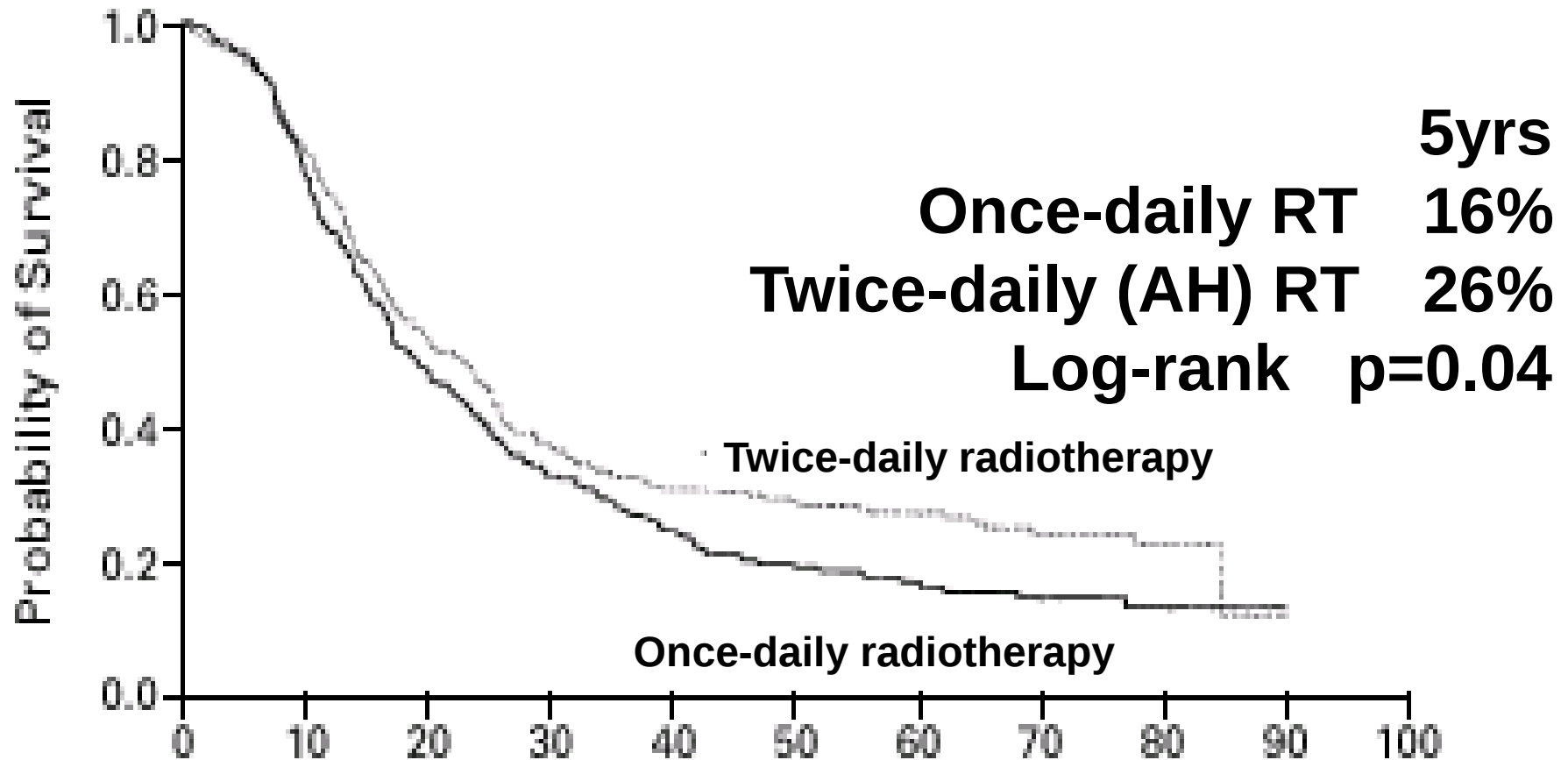
**Lessons
learned from
Amrubicin
trials**



SCLC: State of the art in 1983→2016

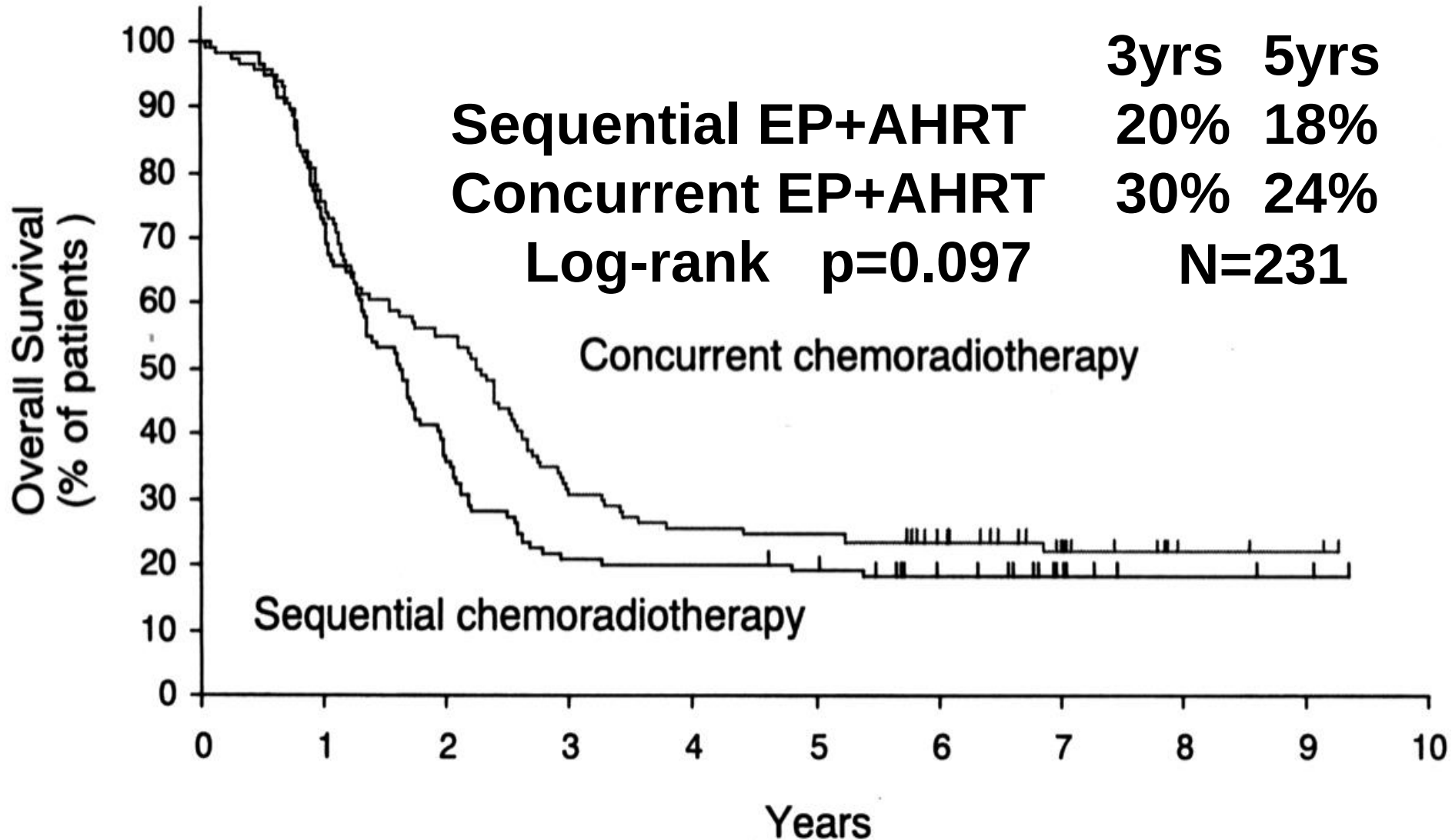
	ED
CR+PR (%)	75
CR (%)	25
Median Survival (mo)	7→9-15
3-year Survival (%)	0→5-10

EP+TRT vs EP+AHTRT for LD-SCLC

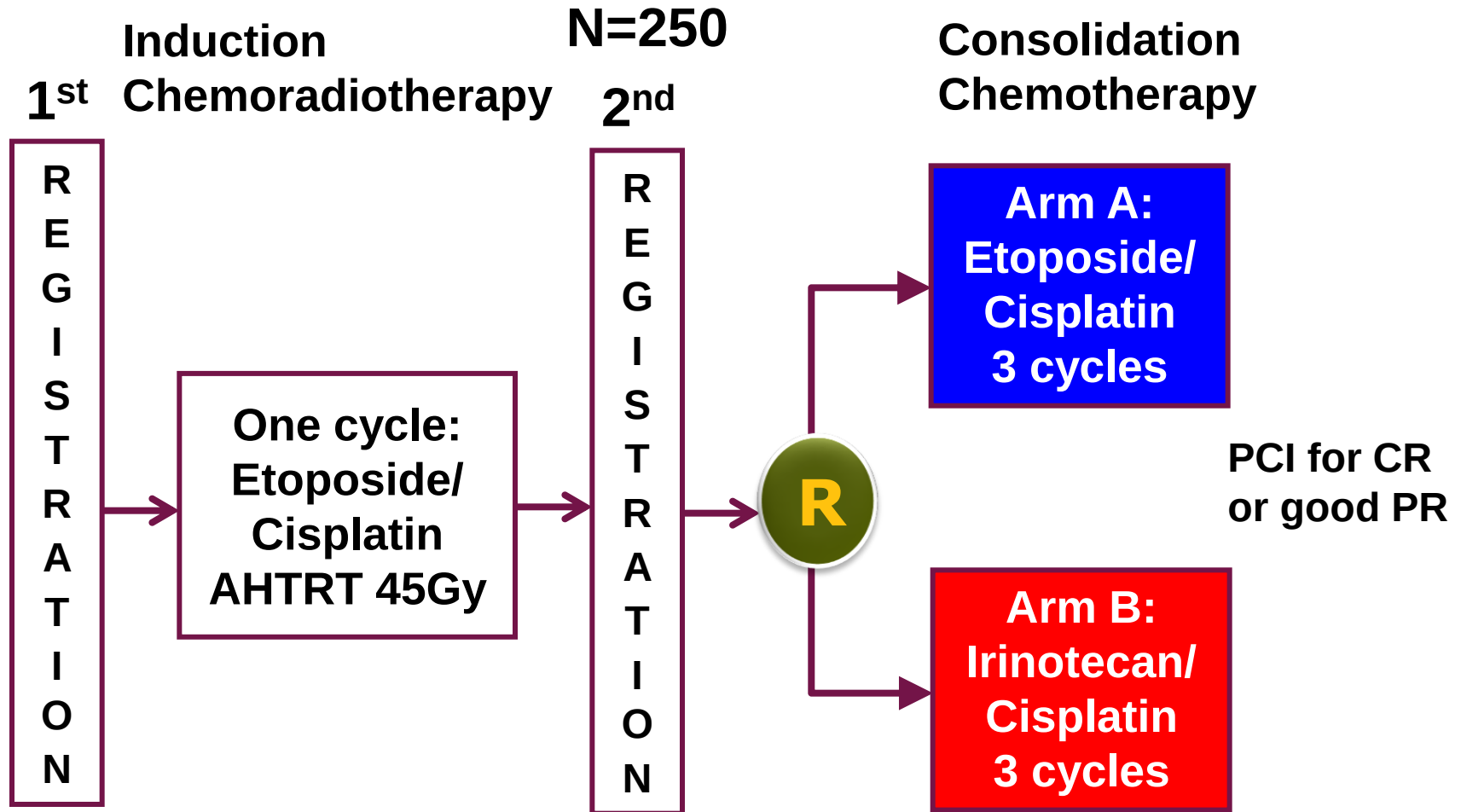


Turrisi AT, et al. NEJM; 340: 265, 1999

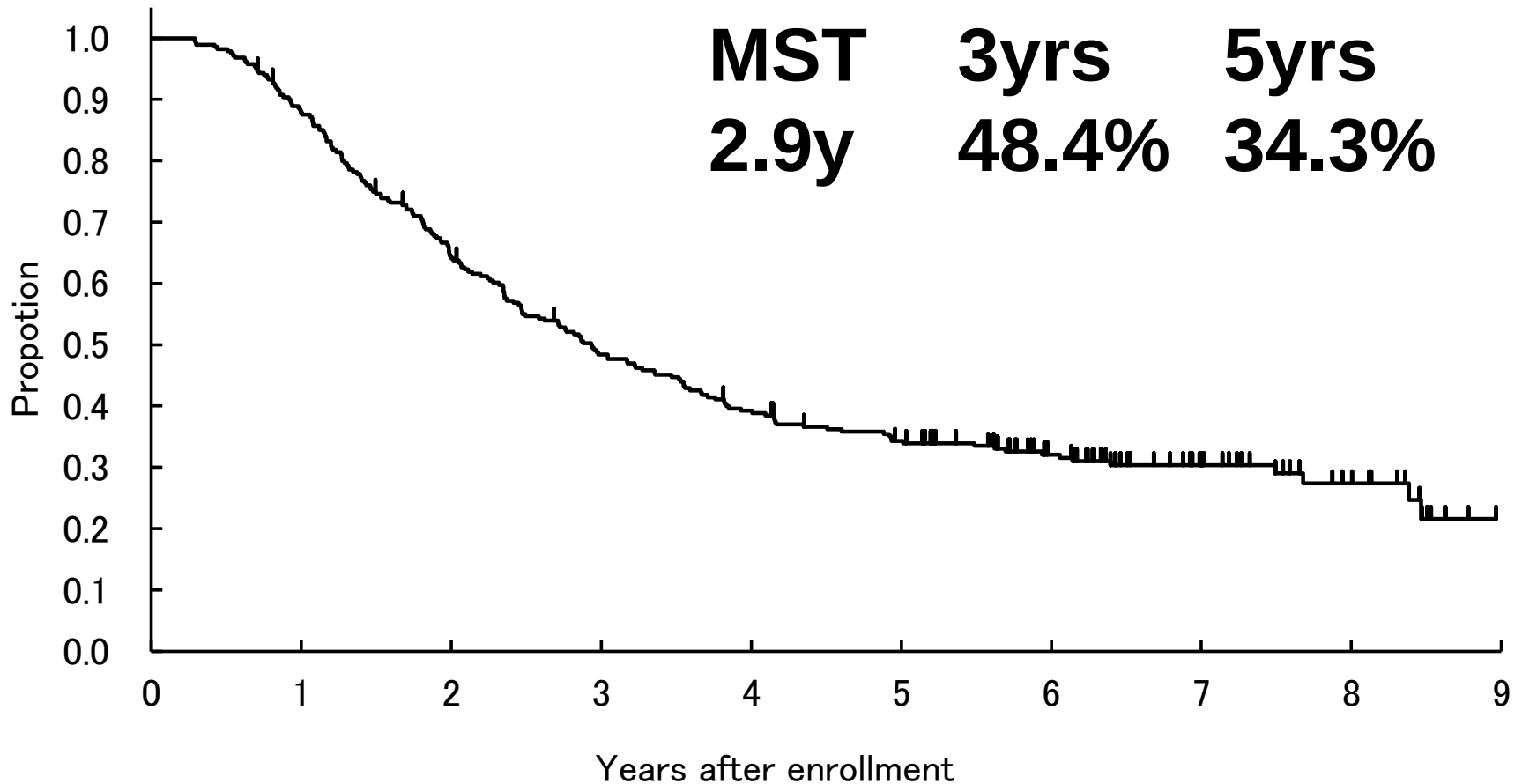
JCOG9104 OS



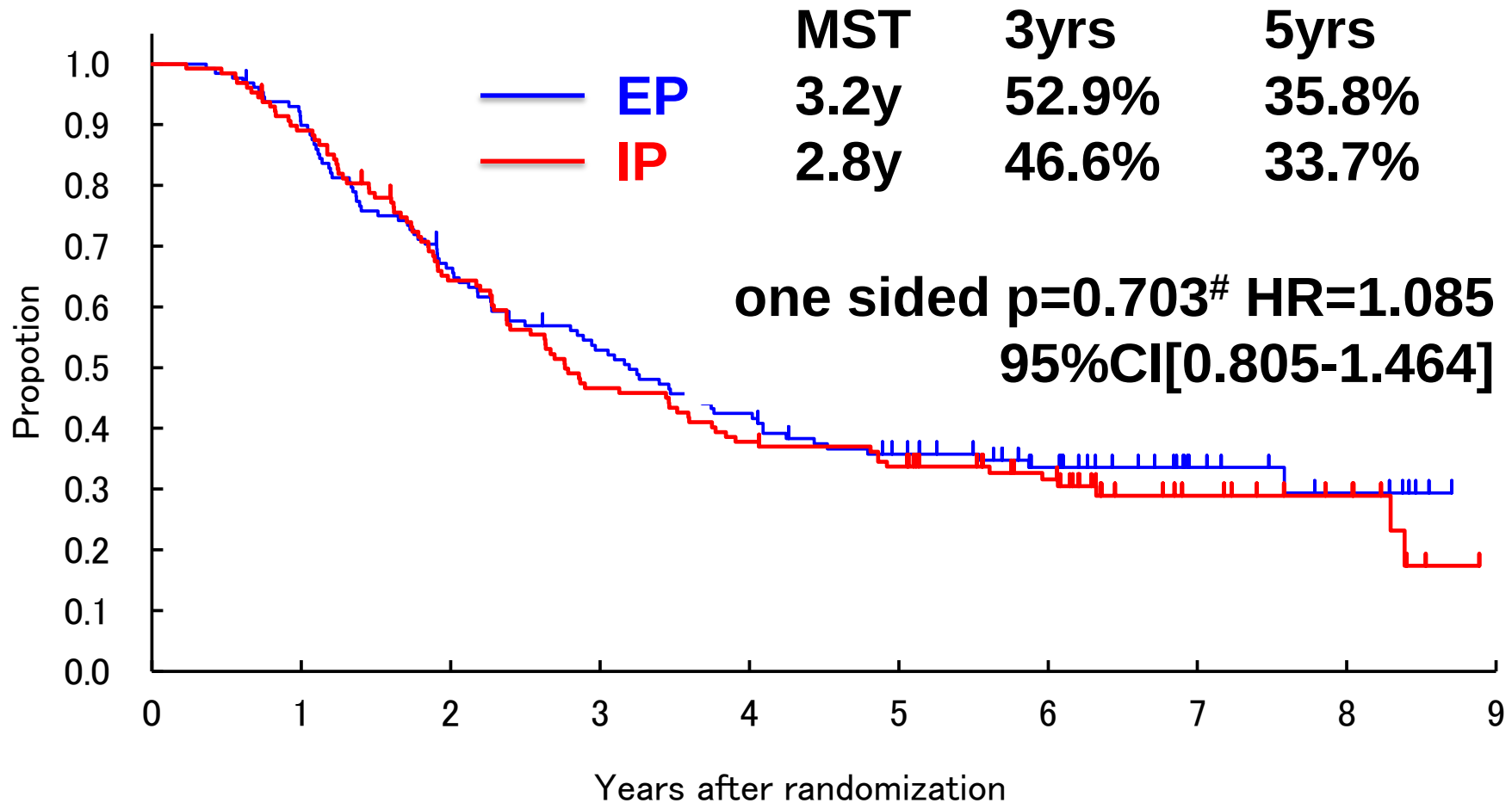
JCOG0202: Study Schema



JCOG0202: OS after 1st Registration



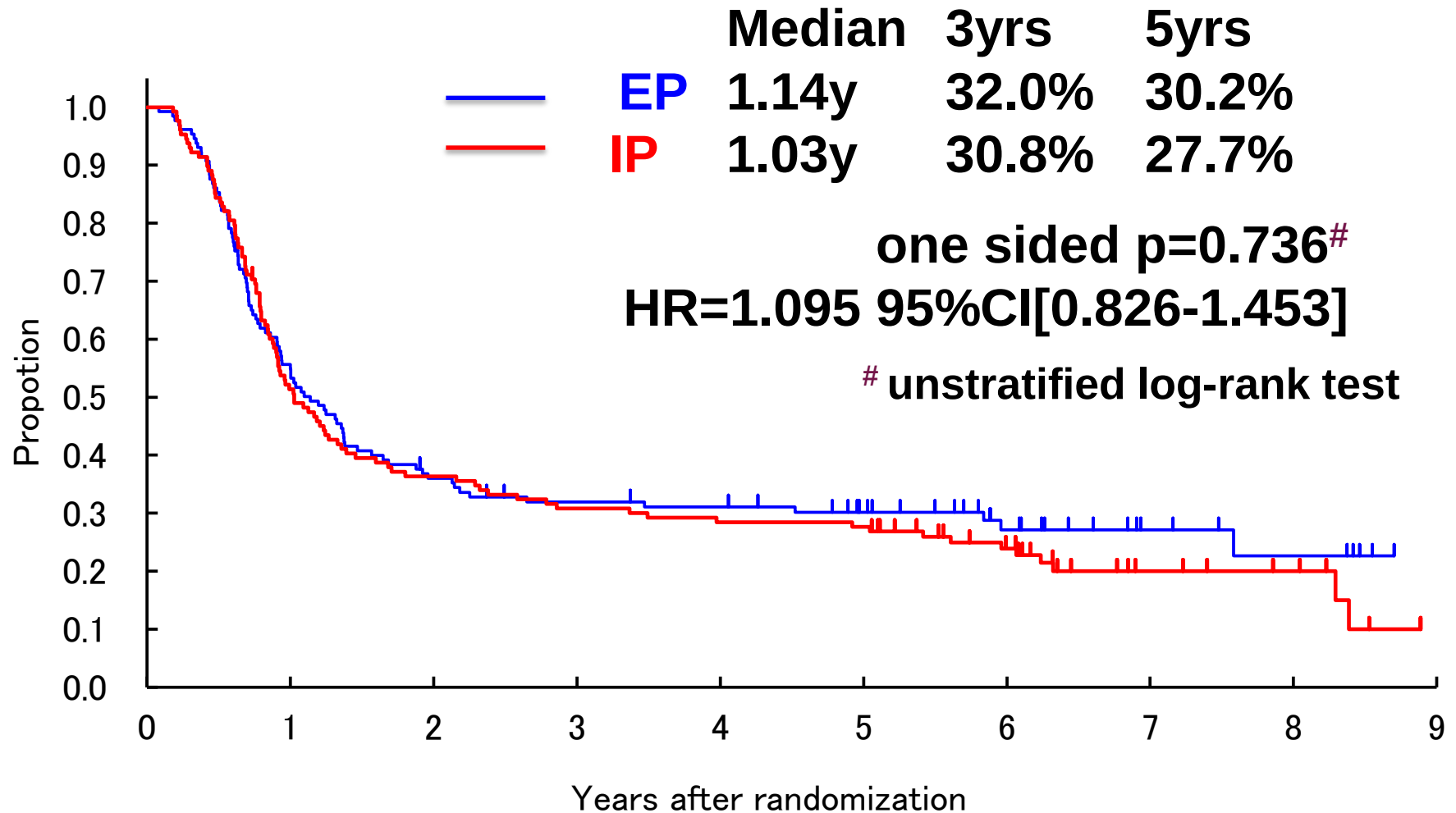
JCOG0202 Primary Analysis: OS after randomization



$^{\#}$ Stratified log-rank test, with PS and Response to Induction Chemoradiotherapy as strata

Kubota K, et al. Lancet Oncol 2014; 15: 106-13

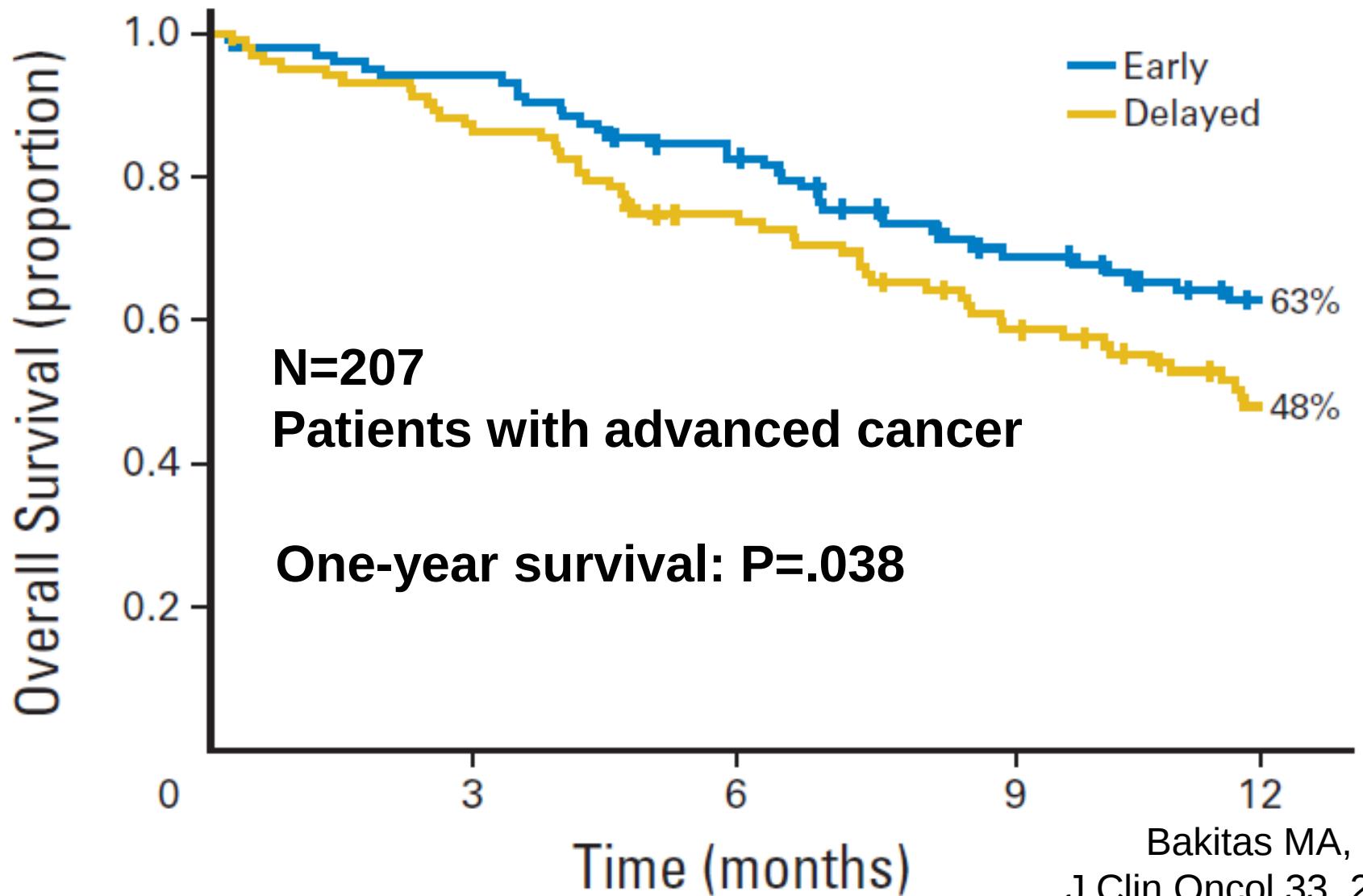
JCOG0202: PFS after randomization



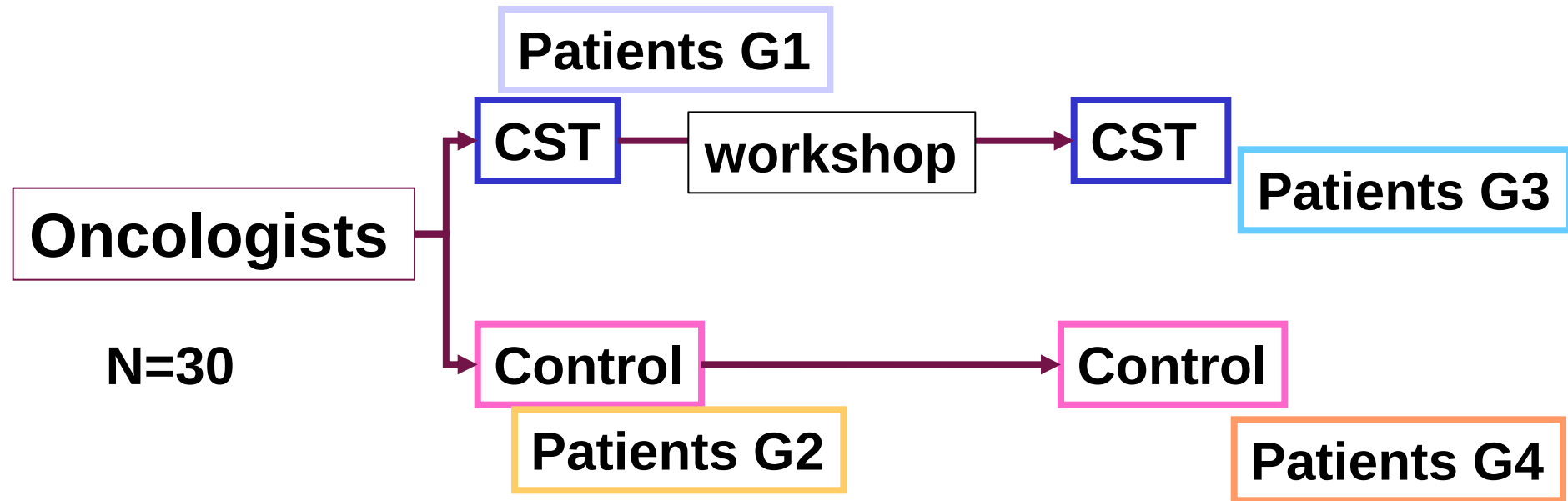
JCOG0202 Favorable Outcome:

- **Patient Selection- PS 0-1, Age: 70≥**
- **Japanese Patients**
- **Radiotherapy Quality Control**
- **Patient Care: Full Disclosure of prognosis, and toxicity management in the consent form of the study**

Early Versus Delayed Concurrent Palliative Oncology Care

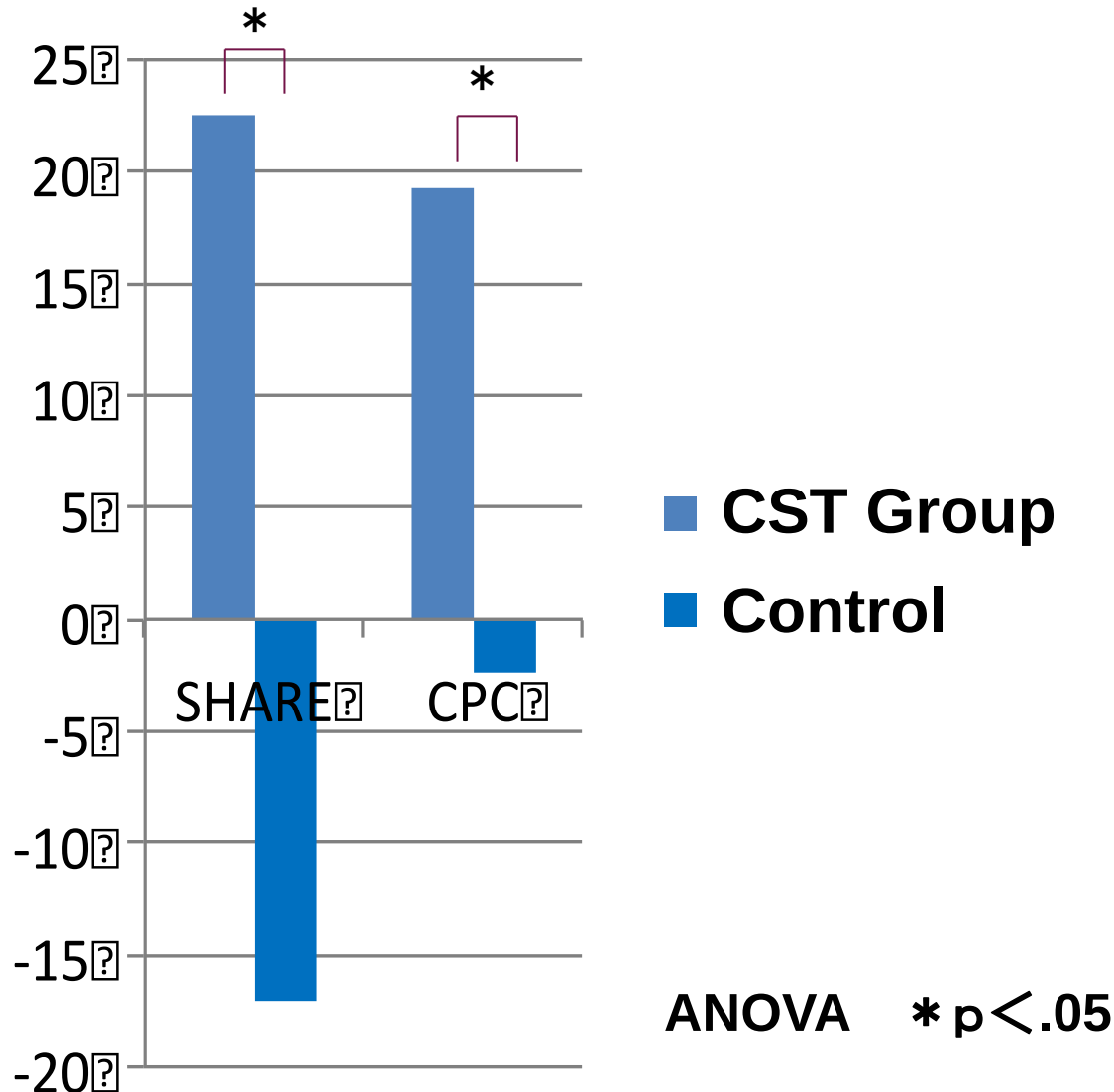


Randomized Trial of Communication Skill Training

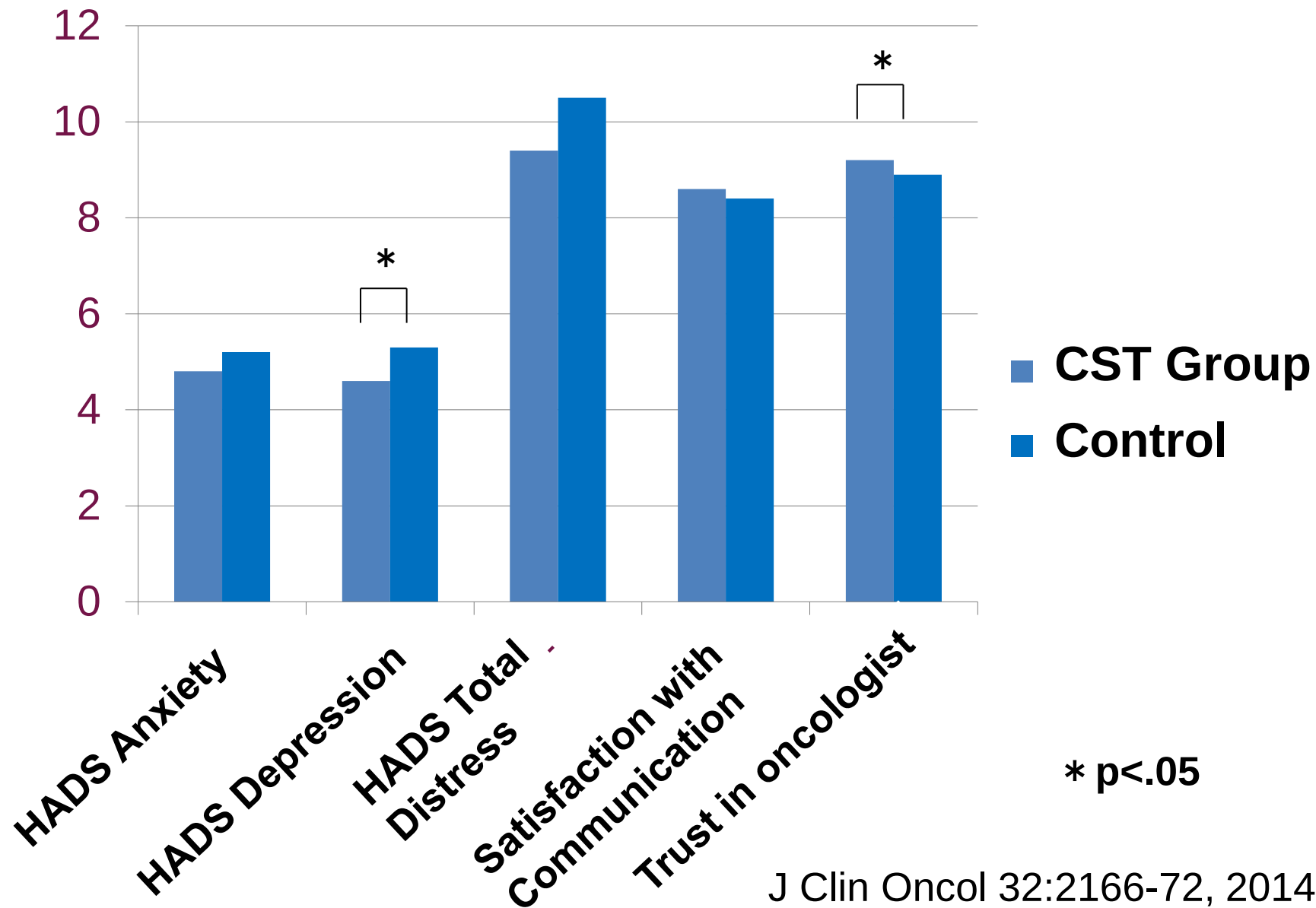


SHARE protocol

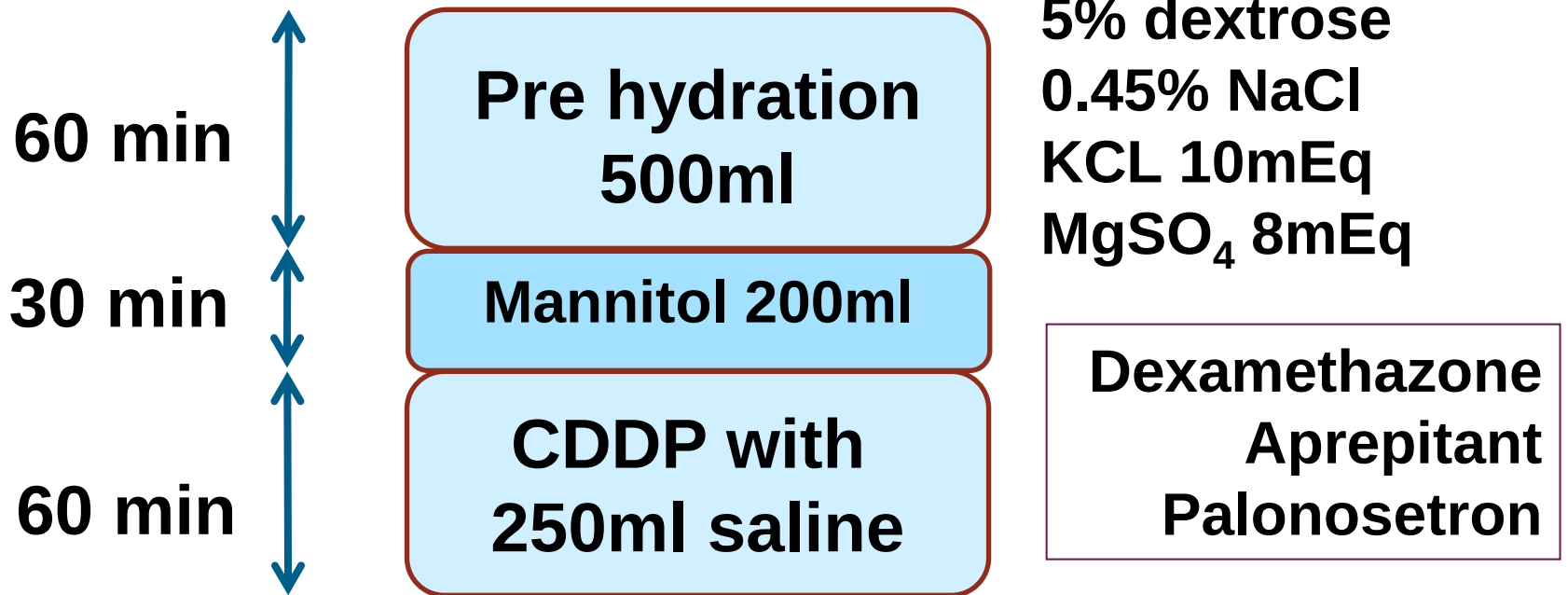
Physician Performance: Self-efficacy



Patient Psychological Distress, Perceived Communication and Satisfaction (N=601)



Prospective Trial of Cisplatin-based chemotherapy using Oral Post Hydration

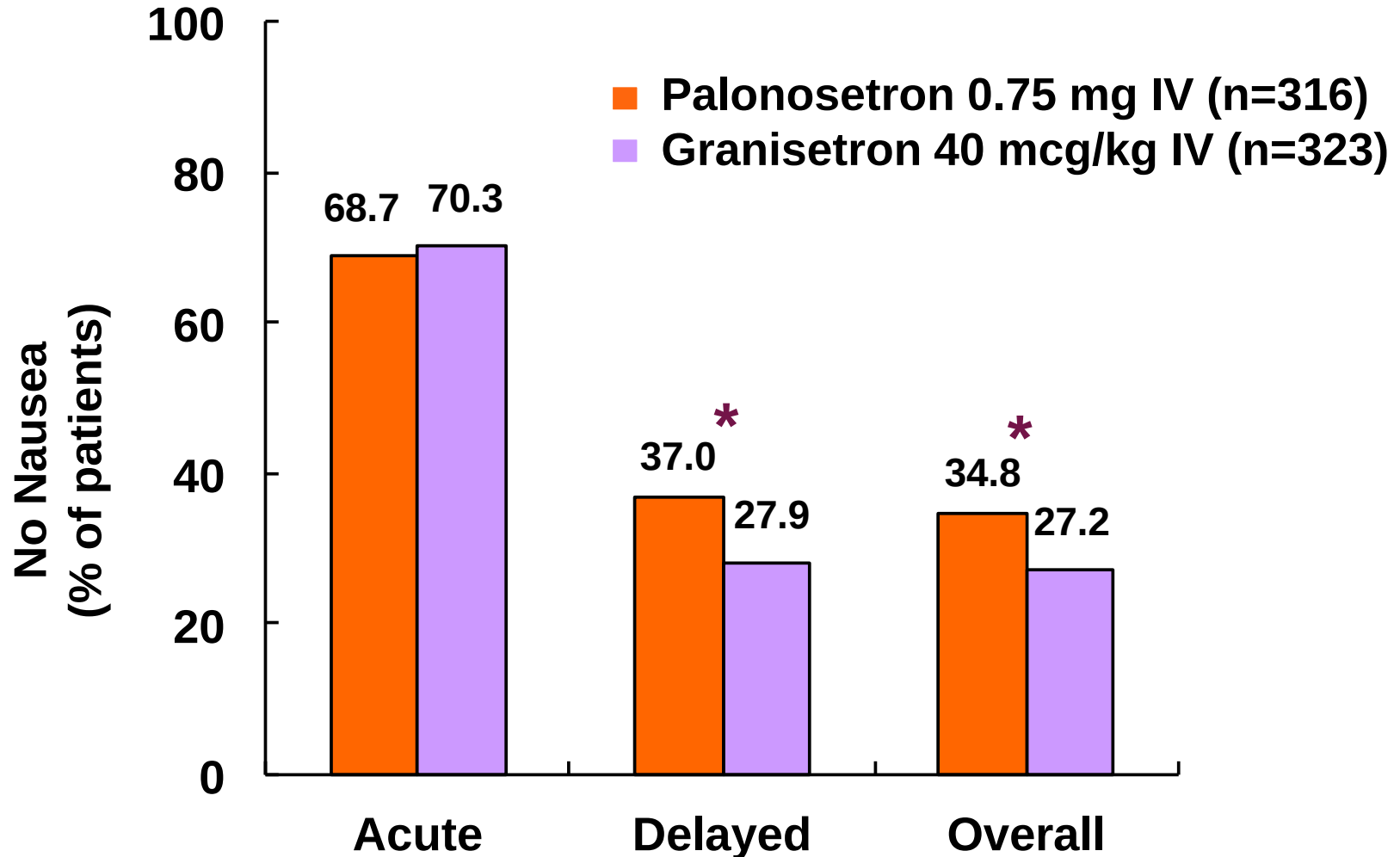


**Oral
500ml**

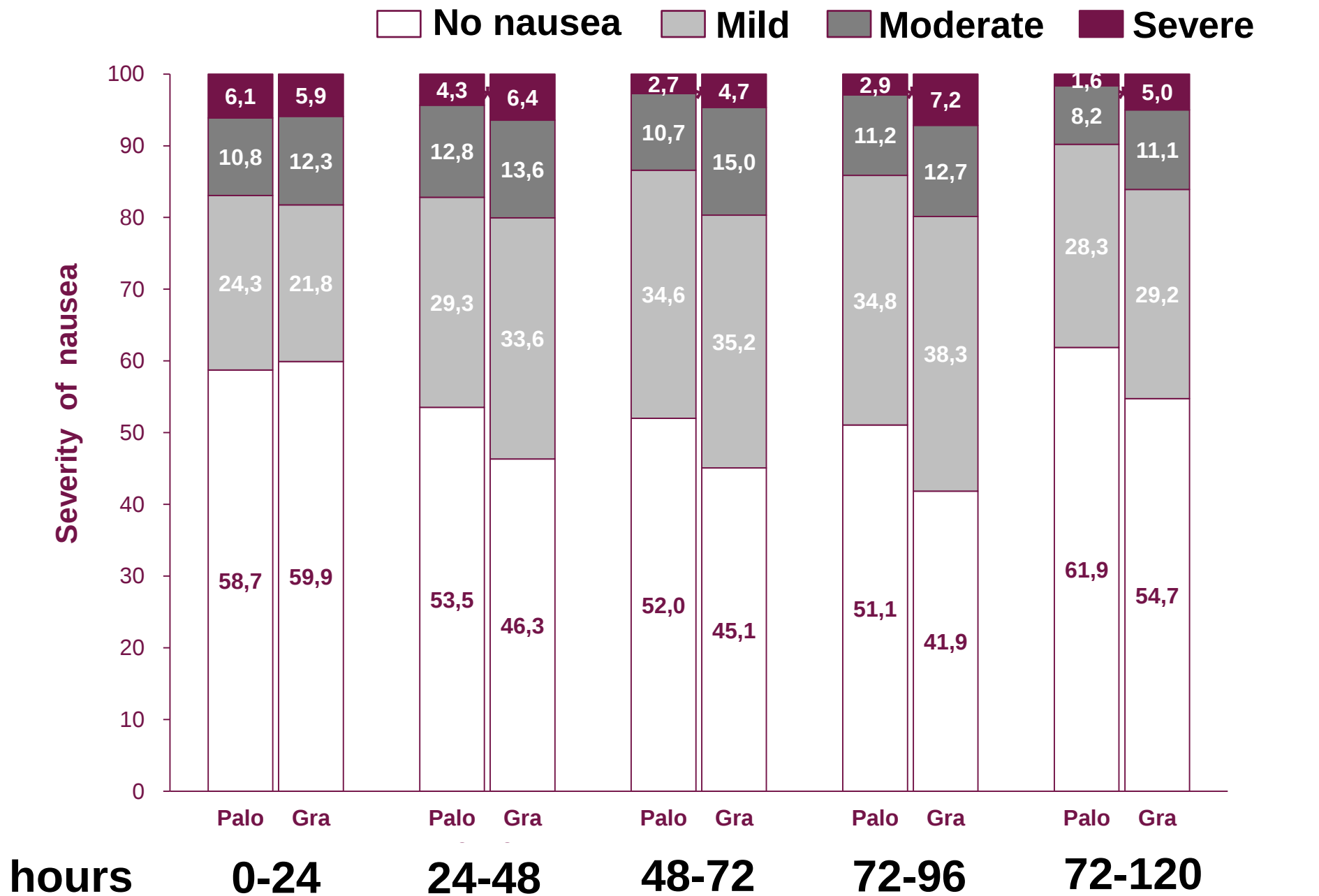
Result (N=46)

Serum Creatinine Elevation	N (%)
Grade 1	1 (2)
Grade 2	1 (2)

No Nausea: CDDP based Chemotherapy



* statistical significance: $p < 0.05$ - Chi-square test



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5-year Survival (%)	25-30	0-5

Acknowledgement

- **Patients and family members**
- **JCOG staff**
- **Co-investigators**

Backup Slide

PROTECT: Randomized Double Blind Trial Comparing Palonosetron+DEX with Granisetron+DEX in either Cisplatin or “AC/EC”

**HEC
N=1114**

**Stratified by
Age (≥ 55 , < 55)
Gender**

Chemotherapy (CDDP, AC/EC)

