

Approach to Stage IIIA Lung Cancer

Current Concepts

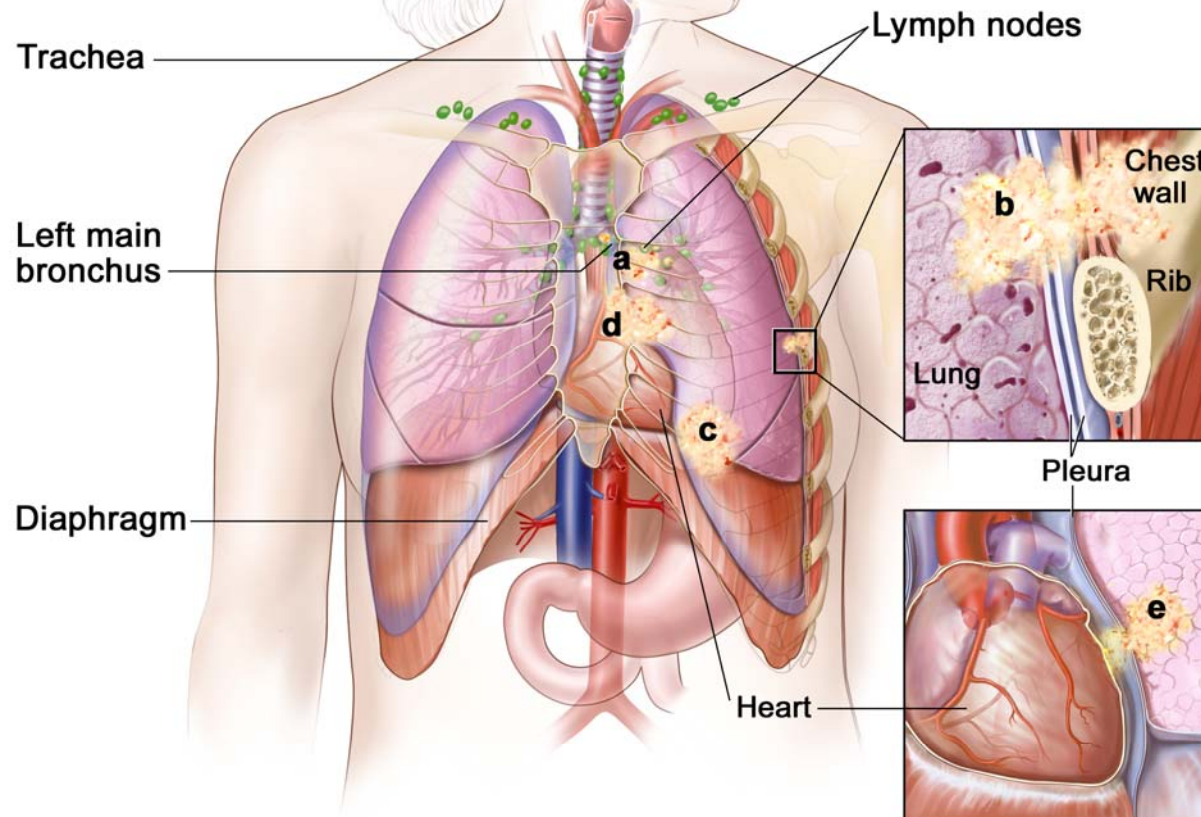
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Stage IIIA



T1-3 N2
T3* N1

***T3: Locally invasive,
or <2 cm from carina,
or obstructive
atelectasis**

National Cancer Institute



Focus on Patients with Ipsilateral Mediastinal Adenopathy

- Three groups of patients:
 - Massive IIIA Clinical – i.e., it is obvious before surgery that the mediastinum is involved
 - Minimal IIIA Clinical – minimal mediastinal involvement pre-op where immediate surgery is thought feasible
 - Accidental IIIA – patients thought to have lesser disease who are discovered to have IIIA at surgery



Ipsilateral Mediastinal Adenopathy

- Focus on Group I: patients thought inoperable by virtue of mediastinal adenopathy
 - Look at pre-op chemotherapy with or without radiation with or without subsequent surgery
 - After several years of doing this, data from studies are now mature as to outcome

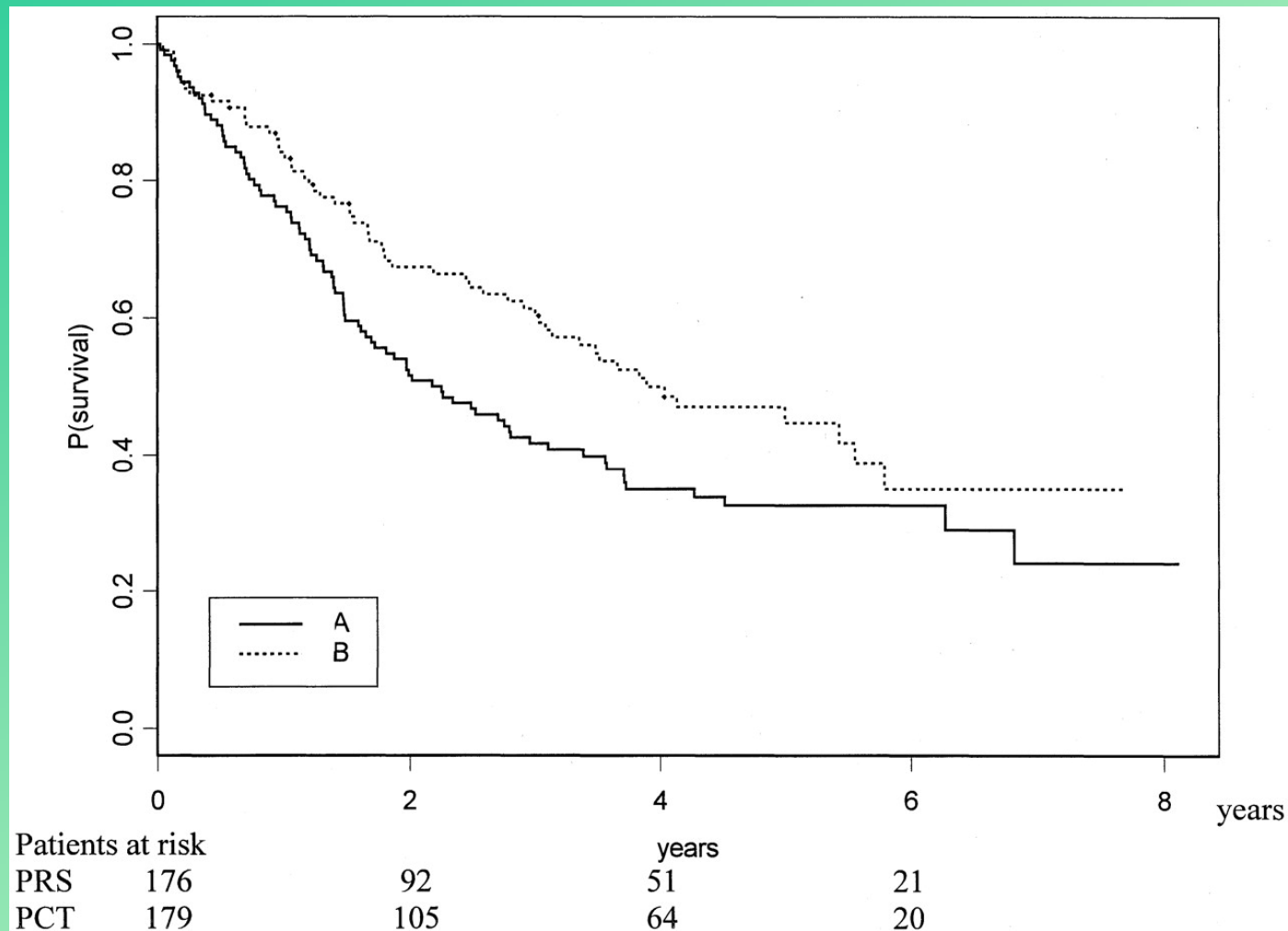


Studies to be Examined

- Pre-op chemo + surgery vs. surgery alone (Depierre, *JCO*, 2002)
- Pre-op chemo → RT versus chemo → surgery (VanMeerbeek, *JNCI*, 2007)
- Non-randomized Chemo → Surgery when feasible (compared to patients inoperable after chemo in same study) (Garrido, *JCO*, 2007)
- Intergroup 0139: Pre-op Chemo/RT with or without subsequent surgery (Albain *Proc Am Soc Clin Onc*, 2005)



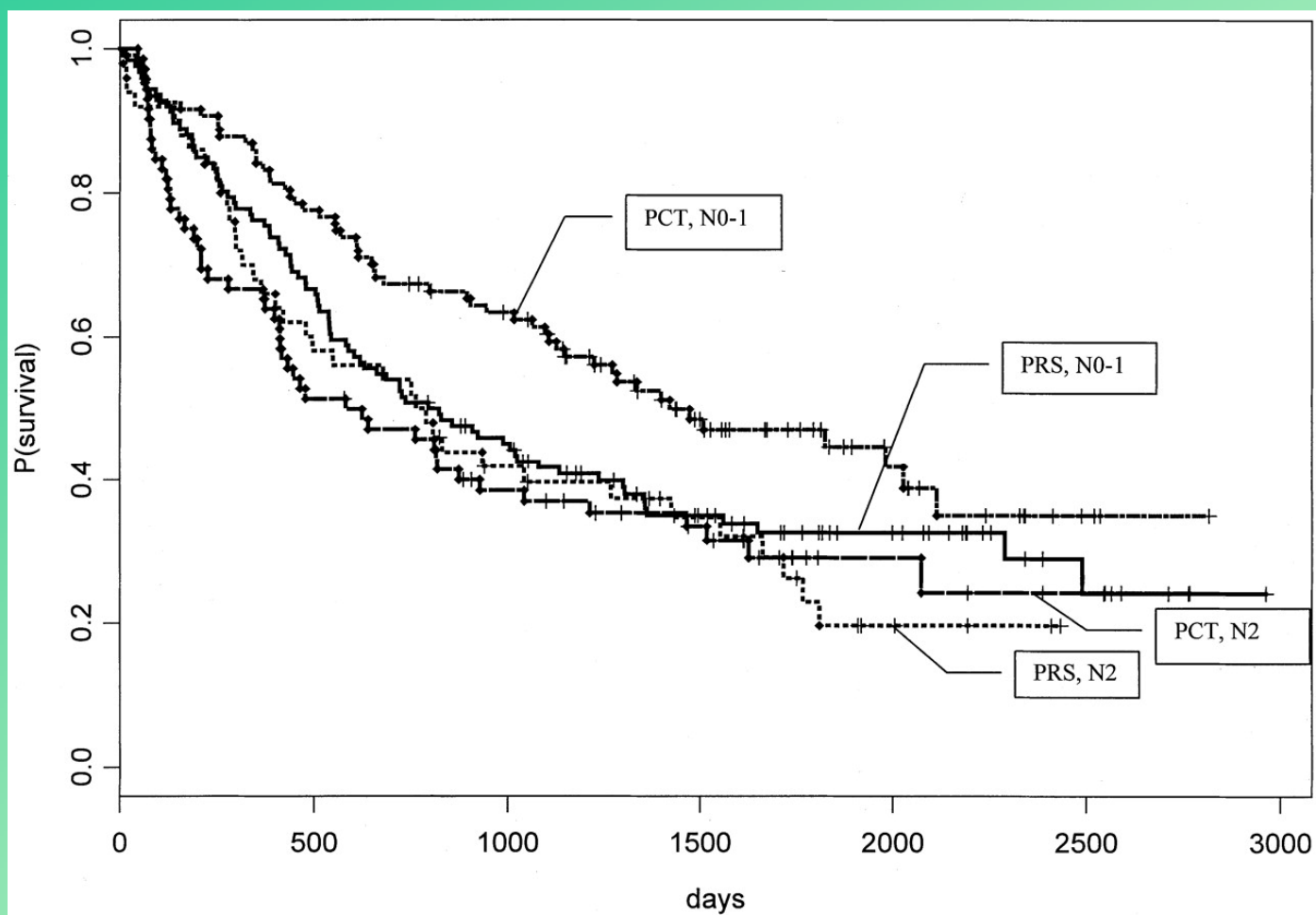
Overall survival by treatment arm: arm A: Surgery only; arm B, PCT + Surgery



Depierre, A. et al. J Clin Oncol; 20:247-253 2002



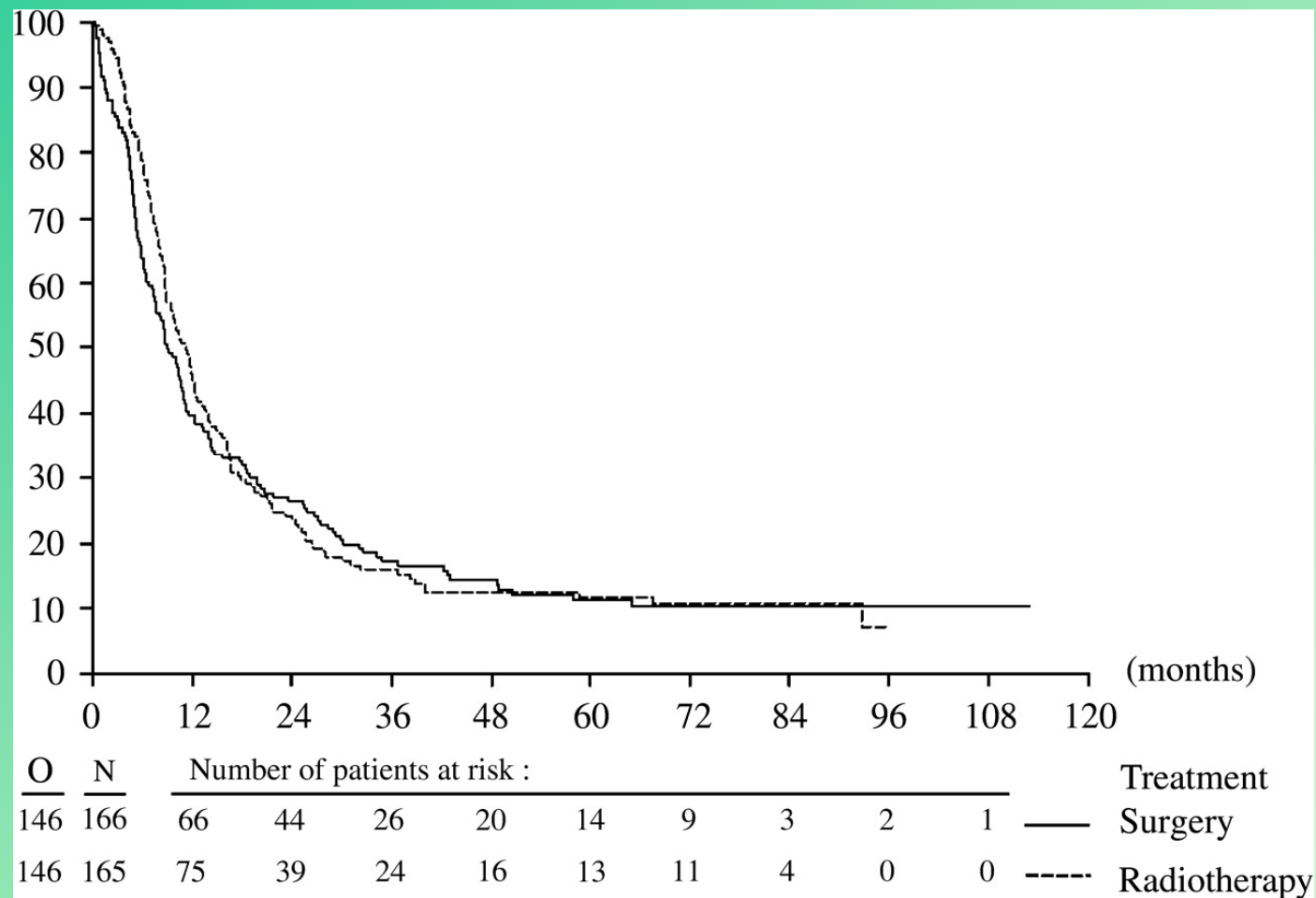
Overall survival by treatment arm and by nodal status



Depierre, A. et al. J Clin Oncol; 20:247-253 2002



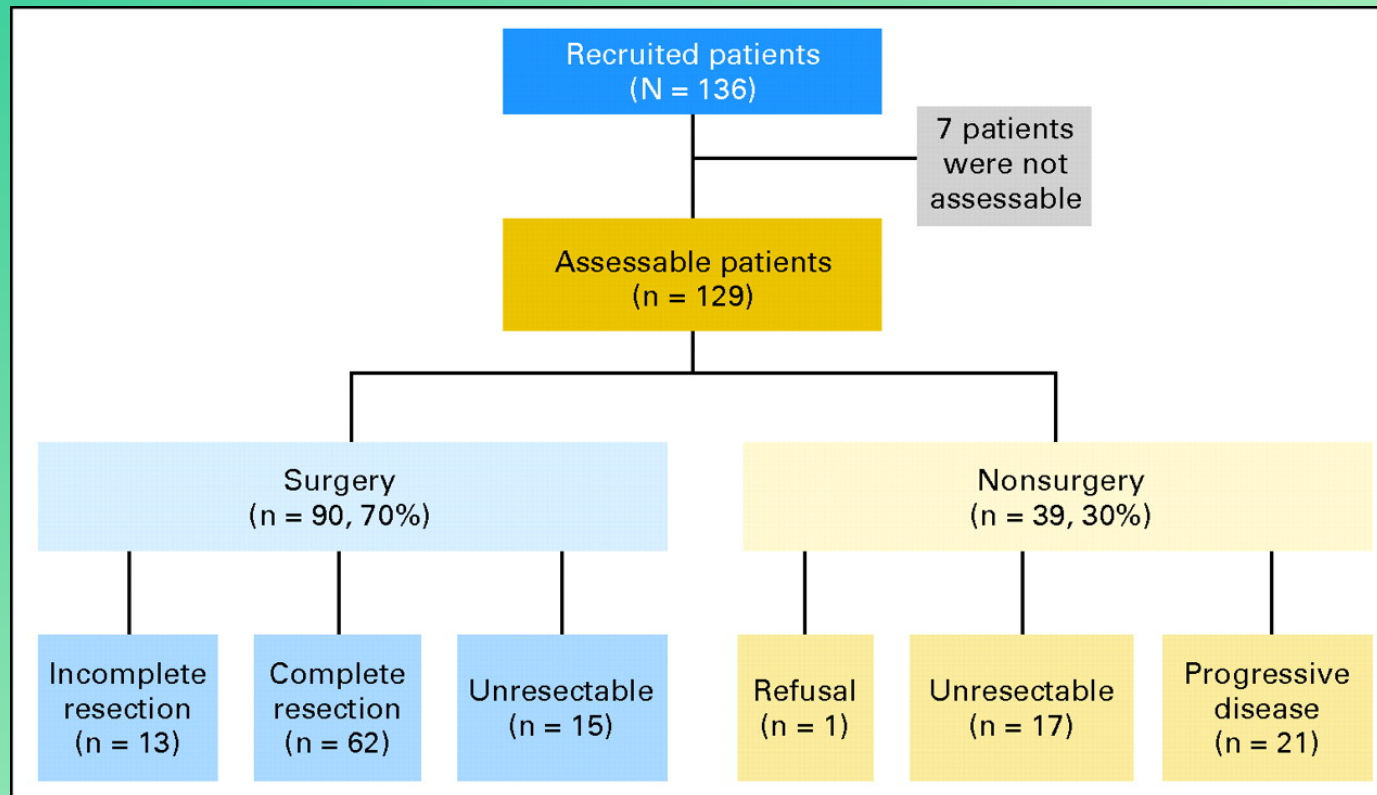
Progression-free survival rates estimated from time of randomization using Kaplan-Meier analyses



van Meerbeeck, J. P. et al. J. Natl. Cancer Inst. 2007 99:442-450;



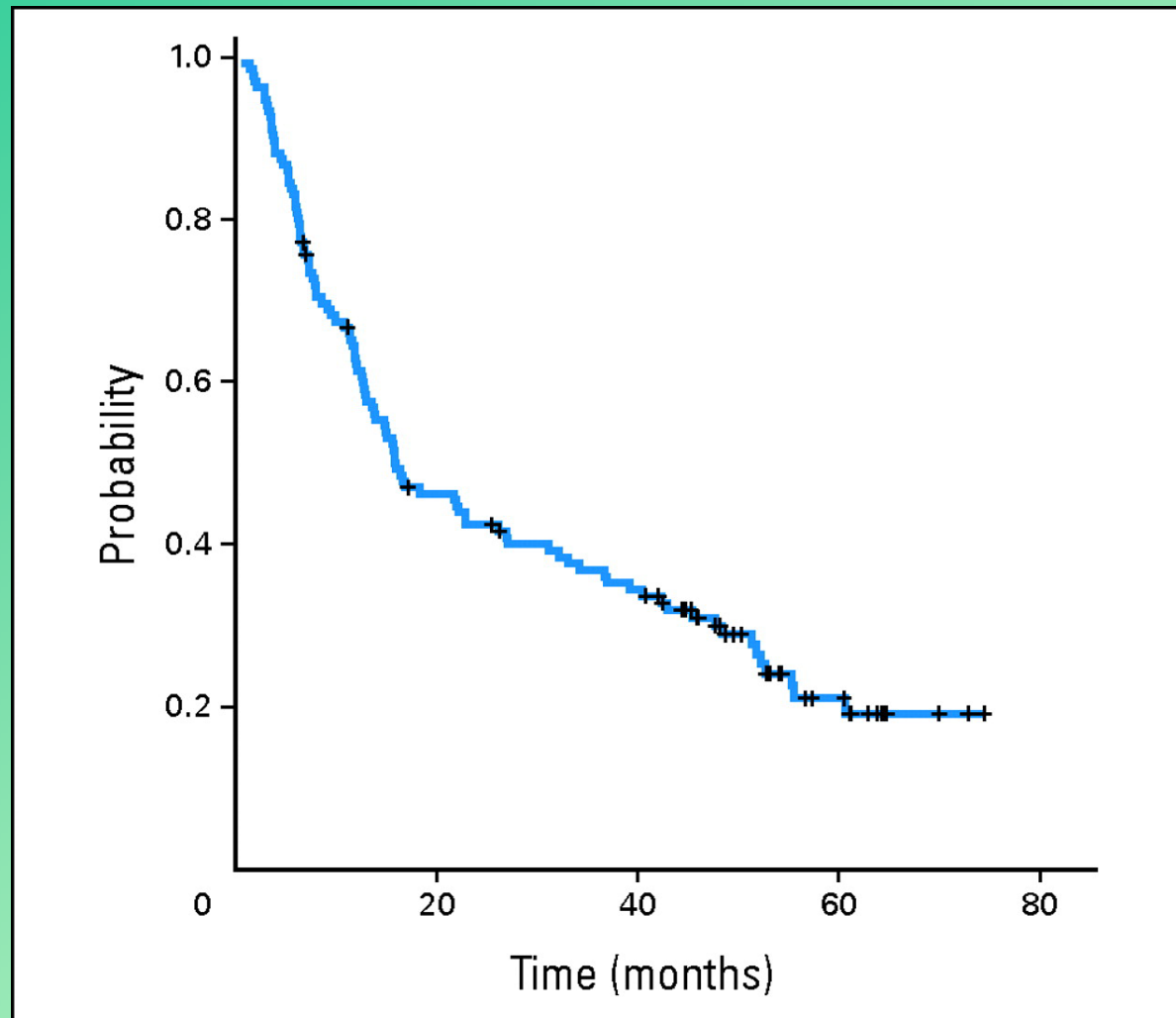
Flow Diagram of non-randomized trial using chemo followed by surgery in patients sufficiently downstaged – a real-world approach



Garrido, P. et al. J Clin Oncol; 25:4736-4742 2007



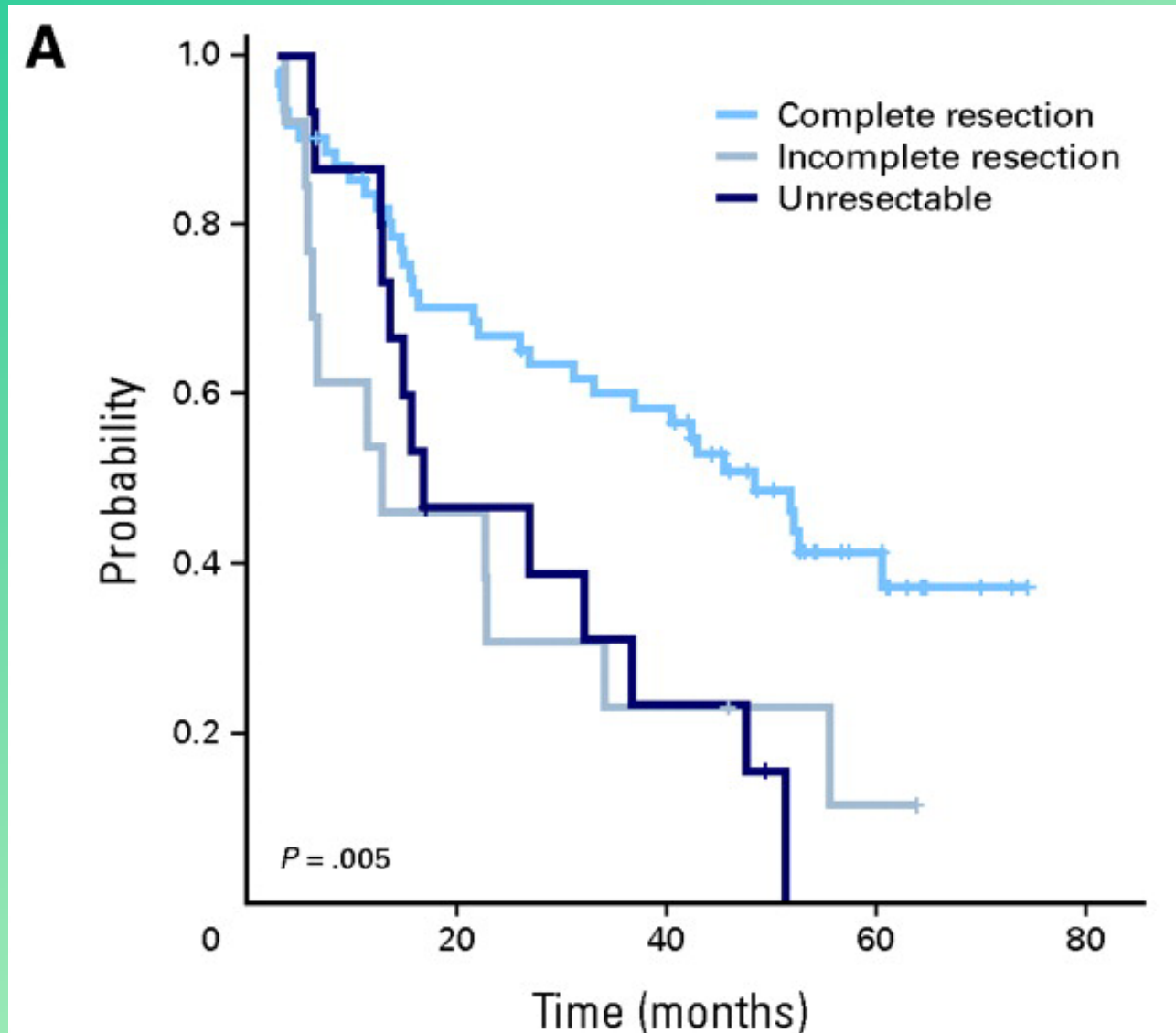
Overall survival curve for all 136 patients



Garrido, P. et al. J Clin Oncol; 25:4736-4742 2007



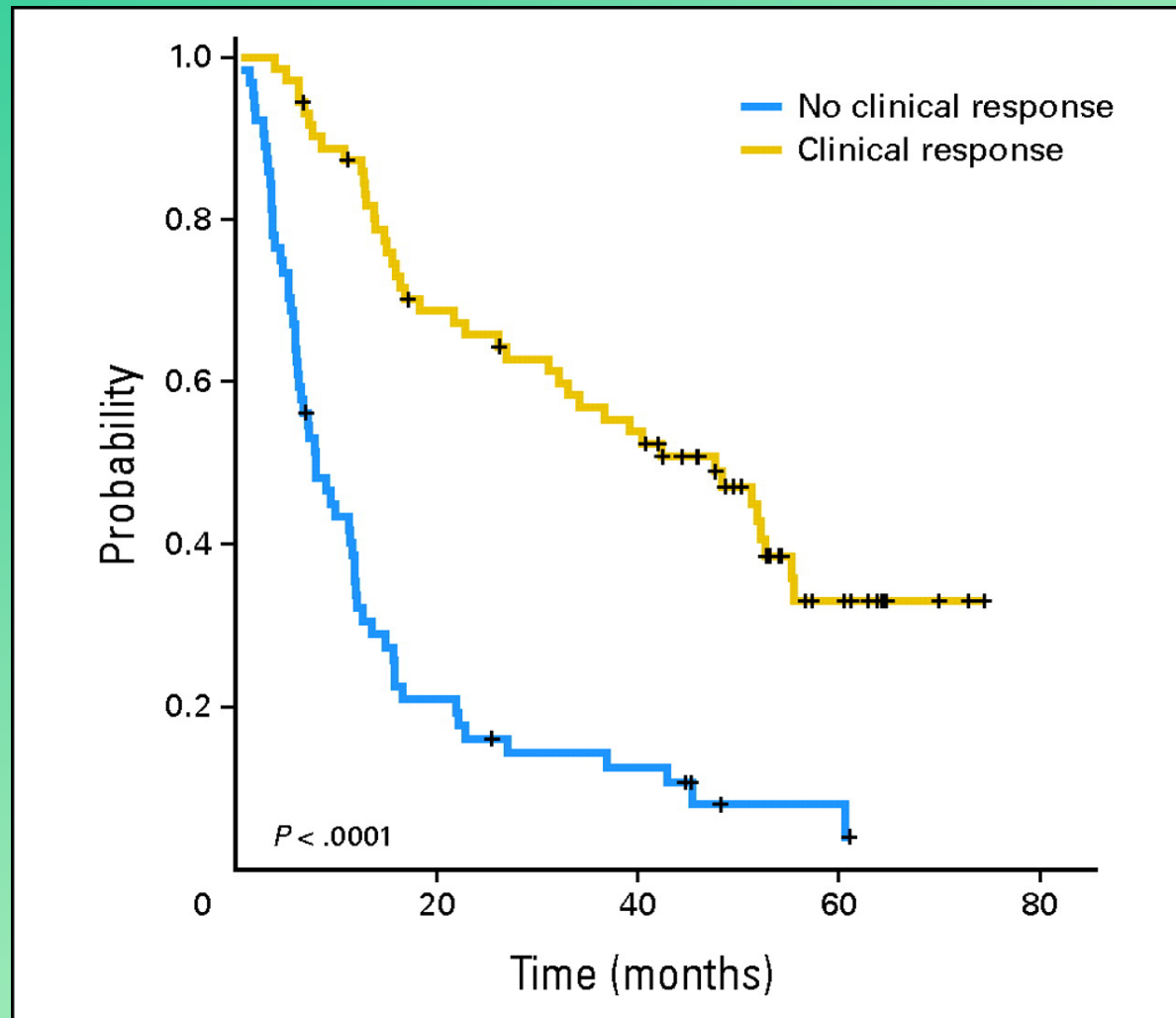
Median survival according to surgical resection



Garrido, P. et al. J Clin Oncol; 25:4736-4742 2007



Overall survival according to clinical response



Garrido, P. et al. J Clin Oncol; 25:4736-4742 2007

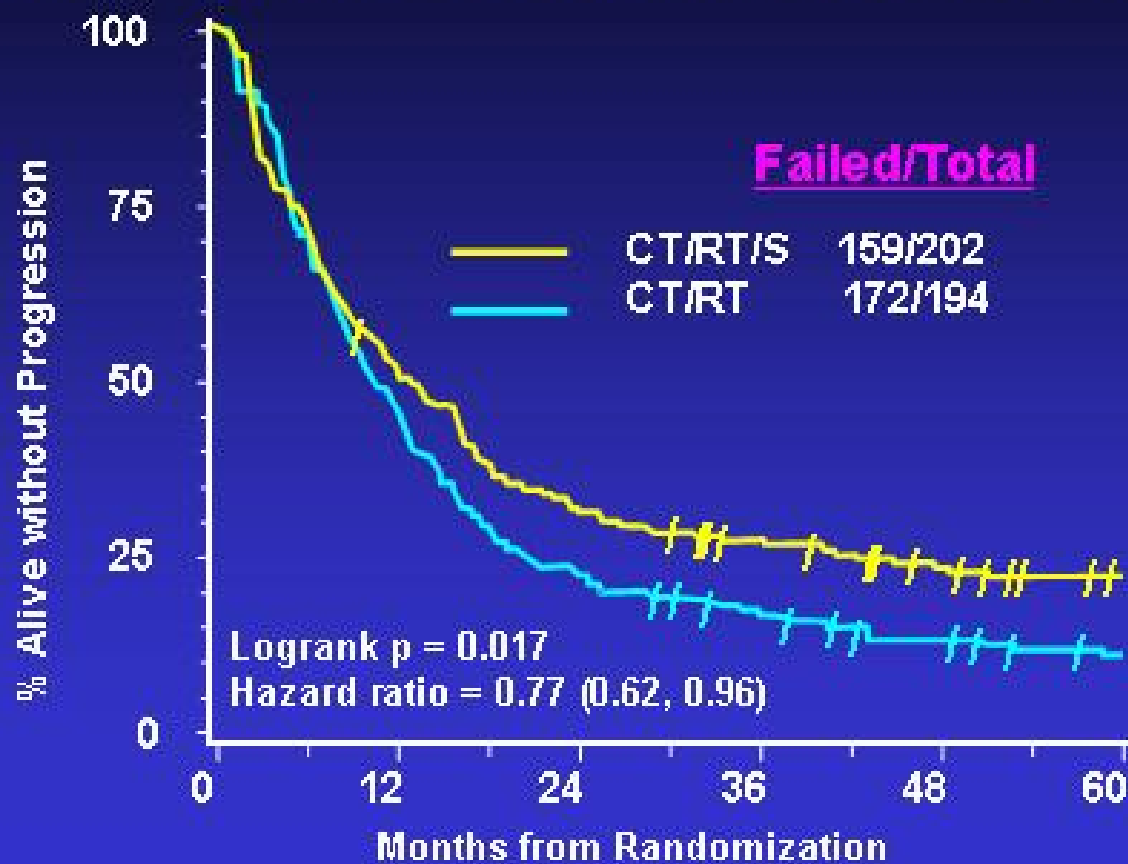


Randomized Trial Looking at Value of Surgery after optimal Chemo/RT

- Intergroup Trial 0139
- Chemo/RT with or without subsequent surgery
- Results published in abstract form only at 2005 ASCO meeting



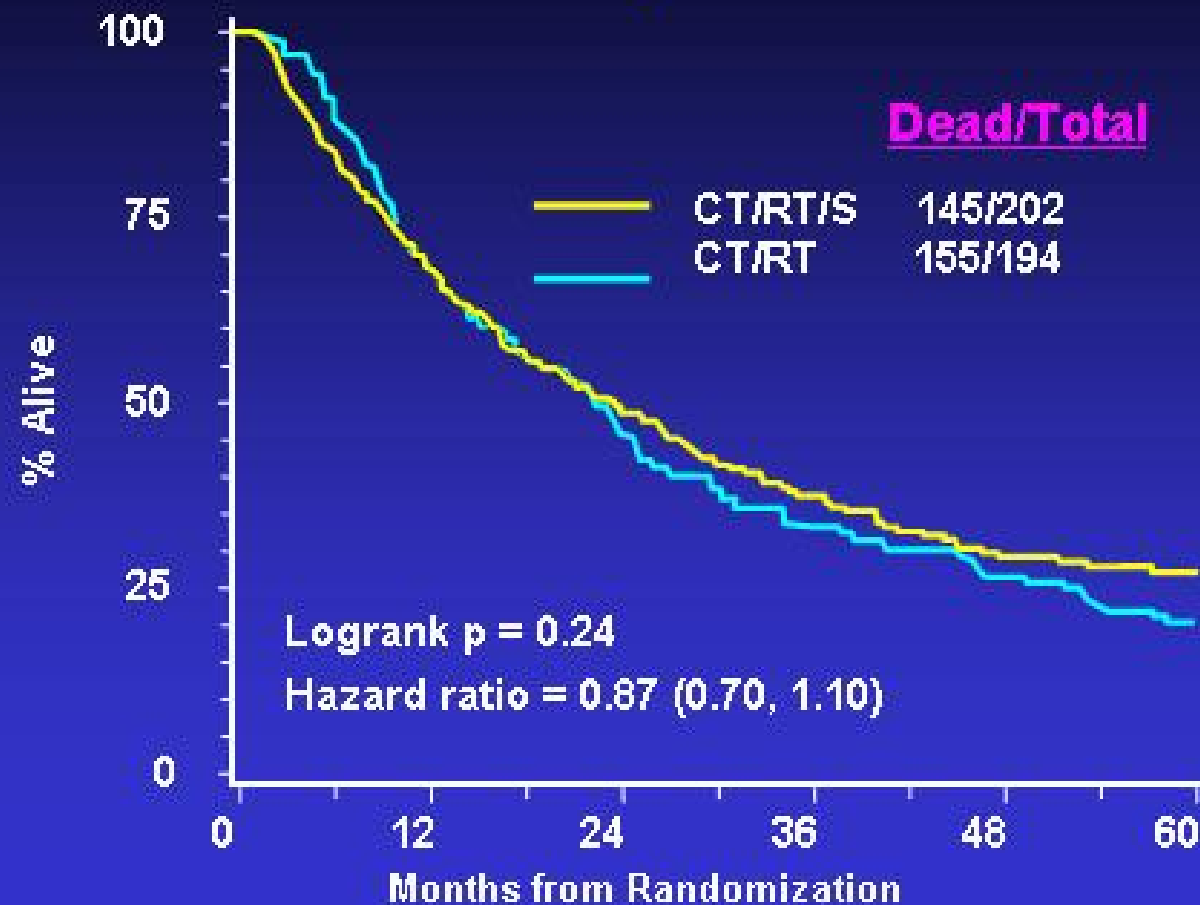
Intergroup 0139/RTOG 9309 Progression-Free Survival by Treatment Arms



Albain et al *JCO* 23, No. 16S, Part I of II (June 1 Supplement), 2005: 7014



Intergroup 0139/RTOG 9309 Overall Survival by Treatment Arms

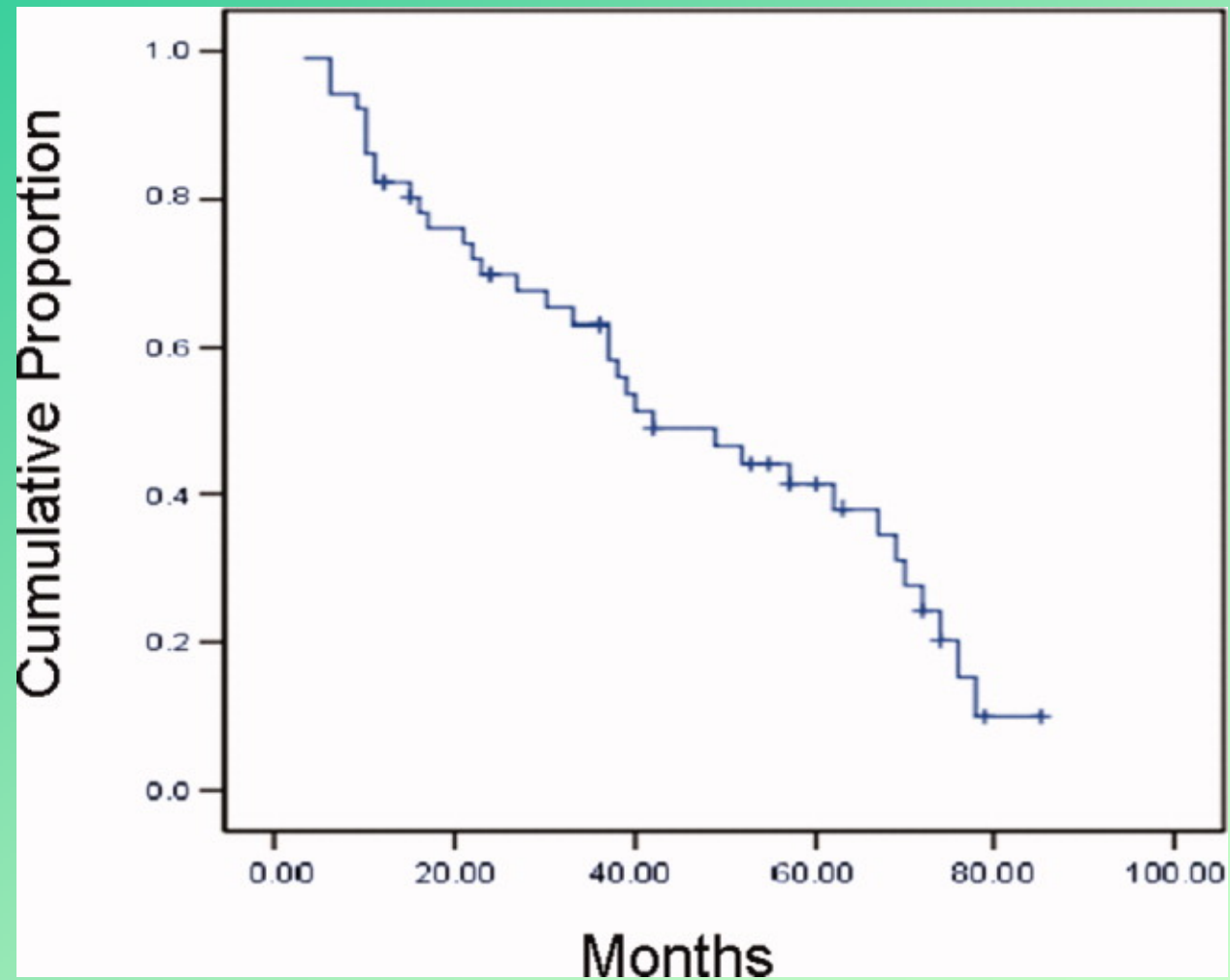


The Problem of Brain Metastases

- Recent study looked at patients who obtained a pathologic complete remission after pre-op chemo±RT followed by surgery (Chen, *CANCER*, 2007)
- 211 patients started study; 51 completed treatment including surgery and had no tumor in resection specimen
- Those 51 patients were further analyzed...



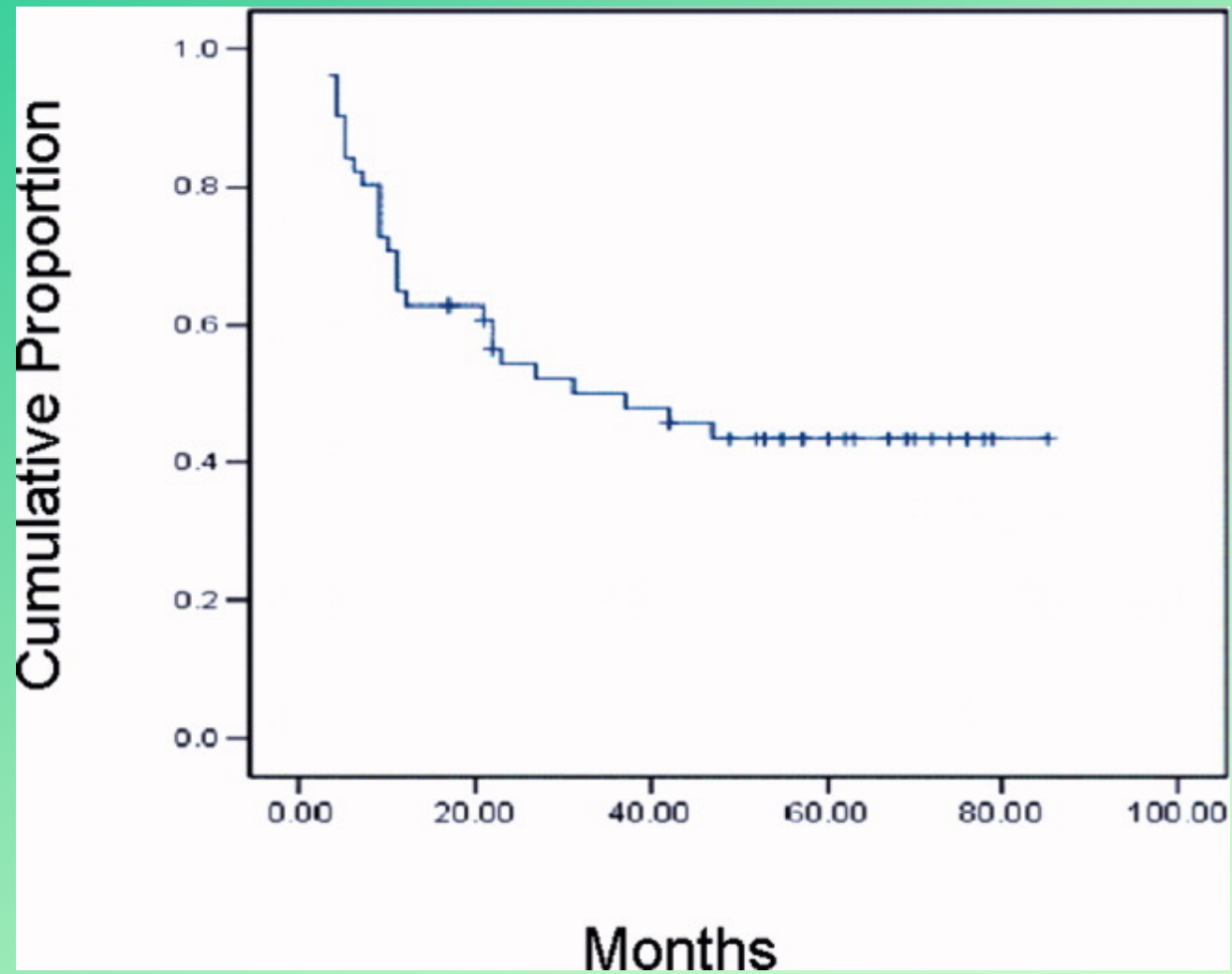
Survival curve for PCR patients after chemo \pm RT followed by surgery
for Stage IIIA lung cancer



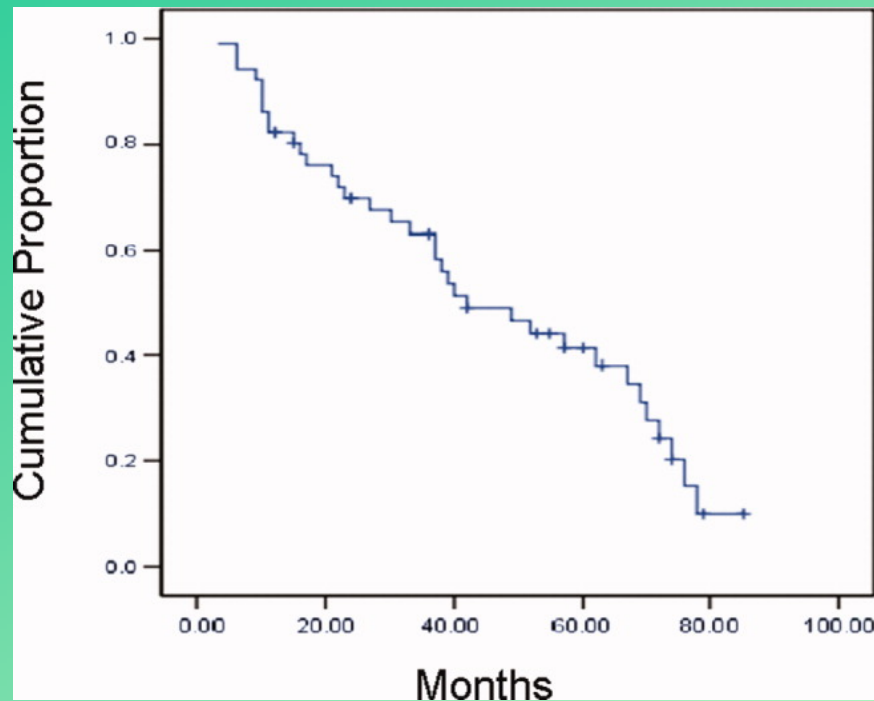
Chen et al *CANCER* 109:1668, 2007



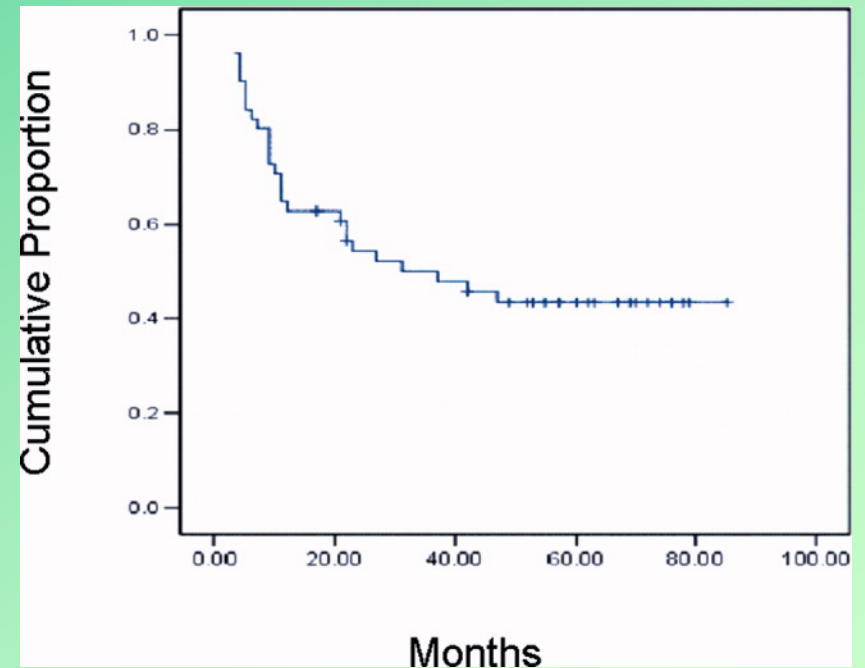
Survival without brain metastases in subset of patients



Side-by-side Comparison



Overall survival of group



Survival if no brain mets

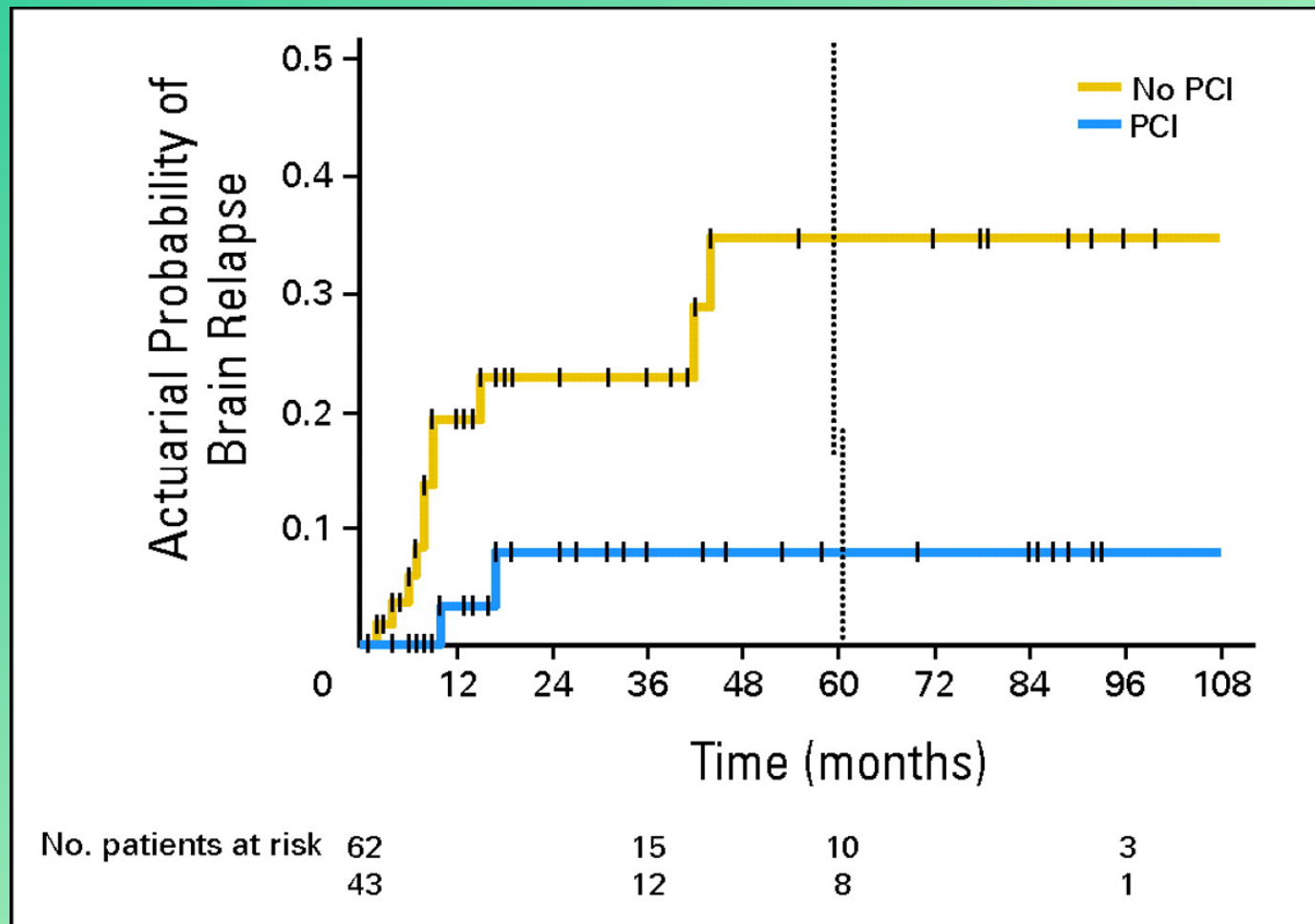


Brain Mets, continued

- Above study raises question of whether with improved systemic therapy for NSCLC we should consider prophylactic cranial radiation
- Preliminary data....just published



Actuarial probabilities of brain relapse at first site of failure according to the treatment actually administered



Pottgen, C. et al. J Clin Oncol; 25:4987-4992 2007

Neurocognitive defects in *both* groups (!)



Conclusions

- Long-term survival now possible with patients with Clinical Stage IIIA NSCLC
- Optimal integration of chemo, radiation and surgery still to be worked out
 - Role of surgery after chemo/RT uncertain
 - Nonetheless pathologic complete response at surgery seems to be important
 - As expected chemo responders do better than non-responders – attests to the value of chemo
- As patients do better we need to worry about brain metastases



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