Timing of Sentinel Node Biopsy:
The Case for Doing it Prior to Pre-operative Systemic Therapy

Jay R. Harris, M.D.
Department of Radiation Oncology
Dana-Farber Cancer Institute
Brigham and Women's Hospital
Harvard Medical School

Considerations for Initial SNB

- Effective local regional treatment is important to long-term survival
- Guidelines for local regional RT have been developed based on the initial stage
- Pre-op treatment downstages disease, but the need for local regional RT based on this ‘down-staged’ disease is not known

The Issue: Who gets RT?

- This question has added significance with *Lancet* 2005 Overview publication showing reductions in LRR > 10% improve survival
- At the same time, nodal RT can be associated with significant side effects
- Hence, over or under treatment is a problem

Guidelines for RT after Initial Surgery

- RT is used if $\geq$ 4 nodes are positive or if T3/N+ based on a risk of LRR > 20% even with post-op chemotherapy
- There is controversy about which patients with T1,2/1-3+ cancers have a LRR rate > 10-15% and should also be treated

Down-Staging with Pre-op Systemic Rx

(Ref: NSABP B-18, Fisher B et al. JCO 15: 2483, 1997)

	Post-op (n = 743)	Pre-op (n = 735)
% Path N+	57%	41%
% Path 1-3+	30%	24%
% Path ≥ 4+	27%	16%

Loss of Information

- 11% of patients initially with ≥ 4 + nodes become either N- or 1-3+
- We don't yet know if these 11% will have low rates of LRR without RT
- There is limited published data on the LRR rates with pre-op treatment and no RT

LRR after Pre-op CTx followed by Mastectomy and no RT

- Retrospective analysis of 150 patients treated with either pre-op Adriamycin regimen or Taxol without post-op RT
- Stage: I - 1%; II - 43%; IIIA - 23%; IIIB - 25%; and IV - 7 %

Ref: Buchholz T et al. J Clin Oncol: 20, 17, 2002

Pre-op Ctx and MRM, No RT

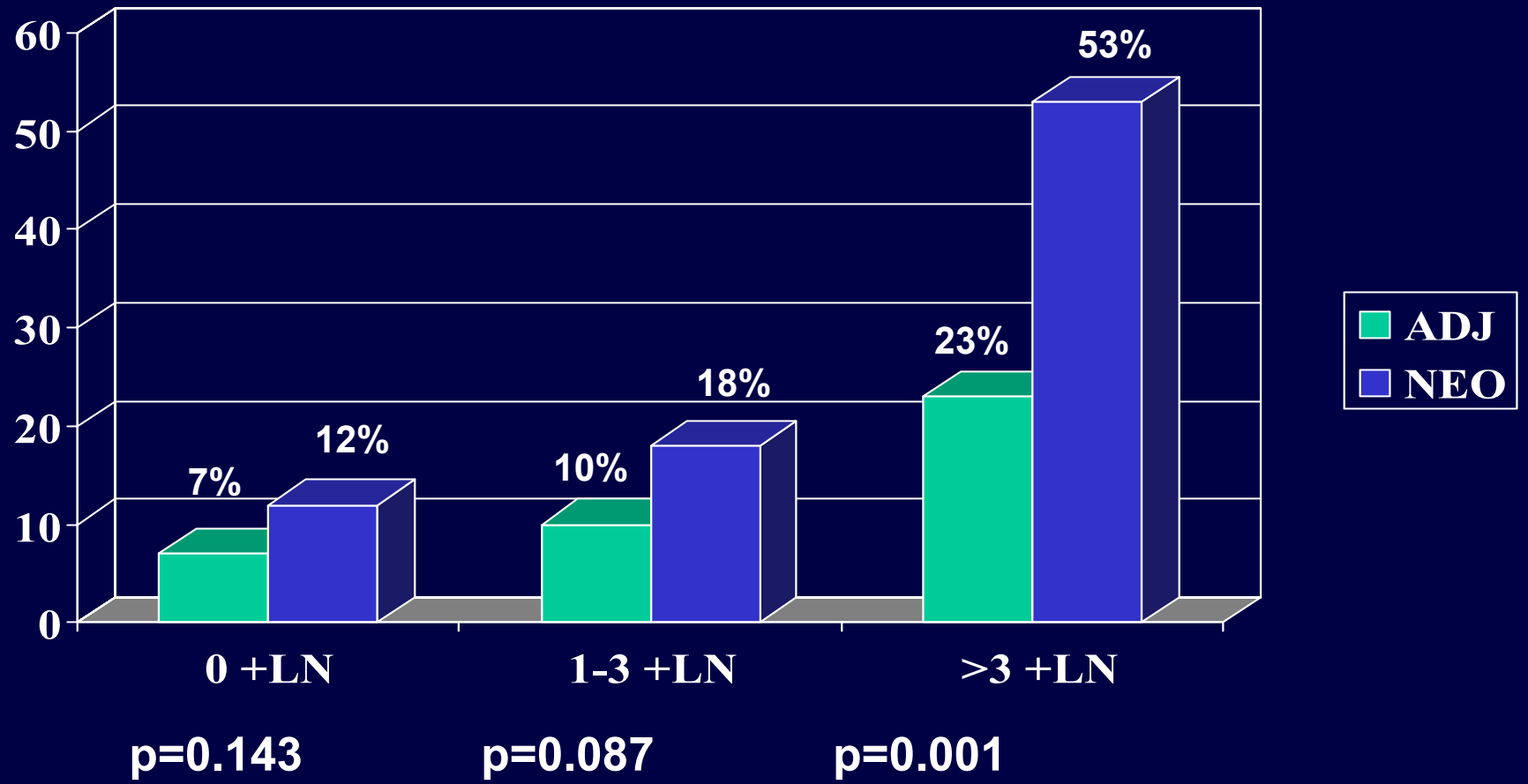
- Crude 5-Yr LRR related to pN:

  0+: 10% 1-3+: 17% 4-9+: 47%

- Among 18 patients with pT&N CR, the 5-Yr rate of LRR = 19% (CI: 6 - 48%)

- LRR rates after pre-op Ctx by nodal stage are greater than rates after initial surgery

5-Year LRR by # + Nodes: Post-op vs. Pre-op

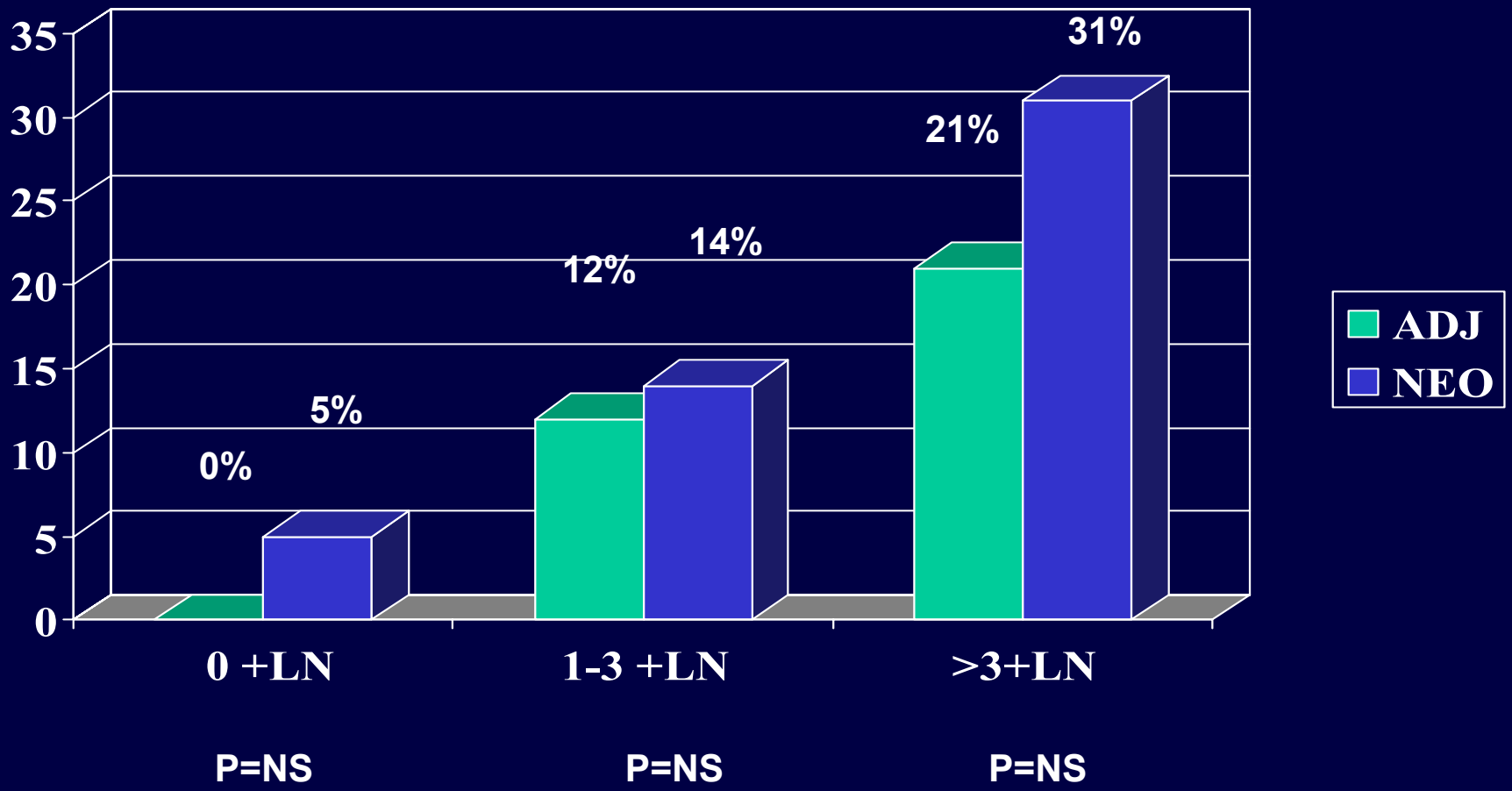


Follow-Up Study (Anderson)

- Same 150 pre-op Ctx patients compared with 1030 patients treated with post-op Ctx without RT
- Clinical stage was more advanced for pre-op patients and here, matched by clinical stage

(Ref: Buchholz TA et al. Int J Radiat Oncol Biol Phys: 53; 880, 2002)

5-Year LRR by # + Nodes: Post-op vs. Pre-op (matched for clinical stage)



Clinical Implications: Pre-op Ctx + MRM

- Response to Ctx does not reduce LRR rate based on final stage to that seen after same staging with initial surgery
- Both the initial and the final stage must be used to determine the LRR risk

Implications: Pre-op Ctx + MRM

- Stage III patients should receive post-mastectomy RT regardless of final path findings
- There is very limited published data on LRR risk after pre-op systemic therapy in patients with cT1,2 N0 breast cancer

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Should This Patient Receive RT?

- 40 yo woman with a cT2 (3 cm) N0 cancer
- Core -> grade 3 IDC, ER low+, PR-, HER2-LVI+
- Receives pre-op dd AC -> T
- Has cPR and mastectomy and SNB reveals some residual disease in the breast (PM 3) and a negative SNB

Timing of SNB

- SNB after pre-op systemic therapy is more convenient and more prognostic
- However, until we have validated prognostic data on LRR risk using this approach, it seems prudent to do SNB prior to pre-op systemic therapy