

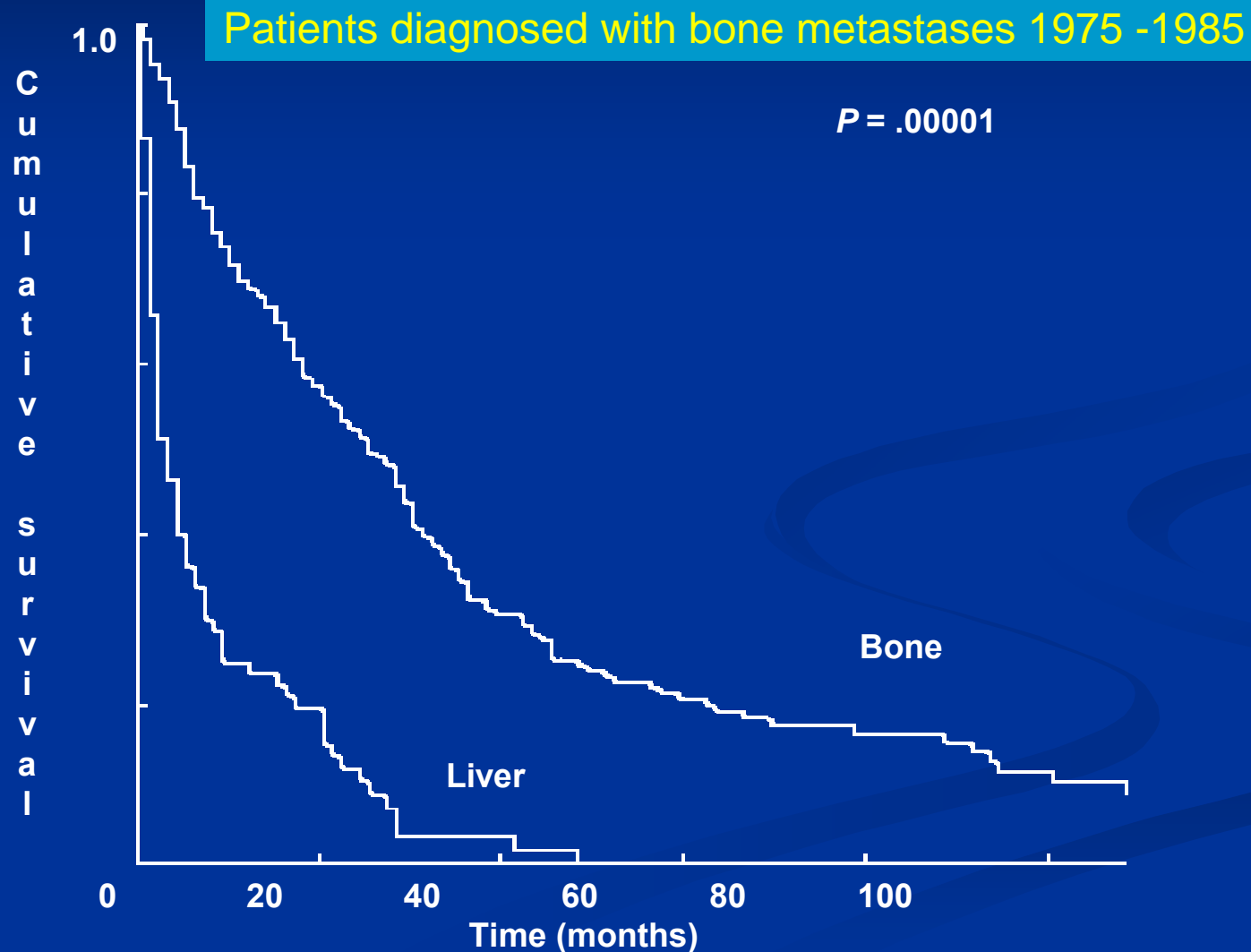
# Bisphosphonate Therapy in Breast Cancer

**Allan Lipton, MD**  
***Hershey Medical Center***  
***Hershey, PA***

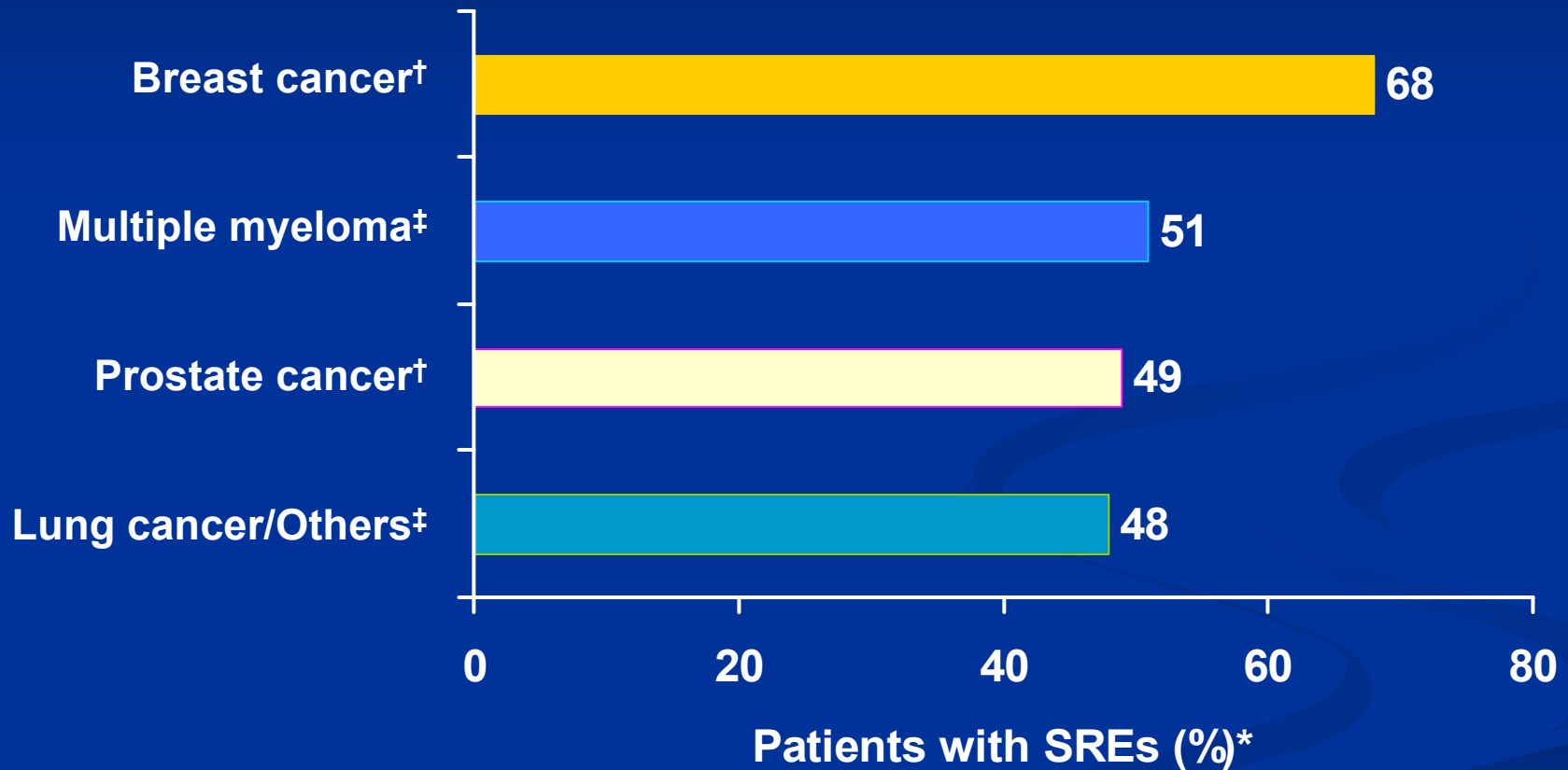
# Scope of the Problem

400,000 new patients per year in the  
United States develop bone  
metastases

# Survival of Patients With Breast Cancer After First Relapse

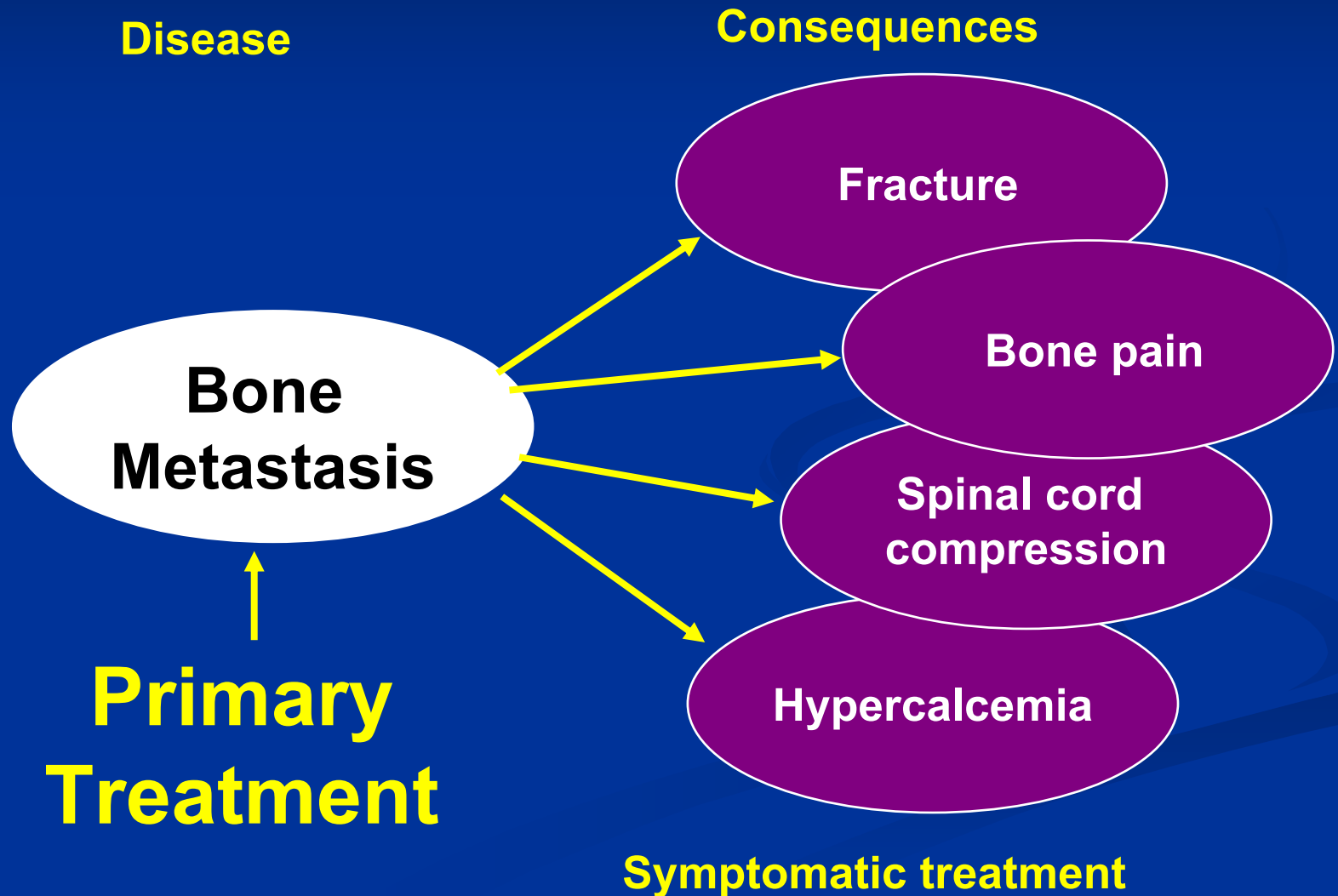


# Incidence of Skeletal-Related Events (SREs) in Clinical Trials

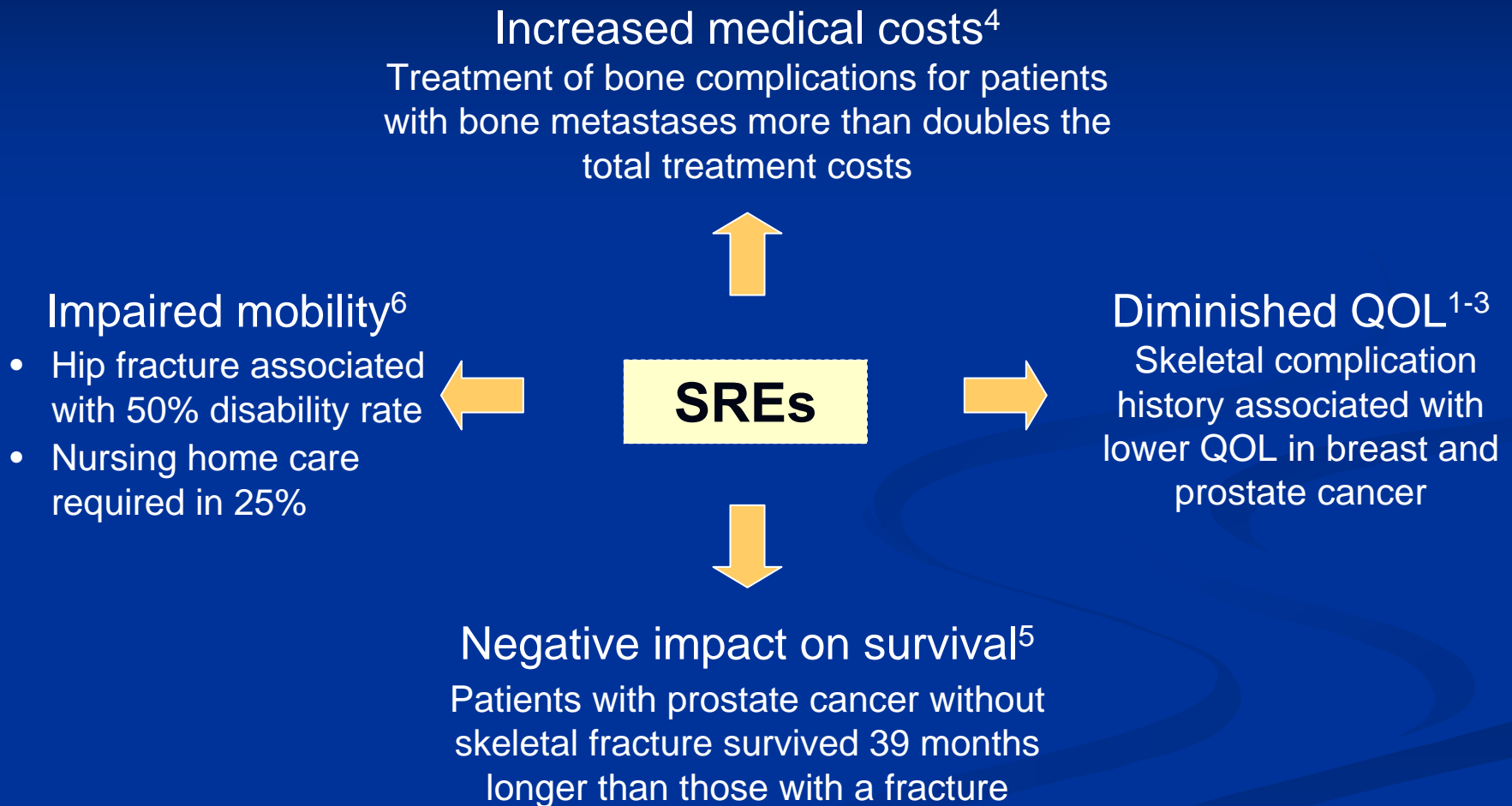


\*Placebo arm of pamidronate or zoledronic acid randomized trials; <sup>†</sup>24 months; <sup>‡</sup>21 months.  
Coleman RE. *The Oncologist*. 2004;9(suppl 4):14-27.

# Optimal Management of Bone Metastases: *Treat the Disease*

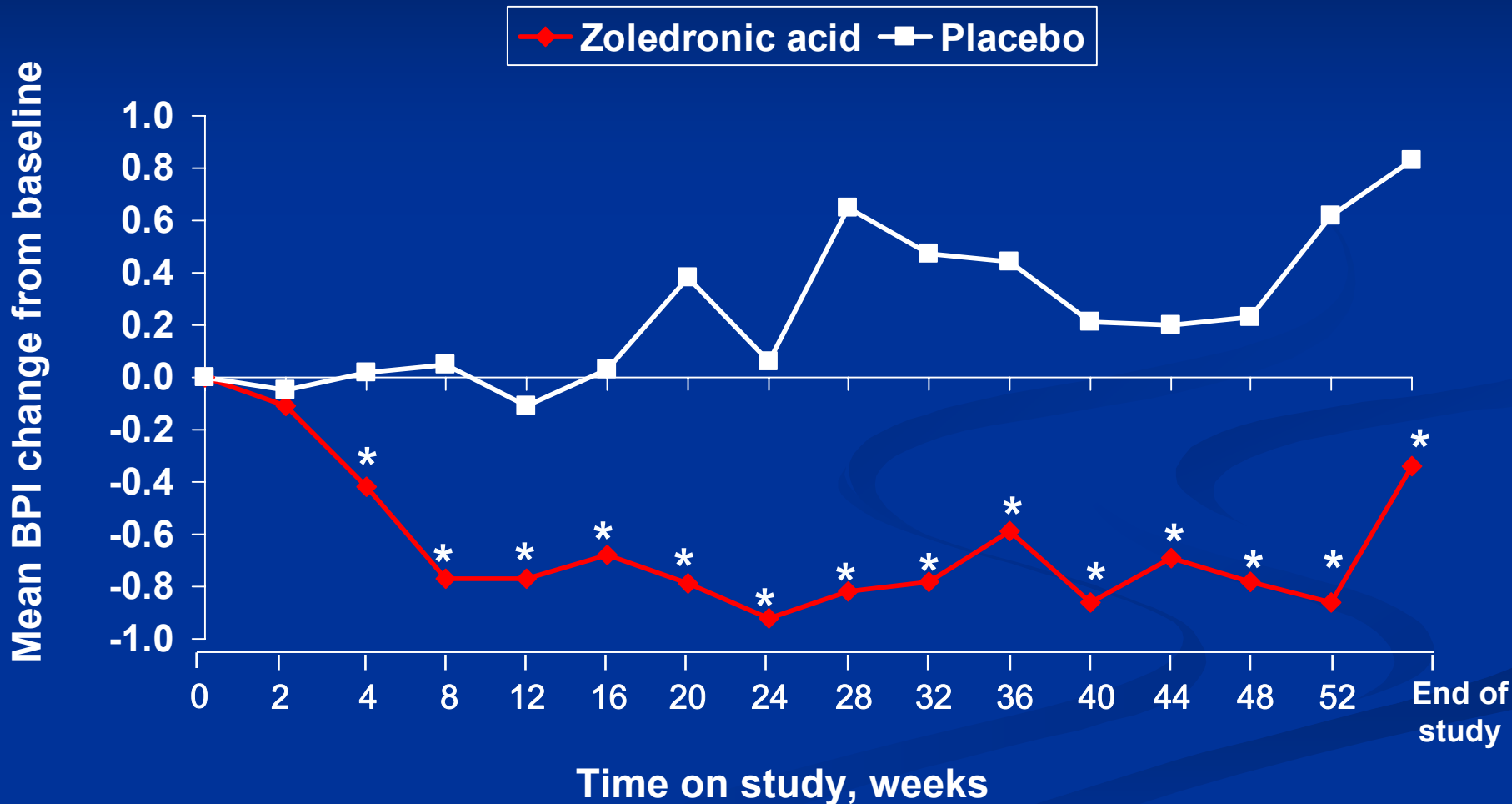


# Quality of Life (QOL) Implications of Bone Complications in Cancer



# Breast Cancer

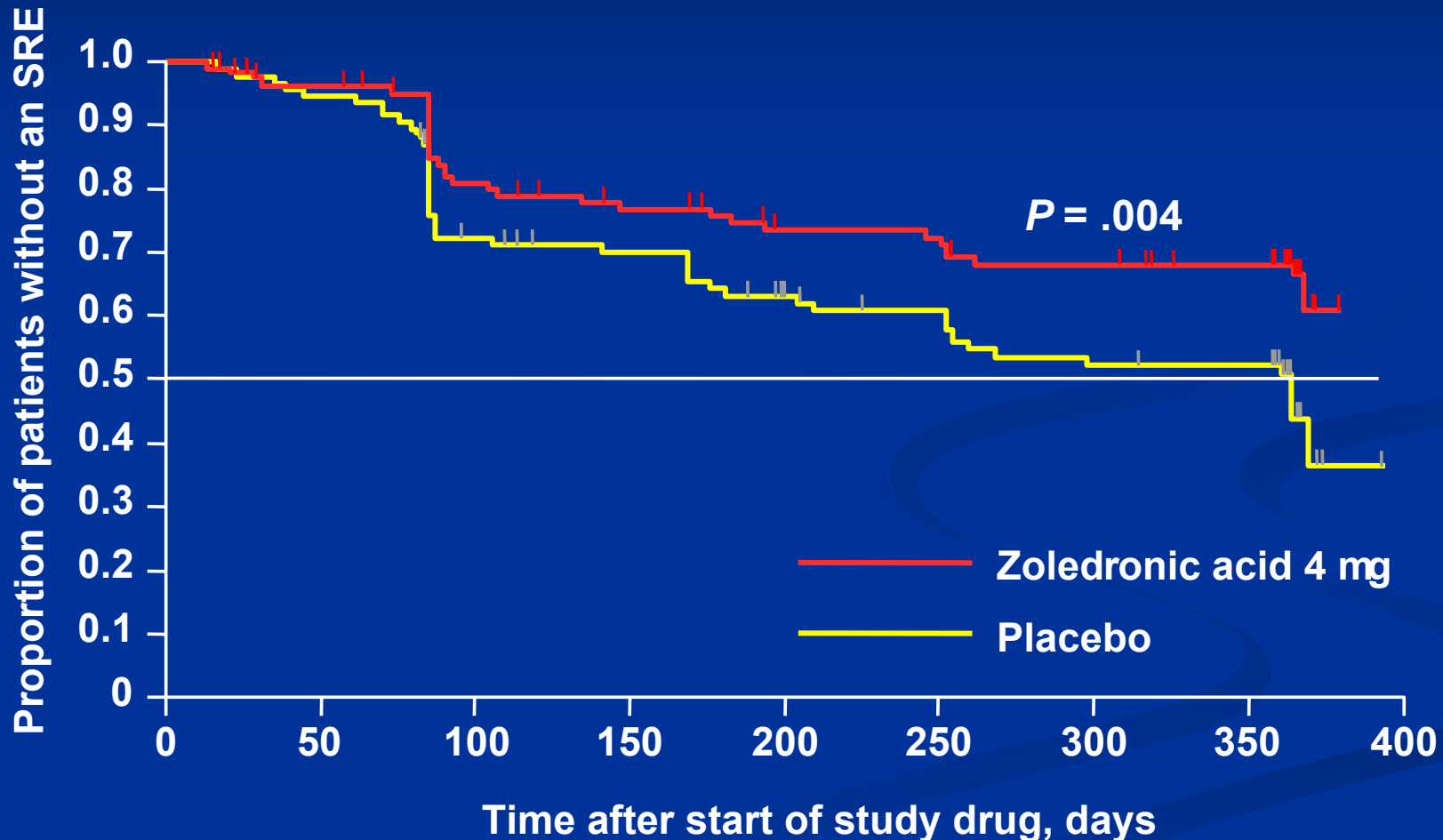
# Long-term Relief of Bone Pain with Zoledronic Acid (Breast Cancer)



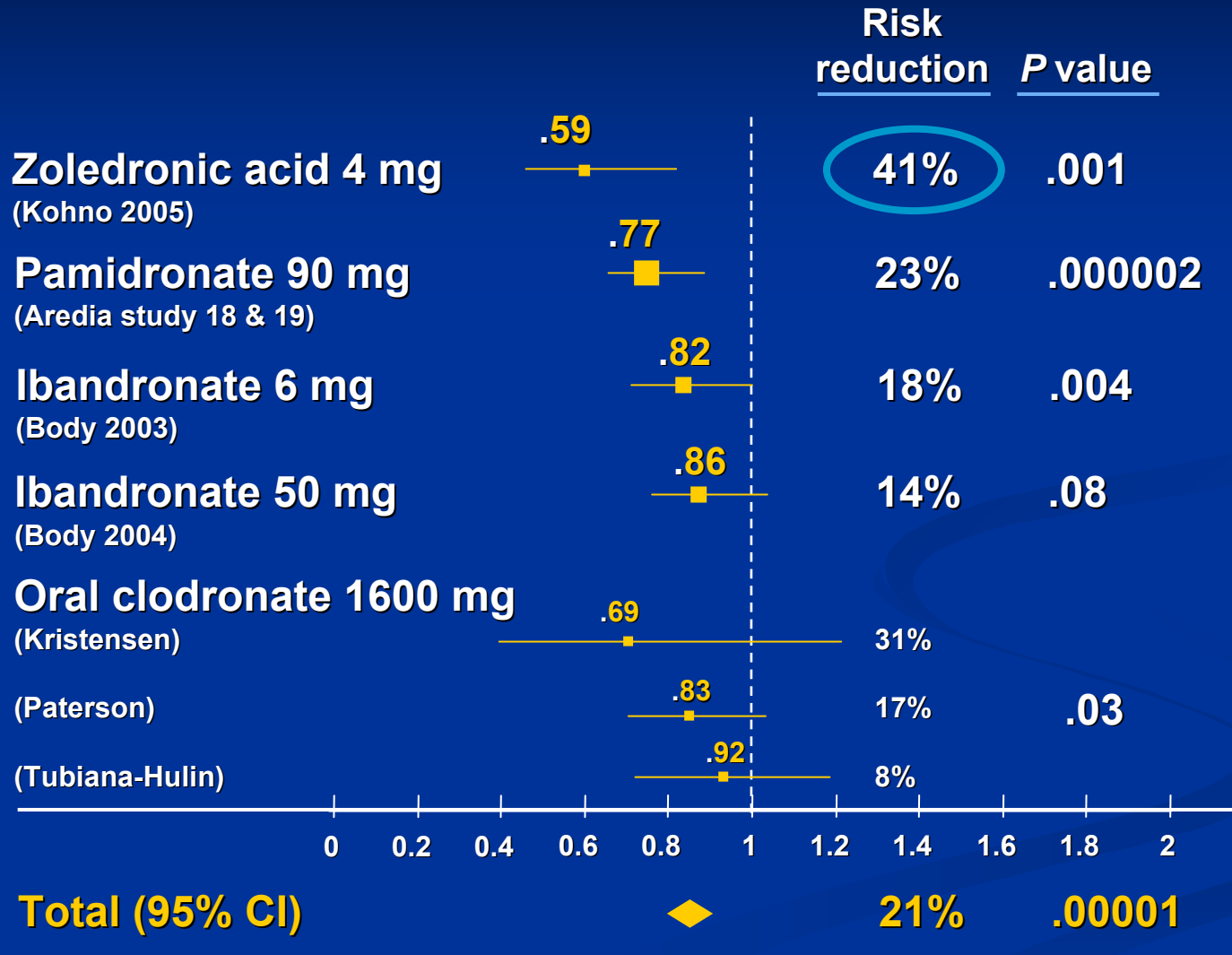
\* $P < .05$  versus baseline.

Reprinted with permission from Kohno N, et al. Presented at: 27th Annual San Antonio Breast Cancer Symposium; Dec 8-11, 2004; San Antonio, Tex. Abstract 3060.

# Zoledronic Acid Significantly Delays Time to First SRE Compared With Placebo

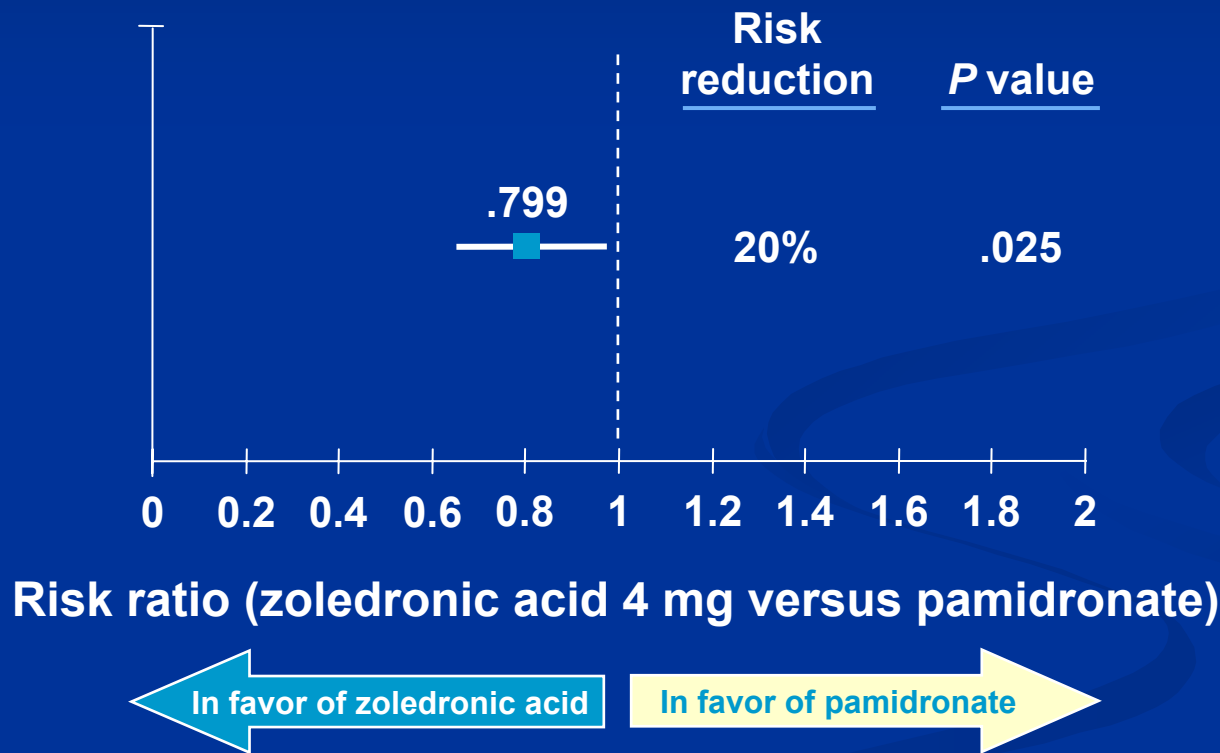


# Bisphosphonates for Breast Cancer



# Zoledronic Acid Versus Pamidronate Multiple Event Analysis\*

Zoledronic acid reduced the risk of developing a skeletal complication by an additional 20% compared with pamidronate



\*HCM included as an SRE.

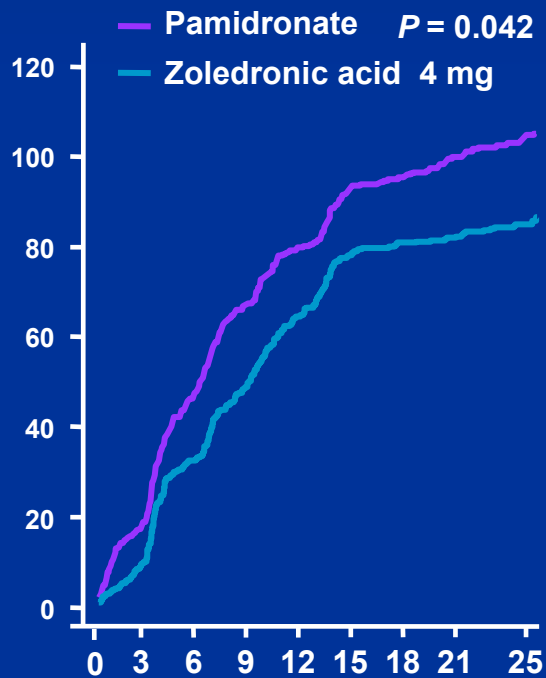
Clinical outcome assessed after 25 months

Rosen LS. *Cancer*. 2003;98:1735-1744.

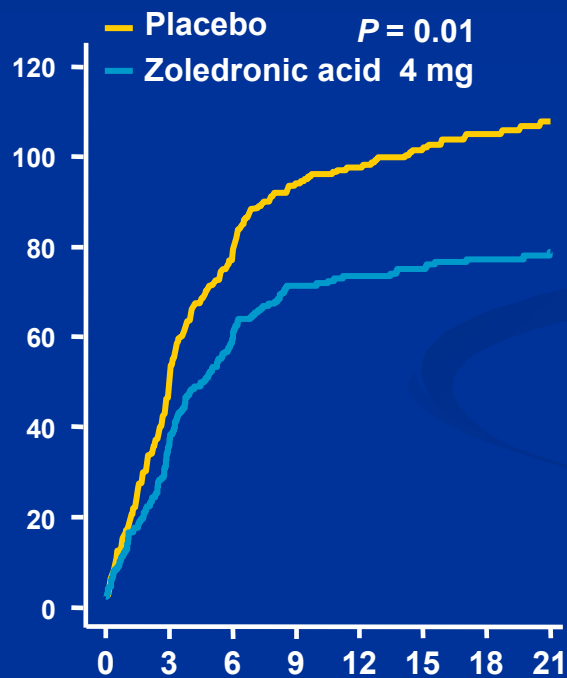
# Zoledronic Acid Reduces the Incidence of Skeletal-Related Events Across Tumour Types

Cumulative expected SREs, (n) / 100 patients

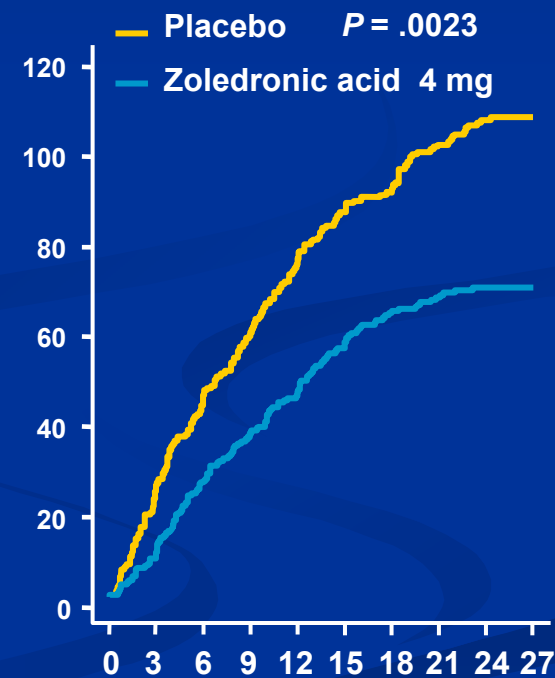
Breast cancer



Solid tumours



Prostate cancer



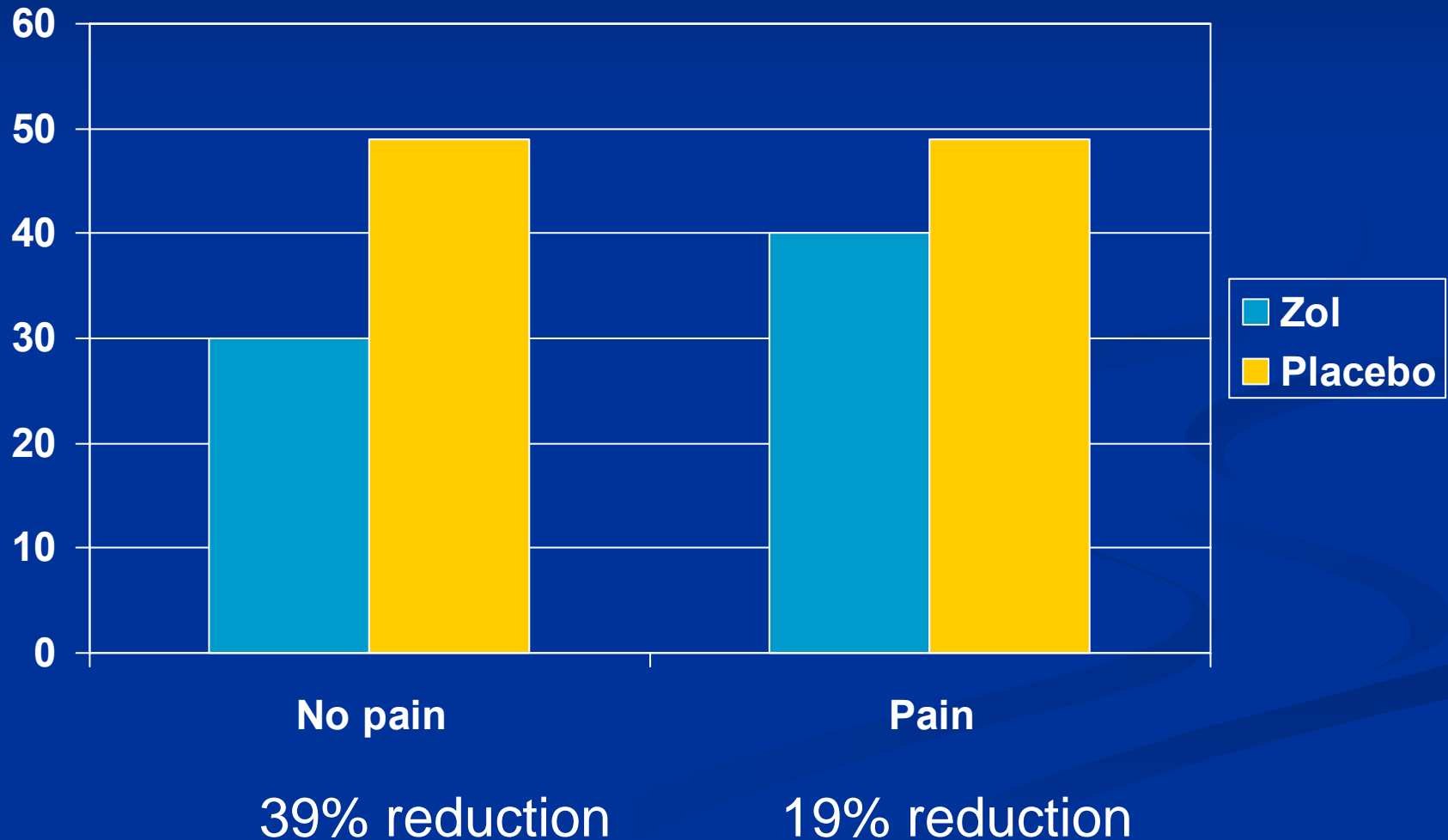
Months since randomization

# Importance of Early and Continued Bisphosphonate Therapy

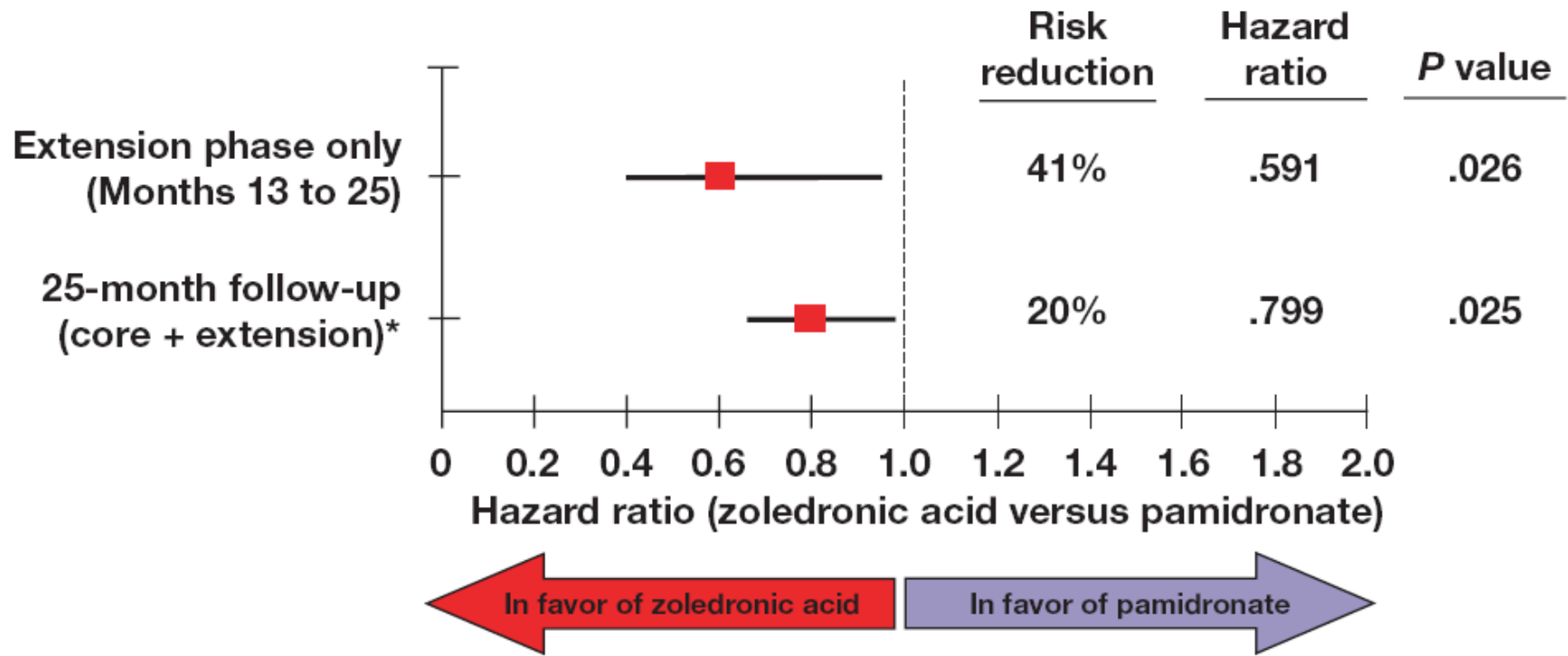
# Importance of Early Treatment to Prevent SREs in Patients With Bone Metastases

- Patients who experience an SRE are at 2-fold greater risk of a subsequent SRE (HR = 2.08)<sup>1</sup>
- Therefore, patients may have a better outcome if bisphosphonate therapy is initiated early and SREs are prevented

# SRE vs Pain on Study Entry

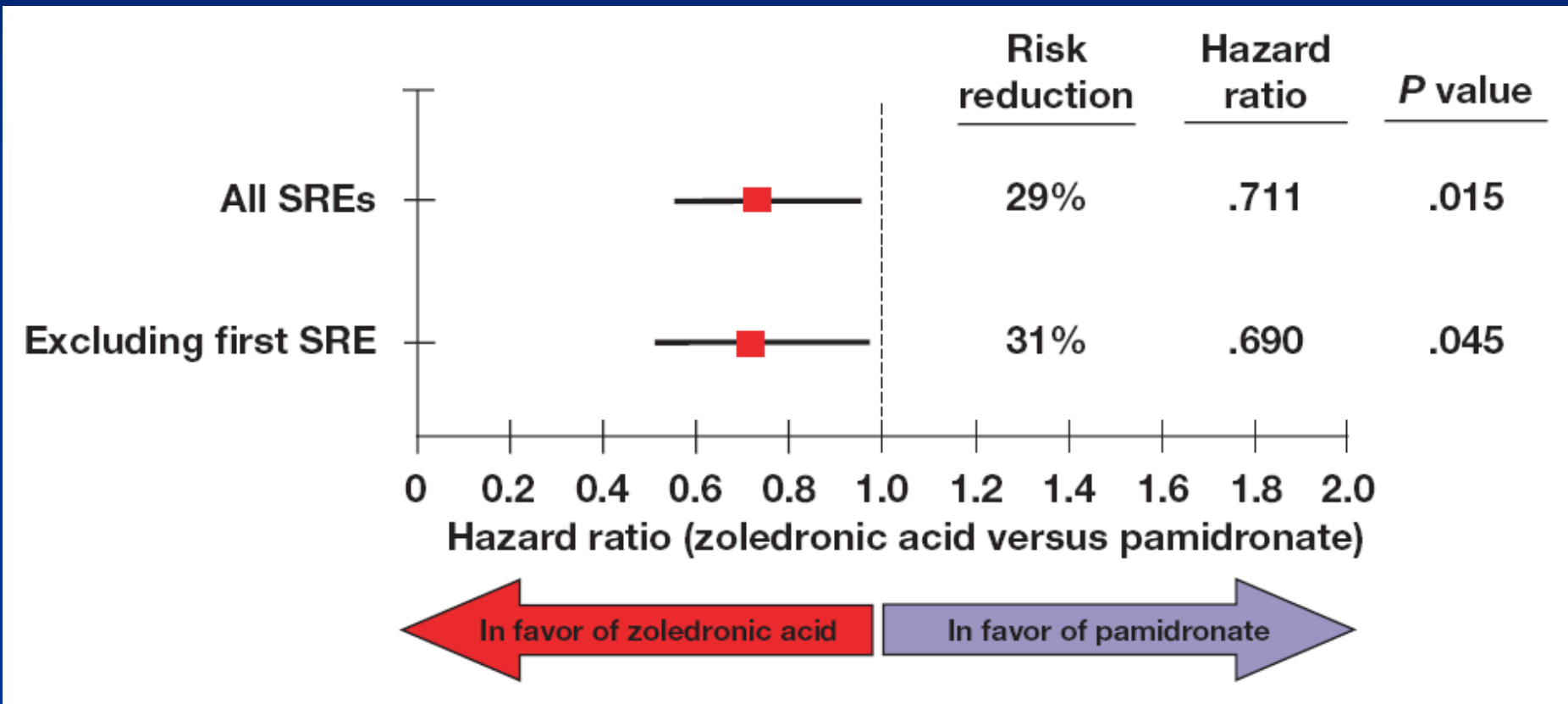


# Breast Cancer: Continuing Reduction in SRE Risk



**During the second year on zoledronic acid, the relative risk of experiencing an SRE remains lower than with pamidronate.**

# Continuing Reduction in the Risk of a Second SRE (Breast ca., 2nd event subset analysis; multiple event analysis)



**Compared with pamidronate, zoledronic acid in breast cancer reduced the risk of experiencing a second SRE by about one-third.**

# Zoledronic Acid May Reduce Time to Progression in Bone and Survival in Subsets of Patients

# Zoledronic Acid Reduces the Risk of Breast Cancer Progression (Exploratory Analysis)

- Compared to pamidronate, zoledronic acid significantly reduced the risk of overall disease progression in specific subsets of breast cancer patients with
  - higher pain scores  
(-21% for pts with BPI score  $\geq 2.75$ )
  - shorter time to development of bone metastases  
(-20% for pts with BM development within <4yrs)

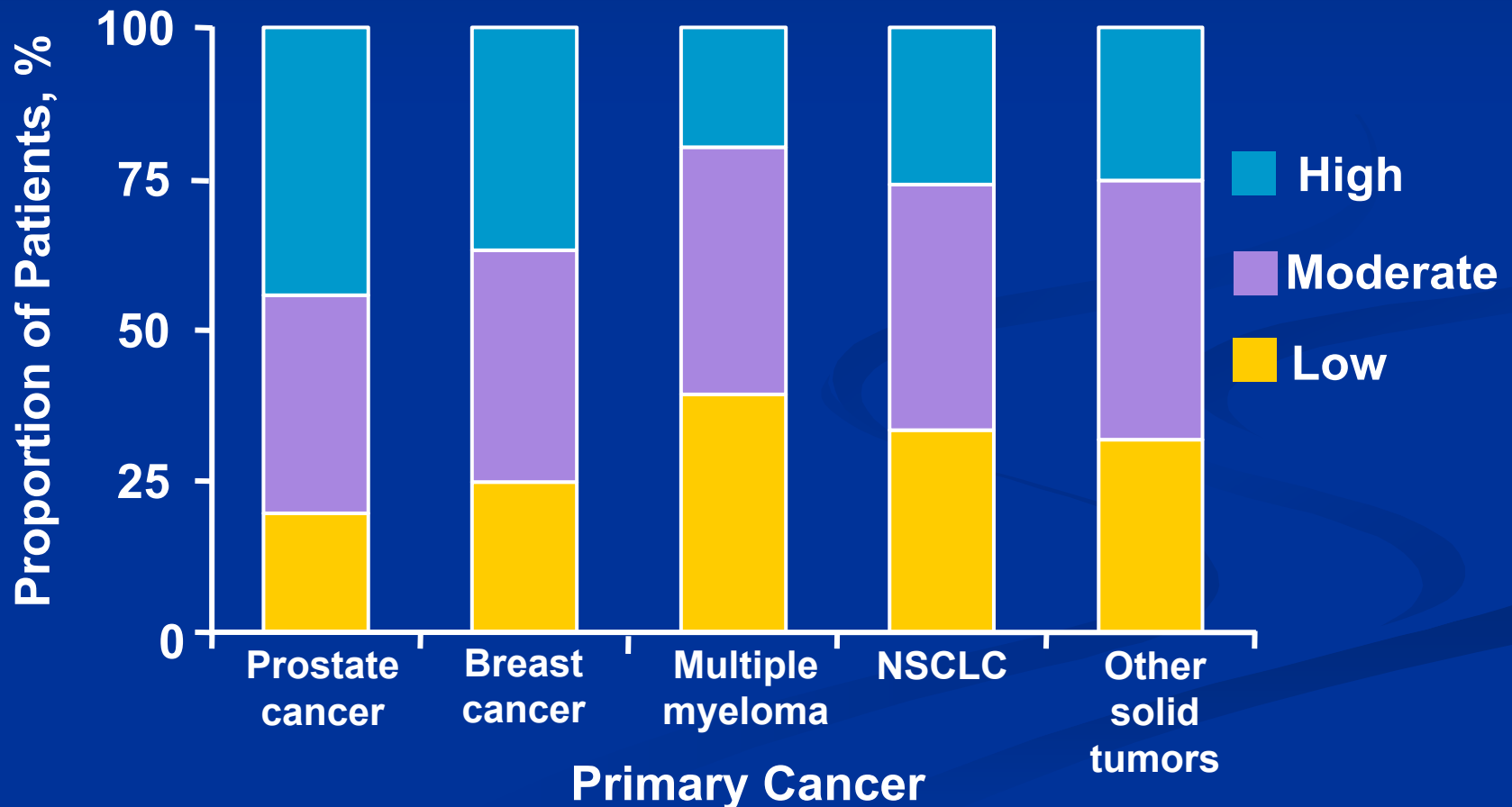
# Collagen Crosslinks Provide Specific Measurement of Bone Resorption

- Free crosslinks
  - Free Dpd
  - Free Pyr
- Protein-bound crosslinks
  - N-telopeptide (NTx)
  - C-telopeptide (CTx)
- Total crosslinks
  - Deoxypyridinoline (Dpd)
  - Pyridinoline (Pyr)

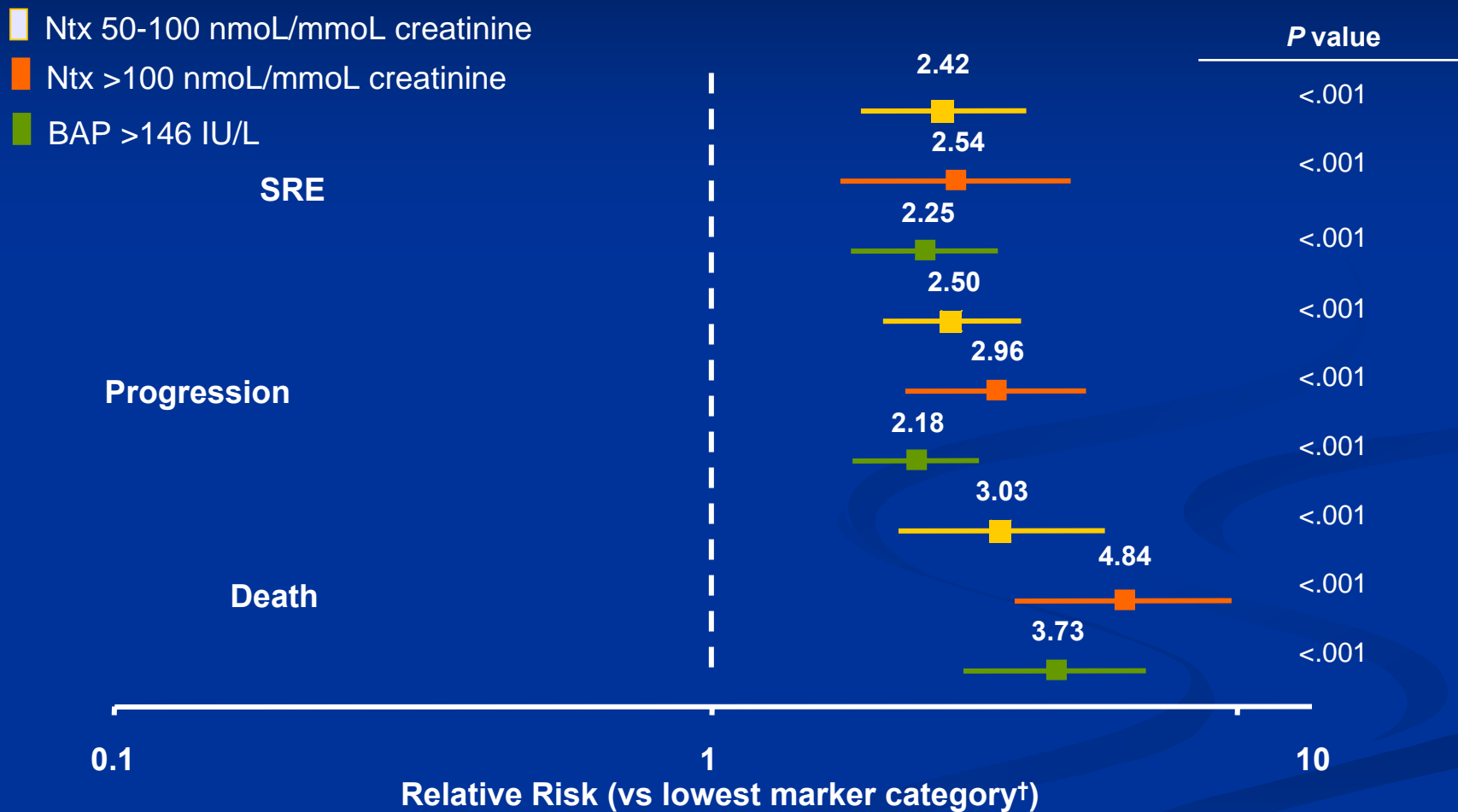


# Baseline NTx Levels by Primary Cancer

- Patients with each cancer type were categorized as low NTx, moderate NTx, or high NTx



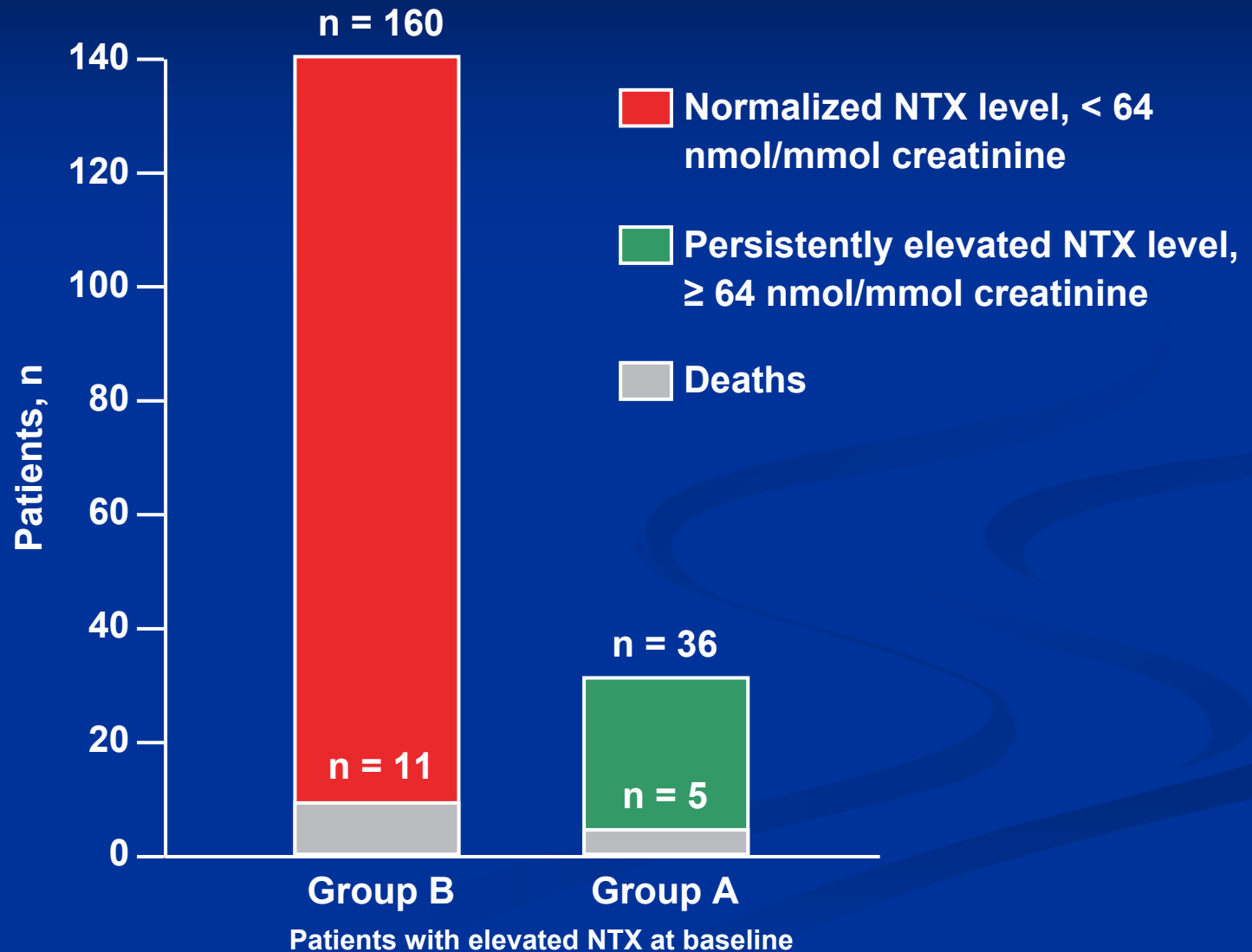
# Breast Cancer



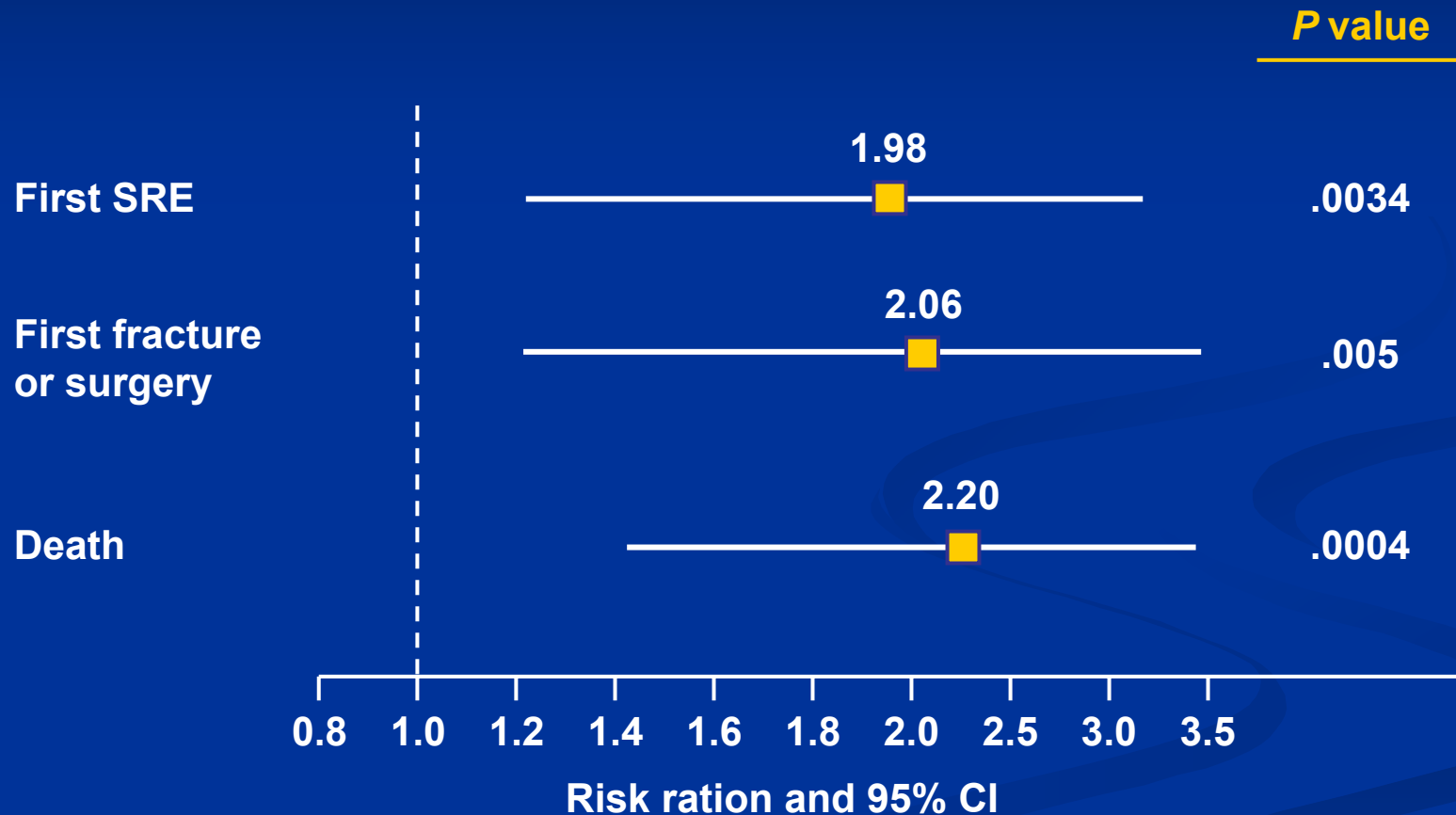
\*Based on most recent on-study marker assessments, univariate analysis.

†< 50 nmol/mmol for Ntx, ≤146 IU/L for BAP.

# Changes in Urinary N-telopeptide (NTX) Levels After 3 Months of Zoledronic Acid Treatment (Breast cancer)



# Relative Risk of Clinical Events in BC Patients With Persistently Elevated NTX Versus Normalized NTX



# Zoledronic Acid in Subsets of Patients: Conclusions

- These data suggest that Zoledronic Acid is associated with improved survival in the subset of breast cancer patients with high bone resorption