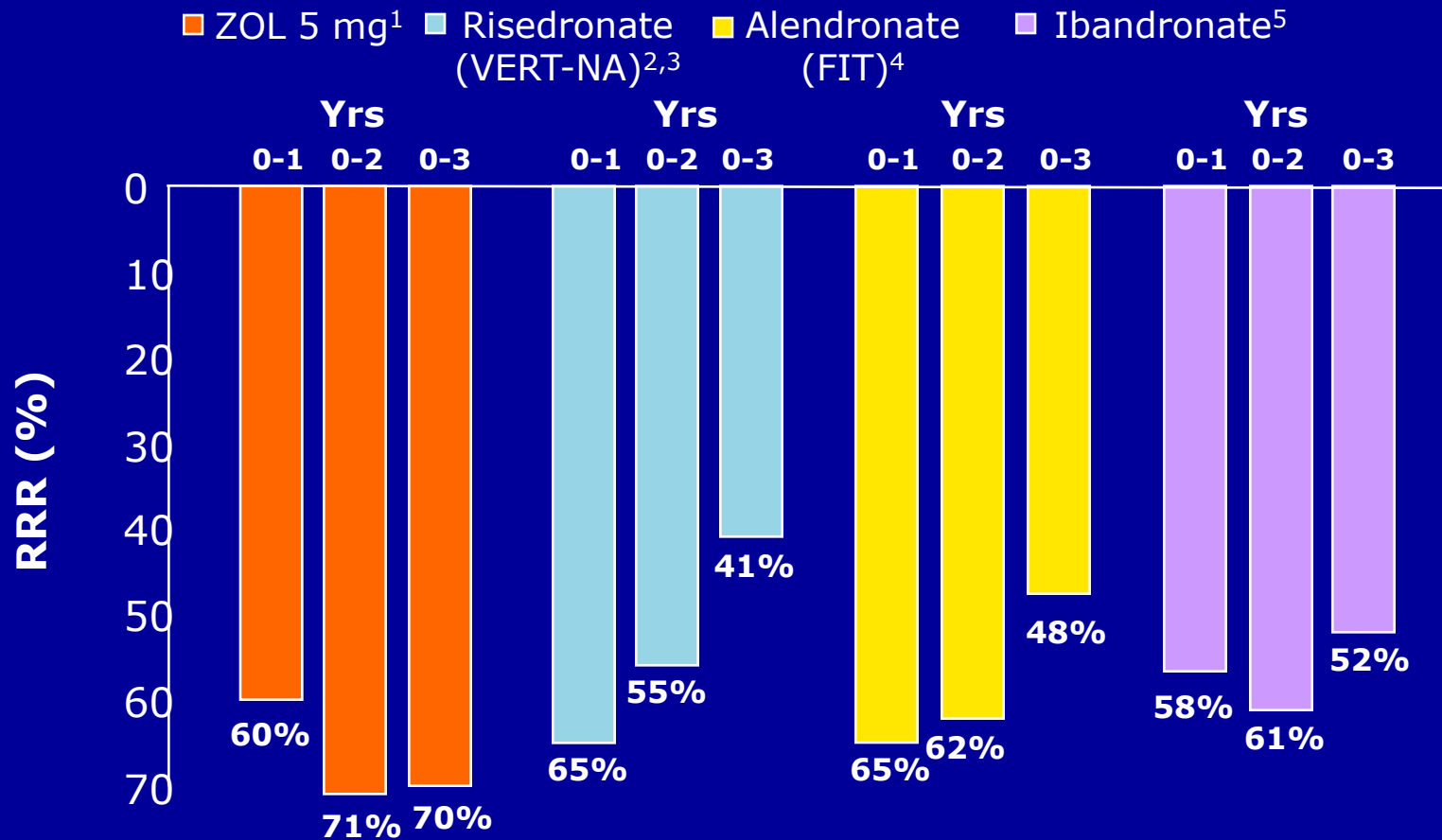


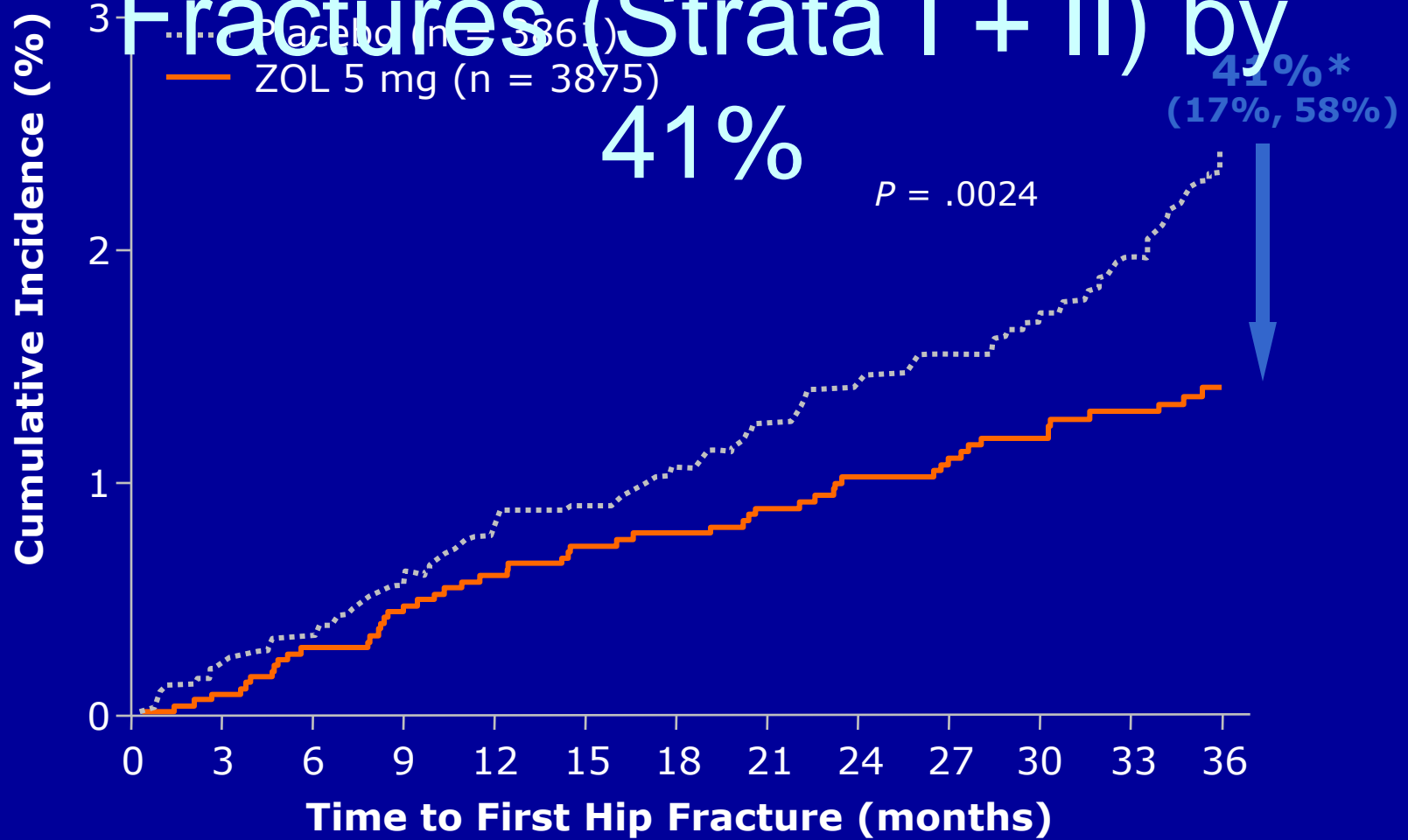
# Comparison of year by year vertebral fracture reduction among bisphosphonates

## Results from independent RCTs



1. Black DM, et al. *N Engl J Med.* 2007;356:1809-1822. 2. Harris ST, et al. *JAMA.* 1999;282:1344.  
 3. Actonel Prescribing Information. 4. Black D, et al. *J Clin Endocrinol Metab.* 2000;85:4118-4124.  
 5. Chesnut CH, et al. *J Bone Miner Res.* 2004;19:1241.

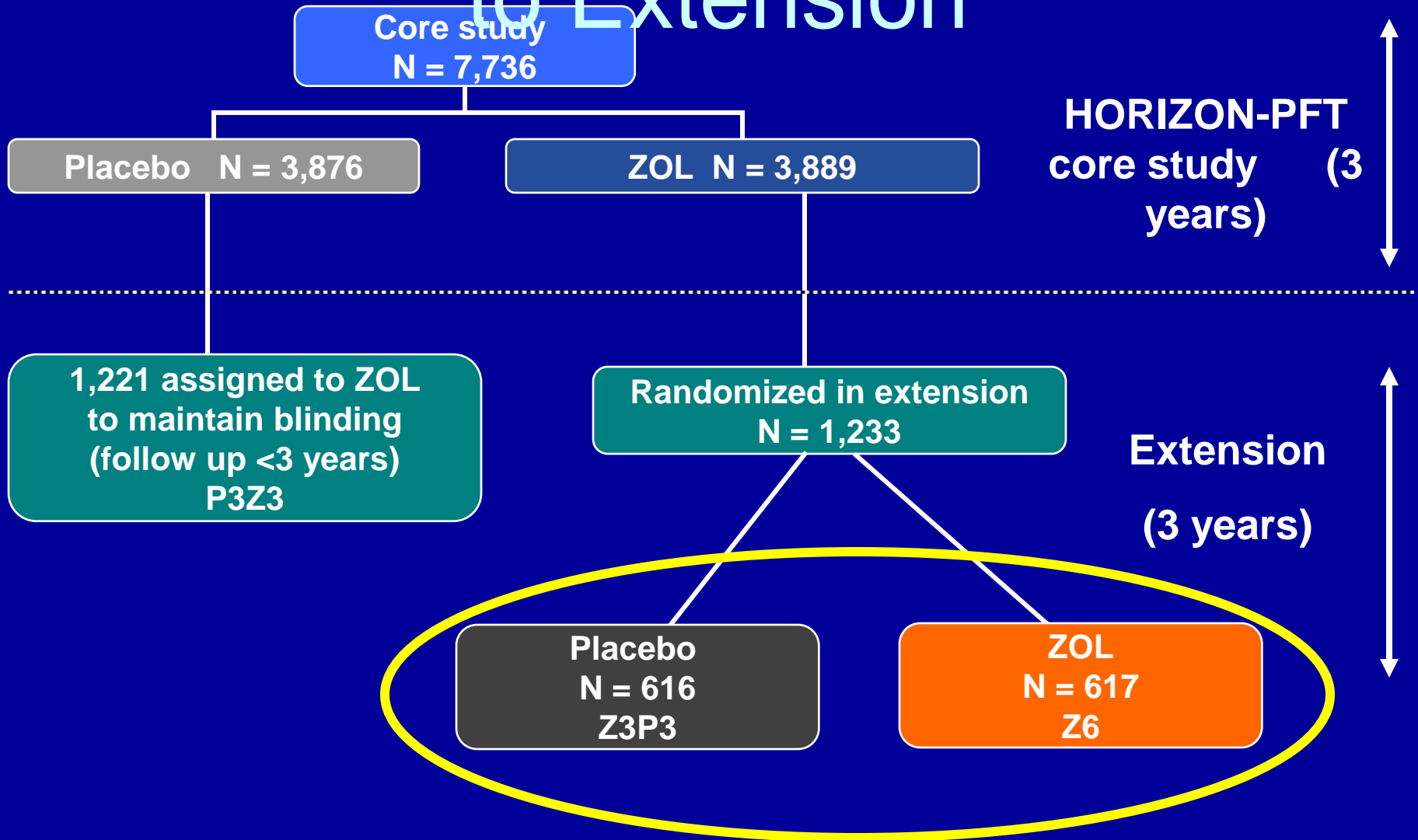
# Zoledronic Acid Reduced Cumulative 3-Year Risk of Hip Fractures (Strata I + II) by



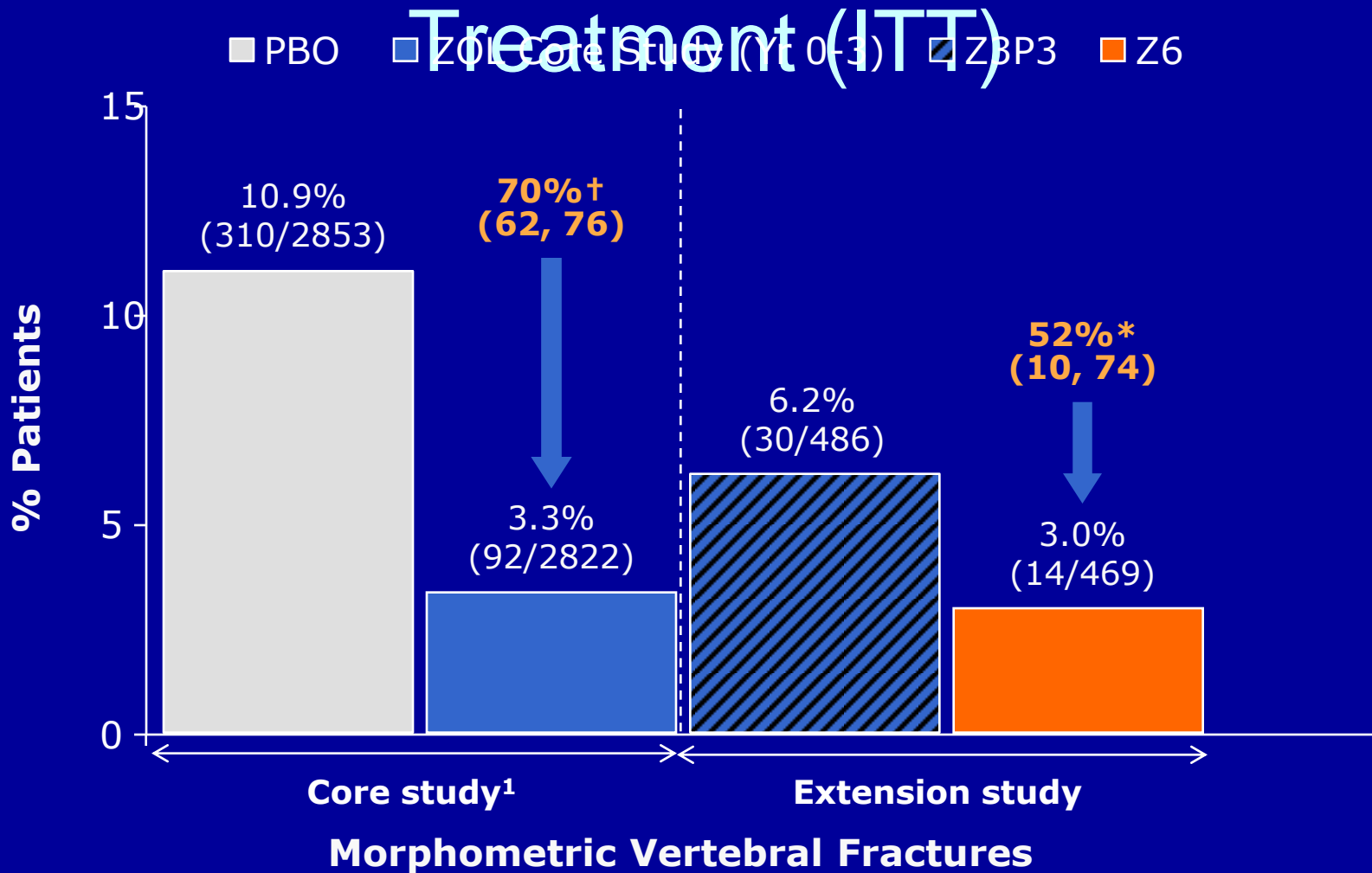
\*Relative risk reduction vs placebo (95% confidence interval)

Adapted from Black DM, et al. *N Engl J Med.* 2007;356:1809-1822.

# Patient Flow From Core Study to Extension



# Morphometric Vertebral Fractures in Years 3-6 Than Discontinuation of Treatment (ITT)



Core study: †P < 0.001 relative risk reduction vs placebo (PBO)

\*P = 0.0348, relative risk reduction vs Z3P3; n = the number of patients in the analysis population with X-rays at Year 3 and Year 6  
 ITT = intention to treat, Z3P3 = ZOL for 3 years and placebo for 3 years, Z6 = ZOL for 6 years

1. Black DM, et al. *N Engl J Med.* 2007;356:1809-1822.

# Bone Safety

Adverse event	Pivotal Fracture Trial <sup>1,2</sup>		Extension Study (New Events) <sup>*3</sup>	
	Z3 (N = 3862)	PBO (N = 3852)	Z6 (N = 613)	Z3P3 (N = 616)
	n	n	n	n
ONJ	1	1	1	0
Subtrochanteric or diaphyseal femur fracture <sup>†</sup>	3	2	0	0
Nonvertebral fracture	292	388	45	47

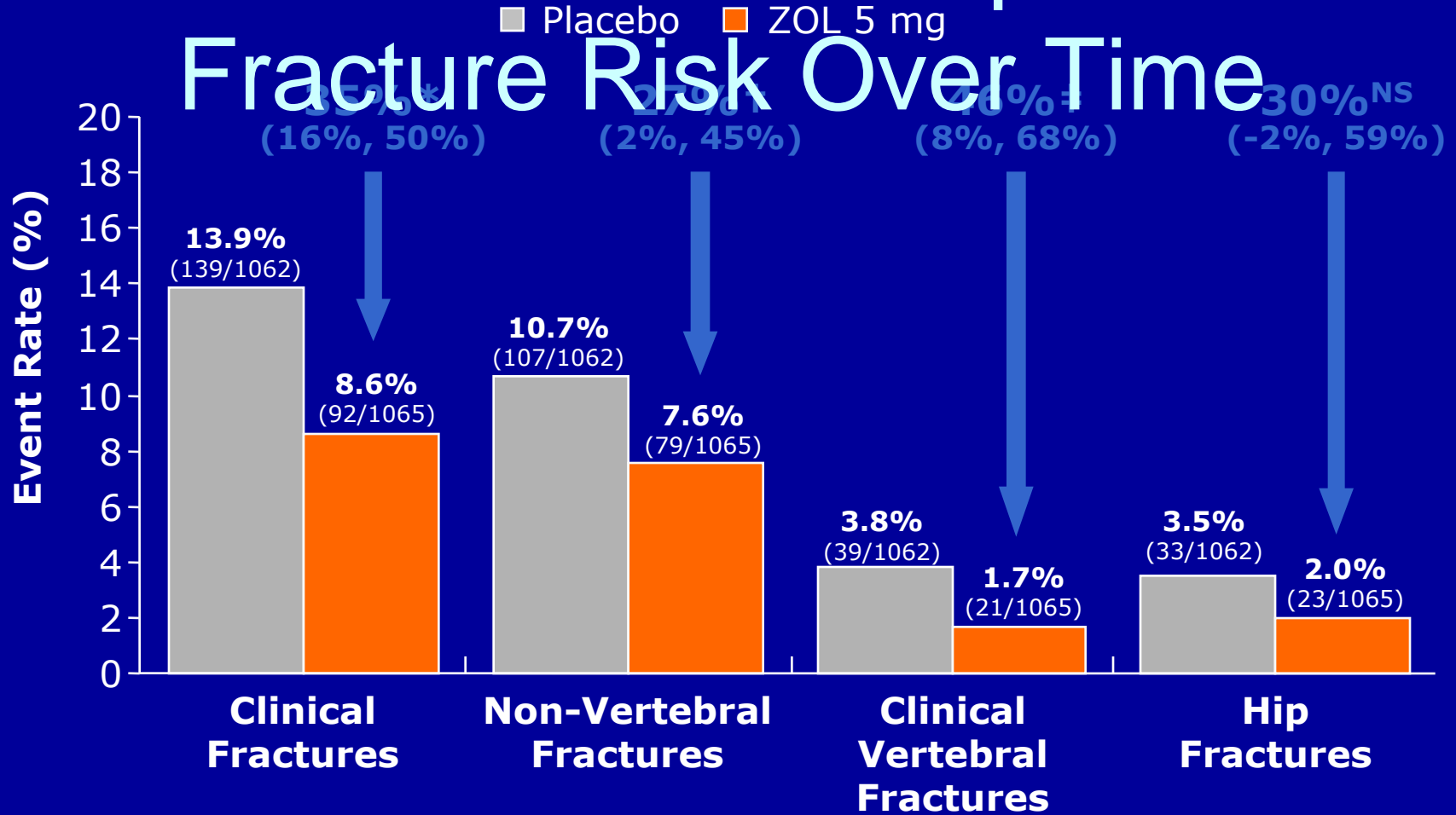
▶ In non-randomized group (P3Z3):

- ▶ 1 ONJ case with several ONJ risk factors
- ▶ 1 subtrochanteric fracture with no atypical features

\*Events were new events that occurred during the extension trial. †Results for the Pivotal Fracture Trial are from a secondary analysis that reviewed fracture records and radiographs (when available) from all hip and femur fractures to identify those below the lesser trochanter and above the distal metaphyseal flare and to assess atypical features.

1. Grbic JT, et al. *JADA*. 2008;139:32-40; 2. Black DM, et al. *N Engl J Med*. 2010; 362:1761-1771. 3. Data on file, Novartis

# Zoledronic Acid 5 mg Reduced Subsequent Fracture Risk Over Time



\* $P = .0012$ ; † $P = .0338$ ; ‡ $P = .0210$ , relative risk reduction vs placebo; NS = not significant. Values above bars are cumulative event rates based on Kaplan-Meier estimates at Month 24.

Lyles KW, et al. *N Engl J Med*. 2007. [e-publication 10.1056/NEJMoa074941 at [www.nejm.org](http://www.nejm.org)]