

**A single tablet multilayer formulation of enteric-coated naproxen coupled with non-enteric-coated omeprazole is associated with a significantly reduced incidence of gastric ulcers vs enteric-coated naproxen: a prospective, randomized, double-blind study**

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## **AGA Disclosure**

I have financial relationships with commercial entities and the content of my presentation includes discussion of off-label/investigative use of medicine(s), medical devices, or procedures.

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# Disclosure and Acknowledgements

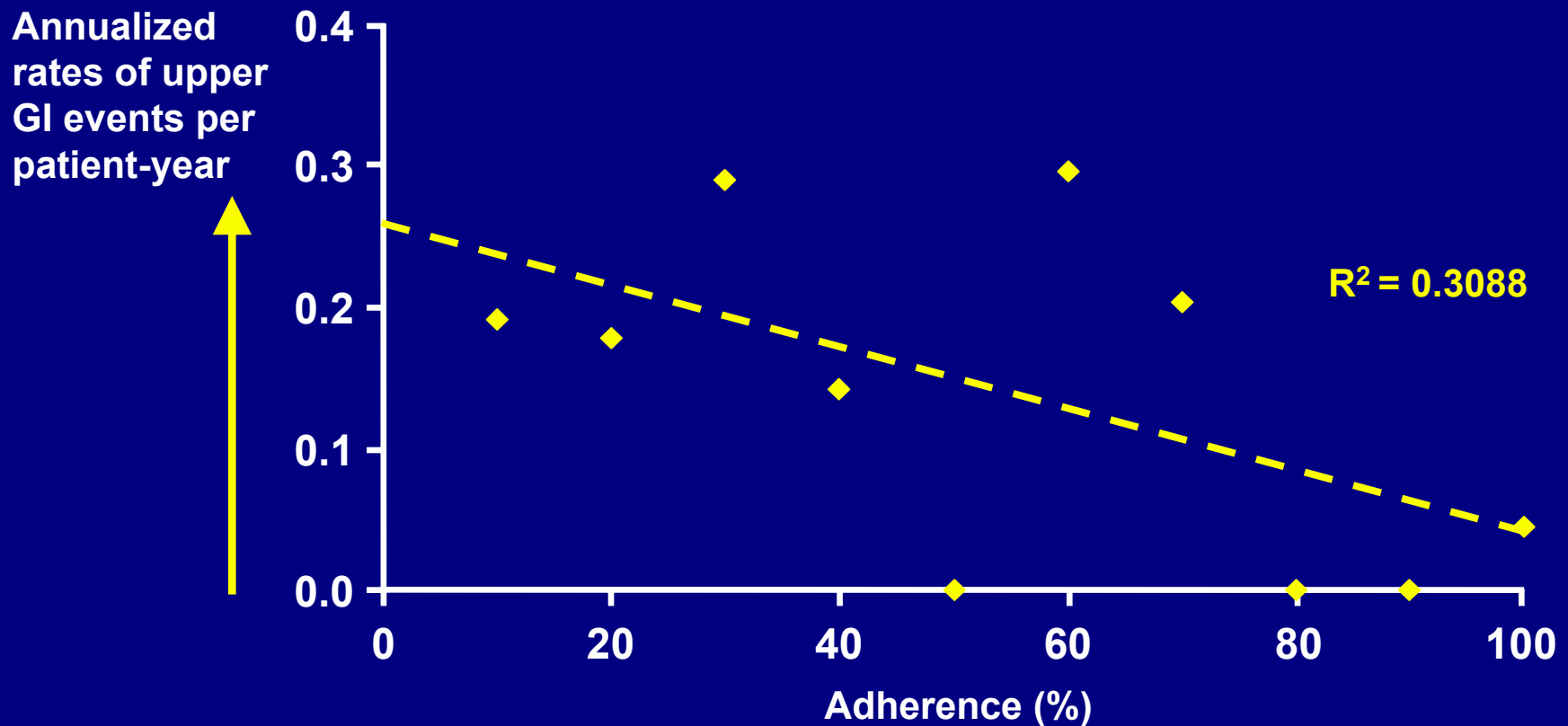
- John G. Fort- POZEN: employee
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- John R. Plachetka- POZEN: employee, patent held/filed; Spouse- POZEN: Stock shareholder, board membership
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# Introduction

- ***Efficacy*** of proton pump inhibitors (PPIs) for the prevention of mucosal injury, endoscopic ulcers, and upper GI symptoms associated with NSAID therapy is well documented<sup>1,2</sup>
- The degree of non-adherence to co-prescribed medications reduces the relative ***effectiveness*** of preventative PPI therapy

<sup>1</sup>Hawkey et al. NEJM 1998; <sup>2</sup>Scheiman Curr Treat Options Gastroenterol 2008

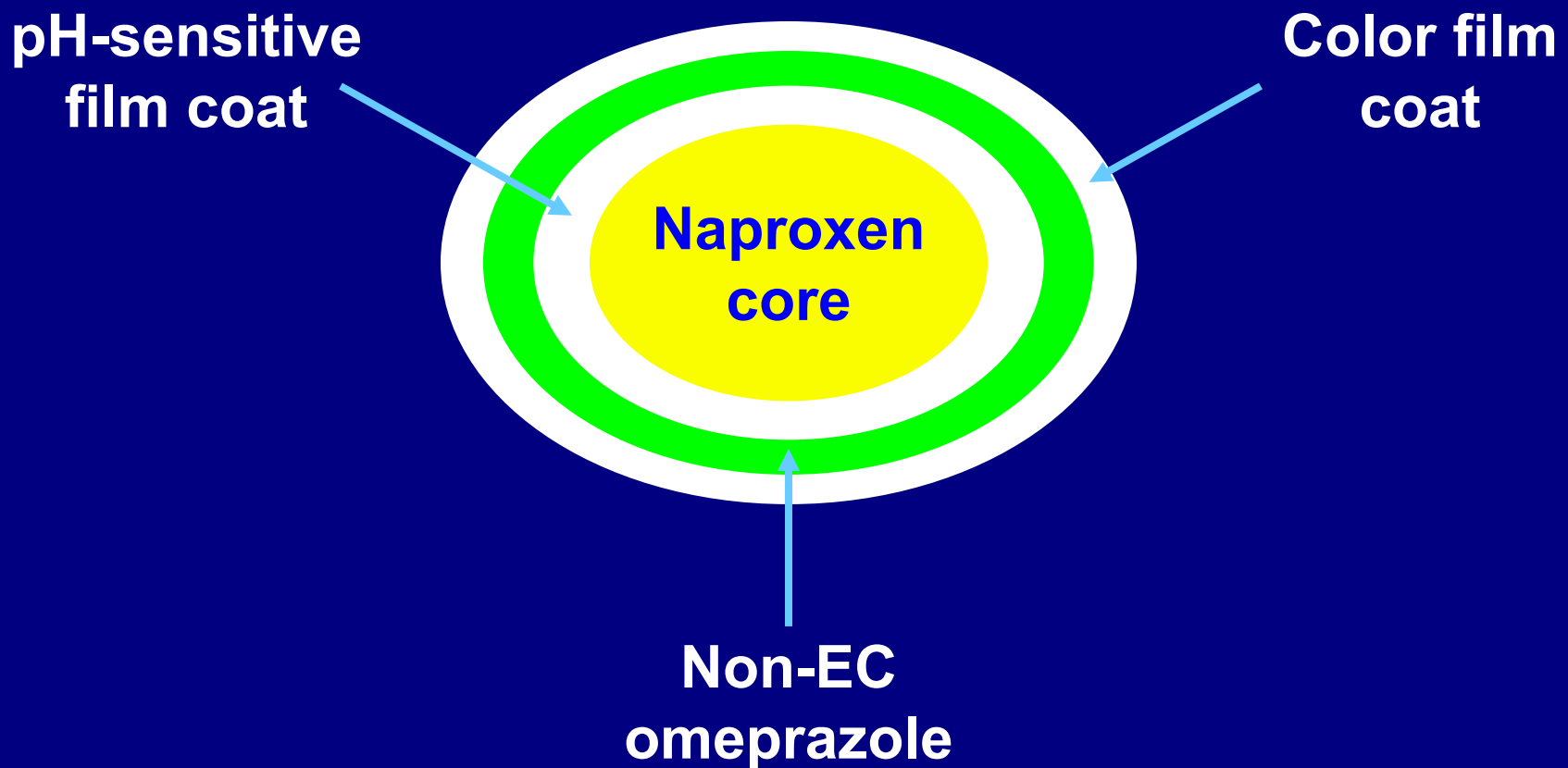
# Non-adherence is associated with decreased relative effectiveness



# Rationale for PN formulation development

- **Non-EC PPI component to optimize PPI delivery prior to exposure to NSAID**
- **A single tablet formulation of a non-EC PPI and an EC NSAID could address the issue of non-adherence**

# PN200: single tablet formulation

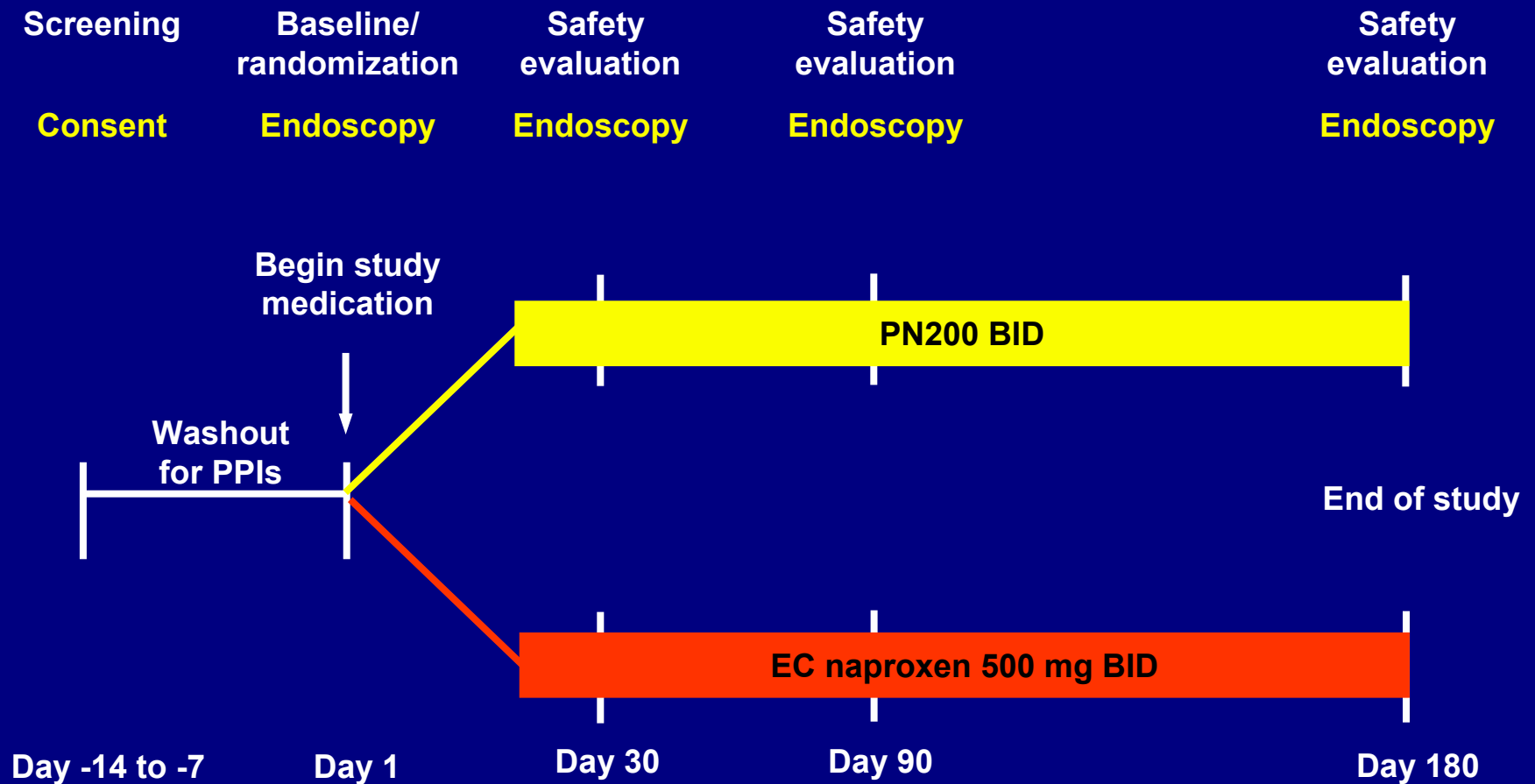


# Study design (1)

- Randomized, double-blind, multicenter, parallel-group, controlled study in patients requiring chronic NSAID treatment\*
  - stratified for ASA use  $\leq 325$  mg
- Inclusion criteria
  - Aged 18-49 with documented Hx of uncomplicated GU or DU within the past 5 years, or aged  $\geq 50$  years (no Hx required)
  - *H. pylori*-negative at screening
  - No antisecretory agents / misoprostol within 14 days
- Patients with baseline endoscopy showing any GU or DU ( $\geq 3$  mm diameter with depth) were excluded

\*included patients with OA, RA, AS or other medical conditions expected to require chronic NSAID treatment

# Study design (2)



# Study endpoints

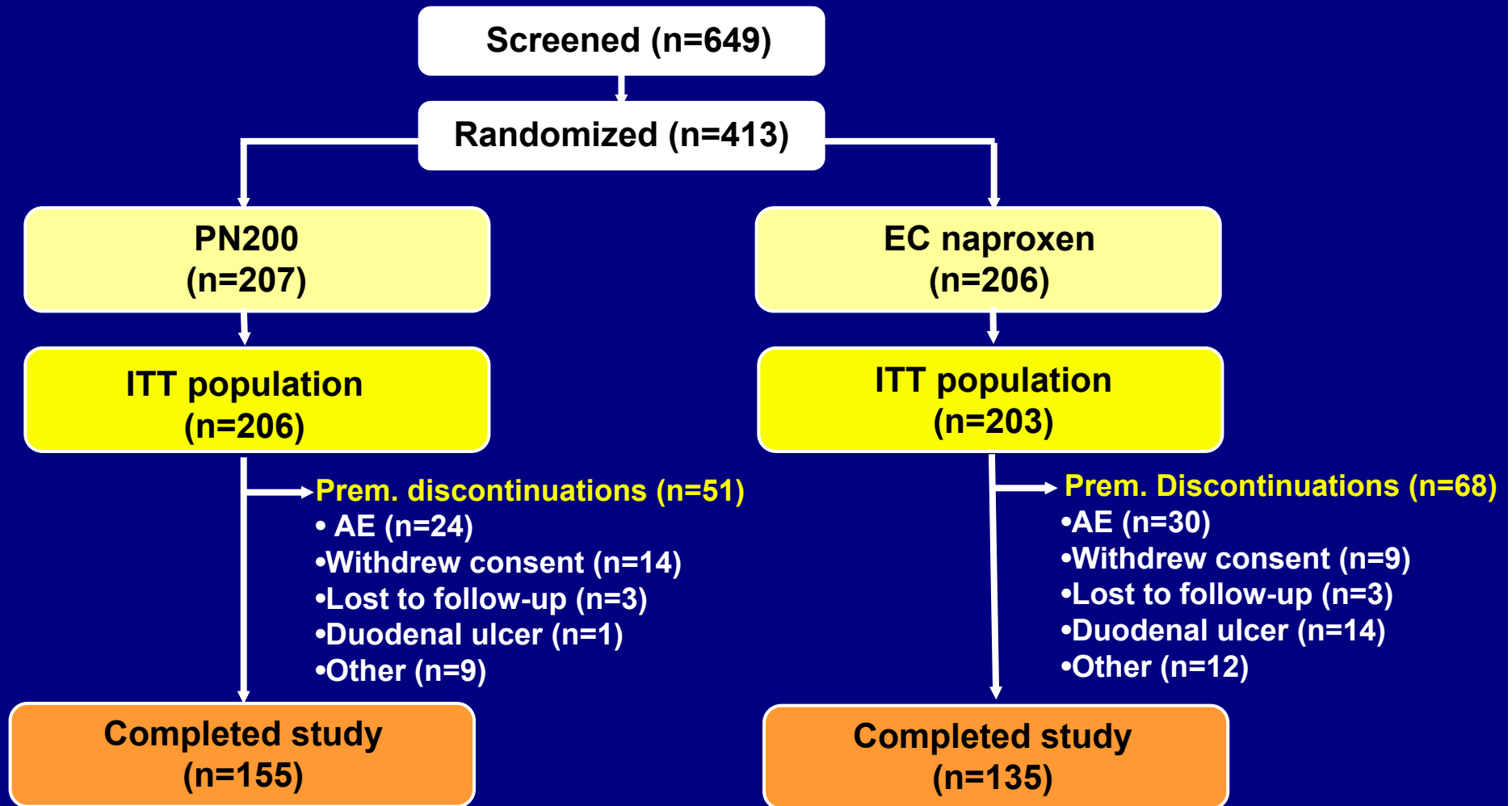
- **Primary endpoint**

- Survival analysis of incidence of GU ( $\geq 3$  mm diameter with depth) over 6 months

- **Secondary endpoints**

- Incidence of DU over 6 months
- Tolerability
- Safety

# Study disposition

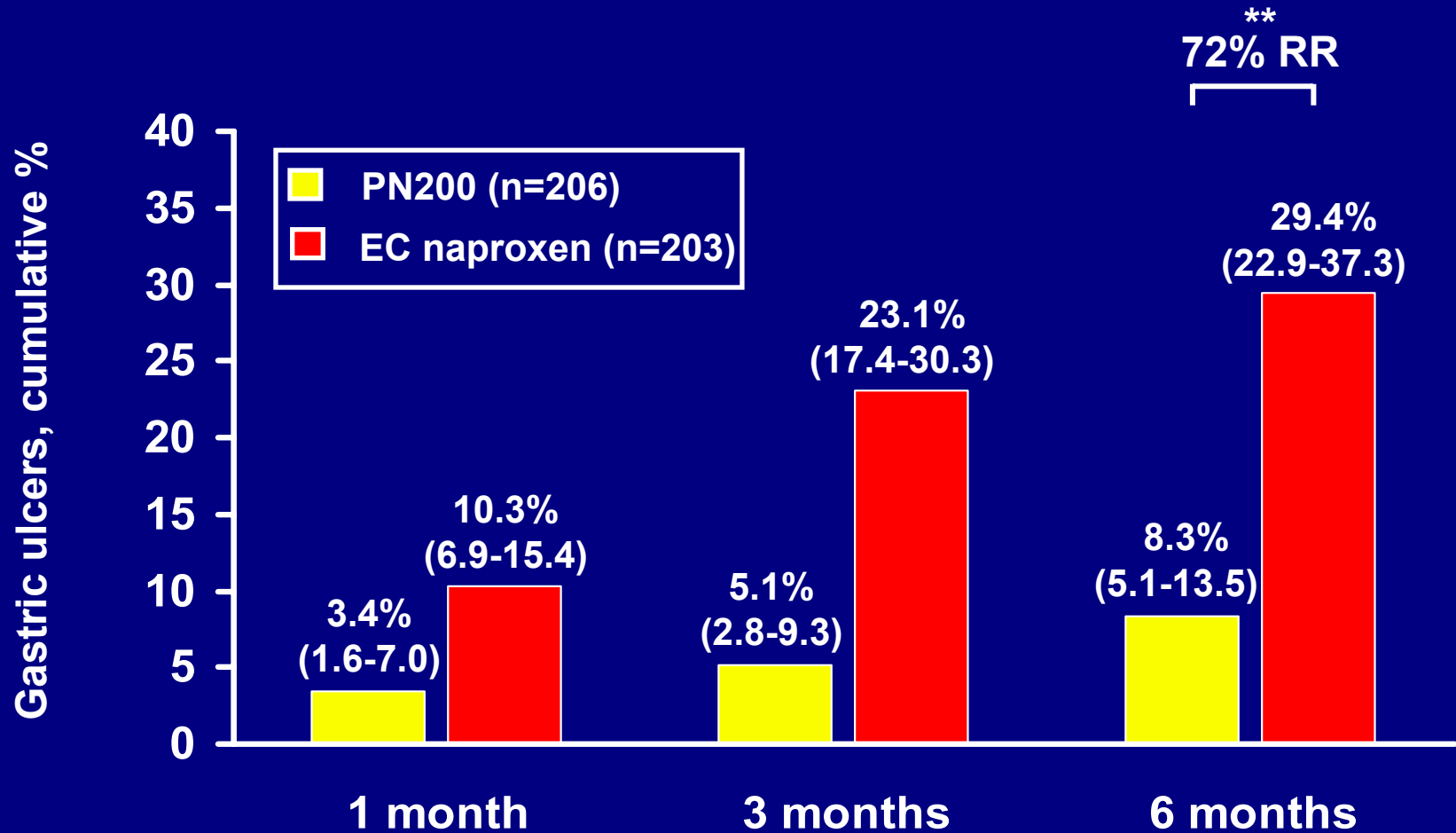


ITT (intent-to-treat) population: all patients randomized who received at least one dose of study drug with no ulcer at baseline  
(At baseline: 4 subjects: 1 PN200, 3 EC naproxen)

# Demographics – ITT

		PN200 (n=206)	EC naproxen (n=203)
Gender, n (%)	Male	73 (35)	60 (30)
Race, n (%)	White	175 (85)	173 (85)
	Black	24 (12)	20 (10)
	Other	7 (3)	10 (5)
Age (years)	Mean	60.8	60.7
	<60 years, n (%)	106 (51)	100 (49)
	≥50 years, n (%)	199 (97)	201 (99)
Aspirin use, n (%)		56 (27.2)	52 (25.6)
Ulcer Hx, n (%)	Gastric only	13 (6.3)	4 (2)
	Duodenal only	2 (1)	0

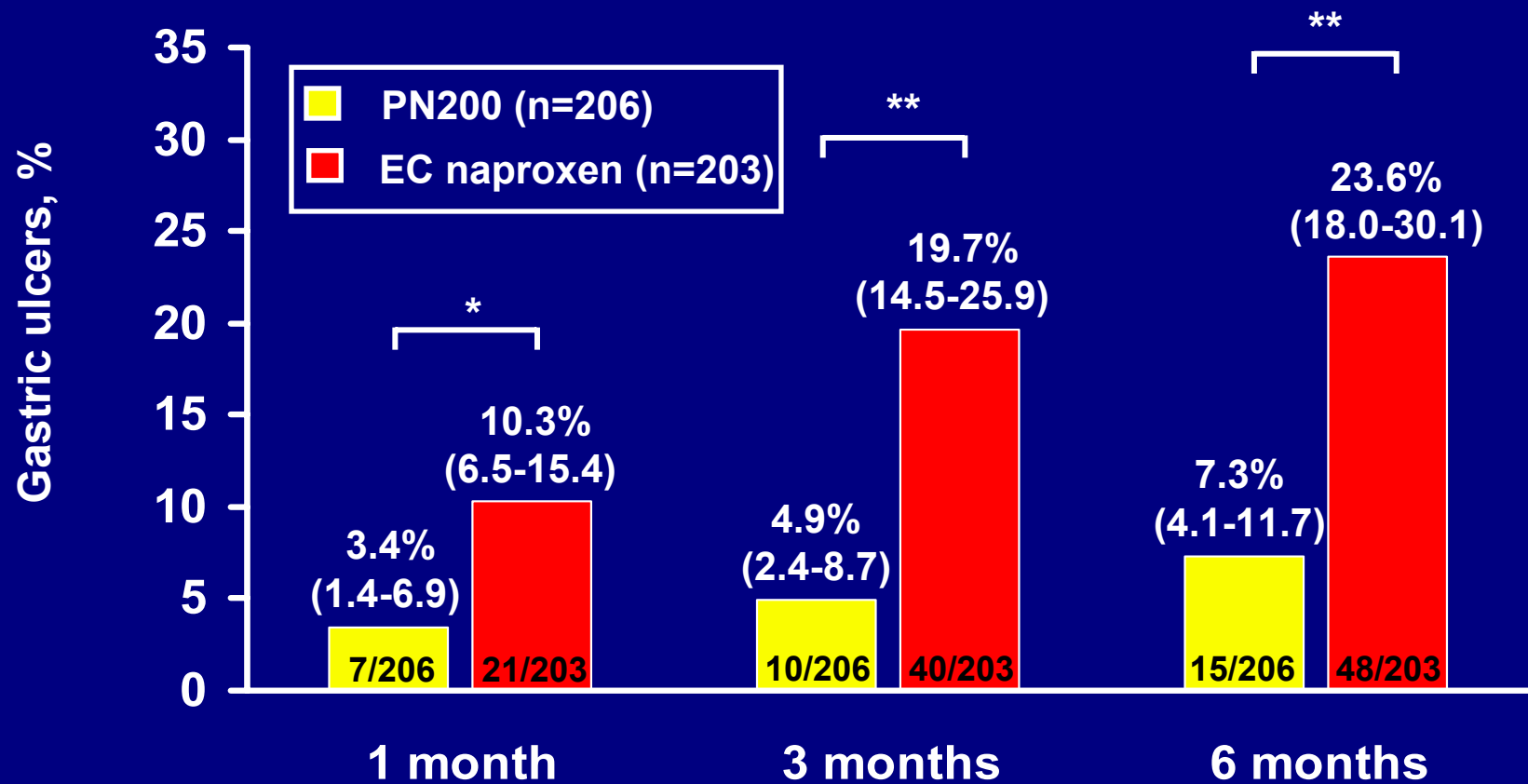
# Primary endpoint: survival analysis of incidence of gastric ulcers – ITT



\*\* p<0.001 between groups over 6 months

Data shown are % (CI)

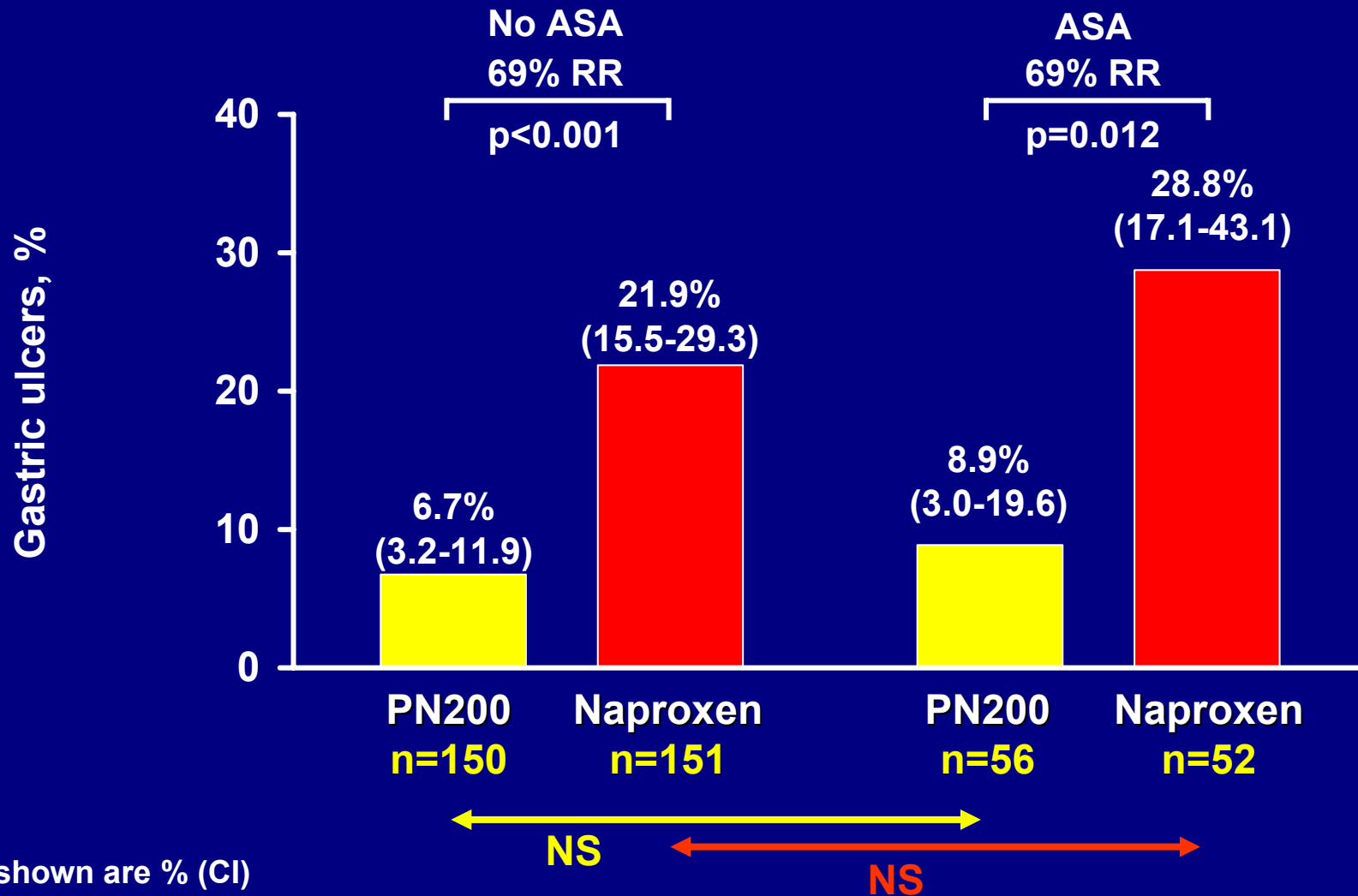
# Cumulative observed incidence of gastric ulcers – ITT



\*p<0.01; \*\*p<0.001

Data shown are % (CI)

# Cumulative incidence of gastric ulcers at 6 months: ASA vs no ASA



Data shown are % (CI)

# Secondary endpoint: survival analysis of incidence of duodenal ulcers at 6 months - ITT

	PN200 (n=206)	EC naproxen (n=203)
Survival analysis, % (CI)		
1 month	0.5 (0.1-3.4)	5.4 (3.0-9.6)
3 months	0.5 (0.1-3.4)	8.9 (5.5-14.2)
6 months**	0.5 (0.1-3.4)	10.8 (6.8-16.8)

\*\*p<0.001, RR 95%

# Safety and tolerability

Proportion of patients, n (%)	PN200 (n=206)	EC naproxen (n=203)	p
Any UGI AE	105 (51.0)	144 (70.9)	<0.001
Any UGI AE related to study drug	86 (41.7)	133 (65.5)	<0.001
Dyspeptic symptoms*	17 (8.3)	18 (8.9)	NS
Use of antacid rescue medication	145 (70.4)	170 (83.7)	0.001
UGI AEs leading to discontinuation	9 (4.4)	22 (10.8)	0.012

\*upper abdominal pain, dyspepsia, eructation, gastric discomfort

# Conclusions

- **Compared with EC naproxen, PN200 was associated with significantly**
  - fewer gastric ulcers
  - fewer duodenal ulcers
- **Concomitant low dose aspirin therapy had no significant effect on the gastric ulcer incidence**