

**Pilot Evaluation of a Novel Combination
Tablet (PN 100) Containing a Proton Pump
Inhibitor and a Nonsteroidal Anti-
Inflammatory Drug in Prevention of Upper
Gastrointestinal Mucosal Injury**

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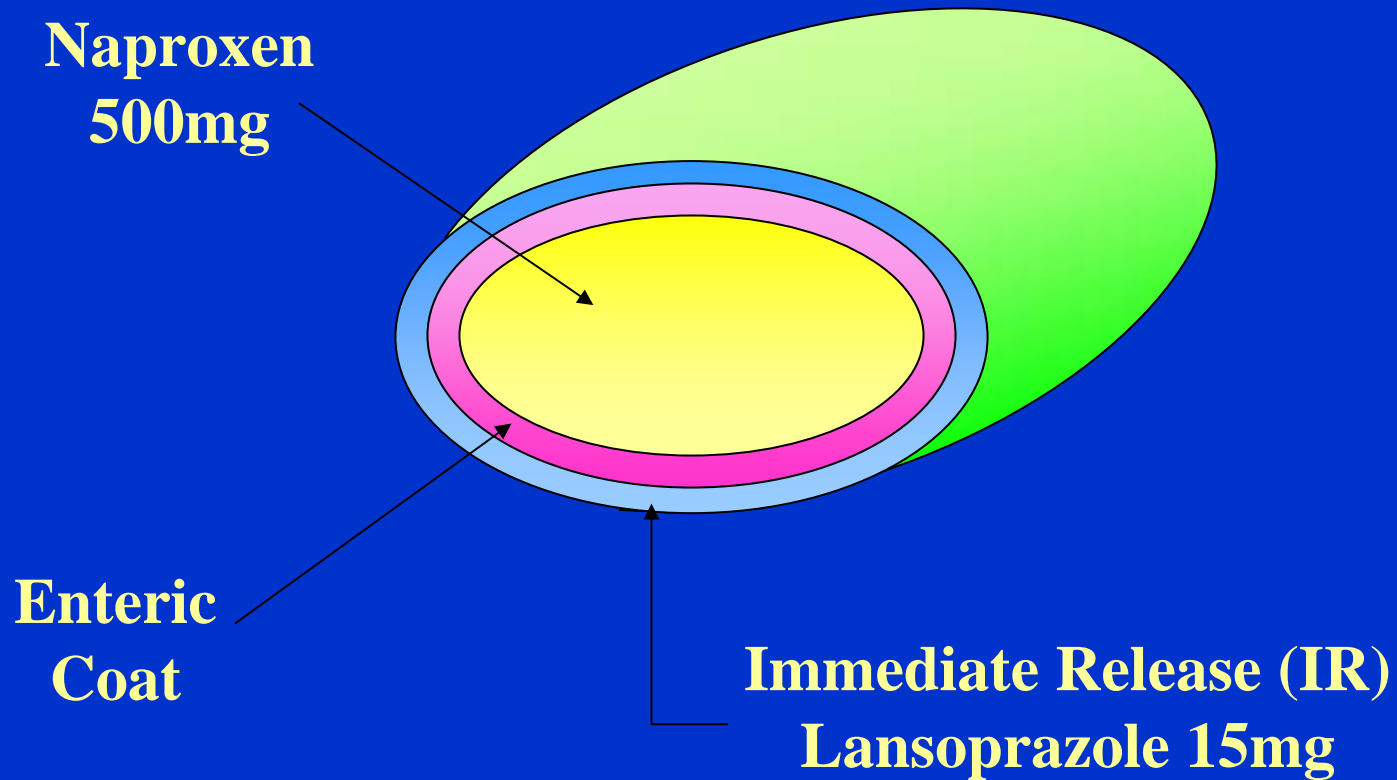
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PN 100 Combination Tablet*

(Immediate Release Lansoprazole and Enteric Coated Naproxen)

[* US Patent 6,926,907]



Study Design

Subjects

60 Volunteers Aged 40-65 Years

Treatments (14 Days)

- PN 100 twice daily**
- Naproxen 500mg twice daily with
DR Lansoprazole 15 q AM**
- EC Naproxen 500mg twice daily**

Endoscopy –Baseline, Day 8, Day 14

Gastric pH and Pharmacokinetics - Day 1 and Day 7

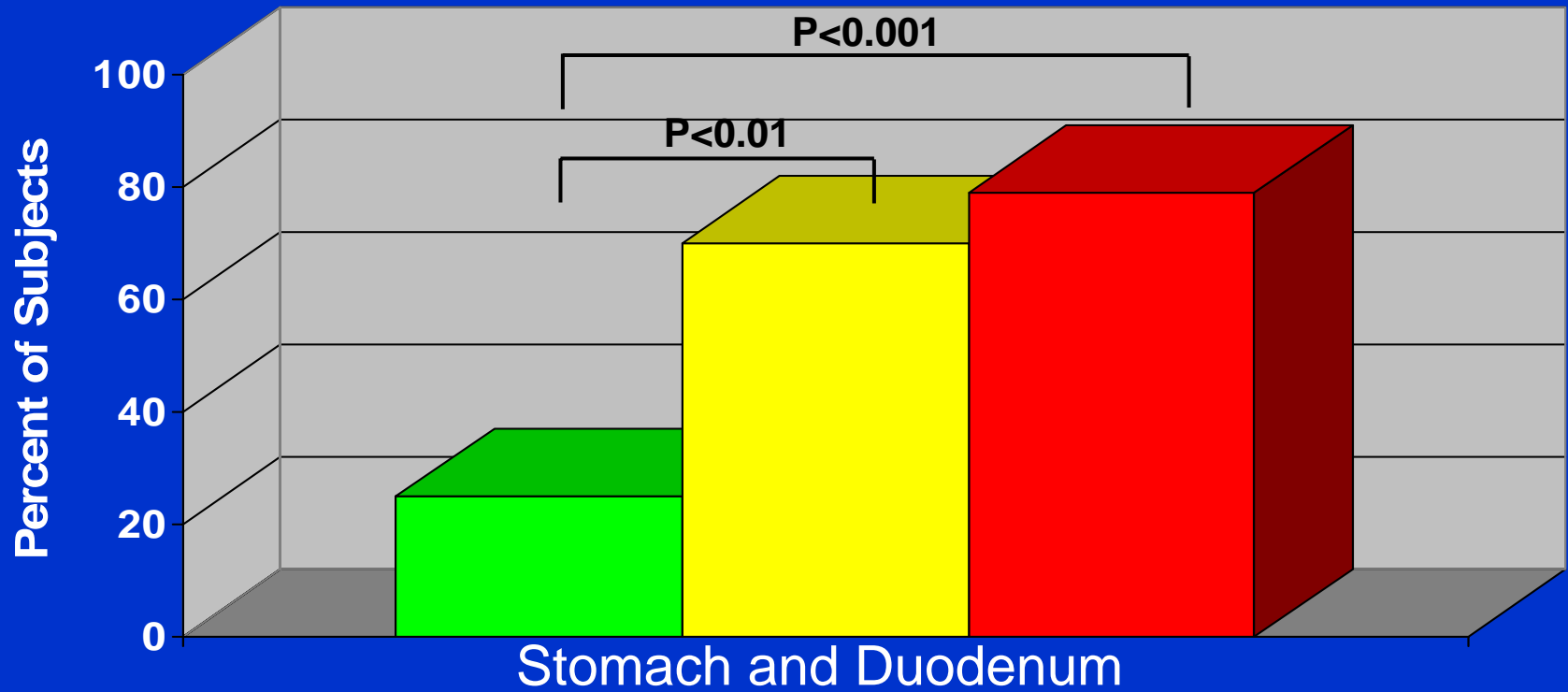
Endpoint--Lanza 3 & 4 Scores at Day 14 Endoscopy

Study Population

Treatment:	PN 100 Twice Daily	Naproxen BID + DR Lansoprazole each morning	EC Naproxen Twice Daily	Total
Number of Subjects:	20	20	20	60
Males	15	12	13	40
Age, yr (mean)	48	51	47	49
Range, yr	(40-59)	(40-58)	(41-54)	(40-59)
H. pylori positive*	5	5	4	14 (35%)
Smoker	2	1	6	9 (23%)
Females	5	8	7	20
Age, yr (mean)	56	51	51	53
Range, yr	(44-63)	(43-59)	(43-64)	(43-64)
H. pylori positive*	3	3	1	7 (35%)
Smoker	1	0	2	3 (15%)

* by serology

Incidence of Lanza 3 & 4 Mucosal Injury by Endoscopy at Day 14



■ PN 100 (15/500) Twice Daily, n=20

■ Naproxen 500 mg Twice Daily with DR Lansoprazole 15 mg each morning; n=20

■ EC Naproxen 500 Twice Daily, n=19

Gastric Mucosa

	PN 100 Twice Daily	Naproxen Twice Daily + DR Lansoprazole each morning	EC Naproxen Twice Daily
<u>Erosions - Day 8 + Day 14</u>			
mean (SD) †	10.1 (12.8)	19.2 (18.3)	26.2 (21.0)
median	5	14	21
<u>Ulcers</u>	0	1 (5%)	2 (11%)

† p = 0.02, Kruskal-Wallis test among 3 groups

p = 0.01, PN 100 vs. EC Naproxen

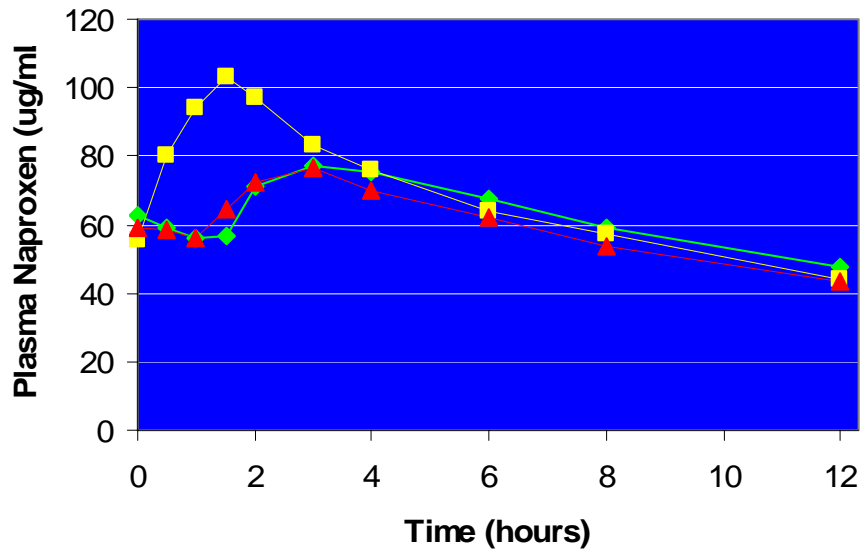
p = 0.07, PN 100 vs. Naproxen + DR Lansoprazole

Lansoprazole Pharmacokinetics

IR Lansoprazole /EC Naproxen (PN 100)				Naproxen + DR Lansoprazole		
	Day 1	Day 7	Change	Day 1	Day 7	Change
C_{max} (ng/mL)						
Mean	331	472	+ 42 %	565	653	+ 16 %
Median	270	421		587	652	
AUC (hr · ng/mL)						
Mean	675	1076	+ 59 %	1527	1796	+ 18 %
Median	386	741		1520	1723	

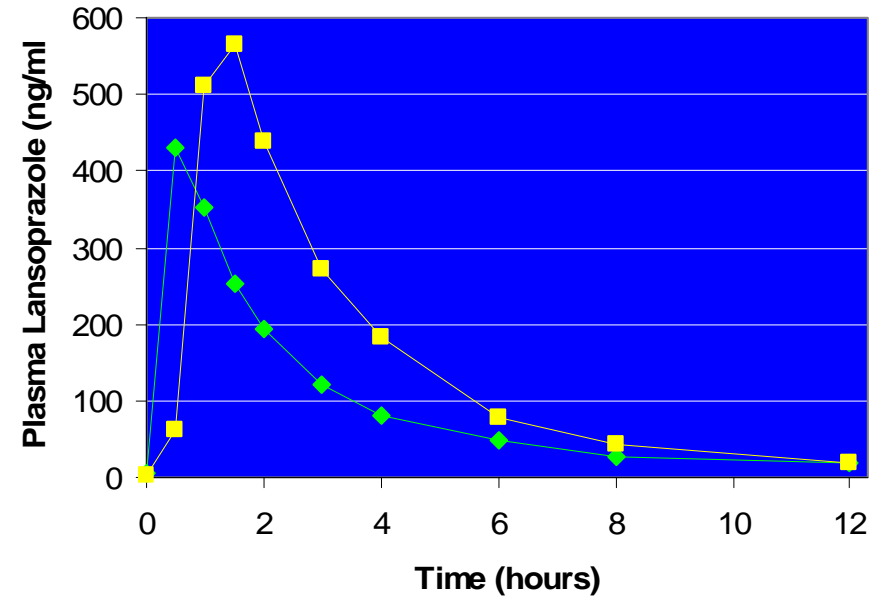
Plasma Time-Concentration Curves for Naproxen and Lansoprazole on Day 7

Plasma Naproxen Day 7



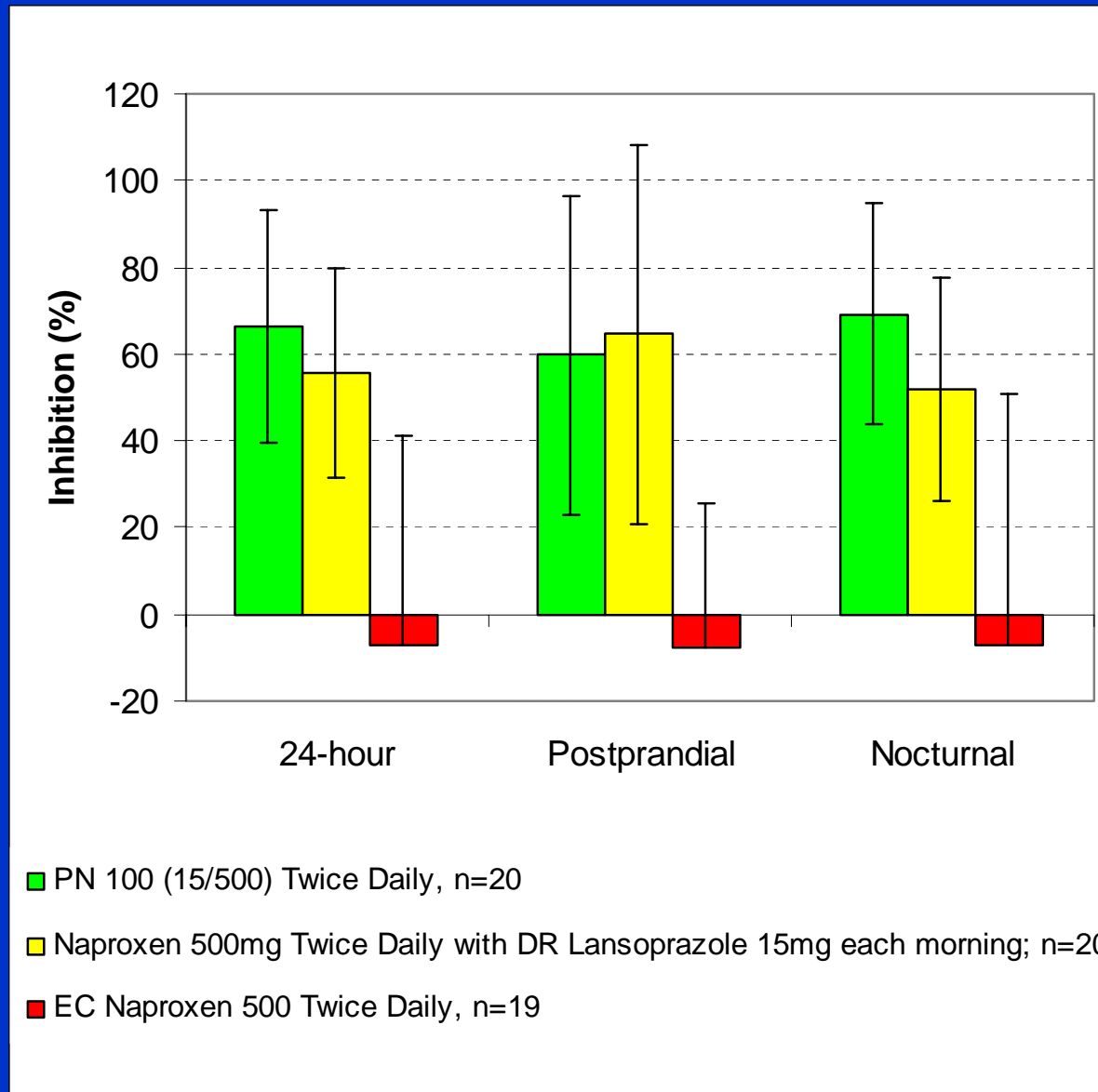
- ◆ PN 100 (15/500) Twice Daily
- Naproxen 500 mg Twice Daily with DR Lanso 15 mg Q AM
- ▲ EC Naproxen 500 mg Twice Daily

Plasma Lansoprazole Day 7



- ◆ PN 100 (15/500) Twice Daily
- Naproxen 500mg Twice Daily with DR Lanso 15 mg Q AM

Inhibition of Integrated Gastric Acidity on Day 7



Postprandial- hours 2 through 13 ; Nocturnal-hours 14 through 2

Adverse Events Reported

	PN 100 Twice Daily	Naproxen BID + DR Lansoprazole each morning	EC Naproxen Twice Daily
No. of Subjects	20	20	20
No. subjects with at least one adverse event (AE)	4 (20%)	6 (30%)	10 (50%)
Any gastrointestinal AE	4	5	8
Diarrhea	1	2	3
Nausea	1	1	4
GI irritation	0	1	3
Abdominal distention	1	3	2
Abdominal discomfort	1	1	1

Summary

- **PN 100 reduced NSAID-associated gastric mucosal injury when administered twice-daily to volunteers over 14 days**
- **These data warrant testing of PN 100 in larger trials**