



TARGETED MEDICAL PHARMA



Safe and Effective Chronic Pain Management

*Cost Savings Associated with the Administration of
Theramine[®] for the Dietary Management of Chronic Pain Syndromes*

Theraproxen™

- Medical Food—***Theramine***®
- Drug—Naproxen
- Dose—once per day of naproxen
- Indications: Pain and Inflammation at reduced dose of NSAID



Theramine[®] and Naproxen Double Blind Trial (Theraproxen Co-Pack)

- 127 patients
- 12 national sites
- Established chronic back pain
- VAS Scales
- Likert Scales
- Roland-Morris disability questionnaire
- Oswestry Back pain index
- Inflammatory markers
- Study completion, April 2009



Theraproxen™ Study Design

- **Inclusion Criteria:**

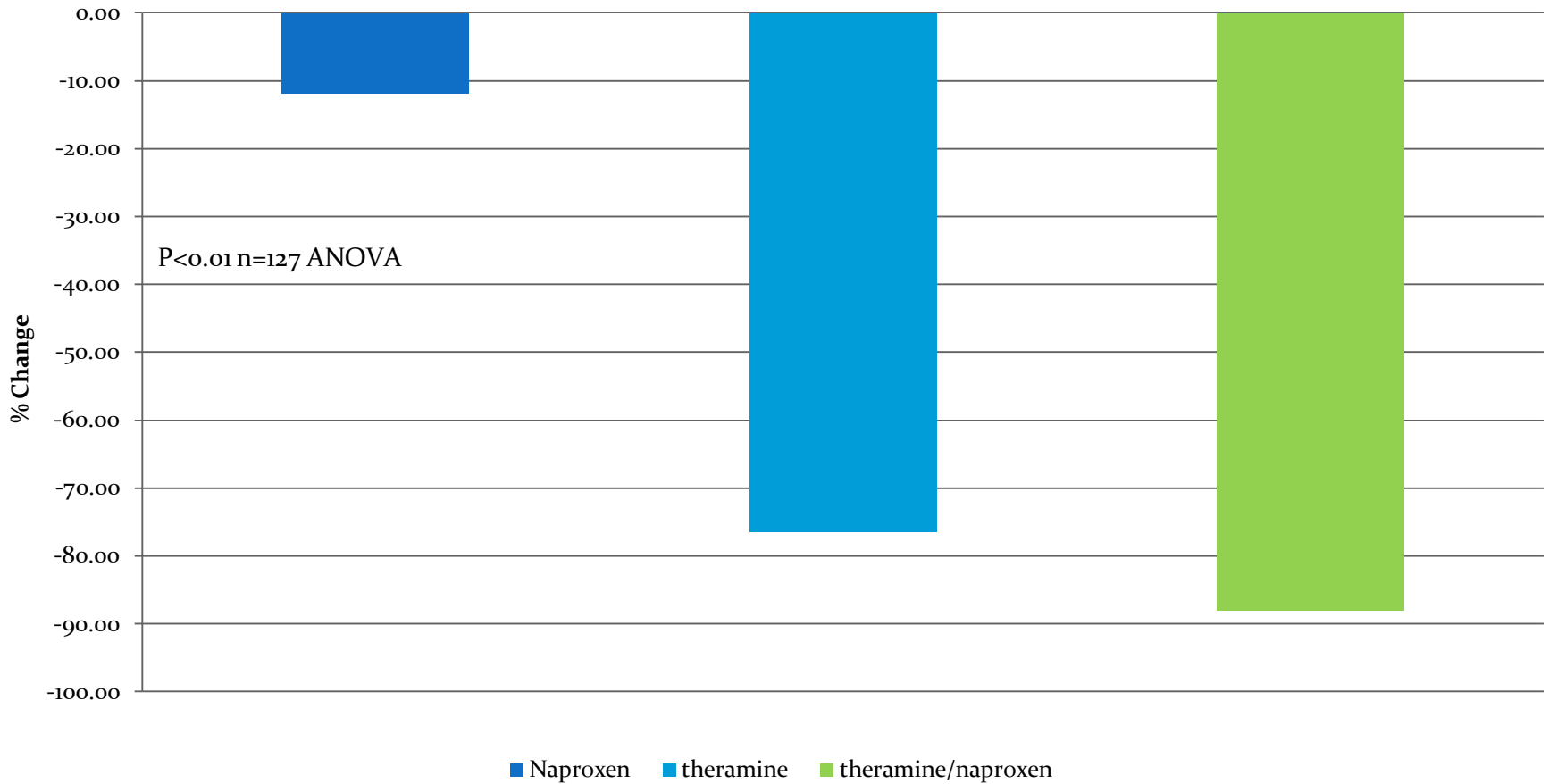
- 1) Back pain lasting greater than six weeks. Pain must be present on at least 5 out of 7 days during each of the two weeks prior to screening visit

- 2) Analgesic medication used to treat pain at least 4 out of last 7 days and at least 10 days in the last month



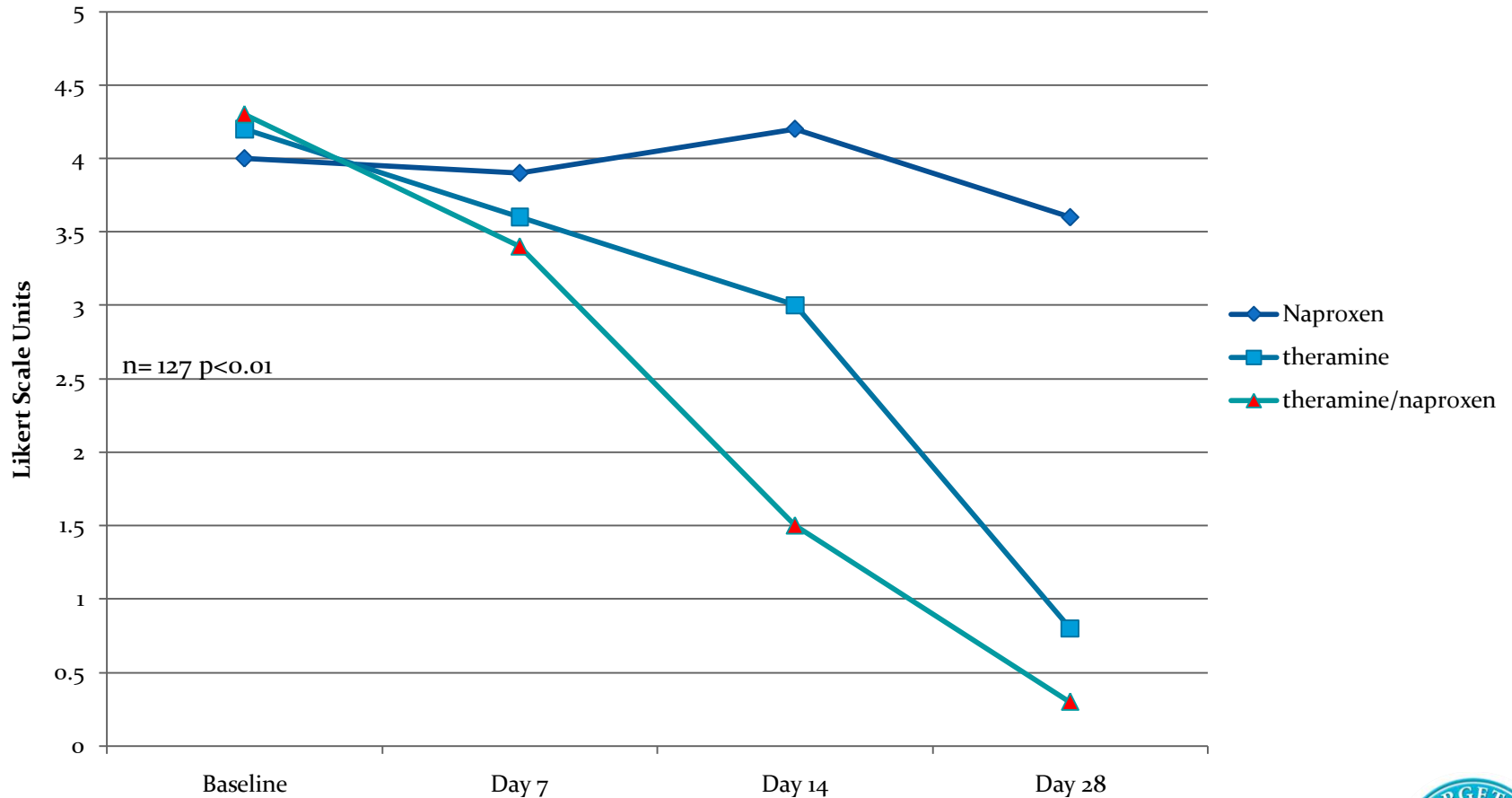
Theraproxen™ Double Blind Trial – Roland Morris Index

The % Change in the Roland Morris Index at Day 28

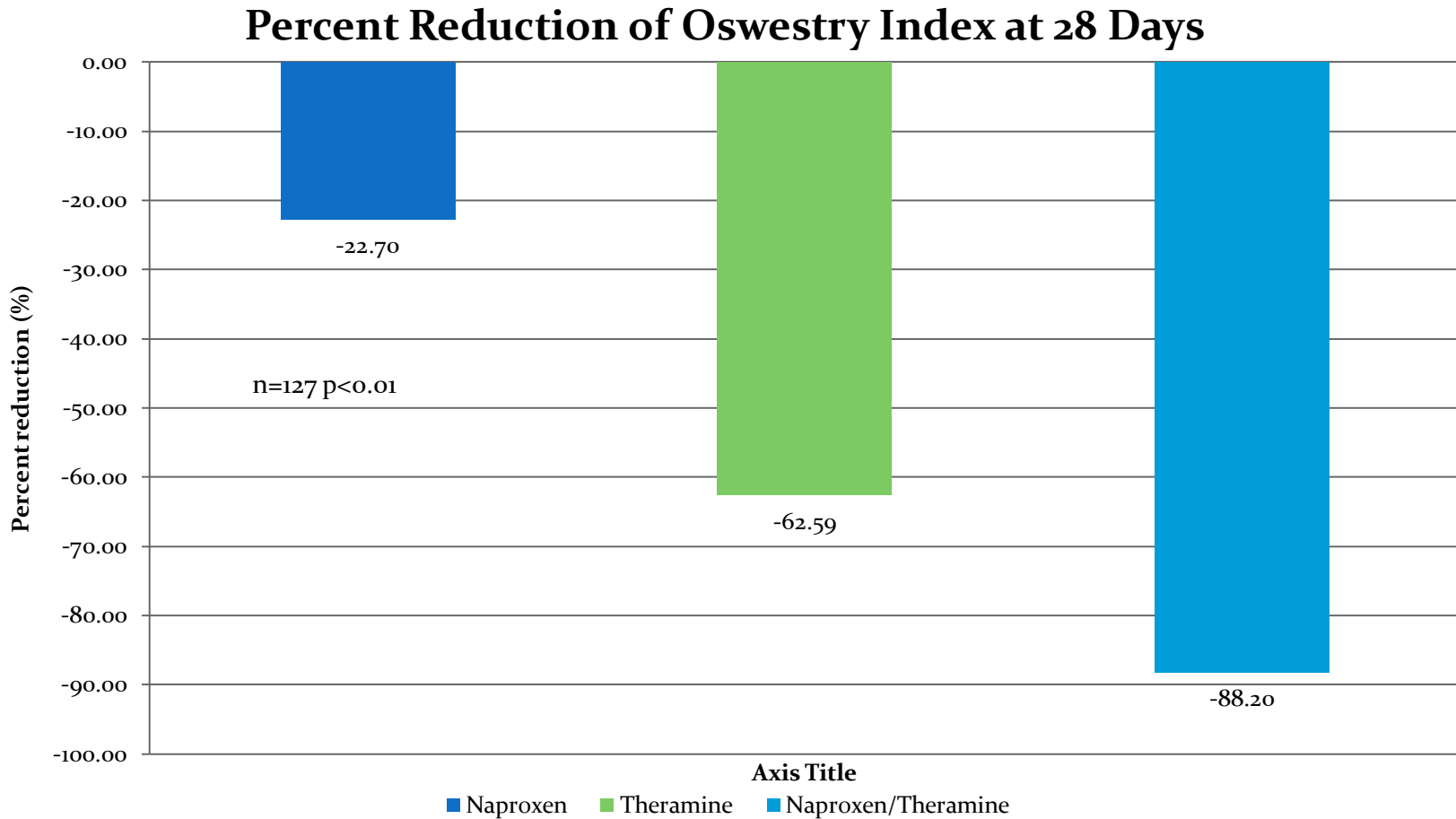


Theraproxen™ Double Blind Trial – Walking on Flat Surface

Sequential Changes in Back Pain Walking on Flat Surface

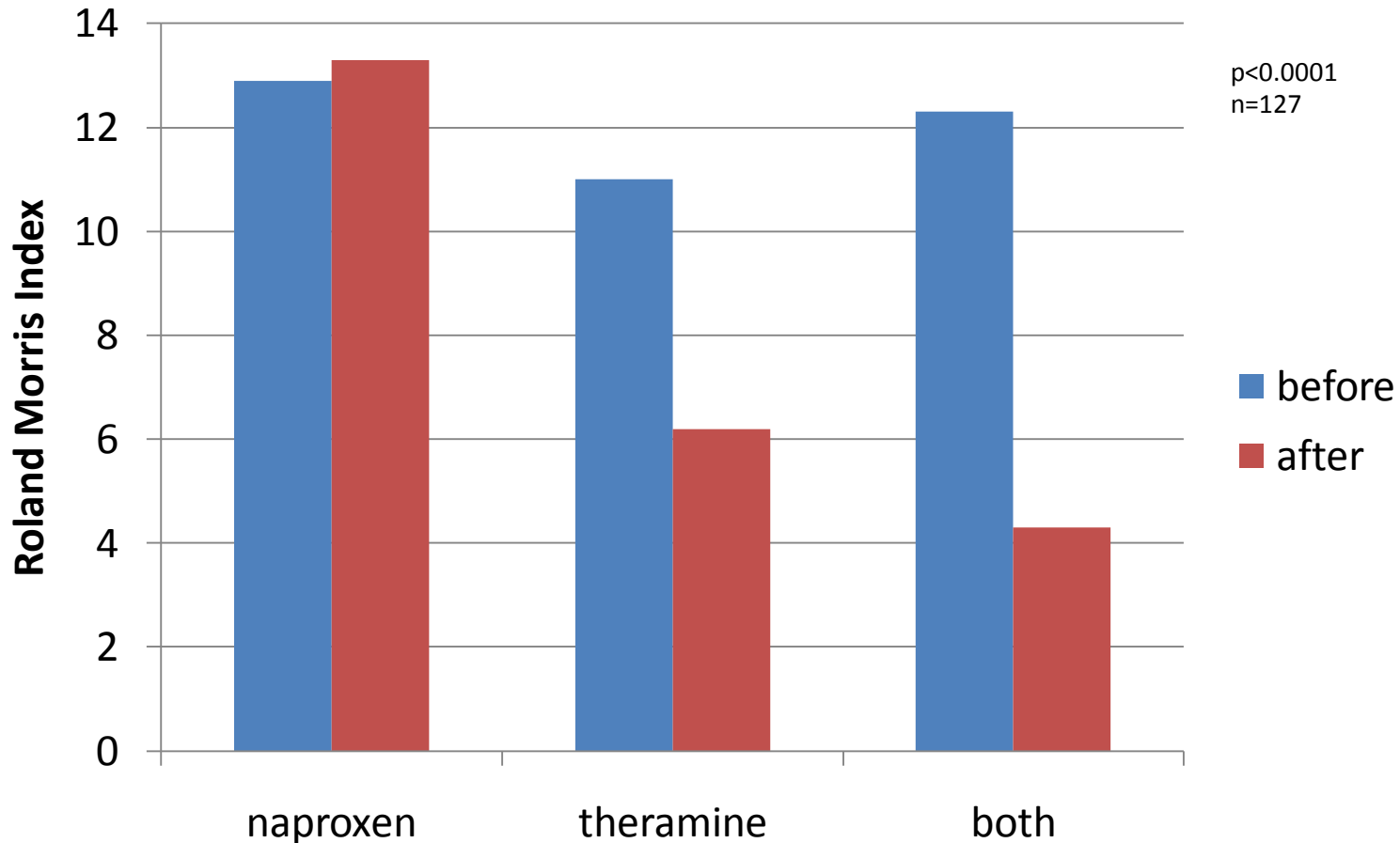


Theraproxen™ Double Blind Trial – Oswestry Index



Theraproxen™ Double Blind Trial – Oswestry Index

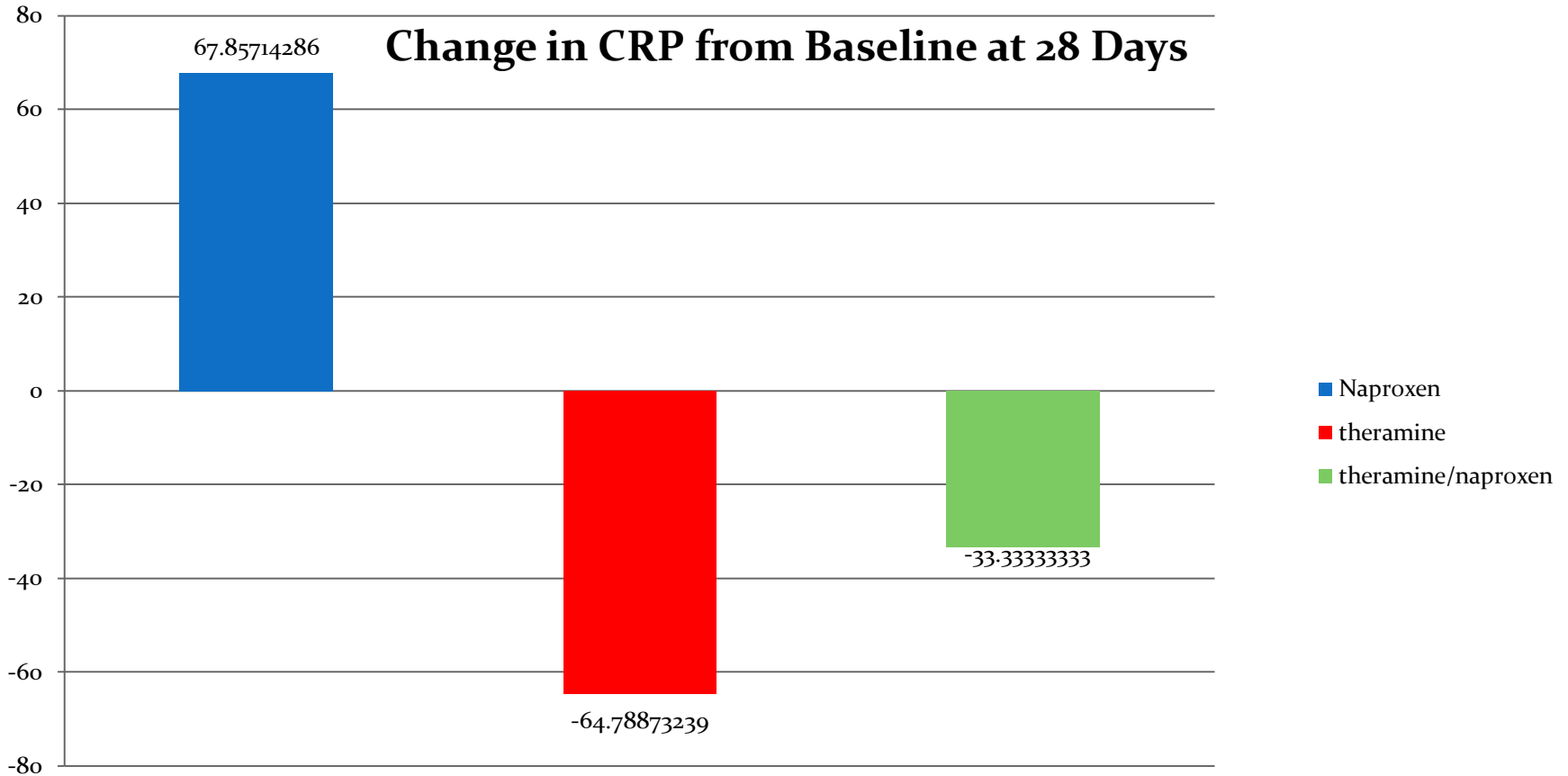
Effect of *Theramine*® and Naproxen on Chronic Back Pain



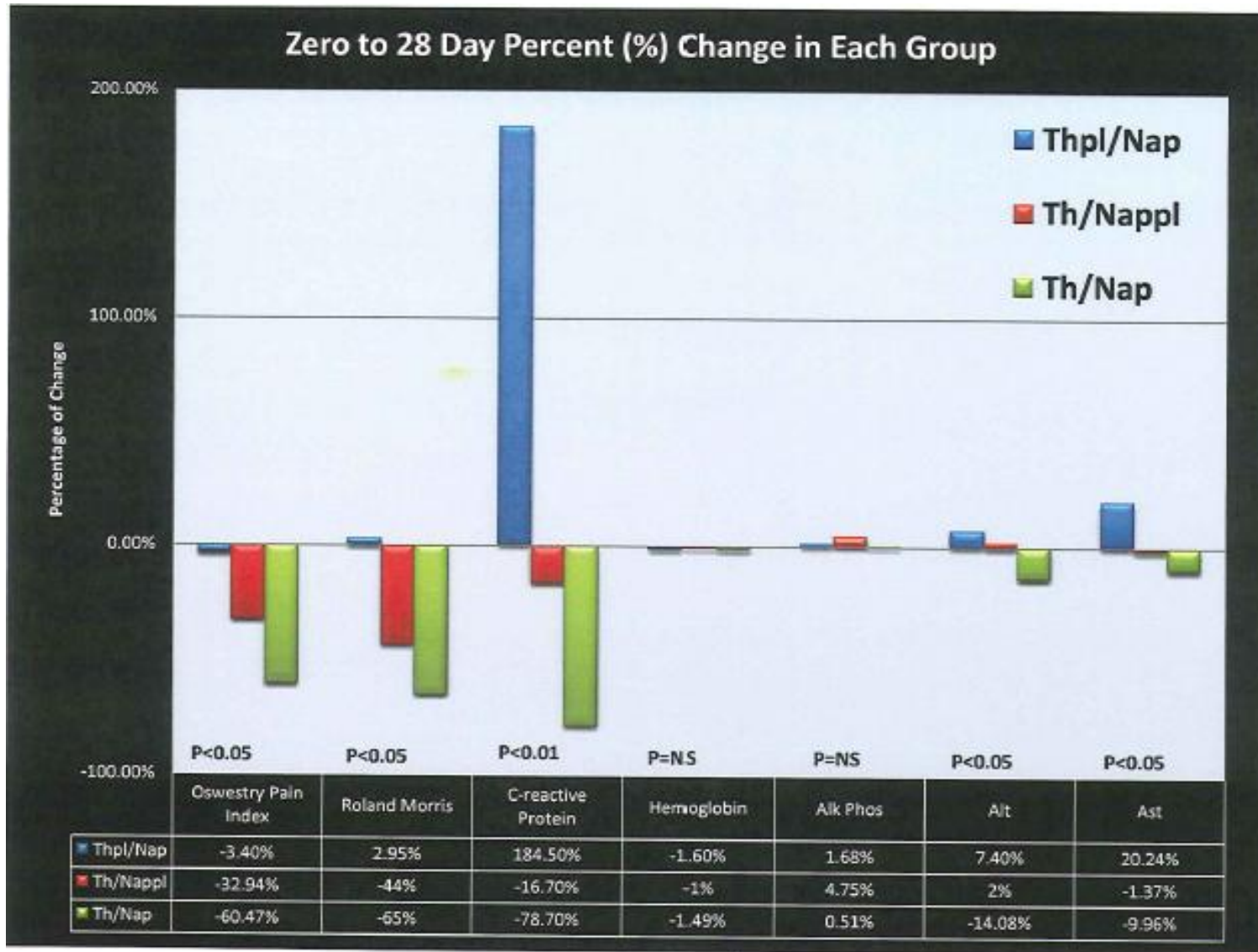
Double Blind Randomized Control Study- 28 days of therapy



Theraproxen™ Double Blind Trial – C-Reactive Protein



Liver Enzyme Activity

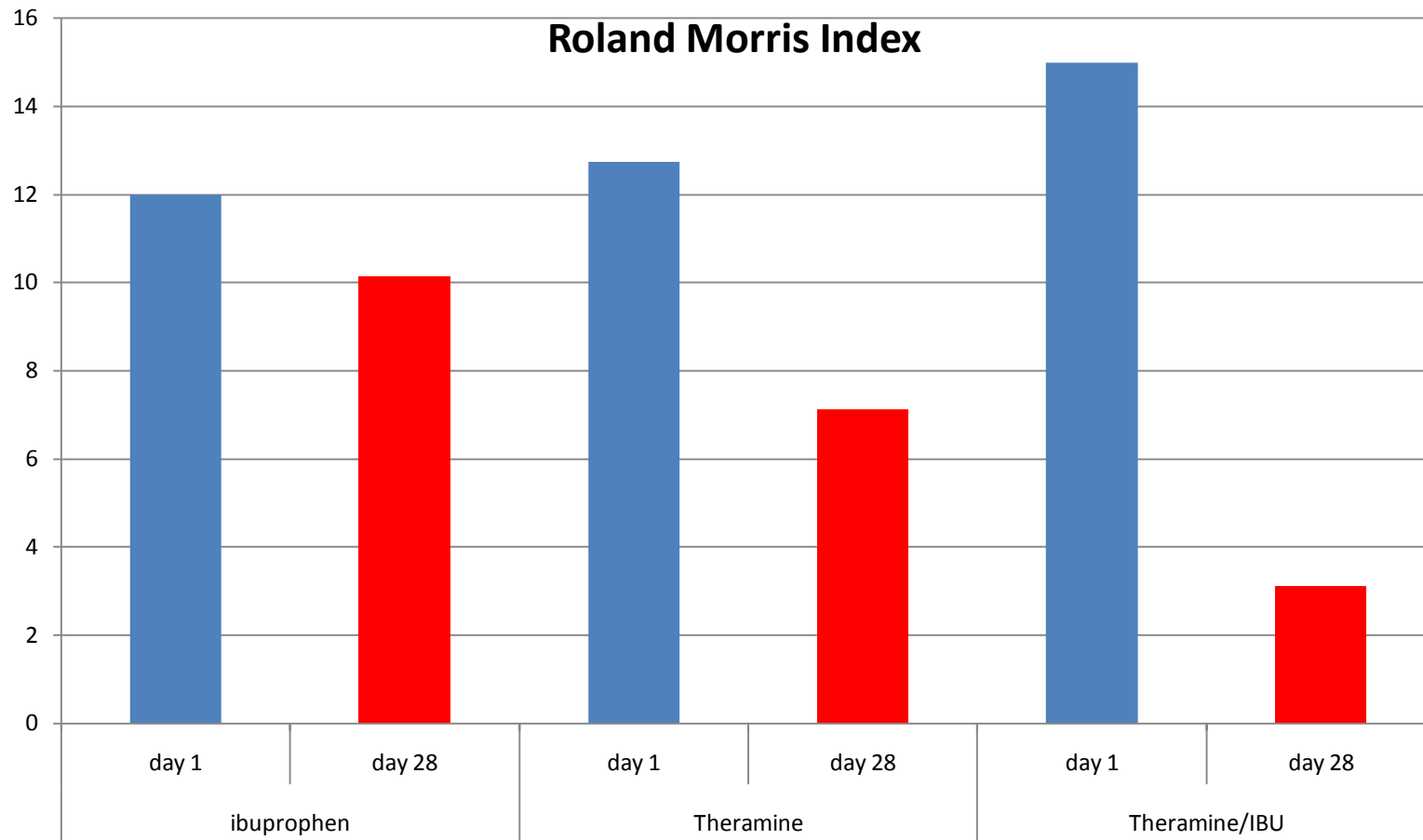


Theramine[®] and Ibuprofen Double Blind Trial (Theraprogen[™] Co-Pack)

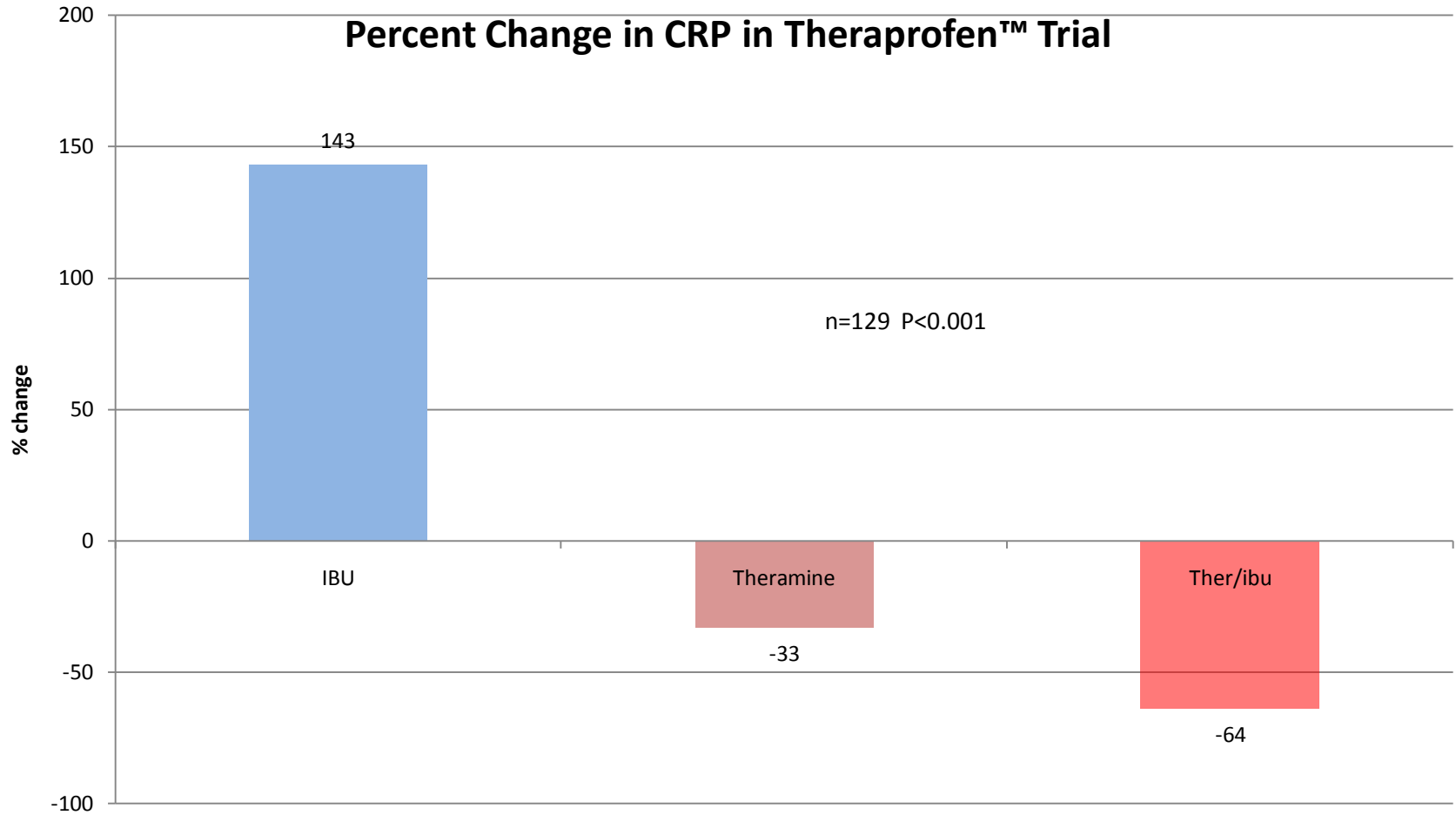
- 129 patients
- 12 national sites
- Established chronic back pain
- VAS Scales
- Likert Scales
- Roland-Morris disability questionnaire
- Oswestry Back pain index
- Inflammatory markers (C-Reactive Protein & Interleukins)
- Amino Acid Turnover
- Study completion, November 2010



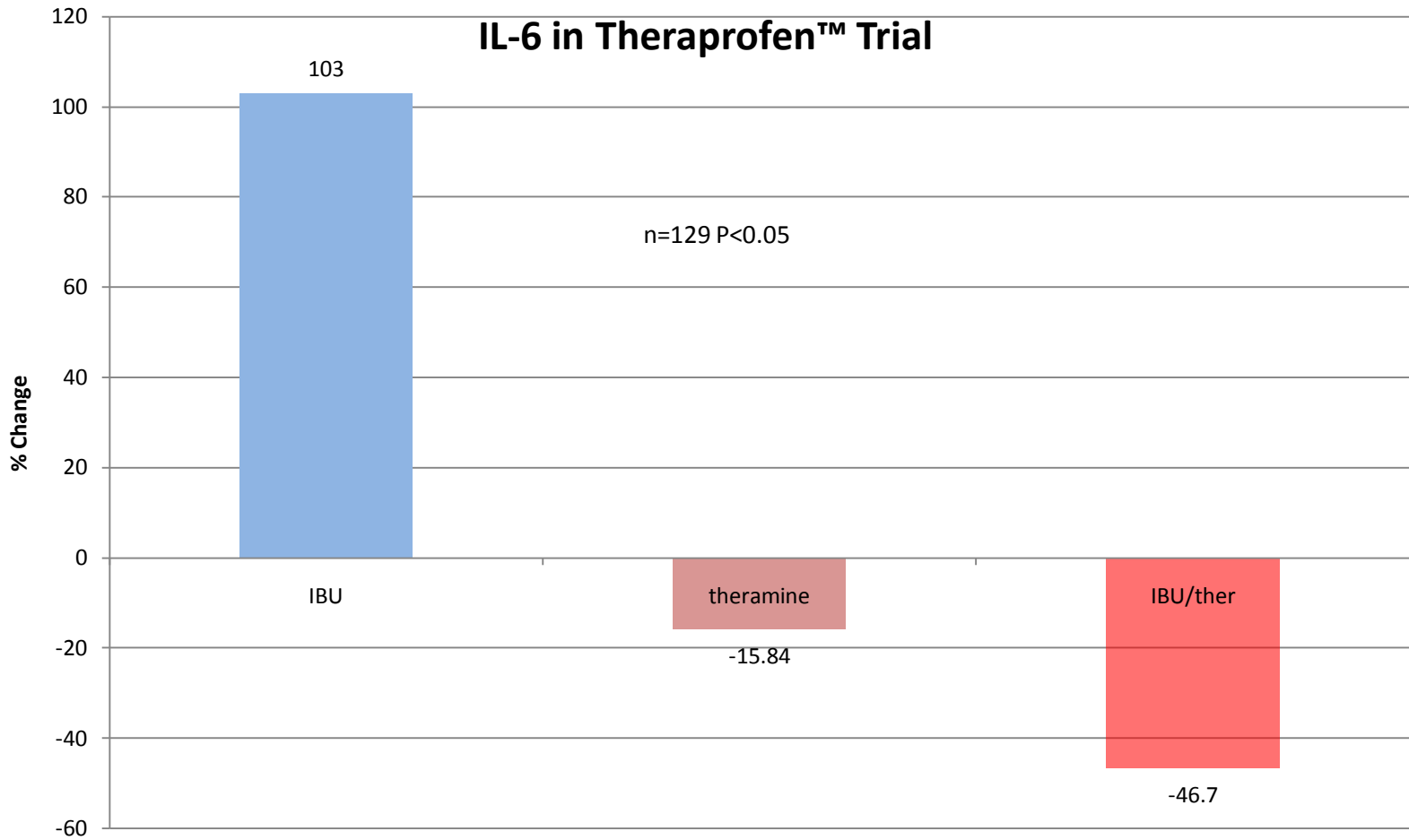
Back Pain Index Over 28 Days



C-Reactive Protein Over 28 Days



Change in IL6



Incidence of Major Events

- ***Theramine***[®] has had no reported GI Bleeds in greater than 16,000,000 dispenses
- ***Theramine***[®] with and without other analgesics --there were no GI bleeds in more than 30,000,000 administrations-30,000 patient years
- Approximately 43 GI bleeds per 1000 patient years were expected—1,290 expected GI bleeds-129 deaths
- No reported kidney or liver abnormalities
- No addiction or abuse potential

**Healthcare cost savings can be achieved by
dose reduction and reduction of drug side effects**



The Real Cost of Pain

- The economic impact of CNP (Chronic Nonmalignant Pain) is substantial
- Back pain, migraines, arthritis and other musculoskeletal conditions alone account for 13% loss in US workforce productivity and \$61.2 billion per year loss in productive work time*.
- Annual total cost of pain from all causes is more than \$80 billion*.
- Under treatment of CNP often results in suicide; an indication of pain's impact on the quality of patients and their families.

*J Occup Environ Med. 2004 Apr;46(4):398-412.

Health, absence, disability, and presenteeism cost estimates of certain physical and mental health conditions affecting U.S. employers. Goetzel RZ, Long SR, Ozminkowski RJ, Hawkins K, Wang S, Lynch W.



Mechanism of GI Protection

- ***Theramine*** produces gut serotonin
 - Gut serotonin increases gut platelet aggregatability
- ***Theramine*** produces gut nitric oxide
 - The overuse of popular NSAIDS (non-steroidal anti-inflammatory drugs) such as Aspirin, Ibuprofen and Naproxen Sodium results in erosion that may permit acid and bacteria to penetrate into the most delicate layers of the stomach.*
- Naproxacoid-Merck in trials
 - Decreases GI bleed by 50% vs. naproxen
 - Only produces gut nitric oxide

*Korean J Physiol Pharmacol, Vol 2: August 1998

Protective Mechanism of Nitric Oxide and Mucus against Ischemia/Reperfusion-Induced Gastric Mucosal Injury

Hyeyoung kim, Kwangsoo, Nam, Kyung Hwan Kim, Dept. of Pharmacology and Institute of Gastroenterology, Yonsei University College of Medicine



Comparative Cost of *Theramine*[®] versus NSAIDs



	per 300,000 Patients/ year	
	Theramine	NSAIDS
product cost	\$633,600,000	\$36,000,000
GI bleed	\$0	\$225,000,000
protective meds	\$0	\$432,000,000
lab testing	\$1,000	\$75,000,000
negative GI workup	\$0	\$144,000,000
total	\$633,601,000	\$912,000,000
deaths/100 pt yrs	0	0.4
deaths/300,000 pt yrs	0	1200

•Silver D. Use of COX-1-Sparing Agents in the Federal Health System. *Pharmacy and Therapeutics*. 2004; 29(7).

•Ilotto A, Franceschi M, Maggi S, et al. Optimal management of peptic ulcer disease in the elderly. *Drugs Aging*. 2010; 27(7):545-58.

•Spiegel B, Chiou C, Ofman J. Minimizing complications from nonsteroidal anti-inflammatory drugs: cost-effectiveness of competing strategies in varying risk groups. *Arth Rheum*. 2005; 53(2):185-97.

•Bardou M, Barkun A. Preventing the gastrointestinal adverse effects of nonsteroidal anti-inflammatory drugs: from risk factor identification to risk factor intervention. *Joint Bone Spine*. 2010; 77(1):6-12.

•Hawkey C, Laine L, Simon T, et al. Comparison of the effect of rofecoxib (a cyclooxygenase 2 inhibitor), ibuprofen, and placebo on the gastroduodenal mucosa of patients with osteoarthritis: a randomized, double-blind, placebo-controlled trial. The Rofecoxib Osteoarthritis Endoscopy Multinational Study Group. *Arth Rheum*. 2000; 43(2):370-7.

•Hawkey C, Laine L, Harper S, et al. Influence of risk factors on endoscopic and clinical ulcers in patients taking rofecoxib or ibuprofen in two randomized controlled trials. *Aliment Pharmacol Ther*. 2001; 15(10):1593-601.

•Jureidini Z, Abdul Walid O. Upper gastrointestinal bleeding: an age based comparative study. *IJGE* 2001; 1(1):22-8.

