

PA32520 (Single-tablet of Immediate-Release Omeprazole 20 mg + Enteric-Coated Aspirin 325 mg): Safer Aspirin Therapy with Greater Thromboxane Suppression

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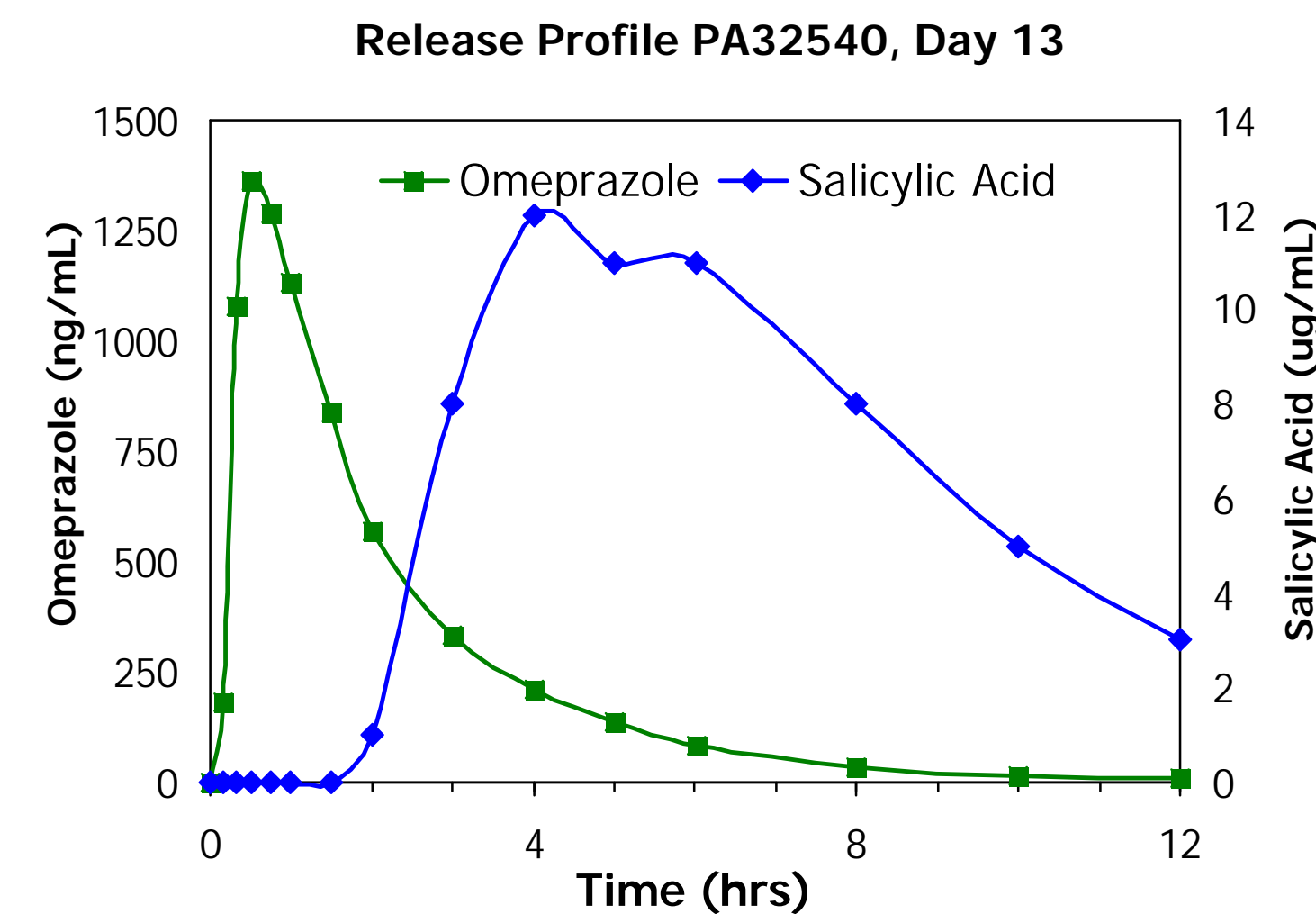
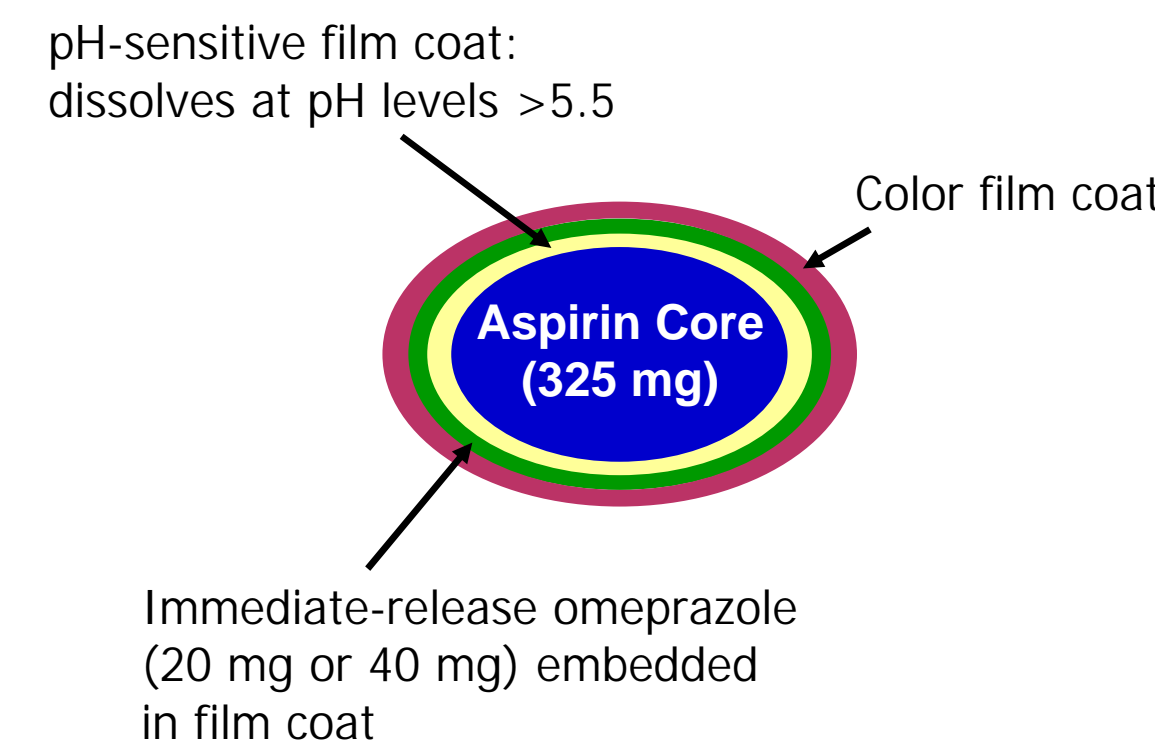
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INTRODUCTION

- Aspirin (ASA) is associated with an increased risk of serious upper gastrointestinal (UGI) damage.^{1,2}
- For cardioprotection, physicians tend to prescribe lower doses of ASA (60% ASA 81 mg/d; 35% ASA 325 mg/d), prompted, in part, by tolerability and safety concerns with higher doses.³
- However, the antiplatelet effect of ASA, as measured by urinary 11-dehydro-thromboxane B₂ (11-dh-TXB₂), appears dose-related.^{4,5}
- ASPECT: significantly greater reduction in urinary 11-dh-TXB₂ with ASA 325 mg/d vs. 81 mg/d (P=0.003).⁴
- CHARISMA⁵
 - ASA ≥150 mg/d associated with lower urinary 11-dh-TXB₂
 - Higher urinary 11-dh-TXB₂ associated with increased risk of CV events
- Urinary 11-dh-TXB₂ is a risk factor for stroke, MI, or CV death.
- ASA dose reduction or use of modified release formulations does not appear to significantly lower the risk of UGI events.^{1,6}
- Proton-pump inhibitors (PPIs) are the preferred agents for therapy and prophylaxis of NSAID- and ASA-associated GI injury.⁷
- PA32520 is a novel fixed-dose combination of enteric-coated aspirin (EC-ASA) and immediate-release omeprazole (a PPI).

1. McQuaid MR, Laine L. *Am J Med* 2006;119:624-38.
 3. Campbell et al. *JAMA* 2007;297:2018-24.
 5. Eikelboom et al. *Circulation* 2008;118:1705-12.
 7. Bhatt et al. *Circulation* 2008;118:1894-909.

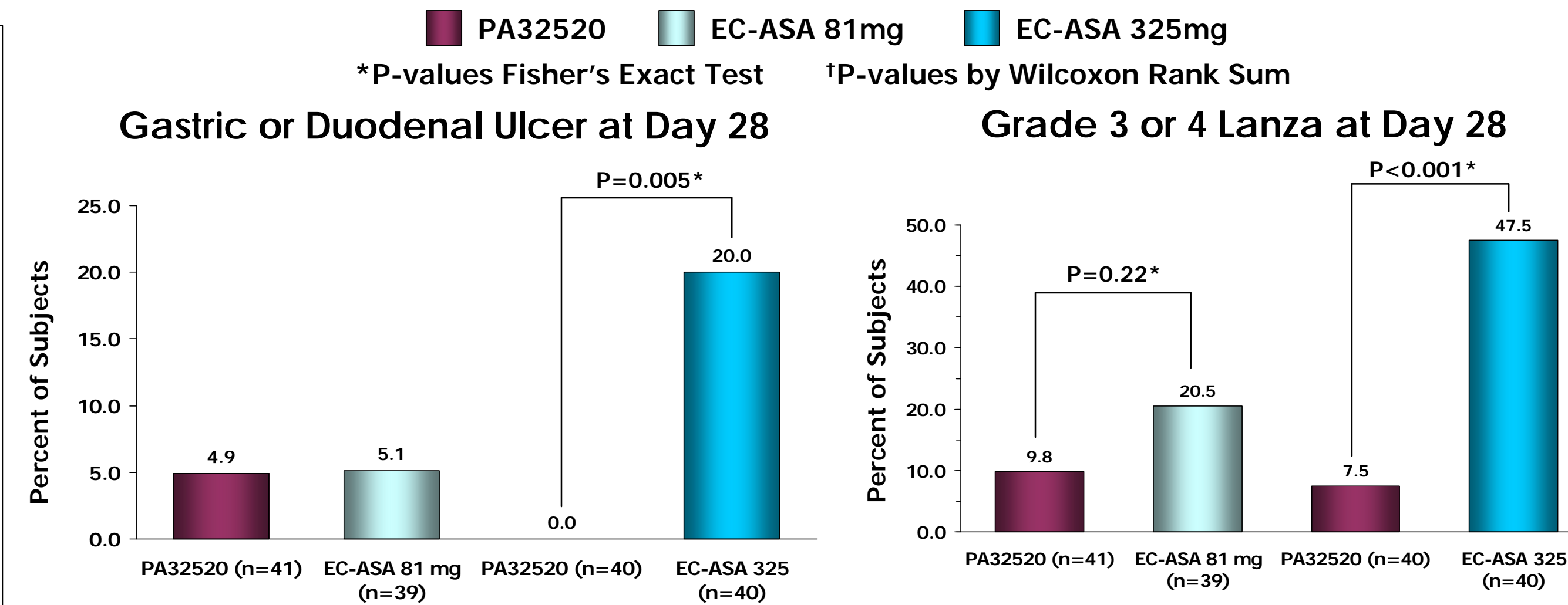
2. Yeomans et al. *Am J Gastroenterol* 2008;103:1-9.
 4. Gurbel et al. *Circulation* 2007;115:3156-64.
 6. García-Rodríguez et al. *Br J Clin Pharmacol* 2001;52:563-71.



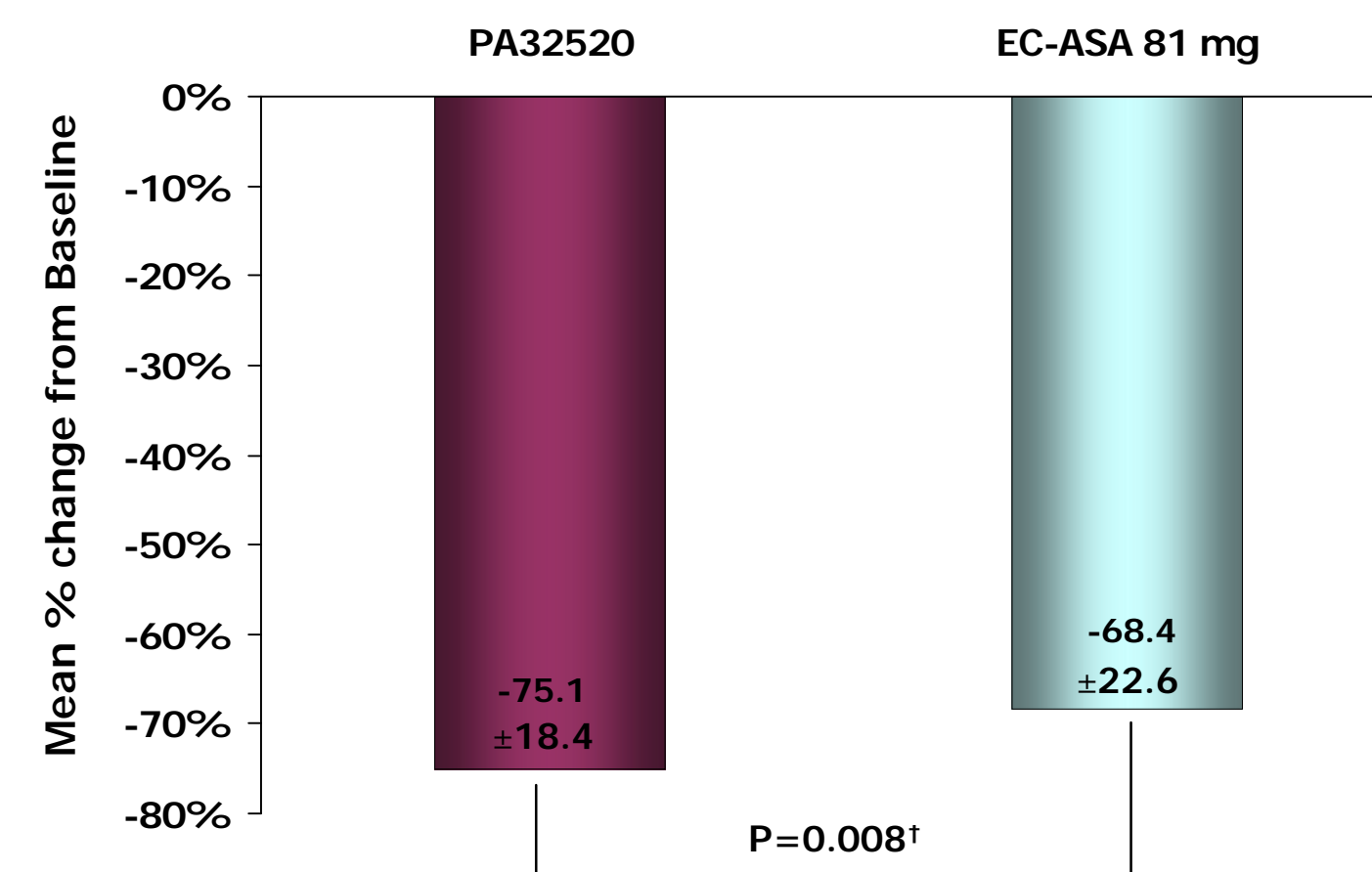
HYPOTHESES

- PA32520 is associated with fewer serious UGI events than EC-ASA 81 mg or EC-ASA 325 mg after 4 weeks of therapy.
- PA32520 is associated with lower urinary 11-dh-TXB₂ levels than EC-ASA 81 mg after 4 weeks of therapy.

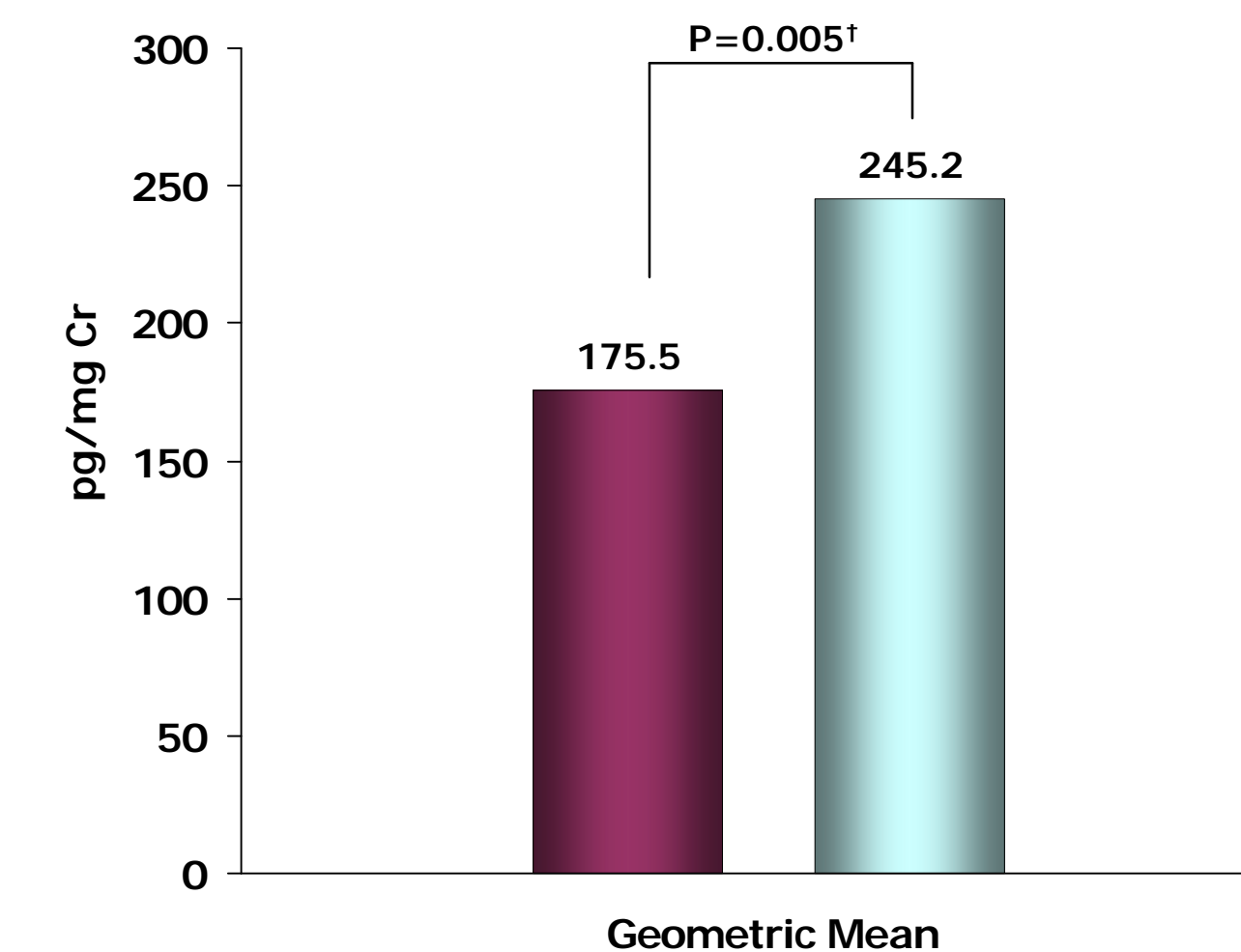
RESULTS



Change in Urinary 11-dh-TXB₂ at Day 28



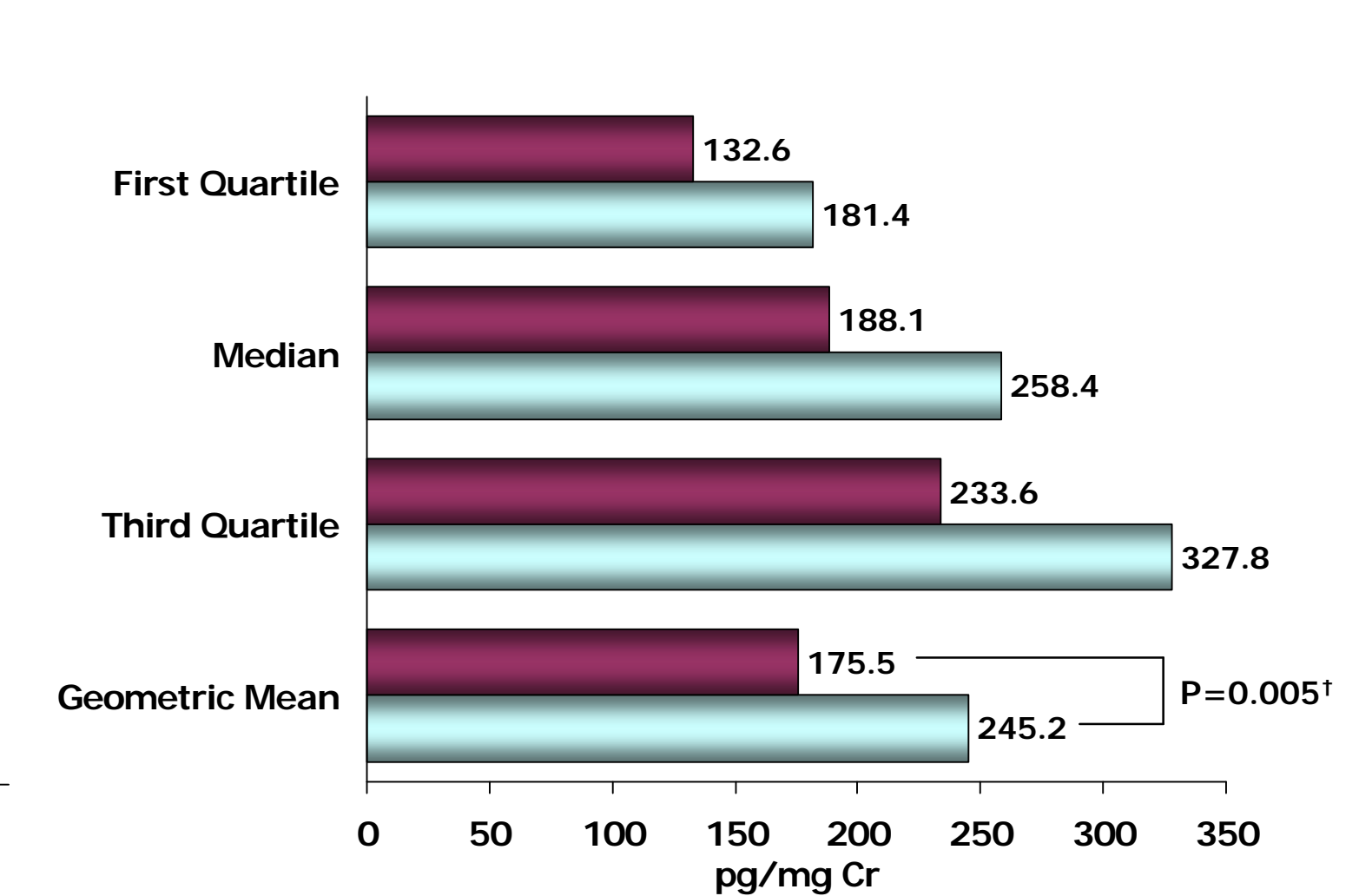
Urinary 11-dh-TXB₂ after 4 Weeks



CONCLUSIONS

- EC-ASA alone was associated with a high incidence of UGI damage
- UGI damage is reduced by PA32520
- Compared to EC-ASA 81 mg, PA32520 produces greater inhibition of in vivo thromboxane generation
- PA may provide an important therapeutic option for patients requiring long-term ASA therapy for cardiovascular protection

Urinary 11-dh-TXB₂ after 4 Weeks



METHODS

Patients

- 2 randomized, investigator-blinded studies in healthy subjects (age ≥50 years)
 - Study 1 (N=80) : PA32520 vs. EC-ASA 81 mg
 - Study 2 (N=80) : PA32520 vs. EC-ASA 325 mg
- All subjects had normal (Grade 0 Lanza score*) endoscopy at baseline
 - Follow-up endoscopies at Day 14 and Day 28
- Dosing was once-daily x 4 weeks
- 24-hour urine collection: pre-treatment (Day -1) and following 4 weeks of therapy by HPLC using an AB/MDS Sciex API Mass Spectroscopy

*Lanza score: 5-grade scoring system based upon endoscopic evaluation of the GI mucosa: 0 (no visible lesions); 1 (1 erosion or hemorrhage); 2 (2-10 erosions or hemorrhages); 3 (11-25 erosions or hemorrhages); 4 (>25 erosions or hemorrhages or any ulcer)

Endpoints

- Primary:
 - Grade 3 or 4 Lanza scores at Day 28
- Secondary:
 - Grade 3 or 4 Lanza scores at Day 14
 - Gastric or duodenal ulcers at Day 28
 - Ulcers >3 mm in diameter with depth on endoscopy
 - Change from baseline in urinary 11-dh-TXB₂ (PA32520 vs. EC-ASA 81 mg) after 4 weeks