Randomized, Double-blind, Multi-center, Parallel-group, Evaluation of the Safety and Efficacy of ADAM Zolmitriptan for the Acute Treatment of Migraine

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ZOSANO PHARMA

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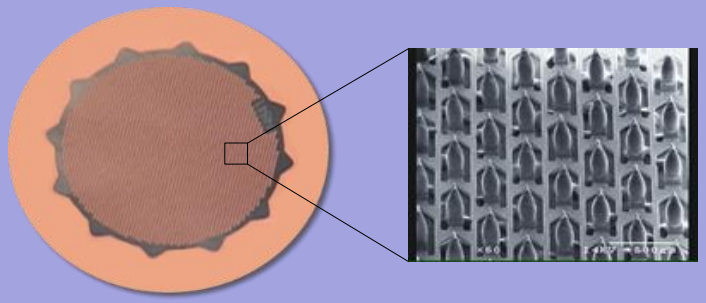
Disclosures

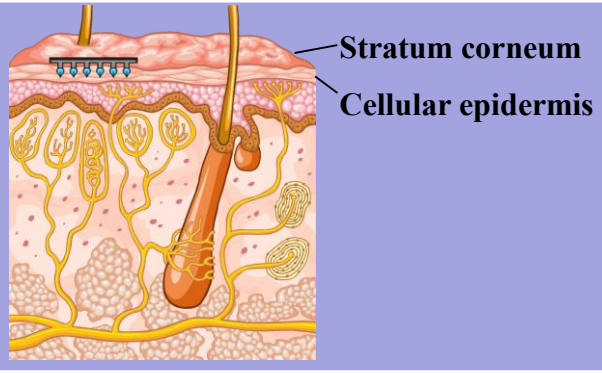
- ELH Spierings
- JL Brandes
- DB Kudrow
- J Weintraub
- J Rubino
- DJ Kellerman, employee of Zosano Pharma
- SJ Tepper
- Primary statistical analysis provided by Clinical Trial Data Services (CTDS), sponsored by Zosano Pharma
- Medical writing support provided by Pamela Foreman, PhD, sponsored by Zosano Pharma

The Adhesive Dermally-Applied Microarray (ADAM) Zolmitriptan System

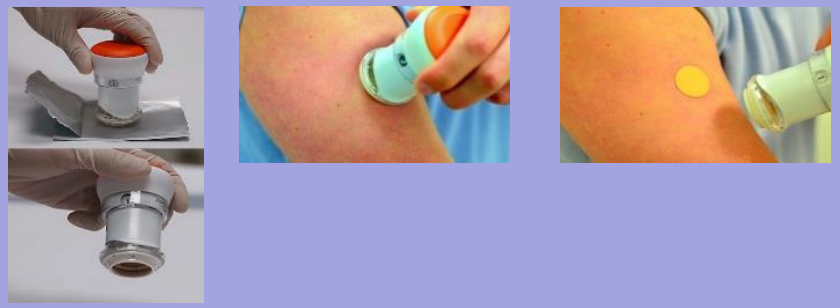
ADAM with Zolmitriptan-Coated Titanium Microprojections (~300 microns in length)



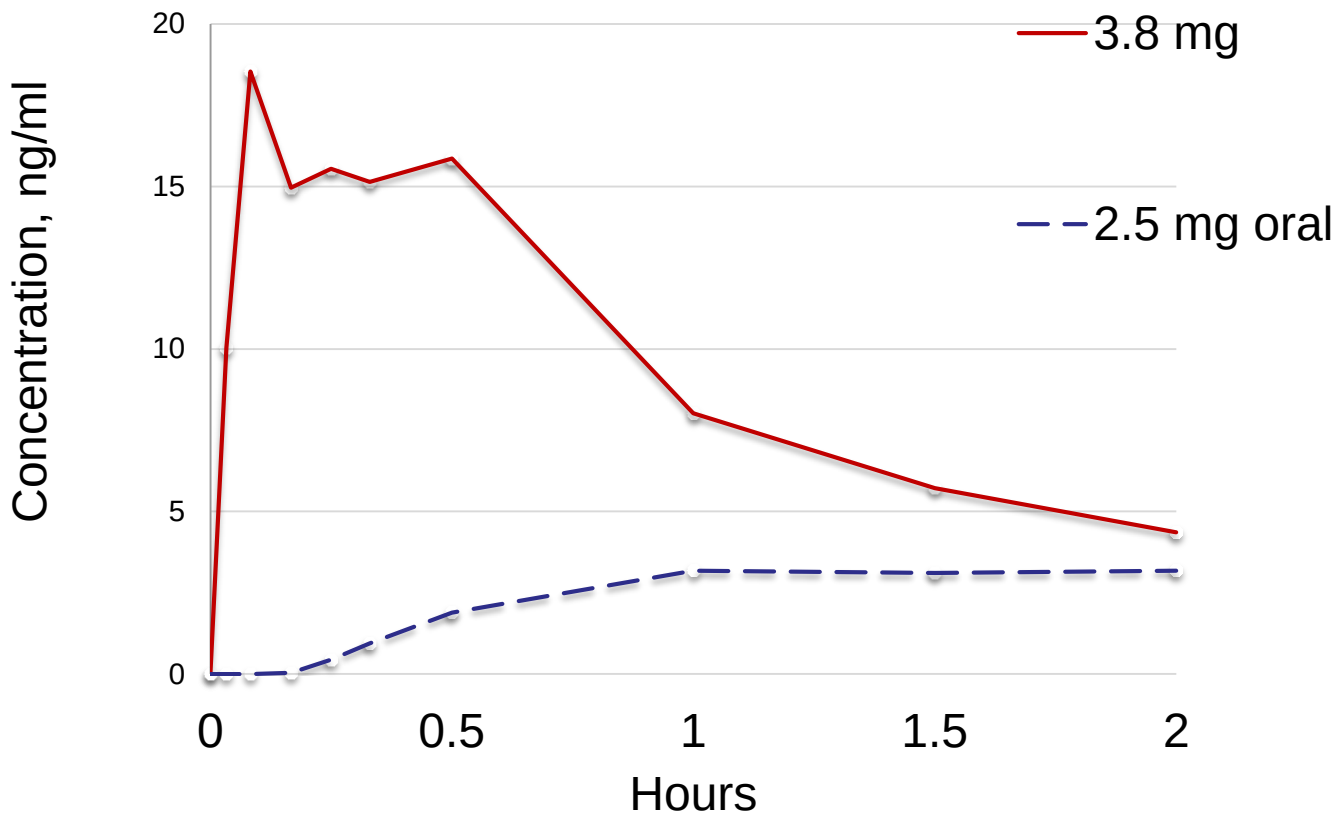
Intradermal zolmitriptan delivery



ADAM Application



Pharmacokinetics of Zolmitriptan Delivery Using ADAM



Study Design and Methods

- Adult patients suffering from migraine with or without aura
- Patients selected most bothersome headache-associated symptom (MBS): photophobia, phonophobia, or nausea (new FDA endpoint)
- Patients randomized 2:2:2:1:1
  - 1 mg: 1.9mg: 2x1.9mg: placebo: 2x placebo
- Primary endpoints: 2-hour pain-free and 2-hour MBS-free
- Efficacy endpoints were tested in a sequential multiple comparison procedure (MCP):

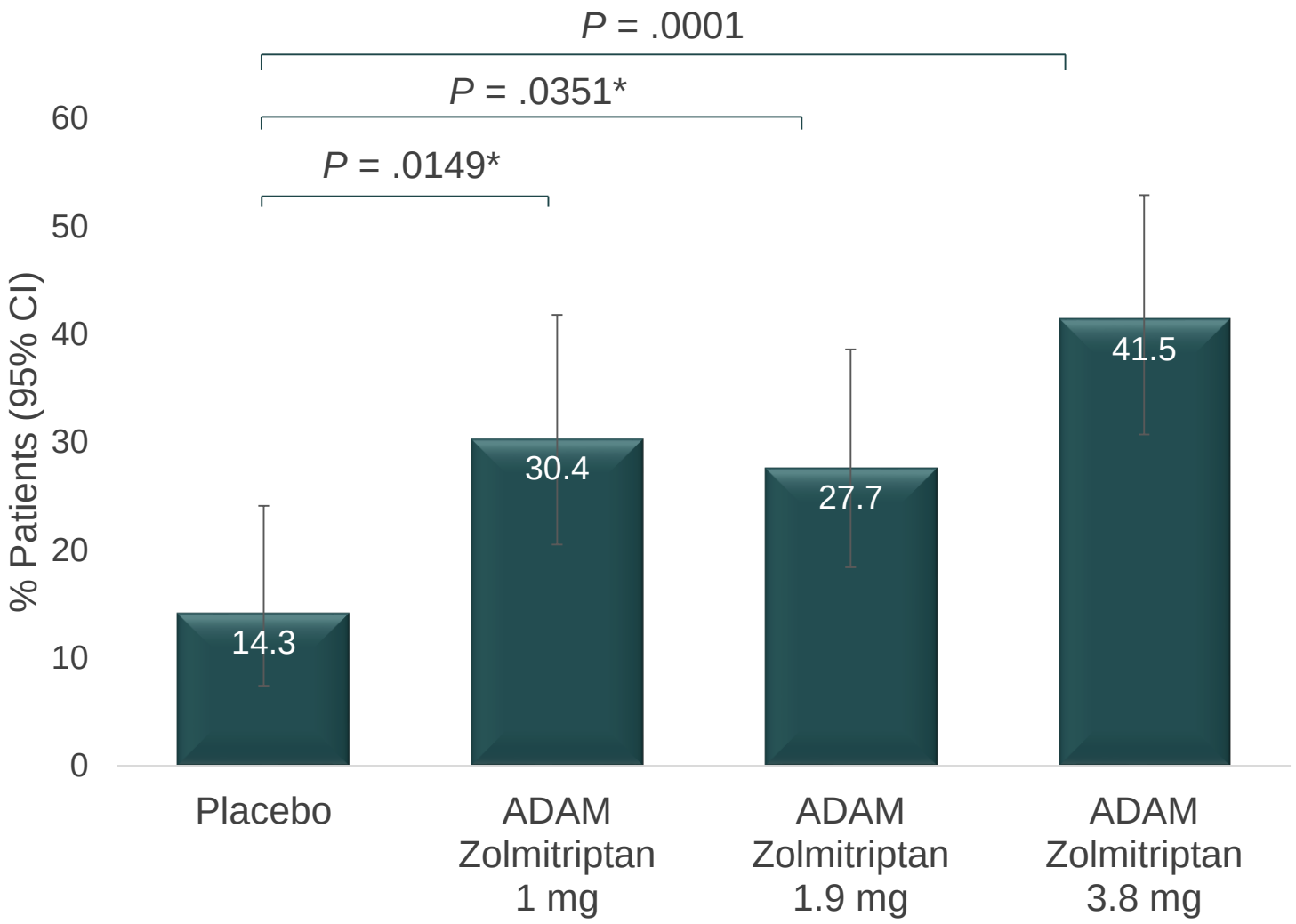
1. Primary endpoints in the 3.8 mg treatment group
2. Primary endpoints in the 1.9 mg treatment group

If significance was not observed for a comparison, subsequent results were not considered statistically significant (regardless of p-value)

Demographics and Baseline Characteristics

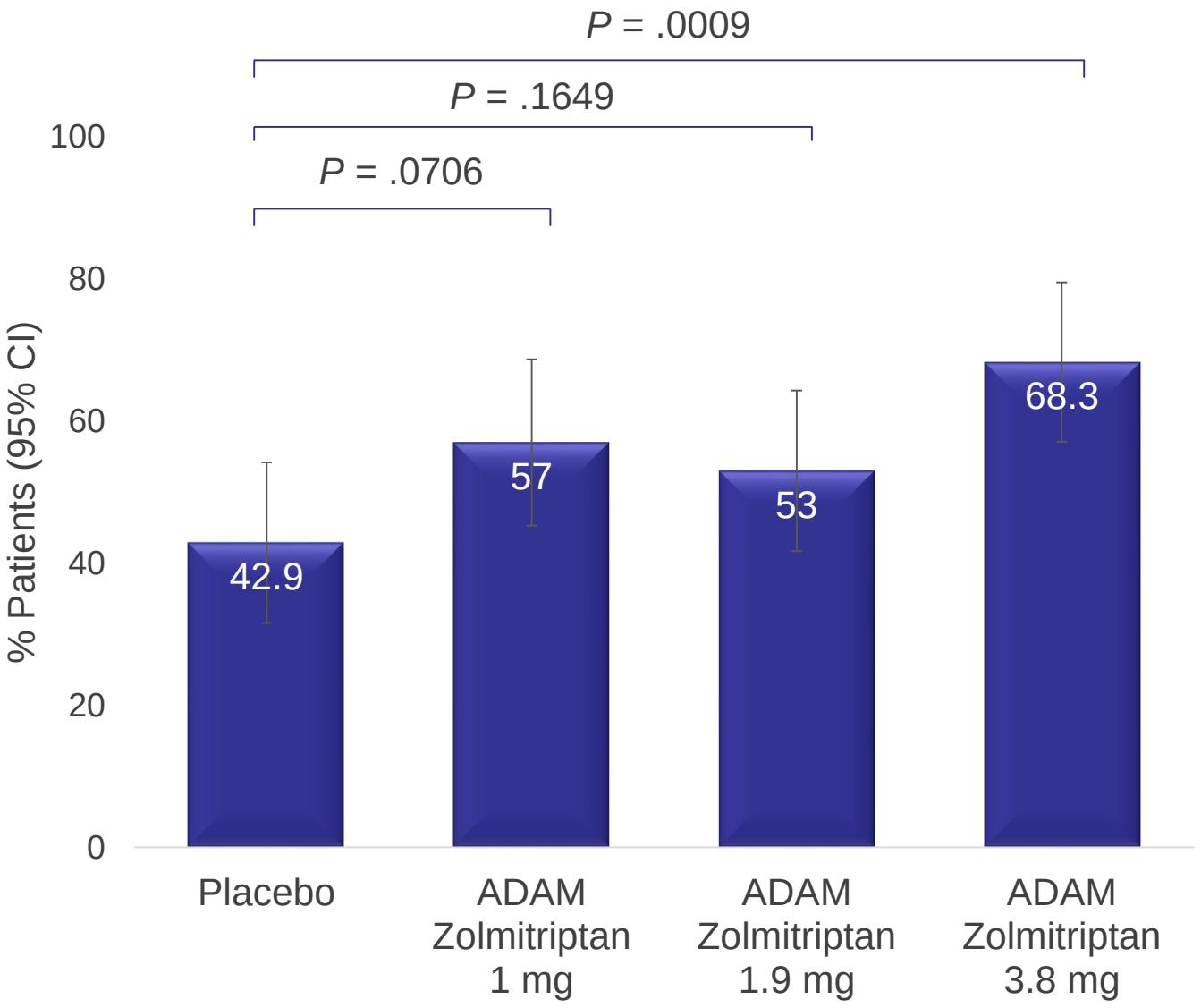
	Treatment Group (mITT Population)				
		ADAM Zolmitriptan			
	Placebo n=77	**1 mg n=79**	**1.9 mg n=83**	**3.8 mg n=82**	**Total n=321**
Female, n (%)	69 (89.6)	70 (88.6)	73 (88.0)	68 (82.9)	280 (87.2)
Age, Mean (SD) Years	42.7 (11.5)	41.7 (11.6)	40.1 (10.9)	41.0 (11.4)	41.3 (11.3)
Race, n (%)					
White	59 (76.6)	58 (73.4)	54 (65.1)	67 (81.7)	238 (74.1)
MBS					
Nausea	20 (26.0)	17 (21.5)	19 (22.9)	17 (20.7)	73 (22.7)
Phonophobia	21 (27.3)	21 (26.6)	22 (26.5)	22 (26.8)	86 (26.8)
Photophobia	36 (46.8)	41 (51.9)	42 (50.6)	43 (52.4)	162 (50.5)

Freedom from Pain at 2 Hours

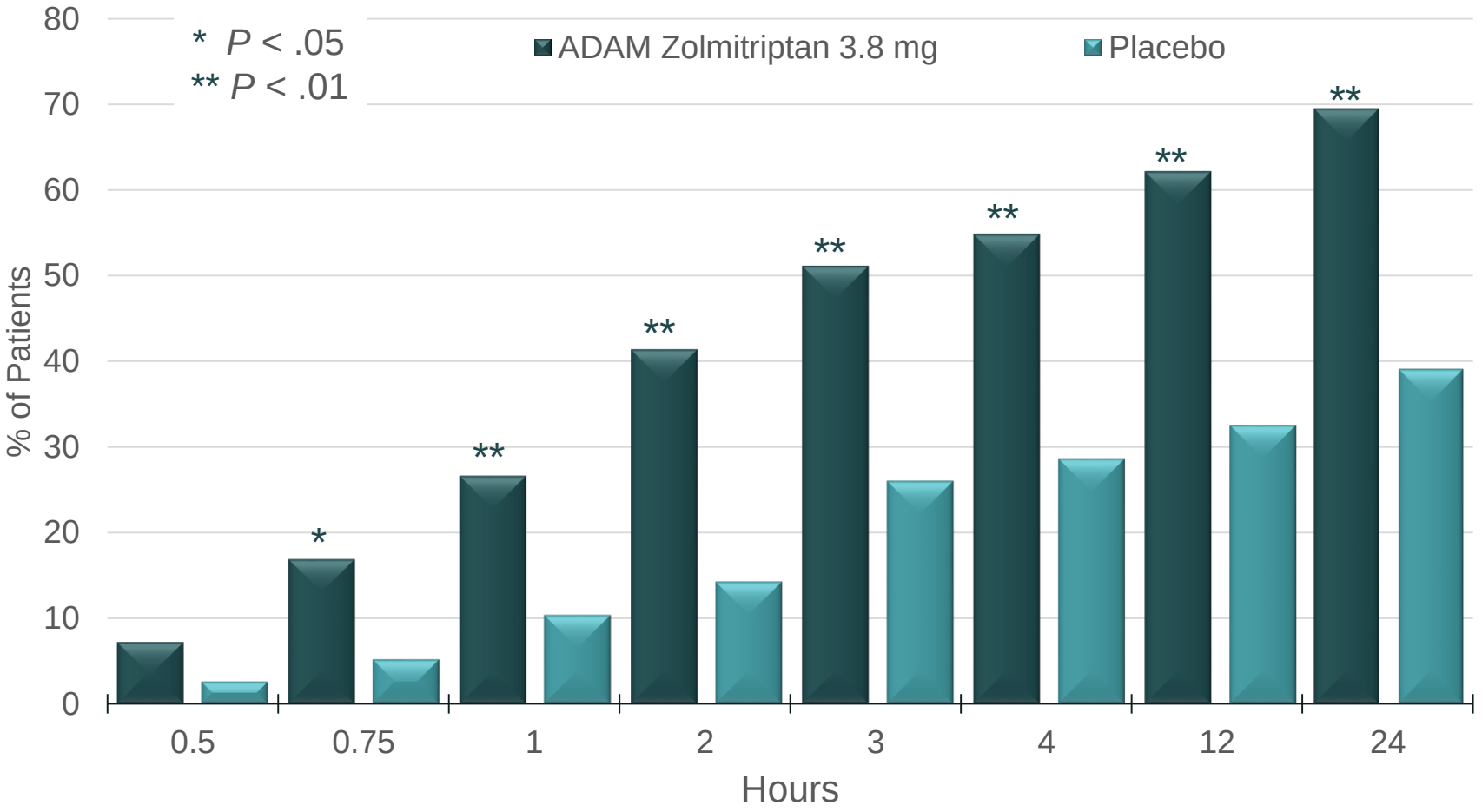


* Not considered significant under MCP

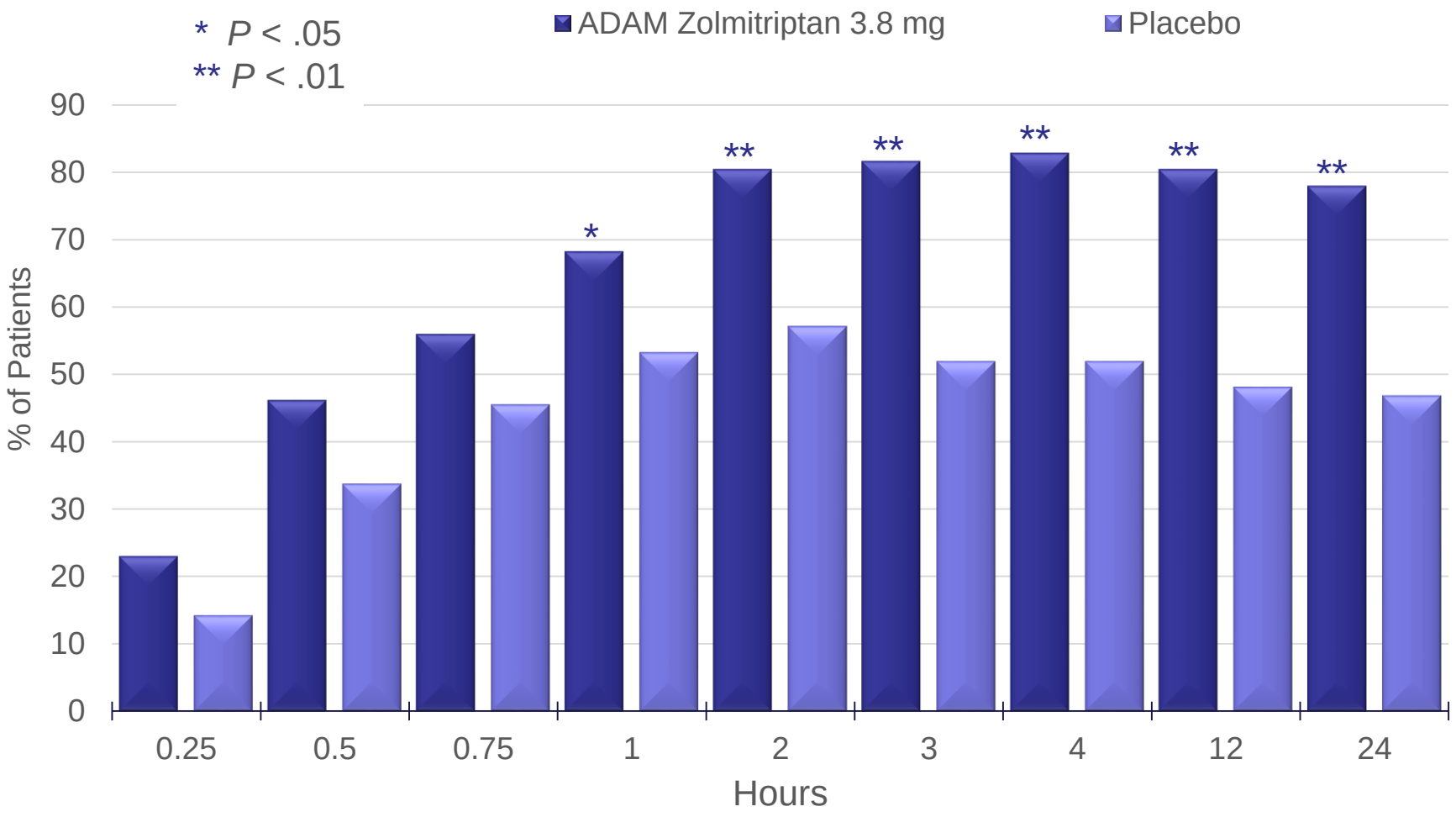
Freedom from Most Bothersome Symptom at 2 Hours



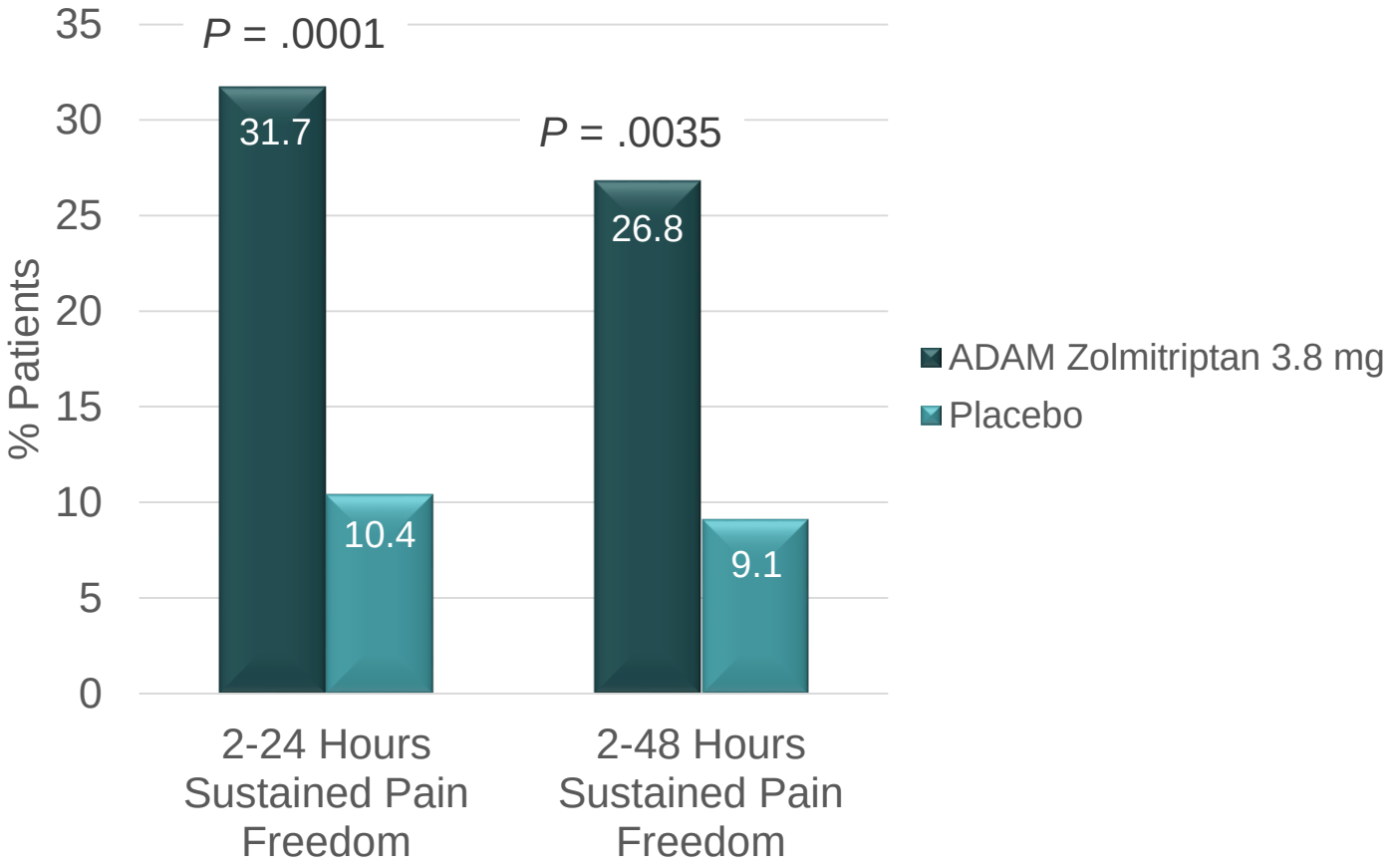
Pain Freedom Over Time



Pain Relief Over Time



Sustained Pain Freedom



Note: post-hoc analysis

Safety and Tolerability

Treatment-Emergent Adverse Events Occurring ≥ 4% in Any Active Treatment Group (Safety Population)

n (%)	Treatment Group			
		ADAM Zolmitriptan		
	Placebo (n=83)	1 mg (n=80)	1.9 mg (n=87)	3.8 mg (n=83)
Application site erythema	9 (10.8)	13 (16.3)	17 (19.5)	22 (26.5)
Application site bruise	3 (3.6)	5 (6.3)	12 (13.8)	12 (14.5)
Application site pain	1 (1.2)	2 (2.5)	2 (2.3)	8 (9.6)
Application site hemorrhage	0 (0.0)	3 (3.8)	5 (5.7)	4 (4.8)

Conclusions

- The proportion of patients who were headache pain-free and most bothersome symptom-free at 2 hours was significantly higher for ADAM zolmitriptan 3.8 mg vs placebo
- For pain-freedom, nominal $P < .05$ was reached at 45 minutes
- Freedom from pain was sustained for the period of two to 24-48 hours in ~one third of patients
- Treatment-emergent adverse events were generally mild; the most common were application site erythema, and bruising
- Intradermal administration of zolmitriptan using ADAM provided significant rapid and sustained freedom from headache pain and most bothersome symptoms in this randomized, placebo-controlled trial