

The Efficacy and Tolerability of LEVADEX™ (orally inhaled DHE) for the Treatment of Migraine in Subjects with Concomitant Asthma – A Subgroup Analysis

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American Headache Society® (AHS) 52nd Annual Scientific Meeting
 June 24-27, 2010 : Los Angeles, California

OBJECTIVES

The results presented here are a subgroup analysis of a large Phase 3 migraine efficacy trial; the overall trial results have been previously presented. (Silberstein et al. September 2009). The analysis was performed to assess whether the efficacy or tolerability of LEVADEX™, an orally inhaled product, was affected by the presence of concomitant asthma.

BACKGROUND

LEVADEX™ (MAPO004) is a novel orally inhaled formulation of DHE under development for the treatment of migraine. Asthma may be a concomitant condition for migraine sufferers, although precise estimates of the incidence of comorbidity are difficult to find. The presence of asthma has the potential to affect the absorption of orally inhaled products, and some inhaled medications are not well-tolerated in subjects with asthma.

A previously performed study in 19 subjects with asthma (Shrewsbury et al. 2008) showed that LEVADEX appeared to be well-tolerated. Pharmacokinetic parameters derived from plasma samples collected from 8 of the subjects were similar to the pharmacokinetics observed in healthy subjects without asthma. Based on these data, subjects with concomitant asthma were included in a large Phase 3 trial of LEVADEX.

This subgroup analysis was performed to assess whether the efficacy or tolerability observed in the large clinical trial appeared qualitatively different in the subgroup of subjects with concomitant asthma.

METHODS

This is a post hoc analysis of a randomized, double-blind, placebo-controlled, two-arm, Phase 3 multicenter study. Any subject who self-reported a diagnosis of asthma was included in the "Asthma Sub Group" analysis. Analyses of the four primary efficacy parameters (2 hour: Pain Relief, Photophobia Free, Phonophobia Free, and Nausea Free) were performed, as well as pulmonary function testing and adverse events. 80 asthmatic subjects were included in the post hoc sub-analyses of the 792 total subjects who treated a migraine. The p-values reported here are not adjusted for multiple comparisons.

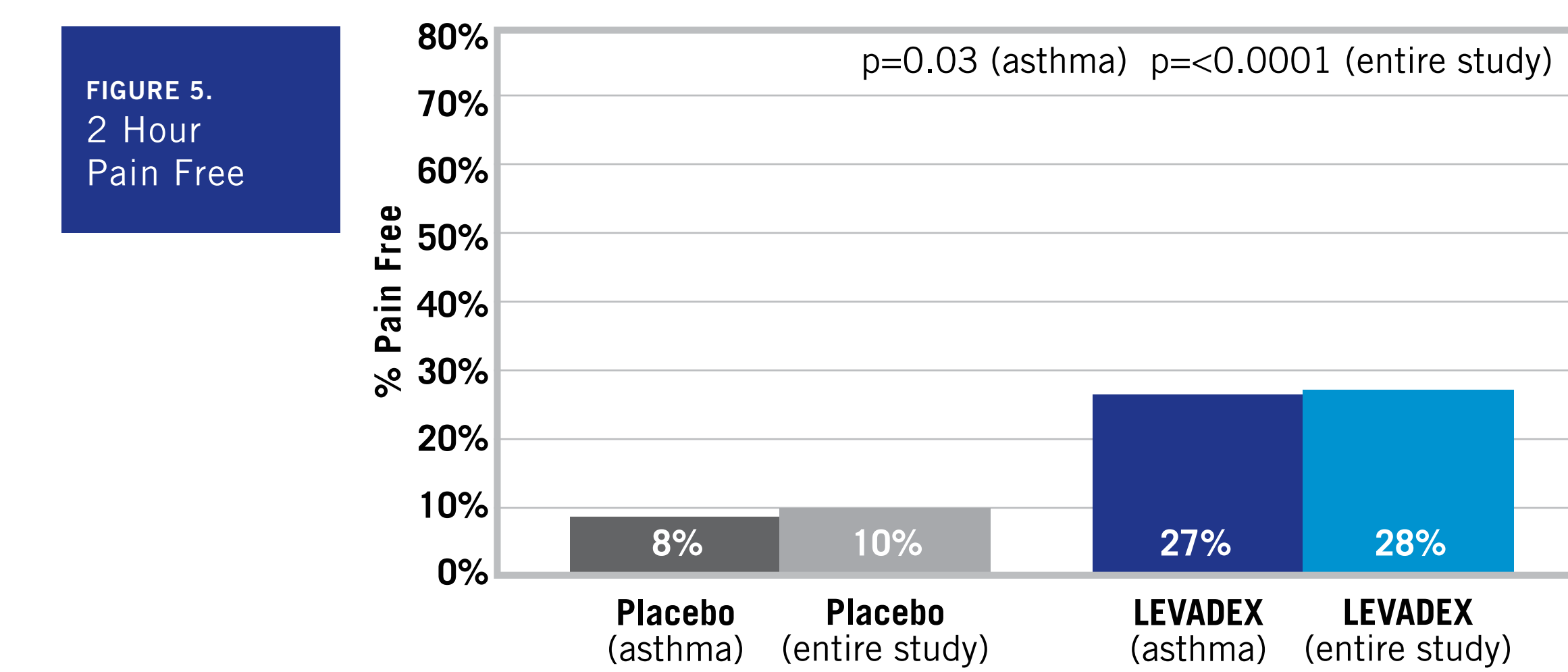
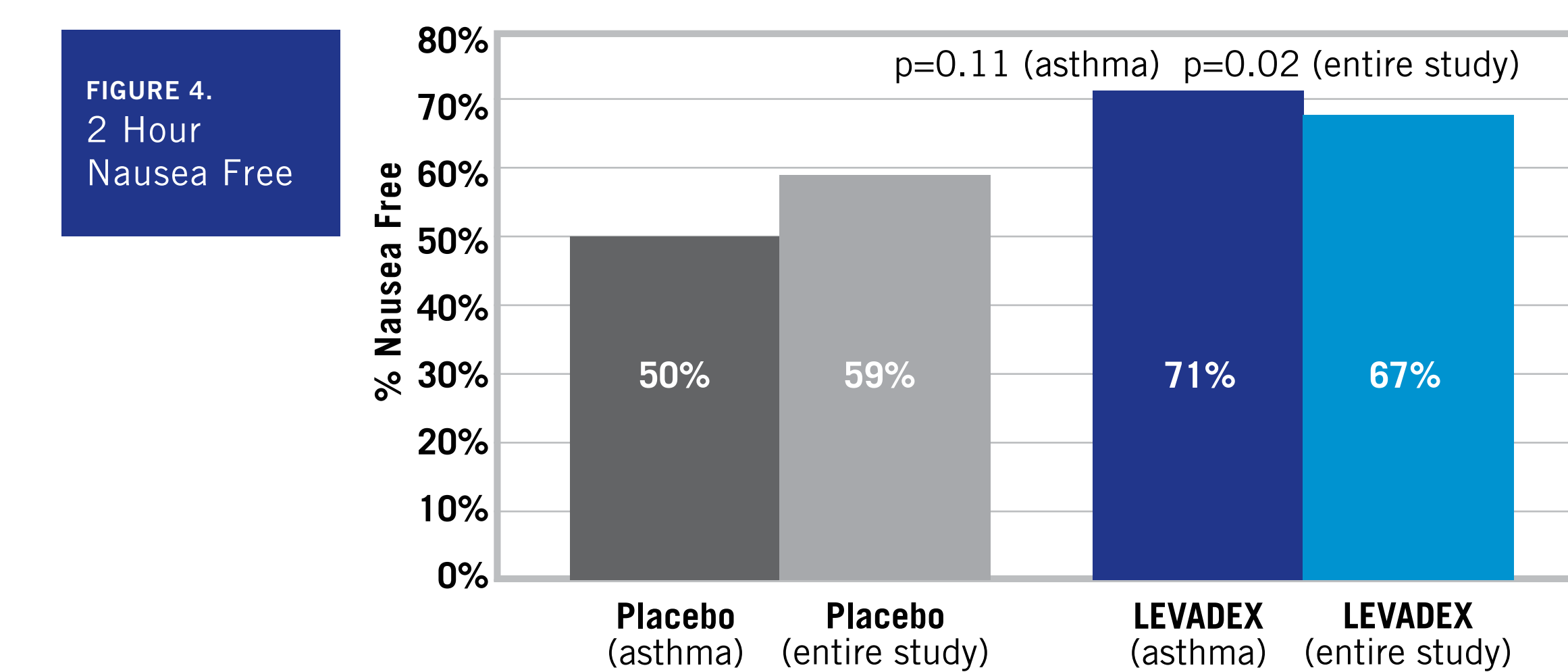
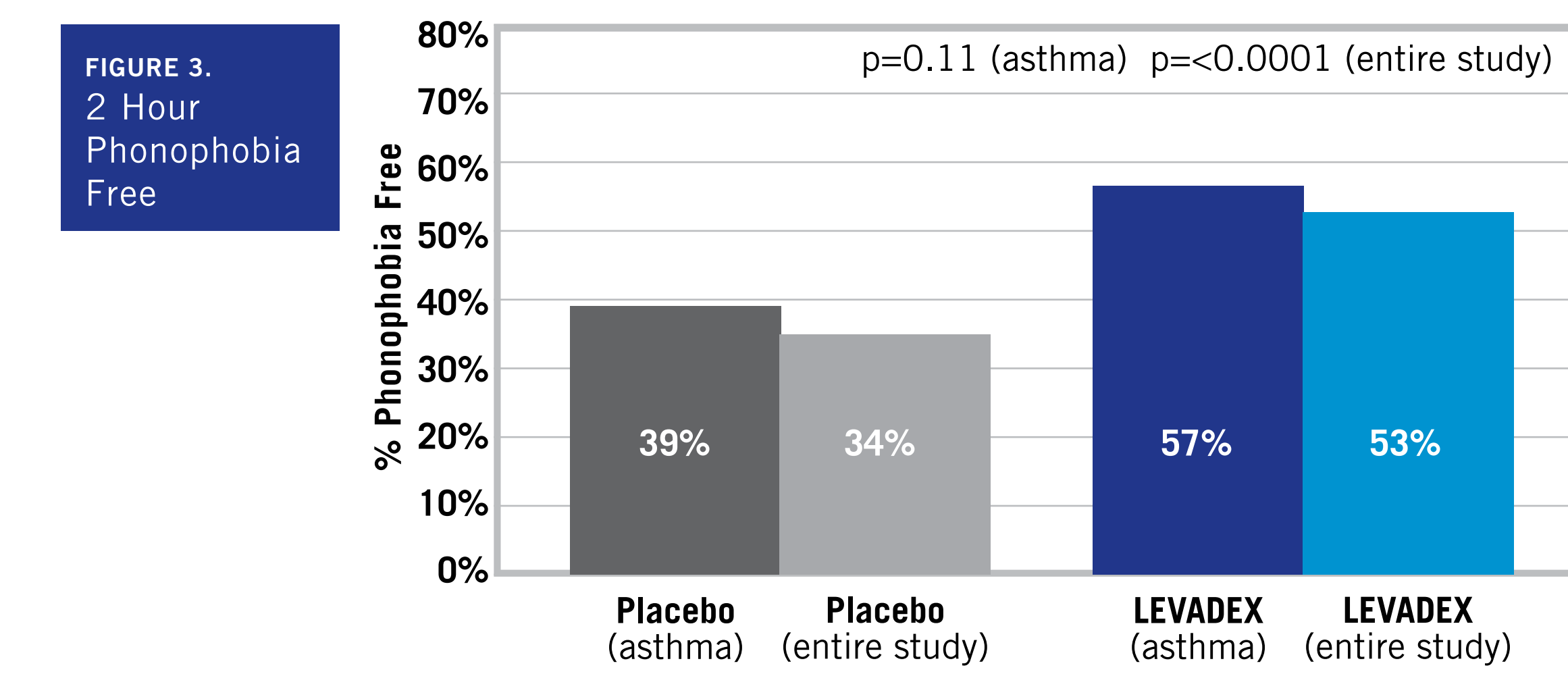
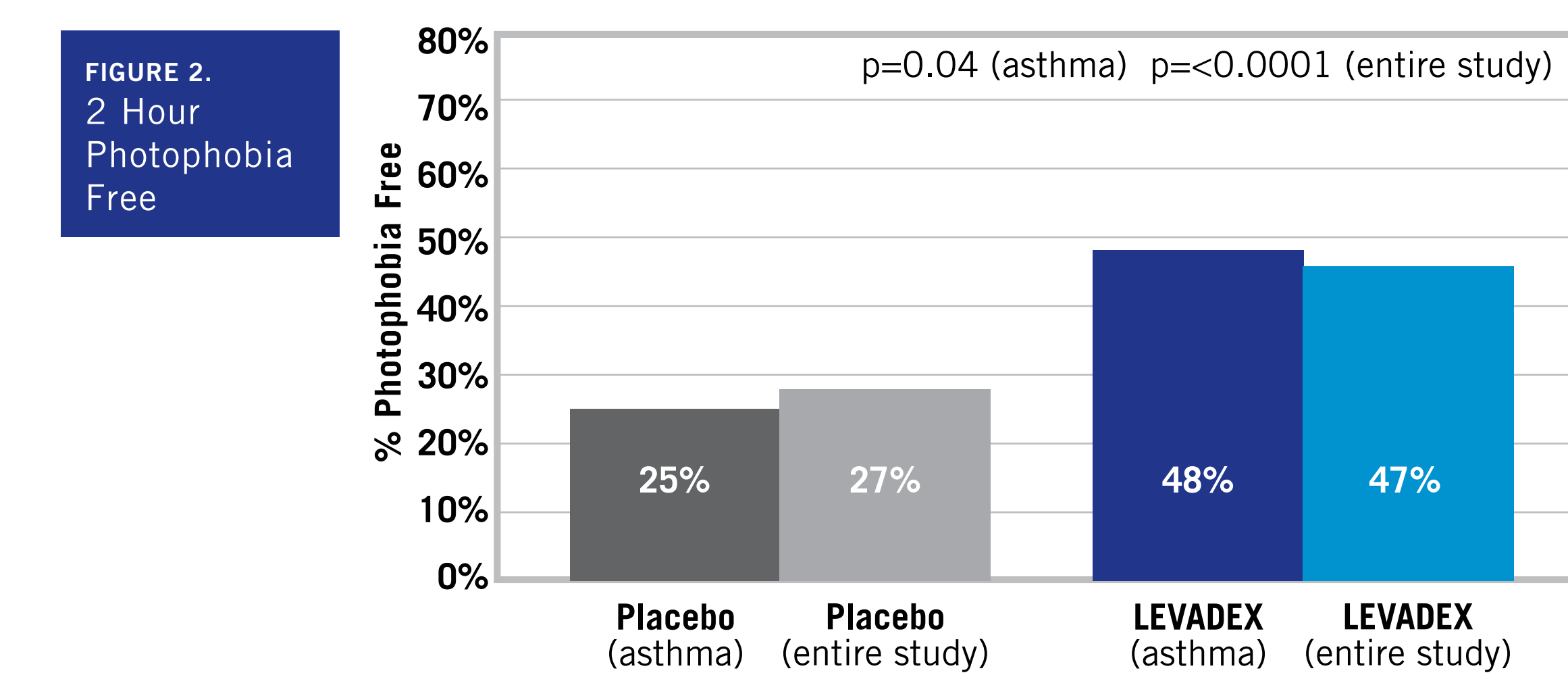
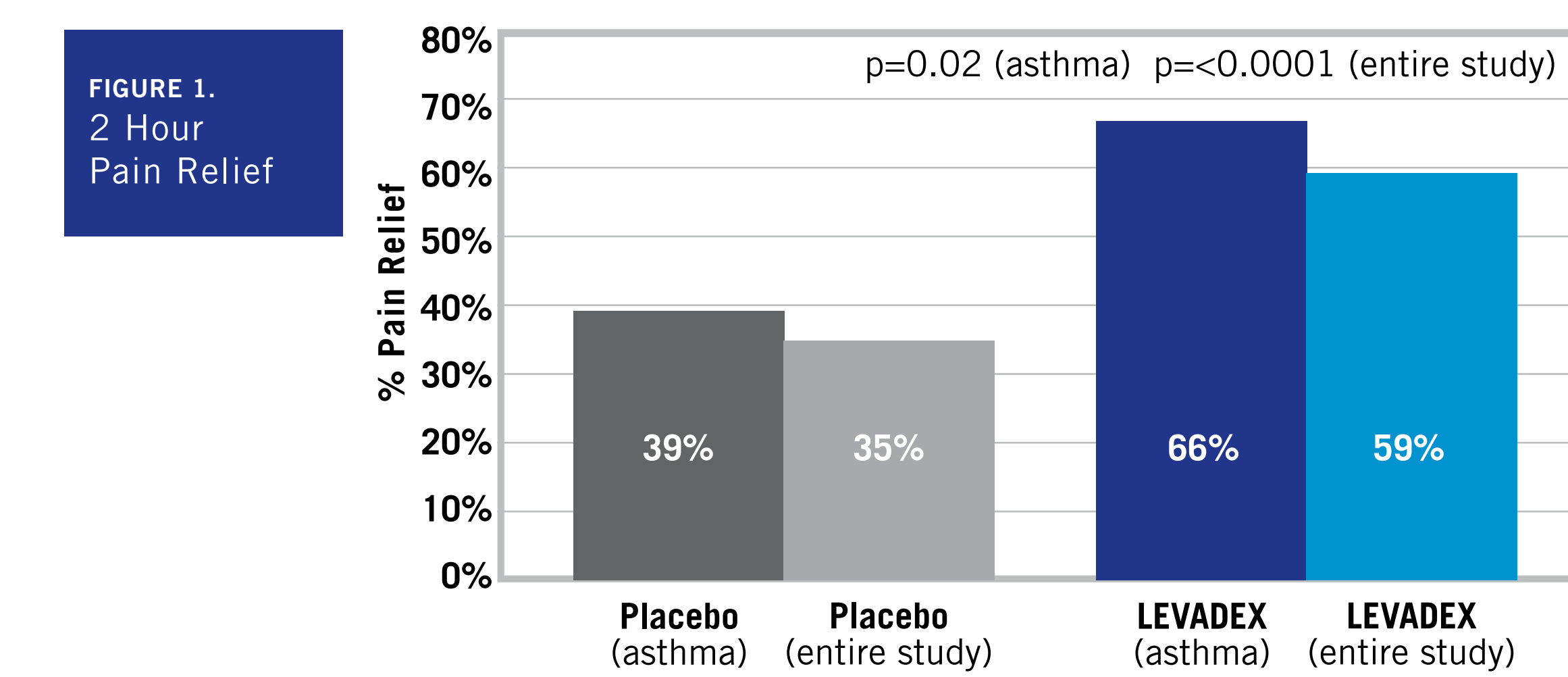
RESULTS

The demographics of the subjects with asthma and the entire study populations are shown in Table 1. Figures 1-5 graphically display the results for the 4 endpoints for the subjects with asthma.

TABLE 1. Demographics of Subjects with Asthma and Entire Study Population

	Placebo		LEVADEX	
	Asthma (n=36)	Entire Study (n=397)	Asthma (n=44)	Entire Study (n=395)
Mean Age (years)	37.6	39.6	37.8	40.5
% Female	97%	91%	91%	92%
Baseline HIT-6	64.6	65.6	64.5	65.5
FEV ₁ , % Predicted	90%	93%	88%	92%
Baseline Migraine Severity - Moderate	47%	53%	59%	55%
Severe	53%	47%	41%	45%

RESULTS



• The therapeutic gains were similar for both the entire study population and also for subjects with asthma.

RESULTS

TABLE 2. Spirometry for Subjects with Asthma and Entire Study

	Placebo		LEVADEX	
	Asthma (n=36)	Entire Study (n=401)	Asthma (n=44)	Entire Study (n=403)
Mean FEV ₁ (L)	2.75	2.86	2.73	2.82
Post-Treatment Mean Change from Baseline (L)	-0.02	0.02	0.06	0.02
Min, Max	-1.12, 0.20	-1.12, 1.09	-0.27, 0.87	-1.37, 1.47
Number with ≥20% Drop from Baseline	1	3	0	4

• There were minimal mean changes from baseline in FEV₁ for both the entire study population and also for the subjects with asthma.

TABLE 3. Adverse Events Overall, and of Interest in Subjects with Asthma

	Placebo (n=36)	LEVADEX (n=44)
Any Adverse Event	13 (36.1%)	14 (31.8%)
Infections and Infestations	7 (19.4%)	7 (15.9%)
Asthma	1 (2.8%)	0 (0%)
Cough	0 (0%)	1 (2.3%)
Chest Discomfort	0 (0%)	2 (4.5%)

CONCLUSION

In this subgroup analysis of subjects who reported a diagnosis of asthma, LEVADEX™ was effective and well-tolerated. The results were consistent with the results of the entire study. The inhaled route of administration appears to present no significant differences in efficacy or safety for subjects with migraine or subjects with migraine and concomitant asthma.

A study evaluating the long term safety of LEVADEX in migraine patients, including those with asthma and those without asthma, is ongoing.