

Evaluation of Safety and Efficacy of MAP0004 in Treating Acute Menstrual Migraine

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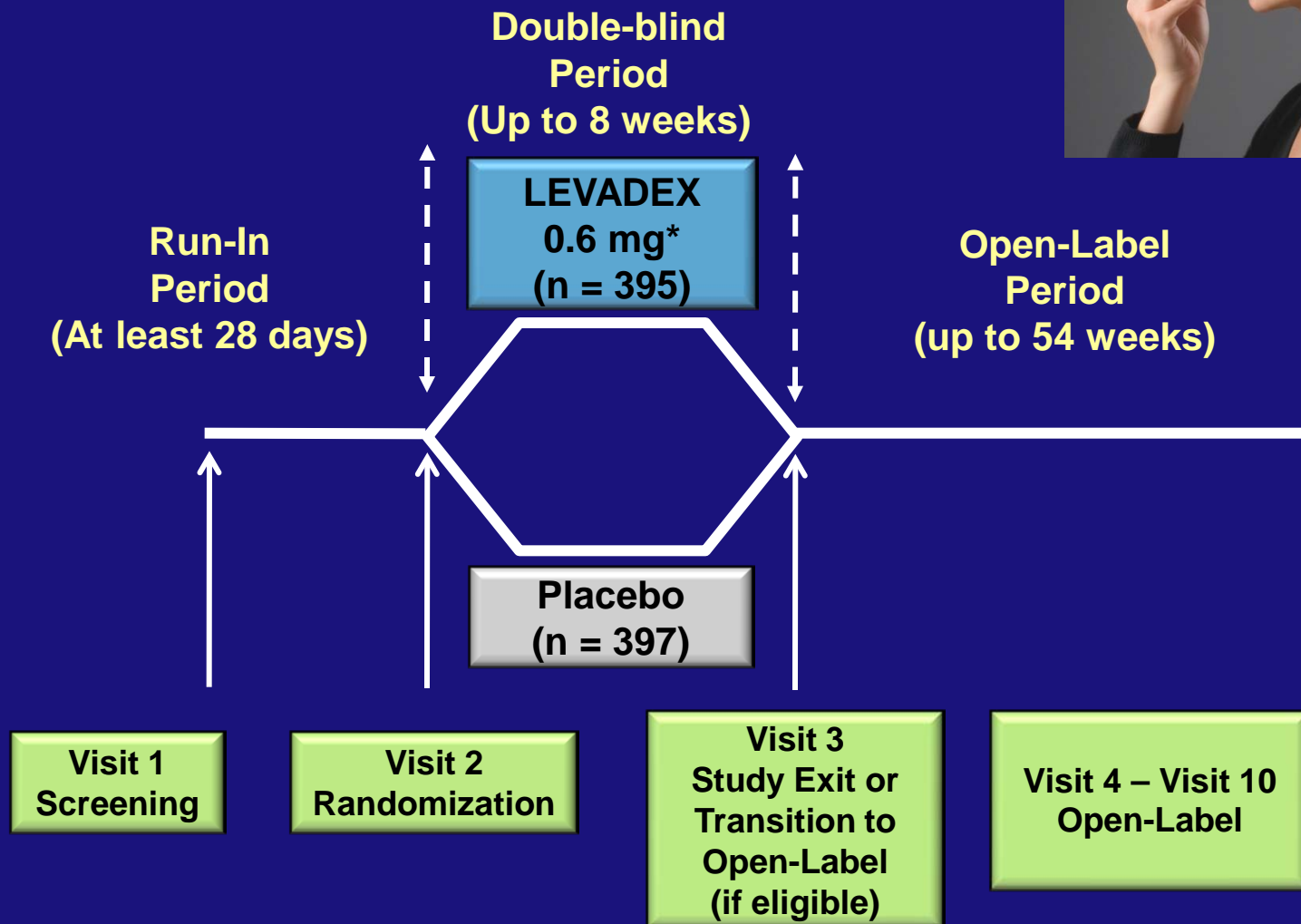
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LEVADEX™ (MAP0004) Phase 3 Clinical Study Design



* 0.6 mg emitted dose (1.0 mg nominal dose)

Post Hoc Analysis of Menstrually Related Migraine (MRM) in Phase 3 Study

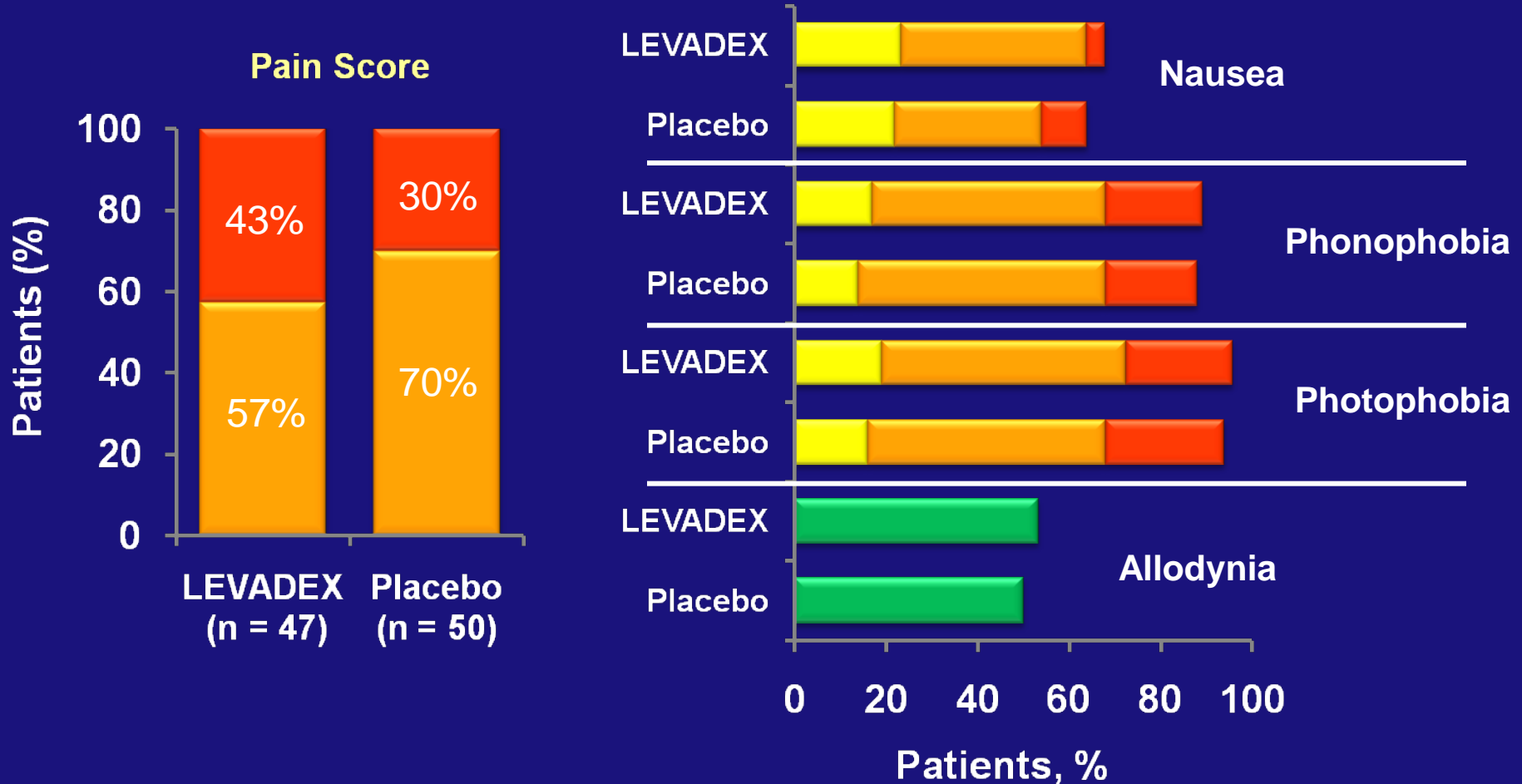
- 903 patients randomized
- 792 patients who treated a qualifying migraine were included in pre-specified efficacy analysis (MITT Population)
- 318 recorded information about last menstrual period
- **97 patients (31%) had menstrually related migraine (MRM)**
 - **Defined as migraine occurring within 2 days before or 3 days after onset of last menstrual flow**

Baseline Demographics for MRM Subgroup

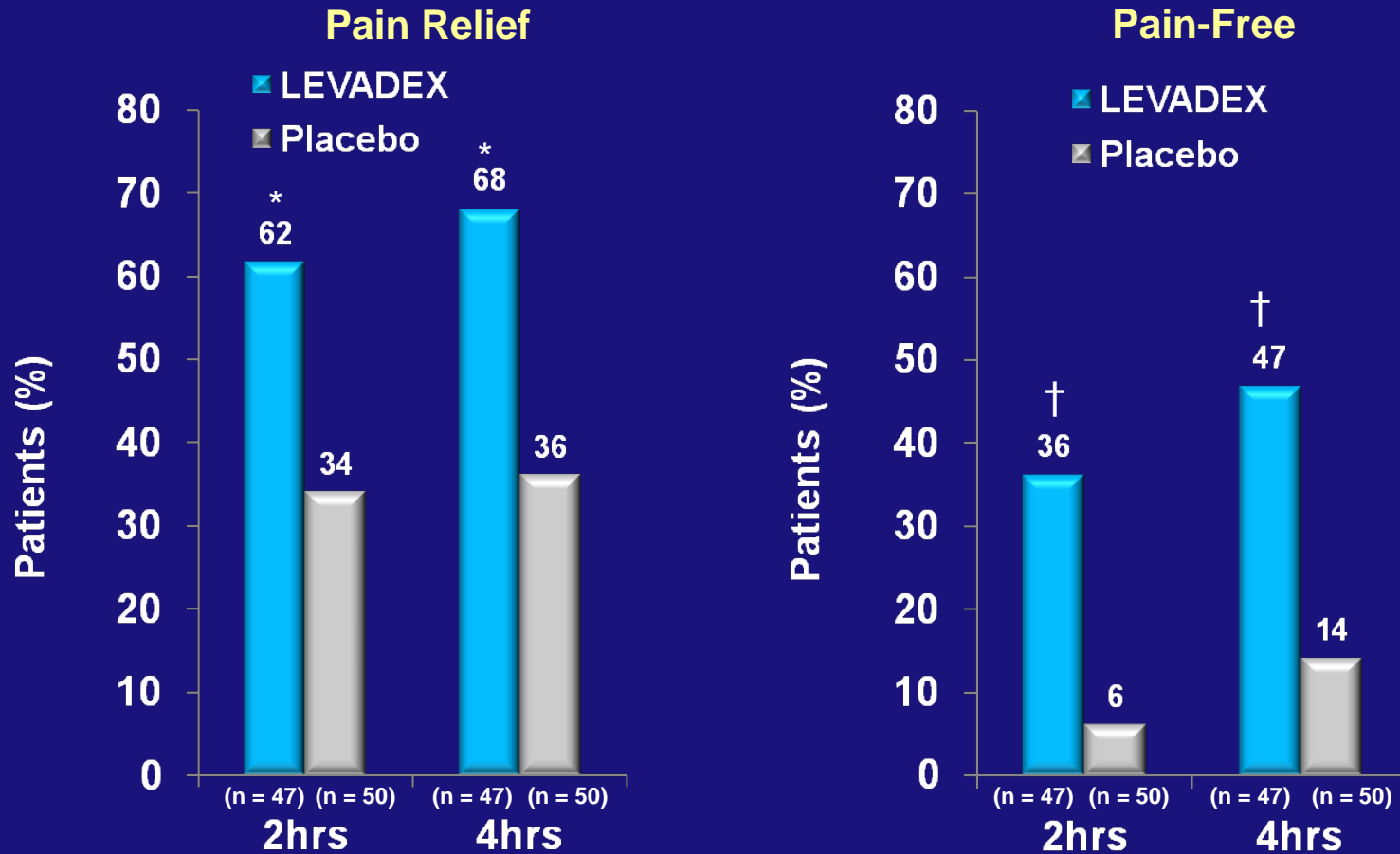
Parameter	LEVADEX 1.0 mg (n = 47)	Placebo (n = 50)
Age, years		
Mean (SD)	35 (8.1)	38 (9.2)
Median (range)	36 (20 – 51)	39 (19 – 53)
HIT-6 Score		
Mean (SD)	66 (4.4)	66 (5.3)
Median (range)	66 (54 – 78)	66 (55 – 78)
Disability due to headache, n (%)		
≥ 60 HIT-6 score	44 (94%)	44 (88%)
< 60 HIT-6 score	3 (6%)	6 (12%)

Intensity of Migraine Symptoms At Time of Treatment for MRM Subgroup

■ = Mild
 ■ = Moderate
 ■ = Severe
 ■ = Allodynia

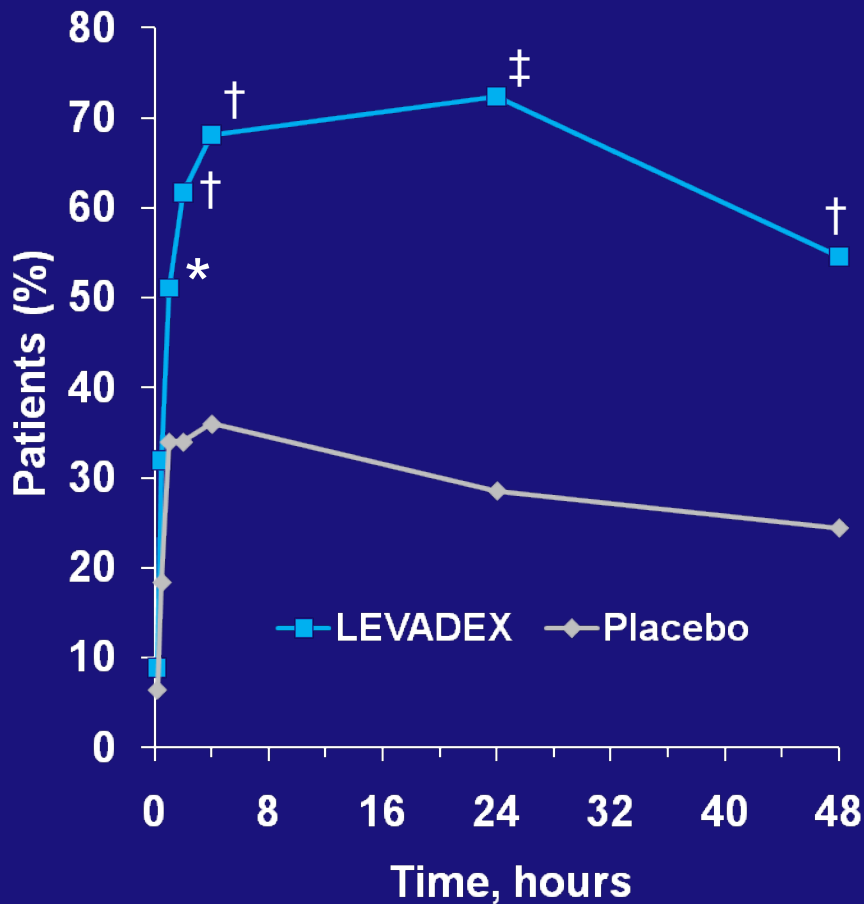
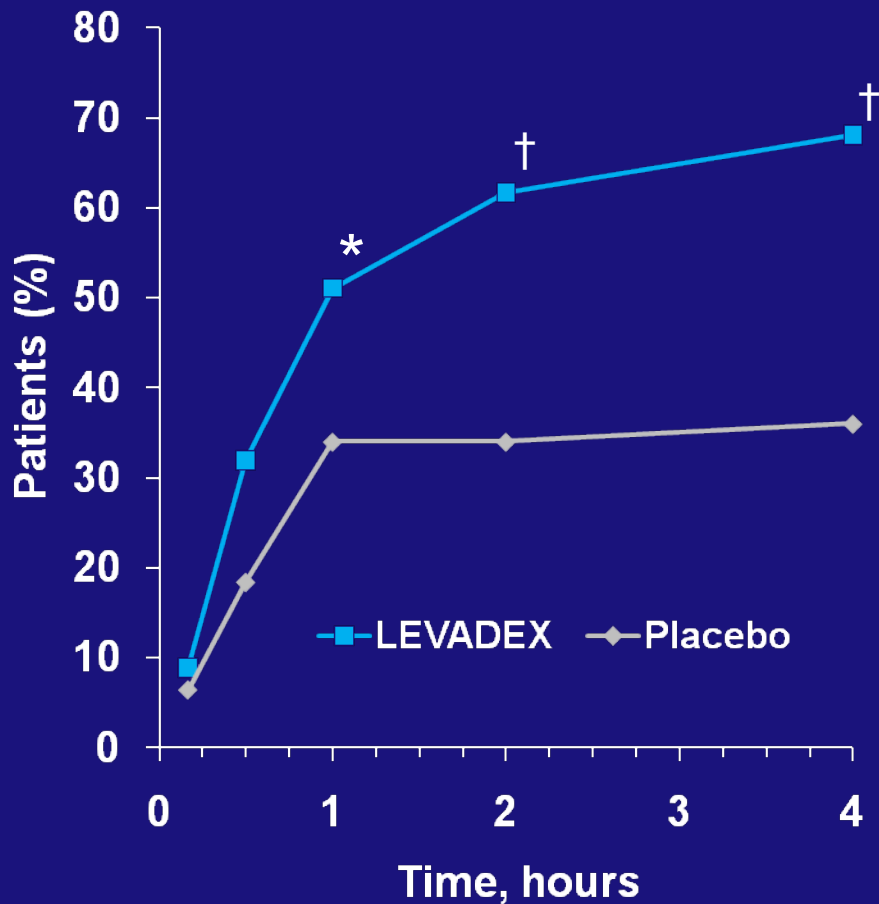


Pain Relief and Pain Free at 2 and 4 Hours for MRM Subgroup



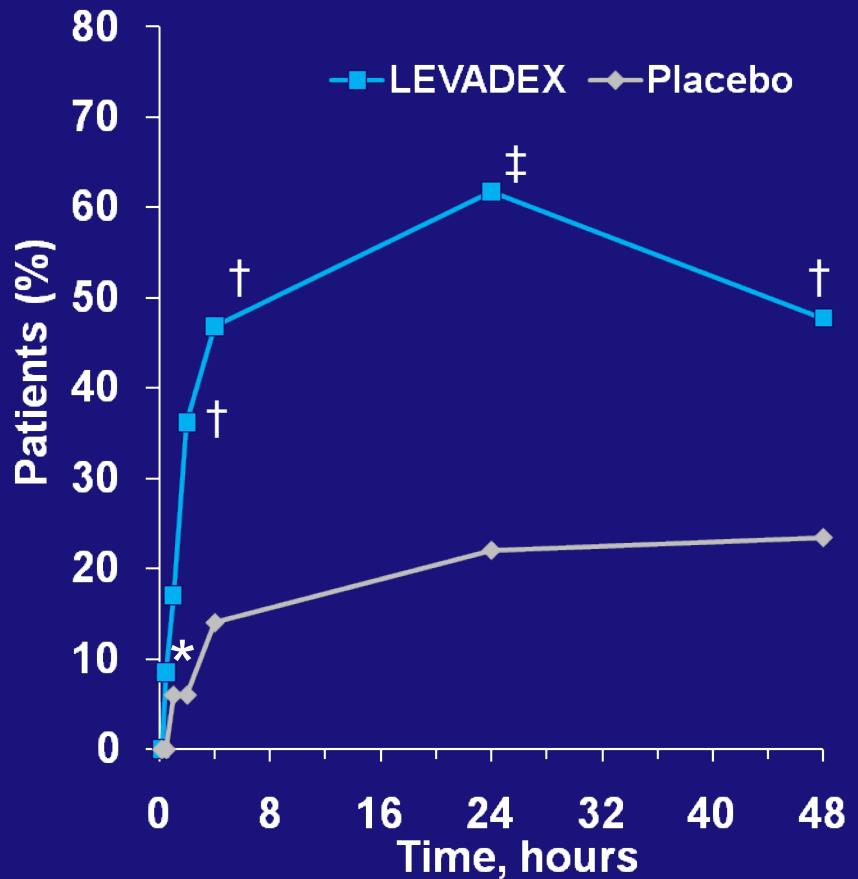
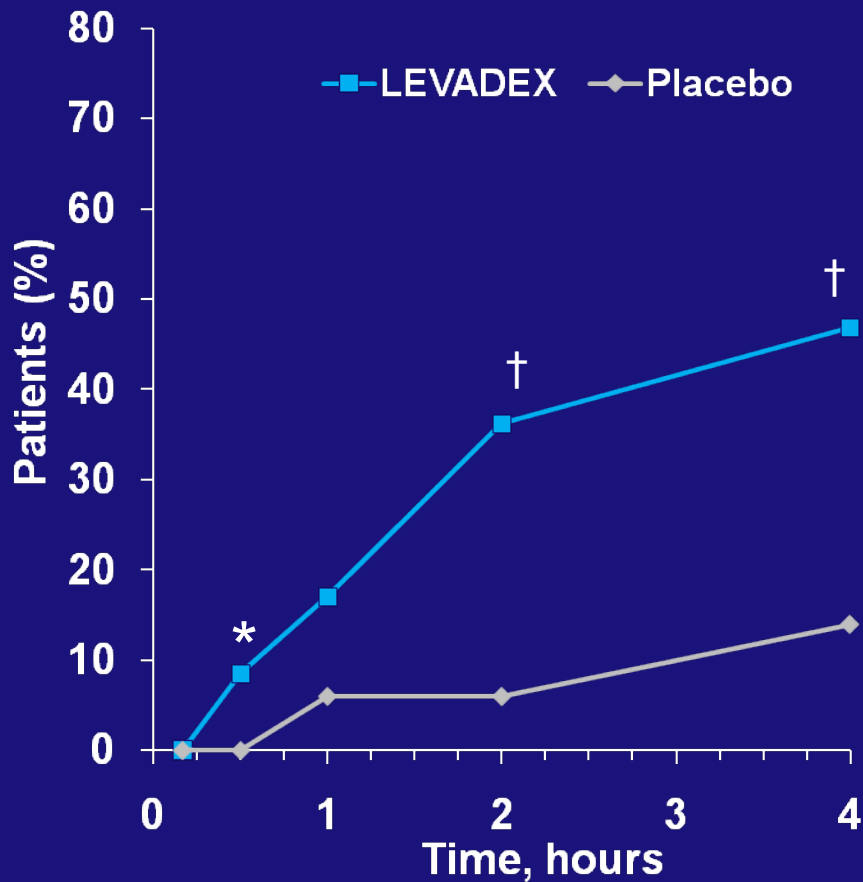
*P <0.01; †P <0.001 compared with placebo calculated using the Cochran-Mantel-Haenszel test controlling for baseline pain score, but not adjusted for multiplicity

Pain Relief over First 4 Hours and over 48 Hours for MRM Subgroup



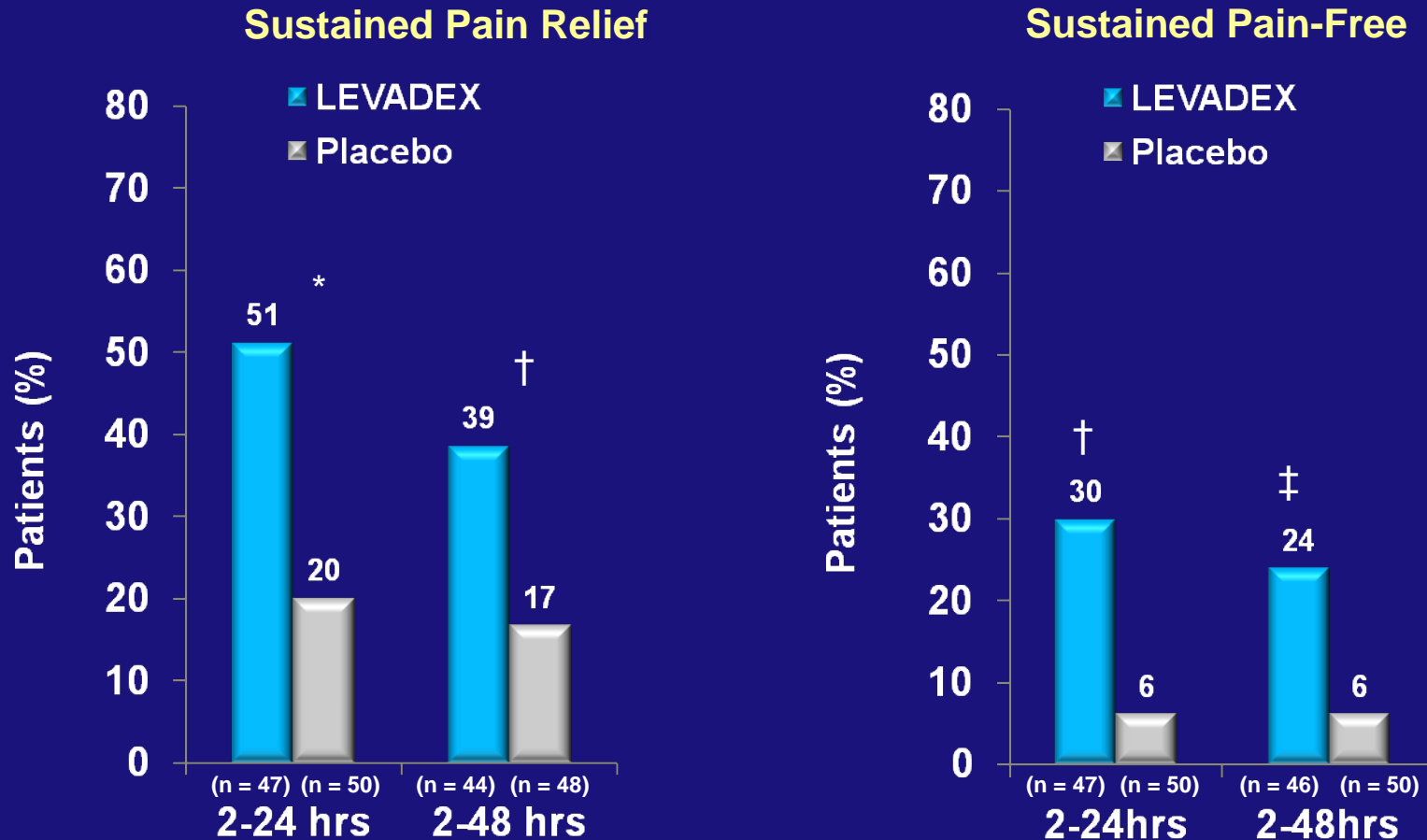
* $P < 0.05$; † $P < 0.01$; ‡ $P < 0.0001$ compared with placebo calculated using the Cochran-Mantel-Haenszel test controlling for baseline pain score, but not adjusted for multiplicity

Pain Free over First 4 Hours and over 48 Hours for MRM Subgroup



* $P < 0.05$; † $P < 0.001$; ‡ $P = 0.0001$ compared with placebo calculated using the Cochran-Mantel-Haenszel test controlling for baseline pain score, but not adjusted for multiplicity

Sustained Pain Relief and Sustained Pain Free from 2-24 and 2-48 Hours (MRM Subgroup)



*P <0.001; †P <0.01, ‡P=0.0108 compared with placebo calculated using the Cochran-Mantel-Haenszel test controlling for baseline pain score, but not adjusted for multiplicity

Tolerability in MRM Subgroup was Similar to that in Overall MITT Population

Adverse Events (Double-Blind Portion, Single Dose)

In MITT population, Adverse Events (AEs) in $\geq 2\%$ of Patients and $>$ Placebo	Overall MITT Population Patients (%)		MRM Subgroup Patients (%)	
	LEVADEX (N = 404)	Placebo (N = 401)	LEVADEX (N = 47)	Placebo (N = 50)
Taste	6.4 %	1.7 %	8.5 %	2.0 %
Nausea	4.5 %	2.0 %	4.3 %	0.0 %
Cough	2.5 %	1.2 %	2.1 %	2.0 %

In both populations:

- There were no significant differences in the AE profiles
- In patients treated with LEVADEX, symptoms and sensitivities typically associated with triptans, such as chest discomfort and chest pain were rare and occurred at similar rates compared with placebo
- No drug related serious adverse events were reported

No Change in Spirometry Measurements in MRM Subgroup or Overall MITT Population

- No clinically meaningful change in lung function in either treatment group in double-blind portion of study (single dose)

Conclusions

- **In this post hoc analysis of MRM in a large Phase 3 study:**
 - **LEVADEX provided significant pain relief at 1, 2, 4, 24 and 48 hours**
 - **LEVADEX provided significant pain freedom at 30 minutes and 2, 4, 24 and 48 hours**
 - **LEVADEX provided significant sustained pain relief and sustained pain freedom from 2-24 and 2-48 hours**
 - **LEVADEX was well tolerated with few triptan-like sensations and no drug-related SAEs reported**

Note: Post hoc analysis. P-values are not adjusted for multiple comparisons.

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