

Efficacy and Safety of Tapentadol Prolonged Release Versus Oxycodone Controlled Release in Opioid-naive and Opioid-experienced Patients With Chronic Pain Associated With Osteoarthritis of the Knee

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Introduction

- **Patients with chronic osteoarthritis pain are often treated with opioid analgesics¹**
 - **Opioid therapy is associated with side effects that often cause patients to discontinue treatment^{2,3}**
- **It is possible that a patient's sensitivity to side effects may be affected by past opioid experience^{4,5}**
- **Purpose of this talk is to describe the efficacy and safety of tapentadol PR in the treatment of moderate to severe chronic osteoarthritis knee pain in subjects with different opioid experience**

1. Avouac J, et al. *Osteoarthritis Cartilage*. 2007;15(8):957-965.

2. Moore RA, McQuay HJ. *Arthritis Res Ther*. 2005;7(5):R1046-R1051.

3. Schug SA, et al. *Drug Saf*. 1992;7(3):200-213.

4. McIlwain H, Ahdieh H. *Am J Ther*. 2005;12(2):106-112

5. Peniston JH, Gould E. *Clin Ther*. 2009;31(2):347-359.

Background on tapentadol

- **A novel, centrally acting analgesic with 2 mechanisms of action^{6,7}**
 - **μ -opioid receptor agonism**
 - **Noradrenaline reuptake inhibition**
- **Prolonged-release formulation under development for moderate-to-severe chronic pain**
 - **Phase 3 studies in OA pain, chronic LBP, painful DPN**

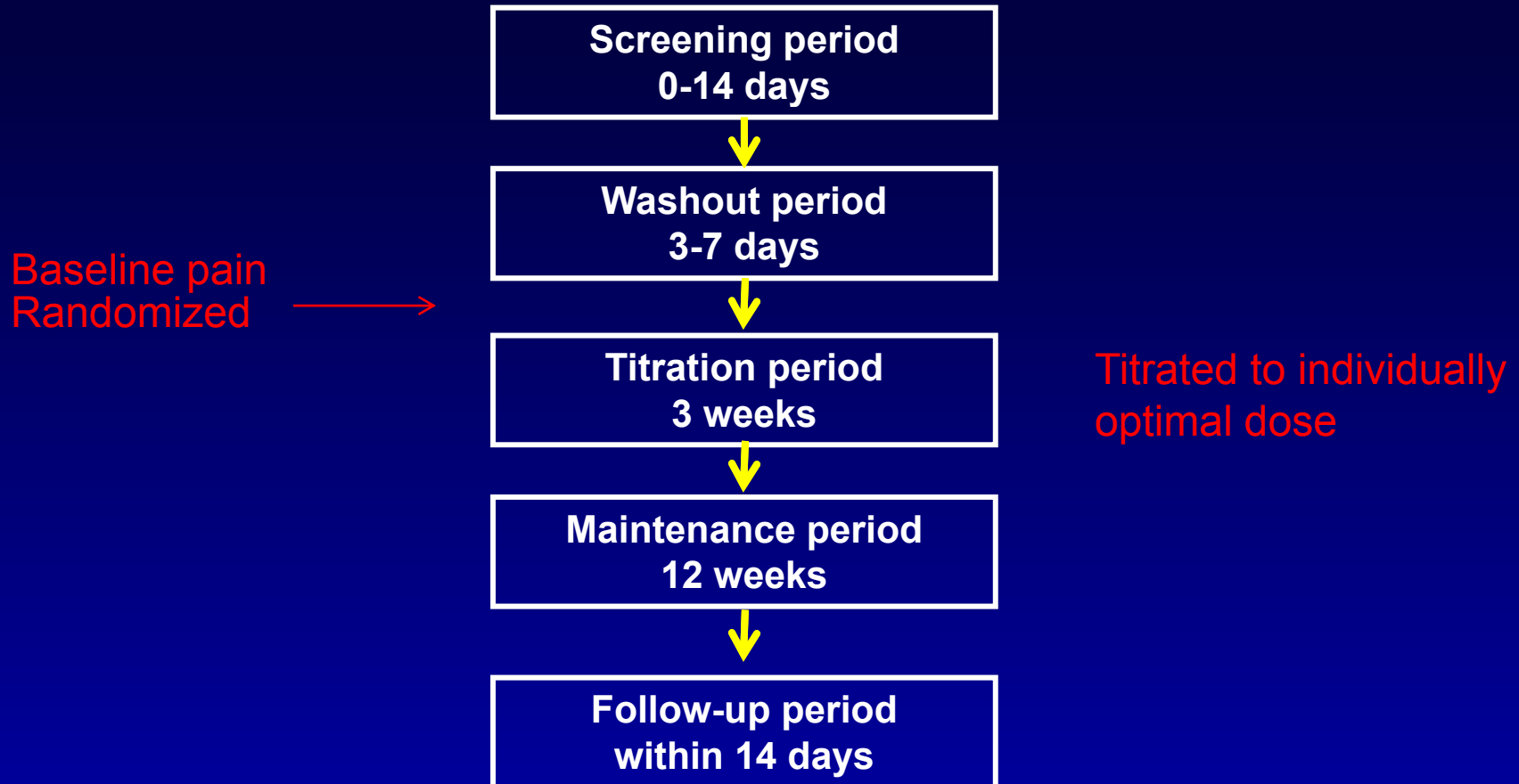
6. Tzschentke TM, et al. *J Pharmacol Exp Ther.* 2007;323(1):265-276.

7. Tzschentke TM, et al. *Drugs Future.* 2006;31(12):1053-1061.

Study Design

- **Randomized, double-blind (DB), active- and placebo-controlled, parallel-arm, multicenter, controlled dose adjustment phase 3 study**
- **3 Treatment groups**
 - **Placebo**
 - **Tapentadol PR, 100 to 250 mg bid**
 - **Oxycodone HCl controlled release (CR), 20 to 50 mg bid**

Study Design



Paracetamol (≤ 1000 mg/day) was allowed during titration (≤ 3 days before the end of the period) and for pain other than osteoarthritis pain during the maintenance period (intermittently for ≤ 3 consecutive days)

Methods

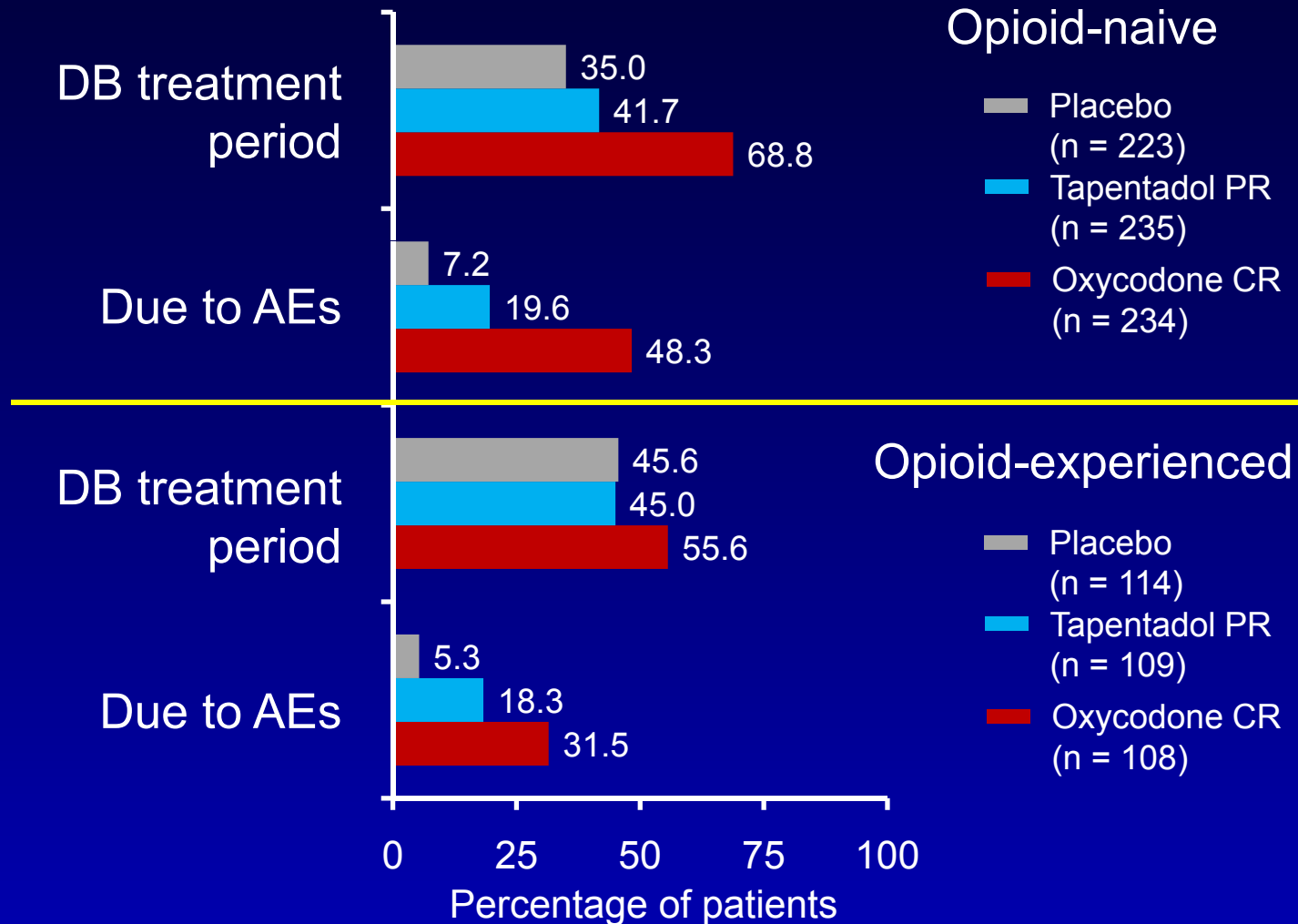
Patients	<p>≥40 years of age</p> <p>Diagnosed and treated for pain from osteoarthritis of the knee for a minimum of 3 months</p> <p>Average baseline pain intensity score of ≥5 on 11-point numerical rating scale (NRS)</p>
Study endpoints ^a	<p>Change from baseline in average pain intensity at Week 12 of the maintenance period and over the 12-week maintenance period for opioid-naïve and opioid-experienced patients</p> <p>Prior opioid experience was defined as taking opioid analgesics during the 3-month period prior to screening</p> <p>Last observation carried forward (LOCF) was used to impute missing values after early treatment discontinuation</p>
Safety assessments ^a	Adverse events (AEs) and discontinuations were monitored

^aIntent-to-treat and safety populations included all randomized patients who received ≥1 dose of study medication.

Results

- **1023 patients received ≥ 1 dose of study medication and were included in efficacy and safety analyses**
- **Opioid-naive patients**
 - Placebo, 66.2%
 - Tapentadol PR, 68.3%
 - Oxycodone CR, 68.4%
- **The majority of patients (83.4%) reported severe baseline pain intensity (≥ 6 on 11-point NRS)**

Treatment discontinuations: 39% placebo, 43% tapentadol PR, 65% oxycodone CR (n = 1023)



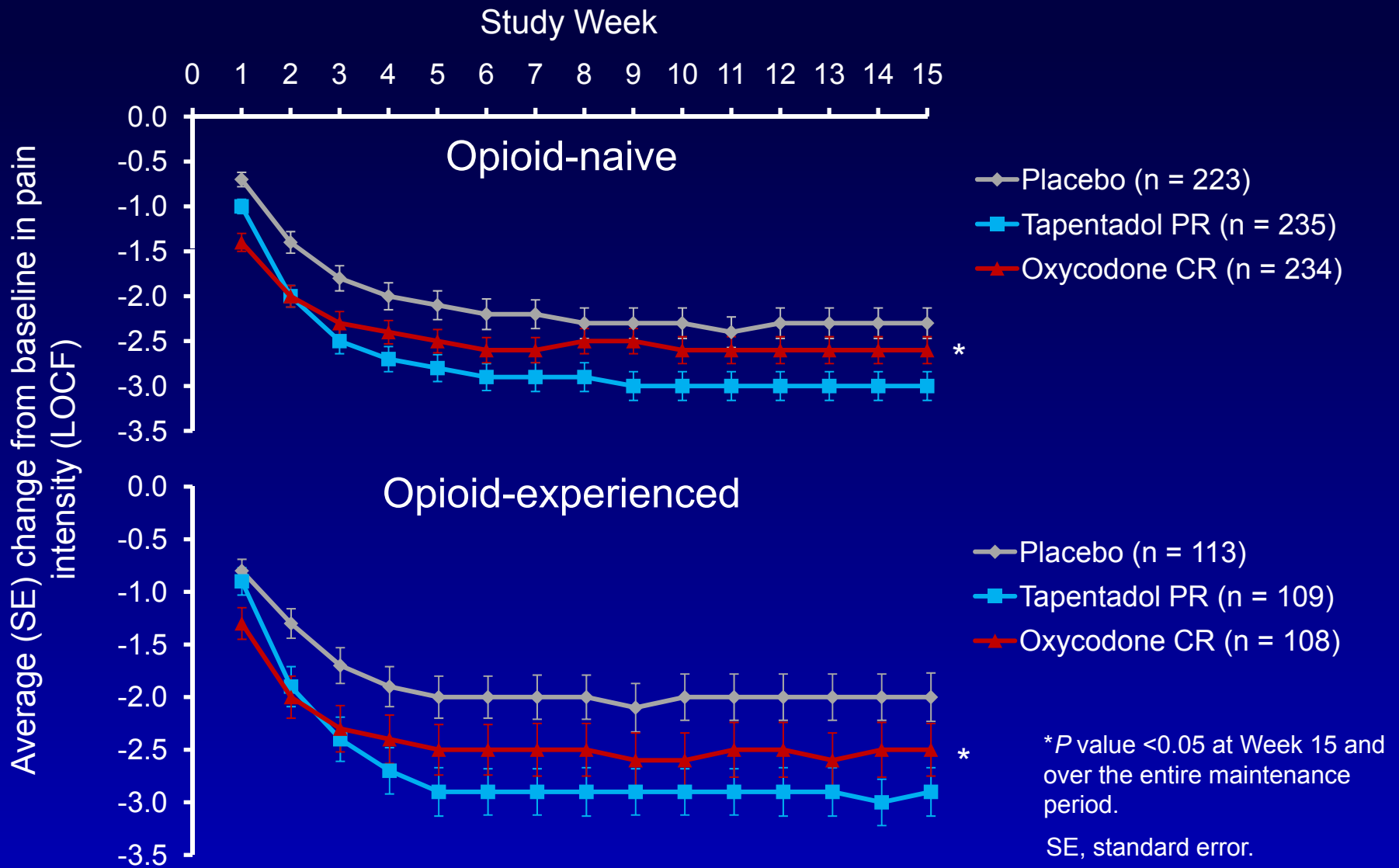
Efficacy – Change From Baseline in Average Pain Intensity

- Overall maintenance period
 - Opioid-naive
 - ◆ Tapentadol PR: $P = 0.001^*$
 - ◆ Oxycodone CR: $P = 0.139$
 - Opioid-experienced
 - ◆ Tapentadol PR: $P = 0.014^*$
 - ◆ Oxycodone CR: $P = 0.101$
- At Week 12
 - Opioid-naive
 - ◆ Tapentadol PR: $P = 0.003^*$
 - ◆ Oxycodone CR: $P = 0.243$
 - Opioid-experienced
 - ◆ Tapentadol PR: $P = 0.012^*$
 - ◆ Oxycodone CR: $P = 0.103$

* P value indicates a significant difference versus placebo (LOCF).

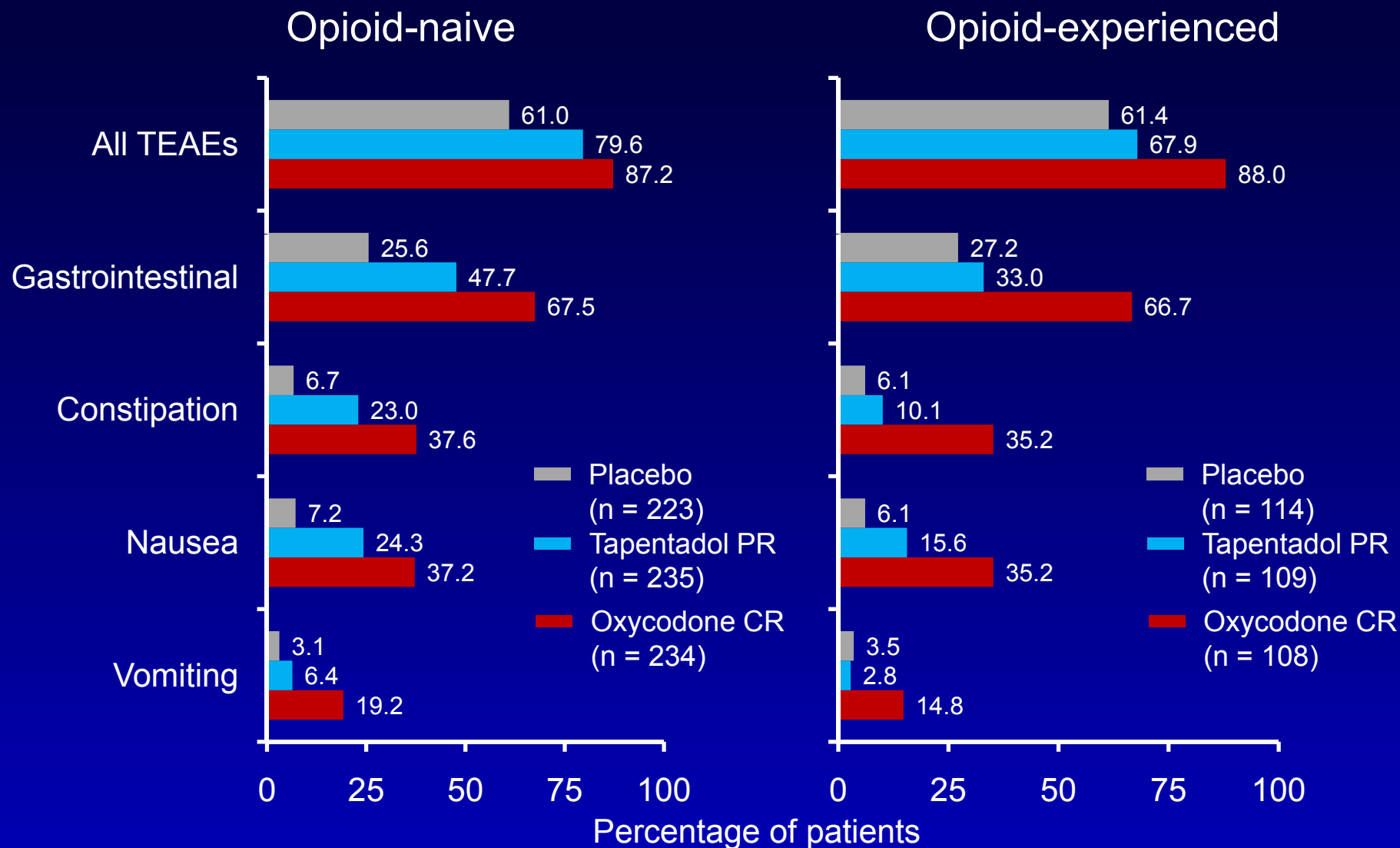
Efficacy

(Intent-to-Treat Population, n = 1023)



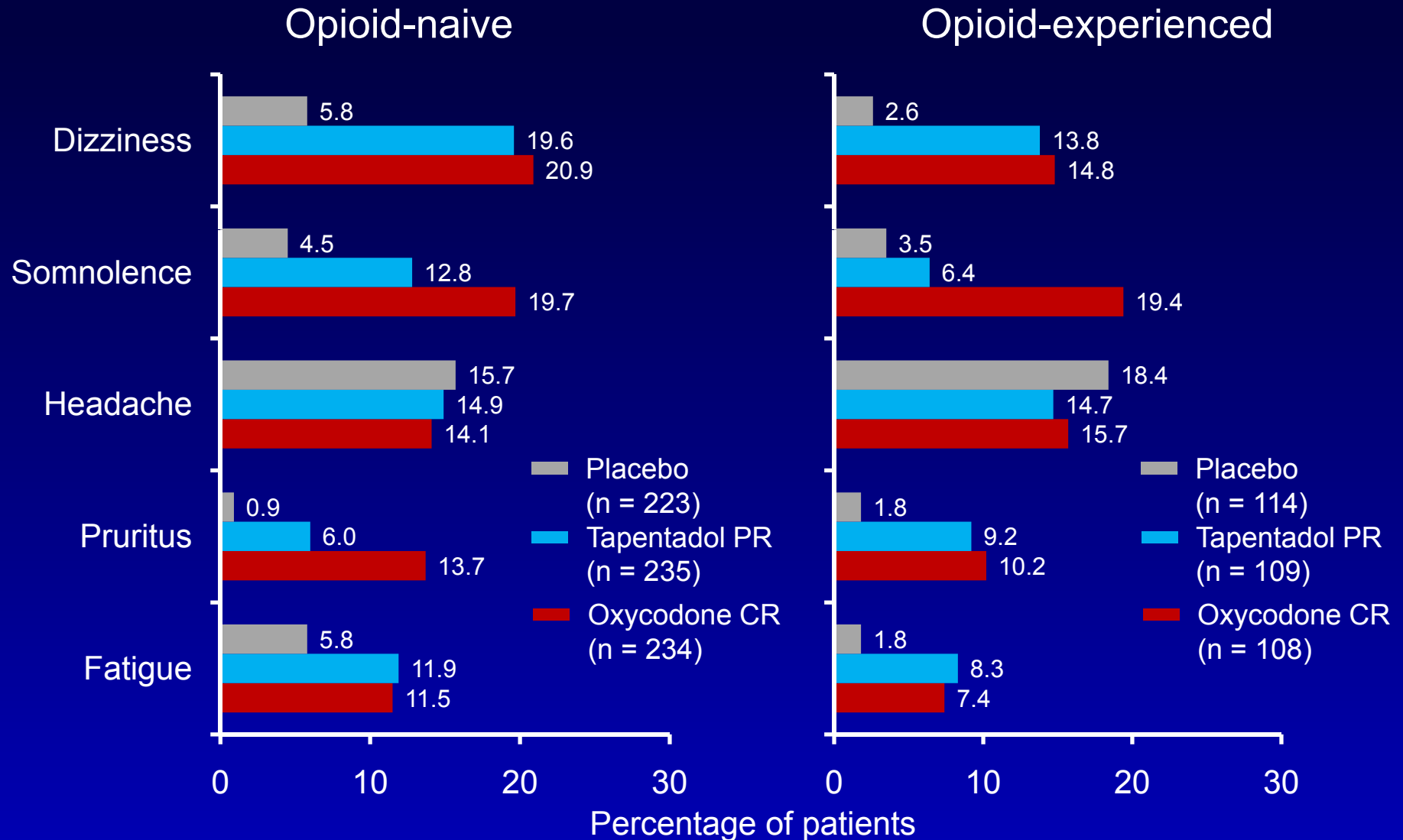
Overall and Gastrointestinal TEAEs Reported by $\geq 10\%$ of Patients

(Safety Population, n = 1023)



TEAEs Reported by $\geq 10\%$ of Patients

(Safety Population, n = 1023)



Conclusions

- **Tapentadol PR (100-250 mg bid) relieved chronic pain for both opioid-naive and opioid-experienced patients**
- **Tapentadol PR was associated with lower incidences of gastrointestinal TEAEs than oxycodone HCl CR (20-50 mg bid), especially for opioid-experienced patients**
- **A lower percentage of patients discontinued treatment with tapentadol PR than with oxycodone CR**