I.V. CR845 Adaptive Phase 2/3 Post Operative Pain Study Results

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Adaptive Design Study Evaluating the Analgesic Efficacy and Safety of I.V. CR845 in Patients Undergoing Abdominal Surgery

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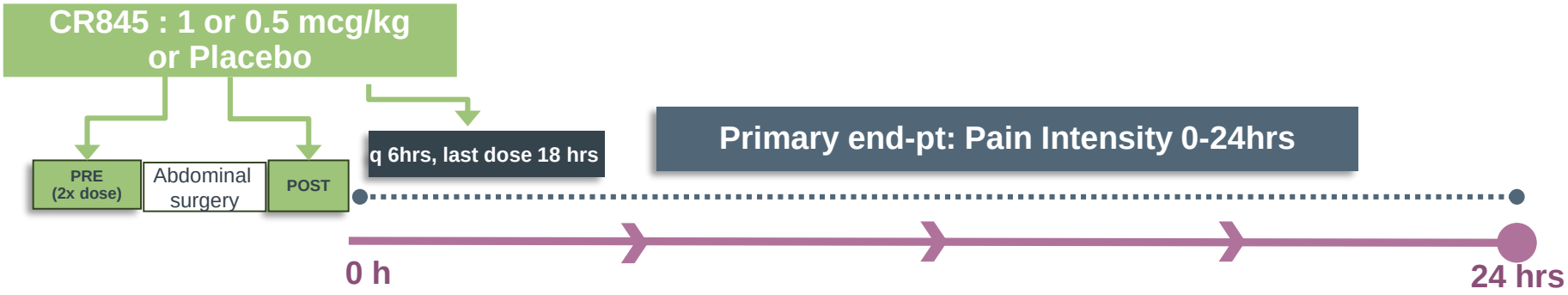
Forward Looking Statements

Statements contained in this presentation regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of these forward-looking statements include statements concerning the future development of IV. CR845 for the management of perioperative pain, potential future meetings with regulators, and the potential for I.V. CR845 to be a therapeutic option for perioperative pain management. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in Cara's filings with the Securities and Exchange Commission, including the "Risk Factors" section of Cara's Annual Report on Form 10-K for the year ended December 31, 2017 and its other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made. Except to the extent required by law, Cara undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Post-Op Pain: Significant Unmet Need

- Multi-modal analgesia (ASA and ERAS)
  - Different MOAs to maximize analgesia
  - Anti-inflammatory benefits vs. mu opioids
- Need to reduce mu opioid usage and side effects
  - Respiratory Depression
  - Nausea / Vomiting
  - Abuse Liability
- Goal to improve patient outcomes, decrease length of hospital stay and reduce overall health care costs

CR845 CLIN3001: Study Design



- Multi-center: 22 U.S. hospital sites, 444 patients
- Randomized, double-blind, placebo controlled, adaptive design
- Dose: 0.5 mcg/kg, 1.0 mcg/kg or placebo
- Primary endpoint: Area Under the Curve (AUC) assessment of the pain intensity measured by Numeric Rating Scale (NRS) from 0 to 24 hrs post surgery
- Secondary endpoints:
  - Incidence of vomiting over 24 hours
  - Post operative nausea & vomiting (PONV) Impact scores
  - Rescue medication used (IV morphine) within 24 hours
  - Patient global assessment of medication at 24 hours
  - Safety

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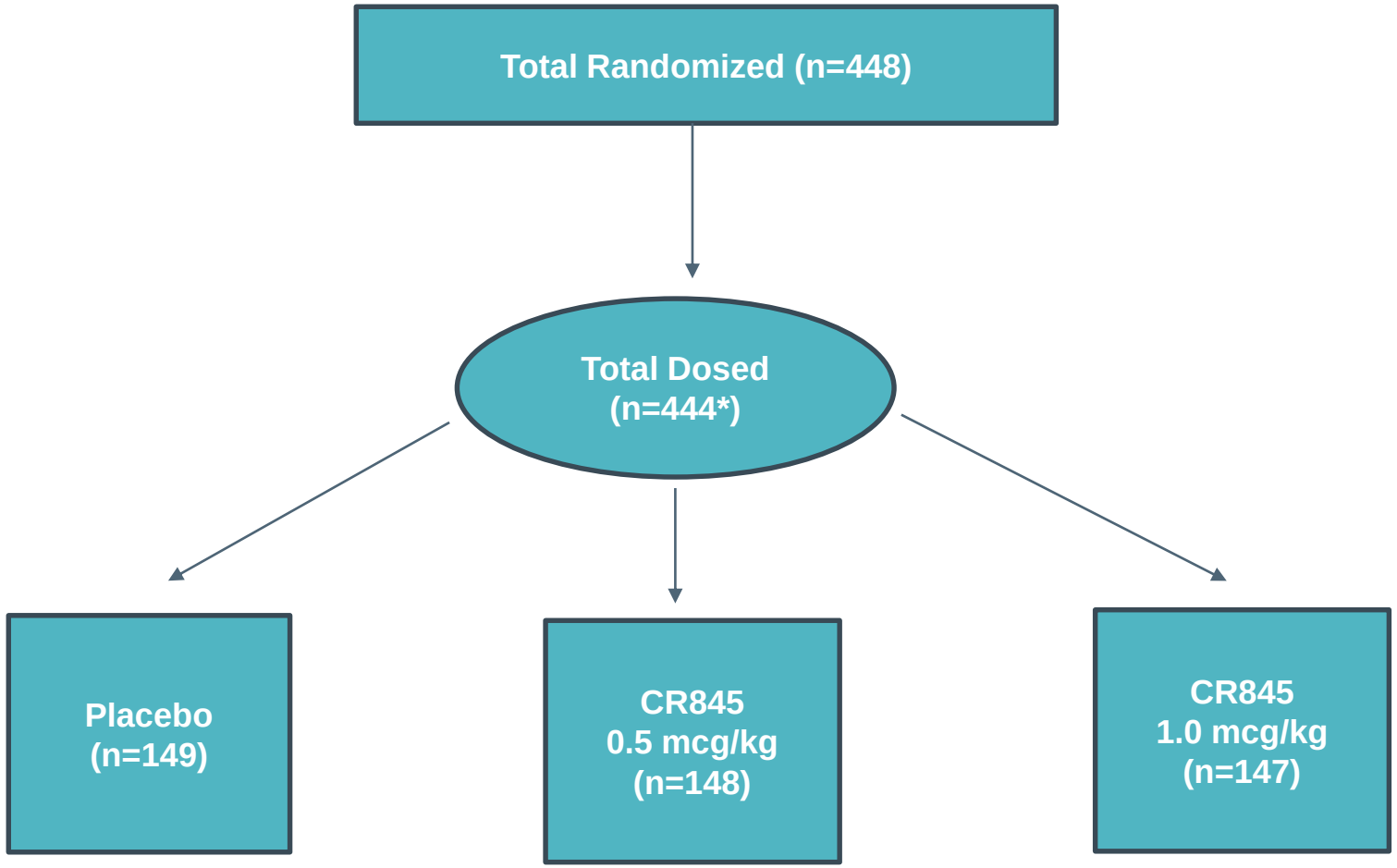
CR845-CLIN3001: Subject Distribution



*4 patients did not report any pain scores and are excluded from the efficacy analyses

Demographics and Baseline Characteristics

Variable	Placebo n= 149	CR845 0.5 mcg/kg n=148	CR845 1.0 mcg/kg n=147
Age at study entry (yrs)			
n	149	148	147
Mean (SD)	46.3 (10.61)	45.1 (10.23)	44.1 (10.92)
Median	46.0	45.0	43.0
Min	23	25	22
Max	80	78	74
Gender, n (%)			
Male	48 (32.2)	51 (34.5)	49 (33.3)
Female	101 (67.8)	97 (65.5)	98 (66.7)
Race, n (%)			
American Indian, Alaskan	1 (0.7)	2 (1.4)	0
Asian	0	0	1 (0.7)
Black or African American	22 (14.8)	16 (10.8)	18 (12.2)
Pacific Islander, Native Hawaiian	0	0	0
White	125 (63.9)	129 (87.2)	128 (87.1)
Other	1 (0.7)	1 (0.7)	0
Type of surgery, n (%)			
Ventral Hernia	78 (52.3)	75 (50.7)	75 (51.0)
Hysterectomy	71 (47.7)	73 (49.3)	72 (49.0)

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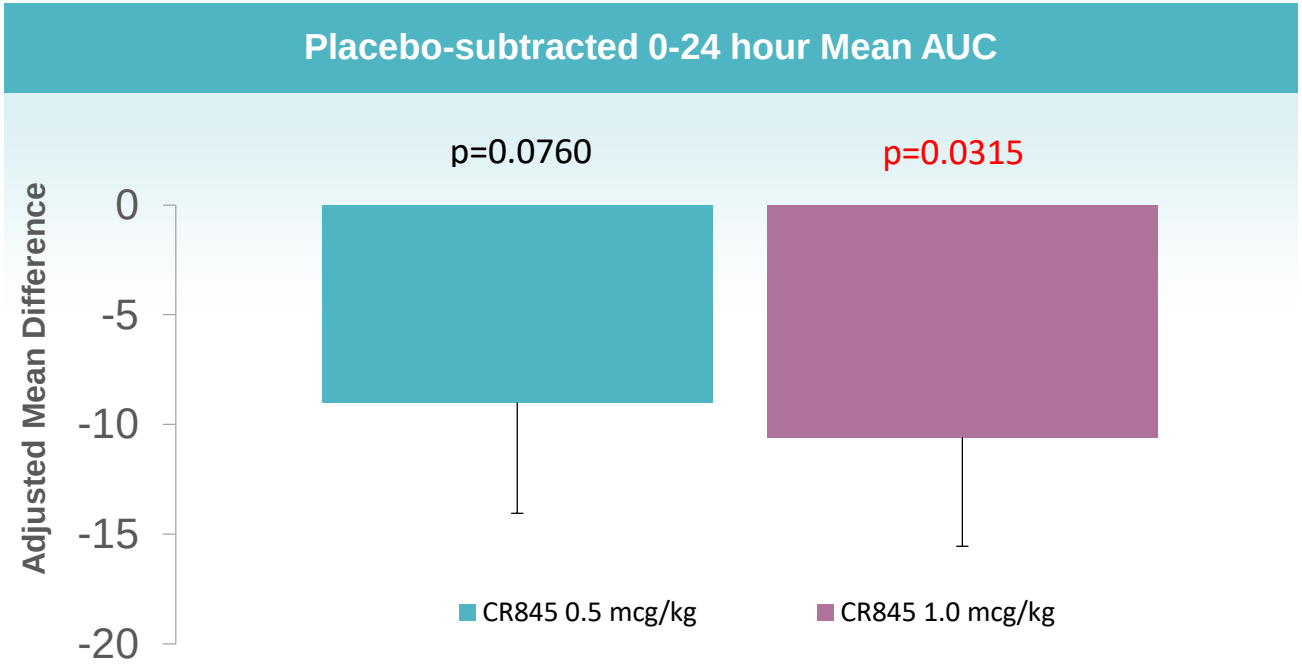
0-24 hour Pain AUC
Primary Endpoint

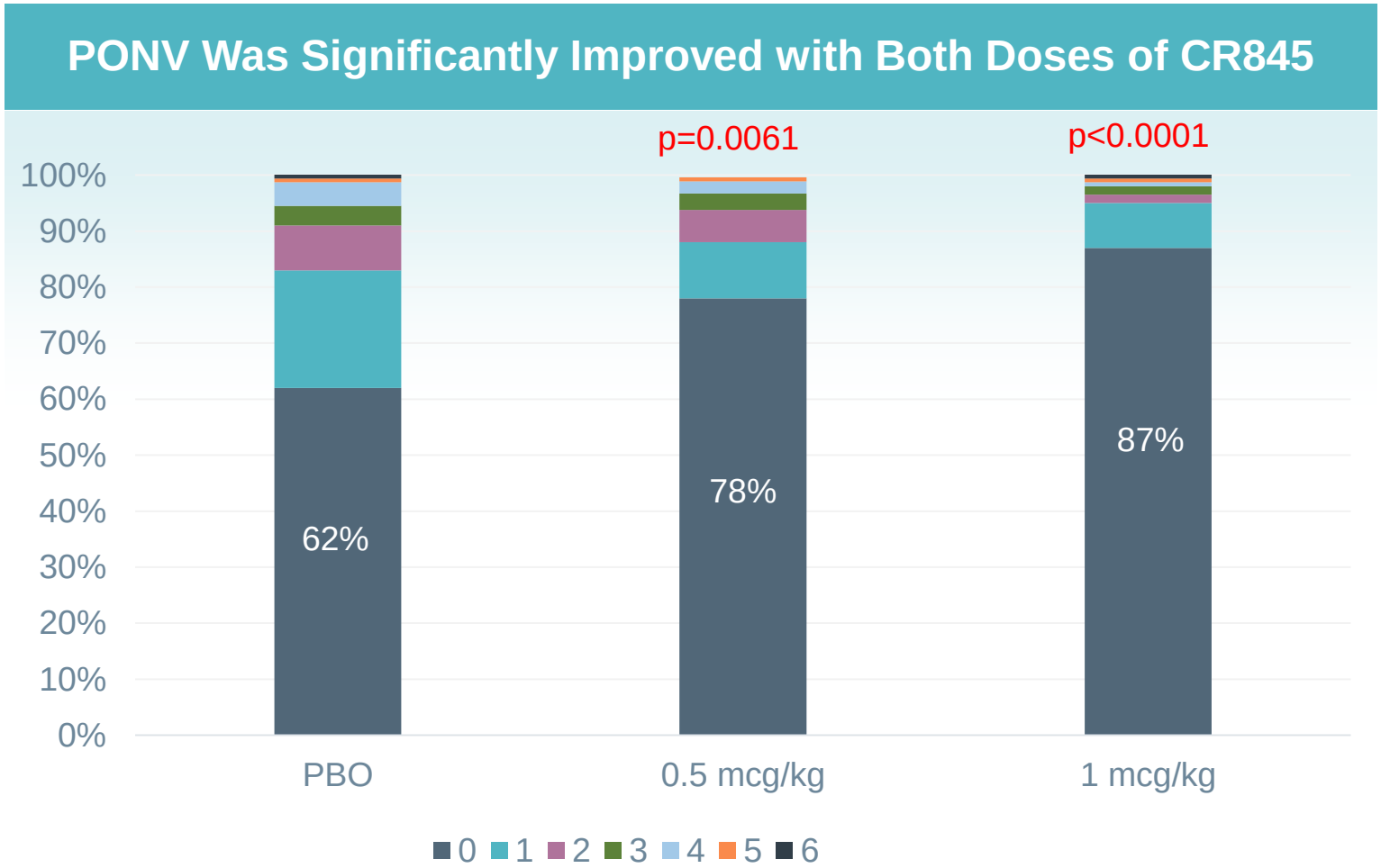
CR845 demonstrated significant improvement in pain relief



Post-Op Interval	0.5 mcg/kg	1.0 mcg/kg
0-6 hours	p=0.041	p=0.001
0-12 hours	p=0.035	p=0.004
0-18 hours	p=0.072	p=0.013

ANCOVA with terms for treatment, surgery type and site nested within surgery type

PONV Impact Score at 24 Hrs:
Secondary Endpoint



% of subjects who did not use any ondansetron was 70% in the CR845 0.5 mcg/ kg and 81% in the CR8451 mcg/kg group versus 56% in the placebo group

PONV Scores: 0- not at all, and 6-Worst score
Wilcoxon rank sum test stratified by surgery type

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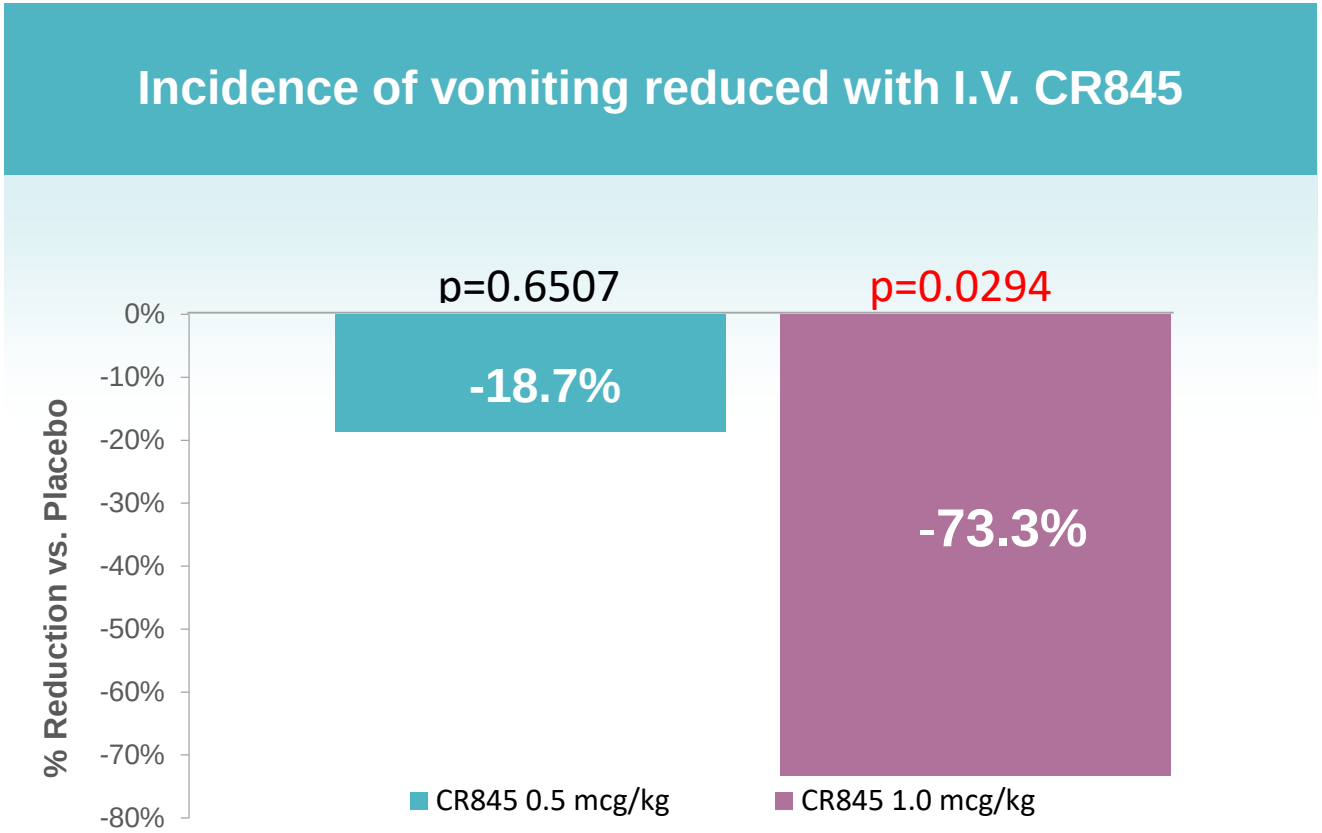
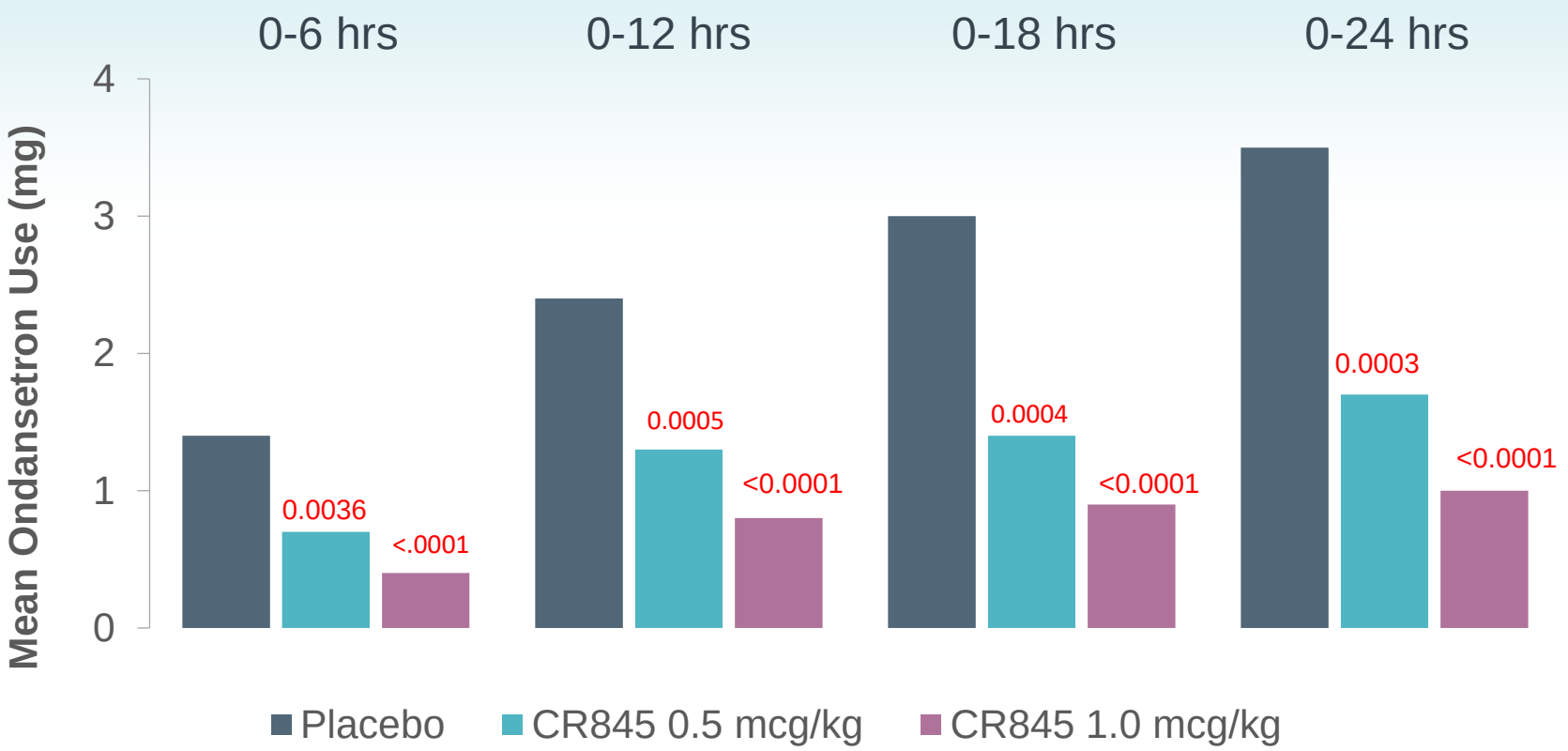
Incidence of Vomiting Over 24 Hrs: Secondary Endpoint



Mantel-Haenszel test stratified by surgery type based on Vollset et al (1991).

Mean Total Ondansetron Use (mg): 0-24 Hrs: Pre-Specified Endpoint

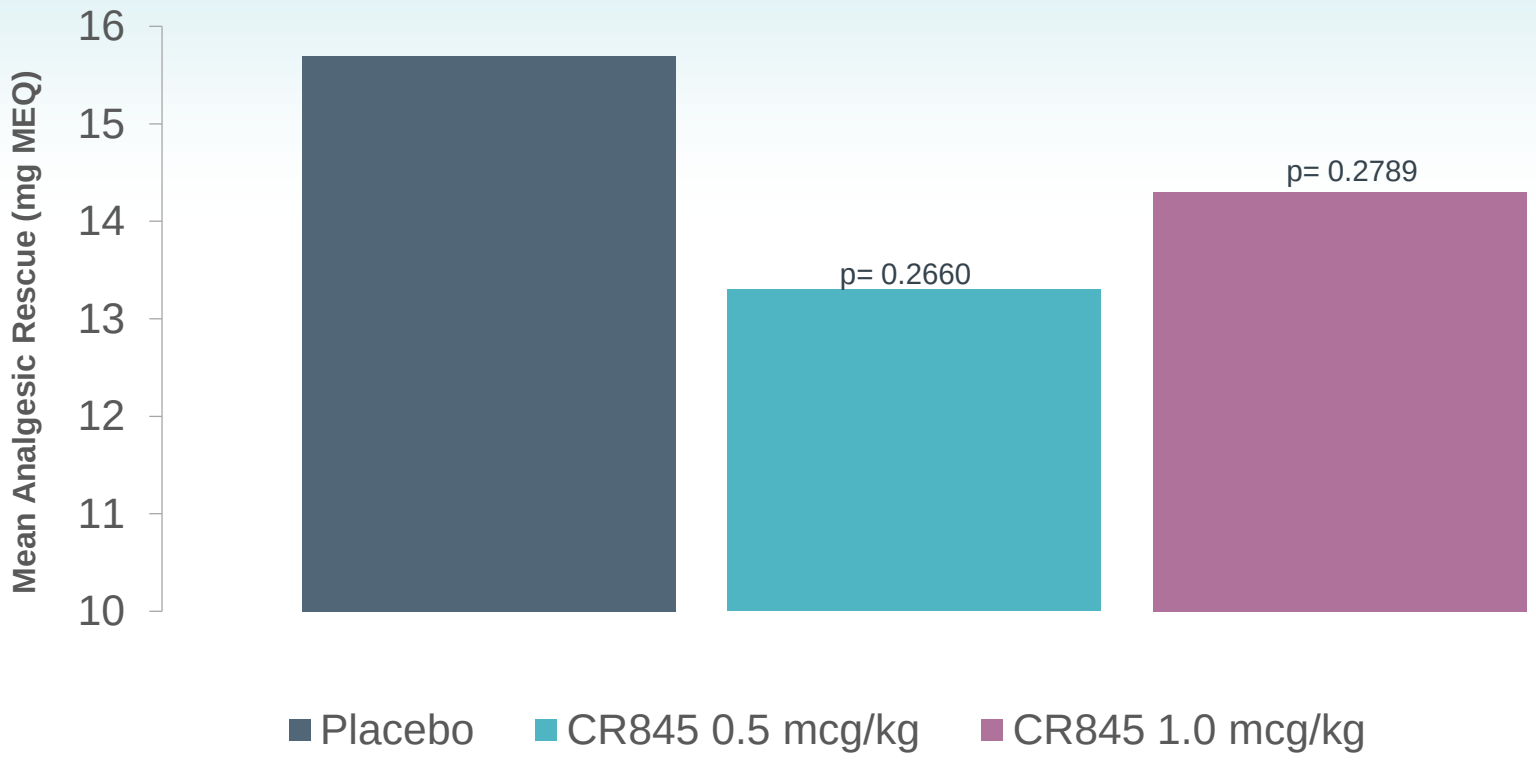
I.V. CR845 Reduced Additional Anti-Emetic Medication Use



Wilcoxon rank sum test stratified by surgery type
Patients who did not take anti-emetic medication (i.e ondansetron) were assigned a dose of 0 mg

Total Analgesic (Morphine) Rescue Use (mg MEQ)- 24 Hrs: Secondary Endpoint

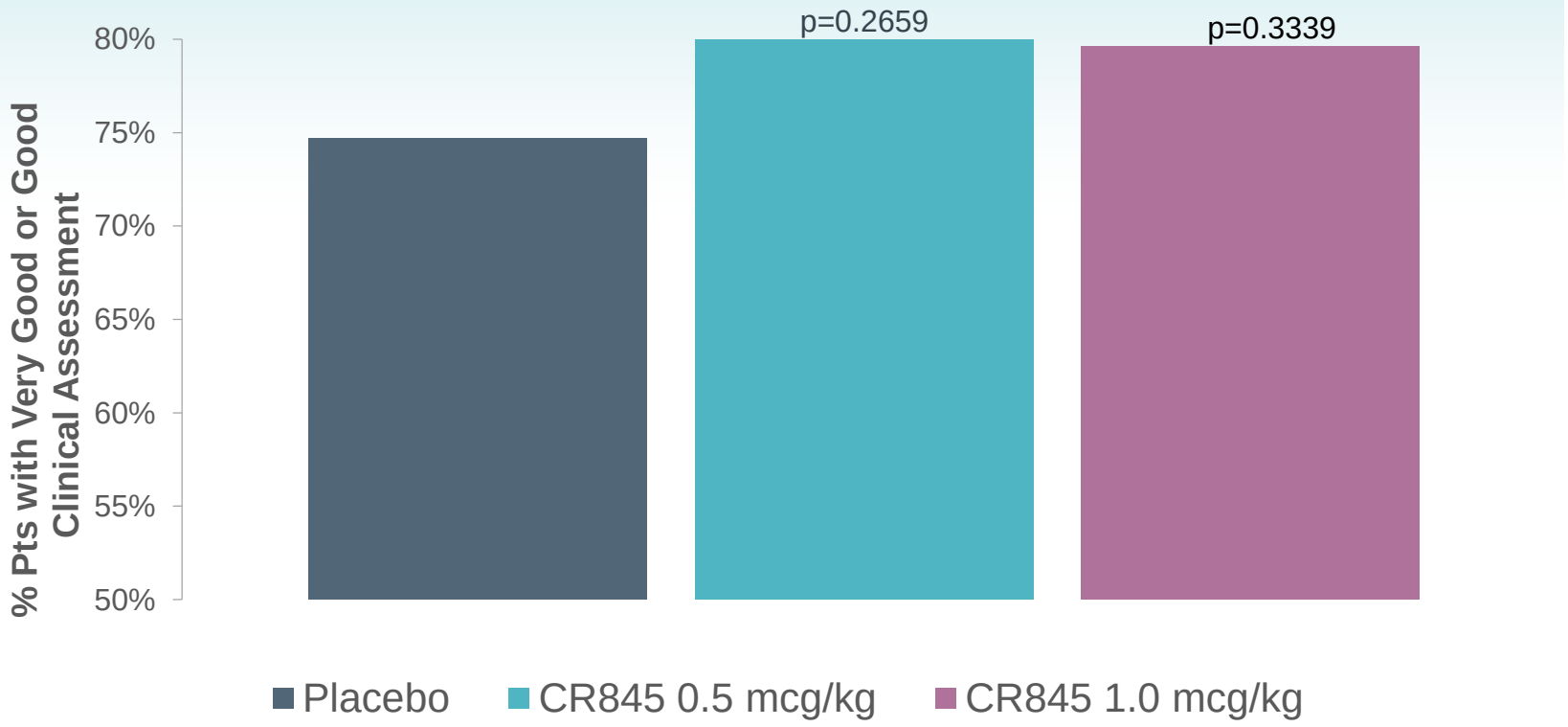
CR845 treatment groups showed trends towards lower rescue analgesic use within 24 hr post surgery



Wilcoxon rank sum test stratified by surgery type
Patients who did not take rescue medication were assigned a dose of 0 mg

Patient Global Assessment (PGA) at 24 hrs:
Secondary Endpoint

% of Patients with a 'Very Good' or 'Good' Clinical Assessment Higher in CR845 Treatment Groups But NS



Mantel-Haenszel test stratified by surgery type

Comparison of Adverse Events ≥ 5%

Adverse Event	Placebo (N=149)	CR845 0.5 mcg/kg (N=148)	CR845 1.0 mcg/kg (N=147)
Nausea	38.9%	29.1%	24.5%
Constipation	19.5%	14.9%	17.0%
Vomiting	11.4%	6.8%	4.1%
Flatulence	6.0%	8.1%	7.5%
Dyspepsia	4.7%	7.4%	8.2%
Pyrexia	4.7%	4.1%	5.4%
Headache	18.1%	15.5%	17.7%
Paraesthesia	0.7%	3.4%	5.4%
Pruritus	5.4%	5.4%	2.7%

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Serious Adverse Events (SAEs)

No SAEs Were Designated As Drug-Related

Adverse Event	Placebo (N=149)	CR845 0.5 mcg/kg (N=148)	CR845 1.0 mcg/kg (N=147)
At least 1 SAE	3 (2.0%)	1 (0.7%)	3 (2.0%)
Atrial Fibrillation	1 (0.7%)	0	0
Ileus	0	1 (0.7%)	0
Gastroenteritis	0	0	1 (0.7)%
Procedural Haemorrhage	0	0	1 (0.7%)
Ureteric Injury	1 (0.7%)	0	0
Hypoxia	1 (0.7%)	0	0
Pulmonary Embolism	0	0	1 (0.7%)

CR845 CLIN3001: Summary

- Met primary endpoint of AUC 0-24 hrs for pain relief at 1.0mcg/kg
  - Significant reductions in AUC (0-6) & AUC (0-12) for both 0.5 mcg/kg & 1.0 mcg/kg
- Met Secondary Endpoints:
  - Significant reduction in PONV impact scores (0.5 mcg/kg & 1.0 mcg/kg)
  - Significant reduction in incidence of vomiting (1mcg/kg)
- Incidence of adverse events generally low and similar between placebo and I.V. CR845 groups