# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 OR 15(d)**
**of The Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): June 27, 2018**

# CARA THERAPEUTICS, INC.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-36279** | **75-3175693** |
|---|---|---|
| **(State or other jurisdiction of incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| | |
|---|---|
| **4 Stamford Plaza**<br>**107 Elm Street, 9th Floor**<br>**Stamford, Connecticut** | **06902** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**Registrant's telephone number, including area code: (203) 406-3700**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2.):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

**Item 8.01 Other Information.**

On June 27, 2018, Cara Therapeutics, Inc. issued a press release announcing top-line data from its adaptive Phase 2/3 trial of I.V. CR845 in patients undergoing abdominal surgeries and held a conference call to discuss the results at 8:30 a.m. EDT on June 27, 2018. A copy of the press release and the presentation discussed on the conference call are attached as Exhibit 99.1 and Exhibit 99.2, respectively, to this Current Report on Form 8-K and are incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

| Exhibit No. | |
|---|---|
| 99.1 | Press release dated June 27, 2018. |
| 99.2 | Presentation dated June 27, 2018. |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**CARA THERAPEUTICS, INC.**

By: /s/ Mani Mohindru, Ph.D.
Mani Mohindru, Ph.D.
Chief Financial Officer
(Principal Financial and Accounting Officer)

Date: June 27, 2018

**Exhibit 99.1**

**Cara Therapeutics Reports Positive Top-Line Data from Adaptive Phase 2/3 Trial of I.V. CR845 in Patients Undergoing Abdominal Surgery**

*-I.V. CR845 achieved statistical significance for the study's primary endpoint of pain relief over the 0 to 24-hour (AUC 0-24) period post-surgery for combined surgeries at the 1.0 mcg/kg dose (p=0.032)-*

*-I.V. CR845 treatment resulted in statistically significant reductions in the secondary endpoint of incidence of nausea and vomiting at 24-hours post-surgery for both the 0.5 and 1.0 mcg doses (p=0.006; p<0.0001 respectively)-*

*-Cara to host conference call today at 8:30 a.m. EDT-*

**STAMFORD, Conn., June 27, 2018 –** Cara Therapeutics, Inc. (Nasdaq:CARA), a biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus and pain by selectively targeting peripheral kappa opioid receptors, today announced positive top-line data from the adaptive Phase 2/3 trial of I.V. CR845 in patients undergoing abdominal surgeries. At the 1.0 mcg/kg dose, I.V. CR845 demonstrated statistically significant reductions in pain intensity compared to placebo at all pre-specified post-operative periods of 0-6 hours (p=0.001); 0-12 hours (p=0.004); 0-18 hours (p=0.013); and 0-24 hours (p=0.032). Additionally, I.V. CR845 treatment resulted in statistically significant reductions in the incidence of post-operative nausea and vomiting over the 24-hour period post-surgery for both 0.5 and 1.0 mcg/kg doses (p=0.006; p<0.0001, respectively).

"We are very pleased that these data demonstrate the overall benefit of I.V. CR845 in both providing pain relief across surgery types up to 24 hours post-surgery and reducing post-operative nausea and vomiting, a significant medical need in the post-operative setting," said Derek Chalmers, Ph.D., D.Sc., President and Chief Executive Officer of Cara Therapeutics. "As there continues to be a critical need for new post-surgical analgesics like I.V. CR845 that lack abuse potential and traditional mu opioid side effects, we will be assessing all options, including discussions with regulators, as to how to best move this program forward."

"The current practice of perioperative pain management anchored around traditional opioids often results in frequent opioid-related adverse events, such as nausea and vomiting, which can be debilitating and delay patients' post-surgical recovery," said Sabry Ayad, M.D., Professor of Anesthesiology, Anesthesiology Institute, Cleveland Clinic and one of the study's investigators. "The ability of I.V. CR845, under standard of care conditions in the present trial, to provide not only additional pain relief but also a considerable decrease in the incidence and degree of post-operative nausea and vomiting underscores the potential of I.V. CR845 to provide meaningful clinical benefit in the immediate post-operative recovery period."

**Phase 2/3 Trial Design and Top-Line Data**

The adaptive Phase 2/3 trial was a randomized, double-blind, placebo-controlled trial designed to evaluate the analgesic efficacy and safety of two doses of I.V. CR845 (0.5 mcg/kg and 1.0 mcg/kg) versus placebo given at pre-specified intervals pre- and post-surgery in 444 patients undergoing abdominal surgery, composed of 228 patients who underwent ventral hernia surgery and 216 patients who completed a hysterectomy procedure. Patients received a 2X loading dose of I.V. CR845 pre-surgery and four additional doses given at 0, 6, 12 and 18 hours after surgery. The primary endpoint was pain relief as measured by Area Under the Curve (AUC) of the Numerical Rating Scale (NRS) pain intensity scores collected over the first 24-hour period after the baseline dose (0 hour) post-surgery for all combined surgeries. In addition to safety, the secondary endpoints included incidence of vomiting, improvement in impact scores of post-operative nausea and vomiting (PONV), reduction in use of rescue analgesic medication, as well as patient global assessment at 24 hours post baseline dose after surgery.

- I.V. CR845 achieved statistical significance for the primary endpoint of pain relief over 24 hours (AUC 0-24) post-surgery with the 1.0 mcg/kg dose versus placebo ($p=0.032$) and also demonstrated statistical significance across two additional pre-specified sensitivity analyses for pain relief ($p=0.040$ and $p=0.041$) for the same period post-surgery. The 0.5 mcg/kg dose did not achieve statistical significance over the 0-24 hour period ($p=0.076$). In addition, improvement in pain AUC was statistically significant for both the 0.5 and 1.0 mcg/kg doses over 0 to 6 hours ($p=0.041$, $p=0.001$) and 0 to 12 hours ($p=0.035$, $p=0.004$) periods and also statistically significant for the 1.0 mcg/kg dose over the 0 to 18-hour period ($p=0.013$) post-surgery.
- At 6 and 24 hours after baseline dose post-surgery, there were statistically significant improvements in PONV impact scores with both doses of I.V. CR845 compared to placebo: 0.5 mcg/kg (6 hrs.: $p=0.0072$, 24 hrs.: $p<0.006$) and 1.0 mcg/kg (6 hrs.: $p<0.0001$, 24 hrs.: $p<0.0001$).
- There were statistically significant differences between placebo and both doses of CR845 with respect to the total use of anti-emetic medication over the first 24 hours post-surgery (0.5 mcg/kg: $p=0.0003$; 1.0 mcg/kg: $p< 0.0001$). The percentage of patients who did not take any anti-emetic medication over 24 hours was 56% for placebo compared to 70% for CR845 0.5 mcg/kg and 81% for CR845 1.0 mcg/kg.
- There was a 73% reduction in the incidence of patient-reported vomiting in the group receiving the 1.0 mcg/kg dose versus placebo ($p=0.029$). Although the 0.5 mcg/kg also showed reduction in vomiting, it did not reach statistical significance.

- Both doses of I.V. CR845 exhibited numerical trends toward reduced use of rescue analgesic medication compared to placebo, but did not achieve statistical significance. There was no significant effect, compared to placebo, on patient's global assessment of medication for either dose of I.V. CR845 over the 24-hour period.
- Common adverse effects reported in the placebo and both I.V. CR845 groups were generally low and similar in incidence, and included nausea, constipation, vomiting, flatulence, headache and dyspepsia.

The full results of this trial will be presented at a future scientific or medical conference.

**Conference Call**

Cara management will host a conference call today at 8:30 a.m. EDT to discuss the data. To participate in the conference call, please dial (855) 445-2816 (domestic) or (484) 756-4300 (international) and refer to conference ID 3863718. A live webcast of the call can be accessed under "Events and Presentations" in the News & Investors section of the Company's website at www.CaraTherapeutics.com.

An archived webcast recording will be available on the Cara website beginning approximately two hours after the call.

**About Cara Therapeutics**

Cara Therapeutics is a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus and pain by selectively targeting peripheral kappa opioid receptors (KORs). Cara is developing a novel and proprietary class of product candidates, led by KORSUVA™ (CR845/difelikefalin), a first-in-class KOR agonist that targets the body's peripheral nervous system, as well as certain immune cells. In Phase 2 trials, KORSUVA injection has demonstrated statistically significant reductions in itch intensity and concomitant improvement in quality of life measures in hemodialysis patients with moderate-to-severe chronic kidney disease-associated pruritus (CKD-aP), and is currently being investigated in Phase 3 trials in hemodialysis patients with CKD-aP. Cara is partnered with Vifor Fresenius Medical Care Renal Pharma Ltd. (VFMCRP) to commercialize KORSUVA injection in dialysis patients with CKD-aP worldwide, excluding the U.S., Japan (Maruishi Pharma), and South Korea (CKD Pharma), and will promote KORSUVA injection, if approved, with VFMCRP in U.S. Fresenius Medical Care North America dialysis clinics under a profit share agreement. Additionally, CR845/difelikefalin has demonstrated efficacy in patients with moderate-to-severe pain, without inducing many of the undesirable side effects typically associated with currently available opioid pain therapeutics. Cara retains rights to all KORSUVA/ CR845 indications, excluding KORSUVA injection in dialysis patients with CKD-aP, worldwide, excluding Japan and South Korea.

The FDA has conditionally accepted KORSUVA™ as the trade name for difelikefalin injection. CR845/difelikefalin is an investigational drug product, and its safety and efficacy have not been fully evaluated by any regulatory authority.

**Forward-looking Statements**

Statements contained in this press release 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 expected future development of I.V. CR845 or 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.

###

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Exhibit 99.2

# 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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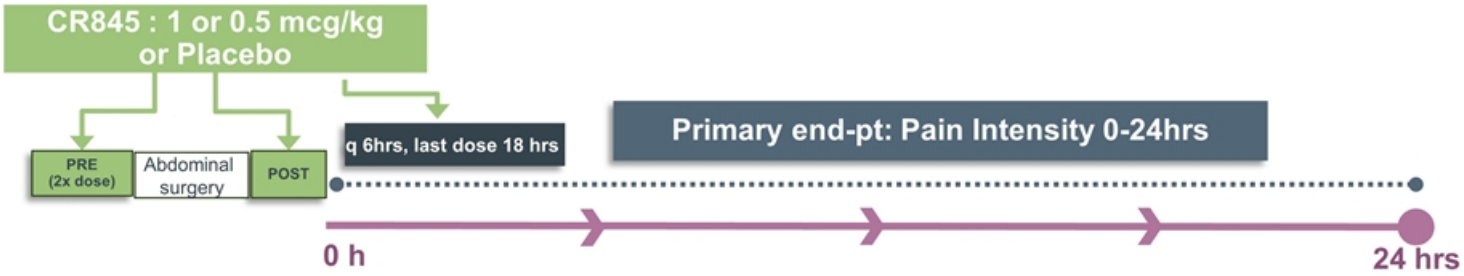
# Forward Looking Statements

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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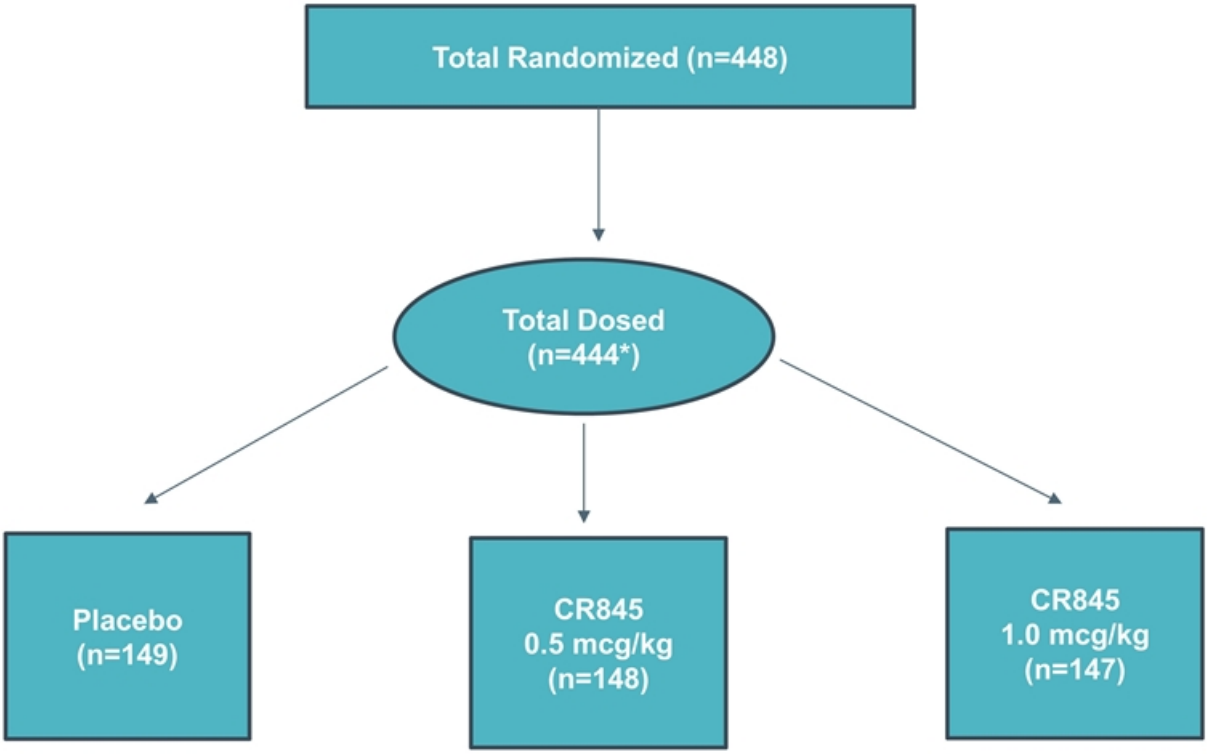
# CR845-CLIN3001: Subject Distribution




*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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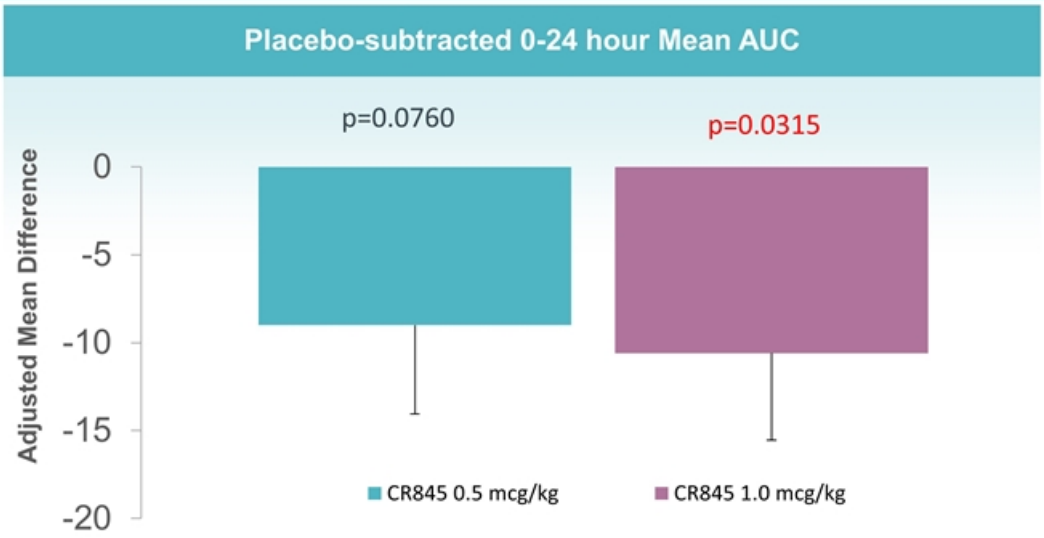
# 0-24 hour Pain AUC
## Primary Endpoint

**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



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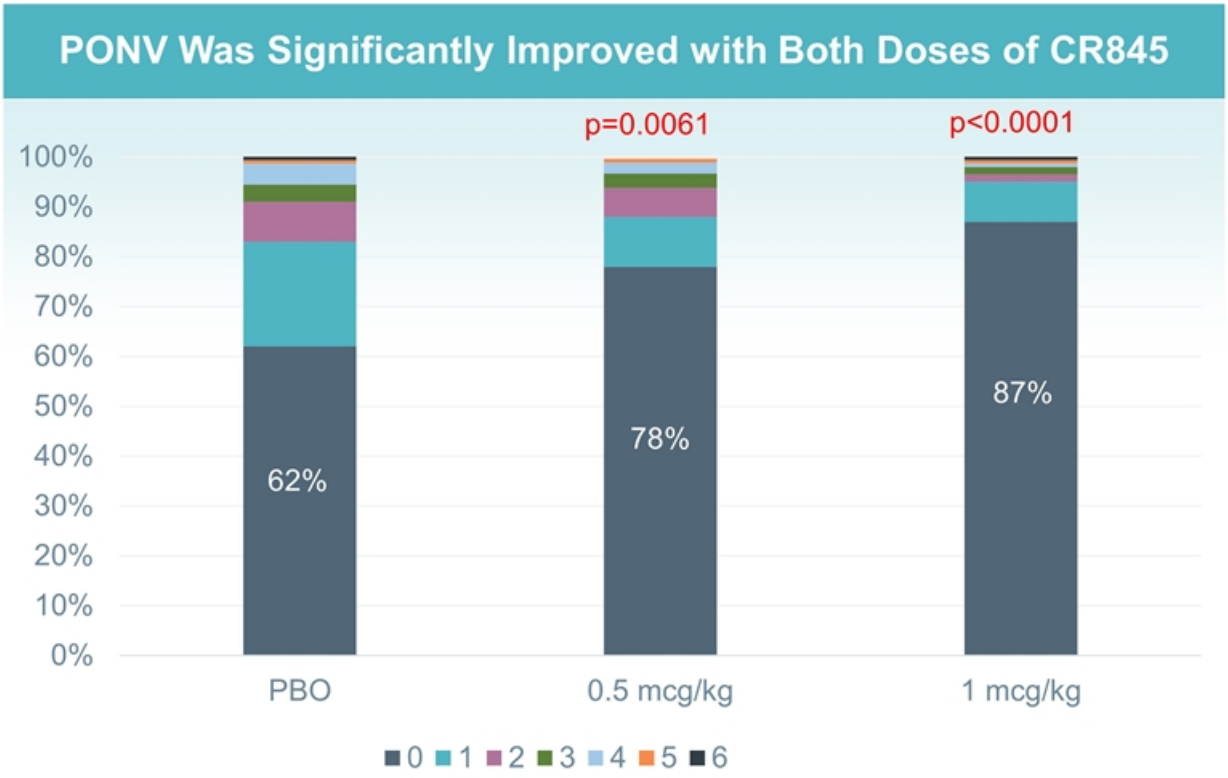
# PONV Impact Score at 24 Hrs:
## Secondary Endpoint




% 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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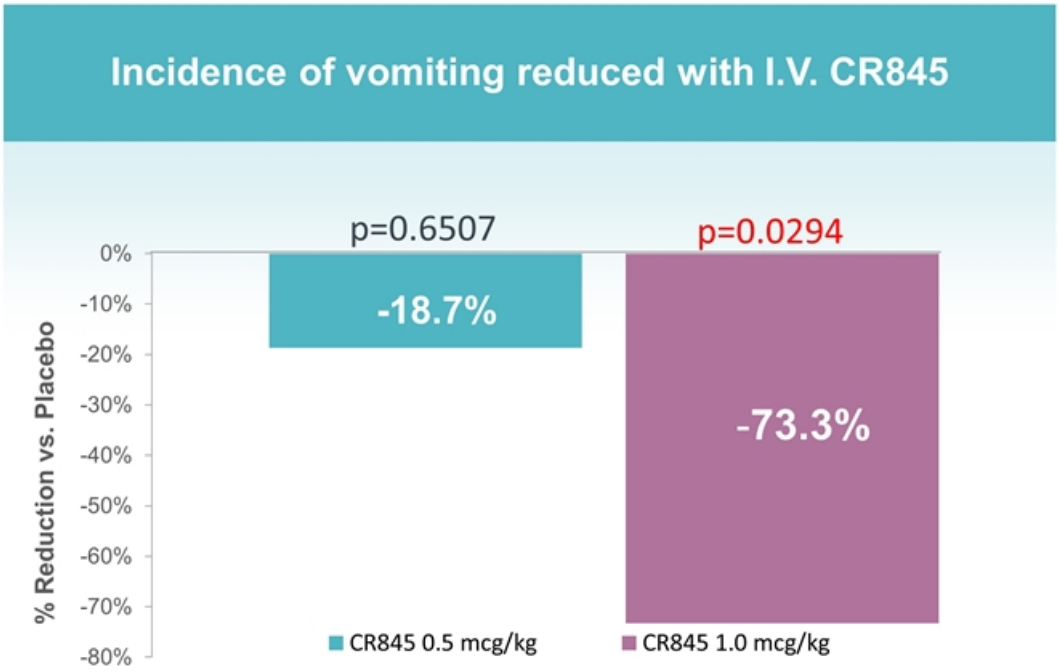
# Incidence of Vomiting Over 24 Hrs:
## Secondary Endpoint






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

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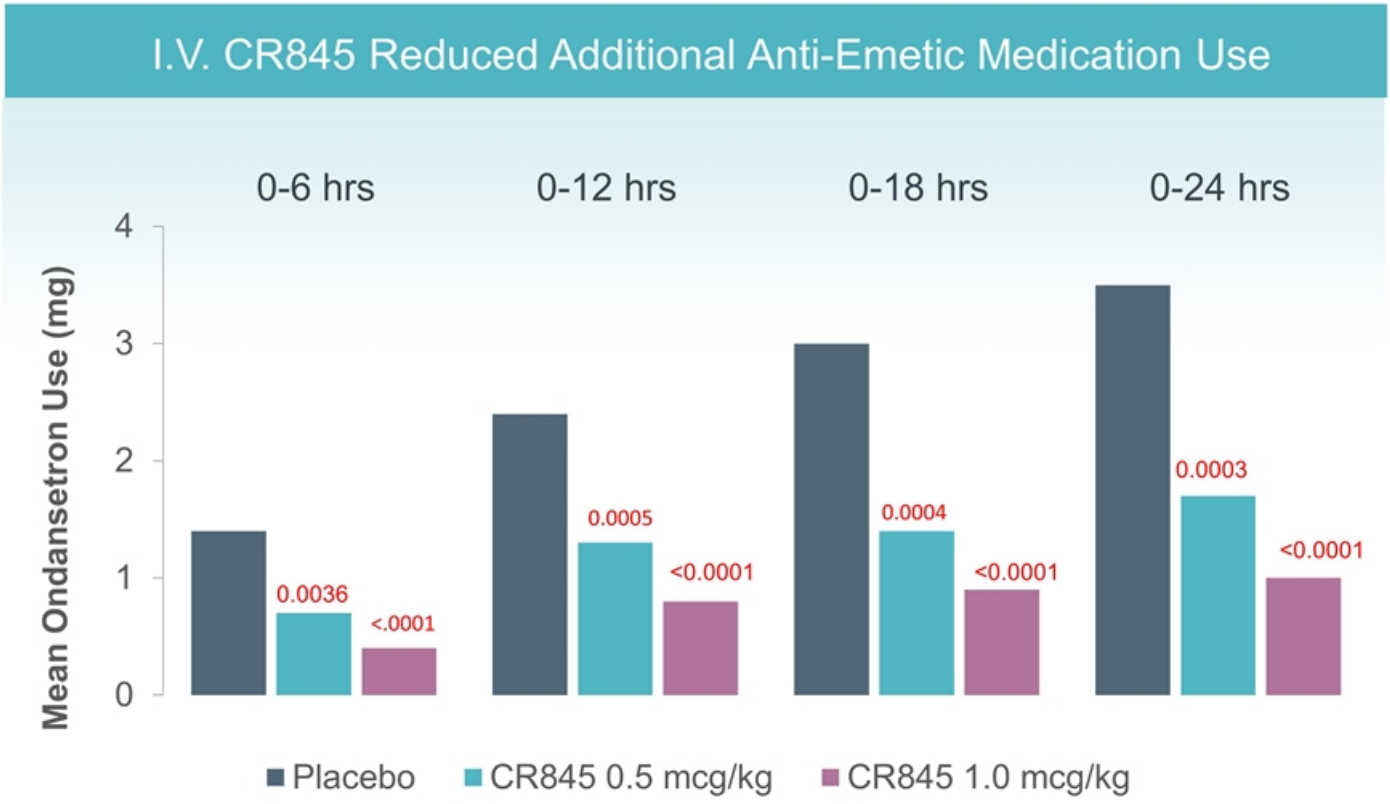
# Mean Total Ondansetron Use (mg): 0-24 Hrs: Pre-Specified Endpoint




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



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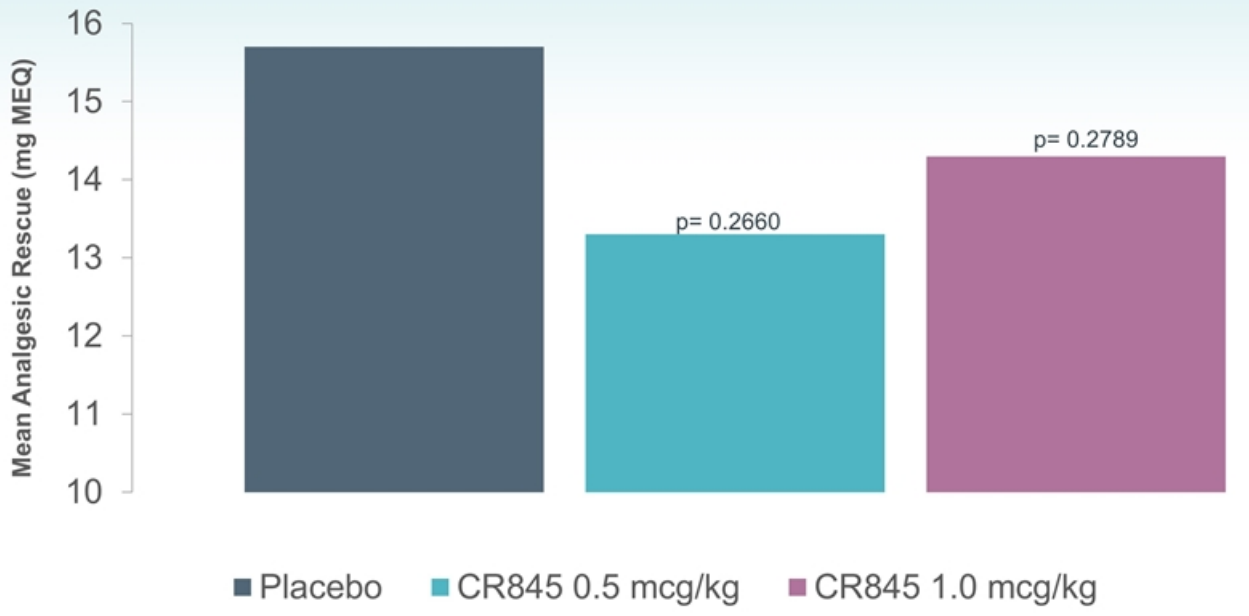
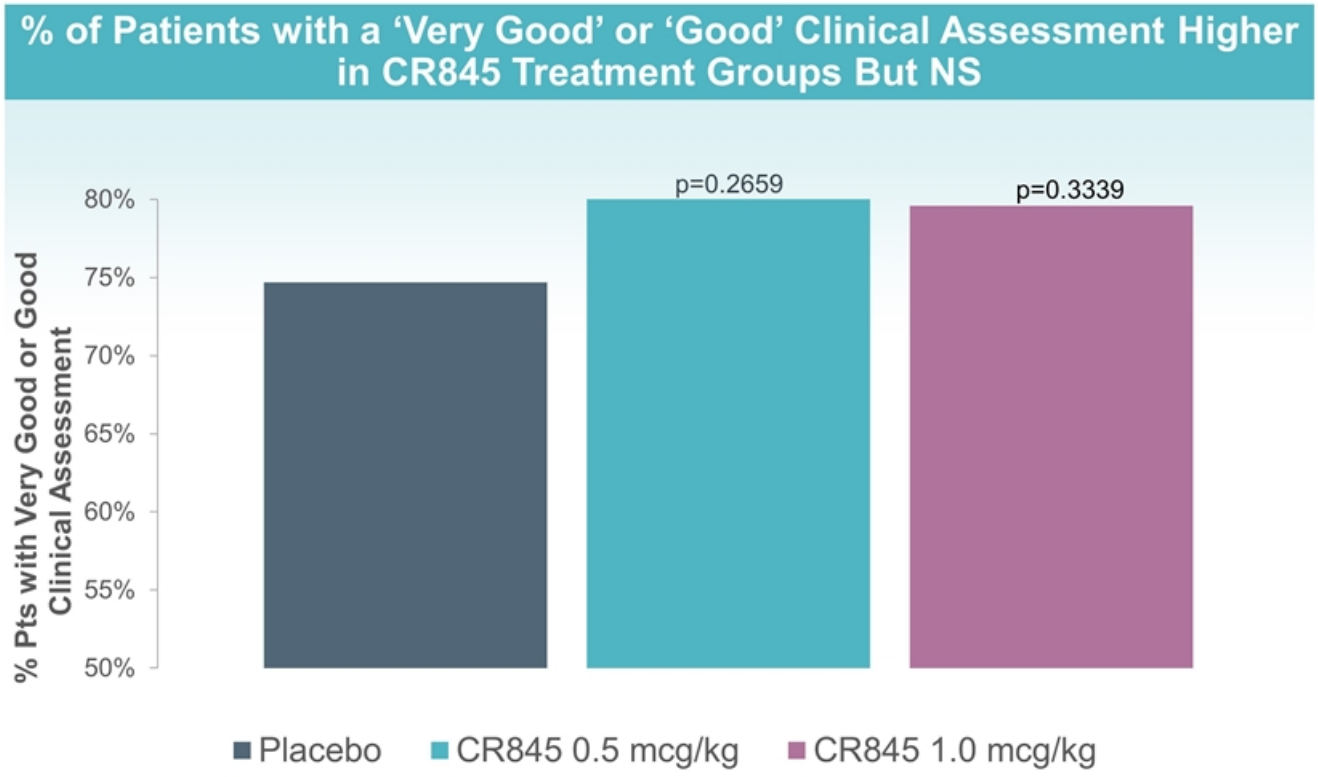
# Total Analgesic (Morphine) Rescue Use (mg MEQ)- 24 Hrs: Secondary Endpoint

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




11 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






Mantel-Haenszel test stratified by surgery type

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# 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%) |



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# 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



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