BACKGROUND

APOLLO-2: A Randomized, Placebo- and Active-Controlled Phase III Study Investigating Oliceridine (TRV130), a Novel μ Receptor G Protein Pathway Selective (μ-GPS) Modulator, for Management of Moderate to Severe Acute Pain Following Abdominoplasty

ER Viscusi1, F Skobieranda2, DG Soergel1, DA Burt3, TJ Gan4

1Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA; 2Trevena, Inc., King of Prussia, PA; 3Stony Brook University, Stony Brook, NY

• Intravenous (IV) opioids are the foundation of moderate to severe pain management in a hospital setting.
• Though conventional opioids provide effective analgesia, they are limited by a variety of opioid-related adverse events (OAREs), including respiratory depression and gastrointestinal intolerance.
• Conventional opioids bind μ receptors and activate 2 signaling pathways: the G protein pathway (providing analgesia) and the β arrestin pathway (associated with OAREs and induction of analgesia).1
• Oliceridine (TRV130) is a novel analgesic that acts as a receptor G protein pathway selective (μ-GPS) modulator which activates G protein signaling with decreased β-arrestin recruitment.
• Oliceridine, therefore, offers the potential for efficacious analgesia with improved tolerability and fewer OAREs.2
• In phase II studies, oliceridine produced rapid analgesia, with an improved safety/tolerability profile compared with morphine.
• APOLLO-2 is a randomized, placebo- and active-controlled, phase III study of oliceridine for moderate to severe pain following abdominoplasty.

METHODS

Patients with moderate to severe pain following surgery were randomized 1 to 5 of 1:2:2:2:2, 24-treatment arms (Table 1).

• Beginning 10 min after an initial clinician-administered IV loading dose, Beginning 10 min after an initial clinician-administered IV loading dose, Beginning 10 min after an initial clinician-administered IV loading dose, Beginning 10 min after an initial clinician-administered IV loading dose, a 6-minute lockout interval. Clinician-administered IV supplemental doses were permitted as often as needed.

Table 1. Treatment Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Morphine</th>
<th>Placebo</th>
<th>Oliceridine Regimen B</th>
<th>Oliceridine Regimen C</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>1.5 mg</td>
<td>0.5 mg</td>
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</tr>
<tr>
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<tr>
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</tbody>
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Secondary endpoints: treatment responders over time, use of rescue medication, and use of supplemental oxygen, use of antacids, and the occurrence of nausea and vomiting.

Analysis of the primary endpoint included a Hochberg adjustment for multiple endpoint comparisons on both unpeaked IV profiles.

RESULTS

Patient demographics were similar across treatment groups (Table 2).

Table 2. Patient Demographics

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• A post hoc analysis demonstrated that oliceridine regimen B was non-inferior to morphine in terms of the percentage of treatment responders at study endpoint (P=0.0123). Regimens A and C did not meet non-inferiority as morphine.
• Oliceridine demonstrated a rapid onset of efficacy as evidenced by the percentage of treatment responders at early time points (Figure 2).

Overall, oliceridine was generally well tolerated (Table 3), with few new treatment-emergent adverse events (TEAEs) associated with oliceridine versus placebo.

Table 3. Summary of Treatment-emergent Adverse Events

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Conclusions

• Overall, oliceridine was generally well tolerated (Table 3), with few new adverse events compared with placebo.
• Oliceridine demonstrated comparable efficacy and rapid onset of action compared with morphine.
• Oliceridine was generally well tolerated and demonstrated favorable safety and tolerability compared with morphine, particularly with respect to gastrointestinal tolerability compared with morphine.
• Overall these data demonstrate the efficacy and safety of oliceridine for the management of moderate to severe pain following abdominoplasty, an established, well-tolerated model of acute pain.

REFERENCES

4. Singla NK. (in development).

DISCLOSURES

This study was supported by Trevena, Inc., F Hoffmann-La Roche and a grant from Singla NK. Data and full treatment profiles are available from E. Viscusi and M. J. Goldsmith. Medical writing support was provided by Matt Westeyn, SHP, EMM, LLC. B. A. Sumiya and A. J. F. de Vries state they have nothing to declare.

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