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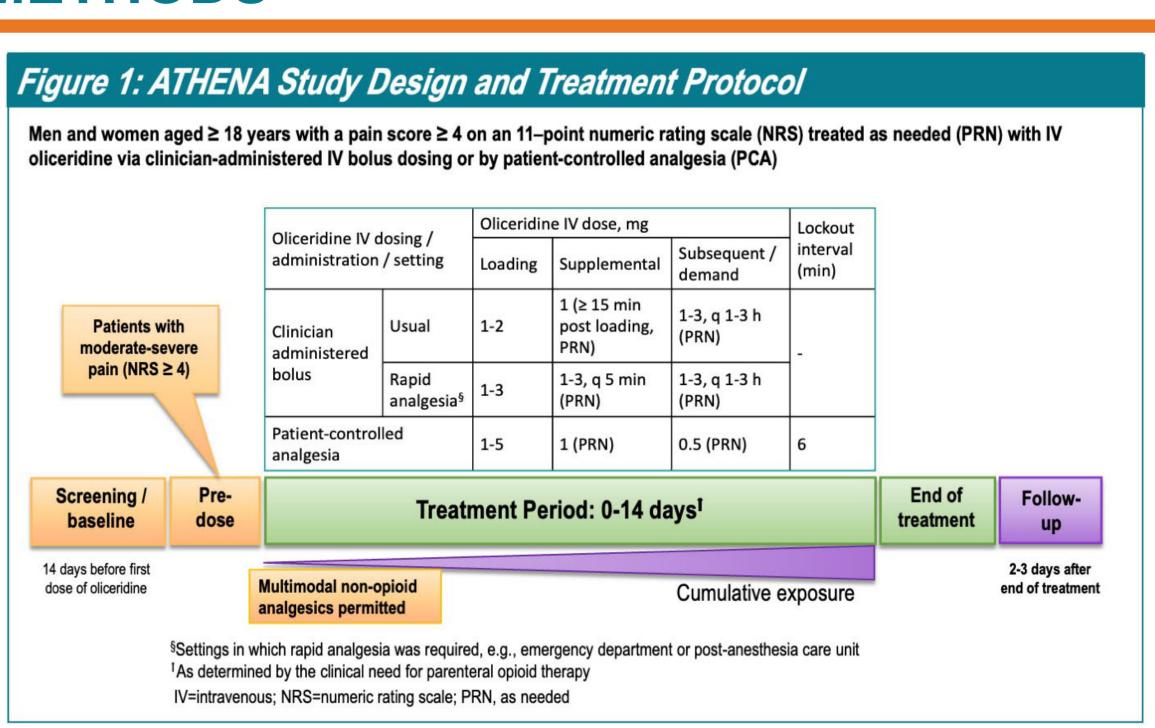




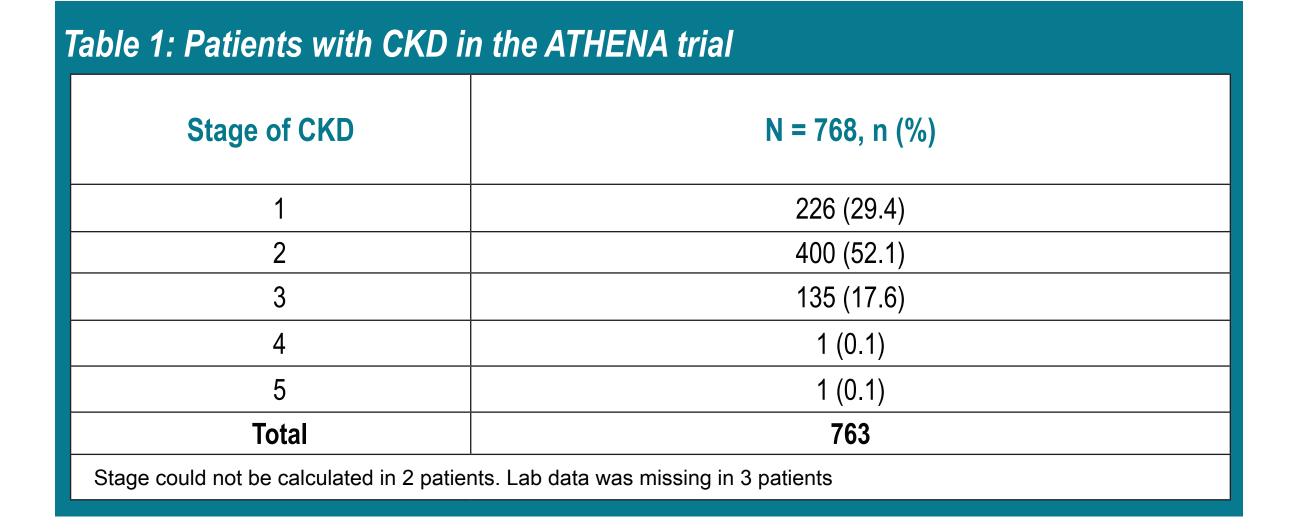
BACKGROUND

- Approximately 15% of the general population in the USA is estimated to have chronic kidney disease (CKD).¹
- In the postoperative setting, patients with CKD are at a high risk of developing serious opioid related adverse events (ORAEs).²
- Furthermore, as most opioids or their metabolites are excreted by the kidneys, dosage adjustment is often required when estimated glomerular filtration rate (eGFR) falls below 50 mL/min.³
- Oliceridine, a new class of IV opioids, that is a G protein-selective agonist at the mu-opioid receptor, was recently approved for use in adults for the management of acute pain severe enough to require an IV opioid analgesic and for whom alternative treatments are inadequate.⁴
- Preclinical findings showed that oliceridine is selective for G-protein signaling (achieving analgesia) with limited recruitment of β-arrestin (associated with ORAEs). The translation of these findings in humans has not been fully established.
- Oliceridine has no active metabolites and findings from a Phase 1 pharmacokinetic study suggest no requirement for dosage adjustment in patients with renal impairment.⁶
- Here we report the safety of oliceridine in patients with renal impairment from the Phase 3 ATHENA open-label, multicenter study.
- The use of opioids for patients with moderate to severe renal insufficiency (stage 3 CKD or higher) poses one of the largest concerns for clinicians.⁷
- Thus, for this report we combined the data for patients with stage 1 (eGFR ≥ 90 mL/min) or 2 CKD (eGFR 60 < 90 mL/min) and compared them with those of patients with stage 3 CKD (eGFR 30 < 60 mL/min).

METHODS



• ATHENA study included a total of 768 patients who received IV oliceridine for moderate to severe pain following a wide variety of surgeries or a medical condition. Based on calculated eGFR, the distribution of patients with CKD is shown in **Table 1**.



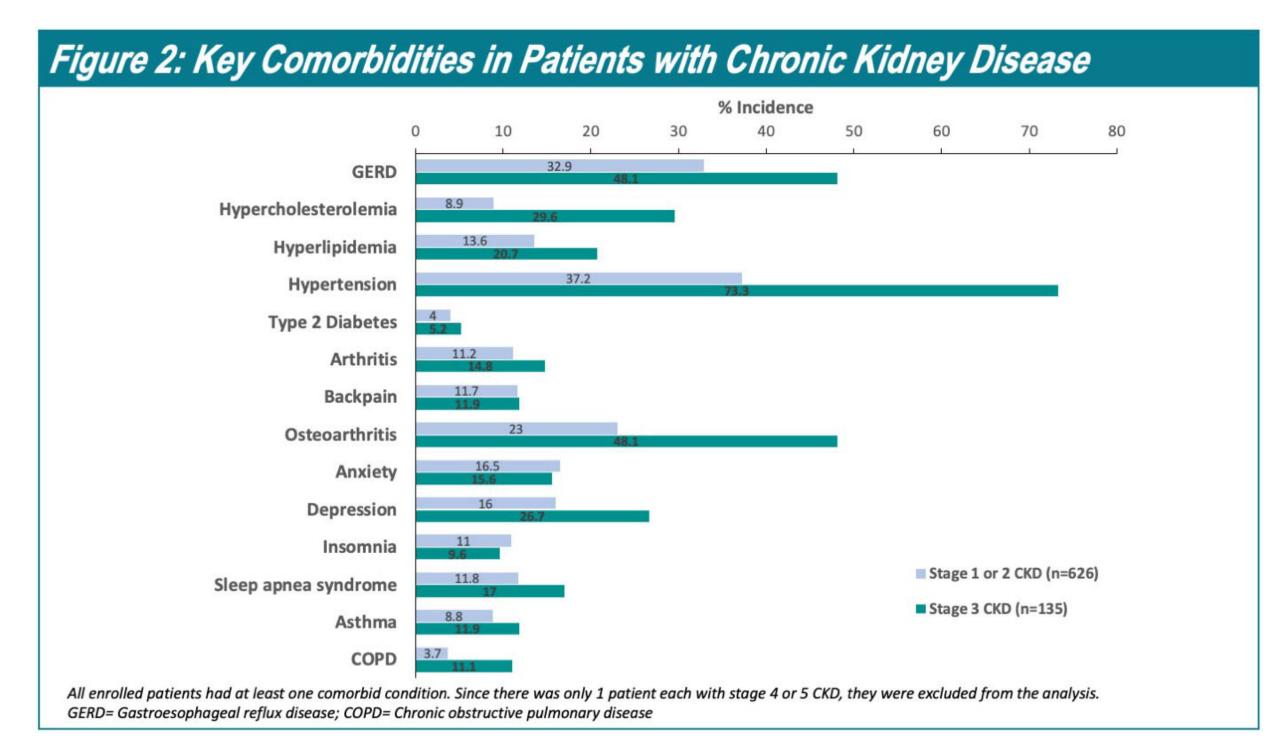
For this analysis:

- A total of 761 patients was included in the overall analysis (for the two patients with stage 4
 or 5 CKD, the adverse events are reported separately).
- The incidence of observed or self-reported adverse events (AEs), coded based on verbatim reported terms, using Medical Dictionary for Regulatory Activities (MedDRA, V19.0) is reported for patients with renal impairment at baseline.
- We also report opioid-induced respiratory depression (OIRD) defined by oxygen saturation (SpO₂) < 90% or respiratory rate (RR) < 10 bpm.

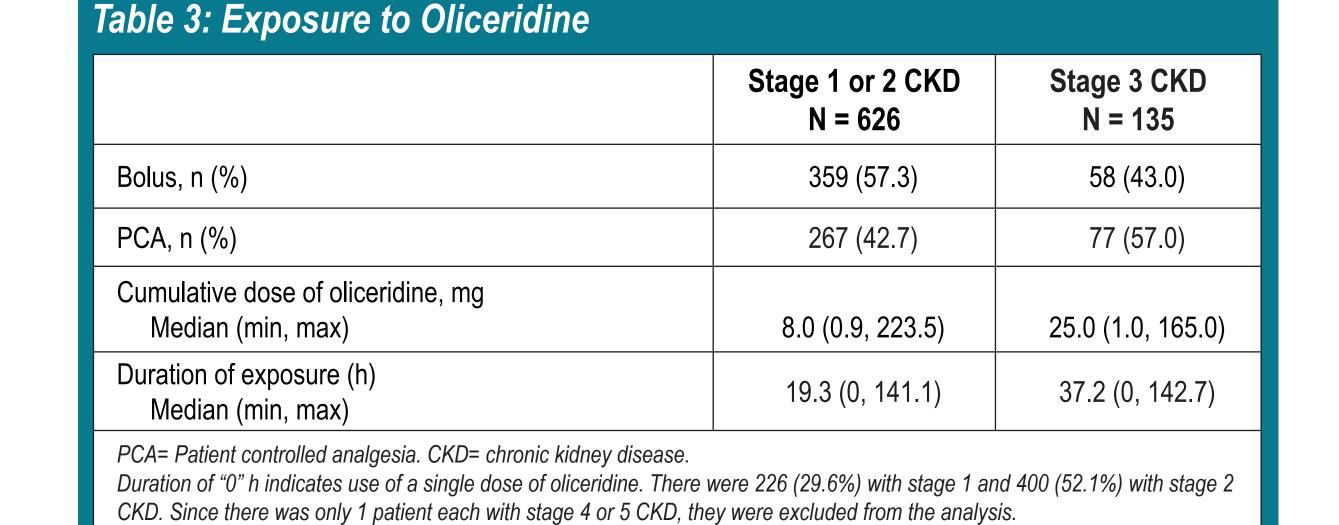
RESULTS

	Stage 1 or 2 CKD N = 626	Stage 3 CKD N = 135
Female, n (%)	404 (64.5)	90 (66.7)
Age, mean ± SD, years ≥ 65 to < 75 years, n (%) ≥ 75 years, n (%)	51.4 ± 15.8 125 (20.0) 35 (5.6)	66.3 ± 10.8 59 (43.7) 26 (19.3)
Race White, n (%) African American, n (%) Asian, n (%) Other, n (%)	470 (75.1) 127 (20.3) 13 (2.1) 16 (2.6)	123 (91.1) 10 (7.4) 0 2 (1.5)
BMI, mean ± SD, kg/m ²	30.3 ± 7.6	31.6 ± 6.4
BMI > 30 kg/m ²	266 (42.5)	78 (57.8)
Baseline NRS pain score, mean ± SD	6.3 ± 2.1	6.1 ± 2.1

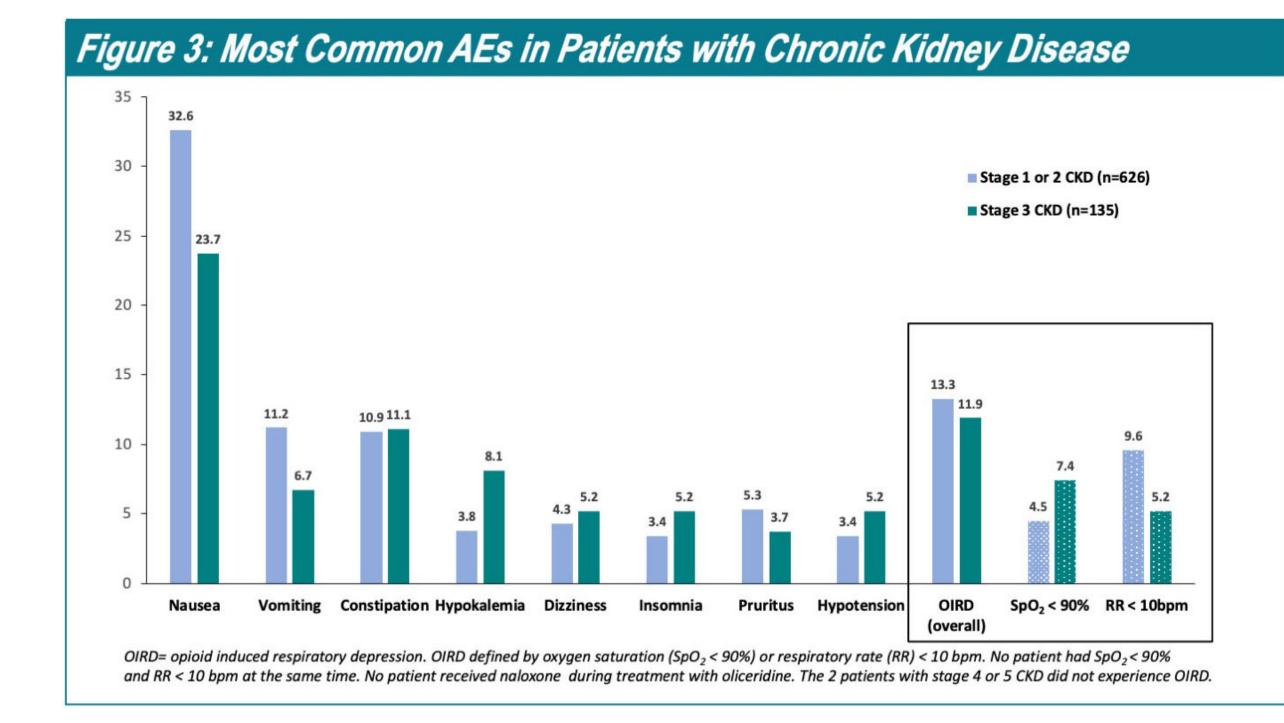
• The most common medical comorbidities are shown in **Figure 2**. The incidence of most comorbidities was numerically higher for the patients with stage 3 CKD.



• Almost half of all patients received oliceridine as a bolus injection; 57% of patients with stage 1 or 2 CKD and 43% of patients with stage 3 CKD (**Table 3**).



- The most common ORAEs were nausea, vomiting, constipation, hypokalemia, dizziness, insomnia, pruritus and hypotension. The incidence of ORAEs was comparable in the two CKD groups (**Figure 3**).
- The two patients with stage 4 or stage 5 CKD reported constipation, nausea or hypokalemia that were of mild intensity. Both of these patients did not experience OIRD.
- No patients received naloxone during treatment with oliceridine.



CONCLUSIONS

- Use of IV oliceridine, did not increase the risk of ORAEs or OIRD in patients with stage 3 or higher CKD compared to those with stage 1 or 2 in this cohort.
- Use of IV oliceridine for moderate to severe acute pain may be clinically appropriate in patients with renal impairment.

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ACKNOWLEDGEMENTS

Layout for the poster was provided by Innovation Communications Group.