NALOXEGOL AND NALDEMEDINE IN THE TREATMENT OF PERSISTENT OPIOID INDUCED CONSTIPATION (OIC) IN PATIENTS WITH CANCER PAIN: A SYSTEMATIC REVIEW

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Introduction

- Opioid-induced Constipation (OIC) has been a major cause of distress in patients treated with opioids for cancer pain. Numerous drugs have been studied so far to manage refractory OIC. Naloxegol (NKTR-118), a pegylated form of naloxone, and Naldemedine, a peripherally acting u-opioid receptor antagonist (PAMORA), have shown to alleviate OIC without affecting central analgesia. We study here the efficacy and safety of Naloxegol and Naldemedine in the treatment of OIC - both in clinical trials and in real-world clinical practice

Methods

PROCESS

01 Following the PRISMA guideline, we performed a comprehensive literature search PubMed, Embase, Cochrane Library, Web of Science, and Clinicaltrials.gov.

IDEA

02 A total of 9 studies assessing the use of Naloxegol and Naldemedine in patients with cancer pain

DATA ANALYSIS

03 STATA version 3.2 was used for data analysis.

Results

Of the 397 studies that were identified by our database search, 9 studies were found to be relevant and met the inclusion criteria. Five studies (three RCT and 2 observational), and four observational studies were included for the assessment of Naldemedine and Naloxegol efficacy respectively.

Results

A total of 953 OIC cancer patients were treated with Naldemedine, and the response rate for Spontaneous Bowel Movements (SBM) is 72 % (95 % CI, p = 0.004). The most common adverse events were diarrhea, abdominal pain, and abdominal bloating. A significant improvement in Quality-of-life scales such as PAC-SYM and PAC-QOL was also reported. A total of 570 patients from four observational studies treated with Naloxegol were included in our review. In all these studies there was a significant improvement in Bowel Function and Quality of Life after adding Naloxegol despite a poor performance status of the participant. The most common adverse events in the Naloxegol group leading to drug discontinuation was diarrhea, and abdominal pain, dysesthesia.

Author & Year	Type of Study	Participants assessed for efficacy (n)	Male n (%)	Follow up period	Spontaneous bowel movements responder RATES (%)	Any Adverse effects N (%)
Naldemedine						
Katakami, 2017	Phase IIb RCT	225, Nal- 169, P- 56	Nal- 100 (69%), P - 34 (60%)	2 weeks	Nal- 122 (72%), P- 21 (37.5%)	Nal- 120 (71%), P - 29 (52%)
Katakami, 2017	Phase III RCT	193, Nal- 97, P- 96	Nal- 59 (61%), P - 60 (62.5%)	2 weeks	Nal- 69 (71%), P- 33 (34%)	Nal- 43 (44%), P - 25 (26%)
Katakami 2017	Open label extension study	Nal- 131	Nal- 74 (56.5%)	12 weeks	NA	Nal- 105 (80%)
Hiruta, 2021	Multicenter Retrospective study	255	Nal- 179 (60.5%)	NA	Nal- 235 (79%)	204 (69%)
Nishiba, 2022	Multicenter Retrospective study	149	Nal- 89 (60%)	NA	Nal- 98 (66%)	116 (78%)
Naloxegol						
Cobo Dols, 2021	Prospective study	126	74(59%)	12 m	98/126 (77.8%	19 (15%)
Lemaire, 2021	Non interventional follow-up study	124	117 (63.2%)	1 m	79 (73.4%)	43 (32.8%)
Ostan, 2021	Observational study	150	77(51.3%)	1 m	NA	51 (33%)
Davies, 2022	Observational study	170, assessed for efficacy - 143, assessed for safety - 170 Group I - 76, Group II - 98	65 (45%)	1 m	Group I 55(72%), Group II 74(75.5%)	89/170 (52.4%)

Naldemedine had a response rate of Spontaneous Bowel Movements (SBM) is 72%

Naloxegol had a response rate (SBM) of 55%

Discussion & Conclusion

Our results suggest that Naloxegol and Naldemedine are safe and effective in the treatment of refractory OIC. More randomized clinical trials are needed to further assess their safety and efficacy in the treatment of OIC in the treatment of cancer pain. This review is significant in terms that it includes the data from first prospective study of its kind and small retrospective studies regarding Naloxegol. The lack of control group and a placebo arm warrants more studies to measure the placebo effect. However, the randomized control trials employing Naldemedine had efficacious and safer profile than placebo which is promising in the treatment of OIC with cancer pain