

Original article

Safety and efficacy of oxycodone/naloxone vs. oxycodone vs. morphine for the treatment of chronic low back pain: results of a 12 week prospective, randomized, open-label blinded endpoint streamlined study with prolonged-release preparations

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Abstract
Background:

Opioid-induced constipation (OIC) is the most prevalent patient complaint associated with opioid use and interferes with analgesic efficacy.

Objectives:

This PROBE trial compares the overall safety and tolerability of oxycodone/naloxone (OXN) with those of traditional opioid therapy with oxycodone (OXY) or morphine (MOR) in the setting of the German healthcare system.

Research design and methods:

This was a prospective, randomized, open-label, blinded endpoint (PROBE) streamlined study (German pain study registry: 2012-0012-05; EudraCT: 2012-001317-16), carried out in 88 centers in Germany, where a total of 453 patients, requiring WHO step III opioids to treat low back pain, were randomized to OXN, OXY or MOR (1:1:1) for 3 months. The primary outcome was the percentage of patients without adverse event-related study discontinuations who presented with a combination of a $\geq 50\%$ improvement of pain intensity, disability and quality-of-life and a $\leq 50\%$ worsening of bowel function at study end.

Results:

Significantly more OXN patients met the primary endpoint (22.2%) vs. OXY (9.3%; OR: 2.80; $p < 0.001$) vs. MOR (6.3%; OR: 4.23; $p < 0.001$), with insignificant differences between OXY vs. MOR ($p = 0.155$). A $\geq 50\%$ improvement of pain intensity, functional disability and quality-of-life has been found for OXN in 75.0/61.1/66.0% of patients and thus for all parameters significantly more than with OXY (58.9/49.0/48.3; $p < 0.001$ for each) or MOR (52.5/46.2/37.3; $p < 0.001$ for each). A total of 86.8% of OXN patients kept normal BFI scores during treatment, vs. 63.6% for OXY ($p < 0.001$) vs. 53.8% for MOR ($p < 0.001$). Overall 189 TEAEs (OXN: 45, OXY: 69, MOR: 75) in 92 patients (OXN: 21, OXY: 44, MOR: 37) occurred, most gastrointestinal (50.8%). One limitation is the open-label design, which presents the possibility of interpretive bias.

Conclusion:

Under the conditions of this PROBE design, OXN was associated with a significantly better tolerability, a lower risk of OIC and a significantly better analgesic efficacy than OXY or MOR.