Nabiximols for Opioid-Treated Cancer Patients With Poorly-Controlled Chronic Pain: A Randomized, Placebo-Controlled, Graded-Dose Trial

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Reference: Russell K. Portenoy, Elena Doina Ganae-Motan, Silvia Allende, Ronald Yanagihara, Lauren Shaiova, Sharon Weinstein, Robert McQuade, Stephen Wright, and Marie T. Fallon
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Abstract:

Background: Patients with advanced cancer who have pain that responds poorly to opioid therapy pose a clinical challenge. Nabiximols (Nabiximols is the US Adopted Name [USAN] for Sativex [GW Pharma Ltd, Wiltshire, UK], which does not yet have an INN), a novel cannabinoid formulation, is undergoing investigation as add-on therapy for this population.

Methods: In a randomized, double-blind, placebo-controlled, graded-dose study, patients with advanced cancer and opioid-refractory pain received placebo or nabiximols at a low dose (1–4 sprays/day), medium dose (6–10 sprays/day), or high dose (11–16 sprays/day). Average pain, worst pain and sleep disruption were measured daily during 5 weeks of treatment; other questionnaires measured quality of life and mood.

Results: A total of 360 patients were randomized; 263 completed.
There were no baseline differences across groups. The 30% responder rate primary analysis was not significant for nabiximols versus placebo (overall P = .59). A secondary continuous responder analysis of average daily pain from baseline to end of study demonstrated that the proportion of patients reporting analgesia was greater for nabiximols than placebo overall (P = .035), and specifically in the low-dose (P = .008) and medium-dose (P = .039) groups. In the low-dose group, results were similar for mean average pain (P = .006), mean worst pain (P = .011), and mean sleep disruption (P = .003). Other questionnaires showed no significant group differences. Adverse events were dose-related and only the high-dose group compared unfavorably with placebo.

Conclusions: This study supports the efficacy and safety of nabiximols at the 2 lower-dose levels and provides important dose information for future trials.
In perspective, nabiximols, a novel cannabinoid formulation, may be a useful add-on analgesic for patients with opioid-refractory cancer pain. A randomized, double-blind, placebo-controlled, graded-dose study demonstrated efficacy and safety at low and medium doses.

Strengths:

1- Multi center trial
2- Randomized, double blind, placebo controlled
3- Graded dose study
4- Focused study on specific group of patients. Since there is not that much of data in terms of synergic effects of opioids and cannabinoids in dose titration in cancer patients, this study gives us some information in this regard.

Weaknesses:

1- Since reducing the scheduled opioid dose was not allowed in this study the potential of opioid sparing effect following the addition of nabixomols could not be assessed.
2- Forced dose titration design
3- Many drop outs due to complicated design of the study.
4- Supported by pharmaceutical company
5- Selection bias, complicated inclusion criteria

Relevance to Palliative Care:

Treatment of neuropathic pain and pain unresponsive to opioids is a challenge in palliative care for cancer patients. Adding cannabinoids might be considered as adjuvant therapy for some of these patients and might cause some improvement in pain control and hence quality of life in this group of patients.