Original Article

A Report on the Long-Term Use of Fentanyl Pectin Nasal Spray in Patients With Recurrent Breakthrough Pain

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Abstract

Context. As patients with cancer are living longer, there is a need to ensure that treatments used for palliative care are well tolerated and effective during long-term use.

Objectives. To investigate the long-term use of fentanyl pectin nasal spray (FPNS) for the treatment of breakthrough pain in cancer (BTPc) in patients receiving regular opioid therapy.

Methods. Adult patients ($N = 401$) taking at least 60 mg/day oral morphine or equivalent, experiencing one to four episodes of BTPc a day, entered an open-label long-term study (NCT00458510). Patients had either completed an FPNS randomized controlled trial or were newly identified. Of these, 171 patients continued into an extension study. Up to four episodes of BTPc a day were treated with FPNS at 100–800 μg titrated doses. During the extension study, patients visited the clinic every four weeks for assessment and reporting of adverse events (AEs).

Results. There were 163 patients with documented FPNS use. The mean duration of use was 325 days; 46 patients used FPNS for ≥360 days; the maximum duration was 44 months. Seventy percent of patients did not change their FPNS dose; 2% of patients withdrew from the study because of the lack of efficacy. The most common AEs, aside from disease progression, were insomnia, 9.9%; nausea, 9.4%; vomiting, 9.4%; and peripheral edema, 9.4%. The overall incidence of FPNS-related AEs was 11.1%, the most common being constipation (4.1%), with no apparent dose relationship. Ten patients (5.8%) experienced nasal AEs, most of which were mild or moderate.

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Conclusion. FPNS appeared to provide sustained benefit and was well tolerated during long-term treatment of BTPc. J Pain Symptom Manage 2014;47:1001−1007.

Key Words
Breakthrough, cancer, fentanyl, FPNS, long-term, palliative care, pain

Introduction

As a result of the advances that have been made in cancer therapies over the last few decades, patients with cancer are living longer, with 50%−65% of patients living for at least two years after diagnosis.[1−3] This, coupled with recommendations that palliative care interventions should be introduced earlier in the course of the disease, has created the need for treatments that can successfully manage symptoms over a prolonged period of time.[1,2,4]

A key component of palliative care is pain management. Analgesic regimens need to have a sustained long-term efficacy with a good safety and tolerability profile; this will facilitate patient adherence and enable patients to benefit from such interventions for as long as possible.[5] It is important to consider analgesics that are being used chronically to treat around-the-clock pain and those being used to manage breakthrough pain in cancer (BTPc), an acute episode of pain with a rapid onset, sharp intensity, and short duration.[6]

Fentanyl pectin nasal spray (FPNS), an opioid analgesic, was developed to control the absorption profile of fentanyl across the nasal mucosa and deliver fentanyl with a concentration-time relationship mirroring the time course of a typical BTPc episode.[7] When administered via the nasal route, the pectin in FPNS forms a gel on contact with the calcium ions present in the nasal mucosa. This gel formation helps to sustain the contact of fentanyl with the nasal mucosa and prevents run off (dripping) or swallowing of the solution, allowing for rapid absorption and onset of action within minutes.[7−10] FPNS was shown to be effective and well tolerated, with a good safety profile, for the treatment of BTPc in two double-blind studies (NCT00459277 and NCT00589823) and a 16-week open-label study (NCT00458510).[7,8,11−15] Herein, we report the results from the extension of the initial open-label study that investigated the long-term use of FPNS in the treatment of patients with BTPc.

Methods

Study Design

This was a long-term extension of a multicenter, open-label, 16-week study in patients with BTPc receiving regular background opioid therapy (Study 045; NCT00458510).[7,15] Patients entering the initial 16-week study had either completed a randomized controlled study with FPNS (Study 043, NCT00459277 and Study 044, NCT00589823) or were newly identified. The original 16-week study began in January 2007 and the extension continued until November 2011; it was conducted at 45 centers worldwide in Argentina, Costa Rica, Czech Republic, The Netherlands, France, Spain, Germany, India, Italy, Poland, and the U.S. The study was conducted in accordance with the International Conference on Harmonisation guidelines on Good Clinical Practice and the Declaration of Helsinki 2000. The clinical study protocol was approved by the appropriate Institutional Review Board/Independent Ethics Committee at each site, and all patients provided written informed consent.

Patients

Patients eligible to enter the extension study were those who had completed the initial 16-week study and were deemed (by the study investigators) suitable to continue FPNS treatment. All patients were adults who were taking at least 60 mg oral morphine/day, or equivalent, to manage background cancer pain, yet continued to experience one to four episodes of moderate-to-severe BTPc a day.[7,15]