

Long-term safety of fentanyl sublingual spray in opioid-tolerant patients with breakthrough cancer pain

Presented by: Jasdeep Gill February 9, 2016

Authors: Minkowitz H, Bull J, Brownlow RC, Parikh N, Rauck R.

Abstract: The current study assessed the long-term safety of fentanyl sublingual spray for managing breakthrough cancer pain (BTCP).

This open-label, multicenter study enrolled both de novo and rollover patients who completed a double-blind, efficacy trial. Eligible patients were ≥ 18 years of age and experiencing pain that was being managed with an around-the-clock opioid yet were experiencing ≤ 4 BTCP episodes daily and were opioid-tolerant (i.e., receiving ≥ 60 mg/day oral morphine or an equivalent dose of another opioid for ≥ 1 week). De novo patients initially entered a 21-day titration period to identify an effective dose of fentanyl sublingual spray (100–1600 μg), then entered a 90-day maintenance period. The incidence of adverse events (AEs), results of laboratory tests, vital sign assessments, and treatment satisfaction were assessed.

Of the 269 patients (de novo, 179; rollover, 90) who entered the maintenance period, 163 (60.6 %) completed the study; the primary reason for discontinuation was an AE (22.3 %). Eighty percent of patients identified an effective dose of fentanyl sublingual spray (median dose, 600 μg). The most common AEs differed from the titration period (nausea (13 %), vomiting (12 %), and somnolence (10 %)) to the maintenance period (malignant neoplasm progression (24 %), vomiting (16 %), and peripheral edema (12 %)). Few changes in laboratory parameters and vital sign assessments were observed. Patients generally reported being more satisfied with fentanyl sublingual spray than with their previous BTCP treatment.

This long-term maintenance study demonstrated that fentanyl sublingual spray was generally safe and well tolerated for managing BTCP over a 90-day period. *Supportive Care in Cancer June 2016, Volume 24, Issue 6, pp 2669–2675*

Strengths- Double-blind study. Safety protocol dictated that 4 or less BTP episodes included in study and dosing of fentanyl had to be 4 hrs apart. Patients who withdrew early had a final visit to collect data via a Treatment Satisfaction Questionnaire for Medication. All adverse events were catalogued with respect to how likely they were caused by fentanyl.

Weaknesses- used patients from a previous study with a positive response to fentanyl and therefore created a confirmation bias. Study was an Open-Label variant. Average age was roughly 54 and lacked a control group for comparison. Patients had to have persistent pain but no more than “moderate” on a pain scale. One death from cardiac arrhythmia could be attributed to the treatment.

Relevance to Palliative Care- fentanyl is a potent opioid that the general public has associated with severe adverse events due to the recent surge of recreational use. The study hints at using fentanyl sprays safely for refractory pain in patients who can be titrated in an in-patient setting. The sub-group of patients that could benefit the most include those with swallowing difficulties and failure/toxicity with the other oral opioid options.