

Breakthrough cancer pain in patients treated with fentanyl sublingual tablets: posthoc analyses of treatment response

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Purpose

Breakthrough cancer pain (BTcP), a transient exacerbation of pain in cancer patients with otherwise stable persistent pain levels, negatively impacts quality of life. In clinical trials, sublingual fentanyl has demonstrated superior efficacy vs placebo and long-term effectiveness in the treatment of BTcP. We investigated the magnitude of pain intensity reductions and pain relief in patients experiencing BTcP after sublingual fentanyl treatment, with a focus on clinically-relevant pain reductions of $\geq 30\%$.

Method

Data were obtained from a randomized, placebo-controlled trial in opioid-tolerant patients (aged ≥ 17 y) experiencing BTcP. The trial consisted of 3 phases: open-label titration with sublingual fentanyl, double-blind treatment (sublingual fentanyl vs placebo), and up to 12 months of open-label sublingual fentanyl treatment. Patients initiated open-label treatment with 100 μg of sublingual fentanyl and titrated to an effective dose between 100 μg to 800 μg . During double-blind treatment, patients randomly received 7 sublingual fentanyl (at the effective dose) and 3 placebo treatments. Posthoc analyses examined overall pain intensity differences (PID), PID of $\geq 30\%$ and $\geq 50\%$ from baseline, and overall pain relief for BTcP episodes occurring during double-blind treatment. Data were assessed based on time postadministration (10 min to 60 min) and baseline pain intensity (≤ 50 mm vs > 50 mm). Response to sublingual fentanyl vs placebo was assessed using Fisher exact tests and paired Wilcoxon tests, respectively, for between- and within-subject comparisons.

Results

A total of 591 BTcP episodes from 64 patients were included in the analyses; the intensity of most episodes was > 50 mm (79%) but ≤ 70 mm (61%). The percentage of BTcP episodes showing $\geq 30\%$ PID from baseline was significantly greater (all $P < .01$; Fisher exact test) with sublingual fentanyl vs placebo at 15 (42% vs 29%), 30 (65% vs 42%), and 60 minutes (77% vs 63%); BTcP episodes showing $\geq 50\%$ PID from baseline were significantly greater (both $P < .05$) with sublingual fentanyl vs placebo at 30 (43% vs 29%) and 60 (61% vs 47%) minutes. Within-subject assessments indicated that the mean percentages of BTcP episodes showing $\geq 30\%$ PID from baseline were significantly greater (all $P < .01$; paired Wilcoxon tests) for sublingual fentanyl vs placebo at 15 (41% vs 27%), 30 (61% vs 38%), and 60 (64% vs 46%) minutes post-treatment; the mean percentages of BTcP episodes showing $\geq 50\%$ PID from baseline were significantly greater (all $P < .01$; paired Wilcoxon tests) for sublingual fentanyl vs placebo at 30 (40% vs 27%) and 60 (49% vs 35%) minutes post-treatment. Overall pain relief from baseline (percentage of scores ≥ 1 on a 5-point scale; 0 [none] to 4 [complete]) was numerically greater with sublingual fentanyl vs placebo at 10 (70% vs 53%), 15 (84% vs 61%), 30 (90% vs 66%), and 60 (93% vs 80%) minutes post-treatment (all $P < .001$; Fisher exact test). Across assessments, treatment differences between sublingual fentanyl and placebo tended to be more pronounced when baseline pain levels were ≤ 50 mm vs > 50 mm.

Conclusions

These posthoc analyses indicate that sublingual fentanyl produced clinically-relevant reductions in BTcP as early as 15 minutes postadministration. The percentage of episodes demonstrating $\geq 30\%$ PID reductions from baseline with sublingual fentanyl at 15 minutes to 60 minutes postadministration was generally comparable to those reported for other transmucosal fentanyl products. A higher percentage of BTcP episodes showed reductions in pain intensity exceeding 30% and 50% following sublingual fentanyl than placebo, with treatment differences being greater among patients with lower baseline pain levels.