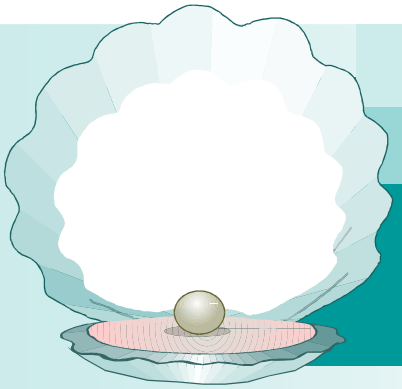

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JOSEPH BRANT MEMORIAL HOSPITAL

Palliative Pearls

Brought to you by the JBMH Palliative Care Program

Cancer breakthrough pain and ROOs…Rapid Onset Opioids

Breakthrough pain is a cause of significant morbidity in cancer patients and is associated with decreased satisfaction in overall pain control and reduced quality of life. Breakthrough pain has a significant impact on sleep, emotional health, personal relationships, ability to perform everyday activities, concentration and thought and work performance. The Association for Palliative Medicine of Great Britian and Ireland Task Force define **breakthrough pain** as "*a transient exacerbation of pain that occurs either spontaneously, or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain.*"

The key elements of this definition are:

- The increase in pain is transient and is either spontaneous or associated with a trigger
- Background pain is adequately controlled, thus pain that occurs during the titration phase of pain management would not be considered breakthrough pain
- The occurrence of an end of dosing interval increase in pain is not considered breakthrough pain, since this phenomenon suggests that the patient requires additional adjustment to their round-the-clock analgesia to improve control of their background pain.

Breakthrough cancer pain can be categorized as either:

- Spontaneous-where it is unpredictable with no identifiable trigger or
- Incident-with a clear trigger eg. Walking/coughing/painful procedures

The ideal agent for managing breakthrough cancer pain would:

- Address the pathophysiology of the pain
- Have a rapid onset of action (several minutes)
- Have a short duration of action (less than 30 minutes)
- Be available in a formulation that is easy and convenient to administer
- Have minimal side effects.

Oral immediate-release morphine has long been considered the "gold standard" treatment for cancer breakthrough pain. However morphine is hydrophilic which means it is primarily absorbed through the gut leaving it prone to first-pass metabolism and slow onset of action (30-45 minutes) and long duration of action (4 hours).

Fentanyl, on the other hand, is highly lipohilic which makes it suitable for transmucosal delivery and allows it to cross the blood-brain barrier quickly. It is a synthetic opioid with an analgesic potency 100 times that of morphine.

Two new Fentanyl products appearing on the market try to address these issues. **(See table)**

It is important to note these products are currently targeting only patients with cancer pain who are on at least the equivalent of 60 mg of morphine per day. They also should not be used for patients on partial opioid agonist like buprenorphine or agents with some opioid effects like tramadol. A potential issue is the conservative starting dose for all patients and need to titrate the dose up gradually which means a delay in reaching an appropriate dose for the patient already on high doses of opioid for their constant pain. But all in all, it is exciting to see some innovative products coming on the market to deal with this difficult aspect of cancer pain.

References available upon request

If you have any questions regarding this publication, please call Ildy Tettero at ext 5743 or Dorothy Vaitekunas at ext 5724

Brand Name	*ABSTRAL*
Dosage Form	**Sublingual tablet** Non-PH dependent rapidly disintegrating Strengths: **100, 200, 300, 400, 600, 800 mcg**
Indication	Breakthrough cancer pain for opioid tolerant patients
Pharmacokinetics	Absorption occurs across the oral mucosa & avoids first-pass metabolism BA: 54% Time to first detectable plasma levels: 8-11 minutes Elimination Half-life: 6 hrs
Onset Duration	**Onset:** After a 400mcg dose significant improvement noted in **10 minutes** **Duration:** at least **60 minutes**
Side effects	Well tolerated Typical opioid side effects • Nausea • Dizziness • Somnolence
Contraindications	Opioid Naïve patients ∅ Use in acute or post-op pain, treating headache or migraine pain, dental pain Severe respiratory depression or severe obstructive lung conditions
Dosing	SL tablet - (Do not suck, swallow or chew) **Tablet dissolves within 30 seconds** **100mcg: repeat dose** if inadequate pain relief **in 15-30 min** If 2 X 100mcg inadequate, ↑ **to 200mcg for next dose** with supplemental 2nd tablet after 15-30 min Continue dose escalation until adequate analgesia Maximum 4 tablets per episode **Each dose must be separated by at least 2 hours**
Brand Name	***ONSOLIS***
Dosage Form	Film Fentanyl **Buccal Soluble Film** Dose: **200, 400, 600, 800, 1200 mcg** buccal strip
Indication	Breakthrough cancer pain for opioid tolerant patients
Pharmacokinetics	BA: 71% (51% from buccal mucosa, 49% from slow GI absorption) Time to first detectable plasma levels: 9 +/-4.8 mins Elimination half-life: 14 hours Median time to max. plasma concentration (for 800 mcg dose): 60 minutes (range 45-240 minutes)
Onset Duration	**Onset: 15** minutes
Side effects	Well tolerated No evidence that mucositis is worsened Typical opioid side effects: • N/V • Dizziness • Somnolence
Contraindications	Opioid Naïve patients - ∅ Use in acute or post-op pain, treating headache or migraine pain, dental pain - Severe respiratory depression or severe obstructive lung conditions
Dosing	Buccal & transmucosal products are not bioequivalent- Do Not substitute mcg per mcg basis- *Always start with recommended start dose for the product and titrate **Titration:** Start 200 mcg buccally X 1 Titrate by 200 mcg/episode prn Each episode must be separated by at least 4 hours Max: 1 dose per episode **Maintenance:** Use single film once dose established **Max:** 1200 mcg/dose - 4 doses/day - Film dissolves within 15-30 minutes