Breakthrough Cancer Pain (BTCP)
25 Years of Study: Key Insights

Henry L. Masters III, MD
Senior Director, Medical Affairs
Arizona Myeloma Network
March 18, 2017
**Definition** – Breakthrough cancer pain is an episode of severe pain that “breaks through” a period of persistent pain at least partly controlled by a stable opioid regimen.

The first survey of BTCP was conducted in 1990 in a sample of 63 patients in which 41 (63%) had flares of painful episodes.

Since that time, a robust amount of literature has been published, describing the prevalence, characteristics and association with adverse outcomes.

Clinical trials of new drug formulations has led to the development of a new class of medications specifically approved for treatment of breakthrough cancer pain in opioid tolerant adults.

---

Cancer Pain Journey

Cancer Pain

Intermittent

Bursts of severe pain without underlying persistent daily pain\(^1,6\)

Persistent

Moderate to severe pain that lasts throughout the day (>12 h)\(^2,3\)

Breakthrough

Transient exacerbation of pain or episodic pain that fails to be controlled and “breaks through” regularly scheduled opioid treatment\(^2-6\)

- Typically severe intensity
- In patients with otherwise stable baseline persistent pain

6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines\(^\text{®}\)) for Adult Cancer Pain V.2.2015. © National Comprehensive Cancer Network, Inc. 2015. All rights reserved. Accessed September 1, 2015. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK\(^\text{®}\), NCCN\(^\text{®}\), NCCN GUIDELINES\(^\text{®}\), and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.
Characteristics of Breakthrough Cancer Pain (BTCP)

Characteristics can vary widely among patients\(^1-6\)

- **Severity\(^1-6\)**
  - Often severe or excruciating
- **Time to peak pain intensity (median)\(^1,2,4-6\)**
  - <1 to 10 minutes
- **Duration (median)\(^1,4-6\)**
  - 15 to 60 minutes
- **Episodes per day (median)\(^1-6\)**
  - 1 to 7 episodes per day
- **Incident-related or idiopathic (predictable or unpredictable)**

It’s terrible – the pain that you have from cancer and the scar tissue

It feels like my body is on fire

It feels like a Mack truck knocked you down and is sitting on top of you

It feels like being beaten with a bat that’s wrapped with barbed-wire

It’s like a monster that hides behind a bush and jumps out to attack you with absolutely no warning!
Testimonial video removed for publication.
How many episodes of pain flares do you usually have in a day?

A. None
B. 1 to 2 flares
C. 3 to 4 flares
D. 5 or more flares

![Bar chart showing percentages of responses.]

- None: 0%
- 1 to 2 flares: 14%
- 3 to 4 flares: 57%
- 5 or more flares: 29%
How quickly does your pain flare usually reach its worst pain intensity?

A. 1 minute or less
B. Between 2 to 5 minutes
C. Between 6 to 10 minutes
D. More than 10 minutes
How long do these episodes of sharp pain flares usually last?

A. Less than 15 minutes
B. Between 16 to 30 minutes
C. Between 31 to 45 minutes
D. More than 45 minutes
BTCP Insights from Patients

- The doctor got mad at me when I told him the pills didn’t work
- Most doctors don’t understand breakthrough pain
- Some oncologists don’t understand pain as well as they need to
- Breakthrough pain occurs right in the hospital and still doesn’t get good treatment
- My doctor was dismissive (Patient was trying to explain her BTCP to her physician)
- When I told my doctor I was still having pain on the medicine, I was labelled as “drug-seeking” and this was put in my chart

Source: Patient and Caregiver Advisory Board on Breakthrough Cancer Pain, October 7, 2016
Cancer Pain Journey

Short-Acting Opioid + NSAIDs
- Oxycodone
- Hydromorphone
- Hydrocodone
- Oxymorphone
- Codeine (NSAIDs)

Long-Acting Opioids
- Oxycodone ER
- Hydrocodone ER
- Methadone
- Fentanyl Transdermal Patch

TIRFS
- Fentanyl Buccal Soluble Film
- Fentanyl Buccal Tablet
- Fentanyl Citrate Oral Transmucosal Lozenge
- Fentanyl Nasal Spray
- Fentanyl Sublingual Spray
- Fentanyl Sublingual Tablet

Intermittent Pain

Persistent Pain

Breakthrough Pain
BTCP Management: Undertreatment vs. Overtreatment

Short-acting oral opioids may not provide timely relief

Increasing the dose of long-acting, around-the-clock, opioids may:

- Increase the risk of opioid tolerance
- Increase side effects such as constipation, sleepiness, and confusion

The ideal treatment for BTCP would match the temporal characteristics of BTCP as much as possible.

Unlike short-acting and long-acting opioids, TIRF Medications offer rapid onset of analgesic effect.
It is important for people fighting cancer to know the Cancer Pain Journey can include intermittent, persistent, and breakthrough pain.

A. Strongly Agree
B. Agree
C. Neutral
D. Disagree
E. Strongly Disagree
Available through the TIRF REMS Access Program

- Fentanyl Buccal Soluble Film
- Fentanyl Buccal Tablet
- Fentanyl Citrate Oral Transmucosal Lozenge
- Fentanyl Nasal Spray
- Fentanyl Sublingual Spray
- Fentanyl Sublingual Tablet
The TIRF Risk Evaluation and Mitigation Strategy (REMS) program is an FDA-required program.

The purpose of the program is to mitigate the risk of misuse, abuse, addiction, overdose and serious complications due to medication errors with the use of TIRF medicines.

Healthcare providers, pharmacies, and patients must enroll in the TIRF REMS Access program for outpatient use of these products.

Enrollment is easy: Log on to www.TIRFREMSaccess.com or call the TIRF REMS Access program call center at 1-866-822-1483 assistance.

To locate a pharmacy able to dispense TIRF products, call: 1-866-822-1483.
IMPORTANCE OF PROPER PATIENT SELECTION, DOSING, and POTENTIAL FOR ABUSE

TRF medicines contain fentanyl, an opioid agonist and a Schedule II controlled substance, with an abuse liability similar to other opioid analgesics. TRF medicines can be abused in a manner similar to other opioid agonists, legal or illicit. Consider the potential for abuse when prescribing or dispensing TRF medicines in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion. Schedule II opioid substances which include morphine, oxycodone, hydromorphone, oxymorphone, and methadone have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

Serious adverse events, including deaths, in patients treated with some oral transmucosal fentanyl medicines have been reported. Deaths occurred as a result of improper patient selection (e.g., use in opioid non-tolerant patients) and/or improper dosing. The substitution of a TIRF medicine for any other fentanyl medicine, including another TIRF medicine, may result in fatal overdose.

TRF medicines are indicated only for the management of breakthrough pain in adult cancer patients 18 years of age and older (16 years of age and older for Actiq® brand and generic equivalents) who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain.

Patients considered opioid tolerant are those who are taking:

- at least 60 mg of oral morphine/daily
- at least 25 mcg transdermal fentanyl/hour
- at least 30 mg of oral oxycodone daily
- at least 8 mg oral hydromorphone daily
- at least 25 mg oral oxymorphone daily
- or an equianalgesic dose of another opioid daily for a week or longer.

TRF medicines are contraindicated in opioid non-tolerant patients and are contraindicated in the management of acute or postoperative pain, including headache/migraine and dental pain, or use in the emergency room. Please see the individual medicine prescribing information for a full list of specific situations in which TRF medicines are not indicated or are contraindicated.

Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with some TIRF medicines.

**Selected Important Safety Information**

**TIRF medicines are contraindicated in opioid non-tolerant patients** and are contraindicated in the management of acute or postoperative pain, including headache/migraine and dental pain, or use in the emergency room. Please see the individual medicine prescribing information for a full list of specific situations in which TIRF medicines are not indicated or are contraindicated. Life-threatening respiratory depression could occur at any dose in opioid non-tolerant patients. Deaths have occurred in opioid non-tolerant patients treated with some TIRF medicines.

When prescribing, do not convert patients on a mcg per mcg basis from another fentanyl medicine to a TIRF medicine, except for substitutions between a branded TIRF medicine and its generic equivalent. Patients beginning treatment with TIRF medicines must begin with titration from the lowest available dose for that specific medicine. Carefully consult the Initial Dosing Instructions in the TIRF medicine-specific Full Prescribing Information.

When dispensing, TIRF medicines are not interchangeable with each other, regardless of route of administration. Differences exist in the pharmacokinetics of TIRF medicines resulting in clinically important differences in the amount of fentanyl absorbed that could cause a fatal overdose. Converting patients from one TIRF medicine to a different TIRF medicine must not be done on a microgram-per-microgram basis, and must be titrated according to the labeled dosing instructions each time they begin use of a new TIRF medicine. The only exception is for substitution between a branded TIRF medicine and its specific generic equivalent.

Special care must be used when dosing TIRF medicines. Refer to the Full Prescribing Information for the individual TIRF medicine for guidance on the maximum number of doses that can be taken per breakthrough pain episode and the time that patients must wait before treating another episode of breakthrough pain with the TIRF medicine.
TIRF medicines are intended to be used only in the care of opioid-tolerant cancer patients and only by healthcare professionals who are knowledgeable of, and skilled in, the use of Schedule II opioids to treat cancer pain.

Patients and their caregivers must be instructed that TIRF medicines contain a medicine in an amount which can be fatal in children, in individuals for whom it is not prescribed, and in those who are not opioid-tolerant. All medicines must be kept out of the reach of children.

The concomitant use of TIRF medicines with cytochrome P450 3A4 inhibitors may result in an increase in tentanyl plasma concentrations, and may cause potentially fatal respiratory depression.

Adverse Reactions
The most commonly observed adverse reactions with TIRF medicines include typical opioid adverse reactions, such as nausea, vomiting, constipation, somnolence, dizziness, and headache. Refer to individual medicine prescribing information for all adverse reactions. Expect opioid side effects and manage them accordingly.

Please see the individual Full Prescribing Information for each TIRF medicine for all information including boxed warnings, and Medication Guide for important safety information for each TIRF medicine.

Adverse Event Reporting
Promptly report suspected adverse events including misuse, abuse, addiction and overdoses directly to the TIRF REMS Access program at 1-866-822-1483. You also may report adverse event information to the FDA MedWatch Reporting System by telephone at 1-800-FDA-1088 or by mail using Form 3500, available at www.fda.gov/medwatch.

Medication Guide
It is important that you discuss the risks of TIRF medicines with your patients and encourage them to read the relevant Medication Guide. The Medication Guide provides important information on the safe and effective use of TIRF medicine and you will need to review the appropriate Medication Guide for the TIRF medicines you prescribe to your patient. Patients should be counseled on the need to store TIRF medicines safely out of the reach of children and other persons for whom the medicine is not prescribed.

You must provide your patient with a copy of the appropriate Medication Guide for the TIRF medicine you prescribe. Medication Guides will be provided to you by the manufacturers of individual TIRF medicines. If you require additional Medication Guides you can:
• Print copies from the TIRF REMS Access program website at www.TIRFREMSAccess.com.
• Contact the TIRF REMS Access program at 1-866-822-1483.
CDC Guideline for Prescribing Opioids for Chronic Pain (released March 18, 2016\(^1\)):

- **Recommendations for primary care clinicians that opioids should not be first-line or routine therapy for chronic pain outside of active cancer, palliative, and end-of-life care**

ASCO Policy Statement on Opioid Therapy: Protecting Access to Treatment for Cancer-Related Pain (released March 23, 2016\(^2\)):

- Cancer Patients Are a Special Population and should be largely exempt from regulations restricting access to or limiting doses of prescription opioids
- There is strong evidence of under treatment of cancer-related pain
- Among patients with cancer, opioid agents remain an essential part of many pain treatment plans

---

1 CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016

2 ASCO Policy Statement issued May 23, 2016
It’s important for people with BTCP to know that the CDC Guideline\(^1\) and ASCO Policy statement\(^2\) protects access to needed pain medication.

A. Strongly Agree
B. Agree
C. Neutral
D. Disagree
E. Strongly Disagree

\(^1\) CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016
\(^2\) ASCO Policy Statement issued May 23, 2016
Key Insights from Cancer Patients, Caregivers, & Advocates

- Want to know what to expect on the Cancer Pain Journey
- Able to learn quickly how to recognize the basic types of cancer pain
- Reassured by the knowledge that there are specific classes of medication available to treat different types of cancer pain
- Quickly understand the value of matching the right type of medication with the correct type of cancer pain
- Fear being stigmatized by healthcare providers as being “drug-seeking” when asking for cancer pain medication
- Glad to know that the Centers for Disease Control and Prevention (CDC) guideline and American Society of Clinical Oncology (ASCO) policy statement both support access to necessary opioid medication for control of cancer-related pain

1 CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016
2 ASCO Policy Statement issued May 23, 2016
Breakthrough Cancer Pain (BTCP)
BACK UP
BTCP Insights from Patients – (Placeholder for Video Clip)