“CANCER may shorten my life... Breakthrough pain is stealing what’s left of it.”

BREAKTHROUGH PAIN

S. Franzoni

UO Medicina Generale
Istituto Clinico Città Brescia
Gruppo Ricerca Geriatrica BS
19 ottobre 2012
Giovanni e il BTP

• Dolore al cuore da alcuni mesi, ma l’Aulin fa bene...
• Così va meglio, la uso anche a casa morfina

COMUNICAZIONE DIAGNOSI + PROGNOSI

• Dottore, è insopportabile.. + diazepam
• Ho paura... se arriva ancora... + citalopram
• Non passa più + promazina
• Dammi qualcosa, ti prego + fentanile TTS
• .....
• Dottore, fammi morire ......
DEFINITION

Original definition “A transitory exacerbation of pain that occurs on a background of otherwise stable pain in a patient receiving chronic opioid therapy” [1]. Updated version “A transitory exacerbation of pain experienced by the patient who has relatively stable and adequately controlled baseline pain” [2]. Recently, an expert group has suggested an extension of the updated version “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” [3].

DOES THE PATIENT HAVE BACKGROUND PAIN?
[Background pain = pain present for ≥ 12 hr / day during previous week (or would be present if not taking analgesia)]

YES →

IS THE BACKGROUND PAIN ADEQUATELY CONTROLLED?
[Adequately controlled = pain rated as “none” or “mild”, but not “moderate” or “severe” for ≥ 12 hr / day during previous week]

NO →

NO →

PATIENT DOES NOT HAVE BREAKTHROUGH PAIN

YES →

DOES THE PATIENT HAVE TRANSIENT EXACERBATIONS OF PAIN?

NO →

YES →

PATIENT HAS BREAKTHROUGH PAIN
Intensità elevata:

≥3 punti vs dolore base

valore assoluto tra 7-10
BTcP

Farmaco inutile

Dolore controllato dalla terapia di base

Tempo

Intensità
CLASSIFICATION

Classified according relationship to specific events [1]:

- **Spontaneous pain** (idiopathic pain): occurs unexpectedly (30-45%)
- **Incident pain** (precipitated or movement-related pain) (30-90%): related to specific events; sub-classified into 3 categories:
  - Volitional incident pain (precipitated by a voluntary act: walking)
  - Non-volitional incident pain (precipitated by an involuntary act: coughing)
  - Procedural pain (related to a therapeutic intervention: wound dressing)

“End-of dose failure” (exacerbation of pain that occurs prior to the next dose of the background analgesic, and reflects declining levels of the background analgesic) is not a subtype of BTP, but it represents inadequately controlled background pain [2].

Figure 2. Subtypes of Breakthrough Pain

Breakthrough Pain

- Idiopathic = Stimulus Independent
- Incidental (Precipitated) = Stimulus Dependent
- “End-of-Dose” Failure = Analgesic Regimen-Related

Volitional
- Movement, Activity

Nonvolitional
- Distension of hollow viscera
- Ischemia
- Coughing, bladder spasm, etc

Common problem in patients with cancer

Prevalence:
19-95%

This disparity reflects a number of factors, including differences in the definition used, in the methods used, and in the populations studied [1-2].

40-80%
BTP is more common in patients with
- advanced disease [13],
- poor performance status [12],
- pain originating from the vertebral column and the nerve plexuses [12].
Raccomandazioni per la gestione del Breakthrough Cancer Pain (BTcP)

Sebastiano Mercadante¹, Dino Amadori², Giovanni Apolone³, Edoardo Arcuri⁴, Alfredo Barbato⁵, Augusto Caraceni⁶, Marco Maltoni⁷, Paolo Marchetti⁸, Consalvo Mattia⁹, Giustino Varrassi¹⁰, Vittorina Zagonel¹¹, Furio Zucco¹²

La prevalenza diminuiva dopo un mese, possibilmente per una progressiva riduzione dell’attività fisica o per una migliore analgesia di base¹³. Il BTP è stato riscontrato anche in numerose altre condizioni di dolore cronico non da cancro, con percentuali di prevalenza abbastanza simili¹⁴-¹⁷. Come negli adulti, il BTcP è abbastanza frequente anche nei bambini,
l'instaurazione di una terapia analgesica di fondo somministrata a orari fissi era ritenuta necessaria ai fini della determinazione di una diagnosi di DEI.

“background pain flare”  “exacerbation of background pain”
AETIOLOGY

Usually the same as the aetiology of the background pain [1,2].

BTP may be due to [3]:

• Direct effect of the cancer (65-76% cases)
• Indirect effect of the cancer (secondary to disability)
• Effect of the anti-cancer treatment
• Effect of a concomitant illness
<table>
<thead>
<tr>
<th>Study</th>
<th>Aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cancer</td>
</tr>
<tr>
<td>Portenoy &amp; Hagen, 1990</td>
<td>76%</td>
</tr>
<tr>
<td>Portenoy, 1999</td>
<td>65%</td>
</tr>
<tr>
<td>Zeppetella, 2000</td>
<td>71%</td>
</tr>
<tr>
<td>Study</td>
<td>Aetiology</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>Nociceptive</td>
</tr>
<tr>
<td>Portenoy &amp; Hagen, 1990</td>
<td>53%</td>
</tr>
<tr>
<td>Portenoy, 1999</td>
<td>38%</td>
</tr>
<tr>
<td>Zeppetella, 2000</td>
<td>75%</td>
</tr>
</tbody>
</table>
CLINICAL FEATURES

- BTP is not a single condition, but a spectrum of very different conditions.

- Clinical features vary from individual to individual, and may vary within an individual [1,2].

Usually reported to be
- frequent in occurrence
- acute in onset
- short in duration
- moderate-to-severe in intensity
- clinical features are often related to the clinical features of the background pain [3].
Mean number of episodes: **4 / day**
(range 1 - 14 / day)


Median duration: **30 min**
(range 1 - 240 min)


**Intense in nature:**  
Slight 16%  
Moderate 46%  
Severe 36%  
Excruciating 2%

• BTP may result in a number of
  – physical problems (insomnia, reduced activity and movement)
  – psychological problems (increased levels of anxiety and depression)
  – social complications (decreased levels of working, social interaction, and IADL; increased use of healthcare and social care resources) [9]

• BTP has a significant negative impact on the QoL of the patient and patient’s family [3,8]
European Association for Palliative Care (EAPC) published updated recommendations on the use of opioid analgesics in the treatment of cancer pain (2012)

Association for Palliative Medicine (APM) of Great Britain and Ireland published recommendations on the management of breakthrough cancer pain (2009)


Most recommendations were based on limited evidence grade of recommendation (D) (based on non-analytical studies or so-called “expert opinion”)*
MANAGEMENT

Principles:
- Assessment
- Treatment
- Re-assessment
1. Patients with pain should be assessed for the presence of BTP (D)

2. Patients with BTP should have this pain specifically assessed (D)

The successful depends on adequate assessment of the
- Aetiology
- Pathophysiology
- Any factors that would indicate or contra-indicate specific interventions

Inadequate assessment may lead to the utilisation of ineffective and / or inappropriate treatment.
ASSESSMENT

- History (pain, general)
- Examination (area of pain, general)
- Assessment tools

Pain history:
- Frequency episodes
- Precipitating / exacerbating factors
- Site pain
- Radiation pain
- Character / quality pain
- Severity / intensity pain
- Duration pain
- Associated physical symptoms
- Interference ADL

Pain Therapy history:
- Relieving factors
- Response analgesics
- Response other treatment
Assessment tools:

a. Breakthrough Pain Questionnaire
b. Episodic Pain Documentation Sheet
c. Alberta Breakthrough Pain Assessment Tool - Research*
d. Breakthrough Pain Assessment Tool (“BAT”)

BTcP  - Assessment tool
Figure 2  Pain diary. (From the American Pain Foundation. Available at: www.painfoundation.org/downloads/Notebook.pdf.)
Table 3  Assessing the Presence of Breakthrough Pain (BTP)

- Do you have episodes of severe pain or BTP?
- How many episodes of BTP do you have each week? Each day?
- How long is it from the time the pain first occurs to when the pain is at its worst?
- How long does each episode of BTP last (minutes, hours)?
- On a scale of 0 to 10, with 0 being no pain and 10 being the worst pain you can imagine, how much does an episode of BTP hurt when it occurs?
- Describe where the BTP occurs. What does it feels like?
- Is the BTP similar to or different from your baseline persistent pain?
- Does your BTP occur with movement or other activity, spontaneously (not associated with any activity), or just before you are supposed to take your next dose of pain medicine?
- What impact does the BTP have on your daily responsibilities at home/work? Are you able to do the things that you want/need to do?
- Are there any things that you avoid doing or that you are able to do only with severe pain?
- What do you do to relieve the BTP?
- What types of treatments have you used? How long did you use them? Were they effective? Are they still effective?
- What drugs have you used to relieve the BTP? What were the doses? Were they effective? Are they still effective?
Treatment:  
- cause of pain  
- pain (symptomatic treatment)  
- complications of pain
3. The management of BTP should be individualised (D)

BTP is not a single entity, but a spectrum of very different entities. (heterogeneous in nature)

Optimal management of BTP depends on a variety of
1) pain-related factors, including the aetiology of the pain (cancer-related, treatment-related, concomitant illness), the pathophysiology of the pain (nociceptive, neuropathic, mixed), and the clinical features of the pain [3].

2) patient-related factors, including the stage of the disease (early,
4. Consideration should be given to treatment of the underlying cause of the pain (D)

The options for treatment are potentially numerous, with new treatments emerging all the time, and so it is important that there is close liaison with the relevant oncology team.

Little evidence for the efficacy of oncological treatments in managing BTP (radiotherapy).

The main reason for the lack of evidence undoubtedly relates to a lack of relevant studies, rather than a lack of efficacy per se.

Oncological treatments may be effective in managing certain types of BTP [5,6] (Bisphosphonate, orthopaedic surgery)
5. Consideration should be given to avoidance / treatment of the precipitating factors of the pain (D)

Incident-type BTP

Movement-related pain is a particularly common problem in patients with bone metastases.

Many patients will benefit from strategies to minimise the amount of movement required, such as provision of simple adaptations to their surroundings, and provision of additional practical support with the ADL [7].
9. **Non-pharmacological methods** may be useful in the management of BTP episodes (D)

A variety of non-pharmacological methods are used by patients, including rubbing / massage [21,22], application of heat [21,22] or cold [21,23], distraction techniques [10,23], and relaxation techniques [10,21].

Little evidence to support the use of these interventions in the treatment of BTP episodes.
10. **Non-opioid analgesics may be useful in the management of BTP (D)**

Paracetamol is sometimes used by patients to treat BTP episodes [24,25] (onset of action of 15-30 min per os [26])

**NSAIDs** [24,25] (especially useful in pain from bone metastases, mucosal and skin lesions)

**Ibuprofen**: onset of action of 15-25 min per os (peak effect at 30-90 min)

Other NSAIDs have a somewhat longer onset of action (30-60 min) [26]. A number of other non-opioid analgesics have been utilised by clinicians to manage episodes of BTP, including ketamine [27], midazolam [28] and nitrous oxide [29].

Little evidence to support the use of these interventions in the treatment of BTP episodes.

11. **Interventional techniques may be useful in the management of BTP (D)**

A variety of different techniques are available [30], including

- neural blockade [31]
- neuromodulation (transcutaneous nerve stimulation: TENS) [32]
- neuroablation [7]
- interventional radiological techniques (direct tumour ablation, cementoplasty, vertebroplasty [34], and balloon kyphoplasty).
6. Consideration should be given to modification of the background analgesic regimen / “around the clock medication” (D)

Modification of the background analgesic regimen has been shown to be a useful approach [8], and may involve the following strategies:

- **Titration of opioid analgesics** can be effective in reducing the intensity and / or frequency of movement-related volitional incident pain [9]. This strategy is often limited by the development of dose-dependent adverse effects (sedation) [10].

- **Switching of opioid analgesics and / or the route of administration of the opioid** can also be effective in reducing the severity of movement-related volitional incident pain [11,12].

- **Addition of “adjuvant analgesics”** (agents whose primary function is not analgesia, but which provide pain relief in certain circumstances) can be effective in reducing the impact of specific BTP syndromes (antiepileptics for neuropathic pain, antispasmodics for visceral pain) [13].
7. **Opioids are the “rescue medication” of choice in the management of BTP episodes (D)**

Cornerstone of the management of BTP episodes is “rescue medication”.
- **taken as required**, rather than on a regular basis
- spontaneous or non-volitional incident pain the treatment should be taken at the **onset** of the BTP
- volitional incident or procedural pain the treatment should be taken **before** the relevant precipitant of the pain

**Most appropriate rescue medication will be an opioid analgesic**

The decision to use a specific opioid preparation should be based on a combination of the:
- pain characteristics (onset, duration)
- product characteristics (pharmacokinetics, pharmacodynamics)
- patient’s previous response to opioids (efficacy, tolerability)
- patient’s preference for an individual preparation.
8. The dose of opioid “rescue medication” should be determined by **individual titration** (B)

Dose of opioid rescue medication should be a **fixed proportion** of the dose of the opioid background medication

**Same opioid**

**Usual dose:** 10% to 20% of the total daily dose of opioids


Data from controlled trials with oral transmucosal fentanyl formulations (or oral morphine [17]) suggest that there is no relationship between the most effective dose of these preparations and the effective dose of the background opioid medication [15-19].

**Dose of all opioid rescue medication should be determined by individual titration**
Because of the rapid onset of fentanyl, fentanyl-based medications are recommended only for **opioid-tolerant patients** receiving daily doses of oral morphine of at least 60 mg for at least 2 weeks.

**Table 6. Baseline Opioid Doses Considered Safe Before Initiating Rapid-Onset Opioids**

<table>
<thead>
<tr>
<th>Patients are considered opioid tolerant when they are taking a minimum of the following for ≥1 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. 60 mg/d oral morphine</td>
</tr>
<tr>
<td>b. 25 mcg/h transdermal fentanyl</td>
</tr>
<tr>
<td>c. 30 mg/d oxycodone</td>
</tr>
<tr>
<td>d. 8 mg/d oral hydromorphone</td>
</tr>
<tr>
<td>e. An equianalgesic daily dose of another opioid</td>
</tr>
</tbody>
</table>
Controlling Breakthrough Pain Doesn't Have to Be a Painful Process

Patient Registers Pain Level on the MOD's Pain Scale.

Patient Waves RFID Wristband Across the Faceplate to Activate the MOD.

Patient Removes and Takes Pill, as per Doctor's Orders!

Better Pain Management Is as Easy as 1...2...3
12. Patients with BTP should have this pain specifically re-assessed (D)

Successful management of BTP depends on adequate re-assessment of the patient.

Objectives of re-assessment are to determine the:
- efficacy and the tolerability of the treatment
- any change in the nature of the BTP

Inadequate re-assessment may lead to an ineffective and/or inappropriate treatment.

The re-assessment of BTP is similar in nature to that of the background pain.
"Ideal" rescue medication:

- Good efficacy
- Rapid onset of action
- Short duration of effect
- Good tolerability
- Easy to use
- Acceptable to the patient
- Available / affordable (NH ???)
Vantaggi dei Rapid Onset Opioid (ROO)

Efficaci nel coprire il dolore da moderato a severo

Bennett et al. Pharm Ther 2005;25:354-61
Vantaggi dei Rapid Onset Opioid (ROO)

Rapidi ad agire: onset paragonabile a quello del BTCP
Breve durata d'azione: ridotto rischio di accumulo

Bennett et al. Pharm Ther 2005;25:354-61
Vantaggi dei Rapid Onset Opioid (ROO)

Personalizzabili alle caratteristiche dell'episodio e alle necessità del paziente

Bennett et al., Pharm Ther 2005;25:354-61
Opzioni di trattamento del BTcP:

Opzioni attuali

- Oramorph— Morfina orale a pronto rilascio
- Actiq – Oral Transmucosal Fentanyl Citrate (OTFC)
- Effentora – Fentanyl Buccal Tablet (FBT)
- Abstral – SubLingual Fentanyl (SLF)
- Instanyl – Intra Nasal Fentanyl Spray (INFS)
- PecFent – Fentanyl Pectin Nasal Spray (FPNS)
Orale:
richiede **20-30 min** per un iniziale effetto analgesico con picco dopo 60 min; durata circa 4 ore
Non adatta a BTP, tranne forme incidentali: prevedibili o procedurali della durata 60 min (somministrare almeno 30 min prima)

EV:
caratteristiche farmacocinetiche e dinamiche favorevoli, ma necessita intenso monitoraggio (strutture terziarie)
Terapie del BTcP


Actiq  EFFENTORA  Abstral  INFS  Pecfent

Data della prima autorizzazione

Oral Transmucosal Lozenge
Effervescent Buccal Tablet
Sublingual Fentanyl
Intranasal Fentanyl Spray
Fentanyl Pectin Nasal Spray
ORAL TRANSMUCOSAL FENTANYL

**Actiq™ (Cephalon)  Effentora™ (Cephalon)**

(200, 400, 600, 800, 1,200, 1600 mcg)

Percentage of fentanyl absorbed by the mouth is about 25% of the dose

Commonly called the fentanyl oralet, oral transmucosal fentanyl citrate is a lozenge containing fentanyl that is rubbed along the buccal mucosa until it dissolves. Placed along the upper gum and cheek; the patient then rubs the outside of the cheek until the tablet dissolves.

Buccal tissue is vascular and allows for rapid absorption within approximately 15 min.

Fentanyl oralets reduce pain levels more and provide better pain relief than oral opioids.

Effective doses range from 200 to 1600 mcg when patients are on baseline opioid therapy for cancer pain.
Fentanyl buccal soluble film (Onsolis)

This drug has 2 layers of water-soluble film, one with fentanyl that adheres to the buccal mucosa. The second layer of film isolates the fentanyl and limits the amount of fentanyl that can be swallowed.

Film dissolves within 15 to 30 min, allowing about 50% of the dose to be absorbed. Total bioavailability of the fentanyl is approximately 71%.

Recommended starting dose is 200 mcg, and subsequent doses should be separated by at least 2 hours. NO more than 4 doses per day and doses higher than 1200 mcg per day.
Sublingual preparations (Fentanyl buccal tablets):
Abstral™ (Prostrakan)  Effentora™ (Cephalon)

Effervescent formulation that can alter the pH in the oral cavity, increasing the rate and extent of absorption
Adequate saliva is required for the tablet to dissolve

Analgesia action can take place 5 to 15 min post-dose

Meaningful pain relief was achieved in approximately 70% of BTP with 400 mcg

Mild mucositis does not change the ability to absorb the dose
**Instanyl™** (Nycomed)  **PecFent™** (Archimedes)

Successfully in Europe to treat BTCP, recently received FDA approval

Pectin-based spray delivery system allows the fentanyl droplets to adhere to the nasal membranes and decreases the potential swallowing of medication.

Absorbed rapidly (starting within 10-15 min)

Significantly **faster onset of meaningful pain relief and more effective** than oral transmucosal fentanyl citrate

Effective doses for patients ranged from 50 to 200 mcg

Patients tend to find the delivery method easy to use

Higher patient preference for this route of administration
RAPIDO ASSORBIMENTO

- l’epitelio altamente vascolarizzato
- Evita il metabolismo di primo passaggio
- Adatta anche in caso di xerostomia o altre affezioni del cavo orale
- Non invasiva
- Facile da utilizzare dal paziente o da chi lo assiste
Curve farmacocinetiche delle formulazioni transmucosali di fentanyl (Confronto indiretto)

**OTFC** – Transmucosal Fentanyl Citrate, 400 mcg; RCP Effentora

**FBT** – Fentanyl Buccal Tablet, 400 mcg; Darwish, Clin Pharmacokin 2006

**FST** – Fentanyl Sublingual Tablet, 400 mcg; Lennernas, Br J Clin Parmacol 2004

**FPNS** – Fentanyl Pectin Nasal Spray, 400 mcg; RCP PecFent

**INFS** – Intranasal Fentanyl Spray, soluzione acquosa, 100 mcg; Chrstrup, Clin Ther 2008
TITOLAZIONE INFS

METODO DI TITOLAZIONE

La concentrazione iniziale deve essere pari a 50 microgrammi in una narice, aumentando secondo necessità seguendo la scala di concentrazioni disponibili (50, 100 e 200 microgrammi).

Se non si raggiunge un’ adeguata analgesia si può somministrare una seconda dose di uguale concentrazione dopo almeno 10 minuti.

Dati da profilo di prodotto
### Table 3. Potential drug–drug interactions.

<table>
<thead>
<tr>
<th>Inhibitors of CYP3A4 isoenzymes</th>
<th>Inducers of CYP3A4 isoenzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir, nelfinavir, ritonavir, saquinavir</td>
<td>Phenobarbital, secobarbital</td>
</tr>
<tr>
<td>Clarithromycin, erythromycin, ciprofloxacin, norfloxacin</td>
<td>Dexamethasone, hydrocortisone, prednisolone, methylprednisolone</td>
</tr>
<tr>
<td>Diltiazem, verapamil</td>
<td>Efavirenz, nevirapine</td>
</tr>
<tr>
<td>Itraconazole, ketoconazole, fluconazole</td>
<td>Carbamazepine, phenytoin</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Modafinil</td>
</tr>
<tr>
<td>Nefazodone, fluvoxamine</td>
<td>Rifabutin, rifampin</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td>St. John’s Wort</td>
</tr>
</tbody>
</table>

**Notes:** Fentanyl is metabolized by the CYP3A4 isoenzyme system. Drug interactions are possible. Inhibition of the CYP3A4 may result in an increase in fentanyl plasma concentrations that could lead to increased or prolonged adverse effects including respiratory depression. Patients should be constantly monitored for signs of opioid toxicity. Concomitant use of fentanyl and CYP3A4 inducers may decrease the efficacy of fentanyl and fentanyl doses may need to be adjusted.¹⁴,⁵⁵
<table>
<thead>
<tr>
<th>Type of study</th>
<th>Drugs compared</th>
<th>Responder rate (%)*</th>
<th>10min</th>
<th>15min</th>
<th>30min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>50% (INF)</td>
<td>70% (INF)</td>
<td>90% (INF)</td>
</tr>
<tr>
<td>Mercadante et al, 2009</td>
<td>Open label RCT</td>
<td>INF vs OTFC</td>
<td>20% (OTFC)</td>
<td>40% (OTFC)</td>
<td>80% (OTFC)</td>
</tr>
<tr>
<td>Kress et al, 2009</td>
<td>Double blind RCT</td>
<td>INF vs placebo</td>
<td>58% (INF)</td>
<td>ND</td>
<td>80% (INF)</td>
</tr>
<tr>
<td>Portenoy et al, 2006</td>
<td>Double blind RCT</td>
<td>FBT vs placebo</td>
<td>ND</td>
<td>13% (FBT)</td>
<td>48% (FBT)</td>
</tr>
<tr>
<td>Slatkin et al, 2007</td>
<td>Double blind RCT</td>
<td>FBT vs placebo</td>
<td>16% (FBT)</td>
<td>30% (FBT)</td>
<td>51% (FBT)</td>
</tr>
</tbody>
</table>

* 33% pain reduction from baseline  
RCT = randomised controlled trial  
INF = intranasal fentanyl  
OTFC = oral transmucosal fentanyl  
FBT = fentanyl buccal tablets

Table 1: Responder rates after different routes of fentanyl administration in trials with homogeneous outcome measures
Intranasal Fentanyl for Breakthrough Pain Control

Claudia F. Clavijo¹, Rachael Rzasa Lynn¹, Uwe Christians¹ and Jeffrey L. Galinkin¹,²

INF has gained popularity due to its ease of administration and rapid absorption through the highly vascular nasal tissues (rapid onset of action, peak effect within 5 min, rapid passage across the brain-blood barrier with an effect site equilibration time of 6.4 min, optimal duration to cover the entire episode of BTP)

INF vs immediate-release morphine sulfate, FBT, OTFC
.... better reducing pain intensity
How can a patient be heavily sedated, but still in excruciating pain?

Patient is only experiencing the side effects of the opioids

Possible explanations:
- pain is not “opioid sensitive” (neuropathic pain)
- tolerance effects (rapid dose escalation with opioids prior to BTP)
- the opioids are not working

Alternative techniques to relieve the pain have to be considered
CONCLUSIONS

R1. Il BTcP è un’esacerbazione transitoria del dolore, di intensità moderata-elevata, che insorge sia spontaneamente sia a seguito di un fattore scatenante, in pazienti con dolore di base mantenuto per la maggior parte della giornata sotto controllo o di intensità lieve.

R2. In tutti i pazienti con BTcP è necessaria una specifica valutazione iniziale (eziologia, durata, intensità e meccanismi fisiopatologici), che va ripetuta dopo l’inizio di un trattamento, una sua modifica o a seguito di variazioni del quadro clinico.

R3. È raccomandato che il dolore di base venga controllato adeguatamente con i farmaci o i trattamenti disponibili, per gestire meglio il BTcP e migliorare la qualità di vita del paziente.

R4. La somministrazione di farmaci al bisogno rappresenta il cardine del trattamento del BTcP.

R5. Nel caso di un dolore spontaneo o non volontario, il farmaco va prescritto all’inizio dell’episodio, mentre in quello di un dolore prevedibile o procedurale il farmaco potrebbe essere somministrato già prima che l’evento previsto si verifichi. La somministrazione di morfina orale, per le sue caratteristiche farmacocinetiche, non si adatta alle caratteristiche temporali del BTcP. La morfina orale può essere quindi raccomandata solo per il trattamento di episodi che s’instaurano lentamente, prevedibili o procedurali, della durata di oltre 60 minuti. La somministrazione deve avvenire circa trenta minuti prima dell’evento, per esempio prima di iniziare l’attività.

R6. Nel trattamento del BTcP nuove formulazioni di fentanyl citrato, come quelle orosolubile, sublinguale e intranasale, offrono oggi sostanziali vantaggi dal punto di vista sia farmacocinetico (rapido assorbimento, maggiore biodisponibilità ed efficacia) sia della compliance (più facile via di somministrazione).