Cost-effectiveness of short-acting opioids for breakthrough pain in cancer patients - a Scottish-based decision-analysis model

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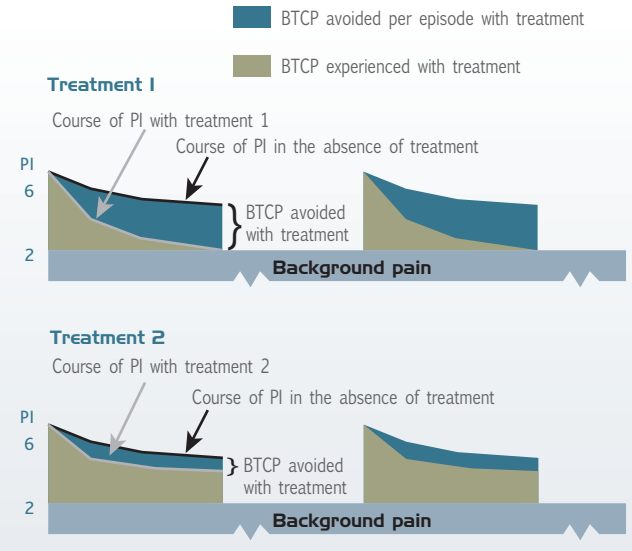
Objective

- Breakthrough cancer pain (BTCP) is a transitory exacerbation of pain that occurs in 24–95% of patients with adequately controlled persistent background pain.[1,2] BTCP is characterised by its frequent occurrence, acute onset and short duration.[3]
- BTCP is associated with increased morbidity, impaired quality of life and increased medical costs.[1,4,5]
- Oral opioids are the mainstay of treatment for BTCP, with normal-release morphine the most widely used. However, the clinical characteristics of normal-release morphine do not match the typical BTCP episode. Oral ingestion of morphine is associated with a delayed time to onset of action and peak analgesic effect, while duration of action may be prolonged beyond the length of the BTCP episode.[6]
- These limitations have encouraged the search for new treatment options that mirror the temporal characteristics of BTCP. Unlike morphine, fentanyl is rapidly absorbed across the mucosal surface, providing a rapid onset of effect. The first fentanyl formulation developed to treat BTCP was oral transmucosal fentanyl citrate (OTFC, Actiq®), a solid drug matrix on a handle. Newer fentanyl formulations for the treatment of BTCP include oral transmucosal fentanyl buccal tablet (FBT, Effentora®) and intranasal fentanyl spray (INFS, Instanyl®).
- A decision-analysis model parameterised for Scotland was used to compare the cost-effectiveness of INFS, OTFC and FBT for the treatment of BTCP.

Methods

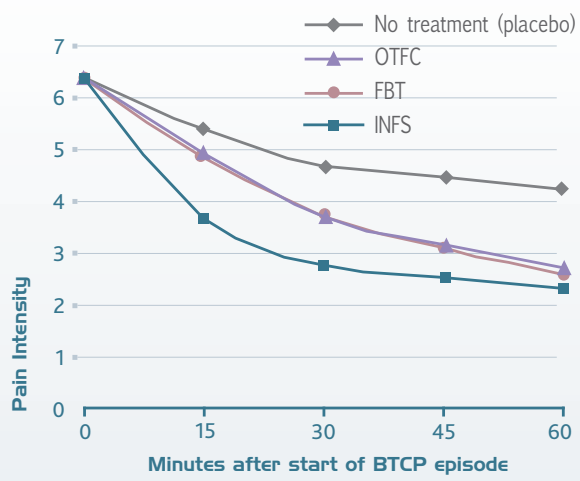
- The basic concept of the model is shown in Figure 1. The pain intensity (PI) of BTCP, measured on a 0–10 scale, decreases over the course of the episode without treatment. With treatment, the PI decreases more rapidly and the total area under the curve (AUC), which represents the total BTCP experienced, is reduced. The area between the PI curves with and without treatment reflects the BTCP avoided. Assuming a certain number of episodes per day, the percentage BTCP avoided with treatment can be calculated for a defined time horizon.

Figure 1. Model concept



- Efficacy data for INFS, OTFC and FBT were obtained from randomised controlled trials and indirectly compared by adjusting for differences in placebo responses via a Bayesian mixed treatment comparison meta-analysis.[7] Estimated PI levels during a BTCP episode after administration of placebo, INFS, OTFC and FBT are shown in Figure 2. In the absence of data beyond 60 minutes, PI curves were cut-off at this time point and the background PI level was assumed.
- Quality of life impact was measured on a utility scale from zero (equivalent to death) to 1 (perfect health). This enabled the evaluation of quality-adjusted life years (QALYs). Utility scores were estimated for a set of PI profiles via a time trade-off study in the UK general population (n=99). Mean utilities for the PI profiles ranged from 0.348 to 0.679. A mathematical function (linear regression: utility = –0.1237*AUC + 0.9536) was used to derive a relationship between the PI profiles and AUC for BTCP experienced.
- The only published data on the impact of BTCP on resource consumption is a US survey in which GP visits, emergency room (ER) visits and hospital admissions were compared for patients with and without BTCP.[8] In order to estimate resource utilisation in the UK, eight clinical experts were interviewed and asked to assess annual probability and frequency for each type of resource consumption for patients with and without BTCP (Table 1). An expert meeting was then held to reach consensus on these data. Resource unit costs were derived from the Personal Social Services Research Unit (PSSRU) *Unit Costs of Health and Social Care 2008* and NHS reference costs (Department of Health, NHS Tariffs, Payment by Results (PbR) 2008/09).

Figure 2. Pain intensity (PI) levels during a BTCP episode with no treatment (placebo), OTFC, FBT and INFS



Data from mixed treatment comparison based on six randomised controlled trials: INFS *versus* placebo (Kress et al. *Clin Ther* 2009;31:1177–91); INFS *versus* OTFC (Mercadante et al. *Curr Med Res Opin*, in press); fentanyl buccal tablet *versus* placebo (n=2) (Portenoy et al. *Clin J Pain* 2006;22:805–11, Slatkin et al. *J Support Oncol* 2007;5:327–34); OTFC *versus* placebo (Farrar et al. *J Natl Cancer Inst* 1998;90:611–6) and OTFC *versus* normal-release morphine sulphate (Coluzzi et al. *Pain* 2001;91:123–30).

Table 1. Treatment-related costs

	Cost/unit	Unit	Source
GP office visits	£36	Per visit	PSSRU 2007/08
A & E visits	£75	Per visit	NHS tariffs: Payment by Results 2008/09
Hospital stay (inpatient)	£400	Oncology ward/day	NHS tariffs: Payment by Results 2008/09
Home care (nurse) visits	£26	Per visit	PSSRU 2007/08
GP home visits	£58	Per visit	PSSRU 2007/08
Hospital outpatient visits (oncology clinic)	£97	Per visit	NHS tariffs: Payment by Results 2008/09
Hospice stay	£82	Per day	PSSRU 2007/08

*Costs indexed for 2009. NHS tariffs: Payment by Results 2008/09: http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_081096
Personal Social Services Research Unit (PSSRU) *Unit Costs of Health and Social Care 2008*: http://www.pssru.ac.uk/pdf/uc/uc2008/uc2008.pdf

- Drug acquisition costs for OTFC and FBT were obtained from the NHS 2009 list price (£5.95 and £5.14 per episode, respectively, MIMS March 2009). INFS is not yet available in the UK so in the absence of cost data, price parity with OTFC was assumed.
- In the base-case scenario, 3 BTCP episodes/day, a background PI of 2, and a time-horizon of 90 days of treatment per year were assumed. Uncertainty in the source data was incorporated by means of one-way sensitivity analyses, probabilistic sensitivity analyses and scenario analyses.

Results

- With INFS, 55% of BTCP (95% uncertainty interval [UI]: 45–67%) measured as PI $AUC_{0–60}$ minutes is avoided per episode compared with placebo, whereas only 29% is avoided with OTFC (95% UI: 22–39%) and 31% with FBT (95% UI: 25–40%).
- Cost estimates by treatment for the base-case scenario are reported in Table 2.
- INFS was dominant over OTFC (i.e. cost savings and a greater reduction in BTCP). Compared with OTFC, INFS is expected to save £27 per patient and avoid an additional 25% of BTCP, which corresponds to a QALY gain of 0.023 (Table 3).
- Compared with FBT, INFS has higher costs (£194) but avoids an additional 24% of BTCP, resulting in a QALY gain of 0.021. The cost/QALY gained (incremental cost-effectiveness ratio, ICER) for INFS versus FBT was estimated at £9037/QALY, well below the generally accepted maximum threshold of £30 000 per QALY gained.
- Despite the uncertainty in the source data, there is a >99% probability that INFS is the most cost-effective intervention. Sensitivity and scenario analyses did not change this conclusion.

Table 2. Cost estimates by treatment for the base-case scenario (90 days of treatment)

	Value (95% uncertainty intervals)			
	No treatment	INFS	OTFC	FBT
Drug costs	NA	£1607	£1607	£1388
GP office visits	£15 (9, 23)	£12 (9, 16)	£14 (9, 19)	£13 (9, 19)
A & E visits	£2 (2, 3)	£1 (1, 2)	£2 (1, 2)	£2 (1, 2)
Hospital stay (inpatient)	£75 (54, 100)	£58 (45, 71)	£66 (50, 85)	£66 (50, 83)
Home care (nurse) visits	£9 (9, 9)	£4 (3, 5)	£6 (6, 7)	£6 (6, 7)
GP home visits	£17 (10, 24)	£12 (12, 16)	£14 (10, 19)	£14 (10, 19)
Hospital outpatient visits (oncology clinic)	£8 (4, 12)	£7 (7, 9)	£8 (5, 10)	£8 (5, 10)
Hospice stay	£56 (28, 92)	£29 (29, 47)	£42 (22, 67)	£41 (21, 64)
Total resource use costs	£183 (145, 226)	£125 (104, 151)	£152 (123, 185)	£150 (122, 182)
Total costs	£183 (145, 226)	£1731 (1710, 1757)	£1758 (1730, 1791)	£1538 (1510, 1570)

All costs over 90 days. NA = not applicable.

Table 3. Cost-effectiveness of INFS compared with OTFC and FBT

	INFS *versus* OTFC	INFS *versus* FBT
Incremental costs (95% UIs)	-£27 (-43, -13)	£194 (179, 205)
Incremental % BTCP avoided (95% UIs)	25% (16%, 36%)	24% (16%, 32%)
Incremental utility (QALY) (95% UIs)	0.023 (0.014, 0.032)	0.021 (0.014, 0.033)
ICER (Cost/QALY gained)	Dominant	£9037

UI = uncertainty intervals, QALY = quality-adjusted life-years, ICER = incremental cost-effectiveness ratio, Dominant = more effective and less costly than comparator.

Conclusions

Treatment with INFS provides a more rapid onset of pain relief and greater reduction in BTCP than achieved with either OTFC or FBT.

Greater efficacy of INFS compared with OTFC and FBT is expected to reduce medical resource use and result in cost-savings for healthcare providers and quality of life gains for patients.

INFS is a cost-effective treatment for BTCP compared with OTFC and FBT in Scotland.

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