COST-UTILITY ANALYSIS OF FENTANYL SUBLINGUAL FORMULATION IN THE TREATMENT OF BREAKTHROUGH PAIN IN ADULTS WITH CANCER, ALREADY ON OPIOID MAINTENANCE THERAPY FOR CHRONIC CANCER PAIN IN ITALY

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BACKGROUND

Breakthrough cancer pain (BTCP) is defined as a transitory exacerbation of pain experienced by a patient who has relatively stable and adequately controlled background pain.[1] Approximately two-thirds of patients with advanced cancer report chronic pain requiring the use of strong opioids.[2] BTCP impacts greatly on patients' quality of life, as it is associated with impairments in daily physical functioning, secondary psychological distress, and a reduced response to routine pharmacotherapy. BTCP also places a high economic burden on society and health care services.[3]

OBJECTIVE

The aim of this analysis was to quantify the advantages and the cost-utility of fentanyl sublingual formulation in terms of pain intensity reduction for each episode of breakthrough cancer pain (BTCP) compared to morphine therapy in Italy.

METHOD

A probabilistic model already proposed by Vissers et al. (2011) [1] was developed for the Italian context considering the NHS perspective. The model compared costs and efficacy of fentanyl sublingual formulation versus immediate-release morphine.
Pain Intensity (PI) measured on a numerical scale from 1 to 10 was used as a measure of effectiveness. A reduction in PI in BTCP episodes was translated into cost savings and quality-adjusted life-year gains (QALYs). The pain intensity values for fentanyl and oral morphine were calculated starting from the respective values of PID (pain intensity difference) at 15, 30 and 60 minutes found in the literature [2, 3]. The estimated PI values are observed for fentanyl and morphine respectively in Table 2.

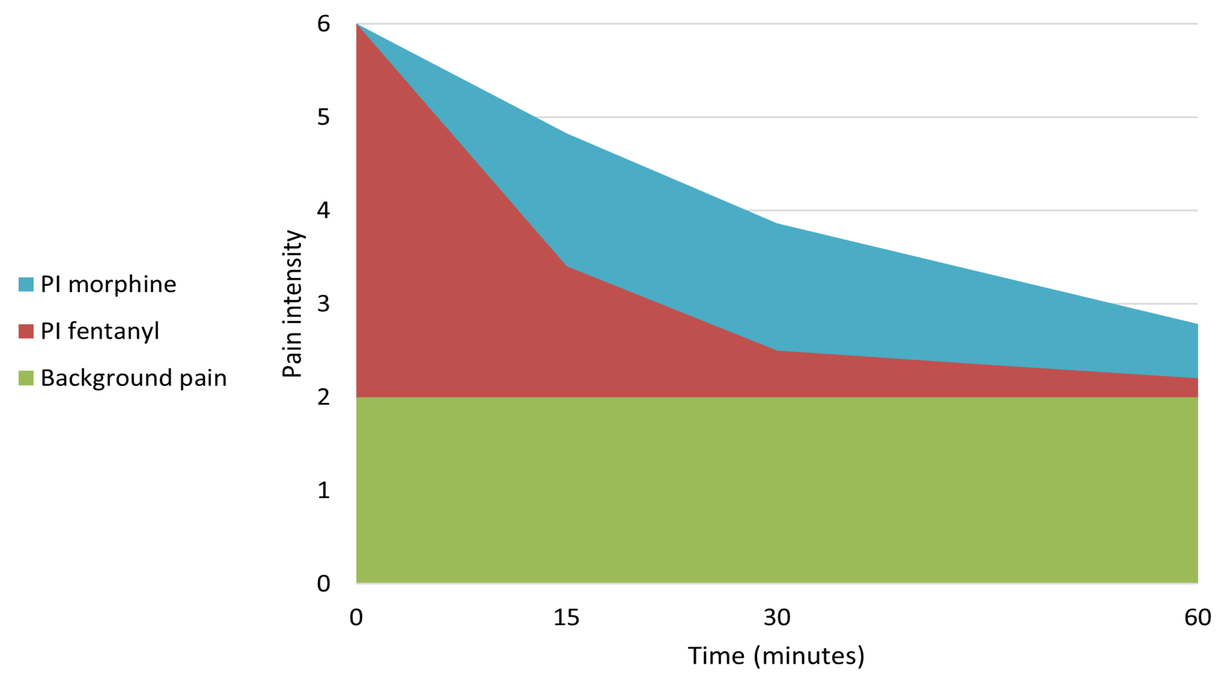
Table 2: Pain Intensity

Time (minutes)	Fentanyl sublingual formulation	morphine
0	6*	6*
15	3.4	4.82
30	2.5	3.86
60	2.2	2.79

** Assumption [1]*

In Figure 1 we can see the graphical representation of the Pain Intensity for the two treatments in a BTCP episode. The blue area under the placebo curve represents the percentage of pain avoided (32.55%) in an episode.

Figure 1: BTCP avoided



The costs considered in the model concerned the cost of therapy and other costs related to the use of resources (medical visits and hospitalizations). As regards the cost of therapy, the cost for a 180-day time horizon [1] of treatment with fentanyl was estimated starting from the net ex-factory price (€ 144.33 [4]) and the dosage as per summary of product characteristics. The cost obtained was € 2,168.16. As regards the morphine, a therapy cost for 180 days was estimated equal to € 581.42 obtained from the net ex-factory price (€ 0.54 [4]) and assuming a maximum number of vials used per day equal to 6 considering the use of a vial every four hours [5].
With regard to medical visits and hospitalizations, the cost estimates were evaluated in consideration of the use of resources per event as per the study by Vissers et al. (2011) [1].

RESULTS

The results obtained show how the treatment with fentanyl sublingual formulation allows a reduction in pain of the patients analyzed by more than 32%. This results in a 24% increase (0.12 QALYs) in the number of years lived in perfect health. Table 2 shows the results of the cost-utility analysis. Overall, the treatment with fentanyl is associated with gains in terms of years lived in perfect health (0.64 QALYs vs 0.51 QALYs), but also higher costs (€ 2,468.61 vs € 1,026.83). An incremental cost-utility ratio (ICUR) is therefore estimated to be € 11,778.85. Considering a willingness to pay threshold as reported by the AIES Guidelines (€ 25,000 - € 40,000) [6], fentanyl is cost-effective compared to oral morphine.

Table 2: Cost-utility results

	Morfina [A]	Vellofent [B]	Differenza [Δ=B-A]	ICUR
Costi	1,026.83 €	2,468.61 €	1,441.78 €	
QALY	0.51	0.64	0.12	**11,778.85 €**

CONCLUSIONS

Considering a willingness to pay threshold as reported by the AIES Guidelines (€ 25,000 - € 40,000), fentanyl sublingual formulation is cost-effective compared to oral morphine.

REFERENCES

[1] Vissers, D.C., et al., *An economic evaluation of short-acting opioids for treatment of breakthrough pain in patients with cancer.* Value Health, 2011. **14**(2): p. 274-81. [2] Novotna, S., et al., *A randomized, placebo-controlled study of a new sublingual formulation of fentanyl citrate (fentanyl ethypharm) for breakthrough pain in opioid-treated patients with cancer.* Clin Ther, 2014. **36**(3): p. 357-67. [3] Zeppetella, G., et al., *A network meta-analysis of the efficacy of opioid analgesics for the management of breakthrough cancer pain episodes.* J Pain Symptom Manage, 2014. **47**(4): p. 772-785.e5. [4] *Codifa - L'informatore farmaceutico*. [5] Canciani M et al. , *CURE PALLIATIVE IN MEDICINA GENERALE Aspetti etici, relazionali, clinici, organizzativi delle cure palliative domiciliari*. 2004. [6] AIES (Associazione Italiana di Economia Sanitaria), *Proposte di linee guida per la valutazione economica degli interventi sanitari.* Pharmacoeconomics-Italian Research Articles. **11**(2): p. 89-93.