

WITHDRAWN

EFFICACY OF OPIOIDS IN THE TREATMENT OF BREAKTHROUGH CANCER PAIN: A BAYESIAN MIXED TREATMENT COMPARISON

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OBJECTIVES: To compare the efficacy of opioids in reducing breakthrough pain within 15 min after taking the medication, in patients with cancer. **METHODS:** Randomised controlled trials investigating the efficacy of opioids administered orally or intranasally were identified with a systematic literature search. The endpoint of interest was the reduction in pain intensity (pain intensity difference (PID)) recorded on a 0–10 numeric rating scale within 15 min after taking the medication. Outcomes of all trials were analysed simultaneously with a Bayesian mixed treatment comparison. **RESULTS:** In addition to one trial report on the use of intranasal fentanyl spray (INFS), four relevant studies were identified, allowing comparisons between INFS, oral transmucosal fentanyl citrate (OTFC), fentanyl buccal tablet (FBT), and morphine sulphate immediate release (MSIR). INFS was

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more efficacious than placebo: the relative treatment effect, PID at 10 min post dosing (PID₁₀), was 1.28 (positive values indicate a reduction in pain), 95% Credibility Interval (CrI): 0.91;1.65. OTFC and FBT at 15 min were also more efficacious than placebo: the relative treatment effect, PID₁₅ (mean ± 95%CrI), was 0.60 (0.11;1.09) for OTFC and 0.51 (0.29;0.73) for FBT. MSIR displayed similar efficacy to placebo: PID₁₅ 0.18 (−0.50;0.86). INFS provided a greater pain reduction after 10 min than the other interventions after 15 min. The relative treatment effects of INFS (PID₁₀) versus other treatments (PID₁₅) were: 0.68 (0.06;1.30) versus OTFC, 0.77 (0.34;1.20) versus FBT and 1.10 (0.32;1.87) versus MSIR, corresponding to a probability of 98% or more of INFS being the most efficacious treatment. **CONCLUSIONS:** The current study demonstrated that in the treatment of breakthrough pain in patients with cancer (i) MSIR has similar efficacy to placebo 15 min after dosing and (ii) INFS is the most efficacious treatment for reducing breakthrough pain within 15 min after dosing compared with OTFC, FBT and MSIR.

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TREATMENT EFFECT OF RITUXIMAB, FLUDARABINE AND CYCLOPHOSPHAMIDE (R-FC) VERSUS FC IN CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL) IN AN OBSERVATIONAL SETTING: AN INVESTIGATION OF PROGNOSTIC FACTORS AND LIFETIME HEALTH OUTCOMES

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OBJECTIVES: Using observational chronic lymphocytic leukaemia (CLL) data collected by Tam et al., (2008), we compared the treatment effect of first line Rituximab, Fludarabine and Cyclophosphamide (R-FC) with FC, inspecting the impact of prognostic factors and modeling life-time health outcomes. **METHODS:** Different lengths of follow-up in FC (1995–2007, n = 108) and R-FC (1999–2007, n = 300) treated patient cohorts was accounted for in a Cox's proportional hazards model. The following prognostic factors were examined for association with treatment outcomes: age, gender, beta-2 microglobulin (β2M) and Binet stage. The best parametric fit (Weibull) was used to extrapolate progression free survival (PFS) with 6 year median follow-up to a 30 year time horizon, and a Markov process to model the transition from the progressed health state to death. Rates of death in the PFS and progressed state were based on background mortality and CLL mortality as observed, respectively. No continued benefit was assumed beyond the observational period. **RESULTS:** Prognostic factors were evenly distributed between treatment groups. In univariate Cox models, age, Binet stage and β2M were confirmed as prognostic factors. For β2M, the hazard ratio (HR) was 2.41 (1.72–3.38)³ 2x upper limit normal (N) compared to <2N. Similar significant increases were observed in the elderly (>70 years) and patients with Binet C stage. The treatment effect of R-FC versus FC adjusted for β2M, binet and age (HR 0.54 (0.38–0.77)), was broadly similar to univariate estimate (HR 0.57 (0.40–0.81)). Patients on R-FC spent on average 2.5 years longer in PFS than FC patients and experienced longer mean life expectancy (9.9 years for R-FC, 7.7 years for FC). **CONCLUSIONS:** The treatment benefit of R-FC over FC in this CLL observational cohort is not affected by prognostic factors and is predicted to generate a considerable increase in life expectancy.

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