**Supplemental Table 1.** Characteristics of included studies that evaluated transdermal buprenorphine formulations for chronic pain.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Subjects** | **Study Duration** | **N** | **Buprenorphine Dose** | **Comparator** | **Scale** | **Mean/Median Pain Score (when calculated)** | **Outcome and Results** |
| Corli *et al*19 | 2016 | Chronic cancer pain | 28 days | 520 | Baseline dose 53.7 + 12.5 mg/day; Final dose: 80.1 + 40.4 (Doses are morphine equivalent) | Oral morphine, oral oxycodone and transdermal fentanyl | NRS | Mean reductions of 3.9 (Buprenorphine), 3.8 (Morphine), 3.7 (Transdermal Fentanyl) and 3.4 (Oxycodone), and reductions of 3.4 (Morphine, Transdermal Fentanyl) and 3.1 (Oxycodone, Buprenorphine).  | No significant differences were observed between morphine and buprenorphine  |
| Simpson *et al*20 | 2016 | Diabetic peripheral neuropathic pain for at least 6 months | 12 weeks | 186 | Commenced with 5 μg/h to a maximum dose of 40 μg/h | Placebo | NRS | The mean average pain at baseline was 5.7 + 1.1 for the buprenorphine group and 5.9 + 1.3 for the placebo group | There was a statistical significant difference between intervention and placebo (p < 0.001), favoring buprenorphine for pain relief. |
| Yarlas *et al*21 | 2014 | Chronic low back pain | 12 weeks | 541 | 10 or 20 μg/h  | Placebo transdermal patch | BPI | Buprenorphine: 2.5 (SE 0.15) Placebo: 3.6 (SE: 0.14) | The scores for the buprenorphine group was statistically significantly lower than the placebo group (p<0.001). |
| Mitra *et al*22 | 2013 | Chronic Non-Cancer Pain | 12 months | 46 | Started on 5 µg/h, and were titrated to optimal dose | Transdermal fentanyl, initial 12.5 µg/h and titrated to optimal dose | VAS | Dose-increment ratio between initial and last dose (mean last dose/mean initial dose) of each patch was comparable (4.58 vs 4.73). | There was no significant difference between the two groups (p<0.05). |
| Steiner *et al*23 | 2011 | Moderate to severe low back pain persisting for a minimum of three months | 12 weeks | 541 | 10 or 20 µg /h | Placebo | 11-point scale (0=no pain, 10= “pain as bad as you can imagine”) | Mean pain score in buprenorphine group 6.9 + 1.21; placebo group: 6.8 + 1.26 | Patients receiving buprenorphine transdermal patch reported statistically significantly lower pain scores compared to placebo (p=0.010) |
| Steiner *et al*24 | 2011 | Chronic moderate to severe lower back pain.  | 12 weeks | 1,160 | 5 µg/h or 20 µg/h | Immediate release Oxycodone 40 mg/day | ‘‘average pain over the last 24 hours’’ score. | For the buprenorphine 5, buprenorphine 20, and the oxycodone 40 mg/daytreatment groups, respective mean pain scores were6.36, 6.46, and 6.46 at screening; 2.84, 2.91, and 2.74 atPre-randomization; and 4.02, 3.35, and 3.26 at week 12, respectively. | Buprenorphine is statistically significantly inferior compared to oxycodone for pain relief (p < 0.001) |
| Gordon *et al*25 | 2010 | Chronic back pain  | 6 months | 78 | Initial 10 µg/h to a maximum of 40 µg/h | Placebo | VAS | Buprenorphine: 45.3 + 21.3 vs Placebo: 53.1 + 24.3 | There was statistically significant relief in buprenorphine intervention (p = 0.022) when compared to placebo. |
| Gordon *et al*26 | 2010 | Moderate to severe chronic low back pain | 6 months | 53 | Initial dose of 5 μg/h, titrated weekly to the maximum tolerated dose (10 μg/h or 20 μg/h)  | Placebo | VAS | Buprenorphine resulted in lower mean daily pain scores than in the placebo group (37.6 + 20.7 versus 43.6 + 21.2 and 1.7 + 0.6 versus 2.0 + 0.7 on the ordinal scale | There was statistical significant difference between buprenorphine and placebo (p=0.0487), favoring buprenorphine in pain relief. |
| Munera *et al*27 | 2010 | Osteoarthritis | 35 days | 315 | 5, 10, or 20 µg/h. | Placebo | Patients with pain > or = on a 0-10 and patient satisfaction score of good, very good, or excellent | Placebo: Baseline 8.1, Days 1-7 7.5, Days 8-14 6.9, Days 15-21 6.8 and Days 22-28 6.6.Buprenorphine: baseline 8.2, Days 1-7 7.4, Days 8-14 6.8, Days 15-21 6.6, Days 22-28 6.4 | The odds of successful treatment from BTDS-treated patients were 66% greater than for placebo (p = 0.036).  |
| Karlsson *et al*28 | 2009 | Osteoarthritis | 12 weeks | 134 | Strengths of 5, 10, and 20 μg/h , with a maximum dosage of 20 μg/h | Tramadol 75-400 mg/day | Box Scale 11 score (BS-11) | Buprenorphine: 3.92 + 2.07; Tramadol: 4.10 + 2.15 | Buprenorphine was noninferior to tramadol (p=0.020).  |
| Poulain *et al*29 | 2008 | Severe Chronic Cancer Pain |  2 weeks | 188 | 70 μg/h patch applied every three days  | Placebo | NRS | Scores in buprenorphine group decreased from 3.5 + 2.2 to 1.5 + 1.5 and in placebo group increasedfrom 1.5 + 1.5 to 2.7 + 1.9 | There was a statistical significant difference between buprenorphine and placebo (p = 0.0003) with regards to response rates, favoring buprenorphine as an analgesic agent. |
| Pace *et al*30 | 2007 | Chronic cancer pain | 8 weeks | 52 | 35 microg/h | 60 mg/day of sustained-release morphine  | 11 Point Likert Scale | Buprenorphine baseline: 6.4 ± 0.2, end of study: 3.9 ± 0.3Morphine baseline: 6.5 ± 0.3, end of study: 5.1 ± 0.2 | There was statistical significant difference between buprenorphine and morphine (p<0.01), favoring buprenorphine for pain relief |
| Sorge *et al*31 | 2004 | Chronic cancer and non-cancer pain | 15 days | 137 | 35 μg/hr | Placebo | VRS (Diary Entries) | In thebuprenorphine group, the proportion of diaryentries relating tosevere and very severe pain intensity decreased arespective 1.1% and 3.0%. In the placebo group, pain intensity worsened during thedouble-blind phase, with the proportion of diaryentries relating to moderate and severe pain increasingby 0.7% and 5.3% respectively | In the double-blind phase, buprenorphine TDS recipients had a more pronounced improvement in pain intensity compared with placebo group, with the difference between treatment groups significant (p<0.05) at all time points favoring buprenorphine.  |
| Bohme *et al*32 | 2003 | Severe to very severe chronic pain of malignant or nonmalignant origin | 15 days | 151 | 35 μg/h, 52.5 μg/h or 70 μg/h | Placebo transdermal patch | VRS | The proportion of responders in each treatment group increased dose-dependently (34%, 37% and 50% for the 35 μg/h, 52.5 μg/h and 70 μg/h groups, respectively) | No statistical significant difference between the groups (p=0.374). |
| Sittl *et al*33 | 2003 | Chronic cancer pain | 15 days | 157 | 35.0, 52.5,and 70.0 μg/h | Placebo | VRS | Buprenorphine 35 μg/hr group: 2.3. Placebo: 1.9. | There was statistical significant difference between buprenorphine and placebo (p= 0.032), favoring buprenorphine with regards to clinical response. |

BPI: Brief Pain Inventory; MPQ: McGill Pain Questionnaire; NRS: Numeric Rating Scale, VAS: Visual Analog Scale, VRS: Verbal Rating Scale