The Impact of Buprenorphine Transdermal System 5 mcg/hour (BTDS 5) and 20 mcg/hour (BTDS 20) on Quality of Life in Opioid-Exposed Patients with Moderate to Severe Chronic Low Back Pain

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INTRODUCTION

Buprenorphine is a semi-synthetic partial mu opioid agonist and a Schedule III controlled substance.

The buprenorphine transdermal system (BTDS) delivers either 5 mcg/hour (BTDS 5), 10 mcg/hour (BTDS 10), or 20 mcg/hour (BTDS 20) of buprenorphine on average continuously over 7 days.

BTDS has been approved by the FDA as Buprenex® for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time.

Data from randomized-controlled trials support BTDS 20 treatments as safe, well-tolerated, and effective for pain relief in patients with moderate to severe chronic low back pain (CLBP).

OBJECTIVES

To examine the degree to which BTDS 20, relative to BTDS 5, improves health-related quality of life (HRQL) for CLBP patients over the course of 12 weeks of treatment.

To examine the degree to which improvements in HRQL are maintained for patients receiving 12 months of continuous BTDS 20 treatment.

METHODS

Study Population and Design

Data in this analysis were from a phase III, multicenter, randomized, double-blind (DB) active comparator trial testing the efficacy and safety of treatment with BTDS 5 or BTDS 20 for opioid-experienced adult patients with moderate to severe CLBP.

This study used an enriched design:

- Prior to the 12-week DB phase, patients were enrolled in an open-label run-in period for the purpose of establishing adequate pain control and tolerability of BTDS 20.
- Patients who did not tolerate or respond to BTDS 20 were excluded from the DB phase.
- An extension phase beginning 3 days after the close of the core study included patients from any DB treatment arm who volunteered to receive treatment with BTDS 5, BTDS 10, or BTDS 20 for up to 12 months.
- Patients were initially treated with BTDS 5 for at least 3 days; dose was then titrated as necessary through the remainder of the extension phase. Most patients received BTDS 20.
- Data for outcomes in the current analyses were collected at screening (baseline), at the end of the run-in period, at weeks 4, 8, and 12 of the DB phase, and at weeks 4, 8, 12, 16, 20, 24, and 52 of the extension phase.
- The primary endpoint in this study was patients averting pain over the last 24 hours (results reported in Steiner et al.); findings presented here are from post-hoc analyses.

Study Outcome: 36-item Short Form Health Survey (SF-36v2)

The SF-36v2 is a 36-item self-reported, generic HRQL survey with a four-week recall period.1

It measures 8 domains of functional health and well-being, as well as 2 summary measures:

- Physical functioning (PF)
- Role physical (RP)
- Bodily pain (BP)
- General health (GH)
- Vitality (VT)
- Social functioning (SF)
- Role emotional (RE)
- Mental health (MH)
- Physical summary (PCS)
- Mental summary (MCS)

The SF-36v2 scoring

- Each scale/summary measure is calculated and standardized into a T score (Mean=50; SD=10) based on a U.S. general population normative sample.
- Higher scores indicate a better health state.
- Minimal important change (MIC) values, which indicate the smallest amount of change in a patient’s score that would be considered clinically meaningful, have been established for all SF-36v2 domains and summary scores.3

Analysis

The impact of BTDS 20 on CLBP patients’ HRQL was analyzed in several ways:

- Analysis of covariance (ANCOVA) models tested for significant differences in week 12 DB SF-36v2 scores between BTDS 20 and BTDS 5 arms (controlling for pre-DB scores).
- Fisher’s exact tests were used to test for significant differences in the proportion of patients in BTDS 20 and BTDS 5 groups that showed clinically meaningful improvement (i.e., an increase ≥ 1 MIC) from baseline to week 12 of the DB phase.
- Linear mixed-models tested for effects of treatment arm and time (and treatment x time) for PCS and MCS scores over the course of the 12-week DB phase.
- Regression models tested for significant changes (i.e., degradation) in PCS and MCS scores over the course of the 12-month extension phase for patients who continued BTDS treatment (other predictors in the model included outcomes and treatment arm in the DB phase).

RESULTS

Impact of BTDS 20 vs. BTDS 5 on CLBP patients’ HRQL

Figure 1. Estimated mean SF-36v2 scores (controlling for screening and run-in period effects) at week 12 of the DB phase for BTDS 20 and BTDS 5 arms.

Figure 2. The percentage of patients showing clinically meaningful improvement (i.e., change ≥ 2 MIC) from baseline to week 12 of the DB phase by treatment arm.

Figure 3. Physical and mental summary scores at screening, run-in, and double-blind phase visits for BTDS 20 and BTDS 5 arms.

Figure 4. Observed mean PCS and MCS scores in the extension phase for patients treated with BTDS 20.

DISCUSSION

Following 12 weeks of DB treatment, patients receiving BTDS 20 had statistically lower role limitations due to pain compared to patients receiving BTDS 5.

However, only the pain dimension showed treatment group differences that were of a magnitude that would be considered clinically meaningful.

The statistically significant advantage of BTDS 20 over BTDS 5 for overall physical HRQL was observed within 4 weeks of treatment following randomization.

The 4-week recall period of the SF-36v2 form used in this trial did not afford examination of earlier visits; thus it remains unknown exactly how rapidly these differences emerge.

No statistical difference across treatment arms was observed for overall mental HRQL; this might be driven by the fact that patients’ mental health at baseline was near normal.

Both overall physical and mental HRQL were fully maintained over a 12-month open-label extension phase in patients who continued receiving BTDS 20.

REFERENCES

