Effects of Tapentadol Prolonged Release (PR) Versus Oxycodone/Naloxone PR on Quality of Life and Function Measures in Patients With Severe Chronic Low Back Pain With a Neuropathic Pain Component

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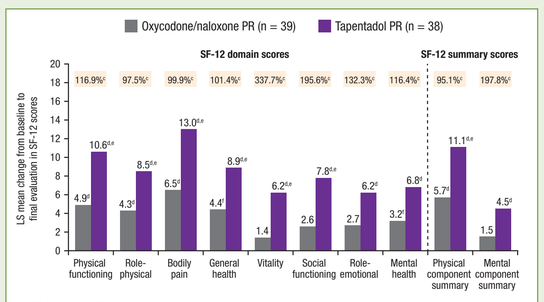
ABSTRACT

Aims: **To evaluate the impact of tapentadol prolonged release (PR) and oxycodone/naloxone PR on quality of life and function measures.**

Methods: **In this ongoing, open-label, phase 3b/4 study, eligible patients (average pain intensity [numerical rating scale-3] ≥6; painDETECT "positive" or "unclear") are randomized to tapentadol PR 50 mg bid or oxycodone/naloxone PR 10 mg/5 mg bid. After titration over 21 days (maximum doses: tapentadol PR 250 mg bid or oxycodone/naloxone PR 40 mg/20 mg bid plus oxycodone PR 10 mg bid), the target dose is continued for 9 weeks. Quality of life and function measures include the Short Form-12 (SF-12) and EuroQol-5 Dimension (EQ-5D) questionnaires. Interim results are presented (77/240 [32.1%] planned patients).**

Results: **All mean SF-12 domain and summary scores improved significantly with tapentadol PR ($P \leq 0.002$), with significantly greater improvements than oxycodone/naloxone PR in 6 domains and the physical component summary score ($P < 0.05$; Figure 1). The mean EQ-5D health status index score improved significantly ($P < 0.001$) from baseline (randomization) to final evaluation (last observation carried forward) with tapentadol PR (mean change, 0.44) and oxycodone/naloxone PR (0.22), with a greater improvement with tapentadol PR ($P = 0.004$).**

Conclusions: **Tapentadol PR was associated with greater improvements in quality of life and function measures than oxycodone/naloxone PR for severe, chronic low back pain with a neuropathic pain component.**



SF-12, Short Form-12; LS, least-squares; LOCF, last observation carried forward; PR, prolonged release; ANCOVA, analysis of covariance.
[a]Descriptive analyses.
[b]LS means and *P* values are obtained from an ANCOVA model that includes treatment and pooled centers as factors and score at randomization (baseline) as a covariate.
[c]Percent difference between tapentadol PR and oxycodone/naloxone PR, using oxycodone/naloxone PR as the base (denominator).
[d]$P \leq 0.002$ for the change from baseline.
[e]$P < 0.05$ versus oxycodone/naloxone PR, in favor of tapentadol PR.
[f]$P \leq 0.03$ for the change from baseline.

Figure 1. Changes from baseline to final evaluation in SF-12 domain and summary scores (LS mean; LOCF; full analysis set, interim results).[a,b]

INTRODUCTION

- Neuropathic pain can have a significant negative impact on health-related quality of life[1]
- Chronic low back pain is often accompanied by a neuropathic pain component, which is often difficult to manage appropriately[2,3]
- Tapentadol prolonged release (PR) is a centrally acting analgesic, with μ-opioid receptor agonist and noradrenaline reuptake inhibitor activities,[4,5] that has been shown to be efficacious and well tolerated for the management of severe, chronic low back pain with or without a neuropathic component in recent phase 3b studies[4,5]
  - In those phase 3b studies,[4,5] tapentadol PR was also associated with significant improvements in health-related quality of life in patients with severe, chronic low back pain with or without a neuropathic pain component
- Furthermore, tapentadol has been shown to be effective and well tolerated for the management of moderate to severe, chronic osteoarthritis knee pain,[6,7] low back pain,[7,8] pain related to diabetic peripheral neuropathy,[9] and cancer pain,[10] with improved tolerability (particularly gastrointestinal tolerability) compared with oxycodone PR (for osteoarthritis and low back pain)[6-8] and morphine controlled release (for cancer pain)[10]
- Fixed-dose combinations of oxycodone/naloxone PR have also been shown to be effective and well tolerated for the management of moderate to severe, chronic low back pain,[11] with better gastrointestinal tolerability compared with oxycodone PR alone[11,12]
  - The naloxone component of oxycodone/naloxone PR is an opioid antagonist that acts on the opioid receptors in the gut, reducing opioid-induced constipation by blocking the effects of oxycodone on these receptors[12]

OBJECTIVES

- To evaluate the effects of tapentadol PR versus oxycodone/naloxone PR on quality of life and function measures, including the Short Form-12 (SF-12) Health Survey and the EuroQol-5 Dimension (EQ-5D) health status questionnaire as secondary endpoints
- Effectiveness results, including results of the primary effectiveness endpoint, from this study are presented in poster <<XX>>, and respective tolerability results are presented in poster <<XX>>

<<Poster numbers will be added upon receipt>>

METHODS

Patients

- Key trial-specific inclusion criteria
  - Diagnosis of chronic low back pain lasting ≥3 months prior to enrollment
  - Pain requiring a strong (World Health Organization [WHO] Step III) analgesic, based on the investigator's assessment at enrollment
  - Score on the painDETECT questionnaire[13] (used to evaluate the likelihood of a neuropathic pain component to low back pain; possible score of 0-38) of "positive" (score of 19-38) or "unclear" (score of 13-18) at enrollment
    - For patients taking a stable regimen of centrally acting co-analgesics, which must be washed out prior to randomization, a "negative" painDETECT score is permitted at enrollment if that score is ≥9
  - For patients taking co-analgesics at enrollment, which must be washed out prior to randomization, average pain intensity score ≥5 on an 11-point numerical rating scale-3 (NRS-3; recalled average pain intensity score [11-point NRS] during the last 3 days prior to the visit; 0 = "no pain" to 10 = "pain as bad as you can imagine") at enrollment
    - For patients who are not taking co-analgesics at enrollment, average pain intensity score ≥6 on an 11-point NRS-3 at enrollment
- Key trial-specific exclusion criteria
  - Low back pain caused by cancer and/or metastatic diseases
  - Severe renal impairment, or history of or current laboratory values reflecting moderate or severe hepatic impairment
  - History of seizure disorder or epilepsy; mild or moderate traumatic brain injury, stroke, transient ischemic attack, or brain neoplasm within 1 year; or severe traumatic brain injury within 15 years, or residual sequelae suggesting transient changes in consciousness
  - Known or suspected paralytic ileus, acute biliary obstruction, or acute pancreatitis
- Permitted medications
  - For patients on a stable pre-study regimen, non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol are permitted at the same stable dose
  - Selective serotonin reuptake inhibitors (for the treatment of uncomplicated depression) are permitted if patients have been taking a stable dose for ≥30 days prior to the randomization visit
  - Other medications used to treat psychiatric or neurological disorders are permitted if patients have been taking a stable dose for ≥3 months prior to the randomization visit
- Prohibited medications
  - All analgesics and co-analgesics, except for study drug and stable doses of NSAIDs and paracetamol, are prohibited during the study (after the washout period)
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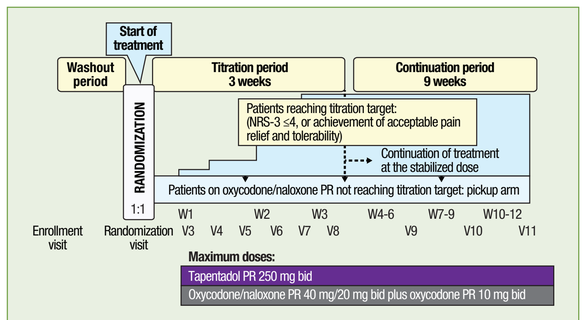
  - Laxatives and anti-emetics as prophylaxis are prohibited within 14 days of enrollment and during the study
  - Monoamine oxidase inhibitors are prohibited within 14 days prior to enrollment and during the study

Study Design

- This on-going, randomized, multicenter, parallel-arm, open-label, active-controlled, phase 3b/4 study (ClinicalTrials.gov Identifier: NCT01838616) includes an optional 3- to 14-day washout period, a 3-week titration period, and a 9-week continuation period (**Figure 2**)



NRS-3, numerical rating scale-3; W, week; V, visit; PR, prolonged release.

Figure 2. Study design.

- During the optional washout period (prior to starting study treatment), centrally acting analgesics and co-analgesics are discontinued prior to the randomization visit; the duration of the washout period is individualized depending on the type and dose of the previous co-analgesics
- At the randomization visit, patients are randomized 1:1 to initial doses of tapentadol PR 50 mg bid or oxycodone/naloxone PR 10 mg/5 mg bid
- During the titration period, doses can be titrated upwards in increments of tapentadol PR 50 mg bid or oxycodone/naloxone PR 10 mg/5 mg bid at minimal 3-day intervals until the minimum target of titration is reached (maximum permitted dose, tapentadol PR 250 mg bid or oxycodone/naloxone PR 40 mg/20 mg bid plus oxycodone PR 10 mg bid)
  - The minimum target of titration at the end of the titration period is defined as 1 of the following:
    - NRS-3 ≤4 with acceptable tolerability, as reported by the patient
    - NRS-3 of ≤5 if pain relief and tolerability are reported as satisfactory by the patient and investigator to continue in the study, and 1) the patient is on the maximum dose of tapentadol PR or oxycodone/naloxone PR or 2) the maximum daily dose cannot be achieved because of side effects
- Patients who reach the minimum target of titration are eligible to enter a 9-week continuation period, during which patients continue on the same stable dose of study drug; for patients not taking the maximum dose, a single titration using the same increments as during titration is permitted during the continuation period
  - Patients in the tapentadol PR group who do not reach the minimum target of titration by the end of the titration period are discontinued from the study
  - Patients in the oxycodone/naloxone PR group who do not reach the minimum target of titration by the end of the titration period can be switched to tapentadol PR in a pickup arm or discontinued from the study (if they do not want to switch to tapentadol PR)

Study Evaluations

- Quality of life is evaluated as a secondary outcome in this study using the EQ-5D health status questionnaire and the SF-12 Health Survey
  - The SF-12 Health Survey[14] includes 12 questions that are used to evaluate 8 dimensions of functional health and well-being (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health); each dimension is scored on a scale from 0 ("lowest level of health") to 100 ("highest level of health")
  - The EQ-5D[15] health status questionnaire includes 5 dimensions of health-related quality of life (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression); patients rate each dimension using a 3-point scale (1 = "no problems," 2 = "some problems," 3 = "extreme problems")
  - The EQ-5D health status questionnaire and SF-12 Health Survey are completed at the enrollment visit, the randomization visit, weekly during titration (Visits 4, 6, and 8), twice during the continuation period (Visits 9 and 10), and at the final evaluation visit
- The mean daily doses of tapentadol PR and oxycodone/naloxone PR were evaluated at the end of titration

Statistical Analyses

- This study has an adaptive 3-stage group-sequential design (O'Brien and Fleming type design[16]), with 1 planned interim analysis after observation of one-third of the total planned study population, the results of which are presented here
- A 2-sample *t* test was used for the calculation of the sample size. The sample size computation for the primary effectiveness endpoint was based on a standard deviation (SD) of 2.5 for the change in pain intensity from baseline and a non-inferiority margin of 1.3; the sample size computation for the second endpoint was based on a SD of 1.0 for the change from baseline in the Patient Assessment of Constipation Symptoms (PAC-SYM) total score, an expected difference of 0.1 in the change from baseline in the PAC-SYM total score in favor of oxycodone/naloxone PR, and a non-inferiority margin of 0.7
  - For both endpoints, a sample size of 96 patients per group in the per protocol set (defined below) is required to show the non-inferiority of tapentadol PR as compared to oxycodone/naloxone PR with 90% power and a 1-sided significance level of $\alpha = 0.0125$
  - Assuming that 80% of patients are available for the per protocol set, a total of 240 patients should receive study treatment in the overall study
  - Statistical methods for the primary endpoints are explained in further detail in posters <<XX>><<Poster numbers will be added upon receipt>>
- The safety set includes all randomized patients who took ≥1 dose of study drug
- The full analysis set includes all randomized patients who took ≥1 dose of study drug and had ≥1 post-baseline pain intensity assessment (NRS-3)
- For the SF-12 Health Survey, physical and mental component summary scores (possible score for each, 0 ["lowest level of health"] to 100 ["highest level of health"]) are calculated by combining scores from the 12 individual questions
- The responses to each of the EQ-5D dimensions are scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 and 1 (0 = "dead" to 1 = "full health")
- The changes from baseline to final evaluation in the SF-12 domain scores and composite scores and the EQ-5D health status index score are evaluated using an analysis of covariance (ANCOVA) model including treatment and pooled center as factors and score at baseline as a covariate
  - The last observation carried forward (LOCF) is used for imputing missing scores
  - The patients who entered the pickup arm were treated as discontinuations using the LOCF. The pickup arm was not analyzed during this interim analysis
- All analyses are exploratory, and all *P* values shown are descriptive

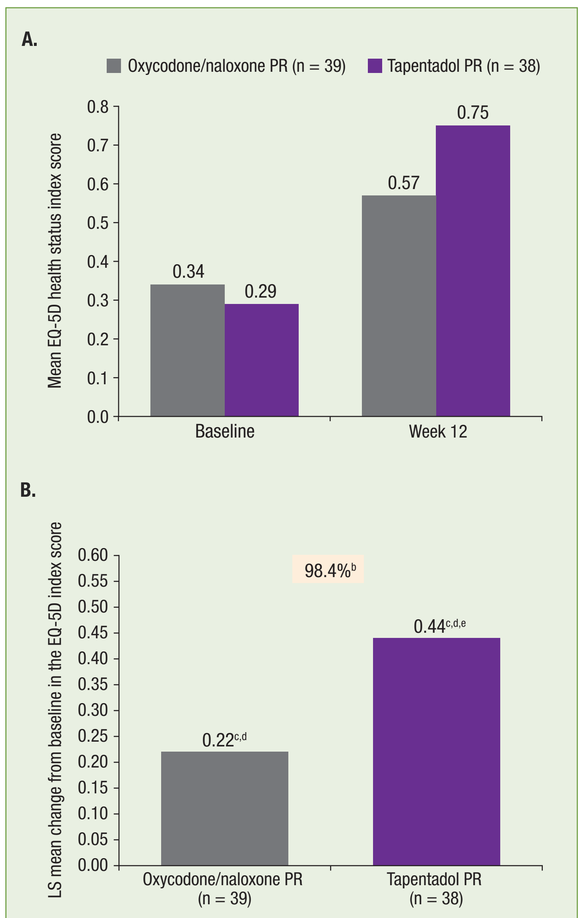
RESULTS

Patients

- For this interim analysis, 77 patients (tapentadol PR, n = 38; oxycodone/naloxone PR, n = 39) were included in the safety set and the full analysis set
- Demographic characteristics were similar in both treatment groups in the safety set
  - All patients in both treatment groups were white and >50% were female (tapentadol PR, 63.2% [24/38]; oxycodone/naloxone PR, 56.4% [22/39])
  - The mean SD age was 55.8 (12.33) years in the tapentadol PR group and 58.7 (11.76) years in the oxycodone/naloxone PR group
- In the tapentadol PR and oxycodone/naloxone PR groups, respectively, 79% (30/38) and 41% (16/39) of patients in the safety set completed study treatment
  - Overall, 92% more patients stayed on tapentadol PR treatment compared with oxycodone/naloxone PR treatment
- At the end of titration, the mean (SD) daily doses were <<X.XX>> mg/day in the tapentadol PR group and <<X.XX>> mg/day in the oxycodone/naloxone PR group

Quality of Life and Function

- In the tapentadol PR group of the full analysis set, significant increases from baseline to final evaluation (LOCF) were observed in all mean SF-12 domain scores (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) and the physical and mental component summary scores (all $P \leq 0.002$; **Figure 1**)
  - In the oxycodone/naloxone PR group of the full analysis set, significant increases from baseline to final evaluation were observed in the SF-12 physical functioning, role-physical, bodily pain, general health, and mental health domain scores, and in the physical component summary score (all $P \leq 0.03$; least-squares mean; **Figure 1**)
  - The improvements observed in the tapentadol PR group from baseline to final evaluation (LOCF) were significantly better than in the oxycodone/naloxone PR group for the SF-12 physical functioning, role-physical, bodily pain, general health, vitality, and social functioning domain scores, and for the physical component summary score (all $P < 0.05$; **Figure 1**)
  - At final evaluation, tapentadol PR was associated with 95.1% to 337.7% greater improvements in the SF-12 domain and summary scores compared with oxycodone/naloxone PR (**Figure 1**)
- Significant increases were observed from baseline to final evaluation (LOCF) in the mean EQ-5D health status index score in both treatment groups in the full analysis set (both $P < 0.001$; **Figure 3**)
  - In the tapentadol PR group of the full analysis set, significant increases from baseline to final evaluation (LOCF) were observed in all mean EQ-5D health status index score (all $P < 0.001$; least-squares mean; **Figure 3**)
  - At final evaluation, tapentadol PR was associated with a 98.4% greater improvement in the EQ-5D health status index score compared with oxycodone/naloxone PR (least-squares mean; **Figure 3**)



EQ-5D, EuroQol-5 Dimension; LS, least-squares; LOCF, last observation carried forward; PR, prolonged release; ANCOVA, analysis of covariance.
[a]Descriptive analyses.
[b]Percent difference between tapentadol PR and oxycodone/naloxone PR, using oxycodone/naloxone PR as the base (denominator).
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Figure 3. Mean EQ-5D health status index score at baseline and Week 12 and changes in EQ-5D index score from baseline to final evaluation (LS mean; LOCF; full analysis set).

CONCLUSIONS

- **In this interim analysis, tapentadol PR was associated with clear improvements in aspects of quality of life, including significant improvements from baseline to final evaluation in all SF-12 domain scores and both summary scores**
  - **Tapentadol PR was associated with significantly greater improvements than oxycodone/naloxone PR group in the SF-12 physical functioning, role-physical, bodily pain, general health, vitality, and social functioning domain scores, and the SF-12 physical component summary score**
- **Tapentadol PR was also associated with significant improvements in the EQ-5D health status index score from baseline to final evaluation, and those improvements were significantly greater than with oxycodone/naloxone PR**
- **This interim analysis is subject to certain limitations**
  - **The current interim analysis is based on a relatively small sample size; the final outcome may differ for the full study population**
  - **All of the *P* values presented here are descriptive and not adjusted for type 1 error inflation, which may lead to an increased false positive rate**
- **Taken together, results of the current interim analysis indicate superior effectiveness[a] and greater improvements in quality of life and function for tapentadol PR versus oxycodone/naloxone PR**

[a]Effectiveness results are presented in poster <<XX>>.

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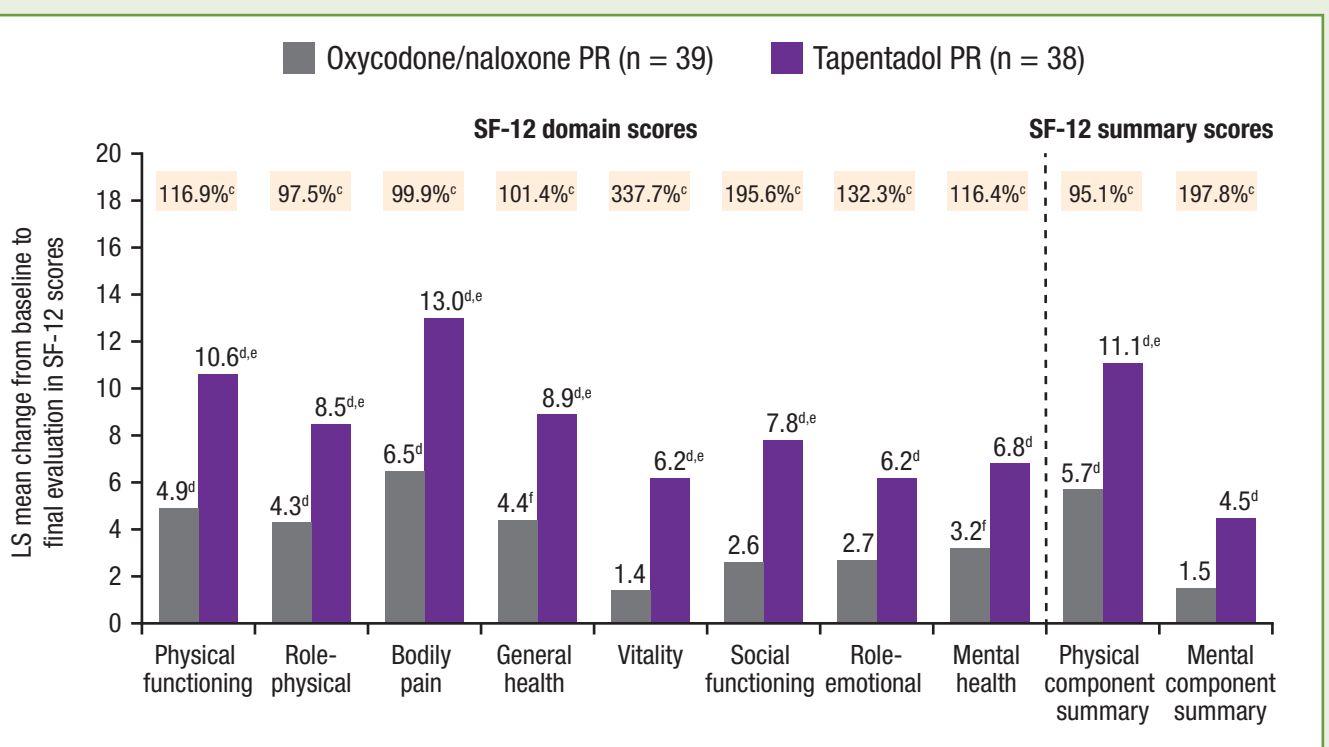

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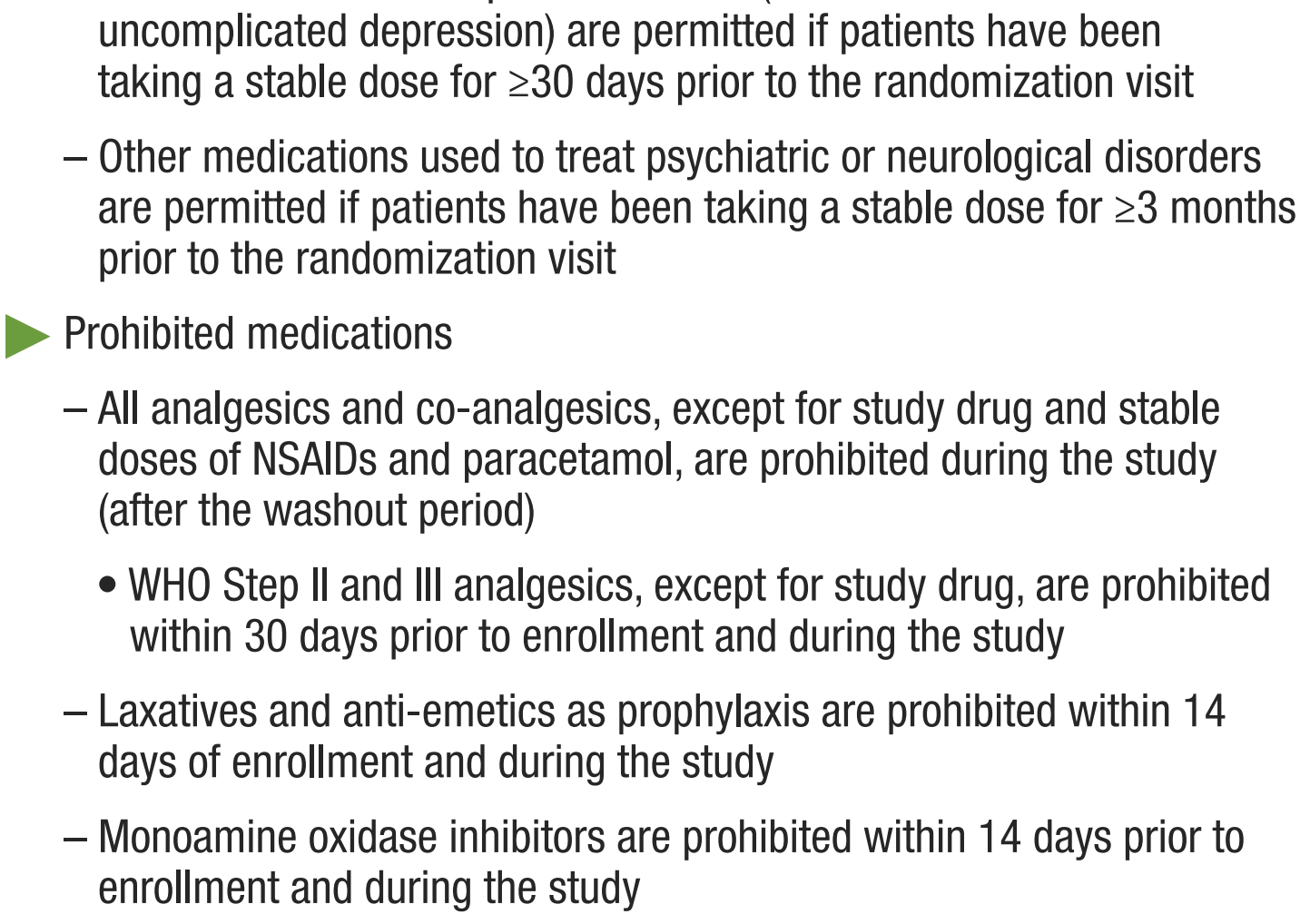

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  - The minimum target of titration at the end of the titration period is defined as 1 of the following:
    - NRS-3 ≤4 with acceptable tolerability, as reported by the patient
    - NRS-3 of ≤5 if pain relief and tolerability are reported as satisfactory by the patient and investigator to continue in the study, and 1) the patient is on the maximum dose of tapentadol PR or oxycodone/naloxone PR or 2) the maximum daily dose cannot be achieved because of side effects
- Patients who reach the minimum target of titration are eligible to enter a 9-week continuation period, during which patients continue on the same stable dose of study drug; for patients not taking the maximum dose, a single titration using the same increments as during titration is permitted during the continuation period
  - Patients in the tapentadol PR group who do not reach the minimum target of titration by the end of the titration period are discontinued from the study
  - Patients in the oxycodone/naloxone PR group who do not reach the minimum target of titration by the end of the titration period can be switched to tapentadol PR in a pickup arm or discontinued from the study (if they do not want to switch to tapentadol PR)

Study Evaluations

- Quality of life is evaluated as a secondary outcome in this study using the EQ-5D health status questionnaire and the SF-12 Health Survey
  - The SF-12 Health Survey[14] includes 12 questions that are used to evaluate 8 dimensions of functional health and well-being (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health); each dimension is scored on a scale from 0 ("lowest level of health") to 100 ("highest level of health")
  - The EQ-5D[15] health status questionnaire includes 5 dimensions of health-related quality of life (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression); patients rate each dimension using a 3-point scale (1 = "no problems," 2 = "some problems," 3 = "extreme problems")

- The EQ-5D health status questionnaire and SF-12 Health Survey are completed at the enrollment visit, the randomization visit, weekly during titration (Visits 4, 6, and 8), twice during the continuation period (Visits 9 and 10), and at the final evaluation visit

- The mean daily doses of tapentadol PR and oxycodone/naloxone PR were evaluated at the end of titration

Statistical Analyses

- This study has an adaptive 3-stage group-sequential design (O'Brien and Fleming type design[16]), with 1 planned interim analysis after observation of one-third of the total planned study population, the results of which are presented here

- A 2-sample *t* test was used for the calculation of the sample size. The sample size computation for the primary effectiveness endpoint was based on a standard deviation (SD) of 2.5 for the change in pain intensity from baseline and a non-inferiority margin of 1.3; the sample size computation for the second endpoint was based on a SD of 1.0 for the change from baseline in the Patient Assessment of Constipation Symptoms (PAC-SYM) total score, an expected difference of 0.1 in the change from baseline in the PAC-SYM total score in favor of oxycodone/naloxone PR, and a non-inferiority margin of 0.7

  - For both endpoints, a sample size of 96 patients per group in the per protocol set (defined below) is required to show the non-inferiority of tapentadol PR as compared to oxycodone/naloxone PR with 90% power and a 1-sided significance level of $\alpha = 0.0125$

  - Assuming that 80% of patients are available for the per protocol set, a total of 240 patients should receive study treatment in the overall study

  - Statistical methods for the primary endpoints are explained in further detail in posters <<XX>><<Poster numbers will be added upon receipt>>

- The safety set includes all randomized patients who took ≥1 dose of study drug

- The full analysis set includes all randomized patients who took ≥1 dose of study drug and had ≥1 post-baseline pain intensity assessment (NRS-3)

- For the SF-12 Health Survey, physical and mental component summary scores (possible score for each, 0 ["lowest level of health"] to 100 ["highest level of health"]) are calculated by combining scores from the 12 individual questions

- The responses to each of the EQ-5D dimensions are scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 and 1 (0 = "dead" to 1 = "full health")

- The changes from baseline to final evaluation in the SF-12 domain scores and composite scores and the EQ-5D health status index score are evaluated using an analysis of covariance (ANCOVA) model including treatment and pooled center as factors and score at baseline as a covariate

  - The last observation carried forward (LOCF) is used for imputing missing scores

  - The patients who entered the pickup arm were treated as discontinuations using the LOCF. The pickup arm was not analyzed during this interim analysis

- All analyses are exploratory, and all *P* values shown are descriptive

RESULTS

Patients

- For this interim analysis, 77 patients (tapentadol PR, n = 38; oxycodone/naloxone PR, n = 39) were included in the safety set and the full analysis set

- Demographic characteristics were similar in both treatment groups in the safety set

  - All patients in both treatment groups were white and >50% were female (tapentadol PR, 63.2% [24/38]; oxycodone/naloxone PR, 56.4% [22/39])

  - The mean SD age was 55.8 (12.33) years in the tapentadol PR group and 58.7 (11.76) years in the oxycodone/naloxone PR group

- In the tapentadol PR and oxycodone/naloxone PR groups, respectively, 79% (30/38) and 41% (16/39) of patients in the safety set completed study treatment

  - Overall, 92% more patients stayed on tapentadol PR treatment compared with oxycodone/naloxone PR treatment

- At the end of titration, the mean (SD) daily doses were <<X.XX>> mg/day in the tapentadol PR group and <<X.XX>> mg/day in the oxycodone/naloxone PR group

Quality of Life and Function

- In the tapentadol PR group of the full analysis set, significant increases from baseline to final evaluation (LOCF) were observed in all mean SF-12 domain scores (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) and the physical and mental component summary scores (all $P \leq 0.002$; **Figure 1**)

  - In the oxycodone/naloxone PR group of the full analysis set, significant increases from baseline to final evaluation were observed in the SF-12 physical functioning, role-physical, bodily pain, general health, and mental health domain scores, and in the physical component summary score (all $P \leq 0.03$; least-squares mean; **Figure 1**)

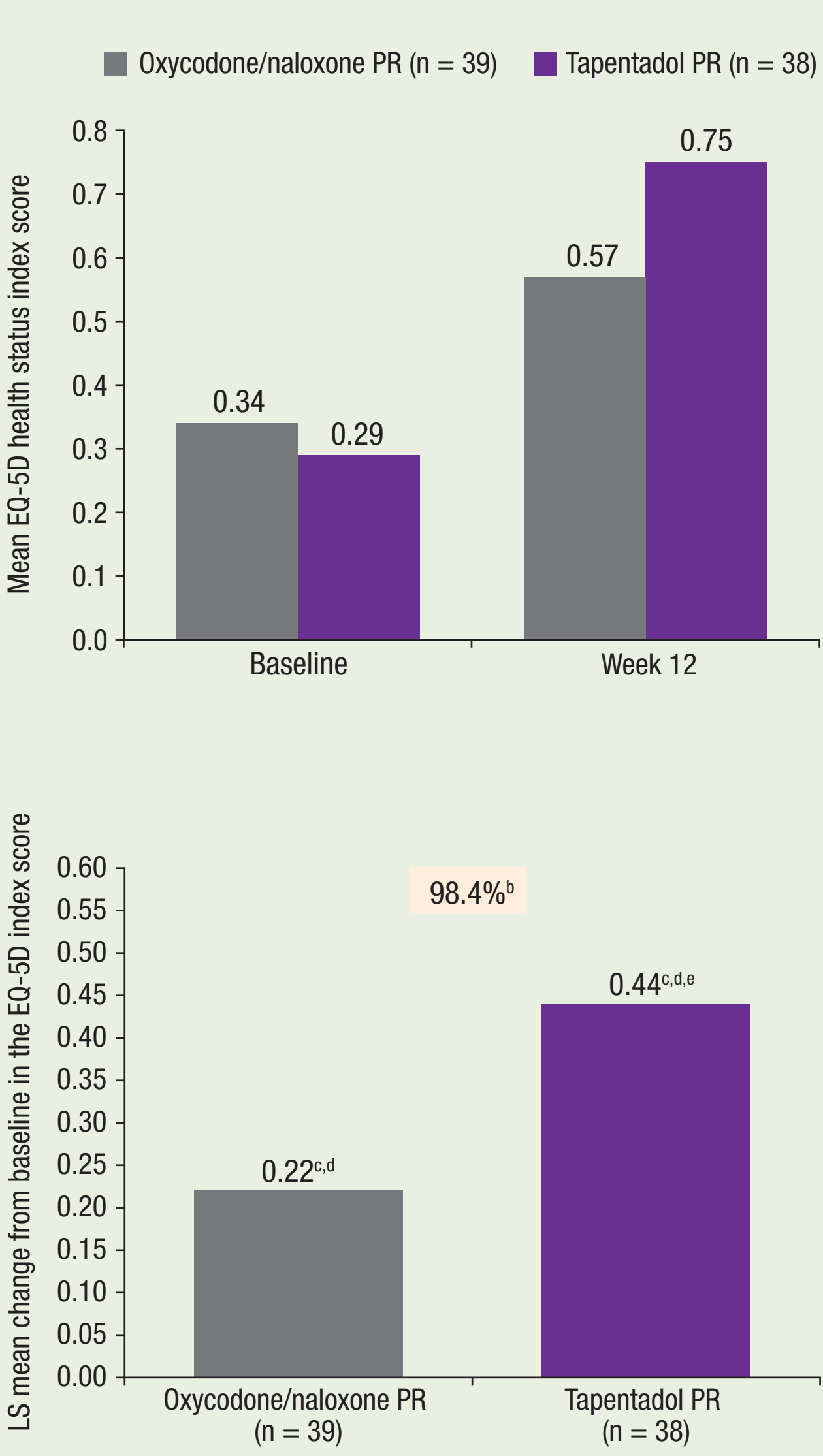
  - The improvements observed in the tapentadol PR group from baseline to final evaluation (LOCF) were significantly better than in the oxycodone/naloxone PR group for the SF-12 physical functioning, role-physical, bodily pain, general health, vitality, and social functioning domain scores, and for the physical component summary score (all $P < 0.05$; **Figure 1**)

  - At final evaluation, tapentadol PR was associated with 95.1% to 337.7% greater improvements in the SF-12 domain and summary scores compared with oxycodone/naloxone PR (**Figure 1**)

- Significant increases were observed from baseline to final evaluation (LOCF) in the mean EQ-5D health status index score in both treatment groups in the full analysis set (both $P < 0.001$; **Figure 3**)

  - The improvement from baseline to final evaluation (LOCF) in the EQ-5D health status index score was significantly greater in the tapentadol PR group than in the oxycodone/naloxone PR group ($P = 0.004$)

  - At final evaluation, tapentadol PR was associated with a 98.4% greater improvement in the EQ-5D health status index score compared with oxycodone/naloxone PR (least-squares mean; **Figure 3**)



EQ-5D, EuroQol-5 Dimension; LS, least-squares; LOCF, last observation carried forward; PR, prolonged release; ANCOVA, analysis of covariance.
[a]Descriptive analyses.
[b]Percent difference between tapentadol PR and oxycodone/naloxone PR, using oxycodone/naloxone PR as the base (denominator).
[c]LS means and *P* values are obtained from an ANCOVA model that includes treatment and pooled centers as factors and score at randomization (baseline) as a covariate.
[d]$P < 0.001$ for the change from baseline.
[e]$P = 0.004$ for tapentadol PR versus oxycodone/naloxone PR (in favor of tapentadol PR).

Figure 3. Mean EQ-5D health status index score at baseline and Week 12 and changes in EQ-5D index score from baseline to final evaluation (LS mean; LOCF; full analysis set).

CONCLUSIONS

- **In this interim analysis, tapentadol PR was associated with clear improvements in aspects of quality of life, including significant improvements from baseline to final evaluation in all SF-12 domain scores and both summary scores**
  - **Tapentadol PR was associated with significantly greater improvements than oxycodone/naloxone PR group in the SF-12 physical functioning, role-physical, bodily pain, general health, vitality, and social functioning domain scores, and the SF-12 physical component summary score**
- **Tapentadol PR was also associated with significant improvements in the EQ-5D health status index score from baseline to final evaluation, and those improvements were significantly greater than with oxycodone/naloxone PR**
- **This interim analysis is subject to certain limitations**
  - **The current interim analysis is based on a relatively small sample size; the final outcome may differ for the full study population**
  - **All of the *P* values presented here are descriptive and not adjusted for type 1 error inflation, which may lead to an increased false positive rate**
- **Taken together, results of the current interim analysis indicate superior effectiveness[a] and greater improvements in quality of life and function for tapentadol PR versus oxycodone/naloxone PR**

[a]Effectiveness results are presented in poster <<XX>>.

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