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| Name of Finished Product: QUTENZA | | |
| Name of Active Ingredient: Capsaicin | | |

## SYNOPSIS

**Title of Study:** A multicentre, single-arm, open-label study of the repeated administration of QUTENZA™ for the treatment of peripheral neuropathic pain.

**Investigators/Coordinating Investigator:** [redacted] France

**Study Centers:** This study was conducted at 63 sites in Europe: 3 sites in Austria, 5 sites in Belgium, 4 sites in Czech Republic, 2 sites in Finland, 6 sites in France, 2 sites in Greece, 1 site in Hungary, 2 sites in Ireland, 9 sites in Italy, 2 sites in the Netherlands, 3 sites in Poland, 2 sites in Romania, 1 site in Slovakia, 2 sites in Slovenia, 10 sites in Spain, and 9 sites in the UK.

**Publication Based on the Study:** Not applicable.

**Study Period:** October 2010 to September 2013

**Study Initiation Date (Date of First Enrollment):** 28 October 2010

**Study Completion Date (Date of Last Evaluation):** 26 September 2013

**Phase of Development:** Phase 4

**Objectives:**
**Primary objective**: To assess the safety of repeated treatments of QUTENZA in patients with peripheral neuropathic pain (PNP).
**Secondary objective:** To assess the efficacy of repeated treatments of QUTENZA in patients with PNP.

**Methodology:** This was a multicenter, open-label study to assess long-term safety of repeated QUTENZA patch applications in patients with PNP. Patients received an initial open-label treatment with QUTENZA and could receive up to 5 additional open-label QUTENZA applications. Patients could not receive more than 6 applications over a period of 1 year (52 weeks of study) and the last administration was no later than week 52. The duration of participation for each patient was up to 65 weeks and consisted of a screening period (1 week prior to first patch application visit [baseline]), a treatment period (baseline visit up to week 52), and a termination (end of study [EoS]) visit (no later than week 65).

**Number of Patients (Planned, Enrolled, and Analyzed):** A total of 300 eligible patients were planned to be treated, 306 patients were enrolled into the study. All of them received QUTENZA.

**Diagnosis and Main Criteria for Inclusion:** Patients were eligible for the study if they met 1 of the population-specific inclusion criteria for postherpetic neuralgia (PHN), human immunodeficiency virus-associated neuropathy (HIV-AN), post-traumatic nerve injury (PNI), or idiopathic small nerve neuropathy (ISNN) or had adequately characterized PNP and if the following applied:

1. Male or female between 18 and 90 years of age, inclusive.
2. In good health as determined by the investigator.
3. Average pain score ≥ 4 during screening period (using the average reported pain from the Brief Pain Inventory [BPI]).

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4. Intact, non-irritated, dry skin over the painful area(s) to be treated.
5. Females of child bearing potential had to be willing to use effective methods of birth control during the study and for 30 days following study termination.
6. Willing and able to comply with protocol requirements for the duration of study participation.
7. Given written informed consent.

**Test Product, Dose, and Mode of Administration, Batch Numbers:** QUTENZA is a high-concentration (8%) capsaicin patch. Up to 4 patches of QUTENZA (1120 $cm^2$ in total) were applied for 60 minutes to the painful areas of the body (as defined by the study physician), except the feet, where a 30-minute application time was used in full accordance with the approved Summary of Product Characteristics. Each patch is 14 cm by 20 cm (280 $cm^2$) and contains a total of 179 mg of capsaicin or 640 µg of capsaicin per 1 $cm^2$ of patch (8% w/w). QUTENZA was provided as a patch stored in a paper coated aluminum foil sachet with acrylnitrile-acrylic acid copolymer heat seal layer.

A topical anesthetic cream (e.g., 5% lidocaine cream) was applied for a period as determined by the prescribing information of the product used. QUTENZA Batches: [redacted] (expiry date: 31 Mar 2013); [redacted] (expiry date: 31 Mar 2013); [redacted] (expiry date: 30 Jun 2014).

**Duration of Treatment (or Duration of Study, if applicable):** The study period was 52 weeks.

**Reference Product, Dose and Mode of Administration, Batch Numbers:** Not applicable.

**Criteria for Evaluation:** This study assessed safety of repeated treatment with QUTENZA by evaluation of adverse events (AEs), including serious AEs (SAEs), treatment-emergent AEs (TEAEs), and the proportion of patients who prematurely terminated from the study due to an AE, and sensory testing, assessed by sensory testing instruments. Sensory testing was performed at screening, at all patch application visits, at week 26, and at the termination visit. Secondary safety variables included use of concomitant mediation, neurological assessments, vital signs, and dermal assessments and were assessed at screening, at all patch application visits, at week 26, and at the termination visit. Tolerability was reported at each patch application. Other safety variables, including laboratory tests and electrocardiogram, were performed at screening and at subsequent visits if clinically indicated.

The evaluation of efficacy was a secondary objective of the study. Secondary efficacy included measurements of pain severity and its interference with daily function by BPI modified short form and of the patients' overall status on a 7-point scale with the Patient Global Impression of Change (PGIC) questionnaire. Self-reported questionnaires were analyzed for the assessment of patients' Quality of Life (QoL, European Quality of life questionnaire in 5 Dimensions [EQ-5D]), anxiety and depression (Hospital Anxiety and Depression Scale [HADS]), and work productivity and activity impairment (Work Productivity and Activity Impairment Questionnaire: Neuropathic Pain [WPAI:NP]). At week 26 and at the termination visit, patients answered a Self-Assessment of Treatment (SAT) questionnaire for the assessment of treatment satisfaction. Concomitant medication use was assessed throughout the study.

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**Statistical Methods:**

Both safety and efficacy analyses were conducted on the Safety Analysis Set (SAF). This population included all patients who received study patch application. All data processing, summarization, and analyses were performed using SAS® Version 9.1 or higher on Unix.

For continuous variables, descriptive statistics included the number of patients, mean, SD, minimum, maximum, 1st quartile, median, and 3rd quartile, and 95% CIs. Percentages by categories were based on the number of patients with no missing data, (i.e., add up to 100%). In general data is summarized overall and patients' individual neuropathic diagnosis (PHN, HIV-AN, PNI, other PNP). The baseline date was the date of the 1st patch application.

AEs (coded by Medical Dictionary for Regulatory Activities [MedDRA] version 13.1) were assessed according to the schedule of assessments, were summarized as counts over the entire study and by patch application and analyzed descriptively. TEAEs, serious TEAEs, drug-related TEAEs (TEAEs with probable or possible relationship to the study drug), and the proportion of patients who prematurely terminated from the study or study drug due to an AE were reported throughout the study. All AEs occurring during the study were to be followed up until resolved or judged to be no longer clinically significant, or until they became chronic to the extent that they could be fully characterized. Sensory testing involved the identification and measurement of most painful areas and corresponding areas of allodynia. Counts by location and absolute value of area size were evaluated. Additionally, evoked sensation assessments were performed at several locations per modality with the most intense sensation evoked being rated. Dermal assessments were summarized as counts and percentage and as worst post-application and worst post-baseline response and neurological assessments were summarized as counts by category.

There was no primary efficacy objective in this study and pharmacokinetics and pharmacodynamics were not evaluated. Secondary efficacy variables were based on the following:

- BPI: Descriptive statistics were performed for BPI Questions 5 (average pain) and 6 (pain now) as absolute values and as changes from baseline and from before patch application for each patch application and as absolute values and as changes from baseline for Questions 1, 3, 4, 5, 6, 8, and 9 prior to and 4 weeks after each patch application, at week 26, and at EoS.
- PGIC questionnaire: Counts by category and by combined category were evaluated prior to and 4 weeks after each patch application, at week 26, and at EoS.
- QoL questionnaires (EQ-5D, HADS, WPAI:NP): Counts by category and descriptive statistics were performed prior to and 4 weeks after each patch application, at week 26, and at EoS.
- SAT questionnaire: Counts by category and by combined category were evaluated at week 26 and EoS.
- Concomitant medications: Change in use of concomitant pain medication was evaluated from screening visit to termination visit.

**Summary of Results/Conclusions:**

**Patient Disposition:** In total, 306 patients were enrolled into the study, all of whom were treated with QUTENZA. Among these 306 patients, 107 had PHN, 80 had HIV-AN, 99 had PNI, and 20 had "other" types of PNP (including 5 patients with ISNN). The safety analysis set (SAF) comprised all treated patients. One

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hundred thirty patients (42.5%) discontinued after treatment was initiated. The discontinuation rates were comparable among the HIV-AN (43.8%), PNI (45.5%), and "other" (45.0%) groups, and the rate was lower in the PHN group (38.3%). The most common reasons for discontinuation were lack of efficacy (17.6%), withdrawal by patient (10.8%), and lost to follow-up (5.6%). The discontinuation rate due to lack of efficacy ranged between 10.0% (HIV-AN) and 30.0% ("other" PNP, N = 6) among the diagnosis groups. The overall completion rate was 57.5%, ranging between 54.5% (PNI) and 61.7% (PHN) among the diagnosis groups. The majority of discontinuations occurred within the first 12 months, with no notable trends over time or among the diagnosis groups. A summary of patient disposition is provided in [Figure 1].

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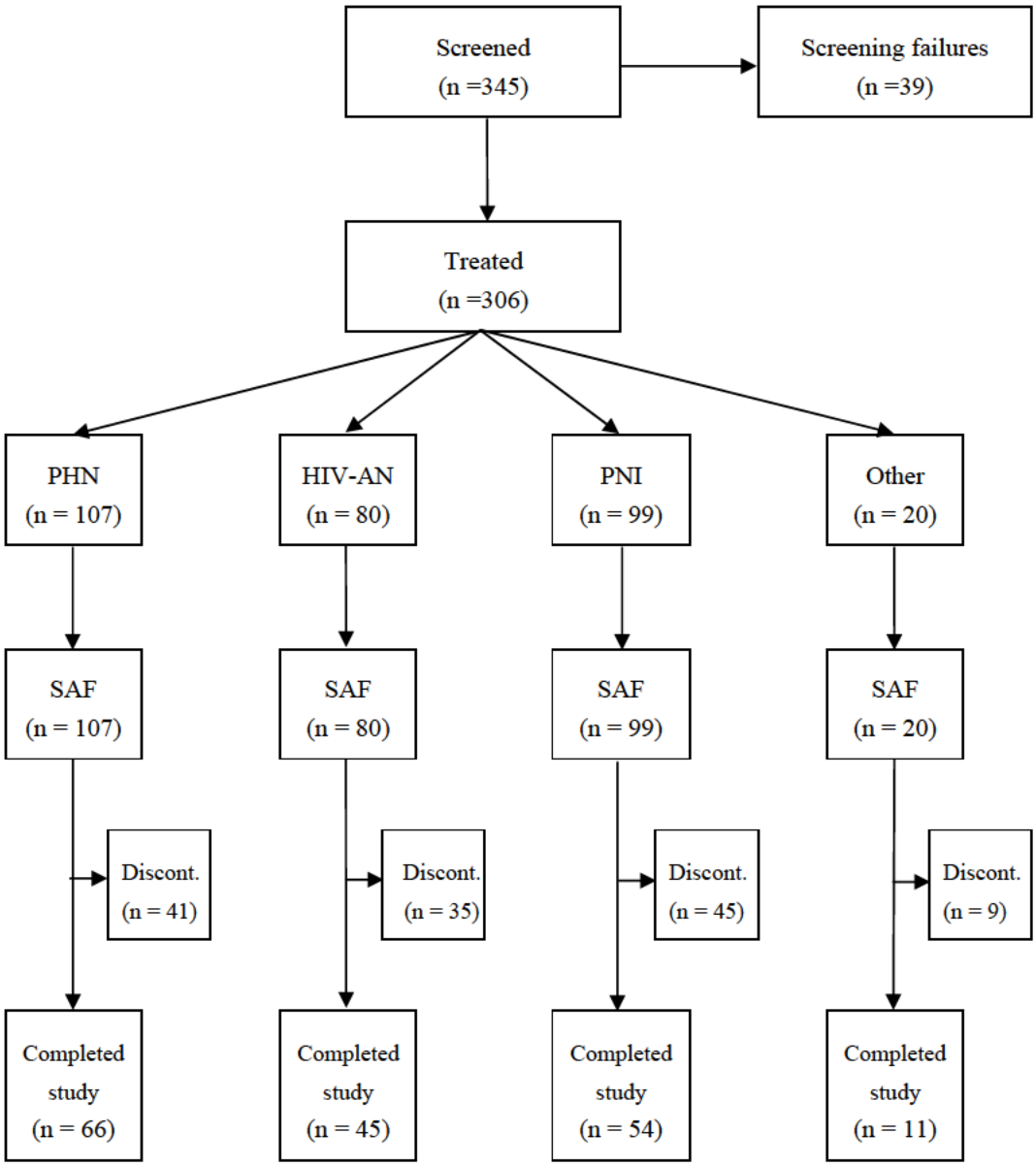
**Figure 1 Disposition of Patients**




Discont.: Discontinued; HIV-AN: Human immunodeficiency virus-associated neuropathy; n: Number of patients; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set (all patients who received at least 1 dose of study drug).

**Patient Demographics:** The mean age of patients enrolled in the study was 57.9 years (range: 20 to 90 years) Table 1. The oldest patients were in the PHN group and the youngest patients were in the HIV-AN and PNI groups. The ratio of men to women was generally balanced except in the HIV-AN group, which included 81.3% men and 18.8% women. The majority of patients in each diagnosis group were White, although the proportion of Black or African American patients was higher in the HIV-AN group (17.5%) than in the other groups (0.9% to 5.0%).

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**Table 1 Summary of Demographics and Baseline Characteristics by Pain Diagnosis (SAF)**

| **Parameter Category/Statistics** | **PHN (N = 107)** | **HIV-AN (N = 80)** | **PNI (N = 99)** | **Other (N = 20)** | **Total (N = 306)** |
|---|---|---|---|---|---|
| Sex, n (%) | | | | | |
| Male | 57 (53.3%) | 65 (81.3%) | 44 (44.4%) | 8 (40.0%) | 174 (56.9%) |
| Female | 50 (46.7%) | 15 (18.8%) | 55 (55.6%) | 12 (60.0%) | 132 (43.1%) |
| Race, n (%) | | | | | |
| White | 104 (97.2%) | 66 (82.5%) | 95 (96.0%) | 19 (95.0%) | 284 (92.8%) |
| Black or African American | 1 (0.9%) | 14 (17.5%) | 4 (4.0%) | 1 (5.0%) | 20 (6.5%) |
| Asian | 2 (1.9%) | 0 | 0 | 0 | 2 (0.7%) |
| Age, years | | | | | |
| Mean (SD) | 70.5 (10.85) | 51.5 (10.97) | 49.7 (13.48) | 56.5 (10.84) | 57.9 (15.04) |
| Median | 72.0 | 51.0 | 47.0 | 55.0 | 56.5 |
| Min; Max | 36; 90 | 22; 76 | 20; 81 | 41; 87 | 20; 90 |
| Age group, n (%) | | | | | |
| ≤ 64 years | 27 (25.2%) | 71 (88.8%) | 83 (83.8%) | 16 (80.0%) | 197 (64.4%) |
| ≥ 65 and ≤ 74 years | 36 (33.6%) | 8 (10.0%) | 11 (11.1%) | 3 (15.0%) | 58 (19.0%) |
| ≥ 75 years | 44 (41.1%) | 1 (1.3%) | 5 (5.1%) | 1 (5.0%) | 51 (16.7%) |

HIV-AN: Human immunodeficiency virus-associated neuropathy; N: Number of patients in the population; n: Number of patients in the sample; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set.

The mean time since diagnosis of PNP in patients enrolled in the study was 5.1 years (range: 0 to 38.3 years). The time since diagnosis of PNP tended to be longer in the HIV-AN group (mean: 7.4 years; range: 0.4 to 25.1 years) than in the PHN (mean: 3.9 years; range: 0 to 38.3 years) and PNI (mean: 4.0 years; range: 0.1 to 20.6 years) groups.

The mean pain baseline characteristics were generally comparable among the PNP diagnosis groups. The proportion of patients with an average pain score of ≥ 5 was higher in the PNI group (93.9%) than in the PHN (84.1%) or HIV-AN (83.8%) groups, and the proportion of patients with an average Pain Severity Index score of ≥ 5 was higher in the PHN (73.8%) and PNI (79.8%) groups than in the HIV-AN group (62.5%).

The baseline neuropathic pain sensory characteristics are summarized in [Table 2]. The mean pain baseline characteristics were comparable among the diagnosis groups for reflexes and cold, where the differences between mean scores among groups were all less than 1.0. Differences among groups were seen for vibration and sharp, where the mean scores were highest in the PNI group (2.4 and 3.4, respectively) and lowest in the HIV-AN group (1.2 and 1.9, respectively), and for heat, where the mean score was highest in the PHN group (2.5) and lowest in the HIV-AN group (1.0).

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**Table 2 Summary of Baseline Neuropathic Pain Sensory Testing by Pain Diagnosis (SAF)**

| Sensory Test Category/Statistics | PHN (N = 107) | HIV-AN (N = 80) | PNI (N = 99) | Other (N = 20) | Total (N = 306) |
|---|---|---|---|---|---|
| Vibration | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Mean (SD) | 2.2 (1.57) | 1.2 (1.40) | 2.4 (1.84) | 1.3 (1.22) | 2.0 (1.67) |
| Reflexes | | | | | |
| n | 104 | 79 | 99 | 20 | 302 |
| Mean (SD) | 1.8 (0.53) | 1.0 (0.85) | 1.8 (0.62) | 1.4 (0.88) | 1.6 (0.76) |
| Heat | | | | | |
| n | 107 | 79 | 99 | 20 | 305 |
| Mean (SD) | 2.5 (1.70) | 1.0 (1.24) | 2.0 (1.76) | 1.4 (1.43) | 1.9 (1.70) |
| Cold | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Mean (SD) | 1.9 (1.50) | 1.5 (1.32) | 2.1 (1.63) | 2.2 (1.90) | 1.9 (1.54) |
| Sharp | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Mean (SD) | 3.3 (1.76) | 1.9 (1.68) | 3.4 (1.84) | 2.1 (1.86) | 2.9 (1.89) |

Vibration: Scale of 0 (not felt) to 5 (felt more than usual, painful); Reflex: Scale of 0 (absent) to 4 (very intense); Heat: Scale of 0 (not felt) to 5 (felt more than usual, painful); Cold: Scale of 0 (not felt) to 5 (felt more than usual, painful); Sharp: Scale of 0 (not felt) to 5 (felt more than usual, painful).

BPI: Brief Pain Inventory; HIV-AN: Human immunodeficiency virus-associated neuropathy; N: Number of patients in the population; n: Number of patients in the sample; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set.

**Efficacy Results:**

**Brief Pain Inventory Modified Short Form**

Analysis of average pain (BPI Question 5) showed a reduction over time in the total population as assessed by the mean change from baseline by month. Patients with PNI showed numerically higher reductions in average pain from baseline compared with patients with HIV-AN or PHN up to month 15 (see Figure 2). However, the majority of differences between the 3 defined diagnosis groups were < 1 point.

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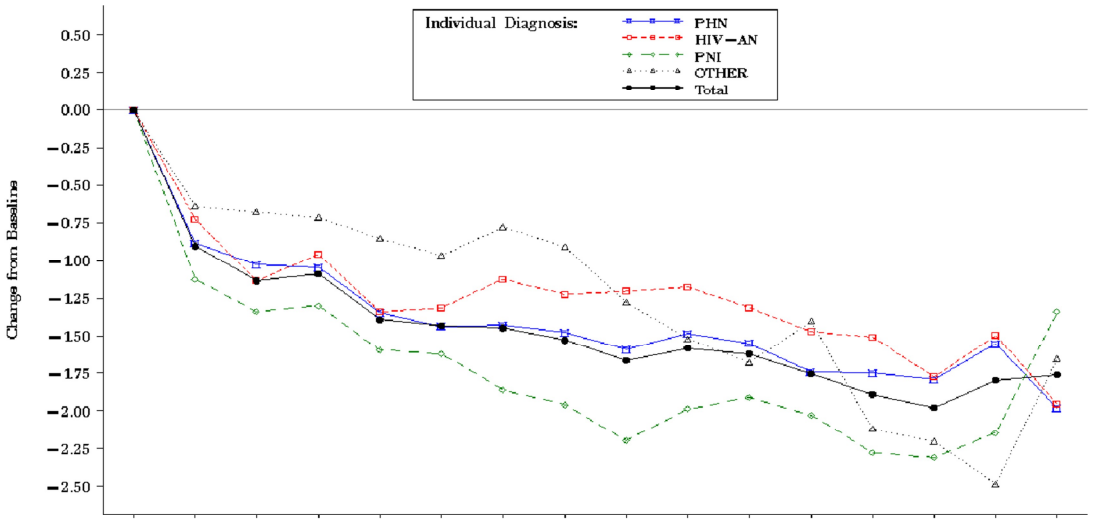
**Figure 2** **Brief Pain Inventory Question 5 (Average Pain) – Change from Baseline by Month by Individual Diagnosis (SAF)**




Number of subjects

| | Baseline | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | >= 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PHN | 107 | 106 | 102 | 97 | 91 | 90 | 81 | 79 | 75 | 70 | 70 | 68 | 63 | 54 | 42 | 36 |
| HIV−AN | 80 | 79 | 69 | 65 | 64 | 58 | 59 | 58 | 56 | 49 | 47 | 43 | 42 | 41 | 29 | 29 |
| PNI | 99 | 99 | 95 | 89 | 85 | 79 | 77 | 72 | 69 | 69 | 64 | 60 | 58 | 49 | 44 | 31 |
| OTHER | 20 | 20 | 19 | 18 | 18 | 18 | 16 | 15 | 15 | 14 | 12 | 11 | 11 | 9 | 5 | 7 |
| Total | 306 | 304 | 285 | 269 | 258 | 245 | 233 | 224 | 215 | 202 | 193 | 182 | 174 | 153 | 120 | 103 |

HIV-AN: Human immunodeficiency virus-associated neuropathy; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set.

A reduction in average pain was also observed across all months and applications (with total number of patients ≥ 50) in the total population when assessed by the mean change from before patch application by month. In general, the reduction from before patch application in average pain was less pronounced as the number of applications increased. For the 1st application, more pronounced reductions were observed in patients with PNI compared with patients in the other 2 defined diagnosis groups (occasionally with differences ≥ 1 between the PNI and HIV-AN groups) and the numerically lowest reductions were observed in the HIV-AN group.

Similar observations to the analyses by month were made for the analyses by week. A reduction in average pain over time in the total population was observed when assessed by the mean change from baseline or from before patch application by week. In general, the reduction from before patch application in average pain was less pronounced as the number of applications increased. Patients with PNI showed numerically higher reductions compared with the other 2 defined diagnosis groups in average pain from baseline over time and from before patch application for the 1st application. Occasional differences in reductions ≥ 1 point between the PNI group and the HIV-AN group were observed.

Analyses of "pain now" (BPI Question 6) showed reductions at 1 hour after patch removal in the total population at all applications (with total number of patients ≥ 50) when assessed by the mean changes from baseline or from pre-patch application. Reductions were also observed in all the 3 defined diagnosis groups. The changes at 5 min after patch removal showed variability, but consistent reductions were observed in the HIV-AN group.

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In general, an improvement in pain control based on the BPI questions and indices was observed at the various time points at all applications in the total population as well as in the individual diagnosis groups. Based on the changes from baseline at 4 weeks after application, more pronounced improvements were observed as the number of applications increased (differences ≥ 1 point between the 1st and 4th application for the majority of BPI questions and indices). The numerically largest changes were generally seen in the PNI group in most of the BPI items and questions (mainly at 4, 8, and/or 12 weeks after patch applications for the 1st and 2nd applications).

**Patient Global Impression of Change**

The majority of patients showed an improvement in their overall status throughout the study as assessed by the PGIC in the total population as well as in the individual diagnosis groups. The highest proportions of patients with improvement in their overall status were observed prior to and 4 weeks after the 4th and the 5th applications (ranging from 79.2% to 87.8%; note that the number of evaluated patients at the 5th application was < 50).

**Quality of Life**

The proportion of patients with no problems in all of the 5 dimensions of the EQ-5D questionnaire (assessing patients' health status) generally increased from prior to 1st application to all time points up to prior to 5th application (where total number of patients were ≥ 50). The proportions of patients with no problems were generally lower compared with the other 2 defined diagnosis groups for mobility and anxiety/depression in the HIV-AN group, and for usual activities in the PNI group, whereas the proportions were higher for self-care in the HIV-AN group.

Analysis of EQ-5D visual analog scale (VAS, assessing patients' self-rated health status) showed an increase for most of the time points (prior to and 4 weeks after patch application for all applications) in the total population as assessed by the mean changes from baseline. An increase in EQ-5D VAS from previous patch application was observed in the 1st, 2nd, and 4th applications, whereas a decrease was observed in the 3rd application in the total population. Regarding the 3 defined diagnosis groups, increases in mean EQ-5D VAS from baseline were observed for most of the time points. However, the mean changes in EQ-5D VAS from baseline at the various time points per application and from previous patch application showed a high degree of variability across and within diagnosis groups.

The proportion of patients with most positive answers generally increased from prior to 1st application at all time points up to prior to 5th application in all HADS items (assessing patients' HRQoL) in the total population. A trend of lower proportions of patients with most positive answers in the HIV-AN group compared with PHN and PNI groups was observed at the 1st to 3rd applications.

Analysis of HADS anxiety score showed a decrease for all applications in the total population as assessed by the mean change from baseline. There were no notable trends in the comparison between the 3 defined diagnosis groups. Analysis of HADS anxiety score by the mean change from previous patch application also showed a reduction at 4 weeks after patch application for the 1st to the 3rd applications in the total population. Increases in the anxiety score at 4 weeks after patch application were observed in the 4th, 5th, and 6th applications (however the number of evaluated patients at 5th and 6th applications was low). In all 3 defined

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diagnosis groups, a reduction at 4 weeks after patch application was observed in patients with PNI for the 1st, 2nd, and 3rd applications and in all 3 defined diagnosis groups for the 1st application.

Analysis of HADS depression score showed a reduction for all applications in the total population (apart from prior to the 6th application where number of evaluated patients was < 50) as assessed by the mean change from baseline. There were no notable trends in the comparison between the 3 defined diagnosis groups. Analysis of HADS depression score by the mean change from previous patch application also showed reductions for the 1st and 2nd applications and increases for the 3rd and 4th applications in the total population. In all 3 defined diagnosis groups changes from previous patch application showed high variability without clear trends.

The majority of patients were employed throughout the study and there were no notable differences in the proportion of employed patients across applications in the total population. The lowest proportions of employed patients were generally observed in the PNI group and highest in the PHN group.

Analyses of WPAI:NP Questions 2 to 5 either showed high variability or did not include enough evaluated patients to allow a reliable interpretation as assessed by the mean change from baseline or from previous patch application. Analysis of mean change from baseline in Question 6 showed a reduction at all time points, with no notable trends in the comparison between the 3 defined diagnosis groups. Analysis of mean change from previous patch application in Question 6 showed a reduction for the 1st to the 3rd applications and an increase for the 4th application. Reductions from previous patch application in Question 6 were observed in patients with HIV-AN and PNI, whereas mainly increases were observed in patients with PHN.

**Self-assessment of Treatment**

The majority of patients provided neutral or positive answers to all assessments of treatment satisfaction at EoS. The proportions of patients in all assessment evaluations were generally comparable between the 3 defined diagnosis groups.

**Medications of Interest and Concomitant Medications**

In general, the proportions of patients using medication of interest (antidepressants, antiepileptic drugs, or opioids) did not show any relevant changes at the different time points from day -30 to day 396 (month 13). The proportion of patients using medication of interest decreased from month 14 to month 18. Similar trends were observed in the individual defined diagnosis groups. The proportions of patients using antidepressants or opioids were comparable between all 3 defined groups for all time points from day -30 to day 396, whereas the proportion of patients using antiepileptic drugs in the HIV-AN group was generally lower compared with the PHN and PIN groups.

The majority of patients remained on a stable number of chronic medications for neuropathic pain from baseline through months 1 to 6. Slightly more patients, mainly in the PHN group, required more treatment than those requiring less treatment, through months 1 to 6. For months 7 to 9, the numbers of patients requiring either more or less treatment than at baseline were generally comparable in the PHN and PNI groups.

The majority of patients received 0 to 1 antidepressants throughout the study.

The majority of patients received 0 to 1 antiepileptics throughout the study. From months 6 to 14, slightly more patients in the PHN and PNI groups required less treatment than at baseline.

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More patients in the PHN and PNI groups required less opioids for pain than at baseline, than those requiring more opioids than at baseline from month 2 to month 14.

**Safety Results:**

**The primary safety variables were:**

- AEs: TEAEs, serious TEAEs, and the proportion of patients who prematurely terminated from the study due to an AE (TEAE resulting in discontinuation).
- Sensory function: change from screening visit of warm, cold, sharp (pinprick), and vibration sensations, light brush, deep tendon reflexes, most sensitive areas, and allodynia, assessed at patch application visits, week 26 (if applicable), and planned or early termination visit.

**Adverse Events**

Overall, 252 (82.4%) patients reported 1244 TEAEs. The proportion of patients with TEAEs was similar between diagnosis (type of neuropathic pain) groups : 87 (81.3%) of patients with PHN reported 466 TEAEs; 62 (77.5%) patients with HIV-AN reported 198 TEAEs; 86 (86.9%) patients with PNI reported 482 TEAEs; and 17 (85.0%) patients with "other" PNP reported 98 TEAEs Table 3. The prevalence of TEAEs (number of TEAEs per number of patients) was also similar between groups with the exception of patients in the HIV-AN group who reported a lower prevalence of TEAEs than in the other diagnosis groups.

In total, 37 (12.1%) patients experienced 72 serious TEAEs. The proportion of patients who reported serious TEAEs was similar between the diagnosis groups Table 4. The prevalence of serious TEAEs reported was also similar between diagnosis groups with the exception of patients in the HIV-AN diagnosis group who reported a higher prevalence of TEAEs than in the other diagnosis groups. No drug-related serious TEAEs were reported.

Eleven patients reported 13 TEAEs that led to discontinuation of QUTENZA; only 5 of these TEAEs leading to discontinuation (reported in 3 patients) were considered to be related to QUTENZA. QUTENZA-related TEAEs leading to discontinuation were application site erythema, application site pain, and PHN (in 1 patient with a diagnosis of PHN), neuralgia (in 1 patient with a diagnosis of PNI), and allodynia (in 1 patient with a diagnosis of "other") [Table 5].

In total, 207 (67.6%) patients reported 766 drug-related TEAEs . The proportion of patients who reported drug-related TEAEs and the prevalence of TEAEs reported was similar between the PHN, PNI, and "other" diagnosis groups. However, fewer patients reported drug-related TEAEs in the HIV-AN diagnosis group (52.5% of patients).

There were 3 deaths reported in the study due to the events of cerebral hemorrhage, pneumonia, and recurrent squamous cell carcinoma; all events leading to death were considered to be not related to QUTENZA.

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**Table 3 Summary of Patients with TEAEs (Reported by ≥ 5.0% of Patients in the Total Population) (SAF)**

| **MedDRA v13.1 System Organ Class Preferred Term** | **Diagnosis group, Number of patients (%)** | | | | |
|---|---|---|---|---|---|
| | **PHN (N = 107)** | **HIV-AN (N = 80)** | **PNI (N = 99)** | **Other (N = 20)** | **Total (N = 306)** |
| **Overall** | 87 (81.3) | 62 (77.5) | 86 (86.9) | 17 (85.0) | 252 (82.4) |
| **General disorders and administration site conditions** | 64 (59.8) | 30 (37.5) | 55 (55.6) | 12 (60.0) | 161 (52.6) |
| Application site pain | 46 (43.0) | 21 (26.3) | 40 (40.4) | 5 (25.0) | 112 (36.6) |
| Application site erythema | 24 (22.4) | 2 (2.5) | 19 (19.2) | 6 (30.0) | 51 (16.7) |
| Pain | 13 (12.1) | 6 (7.5) | 16 (16.2) | 8 (40.0) | 43 (14.1) |
| **Nervous system disorders** | 25 (23.4) | 16 (20.0) | 32 (32.3) | 8 (40.0) | 81 (26.5) |
| Burning sensation | 11 (10.3) | 8 (10.0) | 20 (20.2) | 6 (30.0) | 45 (14.7) |
| **Skin and subcutaneous tissue disorders** | 34 (31.8) | 4 (5.0) | 35 (35.4) | 3 (15.0) | 76 (24.8) |
| Erythema | 29 (27.1) | 1 (1.3) | 29 (29.3) | 3 (15.0) | 62 (20.3) |
| **Musculoskeletal and connective tissue disorders** | 16 (15.0) | 18 (22.5) | 18 (18.2) | 2 (10.0) | 54 (17.6) |
| Pain in extremity | 2 (1.9) | 11 (13.8) | 5 (5.1) | 1 (5.0) | 19 (6.2) |
| **Gastrointestinal disorders** | 11 (10.3) | 12 (15.0) | 13 (13.1) | 6 (30.0) | 42 (13.7) |
| Nausea | 4 (3.7) | 1 (1.3) | 8 (8.1) | 3 (15.0) | 16 (5.2) |

Within a system organ class, a patient may have reported more than 1 type of AE.

A TEAE was defined as an AE which started or increased in severity after application of the study drug.

Sorting order: Descending frequency by system organ class, and within that descending frequency by preferred term based on the total number of patients with TEAEs.

AE: Adverse event; HIV-AN: Human immunodeficiency virus-associated neuropathy; N: Number of patients in the total population and per diagnosis group; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set; TEAE: Treatment-emergent adverse event.

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**Table 4 Serious TEAEs (SAF)**

| **MedDRA v13.1** | **Diagnosis group, Number of patients (%)** | | | | |
|---|---|---|---|---|---|
| **System Organ Class** **Preferred Term** | **PHN (N = 107)** | **HIV-AN (N = 80)** | **PNI (N = 99)** | **Other (N = 20)** | **Total (N = 306)** |
| **Overall** | 14 (13.1) | 8 (10.0) | 13 (13.1) | 2 (10.0) | 37 (12.1) |
| **Infections and infestations** | 2 (1.9) | 6 (7.5) | 2 (2.0) | 0 | 10 (3.3) |
| Pneumonia | 0 | 2 (2.5) | 1 (1.0) | 0 | 3 (1.0) |
| Sepsis | 1 (0.9) | 1 (1.3) | 0 | 0 | 2 (0.7) |
| Bronchitis | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Gastroenteritis | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| HIV peripheral neuropathy | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Influenza | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Lower respiratory tract infection | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Pyelonephritis | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Upper respiratory tract infection | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Urinary tract infection | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Urosepsis | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Viral pericarditis | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| **Musculoskeletal and connective tissue disorders** | 1 (0.9) | 2 (2.5) | 2 (2.0) | 0 | 5 (1.6) |
| Arthralgia | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Fistula | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Mobility decreased | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Musculoskeletal chest pain | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Osteoarthritis | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| **Nervous system disorders** | 1 (0.9) | 1 (1.3) | 3 (3.0) | 0 | 5 (1.6) |
| Cerebral haemorrhage | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Complex regional pain syndrome | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Dizziness | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Neuralgia | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Partial seizures | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| **Surgical and medical procedures** | 4 (3.7) | 0 | 1 (1.0) | 0 | 5 (1.6) |
| Chemotherapy | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Hip arthroplasty | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Hip surgery | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Knee arthroplasty | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Spinal laminectomy | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| **Gastrointestinal disorders** | 0 | 2 (2.5) | 1 (1.0) | 1 (5.0) | 4 (1.3) |
| Abdominal pain upper | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Ascites | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Gastrointestinal ulcer haemorrhage | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Nausea | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Subileus | 0 | 0 | 0 | 1 (5.0) | 1 (0.3) |

*Table continued on next page*

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| **MedDRA v13.1 System Organ Class Preferred Term** | **Diagnosis group, Number of patients (%)** | | | | |
|---|---|---|---|---|---|
| | **PHN (N = 107)** | **HIV-AN (N = 80)** | **PNI (N = 99)** | **Other (N = 20)** | **Total (N = 306)** |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** | 4 (3.7) | 0 | 0 | 0 | 4 (1.3) |
| Basal cell carcinoma | 2 (1.9) | 0 | 0 | 0 | 2 (0.7) |
| B-cell unclassifiable lymphoma high grade | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Squamous cell carcinoma | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| **Cardiac disorders** | 2 (1.9) | 1 (1.3) | 0 | 0 | 3 (1.0) |
| Bradycardia | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Cardiac failure | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Ventricular tachycardia | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| **Injury, poisoning and procedural complications** | 2 (1.9) | 0 | 1 (1.0) | 0 | 3 (1.0) |
| Hip fracture | 2 (1.9) | 0 | 0 | 0 | 2 (0.7) |
| Lumbar vertebral fracture | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| **Renal and urinary disorders** | 1 (0.9) | 1 (1.3) | 1 (1.0) | 0 | 3 (1.0) |
| Bladder disorder | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Haematuria | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Nephrolithiasis | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Renal colic | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| **Vascular disorders** | 0 | 1 (1.3) | 2 (2.0) | 0 | 3 (1.0) |
| Aortic dissection | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Deep vein thrombosis | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Peripheral ischaemia | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| **General disorders and administration site conditions** | 1 (0.9) | 0 | 1 (1.0) | 0 | 2 (0.7) |
| Chest pain | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Malaise | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| Pyrexia | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| **Investigations** | 1 (0.9) | 0 | 1 (1.0) | 0 | 2 (0.7) |
| Biopsy | 1 (0.9) | 0 | 1 (1.0) | 0 | 2 (0.7) |
| Biopsy bone | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| **Respiratory, thoracic and mediastinal disorders** | 1 (0.9) | 0 | 1 (1.0) | 0 | 2 (0.7) |
| Chronic obstructive pulmonary disease | 0 | 0 | 1 (1.0) | 0 | 1 (0.3) |
| Haemoptysis | 1 (0.9) | 0 | 0 | 0 | 1 (0.3) |
| **Endocrine disorders** | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| Hypothyroidism | 0 | 1 (1.3) | 0 | 0 | 1 (0.3) |
| **Psychiatric disorders** | 0 | 0 | 0 | 1 (5.0) | 1 (0.3) |
| Suicidal ideation | 0 | 0 | 0 | 1 (5.0) | 1 (0.3) |

Within a system organ class, a patient may have reported more than 1 type of AE.

A TEAE was defined as an AE which started or increased in severity after intake/application of the study drug.

Sorting order: Descending frequency by system organ class, and within that descending frequency by preferred term based on the total number of patients with serious TEAEs.

AE: Adverse event; HIV-AN: Human immunodeficiency virus-associated neuropathy; N: Number of patients in the total population and per diagnosis group; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set; TEAE: Treatment-emergent adverse event.

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**Table 5 Adverse Events Resulting in Discontinuation**

| Patient Number | Age/ Sex | Adverse Events Resulting in Discontinuation MedDRA (v13.1) Preferred Term (investigator's verbatim term) | Last Applica-tion Day | Onset/ Stop Day | Outcome | Relationship to Study Drug |
|---|---|---|---|---|---|---|
| **Diagnosis group: PHN** | | | | | | |
| [redacted] | [redacted] | Pain ([redacted]) | 1 | 42/- | Not Recovered | Not Related |
| [redacted] | [redacted] | Cerebral haemorrhage ([redacted]) | 169 | 303/303 | Death | Not Related |
| [redacted] | [redacted] | Application site erythema ([redacted]) | 1 | 1/2 | Recovered | Probably Related |
| | | Application site pain ([redacted]) | 1 | 1/23 | Not Recovered | Probably Related |
| | | PHN ([redacted]) | 1 | 23/23E | Not Recovered | Probably Related |
| [redacted] | [redacted] | Facial neuralgia ([redacted]) | 72 | 150/167E | Not Recovered | Not Related |
| [redacted] | [redacted] | Squamous cell carcinoma ([redacted]) | 93 | 133E/161 | Death | Not Related |
| **Diagnosis group: HIV-AN** | | | | | | |
| [redacted] | [redacted] | Pneumonia ([redacted]) | 226 | 252/266 | Death | Not Related |
| **Diagnosis group: PNI** | | | | | | |
| [redacted] | [redacted] | Complex regional pain syndrome [redacted] | 187 | 279/364E | Not Recovered | Not Related |
| [redacted] | [redacted] | Burning sensation [redacted] | 1 | 58/104E | Recover-ing | Not Related |
| [redacted] | [redacted] | Neuralgia [redacted] | 1 | 4/11 | Recovered | Probably Related |
| [redacted] | [redacted] | Renal colic ([redacted]) | 221 | 262E/284E | Recover-ing | Not Related |
| **Diagnosis group: Other** | | | | | | |
| [redacted] | [redacted] | Allodynia [redacted] | 64 | 64/175E | Not Recovered | Possibly Related |

AE: Adverse event; E: Estimated day; HIV-AN: Human immunodeficiency virus-associated neuropathy; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set; TEAE: Treatment-emergent adverse event.

The TEAE reported by the highest proportion of patients was application site pain which was not reported similarly across the diagnosis groups; a lower proportion of patients who were diagnosed with HIV-AN or "other" PNP reported this TEAE than patients diagnosed with PHN or PNI. A relatively high proportion of

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patients reported erythema and application site erythema. Erythema was also not reported similarly across the diagnosis groups; a lower proportion of patients who were diagnosed with HIV-AN or "other" PNP reported this TEAE than patients diagnosed with PHN or PNI. Application site erythema was also reported by a notably lower proportion of patients who were diagnosed with HIV-AN. Of note, investigators did not clearly distinguish between erythema and application site erythema when they reported these TEAEs in the case report form.

Overall, 213 (69.6%) patients experienced at least 1 TEAE within 7 days of any patch application; more patients reported a TEAE within 7 days of patch application than after 7 days of patch application. The general trend for the total population was the proportion of patients who experienced TEAEs decreased over the course of the study, from between 1st and 2nd application to between the 4th and 5th application. The proportion of patients who experienced the TEAEs of application site pain, and application site erythema generally decreased as the study progressed (i.e., in general, less patients reported these events after later patch applications than between 1st and 2nd application), the proportion of patients who experienced erythema generally increased as the study progressed. Of note, the terms "application site erythema" and "erythema" were not reported in a consistent manner by the different investigators in this study.

**Sensory Function**

The majority of patients reported painful areas to the torso (41.2%) or to the feet (34.6%) at screening, and the distribution of painful areas remained similar throughout the study.

For the total population there were fluctuations in the mean area size throughout the study, but a general decrease in mean [SD] sensitive area was observed from 1st application (365.0 [313.85] $cm^2$) to the 5th application (276.6 [260.18] $cm^2$).

The majority of patients reported allodynia to the torso (46.4%) or to the feet (25.0%) at screening, and the distribution of allodynia remained similar throughout the study (with the exception when the number of patients were too low to draw reliable conclusions).

For the total population there were fluctuations in the mean [SD] area of allodynia, but a general decrease in allodynia area from 1st application (241.9 [259.1] $cm^2$ to the 5th application (208 [248.45] $cm^2$).

The change from screening visit of the sensory modalities (light brush, warm, cold, sharp [pinprick], reflex, and vibration sensations), was assessed. The majority of patients reported same or increased sensitivity based on the sensory modalities throughout the study.

For the total population, at the 1st application visit, the majority of patients reported that they had the same or increased sensitivity (from screening) to all the modalities (light brush [90.8%], warm [86.2%], cold [83.9%], pinprick [85.9%], reflex [94.7%], and vibration [85.6%]). Thus the numbers of patients reporting a decrease in sensitivity for these modalities was relatively low (light brush [9.2%], warm [13.8%], cold [16.1%], pinprick [14.1%], reflex [5.3%], and vibration [14.4%]).

By the 2nd application visit the proportion of patients reporting the same or increased sensitivity showed a notable decrease for all modalities except reflex (light brush [79.6%], warm [74.2%], cold [73.0%], pinprick [73.5%], reflex [93.3%], and vibration [71.3%]),and thus the numbers of patients reporting a decrease in

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sensitivity for these modalities showed a notable increase (light brush [20.4%], warm [25.8%], cold [27.0%], pinprick [26.5%], reflex [6.7%], and vibration [28.7%]). Notable differences were based on the lack of overlap between the 95% CIs for patients reporting the decreased sensitivity between 1st application and 2nd application (95% CI: light brush 1st [6.2, 13.0], 2nd [15.4, 26.2]; warm 1st [10.1, 18.2], 2nd [20.2, 31.9]; cold 1st [12.2, 20.7], 2nd [21.3, 33.2]; pinprick 1st [10.4, 18.5], 2nd [20.9, 32.7]; reflex 1st [32.1, 8.5], 2nd [3.8, 10.8] [no relevant difference]; and vibration 1st [10.6, 18.8], 2nd [22.9, 35.0]).

There were no notable differences in the proportion of patients who reported a decrease in sensitivity (thus no notable difference in the proportion of patients who reported the same or increased sensitivity) for any of the modalities between the 2nd application and 3rd application, between the 3rd application and 4th application, and between 4th application and 5th application (based on all of the 95% CIs 2nd versus 3rd, 3rd versus 4th application, and 4th versus 5th application overlapping). These results indicated, in general, the change in sensitivity based on light brush, warm, cold, pinprick, and vibration testing towards a decrease in sensitivity had plateaued by 3rd application. Decreased versus same or increased, dichotomous scores at the last patch application visit are presented in [Table 6].

Shifts in the proportion of patients reporting no sensory changes, changes to below normal (decreased abnormal), increased, increased abnormal from baseline were assessed by diagnosis group and by patch application. Notable shifts (both decreases and increases) in sensitivity were observed for all the sensitivity modalities (light brush, warm, cold, pinprick, vibration, and reflex).

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**Table 6 Sensory Testing – Dichotomous Scores Counts by Category (Last Application) (SAF)**

| Category Dichotomous Scores | Diagnosis group, Number of patients (%) | | | | |
|---|---|---|---|---|---|
| | **PHN (N = 107)** | **HIV-AN (N = 80)** | **PNI (N = 99)** | **Other (N = 20)** | **Total (N = 306)** |
| **Light Brush Rating** | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Decreased | 21 (19.6) | 13 (16.3) | 30 (30.3) | 4 (20.0) | 68 (22.2) |
| 95% CI † | 12.6, 28.4 | 8.9, 26.2 | 21.5, 40.4 | 5.7, 43.7 | 17.7, 27.3 |
| Same or Increased | 86 (80.4) | 67 (83.8) | 69 (69.7) | 16 (80.0) | 238 (77.8) |
| 95% CI † | 71.6, 87.4 | 73.8, 91.1 | 59.6, 78.5 | 56.3, 94.3 | 72.7, 82.3 |
| **Vibration Rating** | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Decreased | 32 (29.9) | 21 (26.3) | 26 (26.3) | 2 (10.0) | 81 (26.5) |
| 95% CI † | 21.4, 39.5 | 17.0, 37.3 | 17.9, 36.1 | 1.2, 31.7 | 21.6, 31.8 |
| Same or Increased | 75 (70.1) | 59 (73.8) | 73 (73.7) | 18 (90.0) | 225 (73.5) |
| 95% CI † | 60.5, 78.6 | 62.7, 83.0 | 63.9, 82.1 | 68.3, 98.8 | 68.2, 78.4 |
| **Warm Rating** | | | | | |
| n | 107 | 79 | 99 | 20 | 305 |
| Decreased | 29 (27.1) | 14 (17.7) | 29 (29.3) | 3 (15.0) | 75 (24.6) |
| 95% CI † | 19.0, 36.6 | 10.0, 27.9 | 20.6, 39.3 | 3.2, 37.9 | 19.9, 29.8 |
| Same or Increased | 78 (72.9) | 65 (82.3) | 70 (70.7) | 17 (85.0) | 230 (75.4) |
| 95% CI † | 63.4, 81.0 | 72.1, 90.0 | 60.7, 79.4 | 62.1, 96.8 | 70.2, 80.1 |
| **Pinprick Rating** | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Decreased | 34 (31.8) | 16 (20.0) | 32 (32.3) | 6 (30.0) | 88 (28.8) |
| 95% CI † | 23.1, 41.5 | 11.9, 30.4 | 23.3, 42.5 | 11.9, 54.3 | 23.8, 34.2 |
| Same or Increased | 73 (68.2) | 64 (80.0) | 67 (67.7) | 14 (70.0) | 218 (71.2) |
| 95% CI † | 58.5, 76.9 | 69.6, 88.1 | 57.5, 76.7 | 45.7, 88.1 | 65.8, 76.2 |
| **Reflex Rating** | | | | | |
| n | 104 | 79 | 97 | 20 | 300 |
| Decreased | 5 (4.8) | 14 (17.7) | 4 (4.1) | 1 (5.0) | 24 (8.0) |
| 95% CI † | 1.6, 10.9 | 10.0, 27.9 | 1.1, 10.2 | 0.1, 24.9 | 5.2, 11.7 |
| Same or Increased | 99 (95.2) | 65 (82.3) | 93 (95.9) | 19 (95.0) | 276 (92.0) |
| 95% CI † | 89.1, 98.4 | 72.1, 90.0 | 89.8, 98.9 | 75.1, 99.9 | 88.3, 94.8 |
| **Cold Rating** | | | | | |
| n | 107 | 80 | 99 | 20 | 306 |
| Decreased | 26 (24.3) | 19 (23.8) | 24 (24.2) | 8 (40.0) | 77 (25.2) |
| 95% CI † | 16.5, 33.5 | 14.9, 34.6 | 16.2, 33.9 | 19.1, 63.9 | 20.4, 30.4 |
| Same or Increased | 81 (75.7) | 61 (76.3) | 75 (75.8) | 12 (60.0) | 229 (74.8) |
| 95% CI † | 66.5, 83.5 | 65.4, 85.1 | 66.1, 83.8 | 36.1, 80.9 | 69.6, 79.6 |

For sensory testing, baseline values are obtained at the screening visit.

Assessments on the day of patch application are recorded prior to patch application.

HIV-AN: Human immunodeficiency virus-associated neuropathy; n: Number of patients with data; N: Number of patients in the total population and per diagnosis group; PHN: Postherpetic neuralgia; PNI: Post-traumatic nerve injury; SAF: Safety analysis set; TEAE: Treatment-emergent adverse event.

† Normal approximation to the binomial distribution for proportion of patients.

**CONCLUSIONS:** QUTENZA was generally well tolerated in patients with PHN, HIV-AN, PNI or other type of PNP. In general, QUTENZA had a beneficial effect on patient's pain relief and QoL. It was observed that patients with PNI had more pronounced analgesia than the other diagnosis groups.

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**Date of Report:** 15 April 2014