A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS OF CAPSAICIN 8% PATCH VERSUS ORAL NEUROPATHIC PAIN MEDICATIONS FOR THE TREATMENT OF PAINFUL DIABETIC PERIPHERAL NEUROPATHY

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INTRODUCTION

• Neuropathies, characterised by damage to peripheral nerve fibre in a common long-term condition of diabetes,1–4
• Painful diabetic neuropathy occurs in 10% to 20% of patients with diabetes.1–4
• Symptoms adversely affect health-related quality of life,4 and can cause sleep problems, anxiety and depression.1–4
• Painful diabetic peripheral neuropathy (PDPN) is a challenging condition to treat.
• Evidence-based treatment guidelines recommend oral agents, including anticonvulsants, tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors.1–5
• Localised and topical treatments are also recognised options,1–4,6,7 including the capsaicin 8% patch (QUTENZA®) that has been shown to achieve pain relief in diabetic patients with peripheral neuropathic pain.1–3,12
• Two phase III randomised controlled trials (RCTs), STEP13 and STEP24 (Figure 1) that evaluated the capsaicin 8% patch in patients with PDPN have recently been completed, leading to an European label extension for the use in adult diabetic patients with peripheral neuropathic pain, either alone or in combination with other pain medications.8
• Currently, there is no direct clinical evidence comparing the capsaicin 8% patch to oral agents in patients with PDPN.

OBJECTIVES

• A network meta-analysis (NMA) was performed to compare the relative efficacy and tolerability of the capsaicin 8% patch with oral agents recommended by the National Institute for Health and Care Excellence (NICE) for patients with neuropathic pain.4

METHODS

Systematic literature review

• A systematic literature review was performed to identify RCTs (published in English after 1950) of pregabalin, gabapentin, duloxetine and amitriptyline in adult patients with PDPN, which were 4–8 weeks in duration.
• – Embase/Medline, Cochrane Library and the National Health Service Centre for Review and Dissemination Database of Abstracts of Reviews of Effects were searched February 2014.
• Data extraction was performed by one reviewer. Extracted data included details of publication, design, treatment, patient baseline characteristics, patient disposition, and efficacy and tolerability outcomes.

Network meta-analysis

• The impact of treatment effect modifiers (i.e. trial duration, number of participants, baseline pain score, treatment dosing, and the degree of enriched enrolment) on outcomes was assessed to ensure a homogeneous set of studies.
• A Bayesian analytical approach was applied to the NMA to obtain estimates of the relative efficacy and tolerability of the capsaicin 8% patch compared with the four oral agents of interest.
• Both fixed-effects and random-effects models were fitted to the data and considered on the basis of model fit.
• The ranking probability of being the best treatment was calculated for each outcome.
• Efficacy outcomes were ≥30% and ≥50% pain reduction from baseline between Weeks 4 to 15, and tolerability outcomes were adverse events commonly associated with the oral comparators (i.e. somnolence, dizziness, nausea, diarrhoea, and the rate of discontinuation due to adverse events).
• Relative effects of treatments were presented as logarithmic odds ratios (OR) with 95% confidence intervals (CI). Forest plots were produced for all outcomes.
• Scenario analyses, which considered different doses (pregabalin, duloxetine), endpoint definitions and inclusion of the open-label PACE trial data, were also performed.

RESULTS

Systematic literature review

• The systematic literature search yielded 400 articles after removing duplicates, of which 21 full text publications were reviewed for eligibility, 24 publications met the inclusion criteria and were fully extracted.

Network meta-analysis

• In addition to the four oral pain medications identified from the literature search, the NMA also included the STEP trial, which had not been published at the time of the literature search.
• – Patients in the STEP trial were allowed to receive concurrent medications, including anticonvulsants, which would have impacted the NMA findings. Therefore, only data from the subpopulation in both arms who did not receive any relevant concurrent oral medications (i.e. pregabalin, gabapentin or duloxetine) at baseline (~15%) were included in the NMA.
• The PACE trial was not included in the base-case NMA as it was an open-label study with safety related primary endpoints.

CONCLUSIONS

• This NMA shows that the capsaicin 8% patch has similar efficacy in terms of pain relief as pregabalin, duloxetine and gabapentin in patients with PDPN.
• Pregabalin, duloxetine and gabapentin were associated with an elevated risk of systemic adverse events compared to placebo, whereas none of these events were reported in association with the capsaicin 8% patch.
• Localised treatment with the capsaicin 8% patch has similar efficacy, but offers the potential for tolerability benefits compared to NICE-recommended oral agents in patients with PDPN.

REFERENCES


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CONTRIBUTIONS AND DISCLOSURES

Full participated in the study research and is employed by Astellas. MC performed the literature search, was employed by Pharmen at the time of analysis and is now employed by UCB Biopharma. SLF participated in the study research, was employed by Astellas at the time of analysis and is now employed by Digital Health Labs Ltd. MR performed the analyses and is employed by Pharmen.

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