

**The impact of canagliflozin on the risk of neuropathy events: results from the CREDENCE trial**

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## The impact of canagliflozin on the risk of neuropathy events: results from the CREDENCE trial

### Background

Sodium-glucose cotransporter 2 inhibitors reduce the risk, and progression, of diabetic kidney disease. We hypothesized that sodium-glucose cotransporter 2 inhibitors could similarly improve the microvascular complication of neuropathy.

### Methods

The CREDENCE trial randomized participants with type 2 diabetes and albuminuria to canagliflozin or placebo. Neuropathy events were defined as any reported adverse event with a Medical Dictionary for Regulatory Activities (MedDRA) term consistent with peripheral or autonomic neuropathy. The effect of canagliflozin on neuropathy events was calculated by Cox regression. In secondary analyses the endpoint was restricted to [sensorimotor polyneuropathy](#), diabetic [neuropathy](#), or non-autonomic neuropathy events, and subgroups were analysed. P-values adjusted for multiplicity using the Holm-Bonferroni correction were derived for the subgroup analyses.

### Results

Half (48.8%) of the 4401 participants had a diagnosis of neuropathy at baseline. Over a median of 2.45 years follow up, 657 people experienced a [first neuropathy event](#) (63.2 per 1000 patient-years). The incidence of neuropathy events was similar in people randomized to canagliflozin and placebo

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(334/2202 vs. 323/2199; HR 1.04, 95% CI 0.89 to 1.21, p=0.66). Canagliflozin had no impact on sensorimotor polyneuropathy (HR 0.93, 95% CI 0.69 to 1.25, p=0.63), diabetic neuropathy (HR 0.91, 95% CI 0.68 to 1.22, p=0.52), or non-autonomic neuropathy (HR 1.03, 95% CI 0.87 to 1.21, p=0.77). The lack of effect on neuropathy events was consistent in subgroup analyses.

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### Conclusions

Canagliflozin did not affect the risk of neuropathy events in the CREDENCE trial despite clear benefits for nephropathy, cardiovascular disease and glycaemic control.

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