# Quality of Life and Objective Measures of Diabetic Neuropathy in a Prospective Placebo-Controlled Trial of Ruboxistaurin and Topiramate

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# Abstract

## Background:

The Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QOL-DN) is a validated comprehensive questionnaire designed to capture the entire spectrum of DN related to large fiber, small fiber, and autonomic neuropathy not captured in existing instruments. We aimed to determine if the Norfolk QOL-DN could be used to capture changes in QOL that correlate with nerve fiber-specific objective measures in a placebo-controlled trial of two agents that affect different nerve fibers.

### Methods:

Sixty patients with DN were allocated to treatment on ruboxistaurin (RBX) (n = 18), topiramate (TPX) (n = 18), or placebo (n = 18). QOL-DN was administered and objective measures of nerve function were performed at entry and end of the study period.

### Results:

Total QOL scores improved significantly in the active treatment groups (RBX -9.56 ± 4.13; TPX -12.22 ± 2.76) but not in placebo (-5.56 ± 3.49). There were differences in nerve function improvement between treatments. Neurological symptom scores (NSS) improved with TPX from 5.5 (2.3) to 4.3 (0.65) (p = .007), sensory scores improved with TPX from 15.5 (1.79) to 8.3 (1.19) (p < .001), motor scores did not change, and sensory and motor impairment scores improved with TPX from 18.8 (2.15) to 12.1 (1.71) (p = .003). Total neuropathy scores (TNS) improved with TPX from 24.35 (2.61) to 16.35 (2.02) (p = .001). Neuropathy total symptom score-6 (NTSS-6) changes were significant for both treatments: RBX 4.38 (0.75) to 1.49 (0.38) (p < .001) and TPX 7.57 (1.3) to 4.26 (0.95) (p = .036). Changes in QOL-DN large fiber subscores correlated (Spearman's rank) significantly with changes in NTSS-6 (r = 0.55; p < .0001), NSS (r = 0.31; p < .04), neuropathy impairment score (NIS) (r = 0.35; p < .02), and TNS (r = 0.48; p < .0006). Changes in QOL-DN small fiber subscores correlated significantly with changes in NTSS-6 total scores (r = 0.40; p < .005) and intraepidermal nerve fiber density (IENFD) (r = -0.29; p < .05).

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Abbreviations: (ADA) American Diabetes Association, (BMI) body mass index, (DN) diabetic neuropathy, (DPN) diabetic peripheral neuropathy, (GABA) gamma-aminobutyric acid, (HbA1c) hemoglobin A1c, (IENFD) intraepidermal nerve fiber density, (MS) motor score, (NCS) nerve conduction studies, (NIS) neuropathy impairment score, (NIS-LL) neurological impairment scores of the lower limb, (Norfolk QOL-DN) Norfolk Quality of Life Diabetic Neuropathy, (NS) not significant, (NSS) neurological symptom score, (NTSS-6) neuropathy total symptom score-6, (PKC-β) protein kinase C-β, (QAFT) quantitative autonomic function, (QOL) quality of life, (QST) quantitative sensory testing, (RBX) ruboxistaurin, (SEM) standard error of the mean, (SkBF) skin blood flow, (SS) sensory score, (TNS) total neuropathy score, (TPX) topiramate

Keywords: diabetic neuropathy, Norfolk QOL-DN, protein kinase C, quality of life, topiramate

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#### Abstract cont.

#### Conclusion:

Ruboxistaurin produced significant improvement in large fiber measures while TPX produced significant changes in small fiber measures. The Norfolk QOL-DN tool differentiated between these changes captured in the fiber-specific domains. Correlations were found between objective measures of neuropathy and total QOL, but those with nerve fiber domain scores were modest and reinforce the need to quantify QOL as an endpoint in neuropathy independent of other measures.

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