Toxicokinetics of CBX129801, a Bio-active C-peptide for Potential Replacement Therapy in Type 1 Diabetic Neuropathy, in Rats and Monkeys After Subcutaneous Injections

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Abstract

To assess the toxicokinetics (TK) of CBX129801 in rats and monkeys following once weekly subcutaneous injection for 5 doses.

Purpose:

To evaluate the toxicokinetics of CBX129801 in rats and monkeys following once-weekly subcutaneous injections for 5 doses of CBX129801. In monkeys, toxicokinetic parameters were determined for CBX129801 in a 28-day toxicity study.

Methods:

To assess the toxicokinetics of CBX129801 in rats and monkeys following once-weekly subcutaneous injection for 5 doses.

Results:

The toxicokinetics of CBX129801 in rats and monkeys following once-weekly subcutaneous injections for 5 doses were determined.

Conclusions:

The toxicokinetics of CBX129801 in rats and monkeys following once-weekly subcutaneous injections for 5 doses were determined.

Introduction

Type 1 diabetes is the leading cause of the diabetic neuropathy, characterized by a complex neuropathic pain. It is estimated that if left untreated, in the U.S. and Europe have type 1 diabetes, and about 15,000,000 children and adults with type 1 diabetes in the U.S. To date, it has been reported that up to 50% of patients with type 1 diabetes are at risk of developing neuropathy, despite recent advances in therapy. It is a prolonged period of high risk for the development of diabetic neuropathy. The purpose of this study was to evaluate the toxicokinetics of CBX129801 in rats and monkeys following once-weekly subcutaneous injections for 5 doses.

Methods

A. Study

Rats received subcutaneous injection of CBX129801 once every week at 2.74, 8.22, 27.4, and 86.0 mg/kg in 5 doses of CBX129801. The toxicity groups were dosed at 0, 27.4 mg/kg, and 86.0 mg/kg. In cynomolgus monkeys, toxicokinetic parameters were determined for CBX129801 in a 28-day toxicity study.

B. Analytical Methods

The plasma samples were analyzed for CBX129801 by validated LC/MS/MS.

C. TL, Analysis

The dose-normalized predose plasma concentrations (nM)/mg were analyzed by a standard independent linear regression.

Table 1

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<tr>
<th>CBX129801 Cmax, nM</th>
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Figure 1

Toxicokinetic parameters of CBX129801 in rats following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Figure 2

Toxicokinetic parameters of CBX129801 in monkeys following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Figure 3

Toxicokinetic parameters of CBX129801 in rats following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Figure 4

Toxicokinetic parameters of CBX129801 in monkeys following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Figure 5

Toxicokinetic parameters of CBX129801 in monkeys following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Conclusions

CBX129801 was readily measurable in rat and monkey plasma with T1/2 ranging from 1.00 to 3.00 days. CBX129801 concentrations appeared to achieve a steady state in both species following once-weekly subcutaneous injections for 5 doses. CBX129801 concentrations in rats and monkeys were determined by standard independent linear regression.

Figure 6

Toxicokinetic parameters of CBX129801 in monkeys following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Figure 7

Toxicokinetic parameters of CBX129801 in rats following subcutaneous injection of CBX129801 in a 28-day toxicity study.

Figure 8

Toxicokinetic parameters of CBX129801 in monkeys following subcutaneous injection of CBX129801 in a 28-day toxicity study.