

Sponsored By:



YKP3089

S. James Lee, Ph.D.

SK Life Science Inc., Fair Lawn, New Jersey, USA

Introduction: YKP3089 is a novel compound with broad-spectrum anticonvulsant activity under clinical development at SK Life Science. In addition to being a candidate for use in epilepsy therapy, YKP3089 has the potential to be a versatile CNS drug with multiple therapeutic uses.

Pharmacology: YKP3089 is effective in a broad range of animal models of seizures and epilepsy, being active against electrically and chemically induced seizures and, more interestingly, in models of refractory epilepsy. Positive effects of YKP3089 have been recorded in many animal models of anxiety, in both mice and rats. YKP3089 is more efficacious than gabapentin in the Bennett and Chung models of neuropathic pain.

Toxicology: In repeated-dose toxicity studies in various rodents and non-rodents, YKP3089 at very high doses displayed predominantly adverse effects related to exaggerated pharmacology in all species tested. YKP3089 was negative in all genotoxicity assays tested. In reproductive studies in rats and rabbits there was no evidence of teratogenicity. YKP3089 did not affect cardiovascular functions in a telemetry cardiovascular study in monkeys.

Clinical pharmacokinetics: In phase I studies completed in the U.S., exposure of YKP3089 following single oral administration was dose proportional with an observed half-life of 30 to 75 h, which would support once daily dosing. In single dose studies, YKP3089 pharmacokinetics was linear over a large dose range. In a multiple-dose 14-day study with once daily dosing, both peak plasma concentrations and AUC correlated linearly with the dose. In a food effect study, there appeared to be no significant differences in pharmacokinetic profile after intake with a high-fat diet compared with the fasted condition.

Tolerability and adverse effect profile: YKP3089 was well-tolerated in phase I studies after single doses and multiple doses ranging with a low incidence of adverse effects. Most common Adverse Events were CNS related, were of mild to moderate intensity and resolved rapidly. No clinically significant changes in ECGs or laboratory parameters were observed.

Efficacy: The photosensitivity epilepsy study, a placebo-controlled, single blind study was conducted at clinical research centers in United States. The photosensitivity model is considered by experts in the field to be useful in the proof of concept for the treatment of epilepsy.

Eligible subjects were those patients with demonstrated epileptiform activity in electroencephalogram (EEG) response in response to photic stimulation. The study measured the ability of YKP3089 to reduce the photic-induced epileptiform EEG response compared to response to placebo.

In this study, YKP3089 demonstrated positive reduction of the photosensitivity response.

Ongoing and planned studies

In view of its good tolerability, possibility of once daily dosing and broad spectrum activity in animal models of epilepsy and other disorders, phase II studies aimed at various indications including epilepsy are currently ongoing.