To make a preliminary assessment of LDL-C lowering by VK2809

Methods

A Phase 1 study was conducted to evaluate the safety, tolerability and pharmacokinetics of VK2809 in 56 subjects with elevated serum cholesterol. Subjects were randomized to receive VK2809 doses of 0.25, 1.0, 2.5, 5.0, 10, 20, and 40 mg in 14 days.

Results

Plasma concentrations of VK2809 and its active metabolite VK2809A each increased in a dose-proportional manner up to 40 mg. The terminal half-life of the active metabolite ranged from 13-41 hours and was longer at higher doses. Less than 3% of VK2809 and its active metabolite were excreted renally. The peak and extent of exposure to the active metabolite VK2809A increased in proportion to increase in plasma drug concentration. The terminal half-life of the active metabolite ranged from 13–41 hours and tended to be shorter following lower doses when compared to higher doses.

Conclusion

VK2809 was found to be well-tolerated in this study. No treatment- or dose-related trends were observed for abnormal vital signs, physical examination assessments, ECGs or Holter-monitored cardiac rhythm. No significant trends for abnormal liver enzymes related to treatment were observed. The observed dose-related elevation in liver enzyme levels was considered to be clinically insignificant.

Safety

VK2809 was found to be safe and well-tolerated in this study. There were no adverse events. No treatment or dose- related trends were observed for serious adverse events, serious adverse reactions, grade 3 or 4 laboratory abnormalities, or dose-related increases in abnormal vital signs, physical examination assessments, ECGs or Holter-monitored cardiac rhythm.

Disclosure

Steven Schoenfeld, MD: Salary – Viking Therapeutics

Title: Safety Evaluation of a Liver-Selective Tri-Beta Agonist in Patients with Non-Alcoholic Fatty Liver Disease

A Phase 1 Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study to Evaluate Safety, Tolerability and Pharmacokinetics of the Liver-Selective TR-Beta Agonist VK2809 (MB07811) in Hypercholesterolemic Subjects, B. Lian, R. Hanley and S. Schoenfeld, Viking Therapeutics, San Diego, CA

Introduction

Selective activation of thyroid beta with the small molecule VK2809 represents an attractive therapeutic approach for treating other conditions such as fatty liver disease. In this 14-day study, the observed LDL-lowering effects were comparable to those historically reported with statin-based therapies. In addition, the observed robust reduction in plasma triglycerides suggest potential application in treating other conditions such as fatty liver disease.

Abstract

Subjects were randomized to receive once-daily oral VK2809 doses of 0.25, 1.0, 2.5, 5.0, 10, 20, or 40 mg, or placebo for 14 days. Subjects were followed for an additional 7 days off drug for safety assessment.

Objectives

• To characterize the pharmacokinetics (PK) of VK2809 and its active metabolite, VK2809A
• To evaluate the safety, tolerability and pharmacokinetics of VK2809 in subjects with elevated serum cholesterol
• To assess the PK profile of VK2809

Methods

A single-center, randomized, double-blind, placebo-controlled, rising multiple-dose Phase 1 study was conducted to evaluate the safety, tolerability and pharmacokinetics of VK2809 in 56 subjects with elevated serum cholesterol. Subjects were randomized to receive VK2809 doses of 0.25, 1.0, 2.5, 5.0, 10, 20, and 40 mg in 14 days.

Results

Plasma concentrations of VK2809 and its active metabolite VK2809A each increased in a dose-proportional manner up to 40 mg. The terminal half-life of the active metabolite ranged from 13–41 hours and was longer at higher doses. Less than 3% of VK2809 and its active metabolite were excreted renally. The peak and extent of exposure to the active metabolite VK2809A increased in proportion to increase in plasma drug concentration. The terminal half-life of the active metabolite ranged from 13–41 hours and tended to be shorter following lower doses when compared to higher doses.

Conclusion

VK2809 was found to be well-tolerated in this study. No treatment- or dose-related trends were observed for abnormal vital signs, physical examination assessments, ECGs or Holter-monitored cardiac rhythm. No significant trends for abnormal liver enzymes related to treatment were observed. The observed dose-related elevation in liver enzyme levels was considered to be clinically insignificant.

Safety

VK2809 was found to be safe and well-tolerated in this study. There were no adverse events. No treatment or dose- related trends were observed for serious adverse events, serious adverse reactions, grade 3 or 4 laboratory abnormalities, or dose-related increases in abnormal vital signs, physical examination assessments, ECGs or Holter-monitored cardiac rhythm. No dose-related or medically important trends were observed for abnormal liver enzyme levels. No dose-related or medically important trends were observed in other testing (weights, BP, or ECG parameters).