Single and Multiple Dose Evaluation of a Novel MetAP2 Inhibitor: Results of a Randomized, Double-Blind, Placebo-Controlled Clinical Trial

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ABSTRACT

METAP2 inhibitors (MetAP2i) are a promising new therapeutic approach for the treatment of obesity, diabetes, and attherosclerotic cardiovascular disease. In this first-in-human clinical trial of single and multiple ascending doses of ZGN-1061 for 4 weeks, we demonstrated 27 kg body weight loss after 26 weeks of treatment in patients with obesity and type 2 diabetes. In addition, there were reductions in waist circumference, food intake, hsCRP, and LDL-cholesterol. However, the trial was halted due to an imbalance of venous thrombotic events. Nonclinical studies revealed potential for thrombosis risk reduction and limit thrombosis.

INTRODUCTION

Beloranib (ZGN-1061) is a novel small-molecule 270 MetAP2 inhibitor (MetAP2i) currently in development as a single agent for the treatment of obesity, diabetes, and cardiovascular disease. In this first-in-human clinical trial of single and multiple ascending doses of ZGN-1061 for 4 weeks, we demonstrated 27 kg body weight loss after 26 weeks of treatment in patients with obesity and type 2 diabetes. In addition, there were reductions in waist circumference, food intake, hsCRP, and LDL-cholesterol. However, the trial was halted due to an imbalance of venous thrombotic events. Nonclinical studies revealed potential for thrombosis risk reduction. Beloranib development was discontinued due to its pro-thrombotic effect. Nonclinical studies revealed potential for thrombosis risk reduction and limit thrombosis.

OBJECTIVE

To evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of ZGN-1061.

METHODS

This was a Phase 1 study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of ZGN-1061 in obese T2DM subjects but development was halted due to its pro-thrombotic effect. Nonclinical studies revealed potential for thrombosis risk reduction.

RESULTS

The most common AEs were mild gastrointestinal issues (similar incidence for ZGN-1061 and placebo). There were no severe or serious events and no events of venous thromboembolism. MetAP2 binding and evidence of endothelial cell exposure and limit thrombosis.

CONCLUSION

Beloranib in Patients with Obesity and Type 2 Diabetes. 76th Scientific Sessions of the American Diabetes Association, June 4-8, 2016. Chicago, IL. 

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