Potential of a novel long-acting glucagon analog, HM15136, for the treatment of obesity

Jung Kuk Kim1, Seon Myeong Lee1, Jinyoung Kim1, CheongByeol Shin1, Jong Soo Lee1, Sang Hyun Lee1, and In Young Choi1
1Hannmi Pharm. Co., Ltd, Seoul, South Korea

ABSTRACT

HM15136, a novel α-7 nAChR agonist, was hypothesized to have potential for obesity treatment. In the present study, the safety and efficacy of HM15136 were evaluated. The pharmacokinetic pattern of HM15136 was extended, and its solubility and physical stability were improved. In a pharmacological study, HM15136 was shown to have satiety and glucose-lowering effects in vivo. In rats fed a high-fat diet, HM15136 improved satiety and reduced body weight gain. In in vitro experiments, the anti-obesity effects of HM15136 were confirmed. These findings suggest that HM15136 could be a candidate for the development of a novel long-acting glucagon analog for obesity treatment.

METHODS

PK of HM15136 was investigated in ICR mice, SD rats, and beagles after single i.v. doses of 0.66–2.0 nmol/kg and 100–150 nmol/kg. In addition, beagles were dosed with multiple i.v. doses of 0.66–2.0 nmol/kg. PK simulation was extended to human. Glucagon was used as a positive control. The solubility and physical stability of HM15136 were improved by pH-adjustment and cryopreservation.

RESULTS

HM15136 showed extended solubility and physical stability. In vivo efficacy in an obesity model

HM15136 showed improved solubility and physical stability at physiological pH. In vitro experiments confirmed the anti-obesity effects of HM15136. In vivo studies demonstrated that HM15136 improved satiety and reduced body weight gain in rats fed a high-fat diet.

CONCLUSIONS

HM15136 is a novel long-acting glucagon analog with improved solubility and stability at physiological pH. In vivo studies demonstrate the potential for obesity treatment. Further clinical development is warranted.

REFERENCES

1. Poitras A et al., Diabetes Obes Metab. 2019
2. Campbell JE and Drucker DJ, Nat Rev Endocrinol. 2019
3. Mullen TD et al., Physiol Rep. 2019
4. Kim T et al., Diabetes, 2018

American Diabetes Association's (ADA) 79th Scientific Sessions, San Francisco, CA, USA; June 07-11, 2019