Clinical Drug Investigation

Electronic Supplementary Material

Pharmacokinetic and pharmacodynamic profiles of canagliflozin in Japanese patients with type 2 diabetes mellitus and moderate renal impairment

Nobuya Inagaki · Kazuoki Kondo · Toru Yoshinari · Manabu Ishii · Masaki Sakai · Hideki Kuki · Kenichi Furihata

N. Inagaki

Department of Diabetes, Endocrinology, and Nutrition, Kyoto University Graduate School of Medicine, Kyoto, Japan

K. Kondo · T. Yoshinari (corresponding author) · M. Ishii · M. Sakai · H. Kuki

Mitsubishi Tanabe Pharma Corporation, 17-10 Nihonbashi-Koamicho, Chuo-ku, Tokyo, Japan

Tel: +81-3-6748-7693

Fax: +81-3-3663-6258

E-mail: yoshinari.toru@mm.mt-pharma.co.jp

K. Furihata

P-One Clinic, Keikokai Medical Corp., Tokyo, Japan

Statistical Methods

Patients were included in the pharmacokinetic, pharmacodynamics and/or safety populations if they had evaluable data in that particular category and had received at least one dose of the study drug. Pharmacokinetic parameters were derived from the plasma concentrations of the unchanged drug and its metabolites (M5 and M7) using Phoenix® WinNonlin® Version 6.2 (Certara USA, Inc., St. Louis, MO, USA). Renal clearance and the amount of canagliflozin excreted into urine from 0 to 72 h were also determined for the unchanged drug. The summary statistics for pharmacokinetic parameters were provided by renal function and dose. For the evaluation of the effects of renal impairment, pharmacokinetic parameters were analyzed using a mixed-effect analysis of variance model. Point estimates and 90% confidence intervals (CIs) for the differences (patients with moderate renal impairment − patients with normal renal function or mild renal impairment) in the natural log-transformed means for C_{max}, area under the curve $(AUC)_{0-\infty}$ were calculated by dose. The percent inhibition of renal glucose reabsorption was calculated from renal glucose reabsorption (eGFR × plasma glucose AUC – urinary glucose excretion) on the preceding day and on the day of administration. The 24-h mean percent inhibition was calculated as a weighted average of the values over four urine collection intervals. Adverse events and adverse drug reactions were summarized by renal function and dose, and their incidence rates were calculated. All statistical analyses were conducted using SAS®, Release 9.2 (SAS Institute Inc., Cary, NC, USA).

Supplementary Fig. 1 Patient flow chart