

Supplemental Table S1. Inclusion and Exclusion Criteria**Inclusion criteria**

- 1) Patients with type 2 diabetes mellitus
- 2) Adults who are at least 19 years old
- 3) Patients who have been treated with a combination therapy of dapagliflozin 10 mg/day+metformin $\geq 1,000$ mg/day (The treatment with a fixed dose combination of dapagliflozin 10 mg+metformin $\geq 1,000$ mg is also allowed.) at stable doses for ≥ 8 weeks prior to visit 1 (screening)
- 4) Patients whose HbA1c and FPG levels at visit 1 (screening) are applicable to the following criteria:
 - a. Patients with $7\% \leq \text{HbA1c} \leq 11\%$, $\text{FPG} \leq 270$ mg/dL at visit 1 (screening) in case patients have not been treated with hypoglycemic agents other than dapagliflozin and metformin within 8 weeks prior to visit 1 (screening).
 - b. Patients with $6.5\% \leq \text{HbA1c} \leq 10.5\%$, $\text{FPG} \leq 270$ mg/dL at visit 1 (screening) in case patients have been treated with other oral hypoglycemic agents added on to dapagliflozin and metformin within 8 weeks prior to visit 1 (screening).
- 5) Patients who or whose legally authorized representatives have signed an informed consent form after receiving explanation about the objectives, methods, effects, etc. of the clinical study.
- 6) Patients who can participate in the clinical study during its entire period and carry out all of the scheduled procedures and visits for it.
- 7) Patients who are applicable to one of the following 3 criteria.
 - a. Surgically infertile patients.
 - b. Postmenopausal female patients of ≥ 45 years of age for whom ≥ 2 years elapsed since their last menstruation.
 - c. Premenopausal fertile female patients or surgically non-infertile male patients who have agreed to use at least 2 kinds of contraceptive measures (certainly including one of the barrier methods) to avoid pregnancy until 14 days after the last treatment with the investigational product.
 - Barrier methods: condom, diaphragm, cervical cap (Pessary), spermicide
 - Hormonal methods: oral contraceptive (Pill), injection (Depot), skin patch, hormonal implant (Implanon), vaginal ring.
 - Intrauterine devices (IUDs): cooper IUD (Loop), hormonal IUD (Mirena).
 - Natural methods: basic body temperature, ovulation period, coitus interruptus, abstinence.

For patients participating in the Washout period, they had to satisfy the following inclusion criteria at visit 1-1 (screening).

- 8) Patients with $7\% \leq \text{HbA1c} \leq 11\%$, $\text{FPG} \leq 270$ mg/dL whose HbA1c and FPG levels at visit 1-1 (screening)

Exclusion criteria

- 1) Patients with type 1 diabetes mellitus, metabolic acidosis such as diabetic ketoacidosis or lactic acidosis, diabetic coma, and precoma
- 2) Patients with gestational diabetes or secondary diabetes
- 3) Patients with NYHA class II–IV congestive heart failure, acute and unstable heart failure, or arrhythmia requiring treatment
- 4) Patients whose thyroid stimulating hormone (TSH) level is out of its normal range and who have thyroidal dysfunction requiring drug therapy (However, those who had been taking thyroid hormone at a certain dose since previous 4 weeks prior to visit 1 [screening] and whose TSH level was within the normal range at visit 1 [screening] or within 4 weeks prior to visit 1 [screening] could participate in the study.)
- 5) Patients with severe infection or severe traumatism
- 6) Patients with pituitary insufficiency or adrenal insufficiency
- 7) Patients with pulmonary infarction, severe pulmonary dysfunction, or who are susceptible to be accompanied by hypoxemia
- 8) Patients with gastrointestinal disturbance including dehydration, diarrhea, and vomiting
- 9) Patients with genetic problems such as galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption
- 10) Female patients who are pregnant or lactating
- 11) Patients with $\text{BMI} > 40$ kg/m² measured at visit 1 (screening)
- 12) Patients whose serology tests including HBsAg, HCV Ab, HIV Ab (tests for hepatitis B, hepatitis C, and HIV) carried out by a local laboratory at visit 1 (screening) or within 4 weeks prior to visit 1 (screening) have turned out to be positive
- 13) Patients with moderate (stage 3B) or severe renal impairment, end-stage renal disease (ESRD) or patients on dialysis, patients with $\text{eGFR} < 45$ mL/min/1.73 m² calculated by using their serum creatinine (utilizing the MDRD formula) at visit 1 (screening) or visit 1-1 (screening, applicable only if carried out)

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Supplemental Table S1. Continued

- 14) Patients with hepatic impairment or who are applicable to the following criteria for the laboratory tests conducted by a local laboratory at visit 1 (screening) or within 4 weeks prior to visit 1 (screening).
 - a. Total bilirubin $> 1.5 \times$ upper limit of normal (ULN)
 - b. AST or ALT $> 2.5 \times$ ULN
- 15) Patients who have been treated with the following drugs for ≥ 2 weeks at visit 1 (screening) or who are required to be treated with them continuously/repeatedly during the clinical study.
 - Cyclosporin, sirolimus, tacrolimus, systemic glucocorticoids, isotretinoin, nicotinic acid ($\geq 1,000$ mg/day)
 - Strong CYP3A4 inducers: rifampicin (Rifampin), phenytoin, carbamazepine, rifabutin, phenobarbital, etc.
 - Cimetidine
 - Organic cation transporters (OCT) inhibitors/inducers: OCT1 inhibitors/inducers, OCT2 inhibitors
 - Warfarin, dicoumarin, digoxin
- 16) Patients who were treated with anti-obesity drugs within 12 weeks prior to visit 1 (screening).
- 17) Patients who were treated with insulin and GLP-1 receptor agonists within 8 weeks prior to visit 1 (screening).
- 18) Patients with a history of malignant tumors within 5 years prior to visit 1 (screening) (However, those with basal cell or squamous cell carcinoma treated properly could participate in the study).
- 19) Patients with a history of alcoholism or drug addiction within 1 year prior to visit 1 (screening).
- 20) Patients who had bariatric surgery within 1 year prior to visit 1 (screening) or who are scheduled to have it during the clinical study.
- 21) Patients to whom coronary artery disease such as myocardial infarction and angina pectoris or cerebrovascular disease newly occurred within 3 months prior to visit 1 (screening).
- 22) Patients who had a surgical operation within 4 weeks prior to visit 1 (screening) (excluding minor surgeries without restriction on food and fluid intake) or who are scheduled to have it during the clinical study.
- 23) Patients who underwent any examination using iodinated contrast (e.g., intravenous urography, intravenous cholangiography, angiography, contrast computed tomography [CT]) within 48 hours prior to visit 1 (screening) or who are scheduled to undergo it during the clinical study.
- 24) Patients with a history of hypersensitivity reactions to the drugs belonging to DPP-4 inhibitors or yellow no. 5.
- 25) Patients with a history of hypersensitivity reactions to the drugs belonging to biguanides.
- 26) Patients with a history of hypersensitivity reactions to the drugs belonging to SGLT2 inhibitors.
- 27) Patients with an experience of participation in another clinical study within 12 weeks prior to visit 1 (screening).
- 28) Patients who are otherwise considered to be ineligible for this study on investigators' judgment.

HbA1c, hemoglobin A1c; FPG, fasting plasma glucose; NYHA, New York Heart Association; BMI, body mass index; HBsAg, hepatitis b surface antigen; HCV, hepatitis C virus; Ab, antibody; HIV, human immunodeficient virus; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease; AST, aspartate transaminase; ALT, alanine transaminase; CYP3A4, cytochrome P450 3A4; GLP-1, glucagon-like peptide-1; DPP-4, dipeptidyl peptidase-4; SGLT2, sodium glucose cotransporter 2.