Title: Nesina Tablets Specified Drug-use Survey "Type 2 Diabetes Mellitus: Combination Therapy With Hypoglycemic Drug (Insulin Preparation or Rapid-acting Insulin Secretagogues, Etc)"

NCT Number: NCT02221284

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Note; This document was translated into English as the language on original version was Japanese.

Statistical Analysis Plan

Nesina Tablets Specified Drug-use Survey "Type 2 Diabetes Mellitus: Combination Therapy With Hypoglycemic Drug (Insulin Preparation or Rapid-acting Insulin Secretagogues, Etc)"

Takeda Pharmaceutical Company Limited.

PPD

Version 3, Created on April 11, 2018

Table of Contents

1.0 Definition of Terms and Handling of Laboratory/Measured Data

1.1 Definitions

Term	Definition
Nesina	Nesina tablet(s) is abbreviated as Nesina in this statistical analysis plan.
SOC	System Organ Class of MedDRA/J MedDRA/J version 20.1 is used for this document.
HLGT	High level group term of MedDRA/J
PT	Preferred term of MedDRA/J
LLT	Lowest level term of MedDRA/J
Registered patients	Patients whose registration was approved
Survey sheet collected patients	Patients whose survey sheets were collected
Survey sheet uncollected patients	Of the registered patients, patients whose survey sheets were uncollected.
Safety Analysis Set	Of the survey sheet collected patients, patients who were evaluated for safety analysis. For tabulation, the description of "total" means the Safety Analysis Set.
Not Safety Analysis Set	Of the survey sheet collected patients, patients who were excluded from safety analysis
Efficacy Analysis Set	Of the Safety Analysis Set, patients who were evaluated for efficacy analysis
Not Efficacy Analysis Set	Of the Safety Analysis Set, patients who were excluded from the efficacy analysis
First date of Nesina treatment	Of the start dates of the Nesina treatment period in patients, the earliest date is defined as the first date of Nesina treatment.
Last date of Nesina treatment	Of the last dates of the Nesina treatment in patients, the latest date is defined as the last date of Nesina treatment. If Nesina treatment is continued and the year, month, and date of the continued treatment period are specified, the year, month, and date of the continued treatment period are defined as the last date of Nesina treatment. If the data for the year, month, and date of the continued treatment period are missing, the following date is defined as the last date of Nesina treatment. (1) First date of Nesina treatment + 1 year (same month and date) for continued treatment of Nesina. (2) Latest date at which the following examinations/observations will be performed for the not-continued treatment of Nesina: ● [Date of examinations/ observations] • Compliance with Nesina treatment

Term	Definition
	• Compliance with diet/exercise therapy • Laboratory tests • Body weight • Waist circumference • Pulse rate • Blood pressure • Electrocardiography • Tests for coronary atherosclerosis and arteriosclerosis
Adverse drug reactions, etc.	Abbreviation of "adverse drug reactions / infections" Of the adverse events, events for which causal relationship to Nesina was assessed as "Not related" by the Investigator. In this statistical analysis plan, "adverse drug reactions / infections" is used in the headings, while "adverse drug reactions, etc." is used in the sentences and tables.
Serious adverse events	Adverse events assessed as "serious" by the Investigator. Events described in the MedDRA coding list in the Takeda Medically Significant AE List will be handled as serious even if the Investigator assesses as "Not serious."
Serious adverse drug reactions	Abbreviation of "serious adverse drug reactions / infections" Of the "serious adverse events," the events for which causal relationship to Nesina was assessed as "Not related" by the Investigator
Number of patients with events	Number of patients with adverse events or adverse drug reactions, etc.
Number of events	Number of adverse events or adverse drug reactions, etc.
Percent of patients with events	[For safety analysis calculation in the Safety Analysis Set] The formula is: Number of patients with events / Number of Safety Analysis Set × 100. [For safety analysis calculation in the Not Safety Analysis Set] The formula is: Number of patients with events / Number of Not Safety Analysis Set × 100.
Percent of events	[For safety analysis calculation in the Safety Analysis Set] The formula is: Number of events / Number of the Safety Analysis Set × 100. [For safety calculation in the Not Safety Analysis Set] The formula is: Number of events / Number of Not Safety Analysis Set × 100.
Onset period	The formula is: Onset date of adverse events (or adverse drug reactions, etc.) − start date of Nesina treatment + 1.

Term	Definition
	If the onset month and date of an adverse event (or adverse drug reaction, etc.) is unknown, calculate the onset month and date as January 1. However, if the start month and date of Nesina treatment are same as the onset month and date of an adverse event (or adverse drug reaction, etc.), the onset period will be calculated as the start date of Nesina treatment. For unknown onset date of adverse events (or adverse drug reactions, etc.), the onset period will be calculated as 1 day. However, if the start month and date of Nesina treatment are same as the onset month and date of adverse events (or adverse drug reactions, etc.), the onset period will be calculated as the start date of Nesina treatment.
Treatment group	Overall: Total patients who will be treated with combination therapy with insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, and other (all are defined below) Combination with insulin preparation: Patients who will be treated with insulin preparation within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with rapid-acting insulin secretagogues or SGLT-2 inhibitors Combination with rapid-acting insulin secretagogues: Patients who will be treated with rapid-acting insulin secretagogues within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with insulin preparation or SGLT-2 inhibitors Combination with SGLT-2 inhibitors: Patients who will be treated with SGLT-2 inhibitors within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with insulin preparation or rapid-acting insulin secretagogues Other: Patients who will not be treated with combination therapy with insulin preparation, rapid-acting insulin secretagogues, or SGLT-2 inhibitors
Patients with diabetic complication	Patients with any of the following complications: diabetic nephropathy, diabetic retinopathy, or diabetic neuropathy.
Patients with diabetic nephropathy	Patients with complication of PT Code 10012660 (diabetic end stage renal disease) or 10061835 (diabetic nephropathy).
Patients with diabetic retinopathy	Patients with complication of PT Code 10012688 (diabetic retinal oedema) or 10012689 (diabetic retinopathy).
Patients with diabetic neuropathy	Patients with complication of PT Code 10012645 (diabetic autonomic neuropathy), 10012676 (diabetic mononeuropathy), or 10012680 (diabetic

Term	Definition
	neuropathy).
Patients with concurrent hypertension	Patients with concurrent disease of the Standardised MedDRA Query (hereinafter SMQ) Code 20000147 (hypertension (SMQ) narrow).
Patients with concurrent dyslipidemia	Patients with concurrent disease of the SMQ Code 20000026 (dyslipidaemia (SMQ) narrow).
Patients with concurrent hyperuricemia	Patients with concurrent disease of the PT code meeting the Takeda MedDRA Query 20.1 (hereinafter, TMQ 20.1) (blood uric acid increased).
Patients with concurrent liver disorder	Patients with concurrent disease of the SMQ Code 20000005 (hepatic disorders (narrow).
Patients with concurrent hepatic steatosis	Patients with concurrent disease of the PT Code 10019708 (hepatic steatosis).
Patients with concurrent alcoholic hepatitis	Patients with concurrent disease of the PT Code 10019728 (hepatitis alcoholic).
Patients with concurrent chronic hepatitis	Patients with concurrent disease of the PT Code 10008909 (chronic hepatitis).
Patients with concurrent hepatic cirrhosis	Patients with concurrent disease of the PT Code 10019641 (hepatic cirrhosis).
Patients with concurrent renal disorder	Patients with concurrent disease of the TMQ 20.1 (renal disease).
Patients with concurrent nephrotic syndrome	Patients with concurrent disease of the PT Code 10029164 (nephrotic syndrome).
Patients with concurrent glomerulonephritis	Patients with concurrent disease of the PT Code 10018364 (glomerulonephritis) or the PT Code 10018367 (glomerulonephritis chronic).
Patients with concurrent chronic renal failure	Patients with concurrent disease of the PT Code 10064848 (chronic kidney disease) or the PT Code 10038435 (renal failure).
Patients with concurrent heart disease	Patients with concurrent disease of the SOC Code 10007541 (cardiac disorders).
Patients with concurrent cardiac failure	Patients with concurrent disease of the SMQ Code 20000004 (cardiac failure (SMQ) narrow).
Patients with concurrent myocardial infarction	Patients with concurrent disease of the SMQ Code 20000047 (myocardial infarction (SMQ) narrow).
Patients with concurrent angina pectoris	Patients with concurrent disease of the SOC Code 10007541 (cardiac disorders) and the PT Code 10036759 (prinzmetal angina), PT Code 10002383 (angina pectoris), PT Code 10058144 (postinfarction angina), PT Code 10002388 (angina unstable), or LLT Code 10065566 (microvascular angina).
Patients with concurrent stroke-related disease	Patients with concurrent disease of cerebral infarction, cerebral haemorrhage, subarachnoid haemorrhage, or transient ischaemic attack, described below.

Term	Definition
Patients with concurrent disease cerebral infarction	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10006147 (brain stem infarction), PT Code 10008118 (cerebral infarction), PT Code 10008119 (cerebral infarction foetal), PT Code 10008034 (cerebellar infarction), PT Code 10019005 (haemorrhagic cerebral infarction), PT Code 10051078 (lacunar infarction), PT Code 10056237 (migrainous infarction), PT Code 10058571 (spinal cord infarction), PT Code 10060839 (embolic cerebral infarction), PT Code 10060840 (ischaemic cerebral infarction), PT Code 10064961 (thalamic infarction), PT Code 10067347 (thrombotic cerebral infarction), or PT Code 10069020 (basal ganglia infarction).
Patients with concurrent cerebral hemorrhage	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10006145 (brain stem haemorrhage), PT Code 10008111 (cerebral haemorrhage), PT Code 10008112 (cerebral haemorrhage neonatal), PT Code 10008030 (cerebellar haemorrhage), PT Code 10018985 (haemorrhage intracranial), PT Code 10022840 (intraventricular haemorrhage), PT Code 10022841 (intraventricular haemorrhage neonatal), PT Code 10042365 (subdural haemorrhage neonatal), PT Code 10049236 (spinal epidural haemorrhage), PT Code 10048992 (spinal cord haemorrhage), PT Code 10050157 (cerebral haemorrhage foetal), PT Code 10052593 (meningorrhagia), PT Code 10058939 (thalamus haemorrhage), PT Code 10058940 (putamen haemorrhage), PT Code 10067057 (basal ganglia haemorrhage), PT Code 10067277 (cerebral microhaemorrhage), PT Code 10071205 (brain stem microhaemorrhage), PT Code 10071206 (cerebellar microhaemorrhage), PT Code 10072043 (central nervous system haemorrhage), or PT Code 10073563 (Spinal subdural haemorrhage).
Patients with concurrent subarachnoid hemorrhage	Patients with concurrent disease of the PT Code 10042316 (subarachnoid haemorrhage), PT Code 10042317 (subarachnoid haemorrhage neonatal), PT Code 10073564 (spinal subarachnoid haemorrhage), LLT Code 10072201 (Asymptomatic subarachnoid haemorrhage).
Patients with concurrent transient ischemic attack	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10044390 (transient ischaemic attack).
Patients with concurrent allergic disease	Patients with concurrent disease of bronchial asthma, pollinosis, allergic rhinitis, or allergic dermatitis, described below.
Patients with concurrent bronchial asthma	Patients with concurrent disease of the SOC Code 10038738 (respiratory, thoracic and mediastinal disorders) and the PT Code 10003553 (asthma), PT Code 10075084 (aspirin-exacerbated respiratory disease), PT Code 10003557 (asthma exercise induced), PT Code 10003559 (asthma late onset), PT Code 10041961 (status asthmaticus), PT Code 10001890 (alveolitis allergic), PT

Term	Definition
	Code 10049585 (infantile asthma), PT Code 10070836 (occupational asthma), or PT Code 10064823 (asthmatic crisis).
Patients with concurrent pollinosis	Patients with concurrent disease of the PT Code 10048908 (seasonal allergy).
Patients with concurrent allergic rhinitis	Patients with concurrent disease of the PT Code 10039085 (rhinitis allergic).
Patients with concurrent allergic dermatitis	Patients with concurrent disease of the PT Code 10012434 (dermatitis allergic).
Patients with concurrent malignant tumor	Patients with concurrent disease of the SOC Code 10029104 (neoplasms benign, malignant and unspecified (incl cysts and polyps)).
Patients with concurrent malignant tumor (narrow sense)	Patients with concurrent disease of the SMQ Code 20000194 (malignant tumour (SMQ) narrow).
Patients with other concurrent disease	Patients with concurrent disease other than the above (diabetic complication, hypertension, dyslipidaemia, hyperuricaemia, liver disease, renal disease, heart disease, stroke-related disease, allergic disease, malignant tumor, or malignant tumor (narrow sense)).
Severity of hepatic impairment	Severity of hepatic impairment will be assessed using AST or ALT at the start of Nesina treatment. Severity will be assessed using the categories described below, and the higher grade of AST or ALT will be used for analysis. Normal: < 50 IU/L Grade 1: ≥ 50 IU/L and < 100 IU/L Grade 2: ≥ 100 IU/L and < 500 IU/L Grade 3: ≥ 500 IU/L Quoted from the Standards for Classification of Serious Adverse Drug Reactions due to Drug Products notified by the director of Pharmaceuticals and Chemicals Safety Division, Pharmaceutical Affairs Bureau, the Ministry of Health and Welfare (No. 80 notification of Pharmaceuticals and Chemicals Safety Division, Pharmaceutical Affairs Bureau: June 29, 1992).
Severity of renal impairment (eGFR)	eGFR* will be calculated based on age and serum creatinine at the start of Nesina treatment to assess the severity according to the categories described below. For unknown serum creatinine and age at the start of Nesina treatment, indicate as unknown. Indicate to one decimal place rounded from two decimals. Normal: ≥ 90 mL/min/1.73 m^2 Mild: ≥ 60 mL/min/1.73 m^2 and < 90 mL/min/1.73 m^2 Moderate: ≥ 30 mL/min/1.73 m^2 and < 60 mL/min/1.73 m^2 Severe: < 30 mL/min/1.73 m^2 *eGFR = $194 \times Cr^{-1.094} \times \text{age (year)}^{-0.287}$(×0.739 for females)

Term	Definition
	Cr: Serum creatinine at the start of Nesina treatment. For serum Cr, indicate to two decimal places. Quoted from the Clinical Practice Guide for CKD, edited by the Japanese Society of Nephrology.
Severity of renal impairment (serum creatinine)	Severity will be assessed based on serum creatinine at the start of Nesina treatment and according to the following categories: Normal + Mild: Males: ≤ 1.4 mg/dL, Females: ≤ 1.2 mg/dL Moderate: Males: > 1.4 mg/dL to ≤ 2.4 mg/dL, Females: > 1.2 mg/dL to ≤ 2.0 mg/dL Severe: Males: > 2.4 mg/dL, Females: > 2.0 mg/dL For undescribed serum creatinine level at the start of Nesina treatment, indicate as unknown.
Age	If the start month and date of Nesina treatment is earlier than the birth month and date, calculate using the following formula: Start year of Nesina treatment − birth year − 1. If the birth month and date is earlier than or equal to the start month and date of Nesina treatment, calculate using the following formula: Start year of Nesina treatment − birth year. For unknown birth date, the birth date will be calculated as the 1st day of the birth month.
BMI	Calculate using the following formula: Weight (kg) / (0.0001 × Height (cm) × Height (cm)). Indicate to one decimal place rounded from two decimals.
Disease duration of type 2 diabetes mellitus (year)	Calculate using the following formula: (start date of Nesina treatment − diagnosis period of type 2 diabetes mellitus + 1) / 365.25. For unknown diagnosis month, calculate as January. Indicate to one decimal place rounded from two decimals.
Prior medication	Medications that patients were taking within 3 months prior to the start of Nesina treatment.
Concomitant medication	Medications that patients were taking after the start date of Nesina treatment.
Start date of other diabetic drug and concomitant medication (other than diabetic drug)	Calculate as the start date of survey sheet. For unknown month and date, calculate as January 1. For unknown date only, calculate as the first day of the relevant month.
End date of other diabetic drug and concomitant medication (other than diabetic drug)	Calculate as the end date of survey sheet. For unknown month and date, calculate as December 31. For unknown date only, calculate as the last day of the relevant month.
Diabetic drugs	Drugs of the National Health Insurance (NHI) Drug List Code starting with 3969, 3961, 3962, 2492, 2499410, 2499411, 2499415, or 2499416.
α-glucosidase inhibitors	Drugs of the NHI Drug List Code starting with 3969003, 3969004, 3969009, or

Term	Definition
	3969102.
Thiazolidines	Drugs of the NHI Drug List Code starting with 3969005, 3969007, 3969100, 3969101, or 3969103.
Sulfonylureas	Drugs of the NHI Drug List Code starting with 3961 or 3969101.
Biguanides	Drugs of the NHI Drug List Code starting with 3962, 3969100, 3969104, or 3969105.
Rapid-acting insulin secretagogues	Drugs of the NHI Drug List Code starting with 3969006, 3969008, 3969013, or 3969102.
Insulin preparations	Drugs of the NHI Drug List Code starting with 2492.
DPP-4 inhibitors	Drugs of the NHI Drug List Code starting with 3969010, 3969011, 3969012, 3969014, 3969015, 3969016, 3969017, 3969024, 3969025, 3969103, 3969104, or 3969105.
GLP-1 receptor agonists	Drugs of the NHI Drug List Code starting with 2499410, 2499411, 2499415, or 2499416.
SGLT-2 inhibitors	Drugs of the NHI Drug List Code starting with 3969018, 3969018, 3969019, 3969020, 3969021, 3969022, or 3969023.
Combination of diabetic drugs	Drugs of the NHI Drug List Code starting with 3969100, 3969101, 3969102, 3969103, 3969104, or 3969105.
Other diabetic drugs	Other diabetic drugs not classified into the above diabetic drug categories (α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, or combination of diabetic drugs).
Hypertension drugs	ARB Drugs of the NHI Drug List Code starting with the following 7 numbers: 2149039, 2149040, 2149041, 2149042, 2149044, 2149046, 2149048, 2149100, 2149110, 2149111, 2149112, 2149113, 2149114, 2149115, 2149116, 2149117, 2149118, 2149119, 2149120, 2149121, 2149122 Ca antagonists Drugs of the NHI Drug List Code starting with the following numbers: 2149019, 2149022, 2149027, 2149030, 2149034, 2149035, 2149037, 2149038, 2149043, 2149400, 2171006, 2171014, 2171019, 2171020, 2171021, 2171022, 2171405, 2190001, 2149114, 2149115, 2149116, 2149117, 2149118, 2149120, 2149121, 2149122 ,2190101 ,2190102 ,2190103 ,2190104 ACE inhibitors Drugs of the NHI Drug List Code starting with the following 4 numbers: 2144 Diuretics Drugs of the NHI Drug List Code starting with numbers 213 or the following 7 numbers: 2149003, 2149007, 2149012, 2149110, 2149111, 2149112, 2149113, 2149119,

Term	Definition
	2149122 α blockers Drugs of the NHI Drug List Code starting with the following numbers: 1234400, 214200210, 2149002, 2149015, 2149023, 2149026, 1152, 1149107, 1149114, 1149115, 2531001, 2149020 αβ/β blockers Drugs of the NHI Drug List Code starting with the following numbers: 2149032, 2149018, 2123014, 2149009, 2123013, 2123003, 2149008, 2149016, 2442001, 2123011, 2149036, 2123016, 2149700, 2149031, 2149010, 2123001, 2123F01, 2149029, 2123008, 2149014, 2149021, 2149028, 2123015, 2123005, 2149025, 2123009, 2123403, 2149033, 2149011 Complication of hypertension drugs Drugs of the NHI Drug List Code starting with the following numbers: 2149110, 2149111, 2149112, 2149113, 2149114, 2149115, 2149116, 2149117, 2149118, 2149119, 2149120, 2149121, 2149122 Other Drugs of the NHI Drug List Code starting with the following numbers: 2149047, 2142004, 2149001, 2149017, 2145
Dyslipidaemia drugs	Statins Drugs of the NHI Drug List Code starting with the following numbers: 2189010, 2189011, 2189012, 2189013, 2189015, 2189016, 2189017, 2190101, 2190102, 2190103, 2190104 Fibrates Drugs of the NHI Drug List Code starting with the following numbers: 2183001, 2183002, 2183003, 2183004, 2183005, 2183006 EPA/DHA Drugs of the NHI Drug List Code starting with the following numbers: 2189019, 3399004 Other Drugs of the NHI Drug List Code starting with the following numbers: Dugs, other than the above, of the NHI Drug List Code starting with 218, 2900002, or 3133001.
Concomitant medication (other)	Drugs other than the above (diabetic drugs, hypertension drugs, or dyslipidaemia drugs).
Protease Inhibitor	Use the results of the drug name in the survey sheet coded with the NHI Drug List (Appendix 1. List of Protease Inhibitors).
Renal excretory drugs	Use the results of the drug name in the survey sheet coded with the NHI Drug List (Appendix 2. List of Renal Excretory Drugs).
Nesina treatment period (days)	Actual treatment period from the start date to the end date of Nesina treatment. However, the washout period is excluded from the treatment period. Calculate using the following formula: End of Nesina treatment − start date of Nesina treatment + 1 (grand total).

Term	Definition
	(Consider the washout period.)
Mean daily dose of Nesina	Calculate using the following formula: Total of "daily dose of Nesina □ Nesina treatment period at the relevant dose" / Nesina treatment period. For the calculation of Nesina treatment period, refer to the above. If the daily dose of Nesina is a number outside specification in the survey sheet , handle the dose as follows: • < 6.25 mg → 3.125 mg • > 25 mg → 50 mg
HbA1c (NGSP value)	The NGSP value only will be used in this analysis. For the HbA1c (JDS value), calculate using the following formula: NGSP value (%) = 1.02 × JDS value (%) + 0.25% The HbA1c (international standard value) will be handled as the NGSP value.
Change in HbA1c	For HbA1c converted to the NGSP value, calculate using the following formula: Laboratory value at each testing time point − Laboratory value at the start of Nesina treatment.
Glycemic control achievement rate	Divide the following two categories for the glycemic control achievement rate: HbA1c (NGSP converted value) [Unit %] NGSP (%): < 6.0, ≥ 6.0 / < 7.0, ≥ 7.0
non-HDL cholesterol	Calculate using the following formula: "Total cholesterol" − "HDL cholesterol."
HOMA-R	Calculate using the following formula: Fasting insulin level (μU/mL) × Fasting blood glucose level (mg/dL) / 405. Indicate to one decimal place rounded from two decimals. For calculation, use the values of fasting insulin level and fasting blood glucose level measured at the same day.
HOMA-β	Calculate using the following formula: Fasting insulin level (μU/mL) × 360 / (Fasting blood glucose level [mg/dL] − 63). Indicate to one decimal place rounded from two decimals. For calculation, use the fasting insulin level and fasting blood glucose level measured at the same day. Do not use the fasting blood glucose level of < 63 for calculation
Summary statistics	Number of patients, mean, standard deviation, minimum, first quartile, median, third quartile, and maximum.

1.2 Important Identified Risks, Potential Risks, and Missing Information

Term	Definition
Important identified risk	
Hypoglycemia	Adverse events of the following PT Codes (term) are defined as hypoglycemia. 10020994(Hypoglycaemia neonatal) 10040576(Shock hypoglycaemic) 10021000(Hypoglycaemic coma) 10020993(Hypoglycaemia) 10065981(Hypoglycaemic unconsciousness) 10021002(Hypoglycaemic encephalopathy) 10048803(Hypoglycaemic seizure) 10020997(Hypoglycaemia unawareness) 10077216(Hyperinsulinaemic hypoglycaemia) 10059035(Postprandial hypoglycaemia)
Acute pancreatitis	Adverse events of the SMQ Code 20000022 (acute pancreatitis (SMQ) narrow scope are defined as acute pancreatitis.
Hepatic impairment / jaundice	Adverse events of the SMQ Code 20000005 (hepatic disorders (SMQ) broad) are defined as hepatic impairment / jaundice.
Skin disorder including oculomucocutaneous syndrome (Stevens-Johnson syndrome) / erythema multiforme	Adverse events of the SMQ Code 20000020 (severe skin adverse reactions (SMQ) narrow) are defined as skin disorder including oculomucocutaneous syndrome (Stevens-Johnson syndrome) / erythema multiforme.
Rhabdomyolysis	Adverse events of the SMQ Code 20000002 (rhabdomyolysis/myopathy (SMQ) narrow) are defined as rhabdomyolysis.
Intestinal obstruction	Adverse events of the SMQ Code 20000105 (gastrointestinal obstruction (SMQ) narrow) or the HLGT Code 10018008 (gastrointestinal stenosis and obstruction) or HLT Code 10052736 (non-mechanical ileus) are defined as intestinal obstruction.
Interstitial pneumonia	Adverse events of the SMQ Code 20000042 (interstitial lung disease (SMQ) narrow) are defined as interstitial pneumonia.
Angioedema	Adverse events of the SMQ Code 20000024 (angioedema (SMQ) narrow) are defined as angioedema.
Important potential risk	
Infection	Adverse events of SOC Code 10021881(infections and infestations) are defined as infection.
Malignant tumor	Adverse events of the SOC Code 10029104 (neoplasms benign, malignant and unspecified (incl cysts and polyps)) are defined as malignant tumor.

Malignant tumor (narrow sense)	Adverse events of the SMQ Code 20000194 (malignant tumors (SMQ) narrow) are defined as malignant tumor (narrow sense).
Pemphigoid	Adverse events of the PT Code 10067776 (ocular pemphigoid) or 10034277 (pemphigoid) are defined as pemphigoid.

Term	Definition
Important missing information	
Cardiovascular system risk	Adverse events of the SMQ Code 20000047 (myocardial infarction (SMQ) broad) or SMQ Code 20000061 (central nervous system haemorrhages and cerebrovascular conditions (SMQ) broad) are defined as cardiovascular system risk. "Central nervous system haemorrhage and cerebrovascular conditions (SMQ) broad" includes the following SMQ classes. ➢ 20000166(Conditions associated with central nervous system haemorrhages and cerebrovascular accidents (SMQ) broad) ➢ 20000064(Cerebrovascular disorder haemorrhagic (SMQ) broad) ➢ 20000063(Cerebrovascular disease ischaemic (SMQ) broad)

1.3 Display digit

Term	Definition
Percentage (%)	Percent of patients with adverse events or adverse drug reactions, etc. or percent of adverse events or adverse drug reactions, etc. : Indicate to two decimal places rounded from three decimals. Other than the above: Indicate to one decimal place rounded from two decimals.
Summary statistics	Mean, median, first quartile, and third quartile: Indicate one lower digit rounded from two lower digits than the digit of the to-be evaluated data (refer to Section 1.6). Standard deviation: Indicate two lower digits rounded from three lower digits of the to-be evaluated data. Minimum and maximum Indicate the same digit number as that of the to-be evaluated data.
p-value	Indicate to three decimal places rounded down from four decimals. If the data is less than 0.001, display as $p < 0.001$.

1.4 Level of Significance and Confidence Coefficient

Two-sided 5%, two-sided 95%.

1.5 Handling of Laboratory/Measured Data

The evaluation time points for vital signs and laboratory tests will be at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment, and last evaluation.

The evaluation time points for electrocardiography, waist circumference, and coronary atherosclerosis and arteriosclerosis will be at the start of Nesina treatment, 12 months after the start of Nesina treatment, and last evaluation.

If multiple data exist within the relevant time point, calculate the absolute value of a difference in number of days from the reference number of days and select the minimum absolute value as the datum of the relevant evaluation time point. If the absolute values are same, select the datum at the latest examination/measurement day.

If "On treatment at 12 months after Nesina treatment" is selected in Section "Current Status of Nesina Treatment" in the survey sheet, all values will be used for analysis. If "On treatment at 12 months after Nesina treatment" is not selected, the values before the next day of the last administration of Nesina will be used for analysis.

The start day of Nesina treatment is defined as 0 days.

[Vital signs and laboratory test values]

Evaluation time point	Reference number of days	Lower limit of window	Upper limit of window
At start of Nesina treatment	0 days	30 days before Nesina treatment	Start day of Nesina treatment
1 month after start of Nesina treatment	30 days	1 day after start of Nesina treatment	60 days after start of Nesina treatment
3 months after start of Nesina treatment	90 days	61 days after start of Nesina treatment	136 days after start of Nesina treatment
6 months after start of Nesina treatment	180 days	137 days after start of Nesina treatment	273 days after start of Nesina treatment
12 months after start of Nesina treatment	360 days	274 days after start of Nesina treatment	456 days after start of Nesina treatment
At last evaluation	Select the latest datum from 1 to 456 days after the start of Nesina treatment		

[Electrocardiography and waist circumference]

Evaluation time point	Reference number of days	Lower limit of window	Upper limit of window
At start of Nesina treatment	0 days	30 days before Nesina treatment	Start day of Nesina treatment
12 months after start of Nesina treatment	360 days	1 day after start of Nesina treatment	456 days after start of Nesina treatment
At last evaluation	Select the latest datum from 1 to 456 days after the start of Nesina treatment		

1.6 Display Data Digit

Display digits are described as below.

Term	Display digit	Unit
HbA1c (NGSP value)	0.1	%
Fasting blood glucose level	1	mg/dL
Fasting insulin level	0.1	μU/mL
Fasting glucagon	0.1	pg/mL
HOMA-R	0.1	―
HOMA-β	0.1	%
Fasting triglyceride	1	mg/dL
Total cholesterol	1	mg/dL
HDL-cholesterol	1	mg/dL
LDL-cholesterol	1	mg/dL
non-HDL cholesterol	1	mg/dL
Serum creatinine	0.01	mg/dL
BUN	0.1	mg/dL
Urinary albumin (corrected by creatinine)	0.1	mg/g•Cre
AST	1	IU/L
ALT	1	IU/L
γ-GTP	1	IU/L
ALP	1	IU/L
Total bilirubin	0.1	mg/dL
Amylase	1	IU/L

Term	Display digit	Unit
Lipase	1	IU/L
Waist circumference	0.1	cm
Pulse rate	1	bpm
Systolic blood pressure	1	mmHg
Diastolic blood pressure	1	mmHg
Weight	0.1	kg
BMI	0.1	kg/m^2
Age	1	Year
Duration of type 2 diabetes mellitus	0.1	Year
Height	1	cm
eGFR	0.1	$mL/min/1.73\ m^2$
Nesina administration period	1	Day
Mean daily dose of Nesina	0.01	mg

2.0 Disposition of Patients (Patient Diagram)

(1) Patients to be tabulated and analyzed

Registered patients

(2) Details of tabulation and analysis

The following will be tabulated: the number of registered patients, number of medical site at which patients is registered, number of patients whose survey sheets are collected, number of patients whose survey sheets are not collected, number of patients in the Safety Analysis Set, number of patients in the Not Safety Analysis Set, number of patients in the Efficacy Analysis Set, and number of patients in the Not Efficacy Analysis Set.

For the number of medical sites at which patients are registered, do not duplicate the same medical site with different departments.

For patients whose survey sheets are not collected, tabulate the number of patients for each reason for not collected survey sheets.

For the Not Safety Analysis Set and Not Efficacy Analysis Set, the number of patients will be tabulated for each reason for exclusion to create the list.

The following is the handling of the decision whether patients who meet the following criteria should be evaluated:

Criterion	Safety evaluation	Efficacy evaluation
Pre-agreement administration [found after administration]	×	×
Registration 15 days after prescription of Nesina [found after registration]	×	×
Nesina taking not confirmed [after the end of patient registration period]	×	×
No data for post-administration of Nesina	×	×
Not using any of the 3 combination drugs (the treatment group will be classified as "Other.") (1) With insulin preparation (2) With rapid-acting insulin secretagogues (3) With SGLT-2 inhibitors	○	×

○ Included, × Excluded or not evaluated

(3) Number of tables and figures

Figure 2.0-1 and Table 2.0-1

3.0 Patient Demographics

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be classified by the categories described below to tabulate the number of patients and frequency.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Sex	Male, Female
Age	Summary statistics
	< 65 years, ≥ 65 years
	< 75 years, ≥ 75 years
	< 20 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, ≥ 80 years
Disease duration of type 2 diabetes mellitus (year)	Summary statistics
	< 2 years, 2 to < 5 years, 5 to < 10 years, ≥ 10 years, Unknown
Height	Summary statistics
Category of clinical practice	Outpatient, Inpatient
Pregnancy (only females)	No, Yes
Severity of renal impairment	Normal, Mild, Moderate, Severe
	Normal + Mild, Moderate + Severe
Concurrent disease	No, Yes
Diabetic complication	No, Yes
Details of diabetic complication (overlapped)	Diabetic nephropathy, diabetic retinopathy, diabetic neuropathy For the proportion, the number of patients with diabetic complication will be denominator.
Concurrent hypertension	No, Yes
Concurrent dyslipidemia	No, Yes
Concurrent hyperuricemia	No, Yes
Concurrent liver disorder	No, Yes

Parameter	Category
Details of concurrent liver disorder (overlapped)	Hepatic steatosis, alcoholic hepatitis, chronic hepatitis, hepatic cirrhosis, or other For the proportion, the number of with concurrent liver disorder will be denominator.
Severity of hepatic impairment	Normal, Grades 1, 2, and 3, or Unknown
Concurrent renal disorder	No, Yes
Details of concurrent renal disorder (overlapped)	Nephrotic syndrome, glomerulonephritis, chronic glomerulonephritis, other For the proportion, the number of with concurrent renal disorder will be denominator.
Severity of renal impairment (eGFR)	Normal, Mild, Moderate, Severe, or Unknown
	Normal + Mild, Moderate + Severe, or Unknown
Severity of renal impairment (serum creatinine)	Normal, Mild, Moderate, Severe, or Unknown
	Normal + Mild, Moderate + Severe, or Unknown
Concurrent heart disease	No, Yes
Details of concurrent heart disease (overlapped)	Cardiac failure, myocardial infarction, angina pectoris, other For the proportion, the number of with concurrent heart disease will be denominator.
Concurrent cardiac failure	No, Yes
Severity classification of cardiac failure (NYHA classification)	Classes NYHA I, NYHA II, NYHA III, and NYHA IV, Unknown For the proportion, the number of with concurrent cardiac failure will be denominator.
Concurrent stroke-related disease	No, Yes
Details of concurrent stroke-related disease (overlapped)	Cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, transient ischaemic attack For the proportion, the number of with concurrent stroke-related disease will be denominator.
Concurrent allergic disease	No, Yes
Concurrent malignant tumour	No, Yes
Concurrent malignant	No, Yes

Parameter	Category
tumour (narrow sense)	
Other concurrent disease	No, Yes
Past medical history	No, Yes, Unknown
Hypersensitivity predisposition	No, Yes, Unknown
Alcohol history (drinking alcoholic drinks almost on a daily basis)	Yes, No, Unknown
Smoking history	Never, Smoking, Smoked, Unknown
HbA1c (NGSP value) (at the start of Nesina treatment)	Summary statistics
	< 6.0%, 6.0% to < 7.0%, 7.0% to < 8.0%, ≥ 8.0%, Unknown
Weight (at the start of Nesina treatment)	Summary statistics
BMI (at the start of Nesina treatment)	Summary statistics
	< 18.5 kg/m^2, 18.5 to < 25 kg/m^2, 25 to < 30 kg/m^2, ≥ 30 kg/m^2, Unknown
	< 25 kg/m^2, ≥ 25 kg/m^2, Unknown
Waist circumference (at the start of Nesina treatment)	Males: < 85 cm, ≥ 85 cm, or Unknown / Females: < 90 cm, ≥ 90 cm, or Unknown

(3) Number of tables and figures

Table 3.0-1

4.0 Details of Treatment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be classified by the categories described below to tabulate the number of patients and frequency.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Initial dose of Nesina	25 mg, 12.5 mg, 6.25 mg, or other
Mean daily dose of Nesina	> 25 mg, 25 to >12.5 mg, 12.5 to > 6.25 mg, or ≤ 6.25 mg
Nesina treatment period	Summary statistics
	1 to 60 days, 61 to 136 days, 137 to 273 days, 274 to 455 days, ≥ 456 days
Administration of prior medication (diabetic drug)	No, Yes, or Unknown
Prior medications (diabetic drugs)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs For the proportion, the number of patients with "Yes" for administration of prior medication (diabetic drug) will be denominator.
Administration of prior medication (other than diabetic drug)	No, Yes, or Unknown
Administration of concomitant medication (diabetic drug)	No, Yes, or Unknown
Concomitant medications (diabetic drugs) (overlapped)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs For the proportion, the number of patients with "Yes" for administration of concomitant medication (diabetic drug) will be

Parameter	Category
	denominator.
Administration of concomitant medication (hypertension drug)	No, Yes, or Unknown
Concomitant medications (hypertension drugs) (overlapped)	ARB, Ca antagonists, ACE inhibitors, diuretics, α blockers, αβ/β blockers, complication of hypertension drugs, or other For the proportion, the number of patients with "Yes" for administration of concomitant medication (hypertension drug) will be denominator.
Administration of concomitant medication (dyslipidaemia drug)	No, Yes, or Unknown
Concomitant medications (dyslipidaemia drugs) (overlapped)	Statins, fibrates, EPA/DHA, or other For the proportion, the number of patients with "Yes" for administration of concomitant medication (dyslipidaemia drug) will be denominator.
Administration of concomitant medication (protease drug)	No, Yes, or Unknown
Administration of concomitant medication (combined with renal excretory drug)	No, Yes, or Unknown
Administration of concomitant medication (other)	No, Yes, or Unknown

(3) Number of tables and figures

Table 4.0-1

4.1 Compliance

4.1.1 Status of compliance with Nesina

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For the status of compliance with Nesina, the frequency will be tabulated at each testing time point (1 month, 3 months, and 6 months after the start of Nesina treatment and last evaluation or treatment discontinuation).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance with Nesina	≥ 90%, ≥ 70%, ≥ 50%, or < 50%

(3) Number of tables and figures

Tables 4.1-1

4.1.2 Status of Compliance with Diet Therapy

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details to be tabulated and analyzed

For the status of compliance with diet therapy, the frequency will be tabulated at each testing time point (at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation or treatment discontinuation). The latest datum will be used for last evaluation.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance with diet therapy	≥ 90%, ≥ 70%, ≥ 50%, < 50%, Not performed, or Unknown

(3) Number of tables and figures

Table 4.1.2

4.1.3 Compliance with Exercise Therapy

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details to be tabulated and analyzed

For the status of compliance with exercise therapy, the frequency will be tabulated at each testing time point (at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation or treatment discontinuation). The latest datum will be used for last evaluation.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance	≥ 90%, ≥ 70%, ≥ 50%, < 50%, Not performed, or Unknown

Parameter	Category
with exercise therapy	

(3) Number of tables and figures

Table 4.1.3

5.0 Safety Tabulation and Analysis

5.1 Occurrence of adverse events and adverse drug reactions / infections

5.1.1 Occurrence of adverse events

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for adverse events.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of analysis
Number of patients with adverse events	Number of patients who experienced adverse events.
Number of adverse events	Number of adverse events. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events	Described in Section 1.1.
Type of adverse events	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse events and percent of patients with events will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse events and percent of events will be described in the ascending order of PT codes. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.

(3) Number of tables and figures

Table 5.1.1-1

5.1.2 Occurrence of adverse drug reactions / infections

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for adverse drug reactions, etc. and serious adverse drug reactions, etc.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse drug reactions, etc.	Number of patients who experienced adverse drug reactions, etc.
Number of adverse drug reactions, etc.	Number of adverse drug reactions, etc. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.
Percent of patients with adverse drug reactions, etc.	Described in Section 1.1.
Type of adverse drug reactions, etc.	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. and percent of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. and percent of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Tables 5.1.2-1 and 5.1.2-2

5.1.3 Important Identified Risks, Important Potential Risks, and Important Missing Information

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for important identified risks, important potential risks, and important missing information (described in Section 1.2).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis

Parameter	Details of tabulation and analysis
Number of patients with adverse events (or adverse drug reactions, etc.)	Number of patients who experienced adverse events (or adverse drug reactions, etc.) with important identified risks, important potential risks, and important missing information.
Number of adverse events (or adverse drug reactions, etc.)	Number of adverse events (or adverse drug reactions, etc.) with important identified risks, important potential risks, and important missing information. Count as an event if the same adverse event (or adverse drug reaction, etc.) (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events (or adverse drug reactions, etc.)	Described in Section 1.1.
Type of adverse events (or adverse drug reactions, etc.)	Will be broadly divided into the important identified risks, important potential risks, and important missing information and tabulated by PT in them. For the PTs, the number of adverse events (or adverse drug reactions, etc.) and percent of adverse events (or adverse drug reactions, etc.) will be described in the ascending order of PT codes. Count as an event if the same adverse event (or adverse drug reaction, etc.) (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Tables 5.1.3-1 and 5.1.3-2

5.2 Occurrence of Adverse Events and Adverse Drug Reactions / Infections in the Not Safety Analysis Set

5.2.1 Occurrence of Adverse Events

(1) Patients to be tabulated and analyzed

Not Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse events	Number of patients who experienced adverse events.
Number of adverse events	Number of adverse events. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events	Described in Section 1.1.
Type of adverse events	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse events and percent of patients with events will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse events and percent of events will be described in the ascending order of PT codes. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Table 5.2-1

5.2.2 Occurrence of adverse drug reactions / infections

(1) Patients to be tabulated and analyzed

Not Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse drug reactions, etc.	Number of patients who experienced adverse drug reactions, etc.
Number of adverse drug reactions, etc.	Number of adverse drug reactions, etc. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the

	same PT.
Percent of patients with adverse drug reactions, etc.	Described in Section 1.1.
Type of adverse drug reactions, etc.	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. and percent of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. and percent of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Table 5.2-2

5.3 Occurrence of Adverse Drug Reactions / Infections by Severity, Onset Period, and Outcome

5.3.1 Occurrence of Adverse Drug Reactions / Infections by Severity, Onset Period, and Outcome

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be categorized by the categories described below to tabulate the type of adverse drug reactions, etc.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Severity	Serious, Not serious, Not described
Onset period	1 to 14 days, 15 to 28 days, 29 to 84 days, 85 to 168 days, 169 to 336 days, 337days or Unknown
Outcome	Resolved, Resolving, Not resolved, Resolved with sequelae, Death, or Unknown

The method for tabulation of type adverse drug reactions, etc. is described below:

Parameter	Details of tabulation and analysis
Type of adverse drug	Will be broadly divided into the SOCs and tabulated by PT in the

Parameter	Details of tabulation and analysis
reactions, etc.	SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT. However, evaluate an event for the same LLT in accordance with the following order of priority: Onset period: earlier event Severity: Serious → Not serious → Not described Outcome: Death → Resolved with Sequelae → Not resolved → Resolving → Resolved → Unknown

(3) Number of tables and figures

Tables 5.3-1 to 5.3-3

5.4 Patient Demographics and Frequency of Adverse Drug Reactions / Infections by Treatment

5.4.1 Patients demographics and Frequency of Adverse Drug Reactions / Infections by Treatment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be categorized by the categories described below to tabulate the percent of patients with adverse drug reactions, etc.

The Fischer exact test will be used for parameters without rank data. The Mann-Whitney U test will be used for parameters with rank data. (The tests will be used for parameters with asterisk [*].)

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Sex*	Male, Female
Age*	< 65 years, ≥ 65 years
	< 75 years, ≥ 75 years
Concurrent liver disorder*	No, Yes
Severity of hepatic	Normal, Grades 1, 2, and 3, or Unknown

Parameter	Category
impairment*	
Concurrent renal disorder*	No, Yes
Severity of renal impairment* (eGFR)	Normal + Mild, Moderate + Severe, or Unknown
Severity of renal impairment* (serum creatinine)	Normal + Mild, Moderate + Severe, or Unknown
Concurrent heart disease*	No, Yes
Details of concurrent heart disease (overlapped)	Cardiac failure, myocardial infarction, or angina pectoris
Concurrent cardiac failure*	No, Yes
Severity classification of cardiac failure (NYHA classification)*	Classes NYHA I, NYHA II, NYHA III, and NYHA IV, or Unknown
Concurrent stroke-related disease*	No, Yes, or Unknown
Mean daily dose of Nesina	> 25 mg, 25 to >12.5 mg, 12.5 to > 6.25 mg, or ≤ 6.25 mg
Administration of concomitant medication (diabetic drug)	No, Yes
Concomitant medications (diabetic drugs) (overlapped)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, or insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs
Administration of concomitant medication (protease drug)*	No, Yes, or Unknown
Administration of	No, Yes, or Unknown

Parameter	Category
concomitant medication (combined with renal excretory drug)*	

(3) Number of tables and figures

Table 5.4.1-1

5.5 Occurrence of Adverse Drug Reactions / Infections by Age

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Age will be classified into < 65 years, ≥ 65 years and < 75 years, and ≥ 75 years for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 5.5-1 to 5.5-2

5.6 Occurrence of Adverse Drug Reactions / Infections by Sex

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Sex will be classified into male or female for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.6-1

5.7 Occurrence of Adverse Drug Reactions / Infections by Liver Disorder

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent liver disorder will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.7-1

5.8 Occurrence of Adverse Drug Reactions / Infections by Liver Impairment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Severity of liver impairment will be classified into Grade 1, 2, or 3 or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.8-1

5.9 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Renal Disorder

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent renal disorder will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.9-1

5.10 Occurrence of Adverse Drug Reactions / Infections by Severity of Renal Impairment

(4) Patients to be tabulated and analyzed

Safety Analysis Set

(5) Details of tabulation and analysis

Severity of renal impairment will be classified into normal + mild, moderate + severe, or unknown, according to the criteria for the severity of renal impairment (eGFR and serum creatinine) for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(6) Number of tables and figures

Tables 5.10-1 and 5.10-2

5.11 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Heart Disease

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent heart disease will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.11-1

5.12 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Heart Failure

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent heart failure will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.12-1

5.13 Occurrence of Adverse Drug Reactions / Infections by Severity of Heart Failure

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Severity of heart failure will be classified into Class NYHA I, NYHA II, NYHA III, or NYHA IV or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.13-1

5.14 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Stroke-related Disease

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent stroke-related disease will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.14-1

5.15 Occurrence of Adverse Drug Reactions / Infections by Mean Daily Dose of Nesina

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The mean daily dose of Nesina will be classified into > 25 mg, 25 to > 12.5 mg, 12.5 to > 6.25 mg, or 6.25 mg for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients will be tabulated.

(3) Number of tables and figures

Table 5.15-1

5.16 Occurrence of Adverse Drug Reactions / Infections by Concomitant Medication (Diabetic Drug)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medications (diabetic drugs) will be classified into the following drugs: α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs, for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.16-1

5.17 Occurrence of Adverse Drug Reactions / Infections by Presence of Concomitant Medication (Protease Inhibitor)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medication (protease inhibitor) will be classified into yes, no, or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.17-1

5.18 Occurrence of Adverse Drug Reactions / Infections by Presence of Concomitant Medication (Renal Excretory Drug)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medication (renal excretory drug) be classified into yes, no, or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.18-1

5.19 Change in Laboratory/Measured Data

5.19.1 Vital Signs

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

In vital signs, summary statistics for pulse rate, blood pressure (systolic/diastolic), and weight will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

Measured values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.1-1 and Figures 5.19.1-1 to 5.19.1-4

5.19.2 Laboratory Values

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

In laboratory values, summary statistics will be calculated for fasting triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol, non-HDL cholesterol, serum creatinine, BUN, urinary albumin (corrected by creatinine), AST, ALT, γ-GTP, ALP, total bilirubin, amylase, lipase at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

These laboratory values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.2-1 and Figures 5.19.2-1 to 5.19.2-15

5.19.3 Electrocardiography

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For assessment of electrocardiogram, cross tabulation will be used for the categories described below.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
ECG results at start of Nesina treatment	Clinical abnormal findings (Yes or No) or Not performed
ECG results at 12 months after start of Nesina treatment	Clinical abnormal findings (Yes or No) or Not performed
ECG results at last evaluation	Clinical abnormal findings (Yes or No) or Not performed

(3) Number of tables and figures

Table 5.19.3

5.19.4 Waist Circumference

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For waist circumference, summary statistics will be calculated at each testing time point (at the start of Nesina treatment, 12 months after the start of Nesina treatment, and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

Measured values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.4 and Figure 5.19.4

5.19.5 Tests for Coronary Atherosclerosis and Arteriosclerosis

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

A listing of the following tests and the test results for coronary atherosclerosis and arteriosclerosis will be created: survey sheet number, treatment group, time point, test day, and details of tests (pulse wave velocity [PWV], cardio-ankle vascular index [CAVI], intima-media thickness [IMT], intra-vascular ultrasound [IVUS], and other [specify the details]).

(3) Number of tables and figures

Table 5.19.5

6.0 Efficacy Tabulation and Analysis

6.1 Changes in HbA1c

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For HbA1c (NGSP values), summary statistics will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes, summary statistics and the mean 95% confidence intervals will be calculated and the paired t-test will be performed.

Measured values of HbA1c (NGSP values) will be plotted and for the changes a bar graph will be created excluding the unknown category.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 6.1-1 and Figure 6.1-1

6.2 Glycemic control achievement rate (HbA1c)

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

The glycemic control achievement rate for HbA1c (NGSP value) will be tabulated ($< 6.0\%$, $\geq 6.0\%$ / $< 7.0\%$, $\geq 7.0\%$) and a bar graph will be created at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation) (the unknown category will be excluded for the bar graph).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 6.2-1 and Figures 6.2-1 and 6.2-2

6.3 Changes in Fasting blood glucose level, Fasting insulin level, Fasting Glucagon, HOMA-R, and HOMA-β

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For fasting blood glucose level, fasting insulin level, fasting glucagon, HOMA-R, and HOMA-β, summary statistics will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes, summary statistics and the mean 95% confidence intervals will be

calculated and the paired t-test will be performed.

Measured values will be plotted and for the changes a bar graph will be created excluding the unknown category.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 6.3-1 and 6.3-5 and Figures 6.3-1 and 6.3-5

6.4 Changes in HbA1c, etc. by Factor Probably Affecting Efficacy

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For changes in HbA1c (NGSP values), summary statistics and the mean 95% confidence intervals will be calculated and the paired t-test will be performed at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation).

The glycemic control achievement rate for HbA1c (< 6.0%, ≥ 6.0% / < 7.0%, ≥ 7.0%) at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation) will be tabulated for the following parameters:

i Sex (Male, Female)

ii Age (< 65 years, ≥ 65 years)

iii Age (< 75 years, ≥ 75 years)

iv Concurrent liver disorder (No, Yes)

v Concurrent renal disorder (No, Yes)

vi HbA1c (NGSP value) at the start of Nesina treatment (< 6.0%, 6.0% to < 7.0%, 7.0% to < 8.0%, ≥ 8.0%, or Unknown)

vii Mean daily dose of Nesina (> 25 mg, 25 to > 12.5 mg, 12.5 to > 6.25 mg, or 6.25 mg)

viii Concomitant diabetic drugs (α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, or insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, combination of diabetic drugs, or other diabetic drugs)

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 6.4-1 to 6.4-16

Statistical Analysis Plan

Nesina Tablets Specified Drug-use Survey "Type 2 Diabetes Mellitus: Combination Therapy With Hypoglycemic Drug (Insulin Preparation or Rapid-acting Insulin Secretagogues, Etc)"

Takeda Pharmaceutical Company Limited.

PPD

Version 2, Created on February 6, 2018

Table of Contents

1.0 Definition of Terms and Handling of Laboratory/Measured Data

1.1 Definitions

Term	Definition
Nesina	Nesina tablet(s) is abbreviated as Nesina in this statistical analysis plan.
SOC	System Organ Class of MedDRA/J MedDRA/J version 20.1 is used for this document.
HLGT	High level group term of MedDRA/J
PT	Preferred term of MedDRA/J
LLT	Lowest level term of MedDRA/J
Registered patients	Patients whose registration was approved
Survey sheet collected patients	Patients whose survey sheets were collected
Survey sheet uncollected patients	Of the registered patients, patients whose survey sheets were uncollected.
Safety Analysis Set	Of the survey sheet collected patients, patients who were evaluated for safety analysis. For tabulation, the description of "total" means the Safety Analysis Set.
Not Safety Analysis Set	Of the survey sheet collected patients, patients who were excluded from safety analysis
Efficacy Analysis Set	Of the Safety Analysis Set, patients who were evaluated for efficacy analysis
Not Efficacy Analysis Set	Of the Safety Analysis Set, patients who were excluded from the efficacy analysis
First date of Nesina treatment	Of the start dates of the Nesina treatment period in patients, the earliest date is defined as the first date of Nesina treatment.
Last date of Nesina treatment	Of the last dates of the Nesina treatment in patients, the latest date is defined as the last date of Nesina treatment. If Nesina treatment is continued and the year, month, and date of the continued treatment period are specified, the year, month, and date of the continued treatment period are defined as the last date of Nesina treatment. If the data for the year, month, and date of the continued treatment period are missing, the following date is defined as the last date of Nesina treatment. (1) First date of Nesina treatment + 1 year (same month and date) for continued treatment of Nesina. (2) Latest date at which the following examinations/observations will be performed for the not-continued treatment of Nesina: ● [Date of examinations/ observations] • Compliance with Nesina treatment

Term	Definition
	• Compliance with diet/exercise therapy • Laboratory tests • Body weight • Waist circumference • Pulse rate • Blood pressure • Electrocardiography • Tests for coronary atherosclerosis and arteriosclerosis
Adverse drug reactions, etc.	Abbreviation of "adverse drug reactions / infections" Of the adverse events, events for which causal relationship to Nesina was assessed as "Not related" by the Investigator. In this statistical analysis plan, "adverse drug reactions / infections" is used in the headings, while "adverse drug reactions, etc." is used in the sentences and tables.
Serious adverse events	Adverse events assessed as "serious" by the Investigator. Events described in the MedDRA coding list in the Takeda Medically Significant AE List will be handled as serious even if the Investigator assesses as "Not serious."
Serious adverse drug reactions	Abbreviation of "serious adverse drug reactions / infections" Of the "serious adverse events," the events for which causal relationship to Nesina was assessed as "Not related" by the Investigator
Number of patients with events	Number of patients with adverse events or adverse drug reactions, etc.
Number of events	Number of adverse events or adverse drug reactions, etc.
Percent of patients with events	[For safety analysis calculation in the Safety Analysis Set] The formula is: Number of patients with events / Number of Safety Analysis Set × 100. [For safety analysis calculation in the Not Safety Analysis Set] The formula is: Number of patients with events / Number of Not Safety Analysis Set × 100.
Percent of events	[For safety analysis calculation in the Safety Analysis Set] The formula is: Number of events / Number of the Safety Analysis Set × 100. [For safety calculation in the Not Safety Analysis Set] The formula is: Number of events / Number of Not Safety Analysis Set × 100.
Onset period	The formula is: Onset date of adverse events (or adverse drug reactions, etc.) − start date of Nesina treatment + 1.

Term	Definition
	If the onset month and date of an adverse event (or adverse drug reaction, etc.) is unknown, calculate the onset month and date as January 1. However, if the start month and date of Nesina treatment are same as the onset month and date of an adverse event (or adverse drug reaction, etc.), the onset period will be calculated as the start date of Nesina treatment. For unknown onset date of adverse events (or adverse drug reactions, etc.), the onset period will be calculated as 1 day. However, if the start month and date of Nesina treatment are same as the onset month and date of adverse events (or adverse drug reactions, etc.), the onset period will be calculated as the start date of Nesina treatment.
Treatment group	Overall: Total patients who will be treated with combination therapy with insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, and other (all are defined below) Combination with insulin preparation: Patients who will be treated with insulin preparation within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with rapid-acting insulin secretagogues or SGLT-2 inhibitors Combination with rapid-acting insulin secretagogues: Patients who will be treated with rapid-acting insulin secretagogues within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with insulin preparation or SGLT-2 inhibitors Combination with SGLT-2 inhibitors: Patients who will be treated with SGLT-2 inhibitors within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with insulin preparation or rapid-acting insulin secretagogues Other: Patients who will not be treated with combination therapy with insulin preparation, rapid-acting insulin secretagogues, or SGLT-2 inhibitors
Patients with diabetic complication	Patients with any of the following complications: diabetic nephropathy, diabetic retinopathy, or diabetic neuropathy.
Patients with diabetic nephropathy	Patients with complication of PT Code 10012660 (diabetic end stage renal disease) or 10061835 (diabetic nephropathy).
Patients with diabetic retinopathy	Patients with complication of PT Code 10012688 (diabetic retinal oedema) or 10012689 (diabetic retinopathy).
Patients with diabetic neuropathy	Patients with complication of PT Code 10012645 (diabetic autonomic neuropathy), 10012676 (diabetic mononeuropathy), or 10012680 (diabetic

Term	Definition
	neuropathy).
Patients with concurrent hypertension	Patients with concurrent disease of the Standardised MedDRA Query (hereinafter SMQ) Code 20000147 (hypertension (SMQ) narrow).
Patients with concurrent dyslipidemia	Patients with concurrent disease of the SMQ Code 20000026 (dyslipidaemia (SMQ) narrow).
Patients with concurrent hyperuricemia	Patients with concurrent disease of the PT code meeting the Takeda MedDRA Query 20.1 (hereinafter, TMQ 20.1) (blood uric acid increased).
Patients with concurrent liver disorder	Patients with concurrent disease of the SMQ Code 20000005 (hepatic disorders (narrow).
Patients with concurrent hepatic steatosis	Patients with concurrent disease of the PT Code 10019708 (hepatic steatosis).
Patients with concurrent alcoholic hepatitis	Patients with concurrent disease of the PT Code 10019728 (hepatitis alcoholic).
Patients with concurrent chronic hepatitis	Patients with concurrent disease of the PT Code 10008909 (chronic hepatitis).
Patients with concurrent hepatic cirrhosis	Patients with concurrent disease of the PT Code 10019641 (hepatic cirrhosis).
Patients with concurrent renal disorder	Patients with concurrent disease of the TMQ 20.1 (renal disease).
Patients with concurrent nephrotic syndrome	Patients with concurrent disease of the PT Code 10029164 (nephrotic syndrome).
Patients with concurrent glomerulonephritis	Patients with concurrent disease of the PT Code 10018364 (glomerulonephritis) or the PT Code 10018367 (glomerulonephritis chronic).
Patients with concurrent chronic renal failure	Patients with concurrent disease of the PT Code 10064848 (chronic kidney disease) or the PT Code 10038435 (renal failure).
Patients with concurrent heart disease	Patients with concurrent disease of the SOC Code 10007541 (cardiac disorders).
Patients with concurrent cardiac failure	Patients with concurrent disease of the SMQ Code 20000004 (cardiac failure (SMQ) narrow).
Patients with concurrent myocardial infarction	Patients with concurrent disease of the SMQ Code 20000047 (myocardial infarction (SMQ) narrow).
Patients with concurrent angina pectoris	Patients with concurrent disease of the SOC Code 10007541 (cardiac disorders) and the PT Code 10036759 (prinzmetal angina), PT Code 10002383 (angina pectoris), PT Code 10058144 (postinfarction angina), PT Code 10002388 (angina unstable), or LLT Code 10065566 (microvascular angina).
Patients with concurrent stroke-related disease	Patients with concurrent disease of cerebral infarction, cerebral haemorrhage, subarachnoid haemorrhage, or transient ischaemic attack, described below.

Term	Definition
Patients with concurrent disease cerebral infarction	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10006147 (brain stem infarction), PT Code 10008118 (cerebral infarction), PT Code 10008119 (cerebral infarction foetal), PT Code 10008034 (cerebellar infarction), PT Code 10019005 (haemorrhagic cerebral infarction), PT Code 10051078 (lacunar infarction), PT Code 10056237 (migrainous infarction), PT Code 10058571 (spinal cord infarction), PT Code 10060839 (embolic cerebral infarction), PT Code 10060840 (ischaemic cerebral infarction), PT Code 10064961 (thalamic infarction), PT Code 10067347 (thrombotic cerebral infarction), or PT Code 10069020 (basal ganglia infarction).
Patients with concurrent cerebral hemorrhage	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10006145 (brain stem haemorrhage), PT Code 10008111 (cerebral haemorrhage), PT Code 10008112 (cerebral haemorrhage neonatal), PT Code 10008030 (cerebellar haemorrhage), PT Code 10018985 (haemorrhage intracranial), PT Code 10022840 (intraventricular haemorrhage), PT Code 10022841 (intraventricular haemorrhage neonatal), PT Code 10042365 (subdural haemorrhage neonatal), PT Code 10049236 (spinal epidural haemorrhage), PT Code 10048992 (spinal cord haemorrhage), PT Code 10050157 (cerebral haemorrhage foetal), PT Code 10052593 (meningorrhagia), PT Code 10058939 (thalamus haemorrhage), PT Code 10058940 (putamen haemorrhage), PT Code 10067057 (basal ganglia haemorrhage), PT Code 10067277 (cerebral microhaemorrhage), PT Code 10071205 (brain stem microhaemorrhage), PT Code 10071206 (cerebellar microhaemorrhage), PT Code 10072043 (central nervous system haemorrhage), or PT Code 10073563 (Spinal subdural haemorrhage).
Patients with concurrent subarachnoid hemorrhage	Patients with concurrent disease of the PT Code 10042316 (subarachnoid haemorrhage), PT Code 10042317 (subarachnoid haemorrhage neonatal), PT Code 10073564 (spinal subarachnoid haemorrhage), LLT Code 10072201 (Asymptomatic subarachnoid haemorrhage).
Patients with concurrent transient ischemic attack	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10044390 (transient ischaemic attack).
Patients with concurrent allergic disease	Patients with concurrent disease of bronchial asthma, pollinosis, allergic rhinitis, or allergic dermatitis, described below.
Patients with concurrent bronchial asthma	Patients with concurrent disease of the SOC Code 10038738 (respiratory, thoracic and mediastinal disorders) and the PT Code 10003553 (asthma), PT Code 10075084 (aspirin-exacerbated respiratory disease), PT Code 10003557 (asthma exercise induced), PT Code 10003559 (asthma late onset), PT Code 10041961 (status asthmaticus), PT Code 10001890 (alveolitis allergic), PT

Term	Definition
	Code 10049585 (infantile asthma), PT Code 10070836 (occupational asthma), or PT Code 10064823 (asthmatic crisis).
Patients with concurrent pollinosis	Patients with concurrent disease of the PT Code 10048908 (seasonal allergy).
Patients with concurrent allergic rhinitis	Patients with concurrent disease of the PT Code 10039085 (rhinitis allergic).
Patients with concurrent allergic dermatitis	Patients with concurrent disease of the PT Code 10012434 (dermatitis allergic).
Patients with concurrent malignant tumor	Patients with concurrent disease of the SOC Code 10029104 (neoplasms benign, malignant and unspecified (incl cysts and polyps)).
Patients with concurrent malignant tumor (narrow sense)	Patients with concurrent disease of the SMQ Code 20000194 (malignant tumour (SMQ) narrow).
Patients with other concurrent disease	Patients with concurrent disease other than the above (diabetic complication, hypertension, dyslipidaemia, hyperuricaemia, liver disease, renal disease, heart disease, stroke-related disease, allergic disease, malignant tumor, or malignant tumor (narrow sense)).
Severity of hepatic impairment	Severity of hepatic impairment will be assessed using AST or ALT at the start of Nesina treatment. Severity will be assessed using the categories described below, and the higher grade of AST or ALT will be used for analysis. Normal: < 50 IU/L Grade 1: ≥ 50 IU/L and < 100 IU/L Grade 2: ≥ 100 IU/L and < 500 IU/L Grade 3: ≥ 500 IU/L Quoted from the Standards for Classification of Serious Adverse Drug Reactions due to Drug Products notified by the director of Pharmaceuticals and Chemicals Safety Division, Pharmaceutical Affairs Bureau, the Ministry of Health and Welfare (No. 80 notification of Pharmaceuticals and Chemicals Safety Division, Pharmaceutical Affairs Bureau: June 29, 1992).
Severity of renal impairment (eGFR)	eGFR* will be calculated based on age and serum creatinine at the start of Nesina treatment to assess the severity according to the categories described below. For unknown serum creatinine and age at the start of Nesina treatment, indicate as unknown. Indicate to one decimal place rounded from two decimals. Normal: ≥ 90 mL/min/1.73 m^2 Mild: ≥ 60 mL/min/1.73 m^2 and < 90 mL/min/1.73 m^2 Moderate: ≥ 30 mL/min/1.73 m^2 and < 60 mL/min/1.73 m^2 Severe: < 30 mL/min/1.73 m^2 *eGFR = $194 \times Cr^{-1.094} \times \text{age (year)}^{-0.287}$(×0.739 for females)

Term	Definition
	Cr: Serum creatinine at the start of Nesina treatment. For serum Cr, indicate to two decimal places. Quoted from the Clinical Practice Guide for CKD, edited by the Japanese Society of Nephrology.
Severity of renal impairment (serum creatinine)	Severity will be assessed based on serum creatinine at the start of Nesina treatment and according to the following categories: Normal + Mild: Males: ≤ 1.4 mg/dL, Females: ≤ 1.2 mg/dL Moderate: Males: > 1.4 mg/dL to ≤ 2.4 mg/dL, Females: > 1.2 mg/dL to ≤ 2.0 mg/dL Severe: Males: > 2.4 mg/dL, Females: > 2.0 mg/dL For undescribed serum creatinine level at the start of Nesina treatment, indicate as unknown.
Age	If the start month and date of Nesina treatment is earlier than the birth month and date, calculate using the following formula: Start year of Nesina treatment − birth year − 1. If the birth month and date is earlier than or equal to the start month and date of Nesina treatment, calculate using the following formula: Start year of Nesina treatment − birth year. For unknown birth date, the birth date will be calculated as the 1st day of the birth month.
BMI	Calculate using the following formula: Weight (kg) / (0.0001 × Height (cm) × Height (cm)). Indicate to one decimal place rounded from two decimals.
Disease duration of type 2 diabetes mellitus (year)	Calculate using the following formula: (start date of Nesina treatment − diagnosis period of type 2 diabetes mellitus + 1) / 365.25. For unknown diagnosis month, calculate as January. Indicate to one decimal place rounded from two decimals.
Prior medication	Medications that patients were taking within 3 months prior to the start of Nesina treatment.
Concomitant medication	Medications that patients were taking after the start date of Nesina treatment.
Start date of other diabetic drug and concomitant medication (other than diabetic drug)	Calculate as the start date of survey sheet. For unknown month and date, calculate as January 1. For unknown date only, calculate as the first day of the relevant month.
End date of other diabetic drug and concomitant medication (other than diabetic drug)	Calculate as the end date of survey sheet. For unknown month and date, calculate as December 31. For unknown date only, calculate as the last day of the relevant month.
Diabetic drugs	Drugs of the National Health Insurance (NHI) Drug List Code starting with 3969, 3961, 3962, 2492, 2499410, 2499411, 2499415, or 2499416.
α-glucosidase inhibitors	Drugs of the NHI Drug List Code starting with 3969003, 3969004, 3969009, or

Term	Definition
	3969102.
Thiazolidines	Drugs of the NHI Drug List Code starting with 3969005, 3969007, 3969100, 3969101, or 3969103.
Sulfonylureas	Drugs of the NHI Drug List Code starting with 3961 or 3969101.
Biguanides	Drugs of the NHI Drug List Code starting with 3962, 3969100, 3969104, or 3969105.
Rapid-acting insulin secretagogues	Drugs of the NHI Drug List Code starting with 3969006, 3969008, 3969013, or 3969102.
Insulin preparations	Drugs of the NHI Drug List Code starting with 2492.
DPP-4 inhibitors	Drugs of the NHI Drug List Code starting with 3969010, 3969011, 3969012, 3969014, 3969015, 3969016, 3969017, 3969024, 3969025, 3969103, 3969104, or 3969105.
GLP-1 receptor agonists	Drugs of the NHI Drug List Code starting with 2499410, 2499411, 2499415, or 2499416.
SGLT-2 inhibitors	Drugs of the NHI Drug List Code starting with 3969018, 3969018, 3969019, 3969020, 3969021, 3969022, or 3969023.
Combination of diabetic drugs	Drugs of the NHI Drug List Code starting with 3969100, 3969101, 3969102, 3969103, 3969104, or 3969105.
Other diabetic drugs	Other diabetic drugs not classified into the above diabetic drug categories (α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, or combination of diabetic drugs).
Hypertension drugs	ARB Drugs of the NHI Drug List Code starting with the following 7 numbers: 2149039, 2149040, 2149041, 2149042, 2149044, 2149046, 2149048, 2149100, 2149110, 2149111, 2149112, 2149113, 2149114, 2149115, 2149116, 2149117, 2149118, 2149119, 2149120, 2149121, 2149122 Ca antagonists Drugs of the NHI Drug List Code starting with the following numbers: 2149019, 2149022, 2149027, 2149030, 2149034, 2149035, 2149037, 2149038, 2149043, 2149400, 2171006, 2171014, 2171019, 2171020, 2171021, 2171022, 2171405, 2190001, 2149114, 2149115, 2149116, 2149117, 2149118, 2149120, 2149121, 2149122 ,2190101 ,2190102 ,2190103 ,2190104 ACE inhibitors Drugs of the NHI Drug List Code starting with the following 4 numbers: 2144 Diuretics Drugs of the NHI Drug List Code starting with numbers 213 or the following 7 numbers: 2149003, 2149007, 2149012, 2149110, 2149111, 2149112, 2149113, 2149119,

Term	Definition
	2149122 α blockers Drugs of the NHI Drug List Code starting with the following numbers: 1234400, 214200210, 2149002, 2149015, 2149023, 2149026, 1152, 1149107, 1149114, 1149115, 2531001, 2149020 αβ/β blockers Drugs of the NHI Drug List Code starting with the following numbers: 2149032, 2149018, 2123014, 2149009, 2123013, 2123003, 2149008, 2149016, 2442001, 2123011, 2149036, 2123016, 2149700, 2149031, 2149010, 2123001, 2123F01, 2149029, 2123008, 2149014, 2149021, 2149028, 2123015, 2123005, 2149025, 2123009, 2123403, 2149033, 2149011 Complication of hypertension drugs Drugs of the NHI Drug List Code starting with the following numbers: 2149110, 2149111, 2149112, 2149113, 2149114, 2149115, 2149116, 2149117, 2149118, 2149119, 2149120, 2149121, 2149122 Other Drugs of the NHI Drug List Code starting with the following numbers: 2149047, 2142004, 2149001, 2149017, 2145
Dyslipidaemia drugs	Statins Drugs of the NHI Drug List Code starting with the following numbers: 2189010, 2189011, 2189012, 2189013, 2189015, 2189016, 2189017, 2190101, 2190102, 2190103, 2190104 Fibrates Drugs of the NHI Drug List Code starting with the following numbers: 2183001, 2183002, 2183003, 2183004, 2183005, 2183006 EPA/DHA Drugs of the NHI Drug List Code starting with the following numbers: 2189019, 3399004 Other Drugs of the NHI Drug List Code starting with the following numbers: Dugs, other than the above, of the NHI Drug List Code starting with 218, 2900002, or 3133001.
Concomitant medication (other)	Drugs other than the above (diabetic drugs, hypertension drugs, or dyslipidaemia drugs).
Protease Inhibitor	Use the results of the drug name in the survey sheet coded with the NHI Drug List (Appendix 1. List of Protease Inhibitors).
Renal excretory drugs	Use the results of the drug name in the survey sheet coded with the NHI Drug List (Appendix 2. List of Renal Excretory Drugs).
Nesina treatment period (days)	Actual treatment period from the start date to the end date of Nesina treatment. However, the washout period is excluded from the treatment period. Calculate using the following formula: End of Nesina treatment − start date of Nesina treatment + 1 (grand total).

Term	Definition
	(Consider the washout period.)
Mean daily dose of Nesina	Calculate using the following formula: Total of "daily dose of Nesina □ Nesina treatment period at the relevant dose" / Nesina treatment period. For the calculation of Nesina treatment period, refer to the above. If the daily dose of Nesina is a number outside specification in the survey sheet , handle the dose as follows: • < 6.25 mg → 3.125 mg • > 25 mg → 50 mg
HbA1c (NGSP value)	The NGSP value only will be used in this analysis. For the HbA1c (JDS value), calculate using the following formula: NGSP value (%) = 1.02 × JDS value (%) + 0.25% The HbA1c (international standard value) will be handled as the NGSP value.
Change in HbA1c	For HbA1c converted to the NGSP value, calculate using the following formula: Laboratory value at each testing time point − Laboratory value at the start of Nesina treatment.
Glycemic control achievement rate	Divide the following two categories for the glycemic control achievement rate: HbA1c (NGSP converted value) [Unit %] NGSP (%): < 6.0, ≥ 6.0 / < 7.0, ≥ 7.0
non-HDL cholesterol	Calculate using the following formula: "Total cholesterol" − "HDL cholesterol."
HOMA-R	Calculate using the following formula: Fasting insulin level (μU/mL) × Fasting blood glucose level (mg/dL) / 405. Indicate to one decimal place rounded from two decimals. For calculation, use the fasting insulin level and fasting blood glucose level measured at the same day.
HOMA-β	Calculate using the following formula: Fasting insulin level (μU/mL) × 360 / (Fasting blood glucose level [mg/dL] − 63). Indicate to one decimal place rounded from two decimals. For calculation, use the fasting insulin level and fasting blood glucose level measured at the same day. Do not use the fasting blood glucose level of < 63 for calculation
Summary statistics	Number of patients, mean, standard deviation, minimum, first quartile, median, third quartile, and maximum.

1.2 Important Identified Risks, Potential Risks, and Missing Information

Term	Definition
Important identified risk	
Hypoglycemia	Adverse events of the following PT Codes (term) are defined as hypoglycemia. 10020994(Hypoglycaemia neonatal) 10040576(Shock hypoglycaemic) 10021000(Hypoglycaemic coma) 10020993(Hypoglycaemia) 10065981(Hypoglycaemic unconsciousness) 10021002(Hypoglycaemic encephalopathy) 10048803(Hypoglycaemic seizure) 10020997(Hypoglycaemia unawareness) 10077216(Hyperinsulinaemic hypoglycaemia) 10059035(Postprandial hypoglycaemia)
Acute pancreatitis	Adverse events of the SMQ Code 20000022 (acute pancreatitis (SMQ) narrow scope are defined as acute pancreatitis.
Hepatic impairment / jaundice	Adverse events of the SMQ Code 20000005 (hepatic disorders (SMQ) broad) are defined as hepatic impairment / jaundice.
Skin disorder including oculomucocutaneous syndrome (Stevens-Johnson syndrome) / erythema multiforme	Adverse events of the SMQ Code 20000020 (severe skin adverse reactions (SMQ) narrow) are defined as skin disorder including oculomucocutaneous syndrome (Stevens-Johnson syndrome) / erythema multiforme.
Rhabdomyolysis	Adverse events of the SMQ Code 20000002 (rhabdomyolysis/myopathy (SMQ) narrow) are defined as rhabdomyolysis.
Intestinal obstruction	Adverse events of the SMQ Code 20000105 (gastrointestinal obstruction (SMQ) narrow) or the HLGT Code 10018008 (gastrointestinal stenosis and obstruction) or HLT Code 10052736 (non-mechanical ileus) are defined as intestinal obstruction.
Interstitial pneumonia	Adverse events of the SMQ Code 20000042 (interstitial lung disease (SMQ) narrow) are defined as interstitial pneumonia.
Angioedema	Adverse events of the SMQ Code 20000024 (angioedema (SMQ) narrow) are defined as angioedema.
Important potential risk	
Infection	Adverse events of SOC Code 10021881(infections and infestations) are defined as infection.
Malignant tumor	Adverse events of the SOC Code 10029104 (neoplasms benign, malignant and unspecified (incl cysts and polyps)) are defined as malignant tumor.

Malignant tumor (narrow sense)	Adverse events of the SMQ Code 20000194 (malignant tumors (SMQ) narrow) are defined as malignant tumor (narrow sense).
Pemphigoid	Adverse events of the PT Code 10067776 (ocular pemphigoid) or 10034277 (pemphigoid) are defined as pemphigoid.

Term	Definition
Important missing information	
Cardiovascular system risk	Adverse events of the SMQ Code 20000047 (myocardial infarction (SMQ) broad) or SMQ Code 20000061 (central nervous system haemorrhages and cerebrovascular conditions (SMQ) broad) are defined as cardiovascular system risk. "Central nervous system haemorrhage and cerebrovascular conditions (SMQ) broad" includes the following SMQ classes. ➢ 20000166(Conditions associated with central nervous system haemorrhages and cerebrovascular accidents (SMQ) broad) ➢ 20000064(Cerebrovascular disorder haemorrhagic (SMQ) broad) ➢ 20000063(Cerebrovascular disease ischaemic (SMQ) broad)

1.3 Display digit

Term	Definition
Percentage (%)	Percent of patients with adverse events or adverse drug reactions, etc. or percent of adverse events or adverse drug reactions, etc. : Indicate to two decimal places rounded from three decimals. Other than the above: Indicate to one decimal place rounded from two decimals.
Summary statistics	Mean, median, first quartile, and third quartile: Indicate one lower digit rounded from two lower digits than the digit of the to-be evaluated data (refer to Section 1.6). Standard deviation: Indicate two lower digits rounded from three lower digits of the to-be evaluated data. Minimum and maximum Indicate the same digit number as that of the to-be evaluated data.
p-value	Indicate to three decimal places rounded down from four decimals. If the data is less than 0.001, display as $p < 0.001$.

1.4 Level of Significance and Confidence Coefficient

Two-sided 5%, two-sided 95%.

1.5 Handling of Laboratory/Measured Data

The evaluation time points for vital signs and laboratory tests will be at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment, and last evaluation.

The evaluation time points for electrocardiography, waist circumference, and coronary atherosclerosis and arteriosclerosis will be at the start of Nesina treatment, 12 months after the start of Nesina treatment, and last evaluation.

If multiple data exist within the relevant time point, calculate the absolute value of a difference in number of days from the reference number of days and select the minimum absolute value as the datum of the relevant evaluation time point. If the absolute values are same, select the datum at the latest examination/measurement day.

If "On treatment at 12 months after Nesina treatment" is selected in Section "Current Status of Nesina Treatment" in the survey sheet, all values will be used for analysis. If "On treatment at 12 months after Nesina treatment" is not selected, the values before the next day of the last administration of Nesina will be used for analysis.

The start day of Nesina treatment is defined as 0 days.

[Vital signs and laboratory test values]

Evaluation time point	Reference number of days	Lower limit of window	Upper limit of window
At start of Nesina treatment	0 days	30 days before Nesina treatment	Start day of Nesina treatment
1 month after start of Nesina treatment	30 days	1 day after start of Nesina treatment	60 days after start of Nesina treatment
3 months after start of Nesina treatment	90 days	61 days after start of Nesina treatment	136 days after start of Nesina treatment
6 months after start of Nesina treatment	180 days	137 days after start of Nesina treatment	273 days after start of Nesina treatment
12 months after start of Nesina treatment	360 days	274 days after start of Nesina treatment	456 days after start of Nesina treatment
At last evaluation	Select the latest datum from 1 to 456 days after the start of Nesina treatment		

[Electrocardiography and waist circumference]

Evaluation time point	Reference number of days	Lower limit of window	Upper limit of window
At start of Nesina treatment	0 days	30 days before Nesina treatment	Start day of Nesina treatment
12 months after start of Nesina treatment	360 days	1 day after start of Nesina treatment	456 days after start of Nesina treatment
At last evaluation	Select the latest datum from 1 to 456 days after the start of Nesina treatment		

1.6 Display Data Digit

Display digits are described as below.

Term	Display digit	Unit
HbA1c (NGSP value)	0.1	%
Fasting blood glucose level	1	mg/dL
Fasting insulin level	0.1	μU/mL
Fasting glucagon	0.1	pg/mL
HOMA-R	0.1	―
HOMA-β	0.1	%
Fasting triglyceride	1	mg/dL
Total cholesterol	1	mg/dL
HDL-cholesterol	1	mg/dL
LDL-cholesterol	1	mg/dL
non-HDL cholesterol	1	mg/dL
Serum creatinine	0.01	mg/dL
BUN	0.1	mg/dL
Urinary albumin (corrected by creatinine)	0.1	mg/g•Cre
AST	1	IU/L
ALT	1	IU/L
γ-GTP	1	IU/L
ALP	1	IU/L
Total bilirubin	0.1	mg/dL
Amylase	1	IU/L

Lipase	1	IU/L
Waist circumference	0.1	cm
Pulse rate	1	bpm
Systolic blood pressure	1	mmHg
Diastolic blood pressure	1	mmHg
Weight	0.1	kg
BMI	0.1	kg/m^2
Age	1	Year
Duration of type 2 diabetes mellitus	0.1	Year
Height	1	cm
eGFR	0.1	mL/min/1.73 m^2
Nesina administration period	1	Day
Mean daily dose of Nesina	0.01	mg

2.0 Disposition of Patients (Patient Diagram)

(1) Patients to be tabulated and analyzed

Registered patients

(2) Details of tabulation and analysis

The following will be tabulated: the number of registered patients, number of medical site at which patients is registered, number of patients whose survey sheets are collected, number of patients whose survey sheets are not collected, number of patients in the Safety Analysis Set, number of patients in the Not Safety Analysis Set, number of patients in the Efficacy Analysis Set, and number of patients in the Not Efficacy Analysis Set.

For the number of medical sites at which patients are registered, do not duplicate the same medical site with different departments.

For patients whose survey sheets are not collected, tabulate the number of patients for each reason for not collected survey sheets.

For the Not Safety Analysis Set and Not Efficacy Analysis Set, the number of patients will be tabulated for each reason for exclusion to create the list.

The following is the handling of the decision whether patients who meet the following criteria should be evaluated:

Criterion	Safety evaluation	Efficacy evaluation
Pre-agreement administration [found after administration]	×	×
Registration 15 days after prescription of Nesina [found after registration]	×	×
Nesina taking not confirmed [after the end of patient registration period]	×	×
No data for post-administration of Nesina	×	×
Not using any of the 3 combination drugs (the treatment group will be classified as "Other.") (1) With insulin preparation (2) With rapid-acting insulin secretagogues (3) With SGLT-2 inhibitors	○	×

○ Included, × Excluded or not evaluated

(3) Number of tables and figures

Figure 2.0-1 and Table 2.0-1

3.0 Patient Demographics

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be classified by the categories described below to tabulate the number of patients and frequency.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Sex	Male, Female
Age	Summary statistics
	< 65 years, ≥ 65 years
	< 75 years, ≥ 75 years
	< 20 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, ≥ 80 years
Disease duration of type 2 diabetes mellitus (year)	Summary statistics
	< 2 years, 2 to < 5 years, 5 to < 10 years, ≥ 10 years, Unknown
Height	Summary statistics
Category of clinical practice	Outpatient, Inpatient
Pregnancy (only females)	No, Yes
Severity of renal impairment	Normal, Mild, Moderate, Severe
	Normal + Mild, Moderate + Severe
Concurrent disease	No, Yes
Diabetic complication	No, Yes
Details of diabetic complication (overlapped)	Diabetic nephropathy, diabetic retinopathy, diabetic neuropathy For the proportion, the number of patients with diabetic complication will be denominator.
Concurrent hypertension	No, Yes
Concurrent dyslipidemia	No, Yes
Concurrent hyperuricemia	No, Yes
Concurrent liver disorder	No, Yes

Parameter	Category
Details of concurrent liver disorder (overlapped)	Hepatic steatosis, alcoholic hepatitis, chronic hepatitis, hepatic cirrhosis, or other For the proportion, the number of with concurrent liver disorder will be denominator.
Severity of hepatic impairment	Normal, Grades 1, 2, and 3, or Unknown
Concurrent renal disorder	No, Yes
Details of concurrent renal disorder (overlapped)	Nephrotic syndrome, glomerulonephritis, chronic glomerulonephritis, other For the proportion, the number of with concurrent renal disorder will be denominator.
Severity of renal impairment (eGFR)	Normal, Mild, Moderate, Severe, or Unknown
	Normal + Mild, Moderate + Severe, or Unknown
Severity of renal impairment (serum creatinine)	Normal, Mild, Moderate, Severe, or Unknown
	Normal + Mild, Moderate + Severe, or Unknown
Concurrent heart disease	No, Yes
Details of concurrent heart disease (overlapped)	Cardiac failure, myocardial infarction, angina pectoris, other For the proportion, the number of with concurrent heart disease will be denominator.
Concurrent cardiac failure	No, Yes
Severity classification of cardiac failure (NYHA classification)	Classes NYHA I, NYHA II, NYHA III, and NYHA IV, Unknown For the proportion, the number of with concurrent cardiac failure will be denominator.
Concurrent stroke-related disease	No, Yes
Details of concurrent stroke-related disease (overlapped)	Cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, transient ischaemic attack For the proportion, the number of with concurrent stroke-related disease will be denominator.
Concurrent allergic disease	No, Yes
Concurrent malignant tumour	No, Yes
Concurrent malignant	No, Yes

Parameter	Category
tumour (narrow sense)	
Other concurrent disease	No, Yes
Past medical history	No, Yes, Unknown
Hypersensitivity predisposition	No, Yes, Unknown
Alcohol history (drinking alcoholic drinks almost on a daily basis)	Yes, No, Unknown
Smoking history	Never, Smoking, Smoked, Unknown
HbA1c (NGSP value) (at the start of Nesina treatment)	Summary statistics
	< 6.0%, 6.0% to < 7.0%, 7.0% to < 8.0%, ≥ 8.0%, Unknown
Weight (at the start of Nesina treatment)	Summary statistics
BMI (at the start of Nesina treatment)	Summary statistics
	< 18.5 kg/m^2, 18.5 to < 25 kg/m^2, 25 to < 30 kg/m^2, ≥ 30 kg/m^2, Unknown
	< 25 kg/m^2, ≥ 25 kg/m^2, Unknown
Waist circumference (at the start of Nesina treatment)	Males: < 85 cm, ≥ 85 cm, or Unknown / Females: < 90 cm, ≥ 90 cm, or Unknown

(3) Number of tables and figures

Table 3.0-1

4.0 Details of Treatment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be classified by the categories described below to tabulate the number of patients and frequency.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Initial dose of Nesina	25 mg, 12.5 mg, 6.25 mg, or other
Mean daily dose of Nesina	> 25 mg, 25 to >12.5 mg, 12.5 to > 6.25 mg, or ≤ 6.25 mg
Nesina treatment period	Summary statistics
	1 to 60 days, 61 to 136 days, 137 to 273 days, 274 to 455 days, ≥ 456 days
Administration of prior medication (diabetic drug)	No, Yes, or Unknown
Prior medications (diabetic drugs)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs For the proportion, the number of patients with "Yes" for administration of prior medication (diabetic drug) will be denominator.
Administration of prior medication (other than diabetic drug)	No, Yes, or Unknown
Administration of concomitant medication (diabetic drug)	No, Yes, or Unknown
Concomitant medications (diabetic drugs) (overlapped)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs For the proportion, the number of patients with "Yes" for administration of concomitant medication (diabetic drug) will be

Parameter	Category
	denominator.
Administration of concomitant medication (hypertension drug)	No, Yes, or Unknown
Concomitant medications (hypertension drugs) (overlapped)	ARB, Ca antagonists, ACE inhibitors, diuretics, α blockers, αβ/β blockers, complication of hypertension drugs, or other For the proportion, the number of patients with "Yes" for administration of concomitant medication (hypertension drug) will be denominator.
Administration of concomitant medication (dyslipidaemia drug)	No, Yes, or Unknown
Concomitant medications (dyslipidaemia drugs) (overlapped)	Statins, fibrates, EPA/DHA, or other For the proportion, the number of patients with "Yes" for administration of concomitant medication (dyslipidaemia drug) will be denominator.
Administration of concomitant medication (protease drug)	No, Yes, or Unknown
Administration of concomitant medication (combined with renal excretory drug)	No, Yes, or Unknown
Administration of concomitant medication (other)	No, Yes, or Unknown

(3) Number of tables and figures

Table 4.0-1

4.1 Compliance

4.1.1 Status of compliance with Nesina

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For the status of compliance with Nesina, the frequency will be tabulated at each testing time point (1 month, 3 months, and 6 months after the start of Nesina treatment and last evaluation or treatment discontinuation).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance with Nesina	≥ 90%, ≥ 70%, ≥ 50%, or < 50%

(3) Number of tables and figures

Tables 4.1-1

4.1.2 Status of Compliance with Diet Therapy

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details to be tabulated and analyzed

For the status of compliance with diet therapy, the frequency will be tabulated at each testing time point (at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation or treatment discontinuation). The latest datum will be used for last evaluation.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance with diet therapy	≥ 90%, ≥ 70%, ≥ 50%, < 50%, Not performed, or Unknown

(3) Number of tables and figures

Table 4.1.2

4.1.3 Compliance with Exercise Therapy

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details to be tabulated and analyzed

For the status of compliance with exercise therapy, the frequency will be tabulated at each testing time point (at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation or treatment discontinuation). The latest datum will be used for last evaluation.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance	≥ 90%, ≥ 70%, ≥ 50%, < 50%, Not performed, or Unknown

Parameter	Category
with exercise therapy	

(3) Number of tables and figures

Table 4.1.3

5.0 Safety Tabulation and Analysis

5.1 Occurrence of adverse events and adverse drug reactions / infections

5.1.1 Occurrence of adverse events

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for adverse events.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of analysis
Number of patients with adverse events	Number of patients who experienced adverse events.
Number of adverse events	Number of adverse events. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events	Described in Section 1.1.
Type of adverse events	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse events and percent of patients with events will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse events and percent of events will be described in the ascending order of PT codes. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.

(3) Number of tables and figures

Table 5.1.1-1

5.1.2 Occurrence of adverse drug reactions / infections

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for adverse drug reactions, etc. and serious adverse drug reactions, etc.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse drug reactions, etc.	Number of patients who experienced adverse drug reactions, etc.
Number of adverse drug reactions, etc.	Number of adverse drug reactions, etc. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.
Percent of patients with adverse drug reactions, etc.	Described in Section 1.1.
Type of adverse drug reactions, etc.	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. and percent of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. and percent of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Tables 5.1.2-1 and 5.1.2-2

5.1.3 Important Identified Risks, Important Potential Risks, and Important Missing Information

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for important identified risks, important potential risks, and important missing information (described in Section 1.2).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis

Parameter	Details of tabulation and analysis
Number of patients with adverse events (or adverse drug reactions, etc.)	Number of patients who experienced adverse events (or adverse drug reactions, etc.) with important identified risks, important potential risks, and important missing information.
Number of adverse events (or adverse drug reactions, etc.)	Number of adverse events (or adverse drug reactions, etc.) with important identified risks, important potential risks, and important missing information. Count as an event if the same adverse event (or adverse drug reaction, etc.) (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events (or adverse drug reactions, etc.)	Described in Section 1.1.
Type of adverse events (or adverse drug reactions, etc.)	Will be broadly divided into the important identified risks, important potential risks, and important missing information and tabulated by PT in them. For the PTs, the number of adverse events (or adverse drug reactions, etc.) and percent of adverse events (or adverse drug reactions, etc.) will be described in the ascending order of PT codes. Count as an event if the same adverse event (or adverse drug reaction, etc.) (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Tables 5.1.3-1 and 5.1.3-2

5.2 Occurrence of Adverse Events and Adverse Drug Reactions / Infections in the Not Safety Analysis Set

5.2.1 Occurrence of Adverse Events

(1) Patients to be tabulated and analyzed

Not Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse events	Number of patients who experienced adverse events.
Number of adverse events	Number of adverse events. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events	Described in Section 1.1.
Type of adverse events	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse events and percent of patients with events will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse events and percent of events will be described in the ascending order of PT codes. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Table 5.2-1

5.2.2 Occurrence of adverse drug reactions / infections

(1) Patients to be tabulated and analyzed

Not Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse drug reactions, etc.	Number of patients who experienced adverse drug reactions, etc.
Number of adverse drug reactions, etc.	Number of adverse drug reactions, etc. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the

	same PT.
Percent of patients with adverse drug reactions, etc.	Described in Section 1.1.
Type of adverse drug reactions, etc.	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. and percent of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. and percent of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Table 5.2-2

5.3 Occurrence of Adverse Drug Reactions / Infections by Severity, Onset Period, and Outcome

5.3.1 Occurrence of Adverse Drug Reactions / Infections by Severity, Onset Period, and Outcome

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be categorized by the categories described below to tabulate the type of adverse drug reactions, etc.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Severity	Serious, Not serious, Not described
Onset period	1 to 14 days, 15 to 28 days, 29 to 84 days, 85 to 168 days, 169 to 336 days, 337days or Unknown
Outcome	Resolved, Resolving, Not resolved, Resolved with sequelae, Death, or Unknown

The method for tabulation of type adverse drug reactions, etc. is described below:

Parameter	Details of tabulation and analysis
Type of adverse drug	Will be broadly divided into the SOCs and tabulated by PT in the

Parameter	Details of tabulation and analysis
reactions, etc.	SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT. However, evaluate an event for the same LLT in accordance with the following order of priority: Onset period: earlier event Severity: Serious → Not serious → Not described Outcome: Death → Resolved with Sequelae → Not resolved → Resolving → Resolved → Unknown

(3) Number of tables and figures

Tables 5.3-1 to 5.3-3

5.4 Patient Demographics and Frequency of Adverse Drug Reactions / Infections by Treatment

5.4.1 Patients demographics and Frequency of Adverse Drug Reactions / Infections by Treatment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be categorized by the categories described below to tabulate the percent of patients with adverse drug reactions, etc.

The Fischer exact test will be used for parameters without rank data. The Mann-Whitney U test will be used for parameters with rank data. (The tests will be used for parameters with asterisk [*].)

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Sex*	Male, Female
Age*	< 65 years, ≥ 65 years
	< 75 years, ≥ 75 years
Concurrent liver disorder*	No, Yes
Severity of hepatic	Normal, Grades 1, 2, and 3, or Unknown

Parameter	Category
impairment*	
Concurrent renal disorder*	No, Yes
Severity of renal impairment* (eGFR)	Normal + Mild, Moderate + Severe, or Unknown
Severity of renal impairment* (serum creatinine)	Normal + Mild, Moderate + Severe, or Unknown
Concurrent heart disease*	No, Yes
Details of concurrent heart disease (overlapped)	Cardiac failure, myocardial infarction, or angina pectoris
Concurrent cardiac failure*	No, Yes
Severity classification of cardiac failure (NYHA classification)*	Classes NYHA I, NYHA II, NYHA III, and NYHA IV, or Unknown
Concurrent stroke-related disease*	No, Yes, or Unknown
Mean daily dose of Nesina	> 25 mg, 25 to >12.5 mg, 12.5 to > 6.25 mg, or ≤ 6.25 mg
Administration of concomitant medication (diabetic drug)	No, Yes
Concomitant medications (diabetic drugs) (overlapped)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, or insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs
Administration of concomitant medication (protease drug)*	No, Yes, or Unknown
Administration of	No, Yes, or Unknown

Parameter	Category
concomitant medication (combined with renal excretory drug)*	

(3) Number of tables and figures

Table 5.4.1-1

5.5 Occurrence of Adverse Drug Reactions / Infections by Age

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Age will be classified into < 65 years, ≥ 65 years and < 75 years, and ≥ 75 years for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 5.5-1 to 5.5-2

5.6 Occurrence of Adverse Drug Reactions / Infections by Sex

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Sex will be classified into male or female for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.6-1

5.7 Occurrence of Adverse Drug Reactions / Infections by Liver Disorder

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent liver disorder will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.7-1

5.8 Occurrence of Adverse Drug Reactions / Infections by Liver Impairment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Severity of liver impairment will be classified into Grade 1, 2, or 3 or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.8-1

5.9 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Renal Disorder

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent renal disorder will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.9-1

5.10 Occurrence of Adverse Drug Reactions / Infections by Severity of Renal Impairment

(4) Patients to be tabulated and analyzed

Safety Analysis Set

(5) Details of tabulation and analysis

Severity of renal impairment will be classified into normal + mild, moderate + severe, or unknown, according to the criteria for the severity of renal impairment (eGFR and serum creatinine) for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(6) Number of tables and figures

Tables 5.10-1 and 5.10-2

5.11 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Heart Disease

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent heart disease will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.11-1

5.12 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Heart Failure

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent heart failure will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total and mild type 2 diabetes mellitus patients will be tabulated.

(3) Number of tables and figures

Table 5.12-1

5.13 Occurrence of Adverse Drug Reactions / Infections by Severity of Heart Failure

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Severity of heart failure will be classified into Class NYHA I, NYHA II, NYHA III, or NYHA IV or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Patients with mild type 2 diabetes mellitus patients or other (individual) will be tabulated.

(3) Number of tables and figures

Table 5.13-1

5.14 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Stroke-related Disease

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent stroke-related disease will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.14-1

5.15 Occurrence of Adverse Drug Reactions / Infections by Mean Daily Dose of Nesina

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The mean daily dose of Nesina will be classified into > 25 mg, 25 to > 12.5 mg, 12.5 to > 6.25 mg, or 6.25 mg for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients will be tabulated.

(3) Number of tables and figures

Table 5.15-1

5.16 Occurrence of Adverse Drug Reactions / Infections by Concomitant Medication (Diabetic Drug)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medications (diabetic drugs) will be classified into the following drugs: α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs, for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.16-1

5.17 Occurrence of Adverse Drug Reactions / Infections by Presence of Concomitant Medication (Protease Inhibitor)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medication (protease inhibitor) will be classified into yes, no, or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.17-1

5.18 Occurrence of Adverse Drug Reactions / Infections by Presence of Concomitant Medication (Renal Excretory Drug)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medication (renal excretory drug) be classified into yes, no, or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.18-1

5.19 Change in Laboratory/Measured Data over Time

5.19.1 Vital Signs

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

In vital signs, summary statistics for pulse rate, blood pressure (systolic/diastolic), and weight will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

Measured values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.1-1 and Figures 5.19.1-1 to 5.19.1-4

5.19.2 Laboratory Values

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

In laboratory values, summary statistics will be calculated for fasting triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol, non-HDL cholesterol, serum creatinine, BUN, urinary albumin (corrected by creatinine), AST, ALT, γ-GTP, ALP, total bilirubin, amylase, lipase at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

These laboratory values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.2-1 and Figures 5.19.2-1 to 5.19.2-15

5.19.3 Electrocardiography

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For assessment of electrocardiogram, cross tabulation will be used for the categories described below.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
ECG results at start of Nesina treatment	Clinical abnormal findings (Yes or No) or Not performed
ECG results at 12 months after start of Nesina treatment	Clinical abnormal findings (Yes or No) or Not performed
ECG results at last evaluation	Clinical abnormal findings (Yes or No) or Not performed

(3) Number of tables and figures

Table 5.19.3

5.19.4 Waist Circumference

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For waist circumference, summary statistics will be calculated at each testing time point (at the start of Nesina treatment, 12 months after the start of Nesina treatment, and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

Measured values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.4 and Figure 5.19.4

5.19.5 Tests for Coronary Atherosclerosis and Arteriosclerosis

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

A listing of the following tests and the test results for coronary atherosclerosis and

arteriosclerosis will be created: survey sheet number, treatment group, time point, test day, and details of tests (pulse wave velocity [PWV], cardio-ankle vascular index [CAVI], intima-media thickness [IMT], intra-vascular ultrasound [IVUS], and other [specify the details]).

(3) Number of tables and figures

Table 5.19.5

6.0 Efficacy Tabulation and Analysis

6.1 Changes in HbA1c

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For HbA1c (NGSP values), summary statistics will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes, summary statistics and the mean 95% confidence intervals will be calculated and the paired t-test will be performed.

Measured values of HbA1c (NGSP values) will be plotted and for the changes a bar graph will be created excluding the unknown category.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 6.1-1 and Figure 6.1-1

6.2 Glycemic control achievement rate (HbA1c)

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

The glycemic control achievement rate for HbA1c (NGSP value) will be tabulated ($< 6.0\%$, $\geq 6.0\%$ / $< 7.0\%$, $\geq 7.0\%$) and a bar graph will be created at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation) (the unknown category will be excluded for the bar graph).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 6.2-1 and Figures 6.2-1 and 6.2-2

6.3 Changes in Fasting blood glucose level, Fasting insulin level, Fasting Glucagon, HOMA-R, and HOMA-β

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For fasting blood glucose level, fasting insulin level, fasting glucagon, HOMA-R, and HOMA-β, summary statistics will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes, summary statistics and the mean 95% confidence intervals will be

calculated and the paired t-test will be performed.

Measured values of will be plotted and for the changes a bar graph will be created excluding the unknown category.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 6.3-1 and 6.3-5 and Figures 6.3-1 and 6.3-5

6.4 Changes in HbA1c, etc. by Factor Probably Affecting Efficacy

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For changes in HbA1c (NGSP values), summary statistics and the mean 95% confidence intervals will be calculated and the paired t-test will be performed at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation).

The glycemic control achievement rate for HbA1c (< 6.0%, ≥ 6.0% / < 7.0%, ≥ 7.0%) at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation) will be tabulated for the following parameters:

i Sex (Male, Female)

ii Age (< 65 years, ≥ 65 years)

iii Age (< 75 years, ≥ 75 years)

iv Concurrent renal disorder (No, Yes)

v HbA1c (NGSP value) at the start of Nesina treatment (< 6.0%, 6.0% to < 7.0%, 7.0% to < 8.0%, ≥ 8.0%, or Unknown)

vi Mean daily dose of Nesina (> 25 mg, 25 to > 12.5 mg, 12.5 to > 6.25 mg, or 6.25 mg)

vii Concomitant diabetic drugs (α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, or insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, combination of diabetic drugs, or other diabetic drugs)

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 6.4-1 to 6.4-14

Statistical Analysis Plan

Nesina Tablets Specified Drug-use Survey "Type 2 Diabetes Mellitus: Combination Therapy With Hypoglycemic Drug (Insulin Preparation or Rapid-acting Insulin Secretagogues, Etc)"

Takeda Pharmaceutical Company Limited.

PPD

Version 1, Created on December 26, 2017

Table of Contents

1.0 Definition of Terms and Handling of Laboratory/Measured Data

1.1 Definitions

Term	Definition
Nesina	Nesina tablet(s) is abbreviated as Nesina in this statistical analysis plan.
SOC	System Organ Class of MedDRA/J MedDRA/J version 20.1 is used for this document.
HLGT	High level group term of MedDRA/J
PT	Preferred term of MedDRA/J
LLT	Lowest level term of MedDRA/J
Registered patients	Patients whose registration was approved
Survey sheet collected patients	Patients whose survey sheets were collected
Survey sheet uncollected patients	Of the registered patients, patients whose survey sheets were uncollected.
Safety Analysis Set	Of the survey sheet collected patients, patients who were evaluated for safety analysis. For tabulation, the description of "total" means the Safety Analysis Set.
Not Safety Analysis Set	Of the survey sheet collected patients, patients who were excluded from safety analysis
Efficacy Analysis Set	Of the Safety Analysis Set, patients who were evaluated for efficacy analysis
Not Efficacy Analysis Set	Of the Safety Analysis Set, patients who were excluded from the efficacy analysis
First date of Nesina treatment	Of the start dates of the Nesina treatment period in patients, the earliest date is defined as the first date of Nesina treatment.
Last date of Nesina treatment	Of the last dates of the Nesina treatment in patients, the latest date is defined as the last date of Nesina treatment. If Nesina treatment is continued and the year, month, and date of the continued treatment period are specified, the year, month, and date of the continued treatment period are defined as the last date of Nesina treatment. If the data for the year, month, and date of the continued treatment period are missing, the following date is defined as the last date of Nesina treatment. (1) First date of Nesina treatment + 1 year (same month and date) for continued treatment of Nesina. (2) Latest date at which the following examinations/observations will be performed for the not-continued treatment of Nesina: ● [Date of examinations/ observations] • Compliance with Nesina treatment

Term	Definition
	• Compliance with diet/exercise therapy • Laboratory tests • Body weight • Waist circumference • Pulse rate • Blood pressure • Electrocardiography • Tests for coronary atherosclerosis and arteriosclerosis
Adverse drug reactions, etc.	Abbreviation of "adverse drug reactions / infections" Of the adverse events, events for which causal relationship to Nesina was assessed as "Not related" by the Investigator. In this statistical analysis plan, "adverse drug reactions / infections" is used in the headings, while "adverse drug reactions, etc." is used in the sentences and tables.
Serious adverse events	Adverse events assessed as "serious" by the Investigator. Events described in the MedDRA coding list in the Takeda Medically Significant AE List will be handled as serious even if the Investigator assesses as "Not serious."
Serious adverse drug reactions	Abbreviation of "serious adverse drug reactions / infections" Of the "serious adverse events," the events for which causal relationship to Nesina was assessed as "Not related" by the Investigator
Number of patients with events	Number of patients with adverse events or adverse drug reactions, etc.
Number of events	Number of adverse events or adverse drug reactions, etc.
Percent of patients with events	[For safety analysis calculation in the Safety Analysis Set] The formula is: Number of patients with events / Number of Safety Analysis Set × 100. [For safety analysis calculation in the Not Safety Analysis Set] The formula is: Number of patients with events / Number of Not Safety Analysis Set × 100.
Percent of events	[For safety analysis calculation in the Safety Analysis Set] The formula is: Number of events / Number of the Safety Analysis Set × 100. [For safety calculation in the Not Safety Analysis Set] The formula is: Number of events / Number of Not Safety Analysis Set × 100.
Onset period	The formula is: Onset date of adverse events (or adverse drug reactions, etc.) − start date of Nesina treatment + 1.

Term	Definition
	If the onset month and date of an adverse event (or adverse drug reaction, etc.) is unknown, calculate the onset month and date as January 1. However, if the start month and date of Nesina treatment are same as the onset month and date of an adverse event (or adverse drug reaction, etc.), the onset period will be calculated as the start date of Nesina treatment. For unknown onset date of adverse events (or adverse drug reactions, etc.), the onset period will be calculated as 1 day. However, if the start month and date of Nesina treatment are same as the onset month and date of adverse events (or adverse drug reactions, etc.), the onset period will be calculated as the start date of Nesina treatment.
Treatment group	Overall: Total patients who will be treated with combination therapy with insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, and other (all are defined below) Combination with insulin preparation: Patients who will be treated with insulin preparation within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with rapid-acting insulin secretagogues or SGLT-2 inhibitors Combination with rapid-acting insulin secretagogues: Patients who will be treated with rapid-acting insulin secretagogues within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with insulin preparation or SGLT-2 inhibitors Combination with SGLT-2 inhibitors: Patients who will be treated with SGLT-2 inhibitors within 3 months prior to Nesina treatment and during Nesina treatment (including at the start of Nesina treatment) and not treated with insulin preparation or rapid-acting insulin secretagogues Other: Patients who will not be treated with combination therapy with insulin preparation, rapid-acting insulin secretagogues, or SGLT-2 inhibitors
Patients with diabetic complication	Patients with any of the following complications: diabetic nephropathy, diabetic retinopathy, or diabetic neuropathy.
Patients with diabetic nephropathy	Patients with complication of PT Code 10012660 (diabetic end stage renal disease) or 10061835 (diabetic nephropathy).
Patients with diabetic retinopathy	Patients with complication of PT Code 10012688 (diabetic retinal oedema) or 10012689 (diabetic retinopathy).
Patients with diabetic neuropathy	Patients with complication of PT Code 10012645 (diabetic autonomic neuropathy), 10012676 (diabetic mononeuropathy), or 10012680 (diabetic

Term	Definition
	neuropathy).
Patients with concurrent hypertension	Patients with concurrent disease of the Standardised MedDRA Query (hereinafter SMQ) Code 20000147 (hypertension (SMQ) narrow).
Patients with concurrent dyslipidemia	Patients with concurrent disease of the SMQ Code 20000026 (dyslipidaemia (SMQ) narrow).
Patients with concurrent hyperuricemia	Patients with concurrent disease of the PT code meeting the Takeda MedDRA Query 20.1 (hereinafter, TMQ 20.1) (blood uric acid increased).
Patients with concurrent liver disorder	Patients with concurrent disease of the SMQ Code 20000005 (hepatic disorders (narrow).
Patients with concurrent hepatic steatosis	Patients with concurrent disease of the PT Code 10019708 (hepatic steatosis).
Patients with concurrent alcoholic hepatitis	Patients with concurrent disease of the PT Code 10019728 (hepatitis alcoholic).
Patients with concurrent chronic hepatitis	Patients with concurrent disease of the PT Code 10008909 (chronic hepatitis).
Patients with concurrent hepatic cirrhosis	Patients with concurrent disease of the PT Code 10019641 (hepatic cirrhosis).
Patients with concurrent renal disorder	Patients with concurrent disease of the TMQ 20.1 (renal disease).
Patients with concurrent nephrotic syndrome	Patients with concurrent disease of the PT Code 10029164 (nephrotic syndrome).
Patients with concurrent glomerulonephritis	Patients with concurrent disease of the PT Code 10018364 (glomerulonephritis) or the PT Code 10018367 (glomerulonephritis chronic).
Patients with concurrent chronic renal failure	Patients with concurrent disease of the PT Code 10064848 (chronic kidney disease) or the PT Code 10038435 (renal failure).
Patients with concurrent heart disease	Patients with concurrent disease of the SOC Code 10007541 (cardiac disorders).
Patients with concurrent cardiac failure	Patients with concurrent disease of the SMQ Code 20000004 (cardiac failure (SMQ) narrow).
Patients with concurrent myocardial infarction	Patients with concurrent disease of the SMQ Code 20000047 (myocardial infarction (SMQ) narrow).
Patients with concurrent angina pectoris	Patients with concurrent disease of the SOC Code 10007541 (cardiac disorders) and the PT Code 10036759 (prinzmetal angina), PT Code 10002383 (angina pectoris), PT Code 10058144 (postinfarction angina), PT Code 10002388 (angina unstable), or LLT Code 10065566 (microvascular angina).
Patients with concurrent stroke-related disease	Patients with concurrent disease of cerebral infarction, cerebral haemorrhage, subarachnoid haemorrhage, or transient ischaemic attack, described below.

Term	Definition
Patients with concurrent disease cerebral infarction	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10006147 (brain stem infarction), PT Code 10008118 (cerebral infarction), PT Code 10008119 (cerebral infarction foetal), PT Code 10008034 (cerebellar infarction), PT Code 10019005 (haemorrhagic cerebral infarction), PT Code 10051078 (lacunar infarction), PT Code 10056237 (migrainous infarction), PT Code 10058571 (spinal cord infarction), PT Code 10060839 (embolic cerebral infarction), PT Code 10060840 (ischaemic cerebral infarction), PT Code 10064961 (thalamic infarction), PT Code 10067347 (thrombotic cerebral infarction), or PT Code 10069020 (basal ganglia infarction).
Patients with concurrent cerebral hemorrhage	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10006145 (brain stem haemorrhage), PT Code 10008111 (cerebral haemorrhage), PT Code 10008112 (cerebral haemorrhage neonatal), PT Code 10008030 (cerebellar haemorrhage), PT Code 10018985 (haemorrhage intracranial), PT Code 10022840 (intraventricular haemorrhage), PT Code 10022841 (intraventricular haemorrhage neonatal), PT Code 10042365 (subdural haemorrhage neonatal), PT Code 10049236 (spinal epidural haemorrhage), PT Code 10048992 (spinal cord haemorrhage), PT Code 10050157 (cerebral haemorrhage foetal), PT Code 10052593 (meningorrhagia), PT Code 10058939 (thalamus haemorrhage), PT Code 10058940 (putamen haemorrhage), PT Code 10067057 (basal ganglia haemorrhage), PT Code 10067277 (cerebral microhaemorrhage), PT Code 10071205 (brain stem microhaemorrhage), PT Code 10071206 (cerebellar microhaemorrhage), PT Code 10072043 (central nervous system haemorrhage), or PT Code 10073563 (Spinal subdural haemorrhage).
Patients with concurrent subarachnoid hemorrhage	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10042316 (subarachnoid haemorrhage), PT Code 10042317 (subarachnoid haemorrhage neonatal), PT Code 10073564 (spinal subarachnoid haemorrhage), LLT Code 10072201 (Asymptomatic subarachnoid haemorrhage).
Patients with concurrent transient ischemic attack	Patients with concurrent disease of the SOC Code 10029205 (nervous system disorders) and the PT Code 10044390 (transient ischaemic attack).
Patients with concurrent allergic disease	Patients with concurrent disease of bronchial asthma, pollinosis, allergic rhinitis, or allergic dermatitis, described below.
Patients with concurrent bronchial asthma	Patients with concurrent disease of the SOC Code 10038738 (respiratory, thoracic and mediastinal disorders) and the PT Code 10003553 (asthma), PT Code 10075084 (aspirin-exacerbated respiratory disease), PT Code 10003557 (asthma exercise induced), PT Code 10003559 (asthma late onset), PT Code

Term	Definition
	10041961 (status asthmaticus), PT Code 10001890 (alveolitis allergic), PT Code 10049585 (infantile asthma), PT Code 10070836 (occupational asthma), or PT Code 10064823 (asthmatic crisis).
Patients with concurrent pollinosis	Patients with concurrent disease of the PT Code 10048908 (seasonal allergy).
Patients with concurrent allergic rhinitis	Patients with concurrent disease of the PT Code 10039085 (rhinitis allergic).
Patients with concurrent allergic dermatitis	Patients with concurrent disease of the PT Code 10012434 (dermatitis allergic).
Patients with concurrent malignant tumor	Patients with concurrent disease of the SOC Code 10029104 (neoplasms benign, malignant and unspecified (incl cysts and polyps)).
Patients with concurrent malignant tumor (narrow sense)	Patients with concurrent disease of the SMQ Code 20000194 (malignant tumour (SMQ) narrow).
Patients with other concurrent disease	Patients with concurrent disease other than the above (diabetic complication, hypertension, dyslipidaemia, hyperuricaemia, liver disease, renal disease, heart disease, stroke-related disease, allergic disease, malignant tumor, or malignant tumor (narrow sense)).
Severity of hepatic impairment	Severity of hepatic impairment will be assessed using AST or ALT at the start of Nesina treatment. Severity will be assessed using the categories described below, and the higher grade of AST or ALT will be used for analysis. Normal: < 50 IU/L Grade 1: ≥ 50 IU/L and < 100 IU/L Grade 2: ≥ 100 IU/L and < 500 IU/L Grade 3: ≥ 500 IU/L Quoted from the Standards for Classification of Serious Adverse Drug Reactions due to Drug Products notified by the director of Pharmaceuticals and Chemicals Safety Division, Pharmaceutical Affairs Bureau, the Ministry of Health and Welfare (No. 80 notification of Pharmaceuticals and Chemicals Safety Division, Pharmaceutical Affairs Bureau: June 29, 1992).
Severity of renal impairment (eGFR)	eGFR* will be calculated based on age and serum creatinine at the start of Nesina treatment to assess the severity according to the categories described below. For unknown serum creatinine and age at the start of Nesina treatment, indicate as unknown. Indicate to one decimal place rounded from two decimals. Normal: ≥ 90 mL/min/1.73 m^2 Mild: ≥ 60 mL/min/1.73 m^2 and < 90 mL/min/1.73 m^2 Moderate: ≥ 30 mL/min/1.73 m^2 and < 60 mL/min/1.73 m^2 Severe: < 30 mL/min/1.73 m^2

Term	Definition
	*eGFR = $194 \times Cr^{-1.094} \times \text{age (year)}^{-0.287}$ ($\times 0.739$ for females) Cr: Serum creatinine at the start of Nesina treatment. For serum Cr, indicate to two decimal places. Quoted from the Clinical Practice Guide for CKD, edited by the Japanese Society of Nephrology.
Severity of renal impairment (serum creatinine)	Severity will be assessed based on serum creatinine at the start of Nesina treatment and according to the following categories: Normal + Mild: Males: ≤ 1.4 mg/dL, Females: ≤ 1.2 mg/dL Moderate: Males: > 1.4 mg/dL to ≤ 2.4 mg/dL, Females: > 1.2 mg/dL to ≤ 2.0 mg/dL Severe: Males: > 2.4 mg/dL, Females: > 2.0 mg/dL For undescribed serum creatinine level at the start of Nesina treatment, indicate as unknown.
Age	If the start month and date of Nesina treatment is earlier than the birth month and date, calculate using the following formula: Start year of Nesina treatment − birth year − 1. If the birth month and date is earlier than or equal to the start month and date of Nesina treatment, calculate using the following formula: Start year of Nesina treatment − birth year. For unknown birth date, the birth date will be calculated as the 1st day of the birth month.
BMI	Calculate using the following formula: Weight (kg) / (0.0001 × Height (cm) × Height (cm)). Indicate to one decimal place rounded from two decimals.
Disease duration of type 2 diabetes mellitus (year)	Calculate using the following formula: (start date of Nesina treatment − diagnosis period of type 2 diabetes mellitus + 1) / 365.25. For unknown diagnosis month, calculate as January. Indicate to one decimal place rounded from two decimals.
Prior medication	Medications that patients were taking within 3 months prior to the start of Nesina treatment.
Concomitant medication	Medications that patients were taking after the start date of Nesina treatment.
Start date of other diabetic drug and concomitant medication (other than diabetic drug)	Calculate as the start date of survey sheet. For unknown month and date, calculate as January 1. For unknown date only, calculate as the first day of the relevant month.
End date of other diabetic drug and concomitant medication (other than diabetic drug)	Calculate as the end date of survey sheet. For unknown month and date, calculate as December 31. For unknown date only, calculate as the last day of the relevant month.
Diabetic drugs	Drugs of the National Health Insurance (NHI) Drug List Code starting with 3969, 3961, 3962, 2492, 2499410, 2499411, 2499415, or 2499416.

Term	Definition
α-glucosidase inhibitors	Drugs of the NHI Drug List Code starting with 3969003, 3969004, 3969009, or 3969102.
Thiazolidines	Drugs of the NHI Drug List Code starting with 3969005, 3969007, 3969100, 3969101, or 3969103.
Sulfonylureas	Drugs of the NHI Drug List Code starting with 3961 or 3969101.
Biguanides	Drugs of the NHI Drug List Code starting with 3962, 3969100, 3969104, or 3969105.
Rapid-acting insulin secretagogues	Drugs of the NHI Drug List Code starting with 3969006, 3969008, 3969013, or 3969102.
Insulin preparations	Drugs of the NHI Drug List Code starting with 2492.
DPP-4 inhibitors	Drugs of the NHI Drug List Code starting with 3969010, 3969011, 3969012, 3969014, 3969015, 3969016, 3969017, 3969024, 3969025, 3969103, 3969104, or 3969105.
GLP-1 receptor agonists	Drugs of the NHI Drug List Code starting with 2499410, 2499411, 2499415, or 2499416.
SGLT-2 inhibitors	Drugs of the NHI Drug List Code starting with 3969018, 3969018, 3969019, 3969020, 3969021, 3969022, or 3969023.
Combination of diabetic drugs	Drugs of the NHI Drug List Code starting with 3969100, 3969101, 3969102, 3969103, 3969104, or 3969105.
Other diabetic drugs	Other diabetic drugs not classified into the above diabetic drug categories (α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, or combination of diabetic drugs).
Hypertension drugs	ARB Drugs of the NHI Drug List Code starting with the following 7 numbers: 2149039, 2149040, 2149041, 2149042, 2149044, 2149046, 2149048, 2149100, 2149110, 2149111, 2149112, 2149113, 2149114, 2149115, 2149116, 2149117, 2149118, 2149119, 2149120, 2149121, 2149122 Ca antagonists Drugs of the NHI Drug List Code starting with the following numbers: 2149019, 2149022, 2149027, 2149030, 2149034, 2149035, 2149037, 2149038, 2149043, 2149400, 2171006, 2171014, 2171019, 2171020, 2171021, 2171022, 2171405, 2190001, 2149114, 2149115, 2149116, 2149117, 2149118, 2149120, 2149121, 2149122 ACE inhibitors Drugs of the NHI Drug List Code starting with the following 4 numbers: 2144 Diuretics Drugs of the NHI Drug List Code starting with numbers 213 or the following 7 numbers:

Term	Definition
	2149003, 2149007, 2149012, 2149110, 2149111, 2149112, 2149113, 2149119, 2149122 α blockers Drugs of the NHI Drug List Code starting with the following numbers: 1234400, 214200210, 2149002, 2149015, 2149023, 2149026, 1152, 1149107, 1149114, 1149115, 2531001, 2149020 αβ/β blockers Drugs of the NHI Drug List Code starting with the following numbers: 2149032, 2149018, 2123014, 2149009, 2123013, 2123003, 2149008, 2149016, 2442001, 2123011, 2149036, 2123016, 2149700, 2149031, 2149010, 2123001, 2123F01, 2149029, 2123008, 2149014, 2149021, 2149028, 2123015, 2123005, 2149025, 2123009, 2123403, 2149033, 2149011 Complication of hypertension drugs Drugs of the NHI Drug List Code starting with the following numbers: 2149110, 2149111, 2149112, 2149113, 2149114, 2149115, 2149116, 2149117, 2149118, 2149119, 2149120, 2149121, 2149122, 2190101, 2190102, 2190103, 2190104 Other Drugs of the NHI Drug List Code starting with the following numbers: 2149047, 2142004, 2149001, 2149017, 2145
Dyslipidaemia drugs	Statins Drugs of the NHI Drug List Code starting with the following numbers: 2189010, 2189011, 2189012, 2189013, 2189015, 2189016, 2189017, 2190101, 2190102, 2190103, 2190104 Fibrates Drugs of the NHI Drug List Code starting with the following numbers: 2183001, 2183002, 2183003, 2183004, 2183005, 2183006 EPA/DHA Drugs of the NHI Drug List Code starting with the following numbers: 2189019, 3399004 Other Drugs of the NHI Drug List Code starting with the following numbers: Dugs, other than the above, of the NHI Drug List Code starting with 218, 2900002, or 3133001.
Concomitant medication (other)	Drugs other than the above (diabetic drugs, hypertension drugs, or dyslipidaemia drugs).
Protease Inhibitor	Use the results of the drug name in the survey sheet coded with the NHI Drug List (Appendix 1. List of Protease Inhibitors).
Renal excretory drugs	Use the results of the drug name in the survey sheet coded with the NHI Drug List (Appendix 2. List of Renal Excretory Drugs).
Nesina treatment period (days)	Actual treatment period from the start date to the end date of Nesina treatment. However, the washout period is excluded from the treatment period.

Term	Definition
	Calculate using the following formula: End of Nesina treatment − start date of Nesina treatment + 1 (grand total). (Consider the washout period.)
Mean daily dose of Nesina	Calculate using the following formula: Total of "daily dose of Nesina □ Nesina treatment period at the relevant dose" / Nesina treatment period. For the calculation of Nesina treatment period, refer to the above. If the daily dose of Nesina is a number outside specification in the survey sheet , handle the dose as follows: • < 6.25 mg → 3.125 mg • > 25 mg → 50 mg
HbA1c (NGSP value)	The NGSP value only will be used in this analysis. For the HbA1c (JDS value), calculate using the following formula: NGSP value (%) = 1.02 × JDS value (%) + 0.25% The HbA1c (international standard value) will be handled as the NGSP value.
Change in HbA1c	For HbA1c converted to the NGSP value, calculate using the following formula: Laboratory value at each testing time point − Laboratory value at the start of Nesina treatment.
Glycemic control achievement rate	Divide the following two categories for the glycemic control achievement rate: HbA1c (NGSP converted value) [Unit %] NGSP (%): < 6.0, ≥ 6.0 / < 7.0, ≥ 7.0
non-HDL cholesterol	Calculate using the following formula: "Total cholesterol" − "HDL cholesterol."
HOMA-R	Calculate using the following formula: Fasting insulin level (μU/mL) × Fasting blood glucose level (mg/dL) / 405. Indicate to one decimal place rounded from two decimals. For calculation, use the fasting insulin level and fasting blood glucose level measured at the same day.
HOMA-β	Calculate using the following formula: Fasting insulin level (μU/mL) × 360 / (Fasting blood glucose level [mg/dL] – 63). Indicate to one decimal place rounded from two decimals. For calculation, use the fasting insulin level and fasting blood glucose level measured at the same day. Do not use the fasting blood glucose level of < 63 for calculation
Summary statistics	Number of patients, mean, standard deviation, minimum, first quartile, median, third quartile, and maximum.

1.2 Important Identified Risks, Potential Risks, and Missing Information

Term	Definition
Important identified risk	
Hypoglycemia	Adverse events of the following PT Codes (term) are defined as hypoglycemia. 10020994(Hypoglycaemia neonatal) 10040576(Shock hypoglycaemic) 10021000(Hypoglycaemic coma) 10020993(Hypoglycaemia) 10065981(Hypoglycaemic unconsciousness) 10021002(Hypoglycaemic encephalopathy) 10048803(Hypoglycaemic seizure) 10020997(Hypoglycaemia unawareness) 10077216(Hyperinsulinaemic hypoglycaemia) 10059035(Postprandial hypoglycaemia)
Acute pancreatitis	Adverse events of the SMQ Code 20000022 (acute pancreatitis (SMQ) narrow scope are defined as acute pancreatitis.
Hepatic impairment / jaundice	Adverse events of the SMQ Code 20000005 (hepatic disorders (SMQ) broad) are defined as hepatic impairment / jaundice.
Skin disorder including oculomucocutaneous syndrome (Stevens-Johnson syndrome) / erythema multiforme	Adverse events of the SMQ Code 20000020 (severe skin adverse reactions (SMQ) narrow) are defined as skin disorder including oculomucocutaneous syndrome (Stevens-Johnson syndrome) / erythema multiforme.
Rhabdomyolysis	Adverse events of the SMQ Code 20000002 (rhabdomyolysis/myopathy (SMQ) narrow) are defined as rhabdomyolysis.
Intestinal obstruction	Adverse events of the SMQ Code 20000105 (gastrointestinal obstruction (SMQ) narrow) or the HLGT Code 10018008 (gastrointestinal stenosis and obstruction) or HLT Code 10052736 (non-mechanical ileus) are defined as intestinal obstruction.
Interstitial pneumonia	Adverse events of the SMQ Code 20000042 (interstitial lung disease (SMQ) narrow) are defined as interstitial pneumonia.
Angioedema	Adverse events of the SMQ Code 20000024 (angioedema (SMQ) narrow) are defined as angioedema.
Important potential risk	
Infection	Adverse events of SOC Code 10021881(infections and infestations) are defined as infection.
Malignant tumor	Adverse events of the SOC Code 10029104 (neoplasms benign, malignant and unspecified (incl cysts and polyps)) are defined as malignant tumor.

Malignant tumor (narrow sense)	Adverse events of the SMQ Code 20000194 (malignant tumors (SMQ) narrow) are defined as malignant tumor (narrow sense).
Pemphigoid	Adverse events of the PT Code 10067776 (ocular pemphigoid) or 10034277 (pemphigoid) are defined as pemphigoid.

Term	Definition
Important missing information	
Cardiovascular system risk	Adverse events of the SMQ Code 20000047 (myocardial infarction (SMQ) broad) or SMQ Code 20000061 (central nervous system haemorrhages and cerebrovascular conditions (SMQ) broad) are defined as cardiovascular system risk. "Central nervous system haemorrhage and cerebrovascular conditions (SMQ) broad" includes the following SMQ classes. ➢ 20000166(Conditions associated with central nervous system haemorrhages and cerebrovascular accidents (SMQ) broad) ➢ 20000064(Cerebrovascular disorder haemorrhagic (SMQ) broad) ➢ 20000063(Cerebrovascular disease ischaemic (SMQ) broad)

1.3 Display digit

Term	Definition
Percentage (%)	Percent of patients with adverse events or adverse drug reactions, etc. or percent of adverse events or adverse drug reactions, etc. : Indicate to two decimal places rounded from three decimals. Other than the above: Indicate to one decimal place rounded from two decimals.
Summary statistics	Mean, median, first quartile, and third quartile: Indicate one lower digit rounded from two lower digits than the digit of the to-be evaluated data (refer to Section 1.6). Standard deviation: Indicate two lower digits rounded from three lower digits of the to-be evaluated data. Minimum and maximum Indicate the same digit number as that of the to-be evaluated data.
p-value	Indicate to three decimal places rounded down from four decimals. If the data is less than 0.001, display as $p < 0.001$.

1.4 Level of Significance and Confidence Coefficient

Two-sided 5%, two-sided 95%.

1.5 Handling of Laboratory/Measured Data

The evaluation time points for vital signs and laboratory tests will be at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment, and last evaluation.

The evaluation time points for electrocardiography, waist circumference, and coronary atherosclerosis and arteriosclerosis will be at the start of Nesina treatment, 12 months after the start of Nesina treatment, and last evaluation.

If multiple data exist within the relevant time point, calculate the absolute value of a difference in number of days from the reference number of days and select the minimum absolute value as the datum of the relevant evaluation time point. If the absolute values are same, select the datum at the latest examination/measurement day.

If "On treatment at 12 months after Nesina treatment" is selected in Section "Current Status of Nesina Treatment" in the survey sheet, all values will be used for analysis. If "On treatment at 12 months after Nesina treatment" is not selected, the values before the next day of the last administration of Nesina will be used for analysis.

The start day of Nesina treatment is defined as 0 days.

[Vital signs and laboratory test values]

Evaluation time point	Reference number of days	Lower limit of window	Upper limit of window
At start of Nesina treatment	0 days	30 days before Nesina treatment	Start day of Nesina treatment
1 month after start of Nesina treatment	30 days	1 day after start of Nesina treatment	60 days after start of Nesina treatment
3 months after start of Nesina treatment	90 days	61 days after start of Nesina treatment	136 days after start of Nesina treatment
6 months after start of Nesina treatment	180 days	137 days after start of Nesina treatment	273 days after start of Nesina treatment
12 months after start of Nesina treatment	360 days	274 days after start of Nesina treatment	456 days after start of Nesina treatment
At last evaluation	Select the latest datum from 1 to 456 days after the start of Nesina treatment		

[Electrocardiography and waist circumference]

Evaluation time point	Reference number of days	Lower limit of window	Upper limit of window
At start of Nesina treatment	0 days	30 days before Nesina treatment	Start day of Nesina treatment
12 months after start of Nesina treatment	360 days	1 day after start of Nesina treatment	456 days after start of Nesina treatment
At last evaluation	Select the latest datum from 1 to 456 days after the start of Nesina treatment		

1.6 Display Data Digit

Display digits are described as below.

Term	Display digit	Unit
HbA1c (NGSP value)	0.1	%
Fasting blood glucose level	1	mg/dL
Fasting insulin level	0.1	μU/mL
Fasting glucagon	0.1	pg/mL
HOMA-R	0.1	―
HOMA-β	0.1	%
Fasting triglyceride	1	mg/dL
Total cholesterol	1	mg/dL
HDL-cholesterol	1	mg/dL
LDL-cholesterol	1	mg/dL
non-HDL cholesterol	1	mg/dL
Serum creatinine	0.01	mg/dL
BUN	0.1	mg/dL
Urinary albumin (corrected by creatinine)	0.1	mg/g•Cre
AST	1	IU/L
ALT	1	IU/L
γ-GTP	1	IU/L
ALP	1	IU/L
Total bilirubin	0.1	mg/dL
Amylase	1	IU/L

Lipase	1	IU/L
Waist circumference	0.1	cm
Pulse rate	1	bpm
Systolic blood pressure	1	mmHg
Diastolic blood pressure	1	mmHg
Weight	0.1	kg
BMI	0.1	kg/m^2
Age	1	Year
Duration of type 2 diabetes mellitus	0.1	Year
Height	1	cm
eGFR	0.1	mL/min/1.73 m^2
Nesina administration period	1	Day
Mean daily dose of Nesina	0.01	mg

2.0 Disposition of Patients (Patient Diagram)

(1) Patients to be tabulated and analyzed

Registered patients

(2) Details of tabulation and analysis

The following will be tabulated: the number of registered patients, number of medical site at which patients is registered, number of patients whose survey sheets are collected, number of patients whose survey sheets are not collected, number of patients in the Safety Analysis Set, number of patients in the Not Safety Analysis Set, number of patients in the Efficacy Analysis Set, and number of patients in the Not Efficacy Analysis Set.

For the number of medical sites at which patients are registered, do not duplicate the same medical site with different departments.

For patients whose survey sheets are not collected, tabulate the number of patients for each reason for not collected survey sheets.

For the Not Safety Analysis Set and Not Efficacy Analysis Set, the number of patients will be tabulated for each reason for exclusion to create the list.

The following is the handling of the decision whether patients who meet the following criteria should be evaluated:

Criterion	Safety evaluation	Efficacy evaluation
Pre-agreement administration [found after administration]	×	×
Registration 15 days after prescription of Nesina [found after registration]	×	×
Nesina taking not confirmed [after the end of patient registration period]	×	×
No data for post-administration of Nesina	×	×
No efficacy data at two time points equivalent to the start of Nesina treatment and 1 month after Nesina treatment	○	×
Not using any of the 3 combination drugs (the treatment group will be classified as "Other.") (1) With insulin preparation (2) With rapid-acting insulin secretagogues (3) With SGLT-2 inhibitors	○	×

○ Included, × Excluded or not evaluated

(3) Number of tables and figures

Figure 2.0-1 and Table 2.0-1

3.0 Patient Demographics

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be classified by the categories described below to tabulate the number of patients and frequency.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Sex	Male, Female
Age	Summary statistics
	< 65 years, ≥ 65 years
	< 75 years, ≥ 75 years
	< 20 years, 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, ≥ 80 years
Disease duration of type 2 diabetes mellitus (year)	Summary statistics
	< 2 years, 2 to < 5 years, 5 to < 10 years, ≥ 10 years, Unknown
Height	Summary statistics
Category of clinical practice	Outpatient, Inpatient
Pregnancy (only females)	No, Yes
Severity of renal impairment	Normal, Mild, Moderate, Severe
	Normal + Mild, Moderate + Severe
Concurrent disease	No, Yes
Diabetic complication	No, Yes
Details of diabetic complication (overlapped)	Diabetic nephropathy, diabetic retinopathy, diabetic neuropathy For the proportion, the number of patients with diabetic complication will be denominator.
Concurrent hypertension	No, Yes
Concurrent dyslipidemia	No, Yes
Concurrent hyperuricemia	No, Yes
Concurrent liver disorder	No, Yes

Parameter	Category
Details of concurrent liver disorder (overlapped)	Hepatic steatosis, alcoholic hepatitis, chronic hepatitis, hepatic cirrhosis, or other For the proportion, the number of with concurrent liver disorder will be denominator.
Severity of hepatic impairment	Normal, Grades 1, 2, and 3, or Unknown
Concurrent renal disorder	No, Yes
Details of concurrent renal disorder (overlapped)	Nephrotic syndrome, glomerulonephritis, chronic glomerulonephritis, other For the proportion, the number of with concurrent renal disorder will be denominator.
Severity of renal impairment (eGFR)	Normal, Mild, Moderate, Severe, or Unknown
	Normal + Mild, Moderate + Severe, or Unknown
Severity of renal impairment (serum creatinine)	Normal, Mild, Moderate, Severe, or Unknown
	Normal + Mild, Moderate + Severe, or Unknown
Concurrent heart disease	No, Yes
Details of concurrent heart disease (overlapped)	Cardiac failure, myocardial infarction, angina pectoris, other For the proportion, the number of with concurrent heart disease will be denominator.
Concurrent cardiac failure	No, Yes
Severity classification of cardiac failure (NYHA classification)	Classes NYHA I, NYHA II, NYHA III, and NYHA IV, Unknown For the proportion, the number of with concurrent cardiac failure will be denominator.
Concurrent stroke-related disease	No, Yes
Details of concurrent stroke-related disease (overlapped)	Cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, transient ischaemic attack For the proportion, the number of with concurrent stroke-related disease will be denominator.
Concurrent allergic disease	No, Yes
Concurrent malignant tumour	No, Yes
Concurrent malignant	No, Yes

Parameter	Category
tumour (narrow sense)	
Other concurrent disease	No, Yes
Past medical history	No, Yes, Unknown
Hypersensitivity predisposition	No, Yes, Unknown
Alcohol history (drinking alcoholic drinks almost on a daily basis)	Yes, No, Unknown
Smoking history	Never, Smoking, Smoked, Unknown
HbA1c (NGSP value) (at the start of Nesina treatment)	Summary statistics
	< 6.0%, 6.0% to < 7.0%, 7.0% to < 8.0%, ≥ 8.0%, Unknown
Weight (at the start of Nesina treatment)	Summary statistics
BMI (at the start of Nesina treatment)	Summary statistics
	< 18.5 kg/m^2, 18.5 to < 25 kg/m^2, 25 to < 30 kg/m^2, ≥ 30 kg/m^2, Unknown
	< 25 kg/m^2, ≥ 25 kg/m^2, Unknown
Waist circumference (at the start of Nesina treatment)	Males: < 85 cm, ≥ 85 cm, or Unknown / Females: < 90 cm, ≥ 90 cm, or Unknown

(3) Number of tables and figures

Table 3.0-1

4.0 Details of Treatment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be classified by the categories described below to tabulate the number of patients and frequency.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Initial dose of Nesina	25 mg, 12.5 mg, 6.25 mg, or other
Mean daily dose of Nesina	> 25 mg, 25 to >12.5 mg, 12.5 to > 6.25 mg, or ≤ 6.25 mg
Nesina treatment period	Summary statistics
	1 to 60 days, 61 to 136 days, 137 to 273 days, 274 to 455 days, ≥ 456 days
Administration of prior medication (diabetic drug)	No, Yes, or Unknown
Prior medications (diabetic drugs)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs For the proportion, the number of patients with "Yes" for administration of prior medication (diabetic drug) will be denominator.
Administration of prior medication (other than diabetic drug)	No, Yes, or Unknown
Administration of concomitant medication (diabetic drug)	No, Yes, or Unknown
Concomitant medications (diabetic drugs) (overlapped)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs For the proportion, the number of patients with "Yes" for administration of concomitant medication (diabetic drug) will be

Parameter	Category
	denominator.
Administration of concomitant medication (hypertension drug)	No, Yes, or Unknown
Concomitant medications (hypertension drugs) (overlapped)	ARB, Ca antagonists, ACE inhibitors, diuretics, α blockers, αβ/β blockers, complication of hypertension drugs, or other For the proportion, the number of patients with "Yes" for administration of concomitant medication (hypertension drug) will be denominator.
Administration of concomitant medication (dyslipidaemia drug)	No, Yes, or Unknown
Concomitant medications (dyslipidaemia drugs) (overlapped)	Statins, fibrates, EPA/DHA, or other For the proportion, the number of patients with "Yes" for administration of concomitant medication (dyslipidaemia drug) will be denominator.
Administration of concomitant medication (protease drug)	No, Yes, or Unknown
Administration of concomitant medication (combined with renal excretory drug)	No, Yes, or Unknown
Administration of concomitant medication (other)	No, Yes, or Unknown

(3) Number of tables and figures

Table 4.0-1

4.1 Compliance

4.1.1 Status of compliance with Nesina

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For the status of compliance with Nesina, the frequency will be tabulated at each testing time point (1 month, 3 months, and 6 months after the start of Nesina treatment and last evaluation or treatment discontinuation).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance with Nesina	≥ 90%, ≥ 70%, ≥ 50%, or < 50%

(3) Number of tables and figures

Tables 4.1-1

4.1.2 Status of Compliance with Diet Therapy

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details to be tabulated and analyzed

For the status of compliance with diet therapy, the frequency will be tabulated at each testing time point (at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation or treatment discontinuation). The latest datum will be used for last evaluation.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance with diet therapy	≥ 90%, ≥ 70%, ≥ 50%, < 50%, Not performed, or Unknown

(3) Number of tables and figures

Table 4.1.2

4.1.3 Compliance with Exercise Therapy

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details to be tabulated and analyzed

For the status of compliance with exercise therapy, the frequency will be tabulated at each testing time point (at the start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation or treatment discontinuation). The latest datum will be used for last evaluation.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Status of compliance	≥ 90%, ≥ 70%, ≥ 50%, < 50%, Not performed, or Unknown

Parameter	Category
with exercise therapy	

(3) Number of tables and figures

Table 4.1.3

5.0 Safety Tabulation and Analysis

5.1 Occurrence of adverse events and adverse drug reactions / infections

5.1.1 Occurrence of adverse events

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for adverse events.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of analysis
Number of patients with adverse events	Number of patients who experienced adverse events.
Number of adverse events	Number of adverse events. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events	Described in Section 1.1.
Type of adverse events	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse events and percent of patients with events will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse events and percent of events will be described in the ascending order of PT codes. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.

(3) Number of tables and figures

Table 5.1.1-1

5.1.2 Occurrence of adverse drug reactions / infections

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for adverse drug reactions, etc. and serious adverse drug reactions, etc.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse drug reactions, etc.	Number of patients who experienced adverse drug reactions, etc.
Number of adverse drug reactions, etc.	Number of adverse drug reactions, etc. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.
Percent of patients with adverse drug reactions, etc.	Described in Section 1.1.
Type of adverse drug reactions, etc.	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. and percent of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. and percent of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Tables 5.1.2-1 and 5.1.2-2

5.1.3 Important Identified Risks, Important Potential Risks, and Important Missing Information

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated for important identified risks, important potential risks, and important missing information (described in Section 1.2).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis

Parameter	Details of tabulation and analysis
Number of patients with adverse events (or adverse drug reactions, etc.)	Number of patients who experienced adverse events (or adverse drug reactions, etc.) with important identified risks, important potential risks, and important missing information.
Number of adverse events (or adverse drug reactions, etc.)	Number of adverse events (or adverse drug reactions, etc.) with important identified risks, important potential risks, and important missing information. Count as an event if the same adverse event (or adverse drug reaction, etc.) (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events (or adverse drug reactions, etc.)	Described in Section 1.1.
Type of adverse events (or adverse drug reactions, etc.)	Will be broadly divided into the important identified risks, important potential risks, and important missing information and tabulated by PT in them. For the PTs, the number of adverse events (or adverse drug reactions, etc.) and percent of adverse events (or adverse drug reactions, etc.) will be described in the ascending order of PT codes. Count as an event if the same adverse event (or adverse drug reaction, etc.) (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Tables 5.1.3-1 and 5.1.3-2

5.2 Occurrence of Adverse Events and Adverse Drug Reactions / Infections in the Not Safety Analysis Set

5.2.1 Occurrence of Adverse Events

(1) Patients to be tabulated and analyzed

Not Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse events	Number of patients who experienced adverse events.
Number of adverse events	Number of adverse events. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT.
Percent of patients with adverse events	Described in Section 1.1.
Type of adverse events	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse events and percent of patients with events will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse events and percent of events will be described in the ascending order of PT codes. Count as an event if the same adverse event (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Table 5.2-1

5.2.2 Occurrence of adverse drug reactions / infections

(1) Patients to be tabulated and analyzed

Not Safety Analysis Set

(2) Details of tabulation and analysis

The following will be tabulated.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Details of tabulation and analysis
Number of patients with adverse drug reactions, etc.	Number of patients who experienced adverse drug reactions, etc.
Number of adverse drug reactions, etc.	Number of adverse drug reactions, etc. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the

	same PT.
Percent of patients with adverse drug reactions, etc.	Described in Section 1.1.
Type of adverse drug reactions, etc.	Will be broadly divided into the SOCs and tabulated by PT in the SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. and percent of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. and percent of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even though they have the same PT.

(3) Number of tables and figures

Table 5.2-2

5.3 Occurrence of Adverse Drug Reactions / Infections by Severity, Onset Period, and Outcome

5.3.1 Occurrence of Adverse Drug Reactions / Infections by Severity, Onset Period, and Outcome

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be categorized by the categories described below to tabulate the type of adverse drug reactions, etc.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Severity	Serious, Not serious, Not described
Onset period	1 to 14 days, 15 to 28 days, 29 to 84 days, 85 to 168 days, 169 to 336 days, 337days or Unknown
Outcome	Resolved, Resolving, Not resolved, Resolved with sequelae, Death, or Unknown

The method for tabulation of type adverse drug reactions, etc. is described below:

Parameter	Details of tabulation and analysis
Type of adverse drug	Will be broadly divided into the SOCs and tabulated by PT in the

Parameter	Details of tabulation and analysis
reactions, etc.	SOCs. In case of the laboratory test-related events, type of adverse events will be broadly divided into the SOCs and HLGTs for tabulation by PT. For the SOCs, the number of patients with adverse drug reactions, etc. will be described in the order of SOCs agreed internationally. For the PTs, the number of adverse drug reactions, etc. will be described in the ascending order of PT codes. Count as an event if the same adverse drug reactions, etc. (LLT) occur multiple times in a patient. Count as different events for different LLTs even if they have the same PT. However, evaluate an event for the same LLT in accordance with the following order of priority: Onset period: earlier event Severity: Serious → Not serious → Not described Outcome: Death → Resolved with Sequelae → Not resolved → Resolving → Resolved → Unknown

(3) Number of tables and figures

Tables 5.3-1 to 5.3-3

5.4 Patient Demographics and Frequency of Adverse Drug Reactions / Infections by Treatment

5.4.1 Patients demographics and Frequency of Adverse Drug Reactions / Infections by Treatment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Each parameter will be categorized by the categories described below to tabulate the percent of patients with adverse drug reactions, etc.

The Fischer exact test will be used for parameters without rank data. The Mann-Whitney U test will be used for parameters with rank data. (The tests will be used for parameters with asterisk [*].)

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
Sex*	Male, Female
Age*	< 65 years, ≥ 65 years
	< 75 years, ≥ 75 years
Concurrent liver disorder*	No, Yes
Severity of hepatic	Normal, Grades 1, 2, and 3, or Unknown

Parameter	Category
impairment*	
Concurrent renal disorder*	No, Yes
Severity of renal impairment* (eGFR)	Normal + Mild, Moderate + Severe, or Unknown
Severity of renal impairment* (serum creatinine)	Normal + Mild, Moderate + Severe, or Unknown
Concurrent heart disease*	No, Yes
Details of concurrent heart disease (overlapped)	Cardiac failure, myocardial infarction, or angina pectoris
Concurrent cardiac failure*	No, Yes
Severity classification of cardiac failure (NYHA classification)*	Classes NYHA I, NYHA II, NYHA III, and NYHA IV, or Unknown
Concurrent stroke-related disease*	No, Yes, or Unknown
Mean daily dose of Nesina	> 25 mg, 25 to >12.5 mg, 12.5 to > 6.25 mg, or ≤ 6.25 mg
Administration of concomitant medication (diabetic drug)	No, Yes
Concomitant medications (diabetic drugs) (overlapped)	α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, or insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs
Administration of concomitant medication (protease drug)*	No, Yes, or Unknown
Administration of	No, Yes, or Unknown

Parameter	Category
concomitant medication (combined with renal excretory drug)*	

(3) Number of tables and figures

Table 5.4.1-1

5.5 Occurrence of Adverse Drug Reactions / Infections by Age

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Age will be classified into < 65 years, ≥ 65 years and < 75 years, and ≥ 75 years for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 5.5-1 to 5.5-2

5.6 Occurrence of Adverse Drug Reactions / Infections by Sex

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Sex will be classified into male or female for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.6-1

5.7 Occurrence of Adverse Drug Reactions / Infections by Liver Disorder

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent liver disorder will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.7-1

5.8 Occurrence of Adverse Drug Reactions / Infections by Liver Impairment

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Severity of liver impairment will be classified into Grade 1, 2, or 3 or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.8-1

5.9 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Renal Disorder

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent renal disorder will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.9-1

5.10 Occurrence of Adverse Drug Reactions / Infections by Severity of Renal Impairment

(4) Patients to be tabulated and analyzed

Safety Analysis Set

(5) Details of tabulation and analysis

Severity of renal impairment will be classified into normal + mild, moderate + severe, or unknown, according to the criteria for the severity of renal impairment (eGFR and serum creatinine) for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(6) Number of tables and figures

Tables 5.10-1 and 5.10-2

5.11 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Heart Disease

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent heart disease will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.11-1

5.12 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Heart Failure

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent heart failure will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total and mild type 2 diabetes mellitus patients will be tabulated.

(3) Number of tables and figures

Table 5.12-1

5.13 Occurrence of Adverse Drug Reactions / Infections by Severity of Heart Failure

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Severity of heart failure will be classified into Class NYHA I, NYHA II, NYHA III, or NYHA IV or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Patients with mild type 2 diabetes mellitus patients or other (individual) will be tabulated.

(3) Number of tables and figures

Table 5.13-1

5.14 Occurrence of Adverse Drug Reactions / Infections by Presence of Concurrent Stroke-related Disease

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concurrent stroke-related disease will be classified into yes or no for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.14-1

5.15 Occurrence of Adverse Drug Reactions / Infections by Mean Daily Dose of Nesina

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

The mean daily dose of Nesina will be classified into > 25 mg, 25 to > 12.5 mg, 12.5 to > 6.25 mg, or 6.25 mg for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients will be tabulated.

(3) Number of tables and figures

Table 5.15-1

5.16 Occurrence of Adverse Drug Reactions / Infections by Concomitant Medication (Diabetic Drug)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medications (diabetic drugs) will be classified into the following drugs: α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT-2 inhibitors, combination of diabetic drugs, or other diabetic drugs, for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.16-1

5.17 Occurrence of Adverse Drug Reactions / Infections by Presence of Concomitant Medication (Protease Inhibitor)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medication (protease inhibitor) will be classified into yes, no, or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.17-1

5.18 Occurrence of Adverse Drug Reactions / Infections by Presence of Concomitant Medication (Renal Excretory Drug)

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

Concomitant medication (renal excretory drug) be classified into yes, no, or unknown for tabulation of type of adverse drug reactions, etc.

The method for tabulation of adverse drug reactions, etc. is same as that described in Section 5.1.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.18-1

5.19 Change in Laboratory/Measured Data

5.19.1 Vital Signs

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

In vital signs, summary statistics for pulse rate, blood pressure (systolic/diastolic), and weight will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after the start of Nesina treatment and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

Measured values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.1-1 and Figures 5.19.1-1 to 5.19.1-4

5.19.2 Laboratory Values

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

In laboratory values, summary statistics will be calculated for fasting triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol, non-HDL cholesterol, serum creatinine, BUN, urinary albumin (corrected by creatinine), AST, ALT, γ-GTP, ALP, total bilirubin, amylase, lipase at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

These laboratory values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.2-1 and Figures 5.19.2-1 to 5.19.2-15

5.19.3 Electrocardiography

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For assessment of electrocardiogram, cross tabulation will be used for the categories described below.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

Parameter	Category
ECG results at start of Nesina treatment	Clinical abnormal findings (Yes or No) or Not performed
ECG results at 12 months after start of Nesina treatment	Clinical abnormal findings (Yes or No) or Not performed
ECG results at last evaluation	Clinical abnormal findings (Yes or No) or Not performed

(3) Number of tables and figures

Table 5.19.3

5.19.4 Waist Circumference

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

For waist circumference, summary statistics will be calculated at each testing time point (at the start of Nesina treatment, 12 months after the start of Nesina treatment, and last evaluation). For changes from the start of Nesina treatment, summary statistics and the mean 95% confidence intervals will be calculated.

Measured values (mean and standard deviation) will be plotted. For the changes, the mean changes will be created using a bar graph.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 5.19.4 and Figure 5.19.4

5.19.5 Tests for Coronary Atherosclerosis and Arteriosclerosis

(1) Patients to be tabulated and analyzed

Safety Analysis Set

(2) Details of tabulation and analysis

A listing of the following tests and the test results for coronary atherosclerosis and arteriosclerosis will be created: survey sheet number, treatment group, time point, test day, and

details of tests (pulse wave velocity [PWV], cardio-ankle vascular index [CAVI], intima-media thickness [IMT], intra-vascular ultrasound [IVUS], and other [specify the details]).

(3) Number of tables and figures

Table 5.19.5

6.0 Efficacy Tabulation and Analysis

6.1 Changes in HbA1c

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For HbA1c (NGSP values), summary statistics will be calculated at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes, summary statistics and the mean 95% confidence intervals will be calculated and the paired t-test will be performed.

Measured values of HbA1c (NGSP values) will be plotted and for the changes a bar graph will be created excluding the unknown category.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 6.1-1 and Figure 6.1-1

6.2 Glycemic control achievement rate (HbA1c)

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

The glycemic control achievement rate for HbA1c (NGSP value) will be tabulated ($< 6.0\%$, $\geq 6.0\%$ / $< 7.0\%$, $\geq 7.0\%$) and a bar graph will be created at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation) (the unknown category will be excluded for the bar graph).

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Table 6.2-1 and Figures 6.2-1 and 6.2-2

6.3 Changes in Fasting blood glucose level, Fasting insulin level, Fasting Glucagon, HOMA-R, and HOMA-β

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For fasting blood glucose level, fasting insulin level, fasting glucagon, HOMA-R, and HOMA-β, summary statistics will be calculated at each at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation). For changes, summary statistics and the mean 95% confidence intervals will be

calculated and the paired t-test will be performed.

Measured values will be plotted and for the changes a bar graph will be created excluding the unknown category.

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 6.3-1 and 6.3-5 and Figures 6.3-1 and 6.3-5

6.4 Changes in HbA1c, etc. by Factor Probably Affecting Efficacy

(1) Patients to be tabulated and analyzed

Efficacy Analysis Set

(2) Details of tabulation and analysis

For changes in HbA1c (NGSP values), summary statistics and the mean 95% confidence intervals will be calculated and the paired t-test will be performed at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation).

The glycemic control achievement rate for HbA1c (< 6.0%, ≥ 6.0% / < 7.0%, ≥ 7.0%) at each testing time point (start of Nesina treatment, 1 month, 3 months, 6 months, and 12 months after Nesina treatment and last evaluation) will be tabulated for the following parameters:

i Sex (Male, Female)

ii Age (< 65 years, ≥ 65 years)

iii Age (< 75 years, ≥ 75 years)

iv Concurrent renal disorder (No, Yes)

v HbA1c (NGSP value) at the start of Nesina treatment (< 6.0%, 6.0% to < 7.0%, 7.0% to < 8.0%, ≥ 8.0%, or Unknown)

vi Mean daily dose of Nesina (> 25 mg, 25 to > 12.5 mg, 12.5 to > 6.25 mg, or 6.25 mg)

vii Concomitant diabetic drugs (α-glucosidase inhibitors, thiazolidines, sulfonylureas, biguanides, rapid-acting insulin secretagogues, or insulin preparations, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, combination of diabetic drugs, or other diabetic drugs)

Total patients and patients who are taking concomitant insulin preparation, rapid-acting insulin secretagogues, SGLT-2 inhibitors, or other drugs will be tabulated.

(3) Number of tables and figures

Tables 6.4-1 to 6.4-14