Inclusion criteria

- Type 2 diabetes
- HbA_{1c} ≥7.0 %
- ***OR*** HbA_{1c} <7.0 % and current insulin treatment corresponding to ≥20 U/day of basal insulin
- Current treatment with one or more oral or injectable antidiabetic agents
- Age ≥50 years at screening and at least one of the following conditions:
  - Prior myocardial infarction
  - Prior stroke or prior TIA
  - Prior coronary, carotid or peripheral arterial revascularization
  - >50% stenosis on angiography or other imaging of coronary, carotid or lower-extremity artery
  - History of symptomatic coronary heart disease documented by positive exercise stress test or any cardiac imaging, or unstable angina pectoris with ECG changes
  - Asymptomatic cardiac ischemia documented by positive nuclear imaging test or exercise test or dobutamine stress echo
  - Chronic heart failure NYHA class II–III
  - Chronic kidney disease corresponding to estimated glomerular filtration rate 30–59 mL/min/1.73m^2 per CKD-EPI
- ***OR*** Age ≥60 years at screening and at least one of the following risk factors:
  - Microalbuminuria or proteinuria
  - Hypertension and left ventricular hypertrophy by ECG or imaging
  - Left ventricular systolic and diastolic dysfunction by imaging
  - Ankle/brachial index <0.9

試験の参加資格条件

Exclusion criteria

- An acute coronary or cerebrovascular event in the previous 60 days
- Planned coronary, carotid or peripheral artery revascularization
- Chronic heart failure NYHA class IV
- Current hemodialysis or peritoneal dialysis or eGFR <30 mL/min/1.73 m^2 per CKD-EPI
- End-stage liver disease, defined as the presence of acute or chronic liver disease and recent history of one or more of the following: ascites, encephalopathy, variceal bleeding, bilirubin ≥2.0 mg/dL, albumin level ≤3.5 g/dL, prothrombin time ≥4 seconds prolonged, international normalized ratio ≥1.7 or prior liver transplant
- Known or suspected hypersensitivity to trial products or related products
- Female of child-bearing potential who is pregnant, breast-feeding or intends to become pregnant, or is not using adequate contraceptive methods as required by local law or practice
- Expected simultaneous participation in any other clinical trial of an investigational medicinal product. Participation in a clinical trial with stent(s) is allowed
- Receipt of any investigational medicinal product within 30 days before randomization. Brazil: Receipt of any investigational medicinal product within 1 year before randomization unless there is a direct benefit to the patient at the investigator's discretion
- Current or past (within the last 5 years) malignant neoplasms (except basal cell and squamous cell skin carcinoma)
- Any condition that, in the investigator's opinion, would make the patient unable to adhere to the initial trial visit schedule and procedures

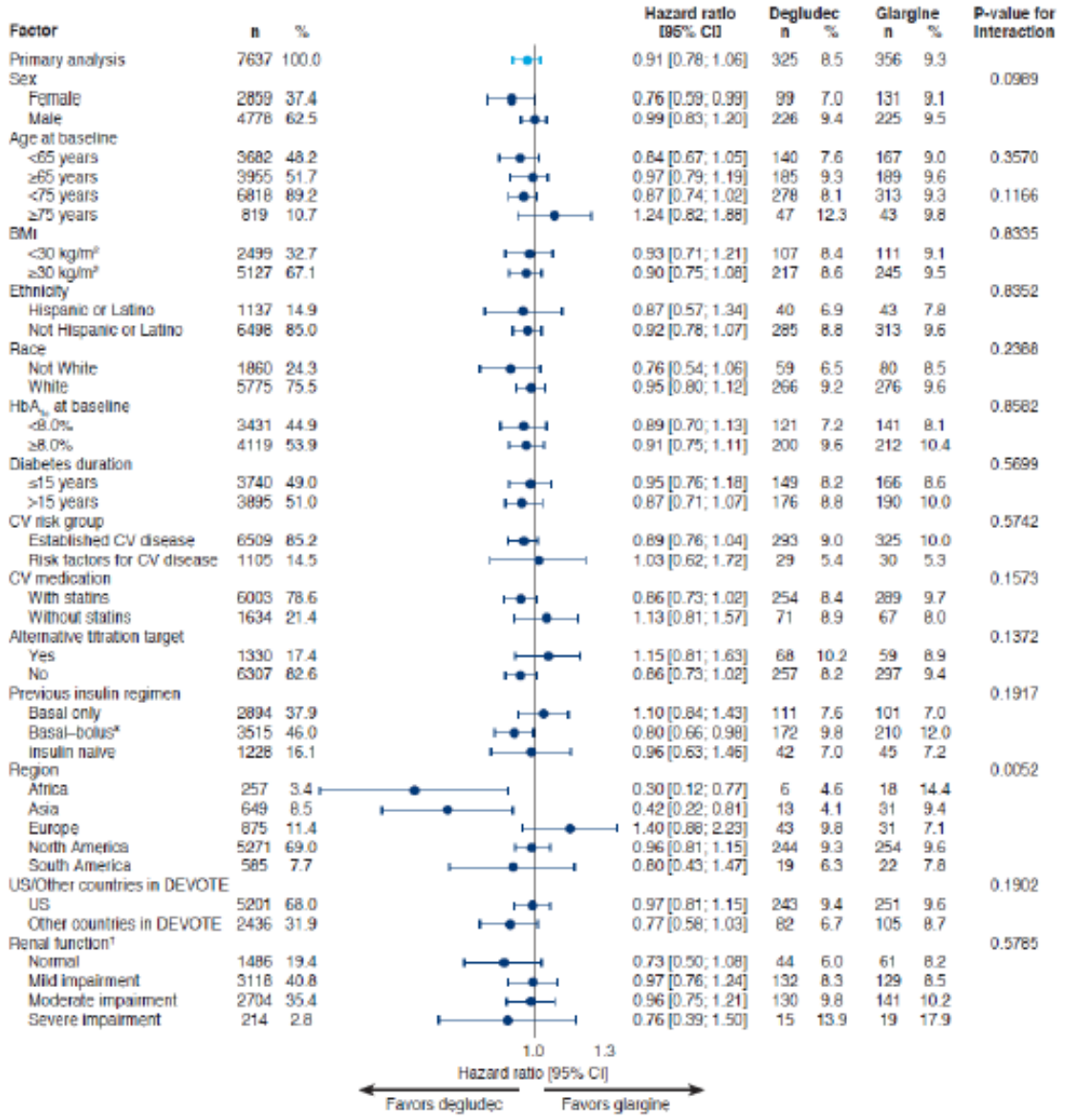
試験参加の除外条件

Table S1: Titration algorithms

Lowest of three pre-breakfast SMPG values		Basal insulin adjustment
mg/dL	mmol/L	Units
<71	<4.0	–2
71–90	4.0–5.0	0
91–126	5.1–7.0	+2
>126	>7.0	+4
Lowest of three pre-prandial or bedtime SMPG values		**Bolus insulin adjustment**
mg/dL	mmol/L	Units
<71	<4.0	–2
71–126	4.0–7.0	0
>126	>7.0	+2

時効型と速効型インスリンの漸増の仕方

Figure S4: Major adverse cardiovascular events subgroup analyses

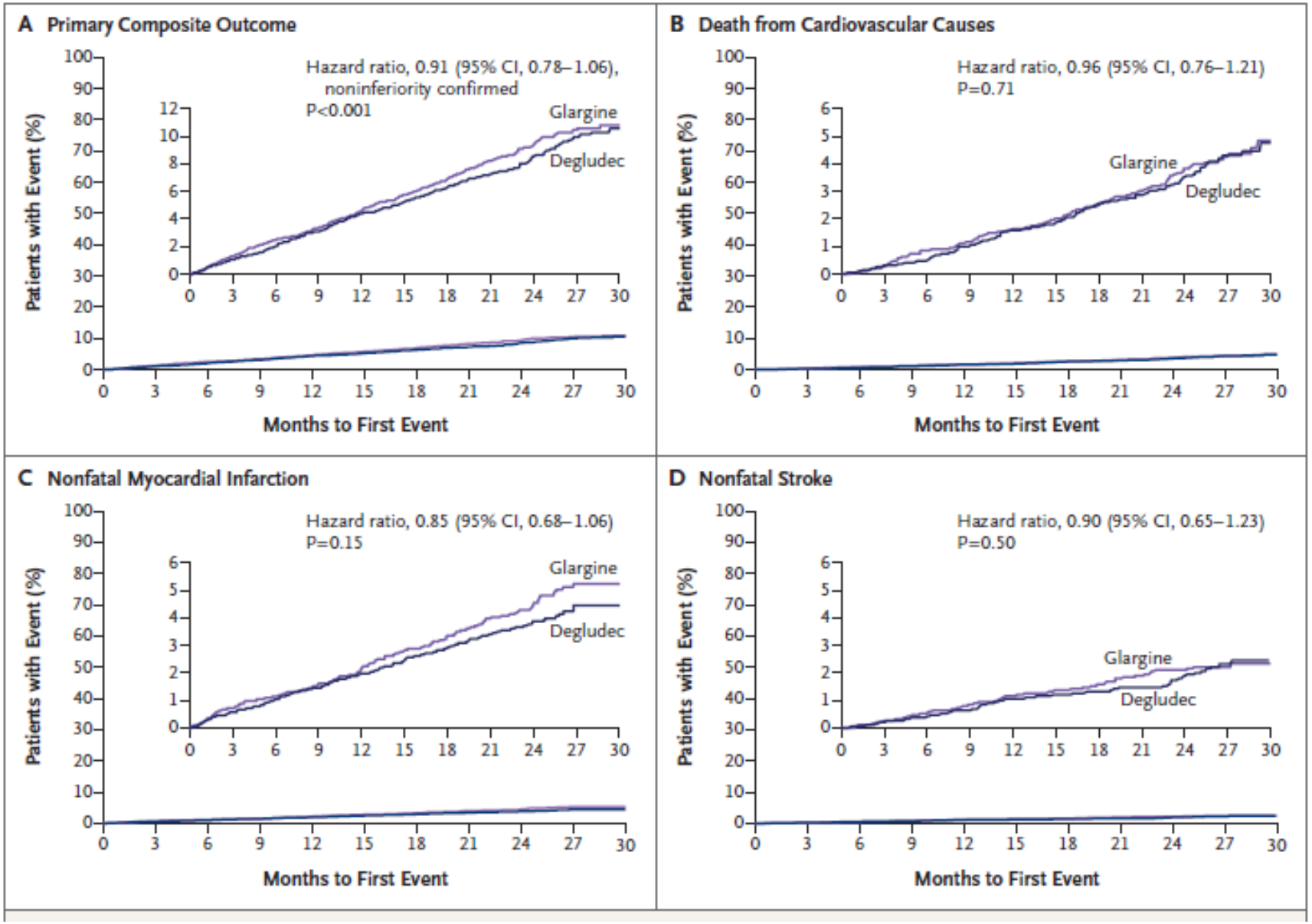


トレシーバとランタスはほぼ同じ結果。低血糖はトレシーバが有利

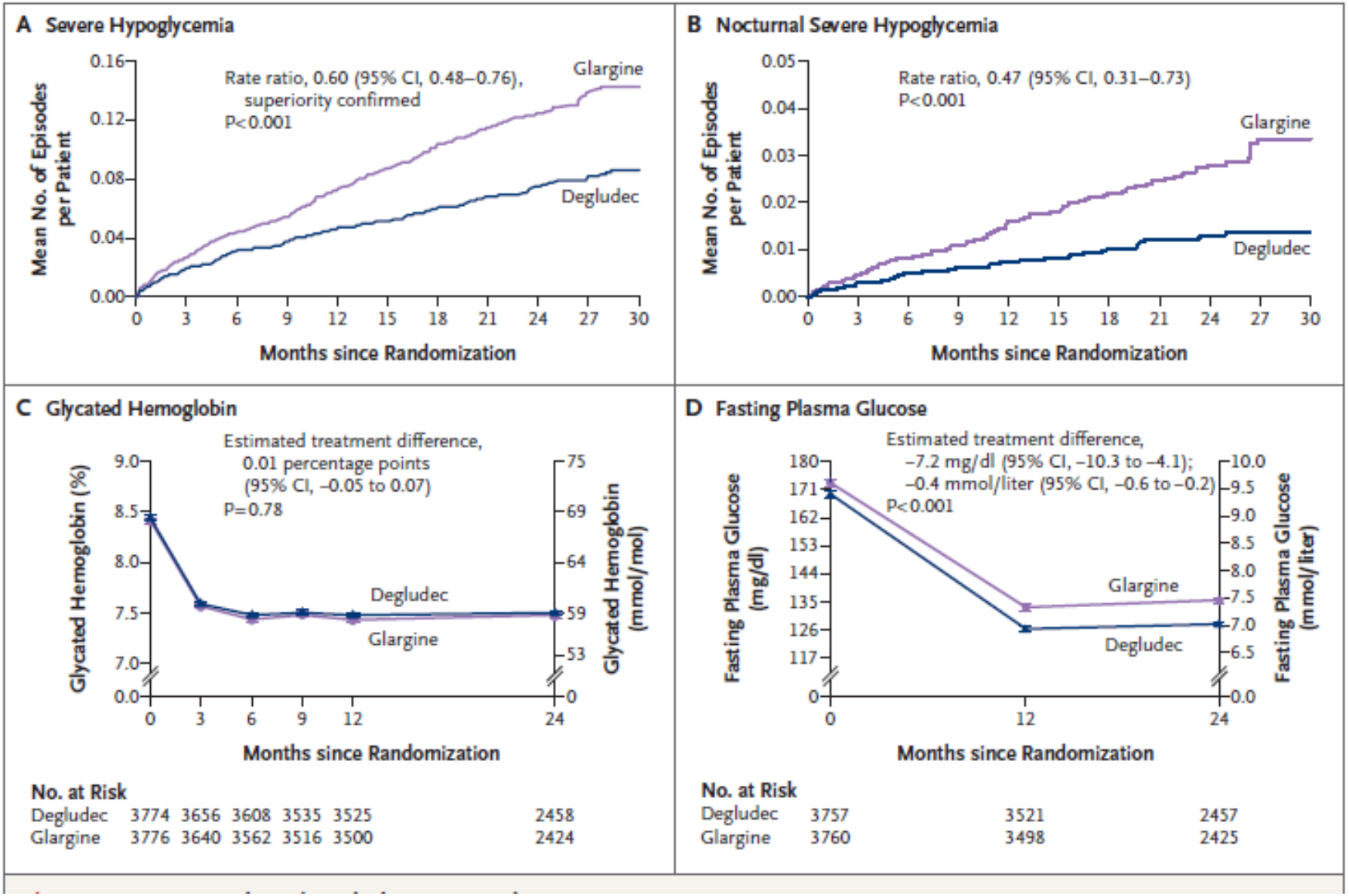
Table S4: Cardiovascular risk factors

Change from baseline to month 24	Degludec	Glargine
Body weight, lb [kg]	4.9 [2.2]	4.2 [1.9]
Body mass index, kg/m^2	0.8	0.7
Systolic/diastolic blood pressure, mmHg	–1.1/–0.8	–0.0/–0.6
Pulse, beats/minute	–0.8	–0.7
Estimated glomerular filtration rate, ml/min/1.73m^2	–2.4	–2.6
Total cholesterol, mg/dL [mmol/L]	–3.86 [–0.10]	–3.66 [–0.09]
High-density lipoprotein cholesterol, mg/dL [mmol/L]	–1.23 [–0.03]	–0.73 [–0.02]
Low-density lipoprotein cholesterol, mg/dL [mmol/L]	–0.98 [–0.03]	–1.09 [–0.03]
Triglycerides, mg/dL [mmol/L]	–9.22 [–0.10]	–12.21 [–0.14]

心血管リスクへの影響も両者ほぼ同じ



同じ結果をグラフにしています。



糖尿病の状態に対する効果は同じ。低血糖はトレシーバが有利