

# SUSTAIN 6



Ozempic® is indicated to reduce the risk of MACE for adults with T2D and established CVD<sup>1,a</sup>

## AUTHORS

Marso SP, Bain SC,  
Consoli A, et al;  
SUSTAIN-6 Investigators

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# Ozempic® and cardiovascular outcomes in patients with type 2 diabetes



**OBJECTIVE:** Assess noninferiority of Ozempic® (semaglutide) vs placebo, both in addition to standard of care, for time to first MACE using a risk margin of 1.3.

<sup>a</sup>Major adverse CV events (MACE) composed of CV death, nonfatal MI, or nonfatal stroke.  
T2D=type 2 diabetes; CVD=cardiovascular disease; CV=cardiovascular; MI=myocardial infarction.

## Indications and Limitations of Use

Ozempic® (semaglutide) injection 0.5 mg or 1 mg is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus and to reduce the risk of major adverse cardiovascular (CV) events (CV death, nonfatal myocardial infarction, or nonfatal stroke) in adults with type 2 diabetes mellitus and established CV disease.

- Ozempic® has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- Ozempic® is not indicated for use in patients with type 1 diabetes mellitus.

## Important Safety Information

### WARNING: RISK OF THYROID C-CELL TUMORS

- In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether Ozempic® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.
- Ozempic® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of Ozempic® and inform them of symptoms of thyroid tumors (eg, a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Ozempic®.

### Contraindications

- Ozempic® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with a prior hypersensitivity reaction to semaglutide or to any of the excipients in Ozempic®. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with Ozempic®.

### Warnings and Precautions

- **Risk of Thyroid C-Cell Tumors:** Patients should be referred to an endocrinologist for further evaluation if serum calcitonin is measured and found to be elevated or thyroid nodules are noted on physical examination or neck imaging.



Please see Important Safety Information throughout. Please see Prescribing Information, including Boxed Warning, at <http://www.novo-pi.com/ozempic.pdf>.

ONCE-WEEKLY  
**OZEMPIC®**  
semaglutide injection 0.5mg/1mg

# STUDY DESIGN<sup>2</sup>



## STUDY DESIGN AND METHODOLOGY

A 104-week, multicenter, multinational, placebo-controlled, double-blind CVOT in 3297 adult patients with inadequately controlled type 2 diabetes and ASCVD. Patients had a mean duration of diabetes of 13.9 years, a mean baseline A1C of 8.7%, and 58% were taking insulin.

### 3297 PATIENTS

#### INCLUSION CRITERIA

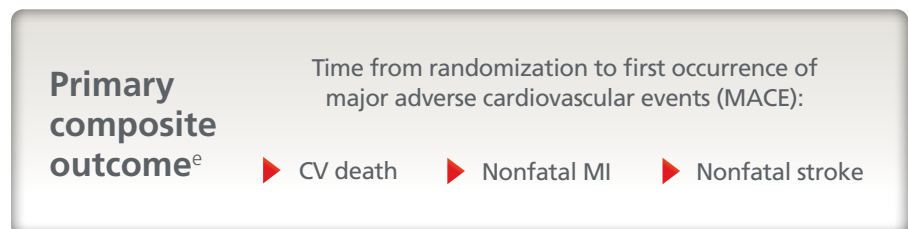
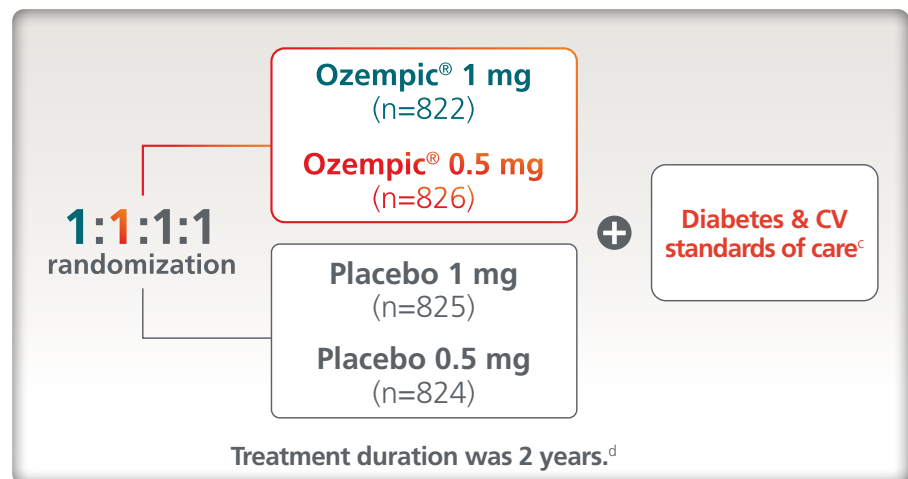
- A1C  $\geq 7\%$
- Previously on 0 to 2 OADs  $\pm$  basal or premixed insulin

$\geq 50$  years of age and established CVD<sup>a</sup>

OR

$\geq 60$  years of age with at least 1 CV risk factor<sup>b</sup>

### STUDY DURATION AND GROUPS



<sup>a</sup>Established CV disease (previous CV, cerebrovascular, or peripheral vascular disease); or chronic heart failure (New York Heart Association class II or III); or chronic kidney disease stage 3 or higher.

<sup>b</sup>Defined as persistent microalbuminuria (30-299 mg/g) or proteinuria, hypertension, and left ventricular hypertrophy by electrocardiogram or imaging, left ventricular systolic or diastolic dysfunction by imaging, or ankle/brachial index  $< 0.9$  of those in the trial.

<sup>c</sup>Standards of care included but were not limited to the following: oral antidiabetic treatments, insulin, antihypertensives, diuretics, lipid-lowering therapies, and antithrombotic medications.

<sup>d</sup>Trial consisted of 104 weeks of treatment (including a 4- to 8-week dose escalation period), with a subsequent 5-week follow-up period.

<sup>e</sup>For the primary analysis, a Cox proportional hazards model was used to test for noninferiority of Ozempic<sup>®</sup> to placebo for time to first MACE using a risk margin of 1.3.

CVOT=cardiovascular outcomes trial; ASCVD=atherosclerotic cardiovascular disease; OADs=oral antidiabetic drugs.

## Important Safety Information (cont'd)

### Warnings and Precautions (cont'd)

- **Pancreatitis:** Acute and chronic pancreatitis have been reported in clinical studies. Observe patients carefully for signs and symptoms of pancreatitis (persistent severe abdominal pain, sometimes radiating to the back with or without vomiting). If pancreatitis is suspected, discontinue Ozempic<sup>®</sup> promptly, and if pancreatitis is confirmed, do not restart.
- **Diabetic Retinopathy Complications:** In a 2-year trial involving patients with type 2 diabetes and high cardiovascular risk, more events of diabetic retinopathy complications occurred in patients treated with Ozempic<sup>®</sup> (3.0%) compared with placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline than among patients without a known history of diabetic retinopathy.

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemetic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.



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semaglutide injection 0.5mg | 1mg

# SUMMARY OF RESULTS<sup>2</sup>

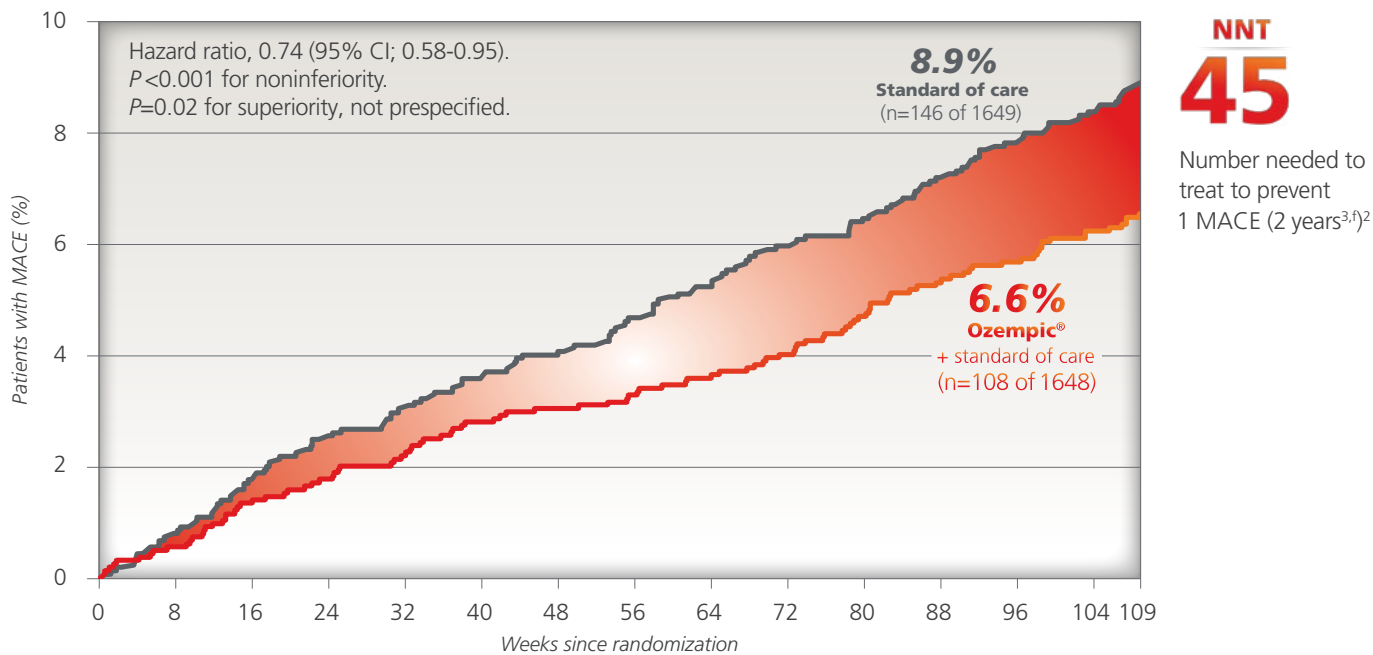
In adults with type 2 diabetes and established CVD, when added to standard of care,

**OZEMPIC® DEMONSTRATED A 26% RRR OF MACE (2.3% ARR AT 109 WEEKS)**



...the rate of first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke was significantly lower in those receiving semaglutide than in those receiving placebo.

## TIME TO FIRST CONFIRMED MAJOR ADVERSE CV EVENT (MACE)<sup>1,2</sup>



Please see Prescribing Information at <http://www.novo-pi.com/ozempic.pdf>.

<sup>1</sup>Estimated cumulative risk of MACE at Week 104 was 6.2% with Ozempic® and 8.4% with placebo.<sup>3</sup>  
RRR=relative risk reduction; ARR=absolute risk reduction; NNT=number needed to treat.

## Important Safety Information (cont'd)

- **Never Share an Ozempic® Pen Between Patients:** Ozempic® pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens.
- **Hypoglycemia:** Patients receiving Ozempic® in combination with an insulin secretagogue (eg, sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. Inform patients using these concomitant medications of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.
- **Acute Kidney Injury:** There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of Ozempic® in patients reporting severe adverse gastrointestinal reactions.
- **Hypersensitivity:** Serious hypersensitivity reactions (eg, anaphylaxis, angioedema) have been reported in patients treated with Ozempic®. If hypersensitivity reactions occur, discontinue use of Ozempic®; treat promptly per standard of care, and monitor until signs and symptoms resolve. Use caution in a patient with a history of angioedema or anaphylaxis with another GLP-1 receptor agonist.



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# ADDITIONAL SAFETY RESULTS<sup>2</sup>

## ADVERSE EVENTS OCCURRING IN ≥5% OF STUDY PARTICIPANTS

	Placebo 0.5 mg (n=824) %	Placebo 1 mg (n=825) %	Ozempic® 0.5 mg (n=826) %	Ozempic® 1 mg (n=822) %
Adverse event leading to treatment discontinuation	5.7	7.6	11.5	14.5
GI disorder <sup>a</sup>	35.7	35.2	50.7	52.3
Diarrhea	11.9	10.5	17.9	18.4
Nausea	7.5	8.1	17.3	21.9
Vomiting	5.2	4.1	10.5	14.8
Cardiac disorder <sup>a</sup>	22.9	21	20.9	18.2
Severe or symptomatic hypoglycemic event <sup>b</sup>	21.5	21	23.1	21.7
Acute renal failure <sup>c</sup>	4.1	4.2	5.1	2.8
Allergic reaction <sup>c</sup>	5.6	6.9	5.9	6
Neoplasm <sup>d</sup>	8.5	8.4	8	10.8
Benign	4.4	4.1	4.8	6.6

- In placebo-controlled trials, the most common adverse reactions reported in ≥5% of patients treated with Ozempic® were nausea, vomiting, diarrhea, abdominal pain, and constipation<sup>1</sup>
- Treatment discontinuation due to adverse events was more frequent in the Ozempic® group than in the placebo group
- Gastrointestinal (GI) disorders were more frequent in the Ozempic® group than in the placebo group

<sup>a</sup>This category was defined according to the system organ class in the *Medical Dictionary for Regulatory Activities* (MedDRA).

<sup>b</sup>This category of hypoglycemic event includes episodes of severe hypoglycemia (defined according to the American Diabetes Association criteria) or symptomatic hypoglycemia as confirmed on plasma glucose testing (<56 mg/dL [3.1 mmol/L]).

<sup>c</sup>This category was based on the group of preferred terms in MedDRA.

<sup>d</sup>This event was confirmed by the event adjudication committee.

## Important Safety Information (cont'd)

### Adverse Reactions

- The most common adverse reactions, reported in ≥5% of patients treated with Ozempic® are nausea, vomiting, diarrhea, abdominal pain, and constipation.

### Drug Interactions

- When initiating Ozempic®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia.
- Ozempic® causes a delay of gastric emptying and has the potential to impact the absorption of concomitantly administered oral medications, so caution should be exercised.

### Use in Specific Populations

- There are limited data with semaglutide use in pregnant women to inform a drug-associated risk for adverse developmental outcomes. Discontinue Ozempic® in women at least 2 months before a planned pregnancy due to the long washout period for semaglutide.

**References:** 1. Ozempic [package insert]. Plainsboro, NJ: Novo Nordisk Inc; 2021. 2. Marso SP, Bain SC, Consoli A, et al; SUSTAIN-6 Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2016;375(19):1834-1844. 3. Data on file. Novo Nordisk Inc; Plainsboro, NJ.



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