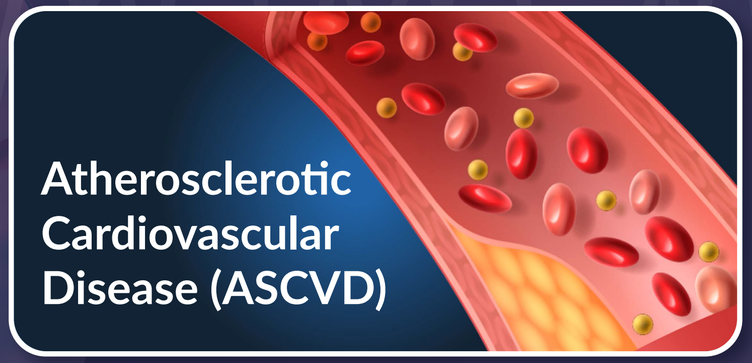
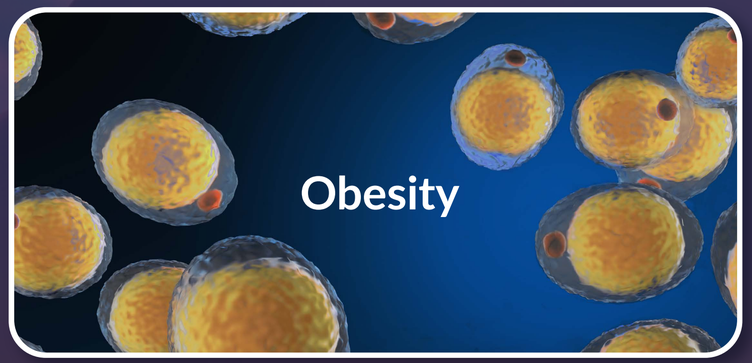
AMGEN

CARDIOVASCULAR AND METABOLIC CLINICAL TRIALS

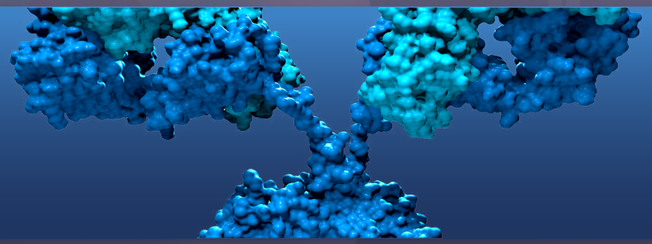
Learn About Active Studies



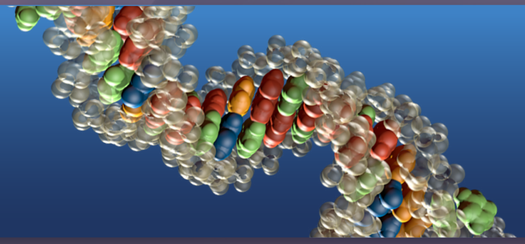


Atherosclerotic Cardiovascular Disease (ASCVD)

Evolocumab
mAb



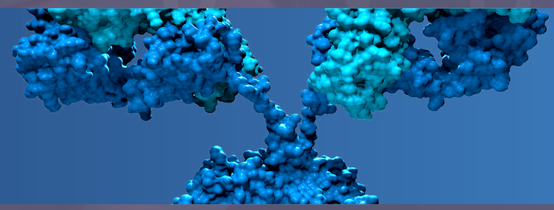
Olpasiran (AMG 890)
siRNA



mAb = monoclonal antibody; siRNA = small interfering RNA.

Evolocumab

mAb



Ongoing phase 3 and 4, and observational studies[1,2]

Evolocumab is a human monoclonal IgG directed against human PCSK9[2,3]

Ongoing trials

IgG = immunoglobulin G; mAb = monoclonal antibody; PCSK9 = proprotein convertase subtilisin/kexin type 9.

1. Amgen Pipeline. www.amgenpipeline.com/pipeline. Accessed September 11, 2023. 2. Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.
3. Langslet G, et al. *Expert Rev Cardiovasc Ther.* 2015;13:477-488.

Clinical Study Program

Evolocumab Investigational Phase 3 and 4 Trials

VESALIUS-CV
Effect of Evolocumab in Patients at High Cardiovascular Risk Without Prior Myocardial Infarction or Stroke

EVOLVE-MI
Effect of Evolocumab in Patients Hospitalized With An Acute Myocardial Infarction

Observational Study

SHENNONG
Effectiveness of Evolocumab Used in Combination With Standard of Care at Long-term in Chinese Patients With Established Atherosclerotic Cardiovascular Disease

Evolocumab Outcomes Trial in High CV Risk Patients

Vesalius-cv

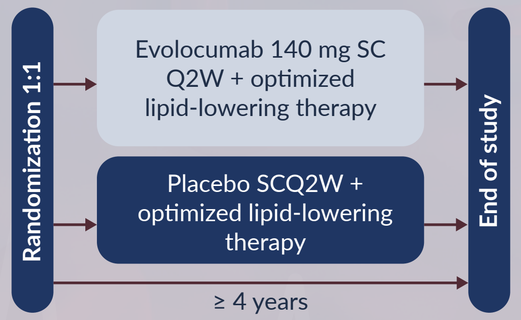
Effect of EVolocumab in PatiEntS at High CArdiovascuLar RIsk WithoUt Prior Myocardial Infarction or Stroke

A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate the Impact of Evolocumab on Major Cardiovascular Events in Patients at High Cardiovascular Risk Without Prior Myocardial Infarction or Stroke

PHASE 3 STUDY DESIGN:*

Patients at high cardiovascular risk without prior MI or stroke:
N = 12,301

- LDL-C ≥ 90 mg/dL or non-HDL-C ≥ 120 mg/dL or ApoB ≥ 80 mg/dL
- Evidence of at least one of the following at screening:
  - Significant CAD
  - Significant atherosclerotic cerebrovascular disease
  - Significant PAD
  - Diabetes mellitus
- At least one high-risk feature



STUDY PURPOSE:

Assess the effect of lowering LDL-C with evolocumab on major cardiovascular events in subjects without a prior MI or stroke who are at high risk for a first cardiovascular event

ADDITIONAL INFORMATION:

www.amgentrials.com (Protocol number: 20170625)
www.clinicaltrials.gov (Identifier: NCT03872401)

Evolocumab is investigational for this population/use.

PRIMARY ENDPOINTS (time to):†

- CHD death, MI, or ischemic stroke, whichever occurs first
- CHD death, MI, ischemic stroke, or any ischemia-driven arterial revascularization, whichever occurs first

SECONDARY ENDPOINTS (time to):†

- MI, ischemic stroke, or any ischemia-driven arterial revascularization
- CHD death, MI, or any ischemia-driven arterial revascularization
- CV death, MI, or stroke
- CHD death or MI
- MI
- Any ischemia-driven arterial revascularization
- CHD death
- CV death
- All-cause death
- Ischemic stroke

KEY INCLUSION CRITERIA: (all 4 needed)

- Adult subjects ≥ 50 (men) or ≥ 55 (women) to < 80 years of age (either sex and meeting lipid criteria)
- LDL-C ≥ 90 mg/dL (≥ 2.3 mmol/L) or non-HDL-C ≥ 120 mg/dL (≥ 3.1 mmol/L) or ApoB ≥ 80 mg/dL (≥ 1.56 µmol/L)
- Evidence of at least one of the following at screening:
  - Significant CAD
  - Significant atherosclerotic cerebrovascular disease
  - Significant PAD
  - Diabetes mellitus
- At least one high-risk feature

KEY EXCLUSION CRITERIA:

- MI or stroke prior to randomization
- CABG < 3 months prior to screening
- Estimated glomerular filtration rate (eGFR) < 15 mL/min/1.73 m^2
- Triglycerides ≥ 500 mg/dL (5.7 mmol/L)
- Last measured left ventricular ejection fraction < 30% or NYHA Functional Class III/IV

*May not be inclusive of all study detail. †For adults at high cardiovascular risk without past MI or stroke and receiving optimized lipid-lowering therapy.
ApoB = apolipoprotein B; CABG = coronary artery bypass graft; CAD = coronary artery disease; CHD = coronary heart disease; CV = cardiovascular; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; NYHA = New York Heart Association; PAD = peripheral arterial disease; Q2W = every 2 weeks; SC = subcutaneous.
Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.

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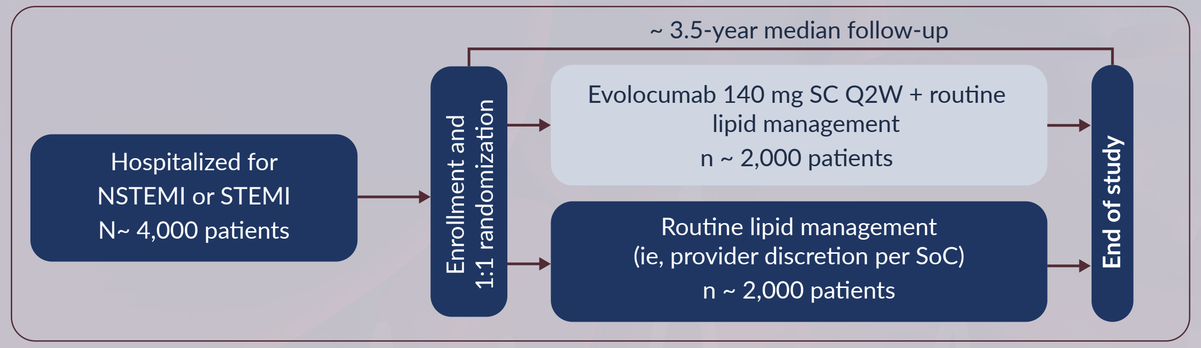
Evolocumab Outcomes Trial in Patients Hospitalized With Acute MI

EVOLVE-MI

A Pragmatic, Randomized, Multicenter Trial of **EVOL**ocumab Administered **V**ery **E**arly to Reduce the Risk of Cardiovascular Events in Patients Hospitalized With Acute **M**yocardial **I**nfarction

An Open-label, Randomized, Multicenter, Pragmatic Study to Evaluate Early Treatment With Evolocumab Plus Routine Lipid Management vs Routine Lipid Management Alone in Patients Hospitalized for an Acute MI

PHASE 4 STUDY DESIGN:[1]



STUDY PURPOSE:[1]

To evaluate the effectiveness of early treatment with evolocumab plus routine lipid management vs routine lipid management alone when administered in the acute setting to reduce MI, ischemic stroke, arterial revascularization, and all-cause death in patients hospitalized for an acute MI (NSTEMI or STEMI)

ADDITIONAL INFORMATION:

www.amgentrials.com (Protocol number: 20190184)
www.clinicaltrials.gov (Identifier: NCT05284747)

PRIMARY ENDPOINTS:[2]

- Total composite of MI, ischemic stroke, any arterial revascularization procedure, and all-cause death

SECONDARY ENDPOINTS:[1]

- Percentage change in LDL-C from baseline to 12 weeks
- Percentage change in LDL-C from baseline to 52 weeks
- Total composite of MI, ischemic stroke, any arterial revascularization procedure, and CV death
- Time to first occurrence of composite MI, ischemic stroke, any arterial revascularization procedure, and all-cause death
- Total MI events
- Total arterial revascularization procedures
- Total ischemia-driven coronary revascularization procedures
- Total ischemic strokes
- Time to CV death
- Time to all-cause death

KEY INCLUSION CRITERIA:[1]

- Adults ≥ 18 years of age
- Hospitalized for primary reason of NSTEMI or STEMI due to presumed atherosclerotic disease

KEY EXCLUSION CRITERIA:[1]

- Invasive hemodynamic and/or vasopressor/ inotropic support at the time of screening
- Elevated biomarkers of myocardial injury due to secondary/nonatherosclerotic etiology*

*Including sepsis, atrial fibrillation, vasospasm, decompensated heart failure, uncontrolled hypertension, stress-induced cardiomyopathy[1].

CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol; mAb = monoclonal antibody; MI = myocardial infarction; NSTEMI= non–ST-segment elevation myocardial infarction; Q2W = every 2 weeks; SC = subcutaneous; SoC = standard of care; STEMI = ST-segmented elevation myocardial infarction.

1. Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023. 2. Amgen Data on File; [2022].

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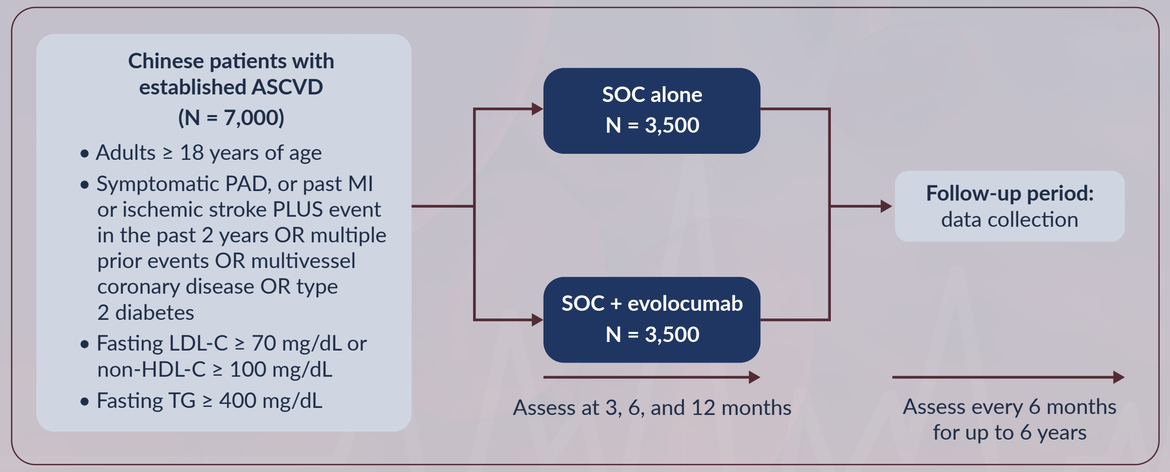
Observational Study of Evolocumab in Chinese Patients With Established ASCVD

shennong
神农

Effectiveness of Evolocumab Used in Combination With Standard of Care At Long-term in Chinese Patients With Established Atherosclerotic Cardiovascular Disease

A Comparative Study to Evaluate the Effect of Treatment With Evolocumab in Combination With SOC, Compared With SOC Alone, on the Risk for Major Cardiovascular Events in Chinese Patients With Established ASCVD

STUDY DESIGN:



STUDY PURPOSE:

To evaluate the effectiveness of evolocumab in combination with SOC, compared with SOC alone, on the risk for CV death, MI, stroke, hospitalization for UA, or coronary revascularization, whichever occurs first, in patients with established ASCVD

PRIMARY OUTCOMES:

- Time to CV death, MI, hospitalization for unstable angina, stroke, or coronary revascularization, whichever occurs first

KEY SECONDARY OUTCOMES

- Baseline characteristics (ie, demographics, medical history, prior and concurrent LLT)
- Time to CV death, MI, or stroke, whichever occurs first
- Change and percentage change in LDL-C from baseline to follow-up
- AEs and ADRs

KEY EXCLUSION CRITERIA:*

- Stroke within the past month
- Past hemorrhagic stroke
- Stroke due to thromboembolic event (ie, atrial fibrillation patient without appropriate anticoagulation)
- NYHA Class III or IV or last known LVEF < 30%
- Any prior use of any PCSK9i within the past 24 weeks

*Not inclusive of all key exclusion criteria.
AE = adverse event; ADR = adverse drug reaction; ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering treatment; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor; PAD = peripheral arterial disease; SOC = standard of care; TG = triglycerides; UA = unstable angina.
Amgen Data on File; [2022].

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Olpasiran (AMG 890)

siRNA

Under investigation for the treatment of atherosclerotic cardiovascular disease[1]

RNA interference therapy designed to reduce production of apolipoprotein(a), a key component of Lp(a)[2]

Ongoing trial

siRNA = small interfering RNA.

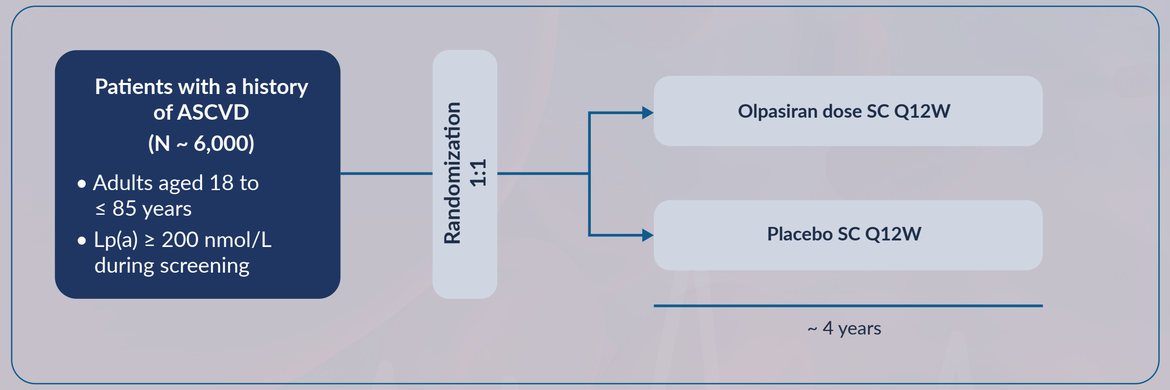
1. Amgen Pipeline. www.amgenpipeline.com/pipeline. Accessed September 11, 2023. 2. Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.

Olpasiran (AMG 890) Phase 3 Cardiovascular Outcomes Trial

OCEAN(a)-Outcomes Olpasiran Trials of Cardiovascular Events And LipoproteiN(a) Reduction (OCEAN(a)) - Outcomes Trial

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study Assessing the Impact of Olpasiran on Major CV Events in Participants With ASCVD and Elevated Lp(a)

PHASE 3 STUDY DESIGN:



STUDY PURPOSE:

To compare the effect of treatment with olpasiran to that of placebo on the risk of CHD death, MI, or urgent coronary revascularization in participants with ASCVD and elevated Lp(a)

ADDITIONAL INFORMATION:

www.amgentrials.com (Protocol number: 20180244)
www.clinicaltrials.gov (Identifier: NCT05581303)

Olpasiran is an investigational drug. Efficacy and safety have not been established.

PRIMARY OUTCOME MEASURES:

- Time to first CHD death, MI, or urgent coronary revascularization

SECONDARY OUTCOME MEASURES:

- Time to first CV death, MI, or ischemic stroke
- Time to first CV death, MI, urgent coronary revascularization, or ischemic stroke
- Percent change in Lp(a) from baseline to week 48
- Time to MI
- Time to first CHD death or MI
- Time to urgent coronary revascularization
- Time to coronary revascularization
- Time to CHD death
- Time to CV death
- Time to death from any cause
- Time to ischemic stroke

KEY INCLUSION CRITERIA:

- Adults aged 18 to ≤ 85 years
- History of ASCVD (MI [presumed type 1 event due to plaque rupture/erosion] and/or coronary revascularization with PCI and ≥ 1 additional risk factor)
- Lp(a) ≥ 200 nmol/L during screening

KEY EXCLUSION CRITERIA:

- Severe renal dysfunction
- AST or ALT > 3 x upper limit of normal, or TBL > 2 x upper limit of normal during screening
- History of hemorrhagic stroke
- History of major bleeding disorder
- Planned cardiac surgery or arterial revascularization
- Severe heart failure
- Current, recent, or planned lipoprotein apheresis
- Previously received RNA therapy specifically targeting Lp(a)

ALT = alanine aminotransferase; ASCVD = atherosclerotic cardiovascular disease; AST = aspartate aminotransferase; CHD = coronary heart disease; CV = cardiovascular; Lp(a) = lipoprotein(a); MI = myocardial infarction; PCI = percutaneous coronary intervention; Q12W = every 12 weeks; RNA = ribonucleic acid; SC = subcutaneous; SoC = standard of care; TBL = total bilirubin.

Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.

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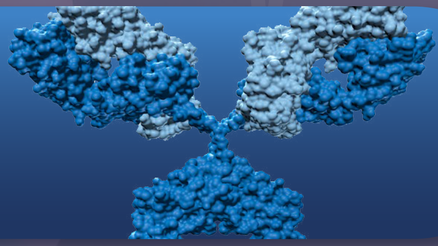
Obesity

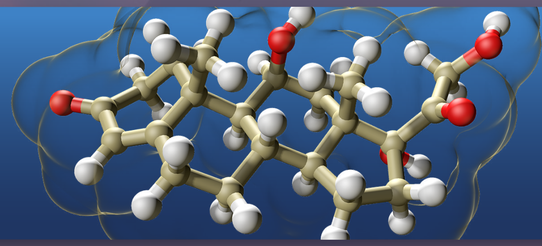
Maridebart Cafraglutide (AMG 133)

Antibody-peptide conjugate



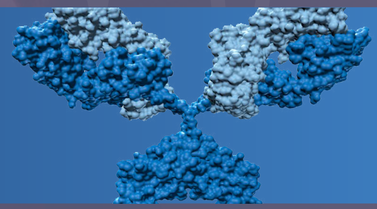
AMG 786

Small molecule



Maridebart Cafraglutide (AMG 133)

Antibody-peptide conjugate



Under investigation for the treatment of obesity[1,2]

Gastric inhibitory polypeptide receptor (GIPR) antagonist and glucagon-like peptide 1 (GLP-1) receptor agonist[1]

Ongoing trial

1. Amgen Pipeline. www.amgenpipeline.com/pipeline. Accessed September 11, 2023. 2. Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.

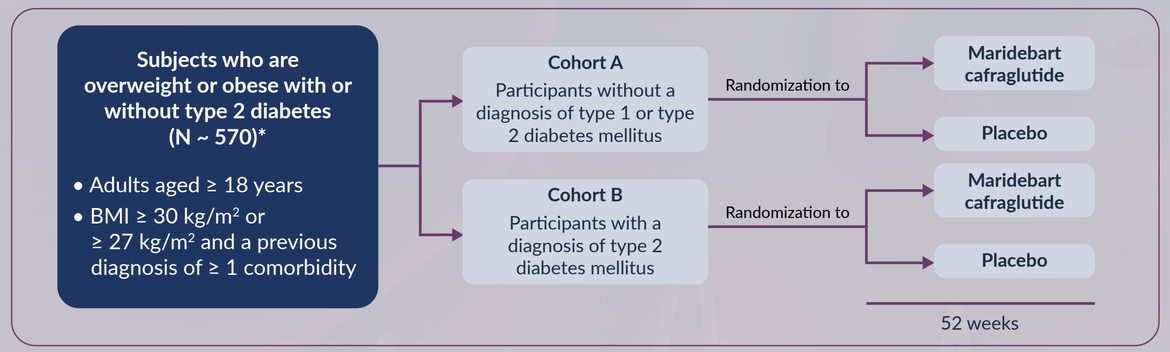
Maridebart Cafraglutide (AMG 133) Phase 2 Dose-ranging Study

Maridebart Cafraglutide

Dose-ranging Study of Maridebart Cafraglutide in Adult Participants With Overweight or Obesity, With or Without Type 2 Diabetes Mellitus

A Phase 2 Randomized, Placebo-controlled, Double-blind, Dose-ranging Study to Evaluate the Efficacy, Safety and Tolerability of Maridebart Cafraglutide in Adult Subjects With Overweight or Obesity, With or Without Type 2 Diabetes Mellitus

PHASE 2 STUDY DESIGN:



STUDY PURPOSE:

To compare and assess the dose response of 3 selected doses of maridebart cafraglutide compared with placebo, on inducing and maintaining weight loss from baseline at week 52 in participants with overweight or obesity without diabetes mellitus (cohort A) and in participants with overweight or obesity with diabetes mellitus (cohort B)

ADDITIONAL INFORMATION:

www.amgentrials.com (Protocol number: 20190218)
www.clinicaltrials.gov (Identifier: NCT05669599)

Maridebart cafraglutide is an investigational drug. Efficacy and safety have not been established.

PRIMARY ENDPOINT:

- Percent change from baseline to week 52 in body weight

KEY SECONDARY ENDPOINTS:

- Percentage of participants achieving ≥ 5%, ≥ 10%, ≥ 15%, and ≥ 20% reduction in body weight from baseline at week 52
- Changes in HbA1c, fasting serum insulin and plasma glucose levels, HOMA2-IR, HOMA2-%B, waist circumference, body weight, SBP, DBP, fat mass using DEXA†, lean body mass using DEXA†, and BMI from baseline to week 52
- Percent changes in hs-CRP, LDL-C, HDL-C, total cholesterol, non-HDL-C, VLDL-C, FFA, and triglycerides from baseline to week 52
- AUC and C_{max} up to week 64

KEY INCLUSION CRITERIA:

- Age ≥ 18 years
- BMI ≥ 30 kg/m², or ≥ 27 kg/m² and previous diagnosis with at least one of the following comorbidities: hypertension, dyslipidemia, obstructive sleep apnea, CVD
- History of ≥ 1 unsuccessful dietary effort to lose body weight
- For participants in cohort B only, HbA1c ≥ 7% and ≤ 10% [(53 to 86mmol/mol)]‡

KEY EXCLUSION CRITERIA:

- Change in body weight > 5 kg within 3 months prior to screening
- Obesity induced by other endocrinologic disorders
- History of major depressive disorder within the last 2 years
- History of pancreatitis, family or personal history of medullary thyroid carcinoma, MEN-2, or other major psychiatric disorder or suicide attempt

*Anticipated participants at enrollment; †Analyzed in a subset of participants; ‡For Cohort B only at screening with an established diagnosis of type 2 diabetes mellitus for ≥ 180 days prior to screening and either treated with diet and exercise alone or on stable (≥ 90 days prior to screening) treatment with metformin, a sulfonylurea, or an SGLT2 inhibitor as monotherapy or combination therapy, per approved local label.
AUC = area under the concentration-time curve; BMI = body mass index; C_{max} = maximum observed plasma concentration; CVD = cardiovascular disease; DBP = diastolic blood pressure; DEXA = dual-energy X-ray absorptiometry; FFA = free fatty acids; HbA1c = glycated hemoglobin; HDL-C = high-density lipoprotein cholesterol; HOMA2-%B = homeostasis model assessment for steady state beta cell function; HOMA2-IR = homeostasis model assessment for insulin resistance; hs-CRP = high-sensitivity C-reactive protein; LDL-C = low-density lipoprotein cholesterol; MEN-2 = multiple endocrine neoplasia syndrome type 2; SBP = systolic blood pressure; SGLT2 = sodium glucose co-transporter-2; VLDL-C = very-low-density lipoprotein cholesterol.
Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.

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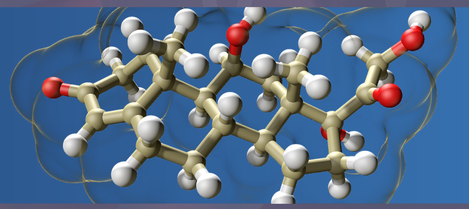
AMG 786

Small molecule



Under investigation for the treatment of obesity[1]

Ongoing trial

1. Amgen Pipeline. www.amgenpipeline.com/pipeline. Accessed September 11, 2023.

AMG 786 Phase 1 Single and Multiple Ascending Dose Study

AMG 786

A Phase 1, Randomized, Double-blind, Placebo-controlled, Single and Multiple Ascending Dose Study in Healthy Subjects and Subjects With Obesity

A Phase 1, Randomized, Double-blind, Placebo-controlled, Single and Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AMG 786 in Healthy Subjects and Subjects With Obesity

PHASE 1 STUDY DESIGN:

Healthy subjects and subjects with obesity (N ~ 72)

- Adults aged 18-65 years
- BMI 18 to < 25 kg/m^2 for healthy subjects and ≥ 25 to ≤ 32 kg/m^2 for otherwise healthy subjects with obesity

PART A

Single ascending dose cohorts

Subjects in 4 cohorts will receive either **AMG 786** or **placebo** in single ascending doses

Food effect cohort

Subjects will receive 1 of 2 **AMG 786** doses in 1 of 2 sequences

Sequence 1: First dose of AMG 786 on day 1 under fed conditions, followed by a 10-day washout period; second dose of AMG 786 on day 11 under fasted conditions

Sequence 2: First dose on day 1 under fasted conditions; second dose on day 11 under fed conditions

PART B

Multiple ascending dose cohorts

Subjects in 4 cohorts will receive either **AMG 786** or **placebo** in multiple ascending doses

STUDY PURPOSE:

To assess the safety and tolerability of AMG 786 as single or multiple doses in healthy subjects and subjects with obesity

ADDITIONAL INFORMATION:

www.amgentrials.com (Protocol number: 20210011)
www.clinicaltrials.gov (Identifier: NCT05406115)

AMG 786 is an investigational drug. Efficacy and safety have not been established.

PRIMARY ENDPOINT:*

- Number of subjects who experience a TEAE (any clinically significant changes in vital signs, 12-lead ECGs, and clinical laboratory tests)

KEY SECONDARY ENDPOINTS:*

- C_{max} of AMG 786 and metabolite M5
- T_{max} of AMG 786 and metabolite M5
- AUC of AMG 786 and metabolite M5

KEY INCLUSION CRITERIA:

- Adults aged 18–65 years
- BMI 18 to < 25kg/m^2 for healthy subjects and ≥ 25 to ≤ 32 kg/m^2 for otherwise healthy subjects with obesity
- Stable body weight prior to screening
- Males; females of non-childbearing potential

KEY EXCLUSION CRITERIA:

- Malignancy, except nonmelanoma skin cancers and cervical or breast ductal carcinoma in situ, within the last 5 years
- Triglycerides ≥ 5.65 mmol/L (ie, 500 mg/dL) at screening
- History or clinical evidence of diabetes mellitus, including fasting glucose level ≥ 125 mg/dL (ie, 6.9 mmol/L) and/or HbA1c ≥ 6.5%
- Untreated or uncontrolled hypothyroidism/hyperthyroidism defined as TSH values outside the normal range
- Obesity induced by other endocrine disorders (eg, Cushing's syndrome)
- Systolic blood pressure ≥ 150 mm Hg or diastolic blood pressure ≥ 90 mm Hg at screening and on day −1

*Day 1 through end of study (approximately 40 days).
AUC = area under the concentration-time curve; BMI = body mass index; C_{max} = maximum observed plasma concentration; ECG = electrocardiogram; HbA1c = glycated hemoglobin; TEAE = treatment-emergent adverse event; T_{max} = time to maximum observed plasma concentration; TSH = thyroid-stimulating hormone.

Clinicaltrials.Gov. www.clinicaltrials.gov. Accessed September 11, 2023.

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