AMGEN'S CARDIOVASCULAR CLINICAL TRIALS
Learn About Active Studies

Heart Failure

Atherosclerotic Cardiovascular Disease (ASCVD)

Scan to explore AMGEN pipeline
Scan to become an investigator site

USA-CCF-80056
Omecamtiv Mecarbil

PHASE 3

Selective activator of cardiac myosin under investigation for the treatment of chronic heart failure

Being developed by Amgen in collaboration with Cytokinetics, Inc. and in collaboration with Servier for certain territories.


GALACTIC-HF
Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure

METEORIC-HF
Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure

Ongoing Trials
Omecamtiv Mecarbil is being investigated by Amgen in collaboration with Cytokinetics and Servier. Efficacy and safety have not been established.

Omecamtiv Mecarbil Phase 3 Study

Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure

Amgen Clinical Study: 20110203

GALACTIC-HF

NCT Clinical Study: 02929329

A Double-Blind, Randomized, Placebo-Controlled, Multicenter Study to Assess the Efficacy and Safety of Omecamtiv Mecarbil on Mortality and Morbidity in Subjects With Chronic Heart Failure With Reduced Ejection Fraction

PHASE 3 STUDY DESIGN:

Chronic HFrEF subjects currently hospitalized with a primary reason of heart failure OR one of the following events within 1 year to screening:
1) Hospitalization with primary reason of HF
2) Urgent visit to ED with primary reason of HF

Omecamtiv Mecarbil + SoC
PO BID for up to 208 weeks*

Placebo + SoC

Screening
Randomization
End of Study

STUDY PURPOSE:
To determine if treatment with omecamtiv mecarbil when added to standard of care (SoC) is well tolerated and superior to placebo and SoC in reducing the risk of cardiovascular (CV) death or heart failure (HF) events in subjects with chronic HF with reduced ejection fraction

PHASE 3 STUDY DESIGN:

BID = twice a day; ED = emergency department; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; PO = orally; SoC = standard of care.
*Dose level determined by periodic blood testing.

STUDY PURPOSE:
To determine if treatment with omecamtiv mecarbil when added to standard of care (SoC) is well tolerated and superior to placebo and SoC in reducing the risk of cardiovascular (CV) death or heart failure (HF) events in subjects with chronic HF with reduced ejection fraction

PRIMARY ENDPOINT:
• Time to CV death or first HF event

SECONDARY ENDPOINTS:
• Time to CV death
• Changes in Kansas City Cardiomyopathy Questionnaire Total Symptom Score from baseline to week 24
• Time to first HF hospitalization
• Time to all-cause death

OTHER OUTCOME MEASURES:
• Incidence of reported adverse events
• Incidence of reported serious adverse events of ventricular arrhythmias requiring treatment
• Incidence of positively adjudicated major cardiac ischemic events

KEY INCLUSION CRITERIA:
• Men or women aged ≥ 18 to ≤ 85 years, with informed consent
• History of chronic HF (defined as requiring treatment for HF for a minimum of 30 days before randomization)
• Left ventricular ejection fraction ≤ 35% per subject’s most recent medical record, within 12 months prior to screening
• New York Heart Association class II–IV at the most recent screening assessment
• Managed with HF SoC therapies consistent with regional clinical practice guidelines according to the investigator’s judgment of subject’s clinical status
• Current hospitalization with a primary reason of heart failure OR one of the following events within 1 year to screening:
  1) Hospitalization with primary reason of HF
  2) Urgent visit to emergency department with primary reason of HF
• Elevated B-type natriuretic peptide (BNP) or N-terminal pro-BNP

KEY EXCLUSION CRITERIA:
• Currently receiving treatment in another investigational device or drug study, or < 30 days since ending treatment on another investigational device or drug study(ies). Participation in other investigational procedures while participating in this study is not allowed
• Malignancy within 5 years prior to randomization with the following exceptions: localized basal or squamous cell carcinoma of the skin, cervical intraepithelial neoplasia, stage 1 prostate carcinoma, or breast ductal carcinoma in situ
• Known sensitivity to any of the products or components to be administered during testing
• Other exclusion criteria may apply

ADDITIONAL INFORMATION:
www.amgentrials.com (Protocol Number: 20110203)
www.clinicaltrials.gov (Identifier: 02929329)

Omecamtiv mecarbil is being investigated by Amgen in collaboration with Cytokinetics and Servier. Efficacy and safety have not been established.
**Omecamtiv Mecarbil Phase 3 Study**

**Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure**

Study to Assess the Effect of Omecamtiv Mecarbil on Exercise Capacity in Subjects With Heart Failure With Reduced Ejection Fraction and Decreased Exercise Tolerance

Cytokinetics Clinical Study: CY 1031

NCT Clinical Study: 03759392

**PHASE 3 STUDY DESIGN:**

A Double-Blind, Randomized, Placebo-controlled, Multicenter Study to Assess the Effect of Omecamtiv Mecarbil on Exercise Capacity in Subjects with Heart Failure With Reduced Ejection Fraction and Decreased Exercise Tolerance

**PRIMARY ENDPOINT:**

- Change in peak oxygen uptake (VO2) CPET from baseline to week 20

**SECONDARY ENDPOINTS:**

- Change in exercise capacity, as measured by the change in total workload during CPET from baseline to week 20
- Change in ventilatory efficiency, as measured by the change in Ventilation (VE)/Carbon dioxide output (VCO2) slope during CPET from baseline to Week 20
- Change in the average daily activity units measured over a 2-week period from baseline (Week -2 to Day 1) to Week 18-20

**KEY INCLUSION CRITERIA:**

- Men or women aged ≥ 18 to ≤ 85 years of age
- History of chronic HF, defined as requiring continuous treatment with medications for HF for a minimum of 3 months before screening
- New York Heart Association (NYHA) class II or III at screening
- Left ventricular ejection fraction ≤ 35%
- On maximally tolerated HF SoC therapies consistent with regional clinical practice guidelines, if not contraindicated and according to investigator judgement of the subject’s clinical status. Beta blocker dose must be stable for 30 days prior to randomization
- N-terminal (NT)-proBNP level ≥ 200pg/mL
- Peak VO2 ≤ 75% of the predicted normal value with respiratory exchange ratio (RER) ≥ 1.05 on a screening CPET, confirmed by a CPET core laboratory

**KEY EXCLUSION CRITERIA:**

- Paroxysmal atrial fibrillation or flutter documented within the previous 6 months, direct-current (DC) cardioversion or ablation procedure for atrial fibrillation within 6 months, or plan to attempt to restore sinus rhythm within 6 months of randomization. Subjects with persistent atrial fibrillation and no sinus rhythm documented in the prior 6 months are permitted
- Ongoing or planned enrollment in cardiac rehabilitation
- Major medical event or procedure within 3 months prior to randomization, including: hospitalization, surgery, renal replacement therapy or cardiac procedure. This includes episodes of decompensated HF that require IV HF treatment
- Chronotropic incompetence (including inadequate pacemaker rate response) during CPET at screening, defined as a maximum heart rate <60% of the maximum predicted heart rate
- Other exclusion criteria may apply

**ADDITIONAL INFORMATION:**

- Omecamtiv mecarbil is being investigated by Amgen in collaboration with Cytokinetics and Servier. Efficacy and safety have not been established.

- [www.amgentrials.com](http://www.amgentrials.com) (Study ID: CY 1031)

- [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (Identifier: 03759392)

Atherosclerotic Cardiovascular Disease (ASCVD)

Dyslipidemia

Evolocumab

Ongoing Trials

Phase 3

Open Label Extension Studies

Registries

AMG 890 Lp(a) Inhibitor

PHASE 1

mAb = monoclonal antibody; Lp(a) = lipoprotein(a)
Atherosclerotic Cardiovascular Disease (ASCVD)

Dyslipidemia

Evolocumab

- Ongoing Phase 3 & 4 and Open Label Extension clinical development¹,²
- Evolocumab is a human monoclonal IgG2 directed against human PCSK9³

PCSK9 = proprotein convertase subtilisin/kexin type 9

**Investigational trial for evolocumab in pediatric subjects**

### HAUSER

**Trial Assessing Efficacy, Safety and Tolerability of PCSK9 Inhibition in Pediatric Subjects With Genetic LDL Disorders (HAUSER-RCT)**

**Amgen Clinical Study: 20120123**

**NCT Clinical Study: 02392559**

**Double-blind, Randomized, Multicenter, Placebo-Controlled Study to Characterize the Efficacy, Safety, and Tolerability of 24 Weeks of Evolocumab for LDL-C Reduction in Pediatric Subjects 10 to 17 Years of Age With HeFH**

**PHASE 3 STUDY DESIGN:**

- **Patients With HeFH (N = ~ 150)**
  - Male or female ≥ 10 to ≤ 17 years of age
  - On an approved statin with stable optimized dose for ≥ 4 weeks
  - Other lipid-lowering therapy stable for ≥ 4 weeks (fibrates must be stable for ≥ 6 weeks)

- **Randomize**

- **Evolocumab SC QM**

- **Placebo SC QM**

- **24 Weeks**

**PURPOSE:**

A study to assess safety and efficacy of evolocumab (AMG-145) in pediatric subjects aged 10–17 years diagnosed with HeFH.

**PRIMARY ENDPOINT:**

- Percentage change from baseline in LDL-C levels at week 24

**SECONDARY ENDPOINTS:**

- Change from baseline in LDL-C levels at week 24
- Percentage change from baseline in ApoB levels at week 24
- Percentage change from baseline in TC:HDL-C ratio at week 24
- Change in ApoB:ApoA1 ratio at week 24
- Percentage change from baseline in non-HDL-C levels at week 24
- Mean percentage change from baseline in LDL-C levels at week 22 and 24

**KEY INCLUSION CRITERIA:**

- Male or female ≥ 10 to ≤ 17 years of age (before 18th birthday)
- Diagnosis of HeFH
- On an approved statin with stable optimized dose for ≥ 4 weeks
- Other lipid-lowering therapy stable for ≥ 4 weeks (fibrates must be stable for ≥ 6 weeks)
- Fasting LDL-C ≥ 130 mg/dL (3.4 mmol/L)
- Fasting triglycerides ≤ 400 mg/dL (4.5 mmol/L)

**KEY EXCLUSION CRITERIA:**

- Type 1 diabetes, or type 2 diabetes that is poorly controlled
- Uncontrolled hyperthyroidism or hypothyroidism
- CETP inhibitor in the last 12 months, or mipomersen or lomitapide in the last 5 months
- Previously received evolocumab or any other investigational therapy to inhibit PCSK9
- Lipid apheresis within the last 12 weeks prior to screening
- Homozygous familial hypercholesterolemia

**ADDITIONAL INFORMATION:**

- www.amgentrials.com (Protocol Number: 20120123)
- www.clinicaltrials.gov (Identifier: NCT02392559)

ApoA1 = apolipoprotein A1; ApoB = apolipoprotein B; CETP = cholesteryl ester transfer protein; HDL-C = high-density lipoprotein-cholesterol; HeFH = heterozygous familial hypercholesterolemia; LDL = low-density lipoprotein; LDL-C = LDL-cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9; QM = once monthly; SC = subcutaneous; TC = total cholesterol.
**Evolocumab Intracoronary Imaging Study**

**High-Resolution Assessment of Coronary Plaques in a Global Evolocumab Randomized Study**

Amgen Clinical Study: 20160184  
NCT Clinical Study: 03570697

**STUDY PURPOSE:**
Evaluate the effect of evolocumab on fibrous cap thickness in subjects with NSTE-ACS who are taking maximally tolerated statin therapy

**PHASE 3 STUDY DESIGN:**
- **Patients With Coronary Artery Disease (N ~ 150)**
  - Clinical indication for coronary angiography due to NSTE-ACS
  - Angiographic evidence of CAD in the vessel targeted for OCT
- **Randomized Assignment:**
  - Evolocumab SC QM
  - Placebo SC QM
- **50 Weeks**

**PRIMARY OUTCOME MEASURE:**
- Absolute change in minimum FCT in a matched segment of artery as determined by OCT from baseline to week 50

**SECONDARY OUTCOME MEASURES:**
- Percent change in minimum FCT in a matched segment of artery at week 50
- Absolute change in mean minimum FCT for all images assessed at week 50
- Absolute change in the maximum lipid arc in a matched segment of artery at week 50
- Absolute change in minimum FCT, maximum lipid arc, and lipid core length in lipid rich plaques† at week 50

**KEY INCLUSION CRITERIA:**
- Clinical indication for coronary angiography due NSTE-ACS
- Angiographic evidence of CAD in the vessel targeted for OCT
- Eligible LDL-C level based on current statin use
- On maximally tolerated statin therapy in accordance with local guidelines

**KEY EXCLUSION CRITERIA:**
- STEMI or left bundle branch block
- ACS likely to be caused by a non-atherosclerotic process
- Any cardiac surgery within 6 weeks prior to screening
- TG ≤ 400 mg/dL (4.5 mmol/L)
- eGFR < 30 mL/min/1.73m²
- Intolerant to statins

**ADDITIONAL INFORMATION:**
- www.amgentrials.com (Protocol Number: 20160184)
- www.clinicaltrials.gov (Identifier: 03570697)

*Note: Not all secondary endpoints listed. Additional exploratory endpoints based on IVUS. †There is no universal definition of a lipid-rich plaque as defined in the study protocol. ‡Note: Not inclusive of all criteria.

**CAD = coronary artery disease; eGFR = estimated glomerular filtration rate; FCT = fibrous cap thickness; IVUS = intravascular ultrasound; LDL-C = low-density lipoprotein cholesterol; NSTE-ACS = non-ST-elevation acute coronary syndrome; OCT = optical coherence tomography; QM = monthly; SC = subcutaneous; STEMI = ST-elevation myocardial infarction; TG = triglycerides.
Investigational trial for evolocumab in high risk patients

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 ~ 13,000)**
  - LDL-C ≥ 100 mg/dL or non-HDL-C ≥ 130 mg/dL
  - Evidence of vascular disease:
    - CAD without prior MI or CABG
    - Cerebrovascular disease without prior stroke or PAD
    - High risk diabetes mellitus
  - At least 1 additional 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

**Primary Outcome Measures** (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 Outcome Measures** (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
- MI
- Any ischemia-driven arterial revascularization

**Key Inclusion Criteria**:
- (All 4 needed)
  - Adult subjects ≥ 50 (men) or ≥ 55 (women) to < 80 years of age (either sex)
  - LDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L) or non-HDL-C ≥ 130 mg/dL (≥ 3.4 mmol/L) at screening, after ≥ 4 weeks of optimized lipid-lowering therapy
  - Evidence of at least one of the following at screening:
    - Significant CAD
    - Significant atherosclerotic cerebrovascular disease
    - Significant PAD
    - Diabetes mellitus
  - At least 1 high-risk feature

**Key Exclusion Criteria**:  
- MI or stroke prior to randomization
- CABG < 3 months prior to screening
- Uncontrolled hypertension (sitting systolic BP > 180 mmHg or diastolic BP > 110 mmHg)
- Fasting triglycerides ≥ 500 mg/dL (5.7 mmol/L)
- Last measured left ventricular ejection fraction < 30% or NYHA Functional Class III/IV

**ADDITIONAL INFORMATION:**
- www.amgentrials.com (Protocol Number: 20170625)
- www.clinicaltrials.gov (Identifier: NCT03872401)

*May not be inclusive of all study details. †For adults at high cardiovascular risk without past MI or stroke and receiving optimized lipid-lowering therapy.

BP = blood pressure; 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.
**Evolocumab HoFH Study in India**

**Safety and Tolerability of Evolocumab in Indian Subjects With Homozygous Familial Hypercholesterolemia**

*Amgen Clinical Study: 20170199  NCT Clinical Study: 03403374*

**PHASE 4 STUDY DESIGN:**

Patients With HoFH (N ~ 30)

- Male or female ≥ 12 to ≤ 80 years of age
- Diagnosis of HoFH based on LDL-C, familial history and xanthoma
- On lipid-lowering therapy stable for 4 weeks

**Evolocumab 420 mg SC QM + Standard of Care**

**12 Weeks**

**STUDY PURPOSE:**

Describe the safety and tolerability of evolocumab in subjects with HoFH in India

**PRIMARY OUTCOME MEASURE:**
- Number of participants with treatment related adverse events (week 12)

**SECONDARY OUTCOME MEASURES:**
- Change in LDL-C (week 12)
- Change in ApoB (week 12)
- Change in Lp(a) (week 12)

**KEY INCLUSION CRITERIA†:**
- Male or female ≥ 12 to ≤ 80 years of age
- Diagnosis of HoFH based on LDL-C, familial history and xanthoma
- On a low-fat diet and receiving background lipid-lowering therapy
- Lipid-lowering therapy stable for 4 weeks prior to screening
- Fasting LDL-C at screening > 130 mg/dL (3.4 mmol/L)
- Fasting TG ≤ 400 mg/dL (4.5 mmol/L)

**KEY EXCLUSION CRITERIA‡:**
- Use of mipomersen or lomitapide within 6 months of screening
- Known active infection or major hematologic, renal, metabolic, GI, hepatic, or endocrine dysfunction
- Currently receiving treatment in another investigational device or drug study, or less than 30 days since ending treatment on another investigational device or drug study(ies)

**ADDITIONAL INFORMATION:**

www.amgentrials.com (Protocol Number: 20170199)  www.clinicaltrials.gov (Identifier: 03403374)

*Note: Apheresis subjects will receive evolocumab SC; subjects on apheresis may initiate 420 mg SC Q2W to correspond with their apheresis schedule to correspond with apheresis schedule. †Note: Not inclusive of all criteria.

ApoB = apolipoprotein B; HoFH = homozygous familial hypercholesterolemia; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a); QM = monthly; SC = subcutaneous; TG = triglycerides.
Study Purpose:
Learn more about evolocumab in Chinese people with primary hypercholesterolemia and mixed dyslipidemia

Primary Outcome Measures:
• Mean percent change from baseline in LDL-C at weeks 10 and 12
• Percent change from baseline in LDL-C at week 12

Secondary Outcome Measures:
• LDL-C
• Non-HDL-C
• ApoB
• Total cholesterol
• Target LDL-C < 70 mg/dL (1.8 mmol/L)

Key Inclusion Criteria:
• Adults ≥ 18 years of age
• On statin ± ezetimibe
• LDL-C ≥ 80 mg/dL (2.1 mmol/L)
• Meets at least one high/very high risk criteria*
• Does not meet high/very high risk criteria, but LDL-C ≥ 130 mg/dL (3.4 mmol/L)

Key Exclusion Criteria:
• MI, unstable angina, PCI, CABG or stroke < 3 months prior to randomization
• Last measured LVEF < 30% or NYHA Functional Class III/IV
• Uncontrolled HTN (defined as sitting SBP > 180 mmHg or DBP > 100 mmHg
• T1DM, NODM (HbA1c ≥ 6.5% or FPG ≥ 126 mg/dL) or poorly controlled (HbA1c ≥ 8.5%) T2DM

Additional Information:
www.amgentrials.com (Protocol Number: 20150172)
www.clinicaltrials.gov (Identifier: 03433755)
Real World Effectiveness of PCSK9 Inhibitors Among Patients With a Recent ASCVD Event

Cardiovascular Multidimensional Observational Investigation of the Use of PCSK9 Inhibitors

Amgen Clinical Study: 20180059

Primary Objective:
To evaluate the real-world effectiveness of PCSK9 inhibitors (PCSK9i) to reduce cardiovascular events in routine practice in a primary objective: composite of all-cause mortality, non-fatal MI, non-fatal IS.

Consented Arm:
1. Age ≥ 40 years with planned follow-up in the enrolling health system
2. One or both of the following:
   - Hospitalization for a clinical ASCVD event: acute MI, UA, IS or CLI within 12 months of enrollment
   - Coronary or peripheral revascularization including percutaneous or surgical revascularization in the past 12 months
3. One of the following:
   - Low-density lipoprotein (LDL) ≥ 70 mg/dL with no plans for immediate initiation or titration of statin therapy (Note: Subjects should not be enrolled into study during initiation/titration of statins until they have a stable LDL-C measurement > 4 weeks after their last statin change and no immediate plans for future titration)
   - Newly started on PCSK9i after the index hospitalization/procedure and prior to enrollment (but no more than 6 months prior to enrollment) with pre-PCSK9i treatment LDL-C value available and measured within 6 months of starting PCSK9i and known background LDL at any time prior to PCSK9i initiation
4. One or both of the following:
   - The presence of an additional ASCVD event: prior history of MI, CVA, or symptomatic PAD

Exclusion Criteria:
- One or more high-risk conditions: age ≥ 65 years old, HeFH, history of CABG, PCI outside of the major event, DM, HTN, chronic renal insufficiency, current smoking, HF, or elevated Lp(a) (≥ 50 mg/dL)
- Planned follow-up within the health system

Key Exclusion Criteria*:
- End stage renal disease (ESRD) or stage 5 chronic kidney disease (CKD)
- Anticipated life expectancy less than 6 months
- On a PCSK9i prior to their index event

Note: Subjects with prior PCSK9i use occurring and ending before the 12-month period prior to enrollment and before the index ASCVD event will be considered for inclusion.

EHR Arm:
- Adults age ≥ 40 years of age
- Have at least 1 inpatient or outpatient diagnosis of clinical ASCVD within 12 months prior to enrollment including CHD, ischemic cerebrovascular disease, PAD, or prior coronary or peripheral revascularization

Exclusion Criteria:
- No exclusion criteria will be applied for the EHR arm

Additional Information:
www.amgentrials.com (Protocol Number: 20180059) www.clinicaltrials.gov (Identifier: NCT04197453)
Evolocumab open label extension study

Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk Open-Label Extension (FOURIER OLE)
Amgen Clinical Study: 20130295, 20160250
NCT Clinical Study: 02867813, 03080935

Two Multicenter, Open-label Extension (OLE), Single-Arm Studies to Assess Long-term Safety of Evolocumab Therapy in Patients With Clinically Evident Cardiovascular Disease

PHASE 3 STUDY DESIGN:

Patients With Hypercholesterolemia and History of Clinically Evident CVD (N = 5,037 in US and Eastern Europe for Study 20130295)* (N = 1,600 in Western Europe for Study 20160250)**

- Completed FOURIER (20110118) study
- Age ≥ 40 to ≤ 85 years

Evolocumab 140 mg Q2W or 420 mg QM, according to patient preference

~ 5 years

PRIMARY ENDPOINT:
- Subject incidence of adverse events

SECONDARY ENDPOINTS:
- Percent change in LDL-C from baseline to each yearly visit
- Achievement of LDL-C < 40 mg/dL (1.03 mmol/L) at each yearly visit

KEY INCLUSION CRITERIA:
- Completed FOURIER (20110118) parent study while still receiving assigned investigational product
- Age ≥ 40 to ≤ 85 years

KEY EXCLUSION CRITERIA:
- Permanent discontinuation of Investigational Product during FOURIER for any reason including an adverse event or serious adverse event

ADDITIONAL INFORMATION:


CVD = cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9; Q2W = once every 2 weeks; QM = once monthly.

*Study 20130295 includes the United States, Czechia, Hungary, Poland, Russian Federation, Slovakia, and Ukraine.
**Study 20160250 includes the following European countries: Belgium, Denmark, France, Germany, Italy, Portugal, and Sweden.
Evolocumab open label extension study in pediatric subjects

HAUSER

Open Label Study to Evaluate Safety, Tolerability and Efficacy of Evolocumab in Pediatric Subjects With Heterozygous Familial Hypercholesterolemia or Homozygous Familial Hypercholesterolemia (HAUSER-OLE)

Ammgen Clinical Study: 20120124

NCT Clinical Study: 02624869

PHASE 3 STUDY DESIGN:

Pediatric patients with HeFH or HoFH (N = 115)

Subjects with HeFH

• Completed study 20120123

Subjects with HoFH

• Male or female ≥ 10 to ≤ 17 years of age

• On lipid-lowering therapy stable for ≥ 4 weeks (fibrates stable for ≥ 6 weeks)

STUDY PURPOSE:

To describe the safety and tolerability of 80 weeks of evolocumab (AMG 145) when added to standard of care in pediatric subjects 10 to 17 years of age with HeFH or HoFH.

PRIMARY OUTCOME MEASURES:

• Number of participants with treatment-related adverse events as assessed by Common Terminology Criteria for Adverse Events V4.0

SECONDARY OUTCOME MEASURES:

• Percent change from baseline in LDL-C at week 80

• Percent change from baseline in non-HDL-C and ApoB at week 80

• Percent change from baseline in total cholesterol/HDL-C ratio and ApoB/ApoA1 ratio from baseline at week 80

• Change from baseline in LDL-C at week 80

• Change from baseline in steroid hormones (FSH, LH, ACTH, DHEA-S, cortisol, estradiol/testosterone [females/males, respectively]) at week 80

• Change from baseline in Carotid intima-media thickness (cIMT) at week 80

• Subject incidence of abnormal muscle enzyme and liver enzyme levels at week 80

• Change from baseline in height, weight, and pubertal development at week 24, 48 and 80

KEY EXCLUSION CRITERIA:

All Subjects:

• Currently receiving treatment in another investigational device or drug study, or less than 30 days since ending treatment on another investigational device or drug study(ies); except Study 20120123

Subjects with HoFH:

• Moderate to severe renal dysfunction

• Active liver disease or hepatic dysfunction

• CK > 3 times the ULN at screening

KEY INCLUSION CRITERIA:

Subjects with HeFH:

• Completed Study 20120123 while still on assigned investigational product and did not experience a treatment-related serious adverse event

Subjects with HoFH:

• Male or female, ≥ 10 to ≤ 17 years of age at time of enrollment

• Diagnosis of HoFH

• On a low-fat diet and receiving background lipid-lowering therapy

• Lipid-lowering therapy unchanged for ≥ 4 weeks prior to LDL-C screening; fibrates must be stable for at least 6 weeks prior to screening

• Fasting LDL-C at screening ≥ 130 mg/dL (3.4 mmol/L)

• Fasting triglycerides ≤ 400 mg/dL (4.5 mmol/L)

ADDITIONAL INFORMATION:

www.clinicaltrials.gov (Identifier: 02624869)

www.amgentrials.com (Protocol Number: 20120124)
READY TO IMPROVE UNDERSTANDING OF LOW-DENSITY LIPOPROTEIN CHOLESTEROL AND DYSLIPIDEMIA MANAGEMENT (GOULD): A REGISTRY OF HIGH CARDIOVASCULAR RISK SUBJECTS IN THE UNITED STATES

Amgen Clinical Study: 20150230

STUDY DESIGN:

Patients With Dyslipidemia and ASCVD (N = ~ 5,000)
- Male or female ≥18 to ≤99 years of age
- Established ASCVD

Prospective data collection

Cohort 1: Patients taking a PCSK9i at baseline (n = ~ 500)
- EOS (24 months)

Cohort 2: Patients with LDL-C ≥ 100 mg/dL (n = ~ 2,000)
- Up to 12 months

Cohort 3: Patients with LDL-C 70–99 mg/dL (n = ~ 2,500)

Retrospective data collection

STUDY DESIGN:

Primary Endpoint:
- LDL treatment patterns through study completion (an average of 3 years)

Secondary Endpoints:
- LDL-C levels and measurement patterns through study completion
- Subject characteristics through study completion
- Subject understanding of CV risk through study completion
- Goals of lipid management through study completion
- Attitudes toward LLT through study completion

Key Inclusion Criteria:
- Male or female ≥ 18 to ≤ 99 years of age
- Established ASCVD defined as meeting ≥ 1 of the following criteria:
  - CAD, prior history of MI, coronary or other arterial revascularization, ischemic stroke or TIA, documented PAD secondary to atherosclerosis, carotid artery stenosis; LDL-C > 69 mg/dL (except in subjects assigned to the PCSK9i cohort)
- For the cohort of ~ 500 subjects taking a PCSK9i at baseline: evidence of a current prescription for an approved PCSK9i and subject confirmation that they have taken a PCSK9i within 30 days prior to enrollment
- For the cohort of ~ 2,000 subjects with LDL-C ≥ 100 mg/dL: confirmation of LDL-C ≥ 100 mg/dL with no change in LLT for 4 weeks
- For the cohort of ~ 2,500 subjects with LDL-C 70–99 mg/dL: confirmation of LDL-C 70–99 mg/dL with no change in LLT for 4 weeks

Key Exclusion Criteria:
- Unable or unwilling to provide informed consent including but not limited to cognitive or language barriers
- Current or planned participation in an interventional clinical study involving any investigational medical device or drug treatment at the time of enrollment or in the 6 months prior to enrollment
- Life expectancy < 12 months
- Currently pregnant, breastfeeding, or planning to become pregnant

*While pregnant subjects are not eligible for the study, if a site investigator has a subject who becomes pregnant while receiving evolocumab, the investigator will be advised to Amgen’s evolocumab pregnancy registry.

ADDITIONAL INFORMATION:

ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; CV = cardiovascular; EOS = end of study; LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering treatment; MI = myocardial infarction; PAD = peripheral arterial disease; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor; TIA = transient ischemic attack.

www.amgentrials.com (Protocol Number: 20150230)

www.clinicaltrials.gov (Identifier: NCT02993120)
Registry

HEYMANS Chart Review of Evolocumab in Subjects With Hyperlipidaemia

Amgen Clinical Study: 20130296

NCT Clinical Study: 02770131

Observational Serial Chart Review of Evolocumab Use in European Subjects With Hyperlipidaemia

STUDY DESIGN:

- Initiation of evolocumab (baseline data)
- Data collected for up to 26 weeks prior to evolocumab initiation
- Data collected for up to 30 months post evolocumab initiation
- Baseline period
- Follow-up period

*Where enrollment occurred after evolocumab initiation, follow-up data between initiation and enrollment were captured retrospectively; patients were followed for up to 30 months irrespective of whether they continued to receive evolocumab.

STUDY PURPOSE:
To review clinical characteristics of patients who are prescribed evolocumab and how their treatment is managed

PRIMARY ENDPOINT:
- Description of clinical characteristics of subjects initiated on evolocumab
  - Age of initiation of evolocumab, gender, familial hypercholesterolaemia status, diabetic status, cardiovascular history, history of statin intolerance

SECONDARY ENDPOINTS:
- Describe LDL-C and other cholesterol values over time
  - Detail all cholesterol assessments recorded during the observation period (Total Cholesterol, LDL-C, HDL-C, Non-HDL-C and Triglycerides)
- Describe evolocumab dose over time in mg
- Describe use of other lipid-modifying therapies over time including Type, dose and dose frequency during the observation period
- Describe physician visits
  - Collect all primary and secondary healthcare visit dates and classify as cardiovascular and non-cardiovascular
- Describe hospitalizations from enrollment to end of study
- Describe evolocumab dose frequency over time (Q2W, QM)
- Describe evolocumab administrative device use over time including device details, personal injector, autoinjector or pre-filled syringe throughout the observation period

KEY INCLUSION CRITERIA:
- Adults ≥ 18 to ≤ 100 years of age with informed consent
- Initiated evolocumab at physicians discretion after August 1st 2015 (and received at least one dose)

KEY EXCLUSION CRITERIA:
- Enrolled in an interventional study of PCSK9 inhibitor within 12 weeks prior to initiation of evolocumab
- Received commercially available PCSK9 inhibitor within 12 weeks prior to initiation of evolocumab

ADDITIONAL INFORMATION:
www.amgentrials.com (Protocol Number: 20130296)
www.clinicaltrials.gov (Identifier: NCT02770131)

LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9.
DID YOUR PATIENT WITH HIGH CHOLESTEROL, FH*, OR ASCVD* BECOME PREGNANT?

MotherToBaby is accepting referrals for a pregnancy registry study in women exposed and not exposed to evolocumab.

MotherToBaby depends on healthcare professionals like you to provide referrals to our pregnancy studies. Our studies are observational; participants are not asked to make any changes to their healthcare routine.

Women may qualify for this study if they reside in the U.S. or Canada. We are enrolling women with hypercholesterolemia associated with FH or ASCVD who have and those who have not used evolocumab in a current or recent pregnancy.

Refer your patients by visiting MotherToBaby.org or by calling 877.311.8972 to speak directly with a member of our research team. We are available: Monday-Friday 7:30am-6pm PST.

THIS IS AN INVESTIGATIONAL STUDY OF EVOLOCUMAB SPONSORED BY AMGEN

*Familial Hypercholesterolemia (FH), Atherosclerotic Cardiovascular Disease (ASCVD)
WHO IS MOTHERTOBABY?

MotherToBaby Pregnancy Studies are conducted by the non-profit Organization of Teratology Information Specialists (OTIS), the nation’s leading authority on the safety of medications and other exposures during pregnancy and lactation, and are coordinated at the University of California, San Diego, CA.

MotherToBaby is dedicated to providing evidence-based information to mothers, healthcare professionals and the general public about medications and other exposures during pregnancy and while breastfeeding.

FOR MORE INFORMATION ABOUT MEDICATION USE OR OTHER ENVIRONMENTAL EXPOSURES IN PREGNANCY AND WHILE BREASTFEEDING:

Visit | MotherToBaby.org
Email | MotherToBaby@ucsd.edu
Call | 877.311.8972

Study Cohort Overview

**group I**
Women diagnosed with hypercholesterolemia associated with FH or ASCVD who were exposed to evolocumab during a current pregnancy.

**group II**
Women diagnosed with hypercholesterolemia associated with FH or ASCVD who were not exposed to a PCSK9 inhibitor during a current pregnancy.

**group III**
Women who have not been diagnosed with hypercholesterolemia associated with FH or ASCVD and who were not exposed to a PCSK9 inhibitor during a current pregnancy.

**group IV (case series)**
Women who were exposed to evolocumab during a current or recent pregnancy but who do not fulfill eligibility criteria for Group 1 (e.g., retrospective pregnancy report).
Amgen is sponsoring a prospective, observational study of pregnant women that have been exposed to Repatha® (evolocumab). The registry is conducted in Europe, South Africa and Australia, and enrolls patients diagnosed with Familial Hypercholesterolemia exposed to Repatha® at any point during pregnancy and/or breast-feeding. Participants are not asked to make any changes to their healthcare routine. If a site investigator/health care practitioner has a subject/patient that has, or may have, been exposed to evolocumab while pregnant or breast-feeding, they will be advised to refer the subject to Amgen’s evolocumab pregnancy registry.

To learn more about this study you can contact the Amgen Call Center:
+ 1 866 572-6436
Atherosclerotic Cardiovascular Disease (ASCVD)

AMG 890 Lp(a) Inhibitor

- RNA interference therapy designed to reduce production of apolipoprotein(a), a key component of Lp(a)
- Under investigation for the treatment of dyslipidemia

AMG 890 Phase 1 RNA Interference Therapy Study

AMG 890

Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Study of AMG 890 in Subjects With Elevated Plasma Lipoprotein(a)

Amgen Clinical Study: 20170544
NCT Clinical Study: 03626662

A Phase 1, Randomized, Double-blind, Placebo-controlled, Single Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AMG 890 in Subjects With Elevated Plasma Lipoprotein(a)

CO-PRIMARY OUTCOME MEASURES:
- Subject incidence of treatment-emergent adverse events (up to 225 days)
- Changes in vital signs, EKG and blood tests (up to 225 days)

SECONDARY OUTCOME MEASURES:
- AMG 890 pharmacokinetics (Cmax, Tmax, AUC) (up to 225 days)
- Change in plasma Lp(a) over time (up to 225 days)
- Percent change in plasma Lp(a) over time (up to 225 days)

KEY INCLUSION CRITERIA:* 
- Male or female ≥ 18 to ≤ 60 years of age
- Protocol-defined elevated plasma Lp(a) level
- BMI ≥ 18 and ≤ 32 kg/m2 at screening
- Women must be non-reproductive potential

KEY EXCLUSION CRITERIA:* 
- Currently receiving treatment in another investigational device or drug study
- Women who are breastfeeding or who plan to breastfeed while on study or through 90 days after receiving the last dose of investigational product
- History or clinical evidence of bleeding diathesis, any coagulation disorder, or peripheral neuropathy

ADDITIONAL INFORMATION: 
www.amgentrials.com (Protocol Number: 20170544) 
www.clinicaltrials.gov (Identifier: 03626662)

*Note: Not inclusive of all criteria.

AUC = area under the curve; BMI = body mass index; Cmax = maximum serum concentration; EKG = electrocardiogram; Lp(a) = lipoprotein(a); Tmax = time drug is at maximum serum concentration.

The study is investigational and efficacy and safety have not been determined