Efficacy and safety of alirocumab in high cardiovascular risk patients with inadequately controlled hypercholesterolaemia on maximally tolerated daily statin: results from the ODYSSEY COMBO II study

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Industry Relationships and Institutional Affiliations

Author	Disclosure
Christopher P. Cannon	Grants from Accumetrics, Arisaph, Astra Zeneca, Boehringer-Ingelheim, Janssen; grants and personal fees from GlaxoSmithKline, Merck, and Takeda; and consulting fees from BMS, CSL Behring, Essentialis, Lipimedix, Pfizer, Regeneron and Sanofi.
Bertrand Cariou	Received research funds from Sanofi Aventis. Consultant/advisory panel for Amgen, AstraZeneca, DebioPharm, Janssen, Eli Lilly, Genfit, Novo-Nordisk and Sanofi-Aventis.
Dirk Blom	Consultant/advisory panel for Aegerion, Amgen, AstraZeneca, MSD and Sanofi Aventis. D.B.'s institution has received payment for conducting clinical trials from Aegerion, Amgen, Eli Lilly, Novartis, and Sanofi/Regeneron. D.B. has participated in a lecture/speaker's bureau or received honoraria from Aegerion, Amgen, AstraZeneca, MSD, Pfizer, Sanofi Aventis, Servier and Unilever.
James M. McKenney	Research grants from Sanofi and Regeneron.
Christelle Lorenzato	Employee of Sanofi.
Robert Pordy	Employee of Regeneron Pharmaceuticals, Inc.
Umesh Chaudhari	Employee of Sanofi.
Helen M. Colhoun	Consultant/advisory panel for Pfizer, Sanofi Aventis, Novartis and Eli Lilly. Received research support from Roche, Pfizer, Eli Lilly, Boehringer Ingelheim, AstraZeneca and JDRF. Participated in a lecture/speaker's bureau and received honorarium from Pfizer. Shareholder in Roche.

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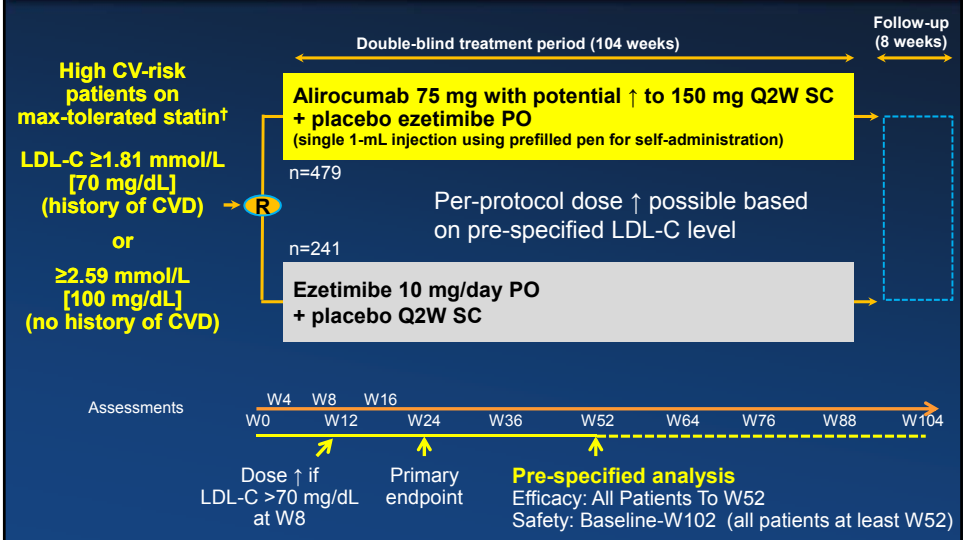
ODYSSEY COMBO II Study Design



†Other LLT not allowed. Clinicaltrials.gov identifier: NCT01644188.

Baseline Characteristics

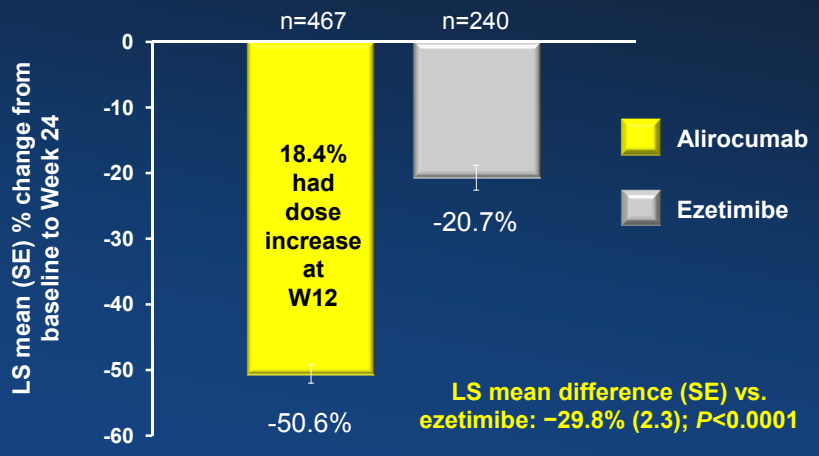
All patients on background max tolerated statin	**Alirocumab** (n=479)	**Ezetimibe** (n=241)
Age, years, mean (*SD*)	**61.7** (*9.4*)	**61.3** (*9.2*)
Male, % (n)	**75.2%** (360)	**70.5%** (170)
Race, White, % (n)	**84.3%** (404)	**85.5%** (206)
BMI, kg/m², mean (*SD*)	**30.0** (*5.4*)	**30.3** (*5.1*)
CHD history, % (n)	**91.2%** (437)	**88.0%** (212)
Hypertension, % (n)	**79.7%** (382)	**82.2%** (198)
Type 2 diabetes, % (n)	**30.3%** (145)	**31.5%** (76)
Any statin†,% (n)	**99.8%** (478)	**100%** (241)
High-intensity statin‡, % (n)	**66.8%** (320)	**66.4%** (160)
LDL-C, calculated mean (*SD*)**, mmol/L [mg/dL]**	**2.8** (*0.9*) **[109** (*37*)**]**	**2.7** (*0.9*) **[105** (*34*)**]**

†Patients should receive either rosuvastatin 20-40 mg, atorvastatin 40-80 mg daily, or simvastatin 80 mg daily unless not tolerated and/or appropriate other dose given according to the judgement of the investigator.

‡High-intensity statin: atorvastatin 40-80 mg or rosuvastatin 20-40 mg daily.

Alirocumab Significantly Reduced LDL-C from Baseline to Week 24 versus Ezetimibe

Primary Endpoint: Percent Change from Baseline to Week 24 in LDL-C
All patients on background of maximally-tolerated statin



5 Intent-to-treat (ITT) analysis

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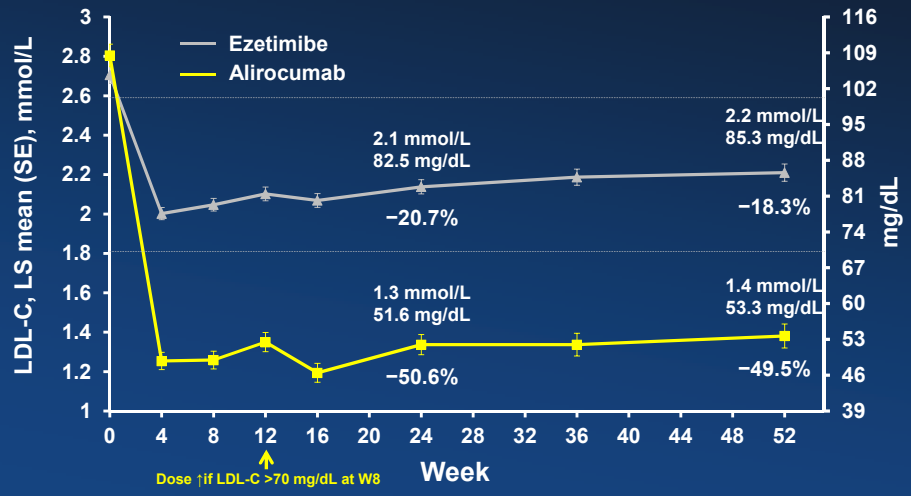
Alirocumab Maintained Consistent LDL-C Reductions over 52 Weeks

Achieved LDL-C Over Time on Background of Maximally-Tolerated Statin



6 Intent-to-treat (ITT) analysis

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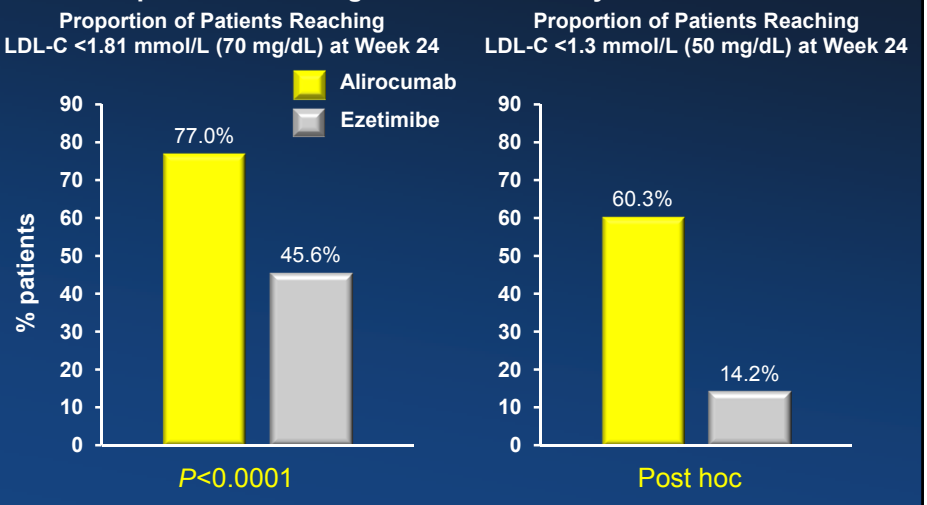
Most of These High CV-Risk Patients Receiving Alirocumab on Background Statin Achieved LDL-C Goal

All patients on background of maximally-tolerated statin



7 Intent-to-treat (ITT) analysis

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Safety Analysis (Baseline-W102)

Including All Data Collected Until Last Patient Visit at Week 52

% (n) of patients All patients on background max tolerated statin	**Alirocumab** (n=479)	**Ezetimibe** (n=241)
TEAEs	**71.2%** (341)	**67.2%** (162)
Treatment-emergent SAEs	**18.8%** (90)	**17.8%** (43)
TEAE leading to death†	**0.4%** (2)	**1.7%** (4)
TEAEs leading to discontinuation	**7.5%** (36)	**5.4%** (13)
Adverse Events of Interest		
Adjudicated CV events‡	**4.8%** (23)	**3.7%** (9)
Injection-site reactions	**2.5%** (12)	**0.8%** (2)
Neurocognitive disorders	**0.8%** (4)	**1.2%** (3)
ALT >3 x ULN	**1.7%** (8/470)	**0.4%** (1/240)
Creatine kinase >3 x ULN	**2.8%** (13/467)	**2.5%** (6/236)

†Both deaths in the alirocumab arm were due to CV events (cardiac arrest and sudden cardiac death). Of the four deaths in the ezetimibe arm, two were due to CV events (malignant lung neoplasm, suicide, defect conduction intraventricular, sudden cardiac death and sudden death – one patient was counted in two categories)

‡Adjudicated CV events include all CV AEs positively adjudicated. The adjudication categories are the following: CHD death, non-fatal MI, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalisation, congestive heart failure requiring hospitalisation, ischemia driven coronary revascularisation procedure [PCI, CABG].

Statistical analyses have not been performed.

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Safety Analysis (Baseline-W102)

TEAEs Occurring in ≥5% of Either Alirocumab or Ezetimibe Patients

% (n) of patients All patients on background max tolerated statin	**Alirocumab** (n=479)	**Ezetimibe** (n=241)
Upper respiratory tract infection	**6.5%** (31)	**5.8%** (14)
Accidental overdose†	**6.3%** (30)	**6.6%** (16)
Dizziness	**4.8%** (23)	**5.4%** (13)
Myalgia	**4.4%** (21)	**5.0%** (12)

†Accidental overdose is an event suspected by the Investigator or spontaneously notified by the patient (not based on systematic injection/capsule counts) and defined as at least twice the intended dose within the intended therapeutic interval (i.e., ≥2 injections from the double-blind treatment kit administered in <7 calendar days or ≥2 capsules from the double-blind treatment kit are administered within 1 calendar day).

Statistical analyses have not been performed.

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Conclusions

- **In this population of high CV-risk patients who had poorly controlled LDL-C on maximally-tolerated statin therapy:**
  - **LDL-C ↓ from baseline maintained with alirocumab: significantly greater ↓ vs. ezetimibe at W24, 51% vs 21% (*P*<0.0001)**
  - **Self-administered alirocumab had good compliance and was well-tolerated**
  - **This "treat-to-target" approach with alirocumab resulted in ~80% pts not requiring a dose ↑ to 150 mg at W12**
  - **77% of alirocumab pts achieved LDL-C <1.81 mmol/L (70 mg/dL) at W24**
  - **Mean achieved LDL-C levels of 1.4 mmol/L (53.3 mg/dL) at W52 with alirocumab**
  - **TEAEs similar between alirocumab and ezetimibe arms**

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Thank you to all principal investigators and national coordinators!
Canada: 4 sites
France: 4 sites
Russia: 15 sites
Hungary: 5 sites
Ukraine: 2 sites
USA: 58 sites
Denmark: 9 sites
Israel: 7 sites
South Korea: 14 sites
South Africa: 8 sites
126 sites worldwide
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