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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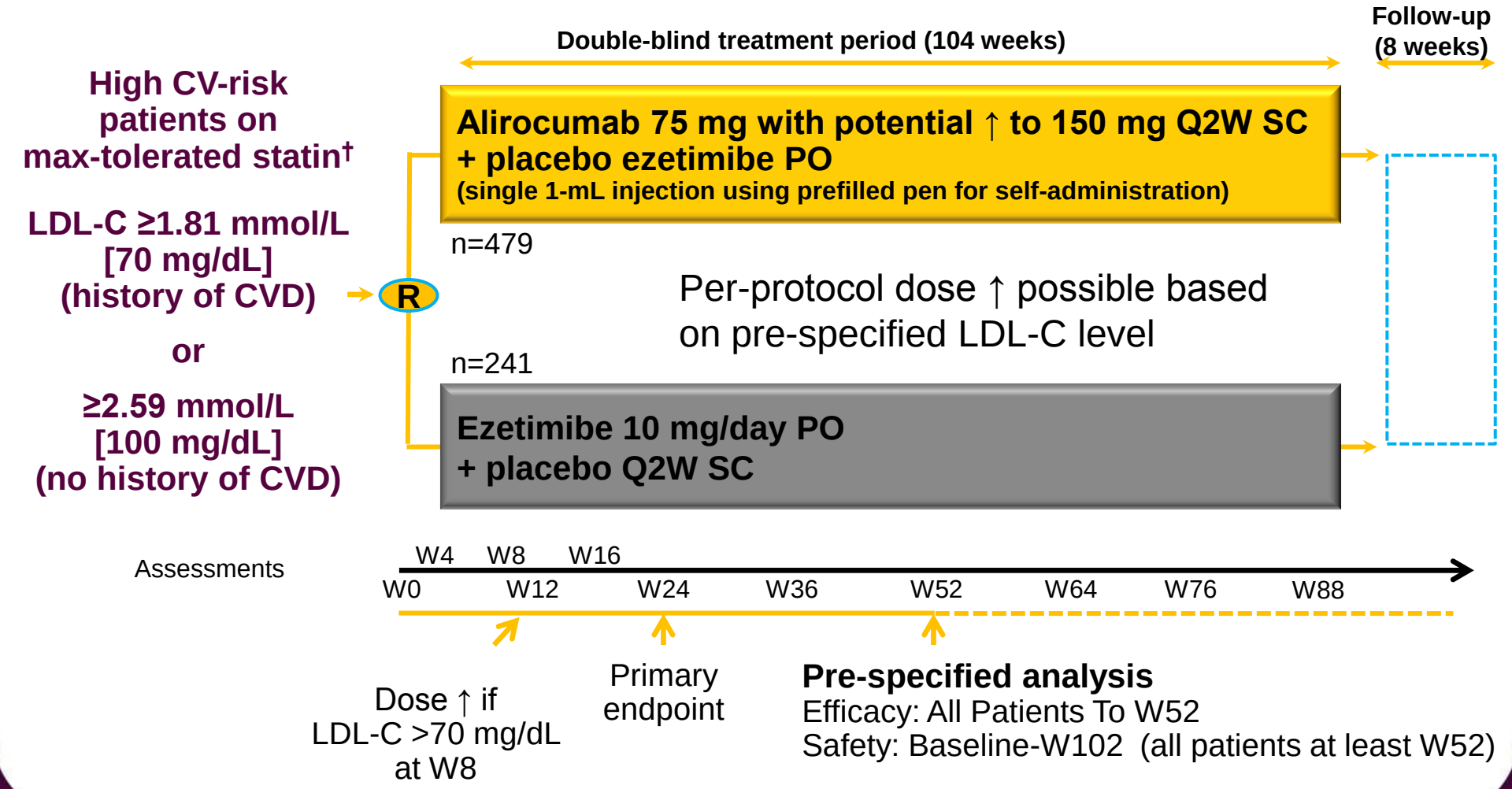
DECLARATION OF INTEREST

- Research contracts
- Consulting/Royalties/Owner/ Stockholder of a healthcare company

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.

ODYSSEY COMBO II Study Design

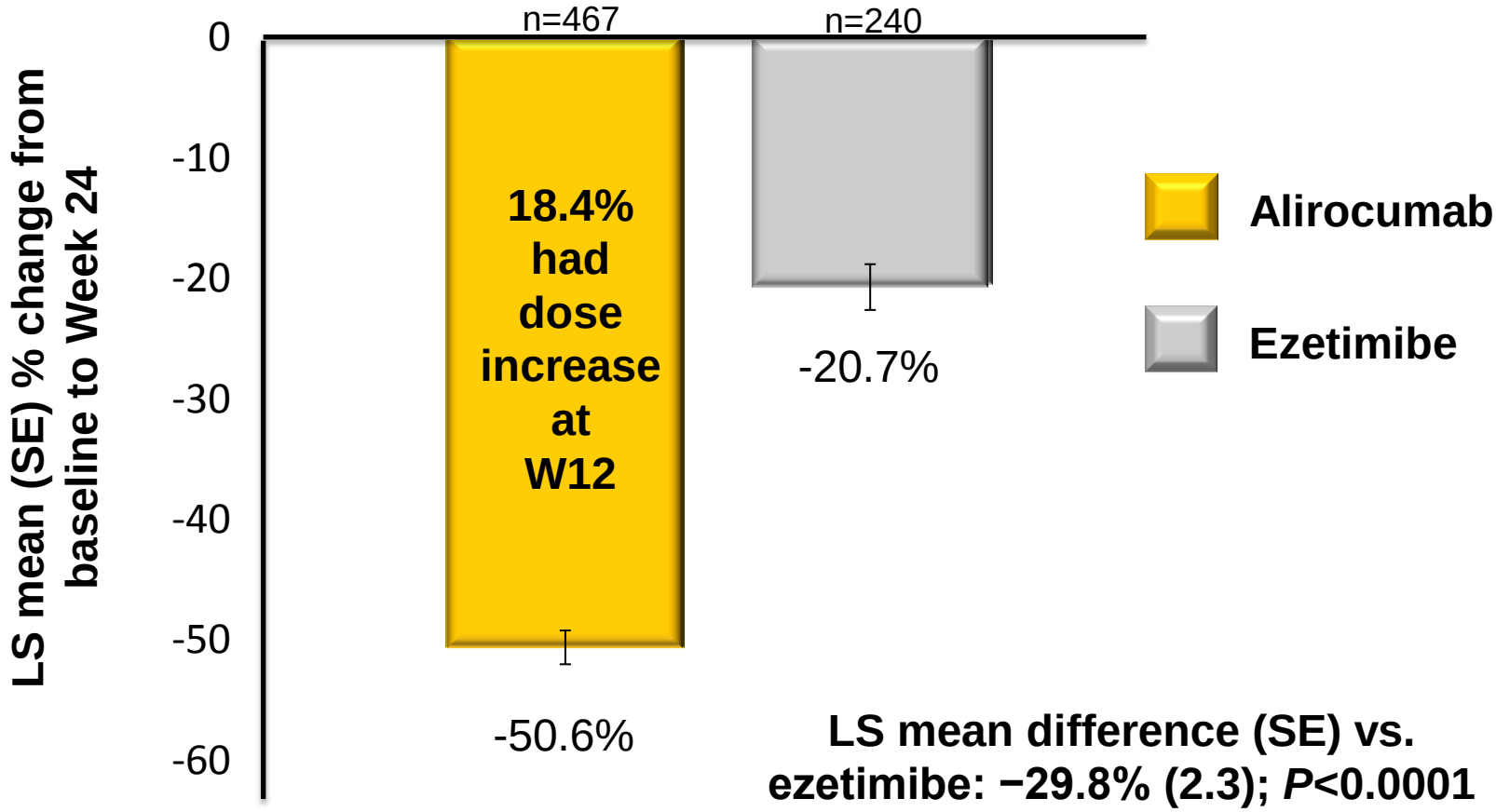


†Other LLT not allowed. Clinicaltrials.gov identifier: NCT01644188.

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

Primary Endpoint: Percent Change from Baseline to Week 24 in LDL-C

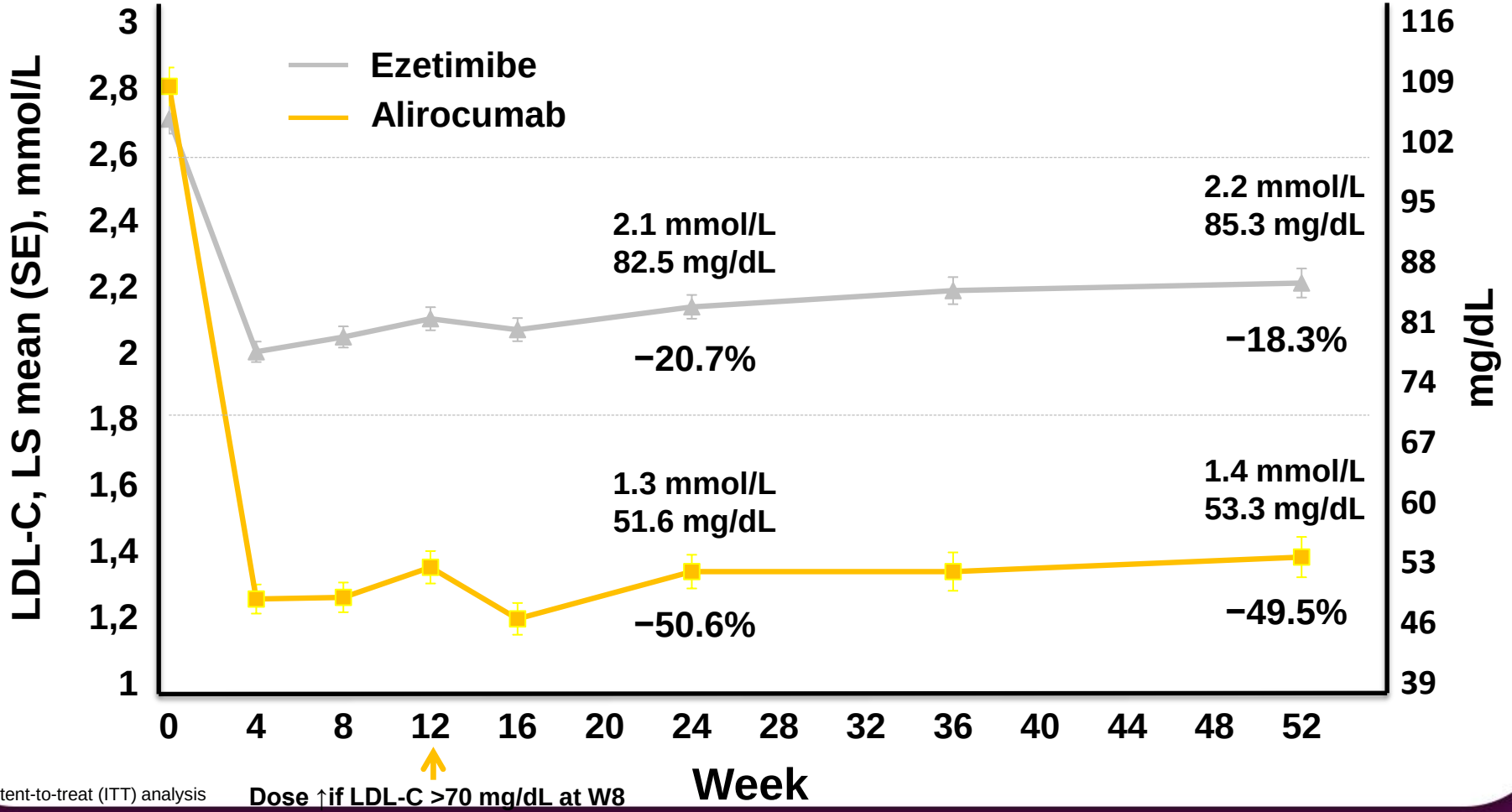
All patients on background of maximally-tolerated statin



Intent-to-treat (ITT) analysis

Alirocumab Maintained Consistent LDL-C Reductions over 52 Weeks

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



Intent-to-treat (ITT) analysis

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.

Conclusions

- High CV-risk patients often **do not reach LDL-C** goal on existing standard-of-care treatments
- In high CV-risk patients on standard-of care therapy (incl. maximum statin doses) alirocumab-treated patients experienced:
  - **51%** reduction in LDL-C levels by Week 24 (**30%** reduction vs. ezetimibe)
  - **77%** achieved LDL-C goal of <1.8 mmol/L (70 mg/dL) at Week 24
  - Approx. **80%** did not require up-titration
  - Adverse events generally comparable with ezetimibe