Efficacy and safety of alirocumab in patients with heterozygous familial hypercholesterolaemia (heFH) not adequately controlled with current lipid-lowering therapy: Results of ODYSSEY FH I and FH II studies

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Industry Relationships and Institutional Affiliations

Author	Disclosure
John J.P. Kastelein	Consultant/honoraria for Regeneron, Sanofi, Eli Lilly, Pfizer, Amgen, Isis, Genzyme, Aegerion and Esperion
Henry N. Ginsberg	Research support from Genzyme (Sanofi) and Sanofi-Regeneron, is a consultant on an advisory board for Sanofi and Regeneron and is or has been a consultant for Amarin, Amgen, AstraZeneca, BristolMyersSquibb, GlaxoSmithKline, ISIS, Kowa, Merck, Novartis, and Pfizer
Gisle Langslet	Advisory board fees from Amgen, Sanofi-Aventis and Janssen Pharmaceuticals
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Robert Dufour	Received consultancy fees from Sanofi
Dirk Blom	Consultant or on an advisory panel for Aegerion, Amgen, AstraZeneca, MSD, and Sanofi Aventis. DB's institution has received payment for conducting clinical trials from Aegerion, Amgen, Eli Lilly, Novartis, and Sanofi/Regeneron; DB has participated in a lecture/speaker's bureau or received honoraria from Aegerion, Amgen, AstraZeneca, MSD, Pfizer, Sanofi Aventis, Servier, and Unilever
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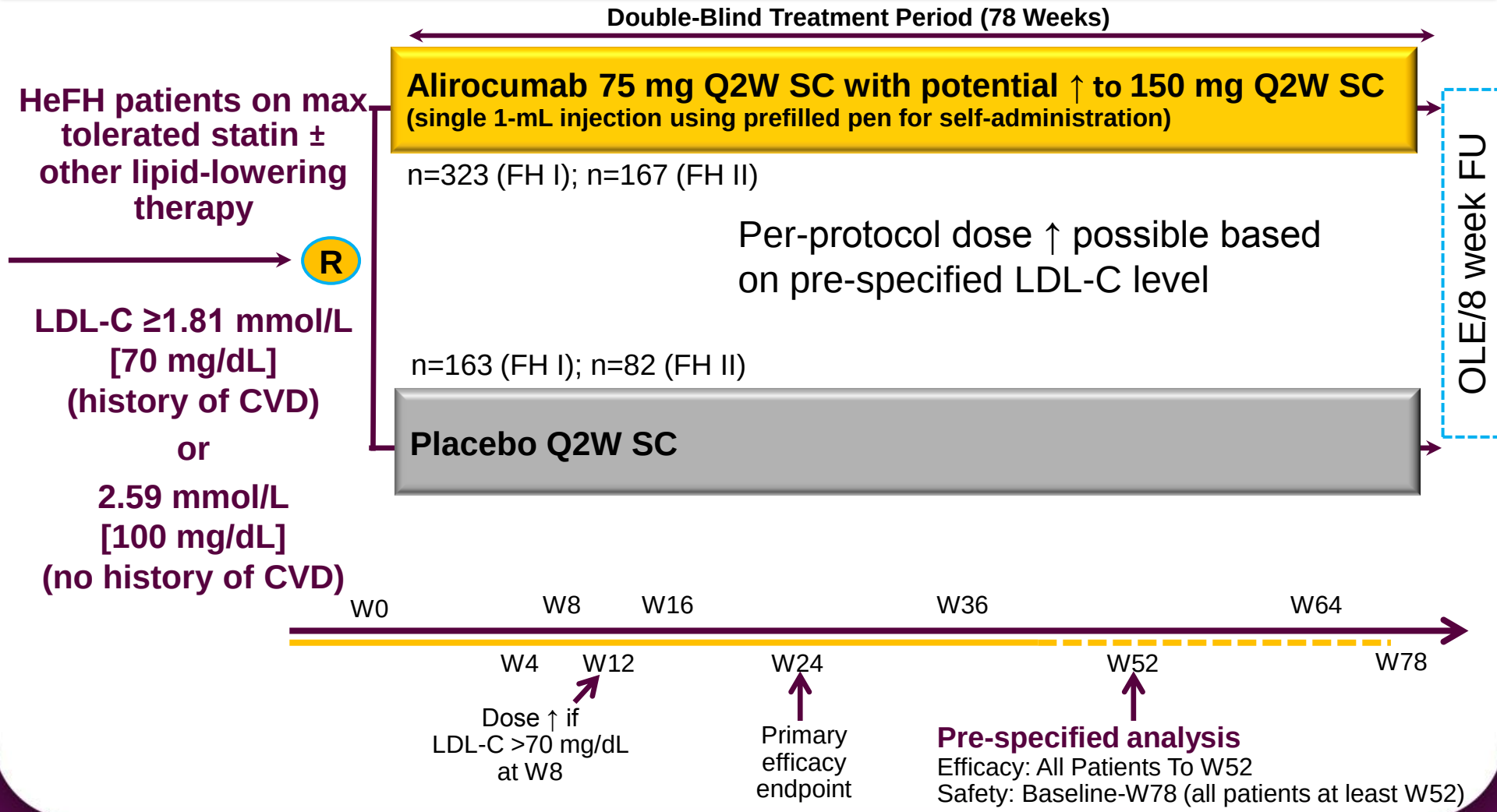
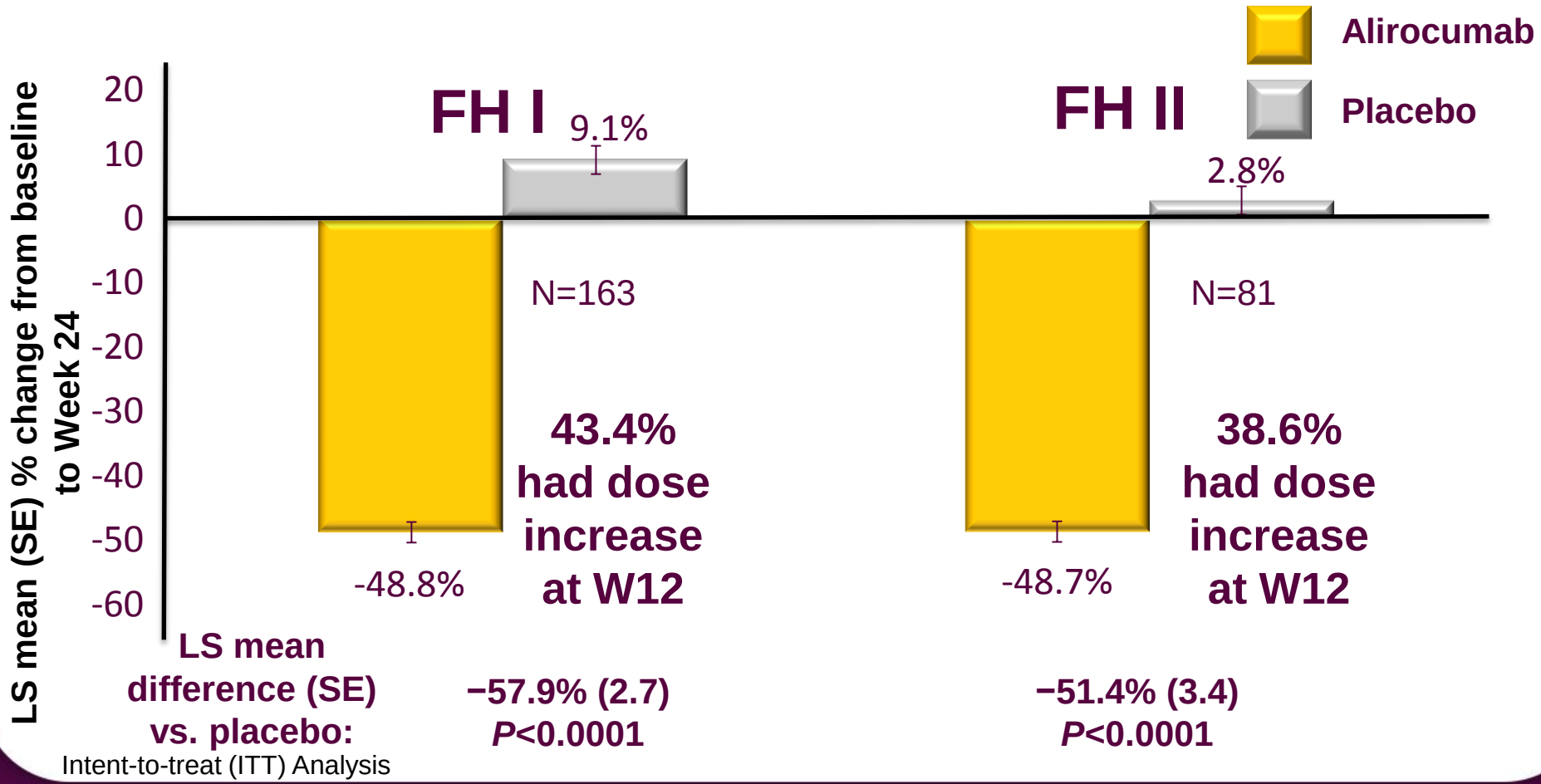
ODYSSEY FH I and FH II Study Design



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

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

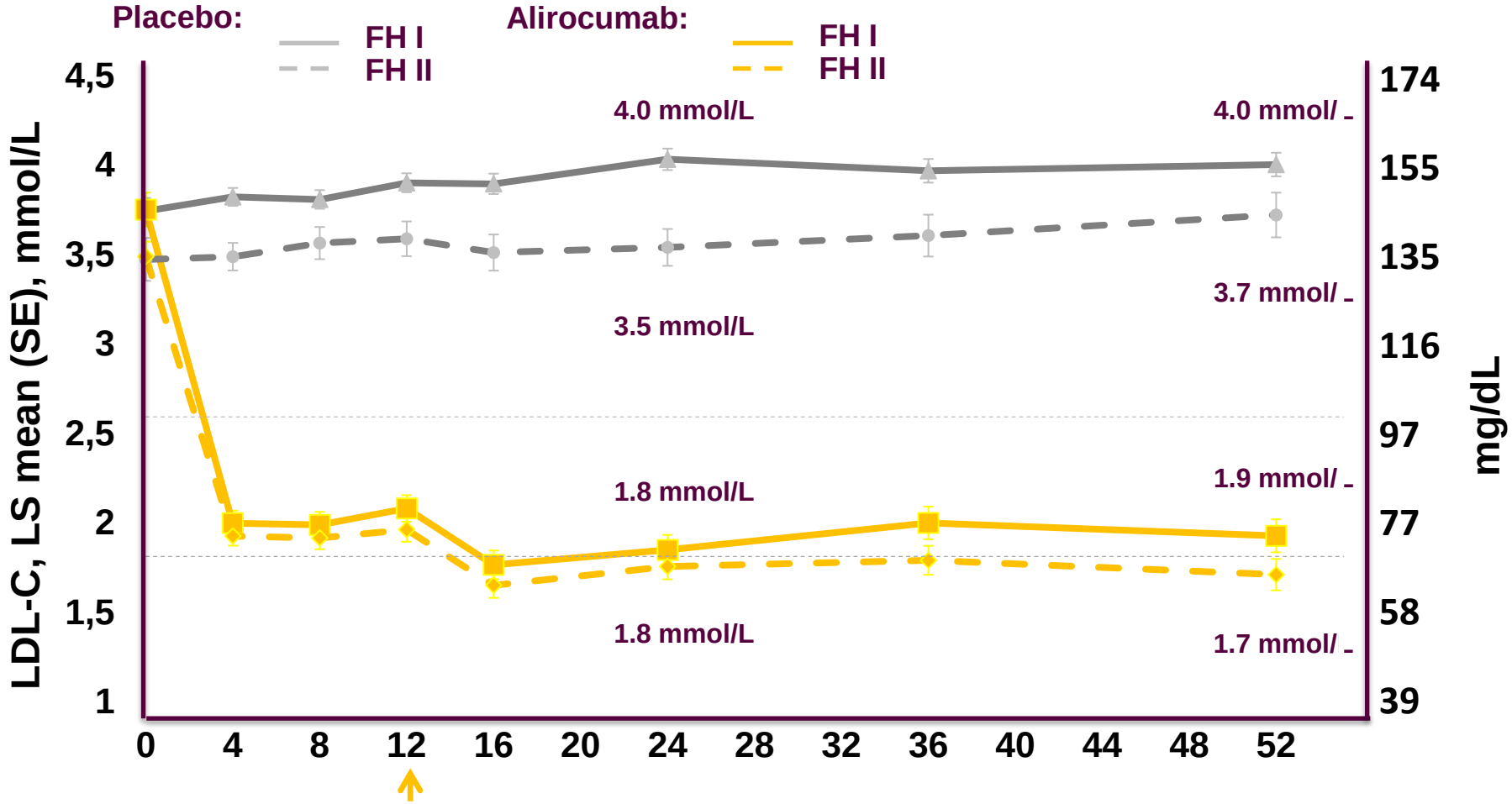
All patients on background max-tolerated statin ±other lipid-lowering therapy



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 ±Other LLT



Intent-to-treat (ITT) Analysis
LLT = lipid-lowering therapy

Safety Analysis (Pooled Data from FH I and FH II)

All Data Collected Until Last Patient Visit at Week 52

% (n) of patients All patients on background of max tolerated statin ± other lipid-lowering therapy	**Alirocumab** (N=489)	**Placebo** (N=244)
TEAEs	**74.8%** (366)	**75.4%** (184)
Treatment-emergent SAEs	**10.0%** (49)	**9.0%** (22)
TEAEs leading to death	**0.8%** (4)	**0**
TEAEs leading to discontinuation	**3.1%** (15)	**3.7%** (9)
Adverse Events of Interest		
Adjudicated CV events†	**1.6%** (8)	**1.2%** (3)
Injection-site reactions	**11.5%** (56)	**9.0%** (22)
Neurocognitive disorders	**0.2%** (1)	**1.2%** (3)
ALT >3 x ULN	**2.1%** (10/488)	**1.2%** (3/244)
Creatine kinase >3 x ULN	**3.5%** (17/483)	**6.2%** (15/243)

4 TEAE-related deaths were all in alirocumab arm, 2 due to metastatic cancer (non-small cell lung and pancreatic), 2 due to MI (1 acute, 1 sudden cardiac death)

†Adjudicated CV events include all CV AEs positively adjudicated. The adjudication categories are the following: CHD death, non-fatal MI, fatal and non-fatal ischaemic stroke, unstable angina requiring hospitalisation, congestive heart failure requiring hospitalisation, ischaemia-driven revascularisation procedure (PCI, CABG).

Statistical analyses have not been performed.

Conclusions

- HeFH is one of the most common inherited diseases, characterized by **extremely high LDL-C levels** and **premature atherosclerosis and CVD**[1]
- In the real-world, **~80% don't reach LDL-C goal** of < 2.5 mmol/L (100 mg/dL)[2]
- **Despite intensive lipid-lowering therapy, HeFH patients require new options**
  - **3.5-3.7 mmol/L** (134-145 mg/dL) average LDL-C levels at beginning of trials, even though **81-88%** on high-dose statin, **56%-67%** on ezetimibe
- In HeFH patients on standard-of care therapy (incl. maximum statin doses) alirocumab-treated patients experienced:
  - **51%-58%** lower LDL-C levels vs. placebo
  - **72%-81%** achieved their LDL-C goal
  - Adverse events generally comparable with placebo

1. Nordestgaard BG et al. Eur Heart J. 2013;34:3478–90
2. Pijlman AH et al. Atherosclerosis. 2010;209(1):189-194.