Effect of alirocumab on the frequency of lipoprotein apheresis: A randomised Phase III trial

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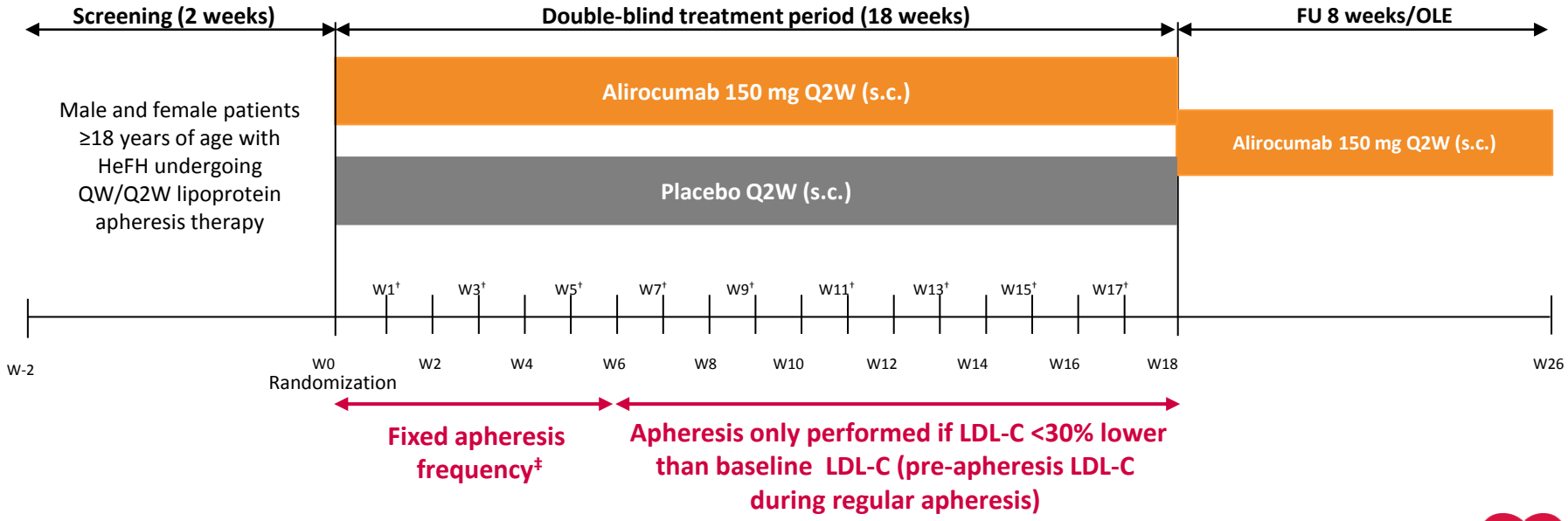
Declaration of Interest

- Regeneron
- Sanofi
- Amgen
- Duke
- Esperion
- Aegerion
- Kowa
- Ionis
- Eliaz Therapeutics
- Alexion)
- Catabasis
- Pfizer
- Novartis
- Kaneka)
- Research contracts (Genzyme
- Consulting/Royalties/Owner/ Stockholder of a healthcare company (Genzyme

Background

- Untreated heterozygous familial hypercholesterolemia (HeFH) is associated with severely elevated LDL-C levels and a high risk for premature CHD[1]
- Despite LDL-C-lowering therapy, many patients with FH do not reach their target LDL-C levels[2]
- Apheresis = Greek for 'taking away'; lipoprotein apheresis is removal of LDL-C[3,4]
- This trial was designed to clarify whether adding alirocumab could reduce or eliminate apheresis therapy

ESCAPE: Study Design



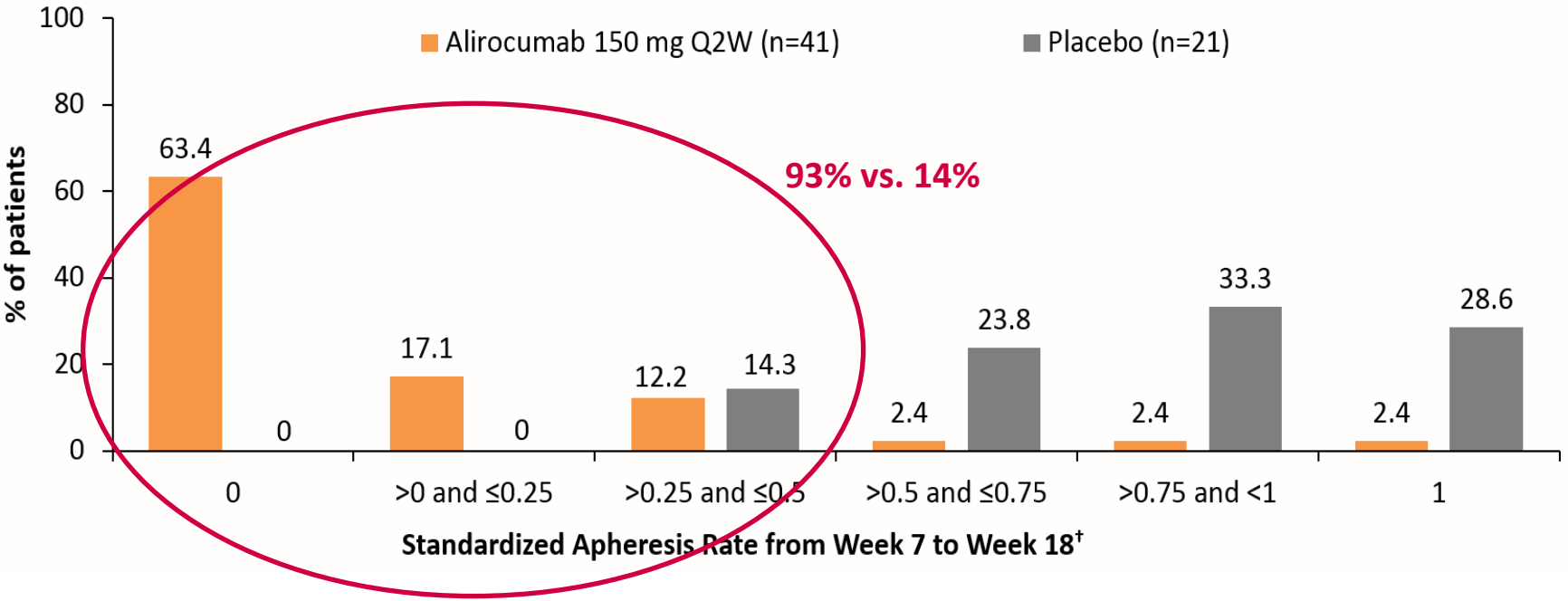
Patients with HeFH were on stable background treatment (statins, ezetimibe, etc.) and had undergone consistent lipoprotein apheresis QW for ≥4 weeks or Q2W for ≥8 weeks (14 study sites in US & Germany)

Dr. Patrick M. Moriarty

1. Ito MK et al. *J Clin Lipidol.* 2011;5:S38–S45; 2. Huijgen et al. *PLoS One*. 2010;5:e9220; CHD, coronary heart disease; FH, familial hypercholesterolemia; He, heterozygous; LDL-C, low-density lipoprotein cholesterol; LLT; lipid-lowering therapies; PCSK9, proprotein convertase subtilisin kexin type 9; Q2W, every 2 weeks; 3. Jacobson TA et al. J Clin Lipidol. 2015;9:129–169; 4. Reiner Z et al. Eur Heart J. 2011; 32:1769–1818

Standardized Apheresis Treatment Rates from Week 7–18

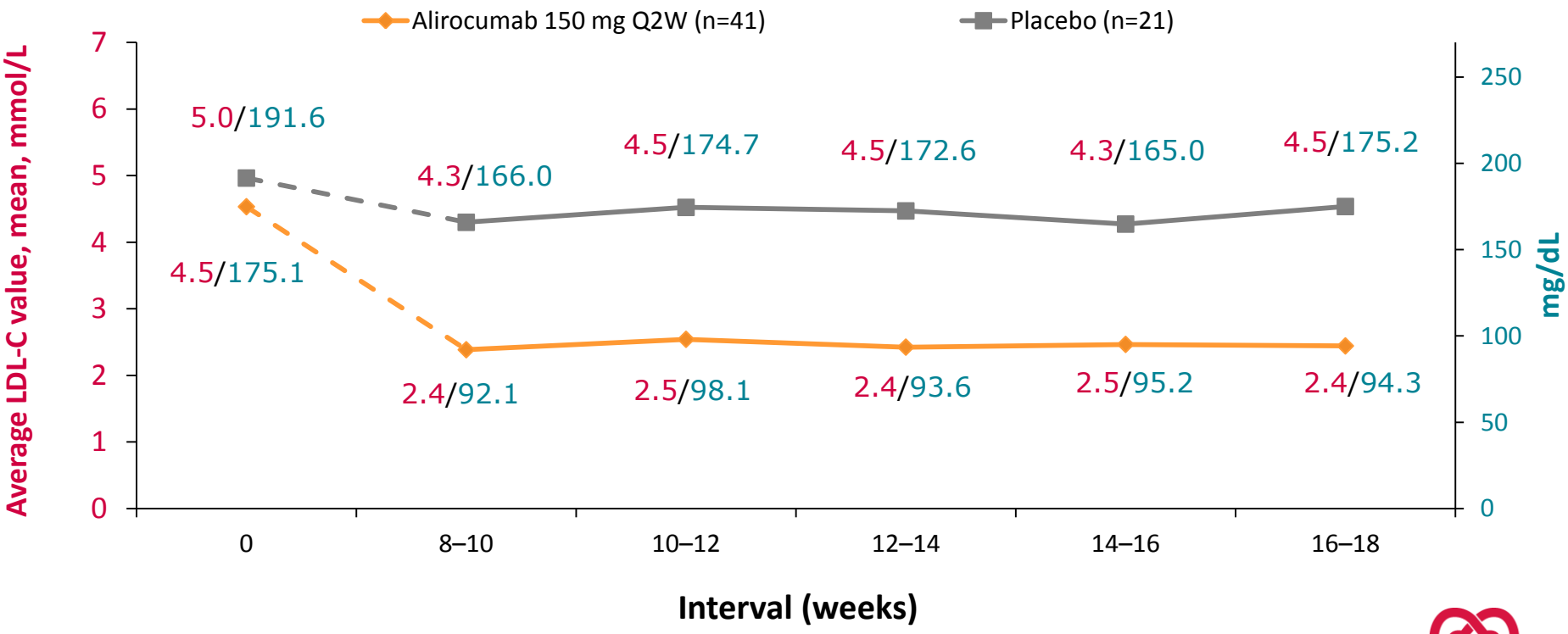
Standardised apheresis treatment rate in the period:	Weeks 7–18	Weeks 15–18
Hodges-Lehmann estimate of median treatment difference (95% CI):	0.75 (0.67 to 0.83)	0.50 (0.50 to 1.00)
p-value versus placebo:	p<0.0001	p<0.0001



†An apheresis rate of 0 indicates that the patient skipped all planned apheresis treatments and an apheresis rate of 1 indicates that the patient received all planned apheresis treatments between Week 7 and Week 18 (apheresis rate of 0.75:, the patient received 75% of planned apheresis treatments)

Time-Averaged Cholesterol Concentrations[1]

LDL-C % change from baseline (%), LS mean (SE):	Alirocumab	Placebo	p-value versus placebo
Week 6	-53.7 (2.3)	1.6 (3.1)	<0.0001
Week 18	-42.5 (4.7)	3.9 (6.3)	<0.0001



Data labels are expressed in both measurements; [1]Kroon Formula; Kroon AA et al. *Atherosclerosis*. 2000;152:519–526. LS, least squares

Safety: Treatment-Emergent Adverse Events

% (n)	Alirocumab 150 mg Q2W (n=41)	Placebo (n=21)
Any TEAE	**75.6 (31)**	**76.2 (16)**
Treatment emergent SAE	**9.8 (4)**	**9.5 (2)**
TEAE leading to death	**0**	**0**
TEAE leading to permanent treatment discontinuation	**4.9** (2)	**4.8** (1)
TEAE of interest: Injection site reaction Pruritus	 **2.4** (1) **4.9** (2)	 **0** **4.8** (1)
TEAE occurring in ≥5% of patients		
Upper respiratory tract infection	**7.3** (3)	**19.0** (4)
Fatigue	**14.6** (6)	**9.5** (2)
Nausea	**4.9** (2)	**14.3** (3)
Diarrhoea	**9.8** (4)	**0**
Myalgia	**9.8** (4)	**4.8** (1)
Nasopharyngitis	**9.8** (4)	**9.5** (2)
Arthralgia	**7.3** (3)	**9.5** (2)
Back pain	**4.9** (2)	**9.5** (2)
Palpitations	**0**	**9.5** (2)
Headache	**7.3** (3)	**4.8** (1)

TEAE, treatment-emergent adverse event; SAE, serious adverse event

Conclusions

- HeFH occurs in approx. 1:200 patients
  - Without effective treatment there is a high risk of premature CVD
- In ODYSSEY ESCAPE, alirocumab significantly reduced the need for apheresis treatment by 75% vs. placebo
- In patients receiving alirocumab:
  - Apheresis was discontinued in 63% of patients
  - LDL-C was reduced by approximately 50% from baseline (vs. 2% increase for placebo)
- Treatment with alirocumab 150 mg Q2W may allow patients with HeFH to terminate or reduce the frequency of lipoprotein apheresis