PEARL: A Non-Interventional Study of Real-World Alirocumab Use in German Clinical Practice

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Supplementary Material

Methods

Familial hypercholesterolemia was defined as follows in paper-based case report form: a. presence of FH (yes, no, unknown); b. patient with LDL-C value >4.9 mmol/L (190 mg/dL; yes, no); c. first degree family member with LDL-C value >4.9 mmol/L (190 mg/dL; yes, no, unknown); d. first degree family member with premature coronary heart disease (yes, no, unknown); e. first degree family member with xanthomas (yes, no, unknown); f. patient with pre-existing tendinous xanthomas (yes, no); g. patient with pre-existing arcus corneae (yes, no).

For this study, the FH criterion was defined as FH, no FH and unknown FH by combining the direct evaluation by item a. and the following algorithm based on previously described FH criteria [1] using items b. to g.:

- If yes was ticked for item a., then the overall FH criterion was FH
- else, if no was ticked for item b., then the overall FH criterion was no FH,
- else, if yes was ticked for item b. and at the same time at least one yes was ticked for items c. to g., the overall FH criterion was FH,
- else, if yes was ticked for item b. and at the same time no is ticked for all items (c. to g) then the overall FH criterion is no FH
- else, the overall FH criterion is set to unknown FH.

Only the composite FH criterion was analysed, not the single items a. to g.

References

1. Klose G, Laufs U, Marz W, Windler E. Familial hypercholesterolemia: developments in diagnosis and treatment. Deutsches Arzteblatt international. 2014;111(31-32):523-9.

Supplementary Table 1 Inclusion and exclusion criteria

Inclusion criteria
1. Treatment with alirocumab due to hypercholesterolemia according to SmPC
2. Informed consent was provided in form of written authorization (signature)
3. Patient aged ≥18 years
Exclusion criteria
1. Participation in alirocumab study ODYSSEY APPRISE (NCT02476006)
2. Contraindication to alirocumab according to SmPC

SmPC, summary of product characteristics.

Supplementary Table 2 Number of statins[a] according to statin intolerance status prior to start of alirocumab therapy (ITT analysis)

n (%)	Total statin intolerance	Partial statin intolerance	No statin intolerance
Number of statins			
0	146 (52.7)	14 (9.0)	10 (6.4)
1	66 (23.8)	131 (84.5)	140 (89.2)
2	26 (9.4)	7 (4.5)	6 (3.8)
3	21 (7.6)	2 (1.3)	1 (0.6)
4	8 (2.9)	0	0
5	5 (1.8)	0	0
6	5 (1.8)	1 (0.6)	0
Total	277 (100)	155 (100)	157 (100)

[a]Entries were limited by data reported by physician; multiple entries were possible. Considered statins included atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin.

ITT, intention-to-treat.

Supplementary Table 3 Initial alirocumab dosing regimen at the start of therapy in PEARL and according to patient subgroups

n (%)	Alirocumab 75 mg Q2W	Alirocumab 150 mg Q2W	Unknown dosing regimen
Overall (*n*=612)	446 (72.9)	150 (24.5)	16 (2.6)
Patient subgroups			
FH status (*n*=612)			
FH	227 (37.1)	75 (12.3)	9 (1.5)
Non-FH	23 (3.8)	11 (1.8)	0
Unknown FH status	196 (32.0)	64 (10.5)	7 (1.1)
DM status (*n*=602)			
Type 1 DM	9 (1.5)	1 (0.2)	0
Type 2 DM	113 (18.8)	37 (6.1)	4 (0.7)
Non-DM	319 (53.0)	109 (18.1)	10 (1.7)
CHD status (*n*=529)			
CHD	320 (60.5)	112 (21.2)	11 (2.1)
Non-CHD	73 (13.8)	11 (2.1)	2 (0.4)
ACS status (*n*=425)			
Post-ACS	150 (35.3)	48 (11.3)	4 (0.9)
No ACS	175 (41.2)	52 (12.2)	≤12 (≤2.8)
Gender (*n*=608)			
Male	278 (45.7)	108 (17.8)	8 (1.3)
Female	164 (59.0)	42 (15.1)	8 (2.9)

ACS, acute coronary syndrome; CHD, coronary heart disease; DM, diabetes mellitus; FH, familial hypercholesterolemia; Q2W, every 2 weeks.

Supplementary Table 4 Alirocumab treatment status at Weeks 0, 12, and 24 (ITT analysis)

n (%)	Alirocumab (*n*=612)
Alirocumab 75 mg Q2W at Week 0 (starting dose)	
75 mg Q2W (no change in dosing regimen) at Weeks 12 and 24	245 (40.0)
150 mg Q2W at Weeks 12 and 24	145 (23.7)
150 mg Q2W at Week 12 and 75 mg Q2W at Week 24	1 (0.2)
150 mg Q2W at Week 12 and treatment discontinuation at Week 24	12 (2.0)
Treatment discontinuation at Weeks 12 and 24	48 (7.8)
Treatment discontinuation at Week 12 and 150 mg Q2W at Week 24	1 (0.2)
Alirocumab 150 mg Q2W at Week 0 (starting dose)	
150 mg Q2W (no change in dosing regimen) at Weeks 12 and 24	128 (20.9)
Treatment discontinuation at Weeks 12 and 24	16 (2.6)
75 mg Q2W at Weeks 12 and 24	11 (1.8)
75 mg Q2W at Week 12 and 150 mg Q2W at Week 24	1 (0.2)
75 mg Q2W at Week 12 and treatment discontinuation at Week 24	2 (0.3)
Missing (no dosage provided)	2 (0.3)

ITT, intention-to-treat; Q2W, every 2 weeks.

Supplementary Table 5 Alirocumab efficacy on LDL-C levels for the PEARL study participants and according to patient subgroups (mITT analysis)

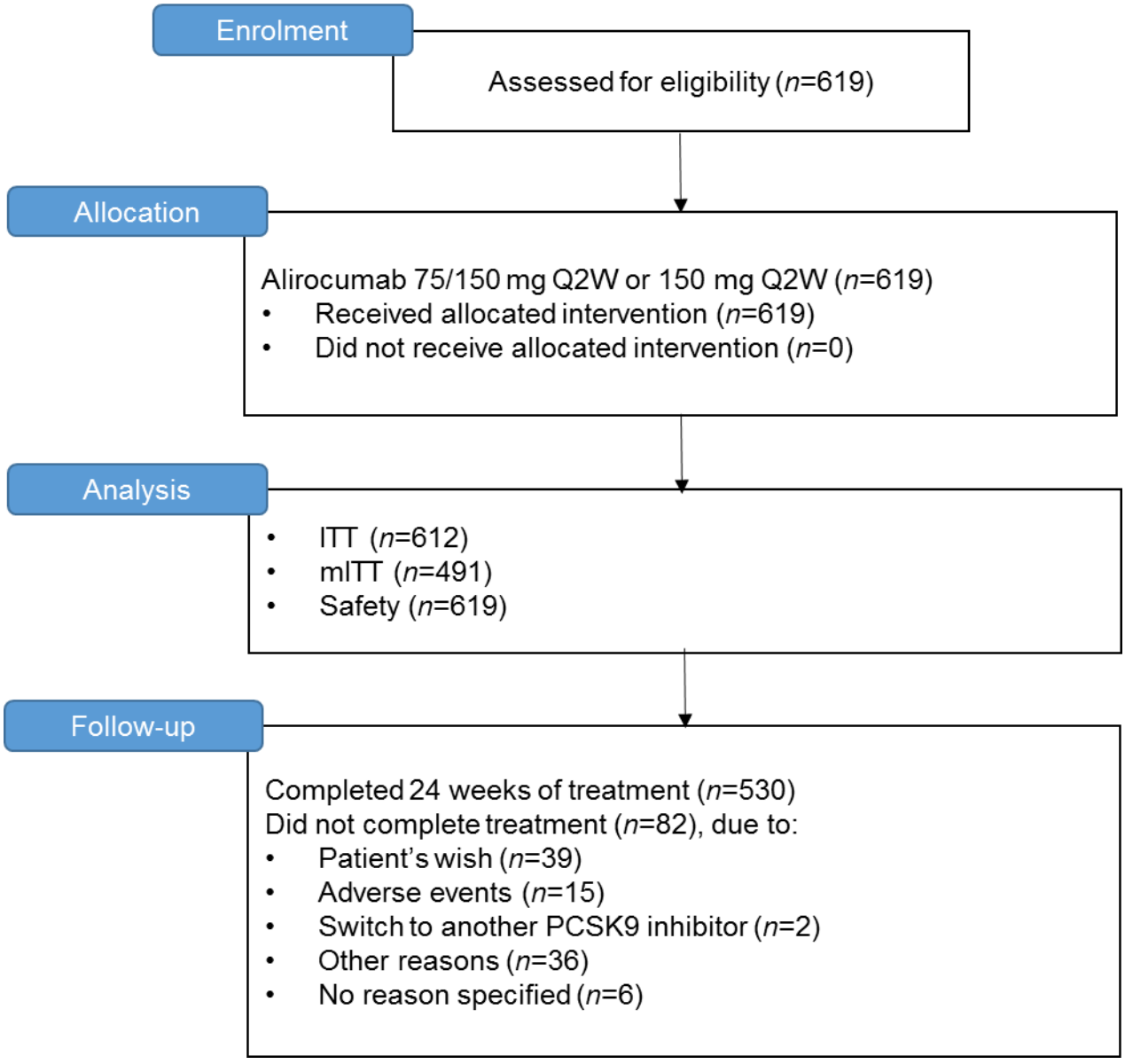
	n	Baseline, mean (SD), mmol/L [mg/dL]	Week 24, mean (SD), mmol/L [mg/dL]	Change from baseline to Week 24, LS mean, %	*p*-value
Total PEARL	491	4.7 (1.6) [180.5 (60.1)]	2.3 (1.2) [90.2 (46.0)]	–48.6	<0.0001
FH	244	5.0 (1.7) [194.9 (67.0)]	2.5 (1.4) [97.5 (54.1)]	–49.1	
Non-FH	28	4.3 (1.0) [164.6 (39.6)]	2.1 (0.9) [79.3 (33.2)]	–51.4	0.6500[a]
Unknown FH status	219	4.3 (1.3) [166.5 (49.5)]	2.2 (0.9) [83.4 (35.1)]	–47.7	
Type 1 DM	7	3.7 (1.0) [144.7 (37.1)]	1.9 (0.5) [73.9 (19.2)]	–48.4	
Type 2 DM	126	4.6 (1.7) [177.6 (64.1)]	2.3 (1.1) [88.1 (42.8)]	–47.4	0.7930[a]
Non-DM	352	4.7 (1.5) [183.3 (58.7)]	2.4 (1.2) [91.8 (47.5)]	–49.0	
CHD	378	4.5 (1.5) [174.6 (58.2)]	2.2 (1.0) [83.9 (40.2)]	–50.0	0.1542[a]
Non-CHD	66	5.0 (1.4) [192.8 (53.3)]	2.6 (1.1) [101.6 (44.4)]	–45.6	
Post-ACS	180	4.3 (1.3) [167.8 (50.5)]	2.1 (1.0) [80.8 (39.5)]	–50.4	0.7891[a]
No ACS	187	4.9 (1.5) [188.1 (58.4)]	2.4 (1.1) [91.4 (42.7)]	–49.8	
Male	323	4.5 (1.5) [172.4 (57.7)]	2.2 (1.2) [84.7 (44.6)]	–49.2	0.3595[a]
Female	166	5.1 (1.6) [197.0 (61.6)]	2.6 (1.2) [101.4 (46.7)]	–47.2	
Baseline LDL-C <3.4 mmol/L (<130 mg/dL)	92	2.7 (0.5) [104.4 (19.6)]	1.7 (0.9) [64.2 (35.1)]	–38.1	<0.0001[a]
Baseline LDL-C ≥3.4 to 4.9 mmol/L	205	4.2 (0.4) [161.8 (17.1)]	2.1 (0.8) [80.3 (31.1)]	–50.1	

(≥130 to ≤190 mg/dL)					
Baseline LDL-C >4.9 mmol/L (>190 mg/dL)	194	6.1 (1.3) [236.5 (48.9)]	2.9 (1.4) [113.0 (53.0)]	–52.0	
Total statin intolerance	220	5.0 (1.5) [194.7 (59.3)]	2.6 (1.2) [99.5 (44.9)]	–47.6	
Partial statin intolerance	127	4.3 (1.4) [166.6 (55.5)]	2.0 (1.0) [78.3 (38.0)]	–52.2	0.1302[a]
No statin intolerance	128	4.4 (1.6) [170.3 (61.2)]	2.2 (1.3) [85.5 (50.8)]	–47.1	

[a]Interaction *p*-value

ACS, acute coronary syndrome; CHD, coronary heart disease; DM, diabetes mellitus; FH, familial hypercholesterolemia; mITT, modified intention-to-treat; LDL-C, low-density lipoprotein cholesterol; LS, least squares; SD, standard deviation.

Supplementary Figure 1. Patient disposition.



For treatment discontinuation, multiple entries were possible. Treatment discontinuation reasons were presented according to a prespecified list: Patient's wish, AEs, switch to another PCSK9 inhibitor, and other reasons.

AE, adverse event; ITT, intention-to-treat; mITT, modified intention-to-treat; PCSK9, proprotein convertase subtilisin/kexin type 9; Q2W, every 2 weeks.