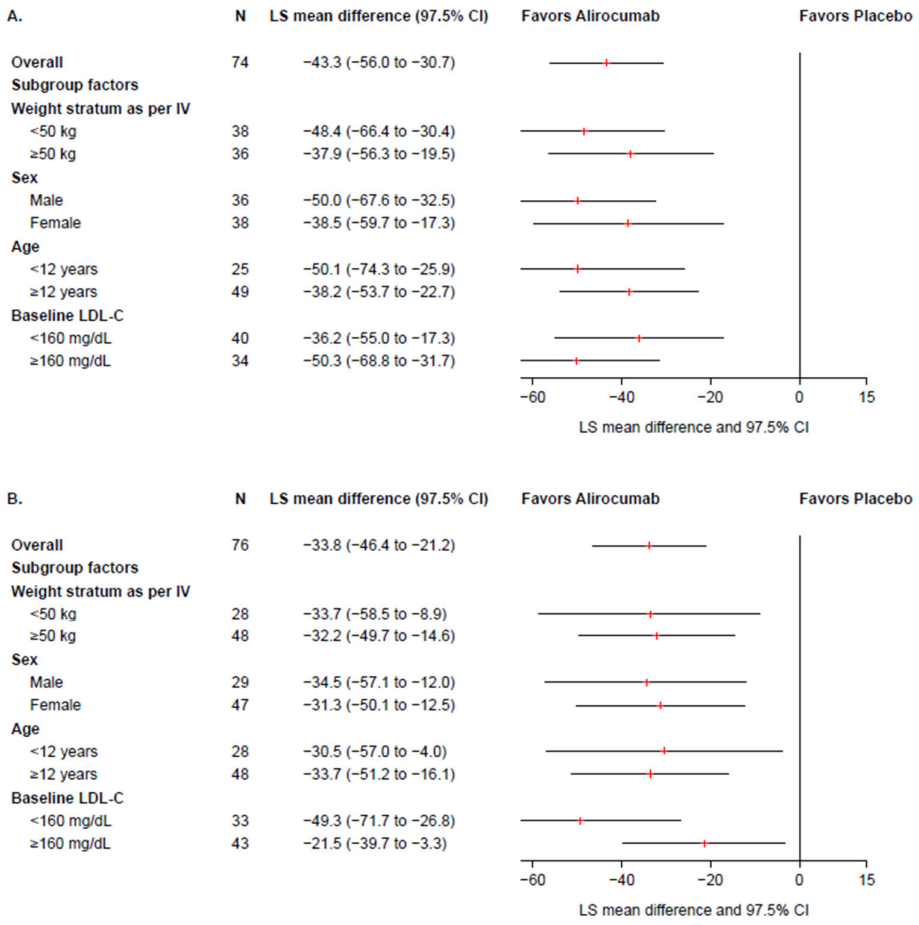
Supplemental Online Content

Santos RD, Wiegman A, Caprio S, et al. Alirocumab in pediatric patients with heterozygous familial hypercholesterolemia: a randomized clinical trial. *JAMA Pediatr*. Published online February 5, 2024. doi:10.1001/jamapediatrics.2023.6477

This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure. Percent change from baseline in LDL-C at Week 24 for subgroup analyses in the a) Q2W and b) Q4W cohorts (ITT population)



LS means and SE taken from MMRM analysis. The model includes the fixed categorical effects of treatment group, stratum previous participation [yes or no] to DFI14223 study (except for Q4W cohort), baseline body weight [<50 or ≥50 kg]), time point (Week 8, Week 12, Week 24), treatment-by-time point interaction, and strata-by-time point interaction, as well as the continuous fixed covariates of baseline LDL-C value and baseline LDL-C value-by-time point interaction.

ITT, intention-to-treat; LDL-C, low-density lipoprotein-cholesterol; LS, least squares; MMRM, mixed-effect model with repeated measures; Q2W, once every 2 weeks; Q4W, once every 4 weeks; SE, standard error

eTable 1. Patient disposition per country

Country, n of sites	Screened, n (%) [n=203]	Randomized, n (%) [n=153]
Argentina, 1	3 (1.5)	2 (1.3)
Austria, 1	3 (1.5)	3 (2.0)
Bulgaria,1	6 (3.0)	3 (2.0)
Brazil, 2	9 (4.4)	6 (3.9)
Canada, 1	13 (6.4)	10 (6.5)
Czech Republic, 2	16 (7.9)	12 (7.8)
Denmark, 1	3 (1.5)	3 (2.0)
Spain, 4	12 (5.9)	9 (5.9)
Finland, 1	3 (1.5)	3 (2.0)
France, 2	4 (2.0)	3 (2.0)
Hungary, 1	4 (2.0)	3 (2.0)
Italy, 3	7 (3.4)	5 (3.3)
Lebanon, 2	6 (3.0)	5 (3.3)
Mexico, 2	17 (8.4)	17 (11.1)
Netherlands, 1	19 (9.4)	18 (11.8)
Norway, 1	10 (4.9)	5 (3.3)
Poland, 2	17 (8.4)	12 (7.8)
Russian Federation, 4	15 (7.4)	8 (5.2)
Slovenia, 1	3 (1.5)	2 (1.3)
Sweden, 1	2 (1.0)	2 (1.3)
Turkey, 2	9 (4.4)	6 (3.9)
Taiwan Province of China, 1	3 (1.5)	2 (1.3)
United States, 5	18 (8.9)	13 (8.5)
South Africa, 1	1 (0.5)	1 (0.7)

n, number.

eTable 2. Safety end points during the open-label period

Adverse events	Q2W Cohort (n=71)		Q4W Cohort (n=74)	
	Alirocumab in double-blind period (n=46)	Placebo in double-blind (n=25)	Alirocumab in double-blind period (n=49)	Placebo in double-blind period (n=25)
Any AE, n (%)[a]	24.0 (52.2)	16.0 (64.0)	27.0 (55.1)	14.0 (56.0)
Most common AE, n (%)[a]				
Headache	5 (10.9)	1 (4.0)	7 (14.3)	4 (16.0)
Nasopharyngitis	3 (6.5)	2 (8.0)	3 (6.1)	1 (4.0)
Syncope	2 (4.3)	0	1 (2.0)	1 (4.0)
COVID-19	1 (2.2)	0	4 (8.2)	1 (4.0)
AESIs, n (%)				
Injection site reaction	3 (6.5)	1 (4.0)	1 (2.0)	1 (4.0)
General allergic reaction	1 (2.2)	3 (12.0)	2.0 (4.1)	1 (4.0)
Memory impairment	1 (2.2)	0	0	0
AE leading to discontinuation, n (%)				
Low density lipoprotein decreased	0	1 (4.0)	0	0
SAE, n (%)				
Pharyngitis streptococcal	1 (2.2)	0	0	0
Pneumonia	1 (2.2)	0	0	0
Hypertension	1 (2.2)	0	0	0
Calculus urinary	1 (2.2)	0	0	0
Appendicitis	0	1 (4.0)	0	0
Syncope	1 (2.0)	1 (4.0)	0	0
Angina pectoris	1 (2.0)	0	0	0
Myocarditis	1 (2.0)	0	0	0
Ligament rupture	1 (2.0)	0	0	0
Treatment related AE, n (%)	4. (8.7)	4 (16.0)	4 (8.2)	3 (12.0)
Developmental parameters				
Height change from baseline at Week 104, cm, mean (SD)	7.51 (6.65)	6.45 (5.47)	5.57 (5.99)	7.57 (6.54)
Weight change from baseline at Week 104, kg, mean (SD)	8.19 (7.83)	9.55 (8.75)	7.37 (5.87)	5.91 (7.85)
Cogstate Battery test change from baseline at Week 104, mean (SD)				
Detection test	−0.05 (0.14)	−0.01 (0.19)	−0.05 (0.07)	−0.07 (0.09)
Identification test	−0.06 (0.10)	−0.03 (0.14)	−0.07 (0.09)	−0.04 (0.11)
One Card Learning test	0.05 (0.16)	0.07 (0.19)	0.02 (0.11)	0 (0.10)
Groton Maze Learning test	−1.57 (14.95)	−22.31 (29.32)	−10.76 (26.80)	−3.47 (26.35)
Composite score	−0.439 (0.917)	−0.601 (1.612)	−0.638 (0.791)	−0.393 (0.764)

eTable 2 (cont). Safety end points during the open-label period (continued)

Adverse events	Q2W Cohort (n=74)		Q4W Cohort (n=79)	
	Alirocumab (n=49)	Placebo (n=25)	Alirocumab (n=52)	Placebo (n=27)
Tanner stage - Boys, n (%)				
Prepubescent				
Baseline	4 (23.5)	1 (5.9)	0	4 (36.4)
W104	1 (6.7)	0	0	1 (12.5)
Pubescent				
Baseline	11 (64.7)	13 (76.5)	14 (77.8)	4 (36.4)
W104	8 (53.3)	6 (46.2)	8 (53.3)	5 (62.5)
Postpubescent				
Baseline	2 (11.8)	3 (17.6)	4 (22.2)	3 (27.3)
W104	6 (40.0)	7 (53.8)	7 (46.7)	2 (25.0)
Tanner stage - Girls, n (%)				
Prepubescent				
Baseline	4 (13.8)	1 (12.5)	6 (19.4)	1 (7.1)
W104	0	0	1 (3.4)	1 (9.1)
Pubescent				
Baseline	16 (55.2)	6 (75.0)	13 (41.9)	7 (50.0)
W104	10 (47.6)	4 (66.7)	17 (58.6)	5 (45.4)
Postpubescent				
Baseline	9 (31.0)	1 (12.5)	12 (38.7)	6 (42.9)
W104	11 (52.4)	2 (33.3)?	11 (37.9)	5 (54.5)

AE, adverse event; AESIs, adverse events of special interest; COVID19, coronavirus disease 2019; HLT, high level term; hs-CRP, high-sensitivity C-reactive protein; n, number of patients; Q2W, dosing every 2 weeks; Q4W, dosing every 4 weeks; SAE, serious adverse event, TEAE, treatment emergent adverse event; W, week.

[a]TEAEs with HLT ≥5% in any treatment group in the safety population.