Poster 1414-220

Reductions in LDL-C within the First Year of Treatment with Inclisiran: Results from a Multicenter Real World Cohort

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KEY FINDINGS & CONCLUSIONS

- This retrospective, observational study demonstrated that inclisiran effectively lowers LDL-C in the real world with 225 patients initiating therapy in 23 physician clinics. Most patients had payor coverage through Medicare (86%) and a diagnosis of ASCVD (82%).
- Patients were adherent, with 91% receiving two doses within the 12-month study period. This led to 51% attaining their target LDL-C of ≤ 70 mg/dL.
- The LDL-C lowering effect of inclisiran in this real world study is consistent with that observed in the ORION clinical development program [2].
- Limitations include the analysis period taking place immediately post-FDA approval with limited follow-up time, the site of care setting restricted to only physician clinics and the time of LDL-C measurements varying among participants.

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INTRODUCTION

- Inclisiran, an injectable small interfering ribonucleic acid (siRNA), inhibits production of PCSK9, thus lowering LDL-C levels.
- Inclisiran was initially approved in the US for use alongside lifestyle modifications and statin pharmacotherapy for the management of LDL-C in patients with heterozygous familial hypercholesterolemia (HeFH) or atherosclerotic cardiovascular disease (ASCVD) [1]. In July 2023, the US FDA approved inclisiran for the management of primary hyperlipidemia.
- Inclisiran is unique in that it is administered subcutaneously every six-months following an initial dose and a day 90 dose [1], potentially reducing patient burden, and improving medication adherence .
- In the phase-3 ORION-10 and ORION-11 clinical trials, inclisiran was shown to reduce LDL-C by 49.9 - 52.2% among patients with HeFH or ASCVD [2]. The lipid lowering capacity of inclisiran in the real world setting has yet to be assessed.
- The objective of this study was to assess the LDL-C lowering effect of inclisiran in a real-world population.

METHODS

- A retrospective, longitudinal cohort study was conducted of patients who initiated inclisiran at independent physician clinics nationwide between February 2022 and May 2023. Patients who received an initial and 90-day dose of inclisiran and had at least one baseline and one LDL-C measurement within 365 days of treatment initiation were eligible for LDL-C reduction assessment.
- The primary outcome was the proportion of patients achieving an LDL-C ≤ 70 mg/dL. For patients with more than one post-initiation LDL-C measurement, the lowest measurement was used. Additional endpoints included adherence to therapy regimen, those who achieved at least a 50% reduction in LDL-C from baseline, and an LDL-C ≤ 55 [3].
- Other variables included demographics, diagnosis and comorbidities. Concurrent therapy with statins, use of ezetimibe and prior use of anti-PCSK9 mAbs were assessed at baseline.
- The cohort was stratified by concurrent statin use and prior treatment with anti-PCSK9 mAbs.

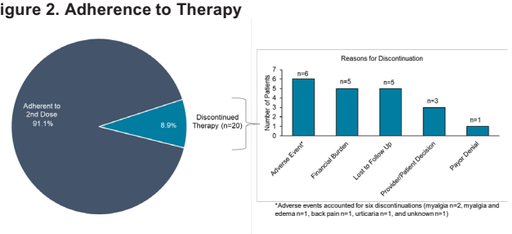
RESULTS

Figure 1. Participant Flow

Study Cohort
N=225

Patients initiating inclisiran between February 2022 to May 2023 in 23 physician clinics across 12 states

Figure 2. Adherence to Therapy



- The median time to 2nd dose was 93.0 days, with 74.1% receiving their dose within 7 days, 85.9% within 14 days, and 91.7% within 30 days of schedule.
- Of 152 patients who received the initial and 2nd dose and had a 12-month follow-up observation period, 86.8% received the maintenance (3rd) dose at a median time of 188 days after the day 90 dose.

Second Dose Cohort
N=205

Patients receiving two injections (Initiation and 90-day dose)

LDL-C Cohort
N=108

Patients with at least one LDL-C measurement at baseline and one within 12 months of initiation

Figure 3. LDL-C Subgroups

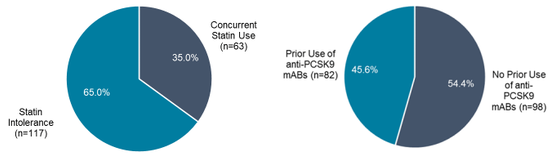


Table 1. Patient Demographics and Clinical Characteristics

Characteristic	All Patients N=180	Subgroups			
		Concurrent Statin Use n=63	Statin Intolerance[1] n=117	No Prior Use of anti-PCSK9 mABs n=98	Prior Use of anti-PCSK9 mABs n=82
Age in years, mean (SD)	69.7 (8.6)	66.7 (10.1)	71.4 (7.2)	70.2 (8.0)	69.2 (9.3)
Age in years, median (IQR)	70.0 (66.0-75.0)	68.0 (64.0-72.0)	71.0 (67.0-75.0)	70.0 (67.0-75.0)	70 (66.0-74.0)
Age <65 years, n (%)	30 (16.7)	16 (25.4)	14 (12.0)	14 (14.3)	16 (19.5)
Age 65-74 years, n (%)	104 (57.8)	37 (58.7)	67 (57.3)	58 (59.2)	46 (56.1)
Age ≥75 years, n (%)	46 (25.6)	10 (15.9)	36 (30.8)	26 (26.5)	20 (24.4)
Sex, n (%)					
Female	89 (49.4)	29 (46.0)	60 (51.3)	46 (46.9)	43 (52.4)
Male	91 (50.6)	34 (54.0)	57 (48.7)	52 (53.1)	39 (47.6)
Body Mass Index					
Body mass index, mean (SD)	30.0 (5.8)	30.7 (5.4)	29.6 (6.0)	30.56 (5.76)	29.4 (5.8)
Body mass index, median (IQR)	30.0 (26.0-34.0)	30.1 (26.0-34.0)	29.8 (26.0-33.0)	30.1 (26.0-34.0)	29.2 (25.0-33.0)
Body mass index ≥30 mg/kg^2, n (%)	87 (48.3)	33 (52.4)	54 (46.2)	52 (53.1)	35 (42.7)
Payor Type, n (%)					
Commercial	26 (14.4)	11 (17.5)	15 (12.8)	7 (7.1)	19 (23.2)
All Medicare	154 (85.6)	52 (82.5)	102 (87.2)	91 (92.9)	63 (76.8)
Medicare, traditional	136 (75.6)	41 (65.1)	95 (81.2)	78 (79.6)	58 (70.7)
Medicare Advantage	18 (10.0)	11 (17.5)	7 (6.0)	13 (13.3)	5 (6.1)
Primary Treatment Indication, n (%)					
ASCVD	147 (81.7)	52 (82.5)	95 (81.2)	81 (82.7)	66 (80.5)
Hyperlipidemia	27 (15.0)	7 (11.1)	20 (17.1)	15 (15.3)	12 (14.6)
Heterozygous familial hypercholesterolemia	6 (3.3)	4 (6.4)	2 (1.7)	2 (2.0)	4 (4.9)
Overall Comorbidities					
Elixhauser Comorbidity Score, mean (SD)	10.4 (11.6)	11.3 (11.9)	9.9 (11.5)	10.5 (11.6)	10.3 (11.7)
Cardiac Comorbidities, n (%)					
Hypertension	159 (88.3)	57 (90.5)	102 (87.2)	90 (91.8)	69 (84.2)
Cardiac Arrythmias	47 (26.1)	18 (28.6)	29 (24.8)	28 (28.6)	19 (23.2)
Valvular Disease	42 (23.3)	18 (28.6)	24 (20.5)	25 (25.5)	17 (20.7)
Heart Failure	17 (9.4)	9 (14.3)	8 (6.8)	12 (12.2)	5 (6.1)
Lipid-Lowering Therapy, n (%)					
Concurrent Ezetimibe Use	52 (28.9)	21 (33.3)	31 (26.5)	32 (32.7)	20 (24.4)
Concurrent Statin Use	63 (35.0)	63 (100.0)	0 (0)	41 (41.8)	22 (26.8)
Low to Moderate Intensity Statin	17 (9.4)	17 (27.0)	0 (0)	11 (11.2)	6 (7.3)
High Intensity Statin	46 (25.6)	46 (73.0)	0 (0)	30 (30.6)	16 (19.5)
Prior anti-PCSK9 mABs	82 (45.6)	22 (34.9)	60 (51.3)	0 (0)	82 (100.0)

[1]: Reasons for no concurrent statin use: statin intolerance (n-114), lack of efficacy (n=3)

- The majority of patients (n=150, 83%) were over the age of 65 years. Most had payor coverage through Medicare, primarily traditional Medicare (Table 1).
- Hypertension was common in the cohort (n=159, 88%), and the average Elixhauser comorbidity score was 10.4 (SD: 11.6).

Figure 4. Median LDL Cholesterol Pre- and Post-Initiation of Inclisiran

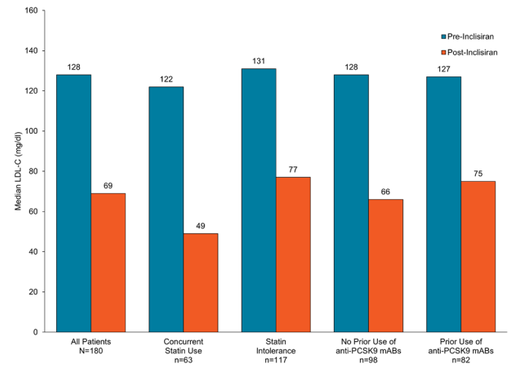


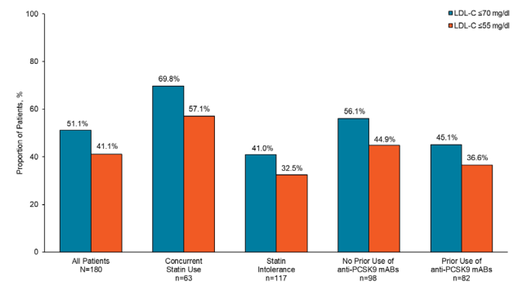
Table 2. Reductions in LDL Cholesterol

Characteristic	All Patients N=180	Subgroups			
		Concurrent Statin Use n=63	Statin Intolerance[1] n=117	No Prior Use of anti-PCSK9 mABs n=98	Prior Use of anti-PCSK9 mABs n=82
LDL-C, mg/dl at Baseline					
Baseline LDL-C, mean (SD)	134.9 (53.2)	125.8 (47.8)	139.8 (55.5)	133.5 (47.8)	136.5 (59.2)
Baseline LDL-C, median (IQR)	128.0 (93.5-167.5)	122.0 (92.0-152.0)	131.0 (100.0-178.0)	128.0 (96.0-154.0)	127.0 (89.0-183.0)
LDL-C <100 mg/dl, n (%)	52 (28.9)	23 (36.5)	29 (24.8)	25 (25.5)	27 (32.9)
LDL-C 100-159 mg/dl, n (%)	78 (43.3)	28 (44.4)	50 (42.7)	52 (53.1)	26 (31.7)
LDL-C ≥160 mg/dl, n (%)	50 (27.8)	12 (19.1)	38 (32.5)	21 (21.4)	29 (35.4)
LDL-C, mg/dl at Follow-up					
LDL-C, mg/dl at follow up, mean (SD)	70.3 (40.7)	54.1 (39.8)	79.0 (38.6)	66.2 (38.6)	75.2 (42.8)
LDL-C, mg/dl at follow-up, median (IQR)	69.0 (42.5-93.0)	49.0 (21.0-79.0)	77.0 (48.0-100.0)	66.0 (39.0-87.0)	75.0 (46.0-96.0)
Initiation to LDL-C measurement, mean days (SD)	157 (85)	145 (83)	164 (86)	149 (80)	168 (90)
Initiation to LDL-C measurement, median days (IQR)	139 (91-210)	112 (89-201)	158 (94-215)	131 (89-196)	150 (104-234)
LDL-C Reduction					
LDL-C ≤70 mg/dl, n (%)	92 (51.1)	44 (69.8)	48 (41.0)	55 (56.1)	37 (45.1)
LDL-C ≤55 mg/dl, n (%)	74 (41.1)	36 (57.1)	38 (32.5)	44 (44.9)	30 (36.6)
Absolute reduction in LDL-C, mean (SD)	64.6 (46.1)	71.7 (50.7)	60.7 (43.2)	67.3 (44.5)	61.4 (48.1)
Percent reduction in LDL-C, mean [95% CI]	45.5% [41.1, 49.7]	55.3% [47.7, 62.8]	40.1% [35.1, 45.2]	48.7% [43.0, 54.3]	41.5% [35.0, 48.1]
LDL-C reduction ≥50% , n (%)	85 (47.2)	37 (58.7)	48 (41.0)	51 (52.0)	34 (41.5)

[1]: Reasons for no concurrent statin use: statin intolerance (n-114), lack of efficacy (n=3)

- A total of 277 LDL-C measurements were observed in the 365 days after initiation. Overall, patients had a mean of 1.5 (SD: 0.70) LDL-C measurements following baseline. The median time from initiation to LDL-C measurement was 110 (IQR: 81-175) days.
- Patients experienced an absolute reduction in LDL-C of 64.6 mg/dl, with 47.2% of patients experiencing an LDL-C reduction of 50% or more. Reductions were seen in all subgroups, with a mean of 55.3% (95% CI: 47.7%-62.8%) reduction in the concurrent statin use group and a mean of 48.7% (95% CI: 43.0%-54.3%) reduction in those without prior anti-PCSK9 mABs (Table 2).
- An LDL-C ≤70 mg/dl was achieved in 51.1% and an LDL-C ≤55 mg/dl in 41.1% of patients. Reductions were most prevalent in those with concurrent statins, with 57.1% achieving an LDL-C goal of ≤55 mg/dl (Figure 5).
- For patients with concurrent ezetimibe use at initiation (n=52), the absolute reduction in LDL-C was 71 (SD: 37.9), and the average percent reduction in LDL-C was 56.8% (95% CI: 51.2%-62.5%). Of these patients on concurrent ezetimibe, 75% (n=39) of patients reached an LDL-C of ≤70 mg/dl and 65.4% (n=34) achieved an LDL-C of ≤55 mg/dl.

Figure 5. Proportion of Patients Reaching Target LDL Cholesterol of ≤70 mg/dl and ≤55 mg/dl



Disclosures

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