Contrasting US Patients with a Fill versus a Prescription for Alirocumab: Early Evidence from Administrative Claims, EMR and Lab Data

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Background

- The clinical management of hypercholesterolemia depends, in part, on ensuring that patients who require additional low-density lipoprotein cholesterol (LDL-C)-lowering are able to access effective medications.
- For decades, statins have been the mainstay for treating hypercholesterolemia, but despite maximally tolerated dose (MTD) of statin therapy, many patients do not reach guideline-recommended LDL-C thresholds.[1–4]
- Alirocumab is a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor approved (on July 24, 2015, by the Food and Drug Administration [FDA] in the USA) as an adjunct to diet and MTD statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of LDL-C.[5]
- Identifying appropriate patients for alirocumab is the initial step towards filling a prescription. However, many US health plans have additional criteria in place for alirocumab (e.g. prior authorization and step-edit requirements) that may delay or limit access to alirocumab. Only after these criteria are met will the prescription be reimbursed by the health plan.

Objective

- The objective of this analysis was to compare the demographic and clinical characteristics of patients with a written prescription but without a pharmacy fill for alirocumab to those of patients with both a written prescription and a pharmacy fill for alirocumab in the first months after the FDA alirocumab approval.

Methods

- The study used de-identified and Health Insurance Portability and Accountability Act 1996-compliant data from four data sources: the QuintilesIMS pharmacy claims (LRx), outpatient medical claims (Dx), ambulatory electronic health records (EHR), and laboratory results databases.†
- Alirocumab prescription information was extracted from the EHR database from July 24, 2015 to December 31, 2015 (the *identification* period). The date of the first alirocumab prescription in the EHR was designated as the *index* date. EHR observations were linked using a unique identifier to Dx and Rx claims, and laboratory data for the same person.
- Inclusion criteria were ≥1 pharmacy claim for any medication and ≥1 medical claim for any reason in the 12-month period before index date (pre-index or baseline period) and ≥1 pharmacy claim for any medication in the 3-month period starting on and following the index date (post-index).
- Patients with an alirocumab prescription were placed into one of the two following mutually-exclusive cohorts, according to the presence versus absence of a pharmacy claim (assumed to indicate a prescription fill) for alirocumab in the post-index period: patients with, versus patients without, an alirocumab prescription fill.
- Baseline demographics (age, gender, geographic region), payer type, clinical characteristics (cardiovascular risk category, Charlson-Quan Comorbidity Index [CCI]‡),[6] prescriber specialty, and treatment characteristics on index date or in the 12 months before index date were described for patients with and without an alirocumab fill (from among patients with an alirocumab prescription). Baseline LDL-C values closest to and before the index date were reported (when available).

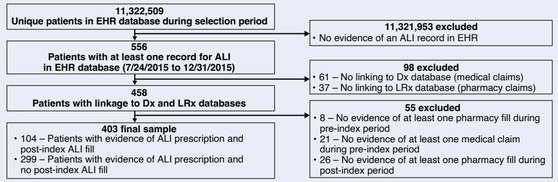
†The LRx database comprises prescription data from retail, mail, long-term care, and specialty pharmacies. The database provides coverage of approximately 88% of all retail prescriptions filled (including cash payments) and approximately 55% of standard mail service in the US, and prescribing information for over 1 million prescribers. The Dx database comprises over 1.1 billion office-based electronic medical claims from office-based health professionals, ambulatory, and health care sites. The EHR database comprises approximately 36 million patient records from approximately 40,000 health care providers from large practices and physician networks. Half of contributing physicians are primary care practitioners, and the remainder are specialists. The laboratory database comprises results from a national warehouse, representing 40% of available US reference laboratory tests.

‡The Charlson-Quan Comorbidity Index is the sum of scores for comorbid conditions (such as, dementia, diabetes , AIDS/HIV, etc.) that might alter the risk of mortality, whereby the higher the index, the higher the risk. The index has been validated and is commonly used in retrospective administrative claims-based analyses.[6]

Results

- Of 11,322,509 patients in the EHR database, 845,513 had an ASCVD ICD diagnosis between July 24, 2014 and December 31, 2015. Of patients in the EHR database, 403 had evidence of alirocumab prescription in the 5-month identification period immediately following FDA approval (104 [25.8%] with and 299 [74.2%] without a post-index alirocumab pharmacy fill) (Figure 1).
  - ASCVD was based on ICD-9 or 10 diagnosis codes for chronic coronary heart disease (CHD) including acute coronary syndrome (ACS), ischemic stroke, or peripheral artery disease (PAD). HeFH was not captured.

Figure 1. Cohort selection for the study



ALI, alirocumab

- Among patients with an alirocumab prescription, more males had evidence of prescription pharmacy fills than females.
- The majority of patients in both cohorts received a prescription for 75 mg alirocumab every 2 weeks (Q2W) (89.4% vs 87.0%, for patients with and without an alirocumab pharmacy fill, respectively, $P>0.05$).
- Most clinical and demographic characteristics did not differ significantly ($P>0.05$) between patients with and without an alirocumab pharmacy fill, as follows:
  - Mean age (65 vs 64 years); payer type (Commercial: 52.9% vs 53.2%; Medicare: 41.3% vs 39.8%), for patients with versus without an alirocumab pharmacy fill, respectively (Table 1).
  - Mean CCI‡ (0.28 vs 0.27); mean pre-index LDL-C (134 vs 132 mg/dL) (Table 2, Figure 2); recent ACS (10.6% vs 8.0%); alirocumab prescriber specialties (cardiologist 20.2% vs 26.4%) (Table 2).
  - History of cardiovascular medications of interest (angiotensin II receptor blockers [ARB], angiotensin-converting enzyme inhibitors [ACEi], beta blockers, calcium channel blockers, diuretics) and anti-diabetic medication use (orals and insulins); current use of any statin within 30 days before index (29.8% vs 27.1%); and current concomitant use of statins plus ezetimibe (11.5% vs 7.4%) were not significantly different between the two cohorts (Table 3).
- Statistically significant differences were observed between patients with versus without an alirocumab pharmacy fill, respectively, for gender (43.3% vs 56.5% female; $P=0.020$), patients in the South region (33.7% vs 49.2%; $P=0.006$) (Table 1), and chronic CHD (i.e. non-ACS CHD, 60.6% vs 48.2%; $P=0.029$) (Table 2). More patients with an alirocumab pharmacy fill had claims for lipid-lowering therapy within 30 days before index (57.7% vs 44.8%; $P=0.024$), and more had an ezetimibe pharmacy fill (28.8% vs 18.4%; $P=0.024$), compared to patients without an alirocumab fill, respectively (Table 3).

Table 1. Demographics of patients with a prescription for alirocumab with, versus without, a pharmacy fill

	With alirocumab pharmacy fill (n=104)	Without alirocumab pharmacy fill (n=299)
Age , years		
Mean ± SD	65 ± 10.9	64 ± 11.4
Median	67	65
Age category, n (%)		
<35 years	2 (1.9)	5 (1.7)
35–44 years	2 (1.9)	12 (4.0)
45–54 years	13 (12.5)	33 (11.0)
55–64 years	25 (24.0)	93 (31.1)
65–74 years	46 (44.2)	108 (36.1)
≥75 years	16 (15.4)	48 (16.1)
Gender, n (%)		
Female*	**45 (43.3)**	**169 (56.5)**
Geographic region, n (%)		
Northeast	14 (13.5)	33 (11.0)
Midwest	18 (17.3)	33 (11.0)
South*	**35 (33.7)**	**147 (49.2)**
West	34 (32.7)	84 (28.1)
Other/Unknown	3 (2.9)	2 (0.7)
Payer type, n (%)†		
Commercial	55 (52.9)	159 (53.2)
Medicaid	1 (1.0)	5 (1.7)
Medicare	43 (41.3)	119 (39.8)
Cash payment	5 (4.8)	16 (5.4)

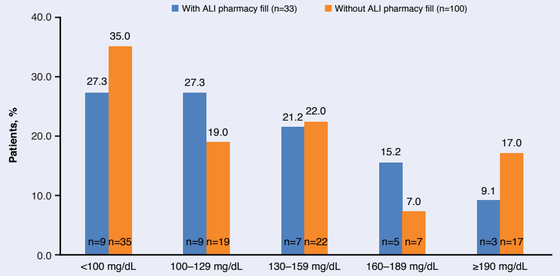
*$P<0.05$. †Payer types as reported in LRx database, associated with the first post-index alirocumab and non-alirocumab pharmacy fill for patients with and without an alirocumab fill, respectively.

Table 2. Clinical characteristics of patients with a prescription for alirocumab with, versus without, a pharmacy fill

	With alirocumab pharmacy fill (n=104)	Without alirocumab pharmacy fill (n=299)
Baseline LDL-C, mg/dL		
Mean ± SD	134 ± 48.5	132 ± 67.3
Median	133	122
Cardiovascular risk category		
Recent ACS, n (%)	11 (10.6)	24 (8.0)
Non-ACS CHD,* n (%)	**63 (60.6)**	**144 (48.2)**
Ischemic stroke, n (%)	3 (2.9)	10 (3.3)
PAD, n (%)	20 (19.2)	56 (18.7)
Diabetes, n (%)	30 (28.8)	89 (29.8)
CCI, mean ± SD	0.28 ± 0.73	0.27 ± 0.81
Prescriber specialties, n (%)		
Primary care	8 (7.7)	36 (12.0)
Internal medicine	3 (2.9)	17 (5.7)
Cardiologist	21 (20.2)	79 (26.4)
Endocrinologist/diabetologist	9 (8.7)	23 (7.7)
Nephrologist	0 (0.0)	1 (0.3)
Other/unknown†	63 (60.6)	143 (47.8)

*$P<0.05$. †Examples of other specialties are pulmonary medicine, hospital medicine, etc.
ACS, acute coronary syndrome; CCI, Charlson-Quan Comorbidity Index; CHD, coronary heart disease; PAD, peripheral artery disease.

Figure 2. Distribution of baseline LDL-C (in patients with baseline laboratory values available)



No statistically significant difference between groups across all LDL-C levels.

Table 3. Medication use of patients with a prescription for alirocumab with, versus without, a pharmacy fill

Measure, n (%)	With alirocumab pharmacy fill (n=104)	Without alirocumab pharmacy fill (n=299)
Lipid-lowering therapy† within 30 days of alirocumab prescription*	**60 (57.7)**	**134 (44.8)**
Statin use	31 (29.8)	81 (27.1)
High-dose‡	19 (18.3)	44 (14.7)
Ezetimibe use*	**30 (28.8)**	**55 (18.4)**
Statin + ezetimibe	12 (11.5)	22 (7.4)
High-dose statin + ezetimibe	11 (10.6)	16 (5.4)
Selected baseline medications 12 months prior to index		
Cardiovascular		
ACEi	34 (32.7)	93 (31.1)
ARB	19 (18.3)	82 (27.4)
Beta blocker	66 (63.5)	170 (56.9)
Calcium channel blocker	26 (25.0)	80 (26.8)
Diuretic	31 (29.8)	89 (29.8)
Statin (including FDC)	56 (53.8)	147 (49.2)
Anti-diabetics		
Basal insulin	14 (13.5)	31 (10.4)
Other insulin	11 (10.6)	34 (11.4)
GLP-1	1 (1.0)	13 (4.3)
SGLT2	3 (2.9)	13 (4.3)
Other oral anti-diabetic medication	27 (26.0)	74 (24.7)

*$P<0.05$. †Lipid-lowering therapy includes statin, ezetimibe, bile acid sequestrant, fibrates, niacin, lomitapide, mipomersen, icosapent ethyl, and omega-3 acid ethyl esters. ‡High-dose statins include atorvastatin 40–80 mg, rosuvastatin 20–40 mg, and simvastatin 80 mg. Statin use, ezetimibe use, and statin + ezetimibe use categories are non-mutually exclusive.
FDC, fixed dose combination; GLP-1, glucagon-like peptide-1; SGLT2, sodium-glucose cotransporter 2.

Limitations

- The small sample size, which is largely due to the relatively short identification period (approximately 5 months, and beginning immediately after the FDA approval), limits the study generalizability and statistical power to detect differences between the two cohorts.
- Follow-up time was limited due to the recent launch of alirocumab and availability of patient data.
- Post-index lipids and diagnoses were not available in these data for the reasons described above.
- The QuintilesIMS LRx, Dx, and EHR databases are open-source data in which patient continuous enrollment of medical and pharmacy benefit cannot be confirmed. Therefore, it is possible that not all medical services and pharmacy fills were completely captured in the databases.

Conclusions

- In the first 5 months after FDA approval, 74.2% of patients with an alirocumab prescription did not have an alirocumab pharmacy fill despite having similar demographic and clinical profiles to patients with an alirocumab pharmacy fill.
- These findings suggest that patients who were prescribed alirocumab and could benefit from alirocumab remain untreated.
- Further research, with longer follow-up and identification periods than were possible in this study, are needed to provide a thorough assessment of the characteristics of patients who are able to fill alirocumab prescriptions.
- These results suggest the need to explore the reasons behind the low fill rate for alirocumab, including analyses with data sources that can capture pharmacy claim reversals and rejections.

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Disclosures

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