Treatment patterns in patients with Familial hypercholesterolemia: evidence from real-world studies in Germany and the UK

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Background: Familial hypercholesterolemia (FH) includes a spectrum of disease as per the number and effect of mutations in specific proteins involved in low-density lipoprotein cholesterol (LDL-C) metabolism, together with other genetic factors. Elevated LDL-C levels have been strongly associated with risk of cardiovascular and coronary heart disease, with up to 10-fold risk in patients (pts) with FH than without FH. The aim of lipid-lowering treatments (LLTs) is to reduce the LDL-C levels, although there is limited research describing treatment patterns and LDL-C outcomes in FH pts in routine care.

Purpose: To characterize the treatment patterns and LDL-C outcomes of FH pts in the real-world setting in Germany (GER) and the UK.

Methods: We conducted two descriptive, non-interventional and retrospective cohort studies. Pts in GER were identified from General Physician (GP) and Cardiology practices available in electronic medical records database Disease Analyzer (January 1992-June 2020). Pts in the UK were identified from the Clinical Practice Research Datalink linked to the Hospital Episode Statistics admitted pts care and Office of National Statistics datasets. Pts were included if they had diagnosis of FH (index date [ID]) and data available within 6-month before and 3-month after the ID. The first diagnosis of FH in the identification period (GER, 1/07/2015–30/06/2019; UK, 01/01/2010–31/05/2018) was considered the ID. Persistence and adherence to the recorded LLT at ID was analyzed for pts with at least 12 months and 24 months of follow-up. Persistence was measured as the duration (in days) with allowed gap of 60 days and adherence as proportion of days covered (PDC).

Results: Analysis included 2,105 FH pts from GER and 9,846 from the UK. Data are presented as GER/UK. The mean (SD) age of pts was 60 (15)/52 (14) years, and 60%/61% were females. Hypertension (53%/27%) and depression (31%/38%) were the common comorbidities. At ID, statin monotherapy (29%/68%) was the most commonly prescribed LLT. The use of ezetimibe, fibrates and PCSK9 inhibitors was very low in both countries (Table 1). Of note, LDL-C measurements at ID (–6m/+3m) were available for 31%/73% of pts. In pts with uncontrolled LDL-C (≥55 mg/dL), 34%/64% were receiving statin monotherapy, whereas there was no use of LLT in 62%/29% of pts. During the 24 months follow-up, the mean (SD) persistence and PDC to statins monotherapy was 471 (264)/489 (289) days and 0.65 (0.36)/0.69 (0.46), respectively, with 50%/70% of pts being adherent (PDC ≥0.80).

Conclusions: In our study, in GER, the rate of LDL-C measurements was low. In both GER and UK, almost all measured patients had LDL-C ≥55mg/dL at ID. Findings indicate low prescriptions of LLTs in GP setting, particularly non-statin LLTs in both countries. The mean adherence (PDC) in GER and the UK was 65% and 69%, respectively within 24 months after ID. Improved LDL-C monitoring and new therapies with potential to lower LDL-C are warranted.

Table 1: Treatment patterns and persistence and adherence to index treatments during 24 months of follow-up in patients with FH in Germany and the UK

Index treatment	Total population		Patients with LDL-C measurement[1]								
			Germany (n=659; 31.3%)		UK (n=7,194; 73.1%)		Persistence[3] (days)/ Adherence[4] (PDC) of index treatment, mean (SD)			Adherent to index treatment (PDC ≥0.8), n (%)	
							Uncontrolled LDL-C[1]				
	Germany (N=2,105) GP+Cardio	UK (N=9,846)	Controlled LDL-C[2] (n=9; 1.4%)	Uncontrolled LDL-C[2] (n=650; 98.6%)	Controlled LDL-C[2] (n=57; 0.8%)	Uncontrolled LDL-C[2] (n=7,137; 99.2%)	N (Germany/ UK)	Germany	UK	Germany	UK
Statins (monotherapy)	618 (29.4%)	6,686 (67.9%)	4 (44.4%)	218 (33.5%)	37 (64.9%)	4,573 (64.1%)	163/6,122	471 (264)/ 0.646 (0.358)	489 (289)/ 0.69 (0.46)	81 (49.7%)	70.0%
Simvastatin	329 (15.6%)	2,477 (25.2%)	2 (22.2%)	108 (16.6%)	18 (31.6%)	1,847 (25.9%)	88/2,276	473 (258)/ 0.660 (0.351)	481 (292)/ 0.7 (0.46)	45 (51.1%)	70.3%
Atorvastatin	245 (11.6%)	3,513 (35.7%)	1 (11.1%)	95 (14.6%)	17 (29.8%)	2,284 (32.0%)	66/3,202	448 (27)/ 0.602 (0.367)	504 (284)/ 0.69 (0.46)	29 (44.0%)	69.8%
PCSK9i	<5 pts	<5 pts	-	-	-	-	-	-	-	-	-
Ezetimibe	5 (0.2%)	652 (6.6%)	1 (11.1%)	3 (0.5%)	7 (12.3%)	402 (5.6%)	2/590	284 (255)/ 0.477 (0.473)	491 (289)/ 0.73 (0.44)	1 (50.0%)	73.7%
Fibrates	7 (0.3%)	179 (1.8%)	0 (0.0%)	5 (0.8%)	<5	100 (1.4%)	5/161	605 (280)/ 0.819 (0.378)	475 (294)/ 0.68 (0.46)	4 (80.0%)	68.3%
Statins + any drug	46 (2.2%)	627 (6.4%)	2 (22.2%)	20 (3.1%)	8 (14.0%)	373 (5.2%)	12/574	665 (185)/ 0.907 (0.246)	515 (280)/ 0.72 (0.45)	11 (91.7%)	72.0%
No LLT	1,426 (67.7%)	2,292 (23.3%)	2 (22.2%)	404 (62.2%)	10 (17.5%)	2,032 (28.5%)	-	-	-	-	-

[1]LDL-C was measured within 6-month before and 3-month after index date. [2]Controlled/uncontrolled were defined as LDL-C levels <55/≥55 mg/dL. [3]Persistence to index treatment(s) was measured as the duration of index treatment with allowed gap of 60 days. [4]Proportion of Days Covered (PDC) was defined as the number of days with drug on-hand divided by the number of days in the specified time interval.

GP, general practice; LDL-C: low density lipoprotein cholesterol; LLT: lipid lowering treatment; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; SD: standard deviation