Long-Term Efficacy and Safety of Evolocumab in Patients With Hypercholesterolemia

Final Report of the 5-year, OSLER-1 Study

Michael J. Koren, MD,[a] Marc S. Sabatine, MD, MPH,[b] Robert P. Giugliano, MD, SM,[b] Gisle Langslet, MD, PhD,[c] Stephen D. Wiviott, MD,[b] Andrea Ruzza, MD, PhD,[d] Yuhui Ma, PhD,[d] Andrew W. Hamer, MD,[d] Scott M. Wasserman, MD,[d] Frederick J. Raal, MBBCh, MMED, PhD[e]

[a]Jacksonville Center for Clinical Research, Jacksonville, FL, USA; [b]Thrombolysis in Myocardial Infarction (TIMI) Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [c]Lipid Clinic, Oslo University Hospital Oslo, Norway; [d]Amgen Inc., One Amgen Center Drive, Thousand Oaks, CA, 91320 (AR, YM, AWH, SMW); [e]The Carbohydrate and Lipid Metabolism Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

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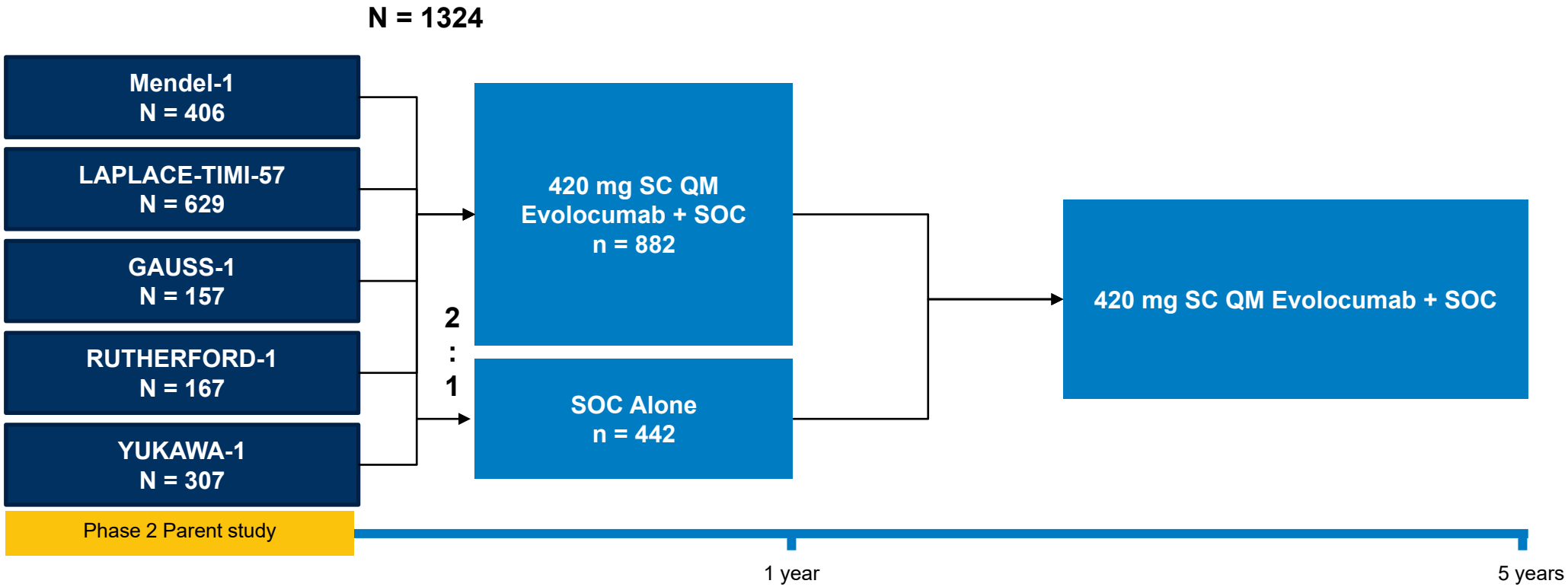
Background

- Evolocumab consistently lowers LDL-C by approximately 60% as monotherapy or in combination with other lipid-lowering therapies in patients with hypercholesteremia[1-6]
- Additionally, evolocumab has demonstrated a consistent efficacy and safety profile in men and women, various ethnicities and racial backgrounds, patients with or without known pre-existing cardiovascular disease, patients with familial hypercholesterolemia or statin intolerant[1-6]
- FOURIER, the evolocumab outcomes study of 27,564 patients with established ASCVD, demonstrated significant reductions in CV events over a median duration of 2.2 years[7]
- Findings from FOURIER support greater relative event reduction with extended LDL-C lowering treatment due to the time accrued cardiovascular benefits of lower LDL-C levels[8]
- OSLER-1, an open-label extension study in patients with hypercholesterolemia with a follow-up period of 5 years, represents the longest PCSK9 inhibitor study to date to evaluate the longer-term safety and efficacy of evolocumab when used in combination with current SOC[9]

LDL-C = low-density lipoprotein; FOURIER = Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk; ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; OSLER-1 = Open Label Study of Long Term Evaluation Against LDL-C Trial; PCSK9 = proprotein convertase subtilisin/kexin type 9; SOC = standard of care.

1. Stein EA, et al. *Eur Heart J* 2014;35:2249-59. 2. Raal FJ, et al. *Lancet* 2015;385:331-40. 3. Raal FJ, et al. *Lancet* 2015;385:341-50. 4. Blom DJ, et al. *N Engl J Med* 2014;370:1809-19. 5. Robinson JG, et al. *JAMA* 2014;311:1870-82. 6. Stroes E, et al. *JACC* 2014;63:2541-8. 7. Sabatine MS, et al. *N Engl J Med* 2017;376:1713-1722. 8. Baigent C, et al. *Lancet* 2010;376:1670-81. 9. Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

OSLER-1 Study Design: Open-Label Extension of 5 Phase 2 Studies With Up to 5 Years Exposure



- At randomization, and for 12 weeks thereafter, central labs lipid results were blinded to investigators
- After 12 weeks, investigators received unblinded lab results and could adjust SOC therapies in either arm at their discretion. Local investigators determined SOC therapy

OSLER-1 = Open Label Study of Long Term Evaluation Against LDL-C Trial; Mendel-1 = Monoclonal Antibody PCSK9 to Reduce Elevated LDL-C in Subects Currently Not Receiving Drug Therapy for Easing Lipid Levels; LAPLACE-TIMI-57 = Low-Density Lipoprotein Cholesterol Assessment With PCSK9 Monoclonal Antibody Inhibition Combined With Statin Therapy; GAUSS-1 = Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects; RUTHERFORD-1 = Reduction of LDL-C With PCSK9 Inhibition in Heterozygous Familial Hypercholesterolemia Disorder Study; YUKAWA-1 = Effects of Evolocumab, a Monoclonal Antibody to PCSK9, in Hypercholesterolemic, Statin-treated Japanese Patients at High Cardiovascular Risk ; SC = subcutaneous; QM = once monthly; SOC = standard of care.

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OSLER-1 Study Endpoints Focused on Longer-Term Efficacy & Safety

- **Efficacy**
  - Assess annual changes in LDL-C, non-HDL-C, ApoB, total cholesterol/HDL-C ratios, ApoB/apoliprotein A-1 ratios
- **Safety**
  - Incidence of AEs, SAEs, and AEs leading to discontinuation
  - Incidence of patients developing anti-evolocumab antibodies (binding or neutralizing)
  - Incidence of new-onset diabetes, injection-site reactions, neurocognitive events, and adjudicated cardiovascular events

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Baseline Demographics Remained Similar Over Time

	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1151
Age, mean (SD), years	57.6 (11.5)	57.1 (11.5)	57.2 (11.3)	57.5 (10.9)	57.6 (10.8)	57.4 (10.7)	57.3 (11.2)
BMI, mean (SD), kg/m^2	29.1 (5.9)	29.0 (5.9)	29.0 (5.9)	29.0 (5.8)	28.9 (5.7)	29.0 (5.7)	29.0 (5.9)
Female, n (%)	241 (54.5)	662 (52.7)	597 (52.0)	554 (51.3)	519 (50.9)	337 (51.1)	600 (52.1)
Race n (%)							
White	325 (73.5)	917 (73.1)	838 (73.1)	786 (72.8)	742 (72.7)	481 (73.0)	834 (72.5)
Asian	87 (19.7)	249 (19.8)	234 (20.4)	226 (20.9)	221 (21.7)	140 (21.2)	239 (20.8)
Black	24 (5.4)	74 (5.9)	61 (5.3)	55 (5.1)	46 (4.5)	30 (4.6)	64 (5.6)
Other	6 (1.4)	15 (1.2)	14 (1.2)	13 (1.2)	11 (1.1)	8 (1.2)	14 (1.2)

Baseline demographics compared similarly between the safety (n=1255) and efficacy (n=1151) analysis populations and were balanced between patients initially randomized to evolocumab + SOC and SOC-only groups.

BMI = body mass index; SOC = standard of care.
*Entered Year 2 and received ≥ 1 dose of evolocumab.
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Baseline Cardiovascular Risk Factors Remained Similar Over Time

	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1151
Coronary artery disease, n (%)	76 (17.2)	249 (19.8)	229 (20.0)	220 (20.4)	215 (21.1)	156 (23.7)	231 (20.1)
Cardiovascular risk factors, n (%)							
Current cigarette use	65 (14.7)	224 (17.8)	203 (17.7)	188 (17.4)	178 (17.5)	125 (19.0)	201 (17.5)
Type 2 diabetes mellitus	58 (13.1)	182 (14.5)	167 (14.6)	161 (14.9)	153 (15.0)	102 (15.5)	166 (14.4)
Family history of coronary heart disease	107 (24.2)	304 (24.2)	280 (24.4)	268 (24.8)	258 (25.3)	176 (26.7)	281 (24.4)
Metabolic syndrome	153 (34.6)	461 (36.7)	422 (36.8)	396 (36.7)	369 (36.2)	258 (39.2)	426 (37.0)

SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

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Baseline Lipid Lowering Therapies and Other Parameters Remained Similar Over Time

	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1151
Statin therapy intensity per ACC/AHA definition, n (%)							
High intensity	80 (18.1)	253 (20.2)	232 (20.2)	221 (20.5)	214 (21.0)	150 (22.8)	226 (19.6)
Moderate intensity	130 (29.4)	393 (31.3)	356 (31.0)	338 (31.3)	318 (31.2)	207 (31.4)	356 (30.9)
Low intensity	76 (17.2)	223 (17.8)	207 (18.0)	198 (18.3)	193 (18.9)	127 (19.3)	211 (18.3)
No statin use	156 (35.3)	386 (30.8)	352 (30.7)	324 (29.9)	295 (28.9)	175 (26.6)	358 (31.1)
Lipid parameters at the *parent study baseline*							
LDL-C by ultracentrifugation mean (SD), mg/dL	144.6 (37.5)	141.4 (37.2)	141.9 (37.2)	142.4 (37.4)	142.6 (37.3)	141.2 (38.0)	142.1 (37.6)
LDL-C calculated, mean (SD), mg/dL	143.2 (39.0)	139.6 (38.1)	140.1 (38.0)	140.7 (38.2)	140.9 (38.2)	139.0 (38.6)	140.3 (38.5)
Total cholesterol, mean (SD), mg/dL	224.8 (42.9)	220.7 (43.1)	221.1 (42.9)	221.8 (42.9)	222.1 (42.9)	219.6 (43.4)	221.5 (43.3)

Of the 1255 patients who received ≥ 1 dose of evolocumab, 71% of patients used statins at the time of receiving their first open-label dose of evolocumab; 20% received high-intensity, 31% moderate-intensity, 18% low intensity statin treatment.

ACC = American College of Cardiology; AHA=American Heart Association; LDL-C = low-density lipoprotein cholesterol; SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

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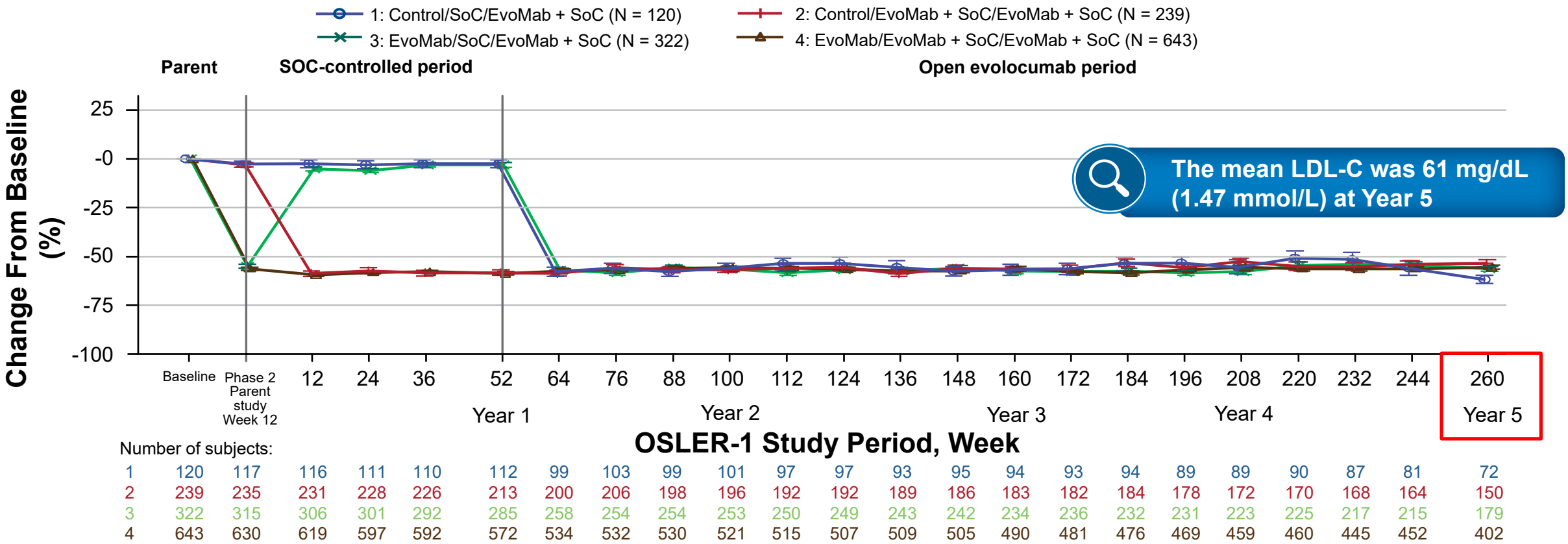
Patients Maintained Their ~60% Reduction in LDL-C Throughout 5 Years With Evolocumab

OSLER-1: LDL-C % Change From Baseline Up to 5 Years



Number of subjects:

1	120	117	116	111	110	112	99	103	99	101	97	97	93	95	94	93	94	89	89	90	87	81	72
2	239	235	231	228	226	213	200	206	198	196	192	192	189	186	183	182	184	178	172	170	168	164	150
3	322	315	306	301	292	285	258	254	254	253	250	249	243	242	234	236	232	231	223	225	217	215	179
4	643	630	619	597	592	572	534	532	530	521	515	507	509	505	490	481	476	469	459	460	445	452	402

In the all-evolocumab efficacy set, 34% (n=393) of patients achieved an LDL-C value <40 mg/dL on two consecutive occasions; 8% (n=91) of patients achieved an LDL-C value <25 mg/dL on two consecutive occasions.

LDL-C = low-density lipoprotein cholesterol; OSLER-1 = Open-Label Study of Long-term Evaluation Against LDL-C; SOC = standard of care.

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Over 5 Years, LDL-C Reduction of ~60% Was Maintained

Visit	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)							
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
LDL-C, mg/dL												
Baseline	442	143.2 (1.9)	NA	NA	882	137.7 (1.3)	NA	NA	1151	140.3 (1.1)	NA	NA
Week 24	412	134.7 (2.1)	–5.2 (1.0)	–6.0 (–16.3, 4.7)	825	58.3 (1.2)	–57.9 (0.7)	–61.5 (–71.3, –49.1)	NA	NA	NA	NA
Year 1	397	137.0 (2.0)	–2.9 (1.1)	–2.4 (–15.2, 9.3)	785	57.3 (1.2)	–58.6 (0.8)	–62.0 (–72.1, –50.0)	NA	NA	NA	NA
Year 2	354	62.3 (1.8)	–56.4 (1.1)	–59.9 (–70.8, –44.5)	717	60.7 (1.2)	–56.1 (0.8)	–59.3 (–71.4, –45.8)	1071	61.2 (1.0)	–56.2 (0.6)	–59.4 (–71.2, –45.2)
Year 3	328	61.2 (2.1)	–57.3 (1.3)	–62.2 (–72.2, –48.0)	673	61.0 (1.5)	–56.3 (1.0)	–60.0 (–72.8, –45.8)	1001	61.1 (1.2)	–56.6 (0.8)	–61.1 (–72.7, –46.4)
Year 4	312	61.8 (2.3)	–57.1 (1.4)	–61.4 (–71.0, –47.7)	631	62.4 (1.5)	–54.8 (1.0)	–60.3 (–71.4, –45.1)	943	62.2 (1.2)	–55.6 (0.8)	–60.7 (–71.2, –45.7)
Year 5	251	59.5 (1.8)	–57.9 (1.2)	–58.7 (–71.0, –46.4)	552	62.2 (1.5)	–55.1 (1.0)	–59.4 (–70.5, –43.8)	803	61.4 (1.2)	–55.9 (0.8)	–59.2 (–70.6, –44.5)

During all study periods, 67% of patients taking evolocumab had LDL-C measurements <70 mg/dL and 87.6% of patients had LDL-C measurements <100 mg/dL.

IQR = interquartile range; EVO = evolocumab; LDL-C = low-density lipoprotein cholesterol; NA = not applicable (based on study design); SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

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Over 70% of Patients Attained An LDL-C <70 mg/dL During the Course of the Study

Time Period	EVO + SOC in SOC-Controlled Period/EVO + SOC in Open EVO Period (n = 882)		
	n	Responders, n (%)	95% CI
Achievement of LDL-C < 70 mg/dL			
Baseline	882	0	NA
By Week 24	859	637 (74.2%)	(71.1%, 77.0%)
By Year 1	862	625 (72.5%)	(69.4%, 75.4%)
By Year 2	862	623 (72.3%)	(69.2%, 75.2%)
By Year 3	862	619 (71.8%)	(68.7%, 74.7%)
By Year 4	862	612 (71.0%)	(67.9%, 73.9%)
By Year 5	862	612 (71.0%)	(67.9%, 73.9%)

CI = confidence interval; EVO = evolocumab; LDL-C = low-density lipoprotein cholesterol; SOC = standard of care.

Responders were required to have at least 2 observed postbaseline LDL-C measurements up to the specified timepoints with time-averaged LDL-C calculated by dividing the area under the LDL-C curve by days from the first postbaseline LDL-C reading until the last LDL-C reading up to the timepoint of interest. No imputation was used for missing values.

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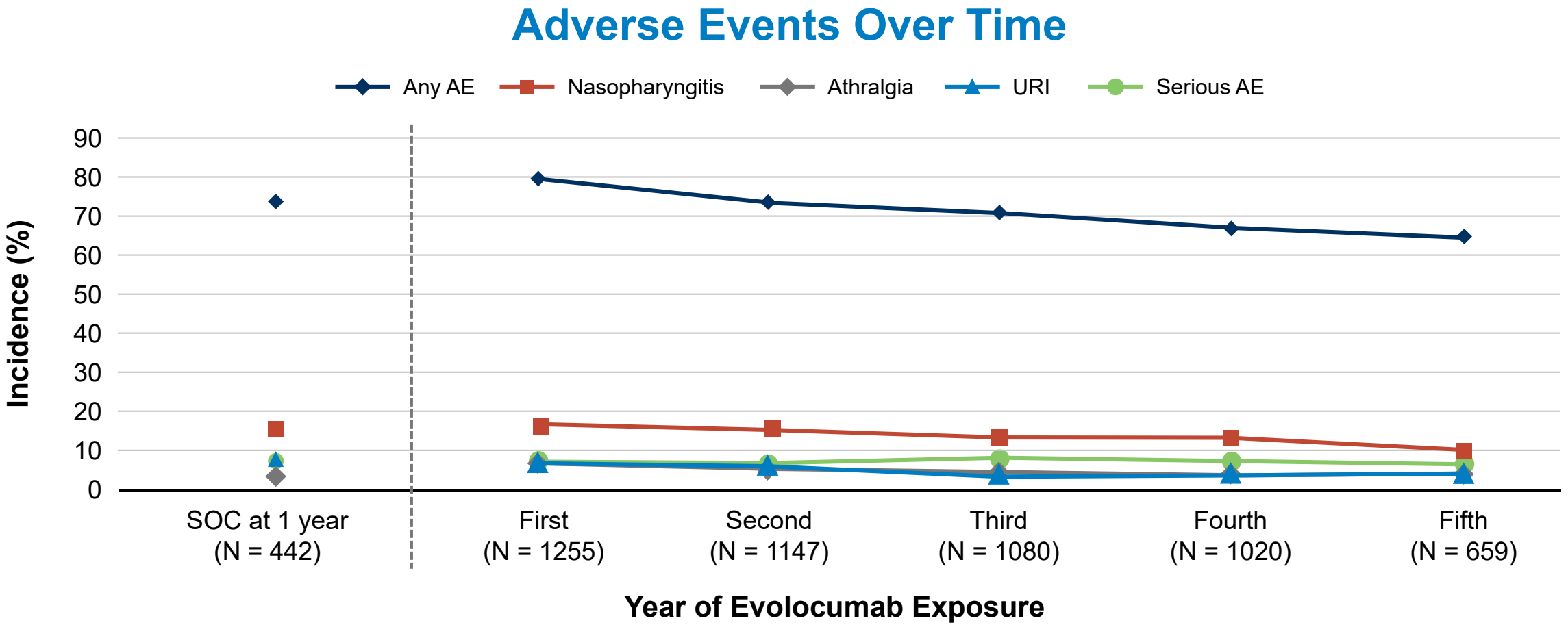
Rates of Adverse Events Over 5 Years in OSLER-1 Did Not Change Over Time



Over 5 years of evolocumab exposure, AEs occurred in 65% of patients; similar to previous years (67%-80%) and to Year 1 SOC control group (74%).

AE = adverse event; SOC = standard of care; URI = upper respiratory infection.

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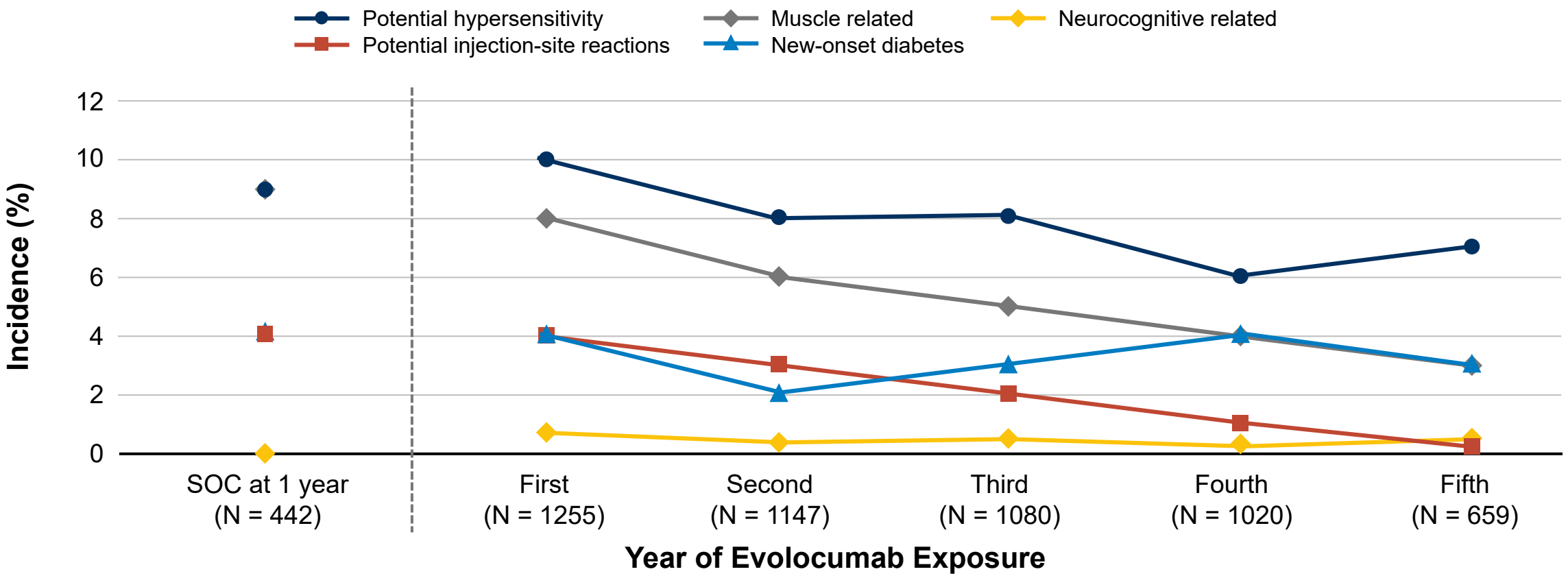
Rates of Adverse Events of Interest Over 5 Years in the OSLER-1 Trial

AEs of Interest Over Time



- **Incidence of new-onset diabetes had little fluctuation ranging from 2% to 4%, respectively.**
- **Rates in evolocumab + SOC group at Year 5 vs. SOC alone during Year 1 of exposure were 0.4% vs. 0% for neurocognitive events.**

AE = adverse event; SOC = standard of care.

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No Neutralizing ADAs Were Detected Over 5 Years

AE, n (%)	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1255
Antibody							
Binding	NA†	2 (0.16)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.16)
Neutralizing	NA	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

No patient tested positive for binding ADAs in the all-evolocumab period.

AE = adverse event; NA = not applicable; SOC = standard of care; ADAs = anti-drug antibodies.

*Observed incidence rates. Also, the length of evolocumab plus SOC exposure in OSLER-1 is defined as per patient-year. For discontinuation due to AEs, events were included in the yearly columns only if the AE onset date was in the same year of evolocumab exposure. Thus, some events were not included in the yearly columns but were included in the overall column. †Two incidences of antidrug antibodies were observed during the SOC-controlled period in patients receiving SOC alone who had received evolocumab during the parent study. No neutralizing antibodies were reported.

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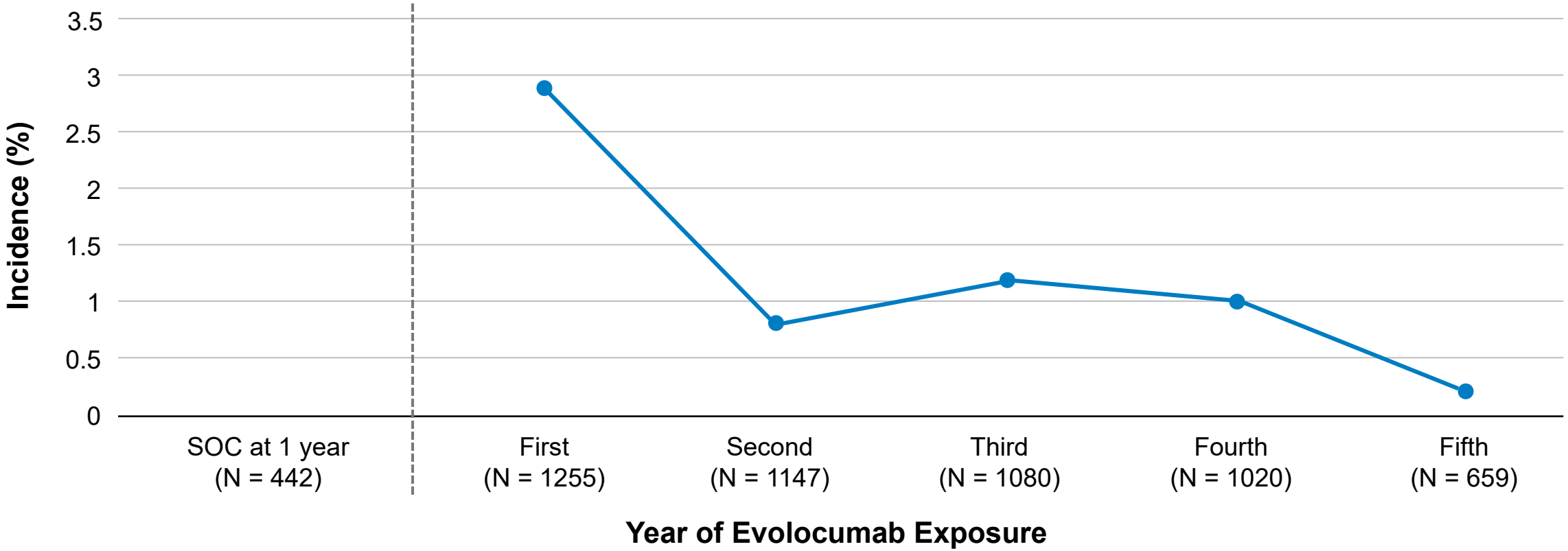
Discontinuation Rates of AEs Over 5 Years in the OSLER-1 Trial

Discontinuation of Evolocumab Due to AE



- **Approximately, 27% of patients in the safety analysis set discontinued evolocumab over the 5 year period; 5.7% of patients discontinued evolocumab due to AEs.**
- **The annualized discontinuation rate was 6.7% (95% CI, 6.0%-7.4%)..**

AE = adverse event; SOC = standard of care.

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In a Multivariate Analysis, Patients With High CV Risk or CAD Were More Likely to Continue Treatment With Evolocumab

Characteristic	Patients, n	Patients With Evolocumab Exposure, n (%)		Hazard Ratio of Drop Out (95% CI)*	*P* Value*
		Discontinued Evolocumab and/or Study (n = 344)	Remained Taking Evolocumab in Study (n = 911)		
Type 2 diabetes, n (%)					
Yes	182	43 (23.6)	139 (76.4)	Yes vs. No: 0.82 (0.60, 1.13)	0.23
No	1073	301 (28.1)	772 (71.9)		
Coronary artery disease, n (%)					
Yes	249	50 (20.1)	199 (79.9)	Yes vs. No: 0.64 (0.48, 0.87)	0.004
No	1006	294 (29.2)	712 (70.8)		
ESC/EAS risk categories					
High/very high risk	625	131 (21.0)	494 (79.0)	High vs. Low: 0.57 (0.46, 0.71)	< 0.0001
Moderate/low risk	630	213 (33.8)	417 (66.2)		

EAS = European Atherosclerosis Society; ESC = European Society of Cardiology.
SI conversion factors: to convert LDL-C to millimoles per liter, multiply by 0.0259.
*Hazard ratio and *P* values are from multivariate Cox regression model where each baseline factor was fit at a time.
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In a Multivariate Analysis, Patients With High CV Risk or CAD Were More Likely to Continue Treatment With Evolocumab *(continued)*

Characteristic	Patients, n	Patients With Evolocumab Exposure, n (%)		Hazard Ratio of Drop Out (95% CI)*	*P* Value*
		Discontinued Evolocumab and/or Study (n = 344)	Remained Taking Evolocumab in Study (n = 911)		
NCEP risk categories					
High risk/moderately high risk	570	127 (22.3)	443 (77.7)	High vs. Low: 0.66 (0.53, 0.82)	0.0002
Moderate/low risk	685	217 (31.7)	468 (68.3)		
Baseline LDL-C, mg/dL					
Mean (SD)		137.2 (36.3)	140.5 (38.7)	NA	0.17
Median (Q, Q3)		131.3 (111.0, 158.0)	133.0 (115.0, 155.0)		

LDL-C = low-density lipoprotein cholesterol; NA = not applicable; NCEP = National Cholesterol Education Program.
SI conversion factors: to convert LDL-C to millimoles per liter, multiply by 0.0259.
*Hazard ratio and *P* values are from multivariate Cox regression model where each baseline factor was fit at a time.
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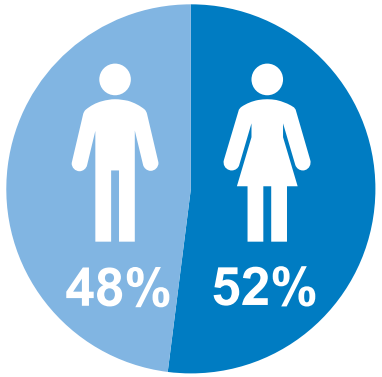
OSLER-1 Demonstrated Consistent LDL-C Efficacy and Safety Over 5 Years of Treatment With Evolocumab

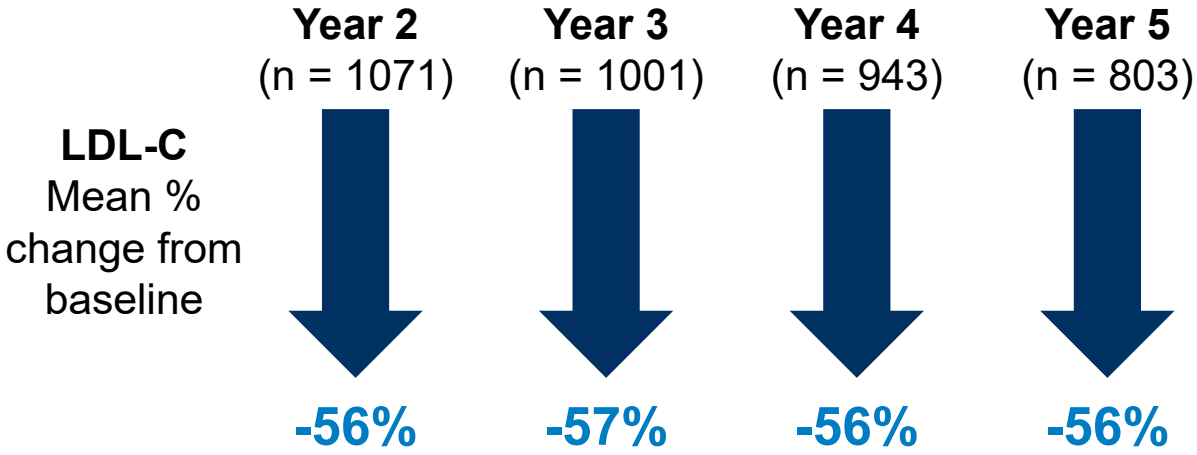
Baseline Characteristics



140 mg/dL

Mean LDL-C

Persistent Reductions in LDL-C Over 5 Years



Consistent safety over 5 years treatment

- AEs stayed stable or tracked lower over the treatment course
- Discontinued evolocumab due to AEs: 1.4%/year
- 4 instances of transient binding antibodies (2 SOC, 2 evolocumab)
- No neutralizing antibodies detected over 5 years

AE = adverse event; LDL-C = low-density lipoprotein cholesterol; SOC = standard of care.

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Summary: OSLER-1 Provides The Longest Follow-Up of Efficacy & Safety With PCSK9i Therapy To Date

- OSLER-1 demonstrated the safety and tolerability of evolocumab for treating hypercholesterolemia in a diverse patient population for up to 5 years, and represents the longest duration of follow-up for a PCSK9 inhibitor
- This study of long-term treatment with evolocumab demonstrated that over 5 years:
  - LDL-C reduction of ~60% was consistently maintained
  - Safety parameters did not change and were consistent with FOURIER
    - Annual incidence of AEs during long-term exposure to evolocumab compared similarly to patients randomized to SOC alone for Year 1
    - AE rates did not increase
    - Rates of injection-site reactions decreased over time
    - No patients developed anti-neutralizing antibodies
    - No clinical evidence of increased hypersensitivity
    - No reports of an increase in neurocognitive events or new-onset diabetes in patients with low LDL-C levels

PCSK9 = proprotein convertase subtilisin/kexin type 9; AEs = adverse events; EVO = evolocumab; SOC = standard of care; ADAs = anti-drug antibodies; LDL-C = low-density lipoprotein cholesterol; FOURIER = Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk; OSLER-1 = Open-Label Study of Long-term Evaluation Against LDL- C.

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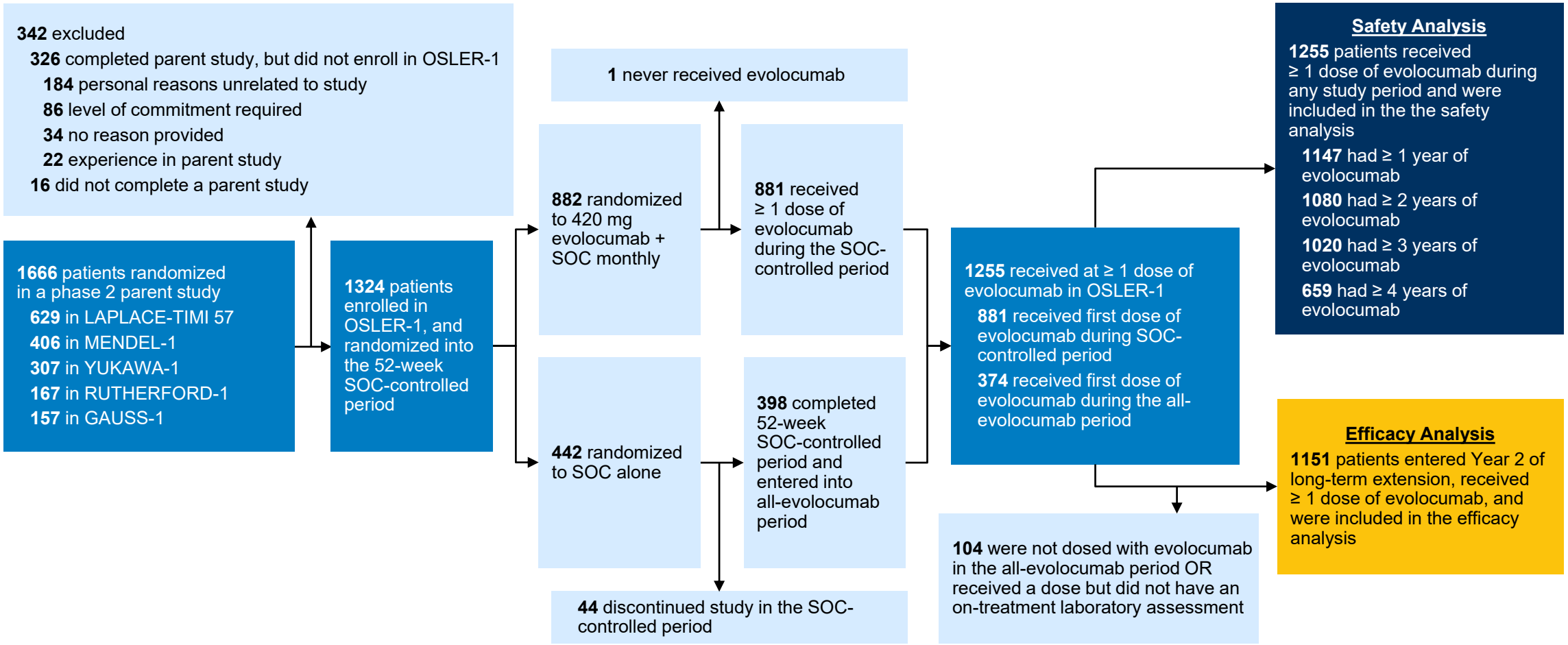
Patient Disposition in OSLER-1



GAUSS-1 = Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects; LAPLACE-TIMI = LDL-C Assessment With Proprotein Convertase Subtilisin Kexin Type 9 Monoclonal Antibody Inhibition Combined With Statin Therapy – Thrombolysis in Myocardial Infarction 57 Trial; MENDEL-1 = Monoclonal Antibody Against PCSK9 to Reduce Elevated Low-Density Lipoprotein Cholesterol in Adults Currently Not Receiving Drug Therapy for Easing Lipid Levels; OSLER-1 = Open-Label Study of Long-term Evaluation Against LDL- C; RUTHERFORD-1 = Reduction of LDL-C With PCSK9 Inhibition in Heterozygous Familial Hypercholesterolemia Disorder; SOC = standard of care; YUKAWA-1 = Study of LDL- Cholesterol Reduction Using a Monoclonal PCSK9 Antibody in Japanese Patients With Advanced Cardiovascular Risk.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

Baseline Lipid Parameters Remained Similar Over Time

	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1151
Lipid parameters at the *parent study baseline (continued)*							
HDL-C, mean (SD)	54.1 (16.5)	53.7 (16.2)	53.5 (15.9)	53.6 (16.0)	53.8 (16.1)	53.0 (15.3)	53.6 (15.9)
Non HDL-C, mean (SD)	170.7 (43.0)	167.0 (41.9)	167.6 (41.7)	168.2 (41.8)	168.3 (41.8)	166.6 (41.9)	167.9 (42.3)
Total cholesterol/HDL-C ratio, mean (SD)	4.5 (1.6)	4.4 (1.5)	4.4 (1.5)	4.5 (1.5)	4.4 (1.5)	4.4 (1.5)	4.4 (1.5)
VLDL-C, median (Q1, Q3)	22.5 (16.0, 31.5)	22.5 (16.5, 31.0)	22.5 (16.5, 31.5)	22.5 (16.5, 31.5)	22.5 (16.0, 31.5)	22.5 (16.5, 31.0)	22.5 (16.5, 31.5)
ApoB, mean (SD), mg/dL	113.2 (25.3)	111.4 (24.5)	111.7 (24.5)	112.1 (24.5)	112.2 (24.4)	111.5 (24.6)	111.9 (24.8)
ApoA1, mean (SD), mg/dL	154.8 (28.1)	154.6 (28.1)	154.5 (27.7)	154.7 (27.6)	154.8 (27.8)	154.2 (27.4)	154.7 (27.6)
ApoB/ApoA1, mean (SD)	0.8 (0.2)	0.7 (0.2)	0.7 (0.2)	0.8 (0.2)	0.8 (0.2)	0.7 (0.2)	0.7 (0.2)

ApoA = apolipoprotein A; ApoB = apolipoprotein B; HDL-C = high-density lipoprotein cholesterol; SOC = standard of care; VLDL-C = very low-density lipoprotein cholesterol.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

Baseline Lipid Parameters Remained Similar Over Time *(continued)*

	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1151
Lipid parameters at the *parent study baseline (continued)*							
Triglycerides, median (Q1,Q3), mg/dL	121.3 (90.5, 167.5)	121.5 (92.5, 168.5)	122.5 (93.0, 169.5)	121.5 (93.0, 170.8)	121.0 (92.0, 170.3)	125.0 (94.5, 172.0)	122.5 (93.0, 169.5)
PCSK9, mean (SD), mg/dL	417.0 (144.8)	427.5 (141.1)	428.4 (142.4)	430.2 (142.4)	429.5 (141.5)	436.9 (138.0)	426.9 (141.8)

SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

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Evolocumab Demonstrated Consistent Effects on Other Atherogenic Lipoproteins Over Time

Visit	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)							
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
ApoB, mg/dL												
Baseline	442	113.2 (1.2)	NA	NA	882	110.4 (0.8)	NA	NA	1151	111.9 (0.7)	NA	NA
Week 24	416	107.9 (1.3)	–4.0 (0.8)	–4.2 (–14.1, 4.9)	834	60.0 (0.8)	–45.5 (0.6)	–48.9 (–57.1, –37.6)	NA	NA	NA	NA
Year 1	401	109.5 (1.3)	–2.3 (0.9)	–2.5 (–12.0, 7.4)	800	60.0 (0.8)	–45.5 (0.6)	–48.3 (–56.9, –37.4)	NA	NA	NA	NA
Year 2	356	60.8 (1.2)	–45.8 (0.9)	–48.5 (–57.5, –36.8)	727	60.0 (0.8)	–45.5 (0.7)	–47.7 (–57.3, –36.9)	1083	60.3 (0.7)	–45.6 (0.5)	–47.9 (–57.4, –36.9)
Year 3	336	61.4 (1.4)	–46.0 (1.1)	–49.0 (–59.0, -37.6)	683	60.9 (0.9)	–45.0 (0.8)	–47.9 (–58.8, –35.5)	1019	61.1 (0.8)	–45.3 (0.6)	–48.4 (–58.9, –36.4)
Year 4	319	61.3 (1.4)	–45.6 (1.1)	–49.5 (–58.1, –36.8)	647	61.9 (1.0)	–44.1 (0.8)	–47.2 (–58.5, –34.0)	966	61.7 (0.8)	–44.6 (0.7)	–47.9 (–58.3, –35.1)
Year 5	255	62.6 (1.4)	–44.7 (1.0)	–46.3 (–56.7, –34.0)	564	63.3 (1.0)	–42.8 (0.8)	–46.0 (–56.3, –32.5)	819	63.1 (0.8)	–43.4 (0.6)	–46.1 (–56.4, –33.3)

At Years 2, 3, 4, and 5 percent reductions from baseline in mean ApoB were 46%, 45%, 45%, and 43% respectively.

ApoB = apolipoprotein B; IQR = interquartile range; EVO = evolocumab; NA = not applicable (based on study design); SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

Evolocumab Demonstrated Consistent Effects on Other Atherogenic Lipoproteins Over Time

	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)							
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
Visit	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
PCSK9, ng/ml												
Baseline	437	417.0 (6.9)	NA	NA	871	431.3 (4.7)	NA	NA	1151	426.9 (4.2)	NA	NA
Week 24	416	441.6 (8.1)	8.9 (1.8)	4.4 (–14.0, 24.6)	828	246.6 (5.1)	–41.8 (1.1)	–44.1 (–64.2, –25.0)	NA	NA	NA	NA
Year 1	401	424.8 (8.2)	5.3 (1.7)	0.9 (–17.1, 20.6)	799	244.9 (5.2)	–42.5 (1.1)	–45.9 (–63.7, –25.7)	NA	NA	NA	NA
Year 2	357	241.5 (8.1)	–42.9 (1.6)	–44.7 (–63.7, –26.5)	726	248.2 (5.5)	–42.6 (1.1)	–44.8 (–62.7, –28.0)	1083	246.0 (4.6)	–42.7 (0.9)	–44.8 (–63.4, –27.5)
Year 3	337	186.5 (7.1)	–55.3 (1.6)	–59.1 (–75.4, –36.3)	676	198.8 (4.9)	–53.3 (1.1)	–58.0 (–74.6, –36.9)	1013	194.8 (4.0)	–54.0 (29.2)	–57.4 (–76.0, –36.9)
Year 4	319	180.1 (7.1)	–56.2 (1.7)	–58.1 (–78.1, –39.4)	648	196.8 (4.9)	–53.9 (1.1)	–55.6 (–75.4, –27.7)	967	191.3 (4.1)	–54.7 (0.9)	–56.5 (–76.5, –38.0)
Year 5	253	221.5 (8.9)	–48.3 (1.9)	–50.8 (–69.3, –35.7)	558	225.7 (5.9)	–47.9 (1.3)	–49.5 (–69.1, –32.9)	811	224.4 (4.9)	–48.0 (1.1)	–49.7 (–69.2, –33.7)

IQR = interquartile range; EVO = evolocumab; NA = not applicable (based on study design); SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

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AE Rates at Year 5 Were Similar to Previous Years and Year 1

AE, n (%)	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1255
Any	327 (74.0)	1000 (79.7)	849 (74.0)	771 (71.4)	680 (66.7)	430 (65.3)	1179 (93.9)
Most common AE†							
Nasopharyngitis	64 (14.5)	195 (15.5)	166 (14.5)	139 (12.9)	134 (13.1)	64 (9.7)	411 (32.7)
Arthralgia	18 (4.1)	83 (6.6)	59 (5.1)	54 (5.0)	39 (3.8)	25 (3.8)	216 (17.2)
Upper respiratory tract infection	29 (6.6)	87 (6.9)	68 (5.9)	42 (3.9)	54 (5.3)	28 (4.2)	214 (17.1)

Achievement of LDL-C <25 or <40 mg/dL at post-baseline visit did not lead to differences in overall rates of AEs compared to patients with LDL-C ≥ 40 mg/dL.

AE = adverse event; SOC = standard of care.

*Observed incidence rates. Also, the length of evolocumab plus SOC exposure in OSLER-1 is defined as per patient-year. For discontinuation due to AEs, events were included in the yearly columns only if the AE onset date was in the same year of evolocumab exposure. Thus, some events were not included in the yearly columns but were included in the overall column. †The 3 most common serious AEs are detailed.

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AEs of Interest Over 5 Years Were Similar to Previous Years and SOC Control

AE, n (%)	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1255
Patients who discontinued owing to AEs	NA	36 (2.9)	9 (0.8)	13 (1.2)	10 (1.0)	1 (0.2)	71* (5.7)
Potential hypersensitivity†	41 (9.3)	128 (10.2)	95 (8.3)	88 (8.1)	57 (5.6)	48 (7.3)	321 (25.6)
Potential injection-site reactions†	NA	52 (4.1)	32 (2.8)	23 (2.1)	10 (1.0)	1 (0.2)	95 (7.6)
Muscle related†	41 (9.3)	104 (8.3)	69 (6.0)	52 (4.8)	40 (3.9)	18 (2.7)	246 (19.6)
New-onset diabetes‡	19 (4.3)	51 (4.1)	22 (2.1)	26 (2.8)	38 (4.4)	14 (2.7)	154 (12.3)
Neurocognitive related§	0 (0.0)	8 (0.6)	3 (0.3)	4 (0.4)	2 (0.2)	2 (0.4)	23 (1.8)

- **Potential hypersensitivity events decreased in frequency over time from 10.2% to 7.3% annually from Year 1 to Year 5.**
- **Potential injection-site reactions decreased from a 4.1% annualized rate in the first year of exposure of evolocumab to 0.2% annually in Year 4 and beyond.**

AE = adverse event; NA = not applicable; SOC = standard of care.

*Observed incidence rates. Also, the length of evolocumab plus SOC exposure in OSLER-1 is defined as per patient-year. For discontinuation due to AEs, events were included in the yearly columns only if the AE onset date was in the same year of evolocumab exposure. Thus, some events were not included in the yearly columns but were included in the overall column. †Based on US Food and Drug Administration broad search terms. ‡Subjects started to take diabetes related contaminant medications, or with post-baseline HbA1c value ≥ 6.5%, or with 2 or more consecutive post-baseline FBG ≥ 126 mg/dL. §Based on Medical Dictionary for Regulatory Activities search terms.

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SAE Rates at Year 5 Were Similar to Previous Years and Year 1

AE, n (%)	SOC Patients at 1 Year n = 442	Length of Evolocumab Exposure, Years					
		First n = 1255	Second n = 1147	Third n = 1080	Fourth n = 1020	Fifth n = 659	All* n = 1255
Serious†	30 (6.8)	90 (7.2)	79 (6.9)	85 (7.9)	71 (7.0)	47 (7.1)	293 (23.3)
Osteoarthritis	1 (0.2)	3 (0.2)	3 (0.3)	6 (0.6)	3 (0.3)	2 (0.3)	17 (1.4)
Angina	2 (0.5)	4 (0.3)	2 (0.2)	2 (0.2)	5 (0.5)	1 (0.2)	14 (1.1)
Chest pain	1 (0.2)	4 (0.3)	3 (0.3)	1 (0.1)	1 (0.1)	2 (0.3)	10 (0.8)

- Cardiovascular events rates during extended exposure to evolocumab remained low.
- Serious AE rates at Year 5 (7%) matches the rates of previous years (7%-8%) and Year 1 SOC control (7%).

AE = adverse event; SOC = standard of care; SAE = serious adverse event.

*Observed incidence rates. Also, the length of evolocumab plus SOC exposure in OSLER-1 is defined as per patient-year. For discontinuation due to AEs, events were included in the yearly columns only if the AE onset date was in the same year of evolocumab exposure. Thus, some events were not included in the yearly columns but were included in the overall column. †The 3 most common serious AEs are detailed.

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Evolocumab Demonstrated Consistent Effects on Other Atherogenic Lipoproteins Over Time

	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)				Total* (N = 1151)			
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
Visit	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
ApoA1, mg/dL												
Baseline	442	154.8 (1.3)	NA	NA	882	154.6 (0.9)	NA	NA	1151	154.7 (0.8)	NA	NA
Week 24	416	156.5 (1.5)	1.4 (0.5)	1.4 (–5.2, 7.8)	834	163.4 (1.0)	6.4 (0.4)	6.5 (–1.8, 14.1)	NA	NA	NA	NA
Year 1	401	157.3 (1.6)	1.8 (0.6)	2.4 (–7.1, 9.5)	800	163.0 (1.0)	6.3 (0.5)	4.8 (–2.6, 14.2)	NA	NA	NA	NA
Year 2	356	166.5 (1.7)	7.9 (0.7)	7.8 (0.2, 15.7)	727	164.2 (1.1)	6.8 (0.5)	6.0 (–1.6, 15.0)	1083	165.0 (0.9)	7.2 (0.4)	6.5 (–1.1, 15.3)
Year 3	336	167.2 (1.7)	8.5 (0.7)	7.6 (1.2, 16.4)	683	165.3 (1.1)	7.8 (0.5)	7.4 (0.0, 14.8)	1019	166.0 (0.9)	8.0 (0.4)	7.4 (0.4, 15.5)
Year 4	319	168.2 (1.8)	9.1 (0.7)	8.5 (1.3, 17.1)	647	166.7 (1.2)	8.9 (0.5)	8.4 (–0.3, 17.5)	966	167.2 (1.0)	9.0 (0.4)	8.4 (0.3, 17.5)
Year 5	255	169.3 (1.9)	9.6 (0.8)	9.8 (1.3, 17.5)	564	167.6 (1.3)	9.4 (0.6)	8.6 (0.8, 17.8)	819	168.1 (1.1)	9.4 (0.5)	8.9 (1.1, 17.5)

Mean ApoA1 increased at Years 2, 3, 4, and 5 by 7%, 8%, 9%, and 9%, respectively.

ApoA = apolipoprotein A; EVO = evolocumab; NA = not applicable (based on study design); SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

Evolocumab Demonstrated Consistent Effects on Other Atherogenic Lipoproteins Over Time

Visit	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)				Total* (N = 1151)			
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
HDL-C, mg/dL												
Baseline	442	54.1 (0.8)	NA	NA	882	53.4 (0.5)	NA	NA	1151	53.6 (0.5)	NA	NA
Week 24	416	56.3 (0.9)	4.1 (0.7)	3.5 (–4.4, 12.0)	834	58.0 (0.6)	9.6 (0.5)	9.5 (0.0,18.2)	NA	NA	NA	NA
Year 1	399	56.5 (0.9)	3.8 (0.8)	3.4 (–6.0, 12.3)	792	58.1 (0.6)	10.0 (0.6)	9.4 (–0.9, 19.2)	NA	NA	NA	NA
Year 2	354	60.5 (1.0)	11.8 (1.0)	10.5 (0.0, 21.9)	722	58.8 (0.6)	11.1 (0.7)	9.7 (0.0, 21.1)	1076	59.3 (0.5)	11.4 (0.5)	10.1 (0.0, 21.2)
Year 3	335	59.4 (1.0)	10.1 (1.0)	9.8 (–2.0, 20.8)	680	58.2 (0.7)	10.2 (0.7)	8.1 (–1.8, 21.3)	1015	58.6 (0.6)	10.2 (0.6)	8.5 (–1.8, 21.3)
Year 4	317	59.9 (1.1)	10.2 (1.0)	9.6 (0.0,20.0)	642	58.2 (0.7)	11.0 (0.7)	9.5 (–2.0, 22.5)	959	58.7 (0.6)	10.7 (0.6)	9.5 (–1.3, 21.6)
Year 5	252	58.8 (1.2)	8.3 (1.2)	7.6 (–3.3, 19.3)	561	57.9 (0.7)	9.8 (0.8)	8.2 (–2.8, 20.4)	813	58.2 (0.6)	9.3 (0.7)	7.9 (–3.0, 20.0)

Increases in mean HDL-C were 11%, 10%, 11%, and 9% at Years 2, 3, 4, and 5, respectively.

EVO = evolocumab; HDL-C = high-density lipoprotein cholesterol; NA = not applicable (based on study design); SOC = standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

Evolocumab Demonstrated Consistent Effects on Other Atherogenic Lipoproteins Over Time

Visit	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)				Total* (N = 1151)			
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
Triglycerides, mg/dL												
Baseline	442	140.0 (3.5)	NA	NA	882	137.3 (2.0)	NA	NA	1151	139.0 (1.9)	NA	NA
Week 24	416	136.2 (3.6)	2.3 (1.7)	–4.2 (–19.8, 20.3)	834	125.1 (2.3)	–5.6 (1.2)	–11.7 (–28.8, 9.0)	NA	NA	NA	NA
Year 1	399	139.7 (3.6)	6.4 (2.0)	0.6 (–18.0, 21.1)	791	127.4 (2.5)	–3.7 (1.4)	–10.9 (–28.4, 10.4)	NA	NA	NA	NA
Year 2	354	120.2 (3.0)	–7.0 (1.8)	–11.6 (–30.5, 10.1)	721	126.9 (2.5)	–4.2 (1.4)	–9.9 (–28.0, 10.8)	1075	124.7 (1.9)	–5.1 (1.1)	–10.6 (–29.0, 10.6)
Year 3	335	125.9 (4.2)	–4.7 (2.3)	–12.0 (–30.3, 10.1)	680	128.5 (2.7)	–2.1 (1.5)	–8.8 (–27.9, 13.3)	1015	127.6 (2.3)	–2.9 (1.3)	–9.7 (–28.5, 12.6)
Year 4	317	128.2 (4.2)	–1.3 (2.4)	–8.4 (–29.3, 13.8)	642	130.6 (2.9)	–0.6 (2.3)	–8.6 (–26.4, 12.4)	959	129.8 (2.4)	–0.8 (1.7)	–8.6 (–27.1, 13.5)
Year 5	252	127.7 (4.0)	–1.8 (2.6)	–8.9 (–30.5, 16.3)	560	134.4 (3.4)	2.6 (2.7)	–6.4 (–28.1, 21.8)	812	132.3 (2.7)	1.2 (1.8)	–6.8 (–28.9, 20.9)

Mean triglyceride reductions occurred at Years 2, 3, and 4 of 5%, 3%, and 1%, respectively.

EVO = evolocumab; NA = not applicable (based on study design); SOC = =standard of care.

*Entered Year 2 and received ≥ 1 dose of evolocumab.

Koren MJ, et al. *J Am Coll Cardiol*. 2019;74(17):2132-2146.

In a Multivariate Analysis, Patients Outside North America or Male Were More Likely to Continue Treatment With Evolocumab

Characteristic	Patients, n	Patients With Evolocumab Exposure, n (%)		Hazard Ratio of Drop Out (95% CI)*	*P* Value*
		Discontinued Evolocumab and/or Study (n = 344)	Remained Taking Evolocumab in Study (n = 911)		
Age group, n (%)					
≥ 65 years	361	101 (28.0)	260 (72.0)	Old vs. Young: 1.05 (0.83, 1.33)	0.68
< 65 years	894	243 (27.2)	651 (72.8)		
Sex, n (%)					
Female	662	202 (30.5)	460 (69.5)	F vs. M: 1.3 (1.07, 1.65)	0.0092
Male	593	142 (23.9)	451 (76.1)		
Region (n (%)					
North America	611	228 (37.3)	383 (62.7)	NA vs. other: 2.28 (1.82, 2.86)	< 0.0001
Other	644	116 (18.0)	528 (82.0)		

NA = not applicable.

SI conversion factors: to convert LDL-C to millimoles per liter, multiply by 0.0259.

*Hazard ratio and *P* values are from multivariate Cox regression model where each baseline factor was fit at a time.

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Hemoglobin A1c Remained Stable Over Time

Visit	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)				Total* (N = 1151)			
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
HbA1c (%)												
Baseline	442	6.0 (0.1)	NA	NA	882	6.0 (0.1)	NA	NA	484*	6.0 (1.0)	NA	NA
Week 24	415	5.9 (0.0)	0.1 (0.0)	0.1 (-0.1, 0.3)	848	5.9 (0.1)	0.1 (0.0)	0.1 (-0.1, 0.3)	NA	NA	NA	NA
Year 1	402	5.8 (0.8)	0.1 (0.0)	0.0 (-0.2, 0.2)	797	5.8 (0.7)	0.0 (0.0)	0.0 (-0.2, 0.2)	NA	NA	NA	NA
Year 2	355	5.9 (0.0)	0.1 (0.0)	0.0 (-0.1, 0.3)	727	5.9 (0.0)	0.1 (0.0)	0.0 (-0.2, 0.3)	467	5.9 (0.0)	0.1 (0.0)	0.0 (-0.2, 0.3)
Year 3	338	6.0 (0.1)	0.2 (0.1)	0.1 (-0.1, 0.3)	679	6.0 (0.0)	0.1 (0.0)	0.1 (-0.1, 0.3)	436	6.0 (0.0)	0.2 (0.0)	0.1 (-0.1, 0.3)
Year 4	320	5.9 (0.0)	0.2 (0.1)	0.1 (-0.1, 0.3)	644	5.9 (0.0)	0.1 (0.0)	0.1 (-0.2, 0.3)	416	5.9 (0.0)	0.2 (0.0)	0.1 (-0.2, 0.3)
Year 5	254	6.0 (0.1)	0.3 (0.1)	0.1 (-0.1, 0.4)	561	6.0 (0.0)	0.1 (0.0)	0.0 (-0.1, 0.3)	373	6.0 (0.0)	0.2 (0.0)	0.1 (-0.1, 0.3)

EVO = evolocumab; HbA1c = hemoglobin A1c.

*Parent study baseline, where HbA1c was not measured for all patients.

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Fasting Plasma Glucose Remained Stable Over Time

Visit	All OSLER-1 Patients (N = 1324)								All-EVO Patients (Efficacy Set)* (n = 1151)			
	SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 442)				EVO + SOC in SOC-Controlled Period/ EVO + SOC in Open EVO Period (n = 882)				Total* (N = 1151)			
			% Change from Baseline				% Change from Baseline				% Change from Baseline	
	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)	n	Observed	Mean (SE)	Median (IQR)
FPG, mg/dL												
Baseline	442	102.4 (1.1)	NA	NA	882	103.2 (0.7)	NA	NA	1151		NA	NA
Week 24	414	102.0 (1.0)	–0.4 (0.9)	0.0 (–6.0, 6.0)	847	105.3 (0.8)	1.8 (0.6)	2.0 (–5.0, 8.0)	NA	NA	NA	NA
Year 1	401	104.0 (1.2)	1.6 (1.1)	1.0 (–4.0, 8.0)	833	105.6 (0.8)	2.2 (0.6)	1.0 (–5.0, 9.0)	NA	NA	NA	NA
Year 2	364	104.8 (1.4)	2.3 (1.0)	1.0 (–4.5, 8.0)	733	106.2 (0.8)	2.3 (0.7)	2.0 (–5.0, 8.0)	1097	105.7 (0.7)	2.3 (0.6)	2.0 (–5.0, 8.0)
Year 3	347	104.8 (1.4)	2.2 (1.2)	2.0 (–5.0, 8.0)	703	106.8 (0.9)	2.9 (0.8)	1.0 (–5.0, 9.0)	1050	106.2 (0.8)	2.7 (0.7)	2.0 (–5.0, 9.0)
Year 4	330	105.2 (1.5)	2.9 (1.0)	1.0 (–5.0, 9.0)	684	107.1 (0.9)	3.4 (0.7)	2.0 (–5.0, 9.0)	1014	106.5 (0.8)	3.2 (0.7)	2.0 (–5.0, 9.0)
Year 5	305	109.5 (1.8)	6.1 (1.4)	4.0 (–3.0, 11.0)	639	109.2 (1.0)	5.4 (0.9)	3.0 (–4.0, 11.0)	944	109.3 (0.9)	5.6 (0.8)	3.0 (–4.0, 11.0)

EVO = evolocumab; FPG = fasting plasma glucose.

*Parent study baseline, where HbA1c was not measured for all patients.

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