

## Supplemental Online Content

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**eTable 1.** LLT Intensification and Achievement of LDL-C <70 mg/dL at 2 Years by Subgroup in the LDL-C Cohorts

**eTable 2.** LLT Intensification and Achievement of LDL- C <70 mg/dL at 2 Years by Site Characteristics and Physician Survey Responses

**eTable 3.** Subject Characteristics at Baseline - Comparing Patients Completing Follow-up vs. Patients Dropping out [not due to death]

**eFigure 1.** Consort diagram

**eFigure 2.** Frequency of lipid panels observed in clinical care over 2 years of follow-up in the GOULD registry

**eFigure 3.** Use of lipid-lowering therapies over time among patients enrolled in the GOULD registry

**eAppendix.** List of Committees and Investigators

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

**eTable 1. LLT Intensification and Achievement of LDL-C < 70 mg/dL at 2 Years by Subgroup in the LDL-C Cohorts**

Characteristics	LLT Intensification at 2 Years, % (n/N)	P Value	LDL-C < 70 mg/dL at 2 Years, % (n/N)	P Value
Baseline LDL-C, mg/dL				
70-99	14.4 (383/2651)	<.001	33.9 (758/2235)	<.001
≥ 100	22.4 (403/1801)		21.0 (308/1464)	
Age, years				
≤ 65	19.1 (315/1650)	.054	28.9 (387/1337)	.898
> 65	16.8 (471/2801)		28.7 (679/2362)	
Gender				
Female	17.8 (310/1741)	.832	23.2 (333/1435)	<.001
Male	17.6 (476/2711)		32.4 (733/2264)	
Race and ethnicity				
White	18.3 (697/3807)	.005	29.6 (946/3191)	.005
Non-white	13.8 (89/645)		23.6 (120/508)	
Hispanic	12.3 (46/375)	.004	22.3 (70/314)	.008
Non-Hispanic	18.1 (736/4056)		29.4 (991/3367)	
College or professional degree				
No	17.7 (475/2689)	.392	27.7 (616/2227)	.002
Yes	18.7 (266/1419)		32.8 (398/1213)	
Married				
No	15.8 (233/1474)	.005	26.8 (322/1201)	.015
Yes	19.3 (513/2652)		30.8 (693/2253)	
Annual household income ≥ \$75 000				
No	16.1 (496/3075)	<.001	27.9 (712/2548)	<.001
Yes	23.7 (245/1034)		33.8 (302/893)	
BMI > 30 kg/m <sup>2</sup>				
No	18.1 (417/2310)	.550	27.8 (539/1936)	.166
Yes	17.4 (365/2102)		29.9 (519/1735)	
ASCVD <sup>a</sup>				
Minor	17.7 (361/2045)	.997	29.0 (493/1702)	.855
Major	17.7 (425/2407)		28.7 (573/1997)	
Diabetes				
No	18.1 (511/2829)	.346	27.4 (645/2350)	.015
Yes	16.9 (275/1623)		31.2 (421/1349)	
Insurance (private, Medicare, Medicaid)				
No	14.6 (94/644)	.028	25.2 (124/493)	.054
Yes	18.2 (692/3808)		29.4 (942/3206)	

Data are as of October 5, 2020.

<sup>a</sup>Major ASCVD events include: MI, CVA, TIA, and PAD. Minor ASCVD events include: CAD, PCI, CABG, percutaneous carotid intervention, and carotid endarterectomy.

For LDL-C, 1mg/dL = 1/38.6 mmol/L

ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CVA, cerebrovascular accident; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

**eTable 2. LLT Intensification and Achievement of LDL-C < 70 mg/dL at 2 Years by Site Characteristics and Physician Survey Responses**

Characteristics	Total, % (n/N) (N = 113 Physicians)	LLT Intensification at 2 Years, % (n/N)	P Value	LDL-C < 70 mg/dL at 2 Years, % (n/N)	P Value
<b>Geographic regions</b>					
Northeast	15.0 (17/113)	11.6 (62/534)	<.0001	27.1 (112/414)	.5654
Northwest	20.4 (23/113)	22.3 (178/798)		30.3 (206/679)	
South	46.0 (52/113)	18.3 (399/2176)		28.1 (501/1784)	
West	18.6 (21/113)	15.8 (109/688)		29.6 (177/597)	
<b>Type of practice</b>					
Teaching	16.8 (19/113)	25.1 (148/589)	<.0001	35.5 (173/488)	<.0005
Nonteaching	83.2 (94/113)	16.6 (600/3607)		27.6 (823/2986)	
<b>Location</b>					
Rural	14.2 (16/113)	15.4 (106/687)	.0726	28.0 (152/542)	.7258
Urban	85.8 (97/113)	18.3 (642/3509)		28.8 (844/2932)	
<b>Presence of lipid management protocols</b>					
Yes	40.7 (46/113)	22.3 (359/1612)	<.0001	32.0 (451/1411)	.0004
No	59.3 (67/113)	15.1 (389/2584)		26.4 (545/2063)	
<b>Lead physician specialty</b>					
Cardiology	45.1 (51/113)	21.7 (452/2087)	<.0001	30.1 (523/1686)	.0028
Internal medicine or family medicine	45.1 (51/113)	11.7 (204/1745)		25.6 (377/1472)	
Other	9.7 (11/113)	25.3 (92/364)		30.4 (96/316)	
<b>LDL-C goal to achieve with LLT</b>					
< 50 mg/dL	4.5 (5/112)	13.4 (25/187)	0.00004	20.9 (34/163)	<.0001
< 70 mg/dL	68.8 (77/112)	19.3 (578/2995)		30.8 (767/2487)	
Others <sup>a</sup>	26.8 (30/112)	14.3 (142/995)		23.6 (191/810)	
<b>How strong is the scientific evidence supporting the use of high-intensity statins vs low-/moderate-intensity statins among patients with ASCVD?</b>					
Very strong	43.6 (48/110)	20.9 (399/1905)	<.0001	29.7 (470/1583)	.4473
Strong	34.5 (38/110)	15.9 (225/1417)		28.1 (338/1201)	
Moderate/weak/very weak	21.8 (24/110)	14.1 (120/850)		27.3 (183/671)	
<b>Frequently prescribing non-statin LLT for the following scenarios (most or always)</b>					
LDL-C remains high despite statin use - yes	67.0 (75/112)	19.1 (558/2922)	0.0012	29.9 (718/2405)	.0201
LDL-C remains high despite statin use - no	33.0 (37/112)	14.9 (187/1255)		26.0 (274/1055)	
Further cardiovascular disease risk reduction above and beyond statin use - yes	50.9 (57/112)	17.2 (378/2204)	0.2215	29.2 (534/1831)	.4958
Further cardiovascular disease risk reduction above and beyond statin use - no	49.1 (55/112)	18.6 (367/1973)		28.1 (458/1629)	

Data are as of October 5, 2020.

<sup>a</sup>Others include LDL-C goal < 100 mg/dL, LDL-C goal < 130 mg/dL, “it depends on patients’ other risk factors,” and “do not use LDL-C goals.”

For LDL-C, 1mg/dL = 1/38.6 mmol/L

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy.

**eTable 3. Subject Characteristics at Baseline - Comparing Patients Completing Follow-up vs Patients Dropping out [not due to death]**

Characteristics	Patients completing follow-up (N=4230)	Patients dropping out [not due to death] (N=576)	P Value
<b>Demographic</b>			
Age, years			
Mean $\pm$ SD (N)	67.7 $\pm$ 9.8 (4230)	67.4 $\pm$ 10.6 (575)	.629
Median (Q1, Q3)	69.0 (61.0, 74.0)	68.0 (60.0, 75.0)	
Range (min, max)	(30.0, 94.0)	(35.0, 93.0)	
Male	60.6% (2562/4230)	57.6% (332/576)	.178
Ethnicity			.002
Hispanic or Latino	7.6% (321/4230)	11.8% (68/576)	
Not Hispanic or Latino	91.8% (3882/4230)	87.7% (505/576)	
Missing	0.6% (27/4230)	0.5% (3/576)	
Race			.022
American Indian or Alaska Native	0.1% (5/4230)	0.3% (2/576)	
Asian	1.7% (72/4230)	3.0% (17/576)	
Black or African American	10.0% (424/4230)	9.9% (57/576)	
Native Hawaiian or Other Pacific	0.1% (4/4230)	0.3% (2/576)	
White	86.5% (3657/4230)	83.7% (482/576)	
Other or multiple	1.6% (68/4230)	2.8% (16/576)	
<b>Physical measurements</b>			
Weight, kg			
Mean $\pm$ SD (N)	88.6 $\pm$ 19.7 (4214)	88.9 $\pm$ 20.1 (563)	.729
Median (Q1, Q3)	87.0 (74.5, 100.1)	87.0 (75.0, 101.8)	
Range (min, max)	(39.5, 189.5)	(44.5, 156.8)	
BMI, kg/m <sup>2</sup>			
Mean $\pm$ SD (N)	30.5 $\pm$ 6.0 (4204)	30.9 $\pm$ 6.1 (560)	.168
Median (Q1, Q3)	29.6 (26.5, 33.7)	30.0 (26.7, 34.5)	
Range (min, max)	(14.5, 79.5)	(18.8, 58.5)	
BMI categories			<.001
Underweight (BMI $\leq$ 18.5)	0.5% (21/4230)	0.0% (0/576)	
Normal (18.5 < BMI $\leq$ 25)	15.0% (635/4230)	13.7% (79/576)	
Overweight (25 < BMI $\leq$ 30)	37.0% (1564/4230)	34.9% (201/576)	
Obese (BMI > 30)	46.9% (1984/4230)	48.6% (280/576)	
Missing	0.6% (26/4230)	2.8% (16/576)	
Waist circumference, cm			
Mean $\pm$ SD (N)	100.8 $\pm$ 16.4 (2400)	102.9 $\pm$ 18.6 (327)	.046
Median (Q1, Q3)	99.1 (91.4, 110.5)	101.6 (88.9, 114.3)	
Range (min, max)	(45.0, 203.2)	(45.0, 167.6)	
Systolic BP, mmHg			
Mean $\pm$ SD (N)	129.7 $\pm$ 16.4 (4220)	131.3 $\pm$ 17.7 (563)	.034
Median (Q1, Q3)	128.0 (120.0, 139.5)	130.0 (120.0, 140.0)	
Range (min, max)	(58.0, 228.0)	(85.0, 221.0)	

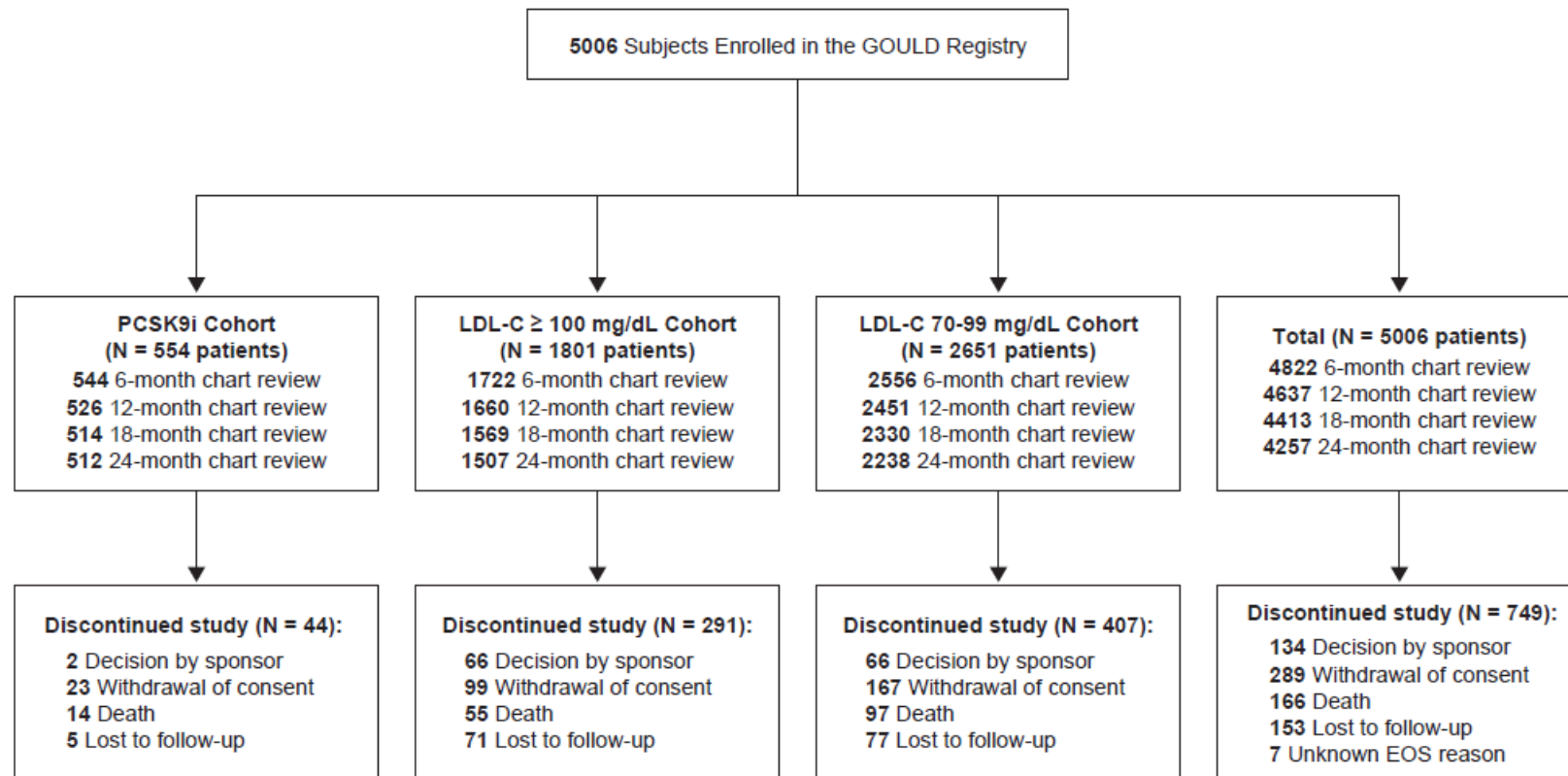
<b>Characteristics</b>	<b>Patients completing follow-up (N=4230)</b>	<b>Patients dropping out [not due to death] (N=576)</b>	<b>P Value</b>
Diastolic BP, mmHg			
Mean ± SD (N)	74.7 ± 9.9 (4220)	76.1 ± 10.3 (563)	.002
Median (Q1, Q3)	74.0 (68.0, 80.0)	76.0 (70.0, 81.0)	
Range (min, max)	(40.0, 144.0)	(50.0, 116.0)	
<b>Composite cardiovascular medical history or procedure before enrollment<sup>a</sup></b>	95.2% (4025/4230)	82.5% (475/576)	<.001
<b>Cardiovascular medical history</b>			
<i>Atherosclerotic cardiovascular disease (ASCVD)</i>			
Congestive heart failure (CHF)	11.5% (485/4230)	10.1% (58/576)	.321
Cerebrovascular accident (CVA)	9.7% (411/4230)	12.0% (69/576)	.089
Transient ischemic attack (TIA)	8.1% (341/4230)	10.9% (63/576)	.020
Peripheral arterial disease (PAD)	13.4% (568/4230)	10.4% (60/576)	.044
Myocardial infarction (MI)	32.4% (1370/4230)	24.5% (141/576)	<.001
Coronary artery disease (CAD)	82.4% (3486/4230)	65.1% (375/576)	<.001
<i>Other risks</i>			
Type I diabetes mellitus	1.7% (72/4230)	1.7% (10/576)	.953
Type II diabetes mellitus	32.5% (1376/4230)	38.0% (219/576)	.009
Hypertension (HTN)	86.4% (3654/4230)	84.7% (488/576)	.279
Atrial fibrillation	13.7% (578/4230)	11.3% (65/576)	.116
Cigarettes			
Never	40.9% (1729/4230)	40.6% (234/576)	.909
Former	43.2% (1828/4230)	36.5% (210/576)	.002
Current	10.5% (446/4230)	13.5% (78/576)	.030
Missing	5.4% (227/4230)	9.4% (54/576)	<.001
<b>Cardiovascular procedure before enrollment</b>			
Percutaneous coronary intervention	14.0% (593/4230)	3.3% (19/576)	<.001
Coronary artery bypass graft (CABG)	6.3% (268/4230)	3.1% (18/576)	.002
Percutaneous carotid intervention	0.3% (14/4230)	0.0% (0/576)	.167
Carotid endarterectomy	0.7% (29/4230)	0.0% (0/576)	.046
Percutaneous peripheral intervention	1.7% (72/4230)	0.2% (1/576)	.005
Peripheral artery bypass graft	0.2% (9/4230)	0.0% (0/576)	.268
<b>Family history of premature ASCVD</b>	35.4% (1496/4230)	29.9% (172/576)	.009

Data are as of October 5, 2020.

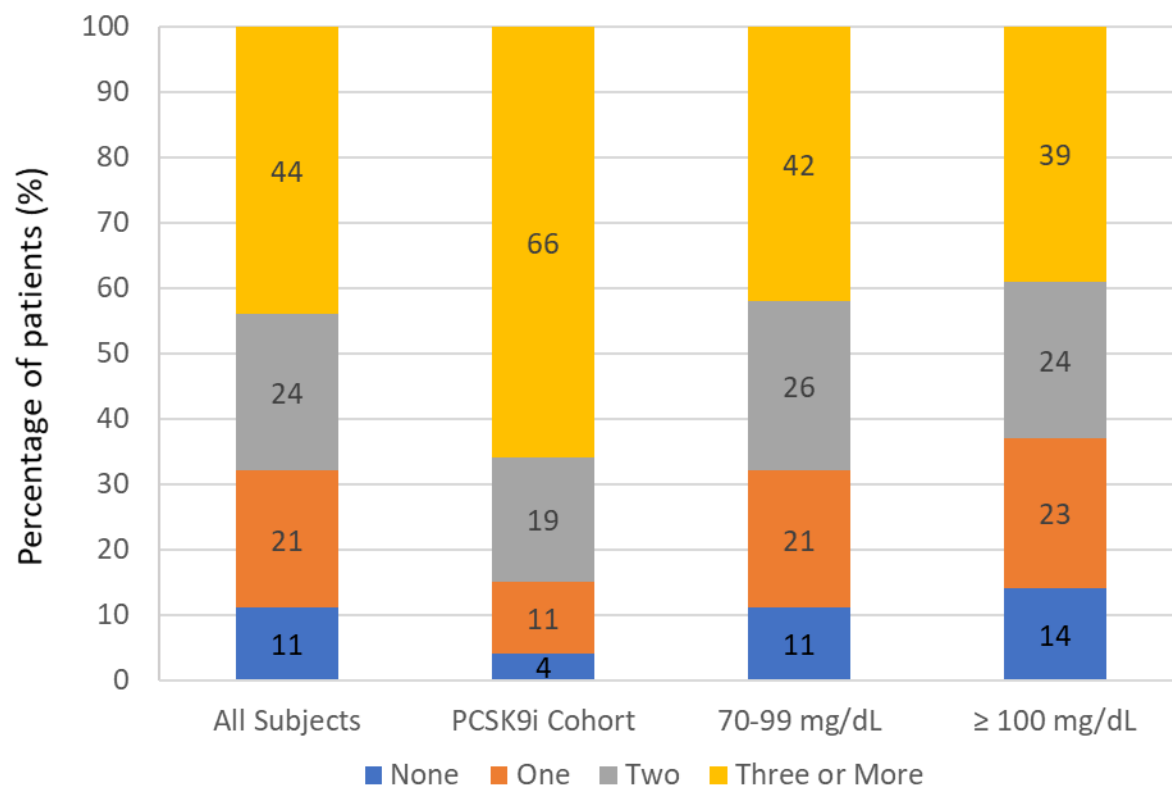
Note: Baseline is defined as the last record before enrollment

<sup>a</sup> Composite cardiovascular medical history or procedure before enrollment includes CVA, TIA, PAD, MI, CAD, PCI, CABG, percutaneous carotid intervention, carotid endarterectomy, percutaneous peripheral intervention, and peripheral artery bypass graft. ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass graft; CAD, coronary artery disease; CVA, cerebrovascular accident; MI, myocardial infarction; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; Q, quartile; TIA, transient ischemic attack.

**eFigure 1.** Consort Diagram



**eFigure 2. Frequency of lipid panels observed in clinical care over 2 years of follow-up in the GOULD registry**

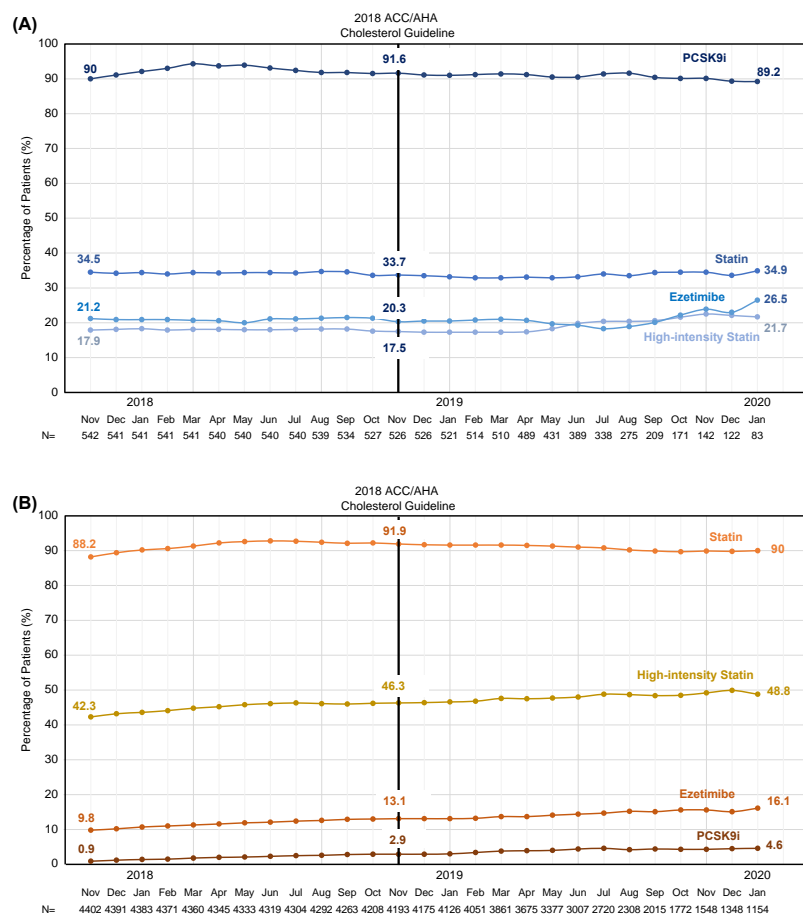


Abbreviations: PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.



**eFigure 3. Use of lipid-lowering therapies over time among patients enrolled in the GOULD registry. A)** Subjects enrolled in the PCSK9i cohort; **B)** Subjects enrolled in both LDL-C cohorts (LDL-C 70-99 mg/dL cohort and LDL-C  $\geq$  100 mg/dL cohort)

Abbreviations: LDL-C, low-density lipoprotein cholesterol; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.



## Appendix: List of Committees and Investigators

### Steering Committee

Christopher Cannon, MD (Co-chair), Mikhail Kosiborod, MD (Co-chair), Christie Ballantyne, M.D, Deepak L. Bhatt, M.D, M.P.H, James De Lemos, M.D, Robert S. Rosenson, M.D

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**Sponsor Acknowledgement:** CJ Bell (Global Clinical Program Management), Blai Coll (Executive Medical Director), Mary Elliott-Davey (Biostatistics), Jason Exter (US Medical Lead), Jo Krol (Global Clinical Program Management), Katie Mues (US Medical Director and Study Lead), Tamara Palagashvili (Senior Medical Scientist)

**Investigators:** Included are primary investigators representing the 119 enrolling sites in the US. Investigators are listed in order of enrollment contribution.

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