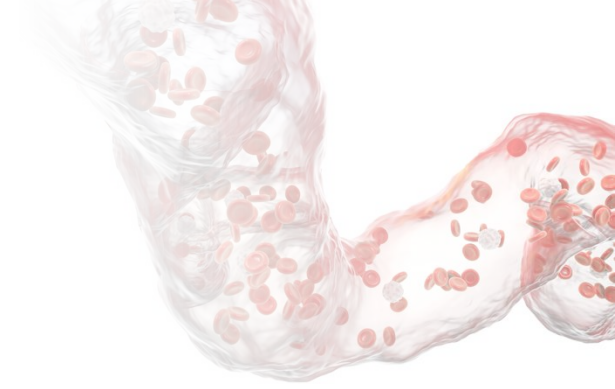


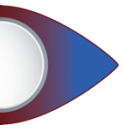
# rose<sup>2</sup>



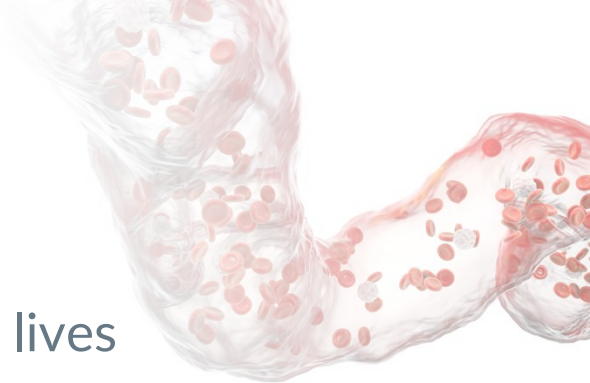
**The combination of obicetrapib and ezetimibe lowers  
LDL-C in patients on high-intensity statins:  
results from the ROSE2 Trial (NCT05266586)**

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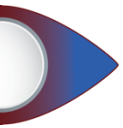
Christie M Ballantyne, Stephen J Nicholls, Marc Ditmarsch, John J Kastelein,  
Douglas Kling, Danielle L Curcio, Michael H Davidson



## Rationale

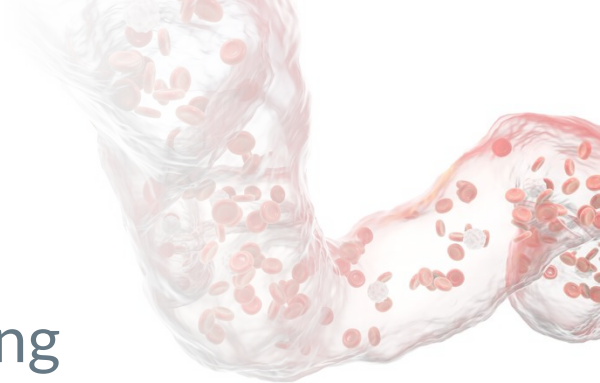


- Cardiovascular disease is a leading cause of death worldwide, claiming more lives than cancer and chronic respiratory disease
- CVD deaths in the United States is on the rise increasing from 784,454 in 2010 to 928,741 in 2020
- The 2022 ACC Expert Consensus recommends that adults with ASCVD at very high risk on statin therapy:
  - Reduce LDL-C  $\geq 50\%$  on maximally tolerated statin therapy **AND**
  - Target an LDL-C goal  $< 55$  mg/dL
- Less than 25% of ASCVD patients are on high-intensity statin therapy (HIS), and less than 25% of these patients have an LDL-C level  $< 70$  mg/dL. As a result, there is an ongoing need for effective, safe, convenient therapies that serve as an adjunct to HIS



## Objective

The primary objective of ROSE2 was to evaluate the lipid-lowering efficacy, safety, and tolerability of obicetrapib 10mg in combination with ezetimibe 10mg in patients treated with high-intensity statin therapy compared with placebo.



# ROSE2 Trial: obicetrapib and high-intensity statin therapy

**Objective** To evaluate the effect of obicetrapib 10mg in combination with ezetimibe 10mg on top of HIS on LDL-C

## Inclusion criteria

- Stable dose of high-intensity statins (A 40/80, R 20/40) 8 weeks before screening
- Fasting LDL-C levels >70 mg/dL (1.8 mmol/L)

## Exclusion criteria

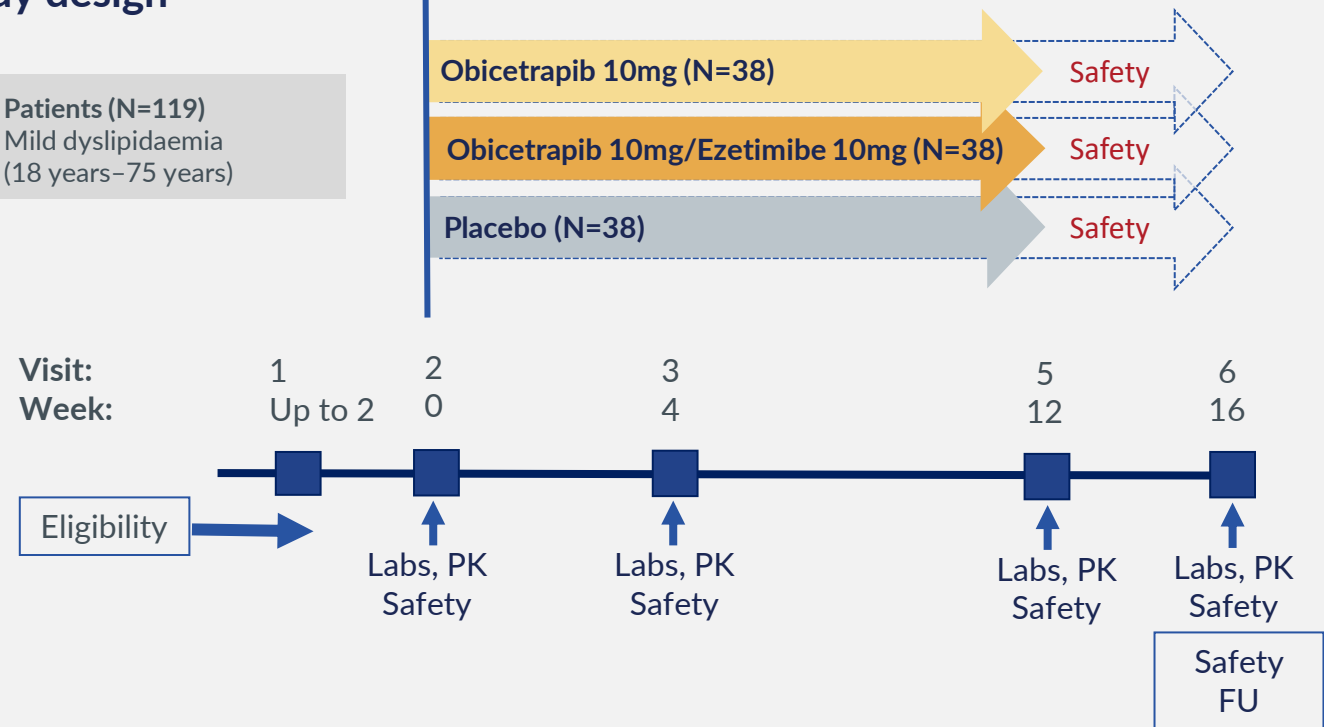
- Current significant CV disease
- HbA1c  $\geq 10\%$
- Uncontrolled hypertension

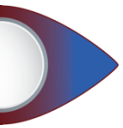
## Primary efficacy endpoint

- Percent change from baseline in LDL-C compared with the placebo group

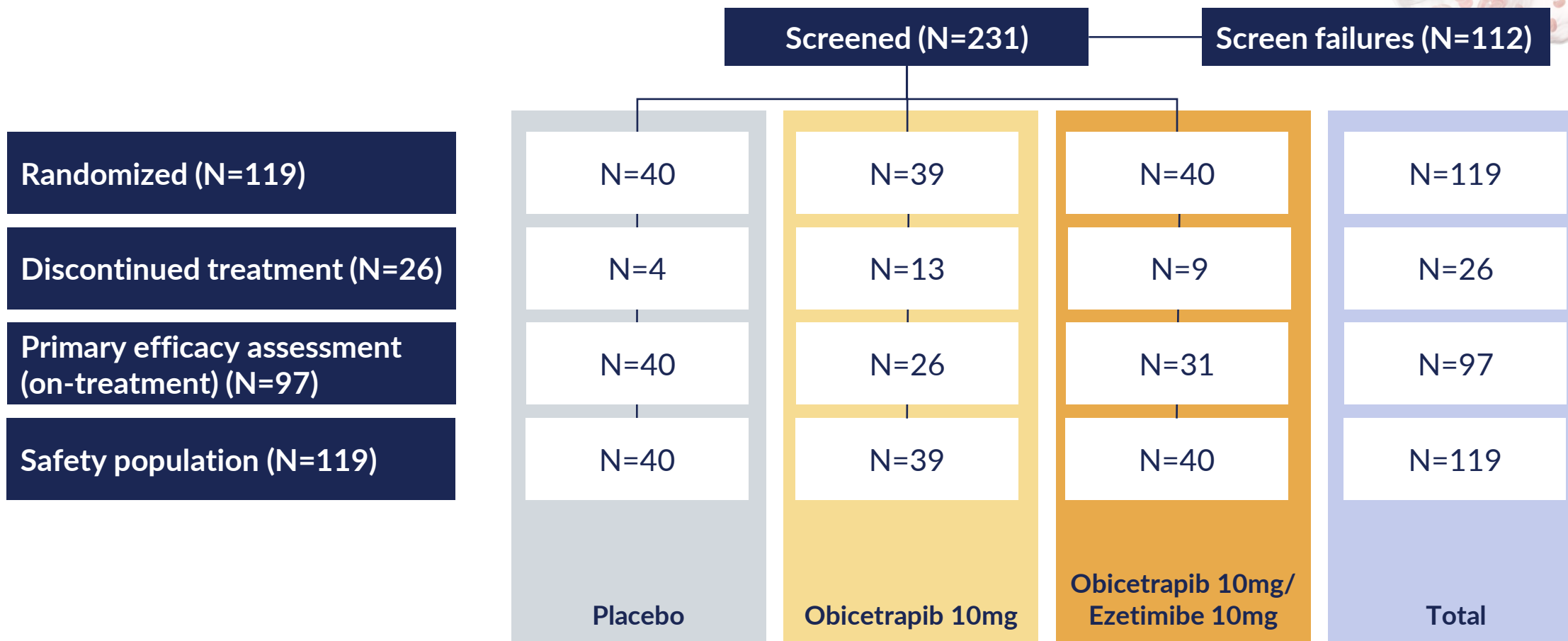
## Study design

Patients (N=119)  
Mild dyslipidaemia  
(18 years-75 years)





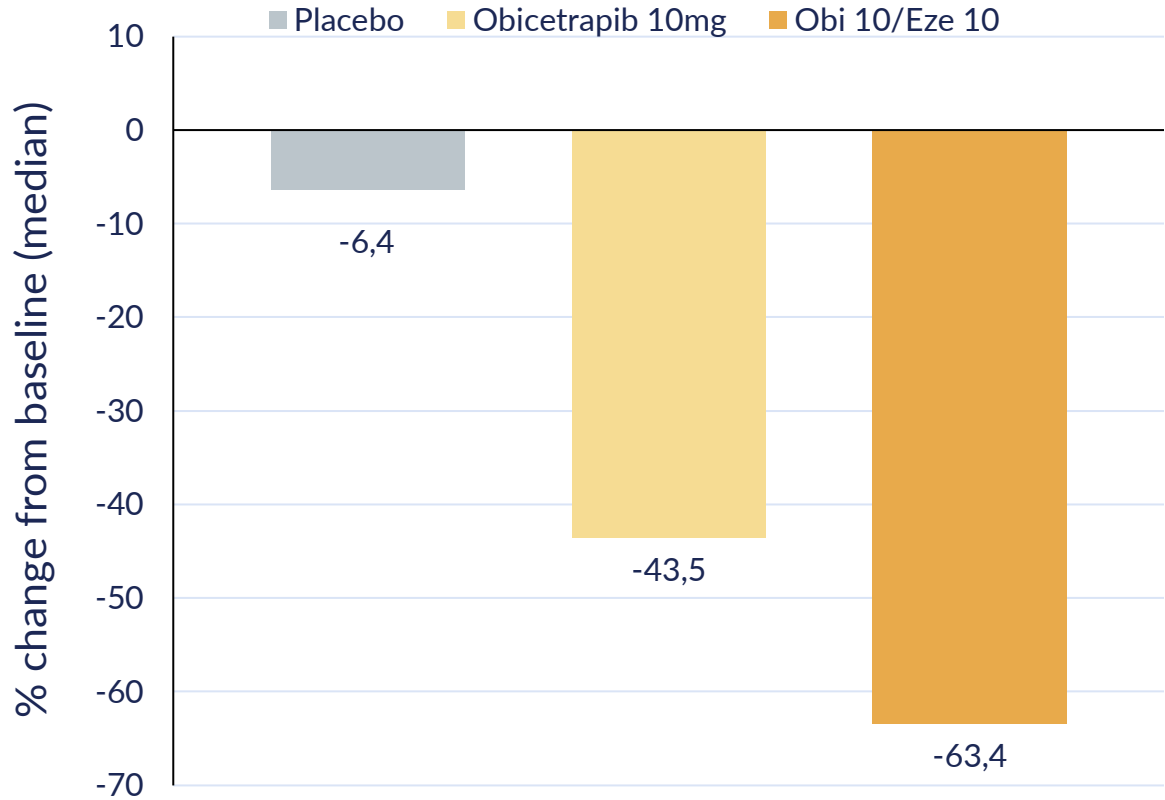
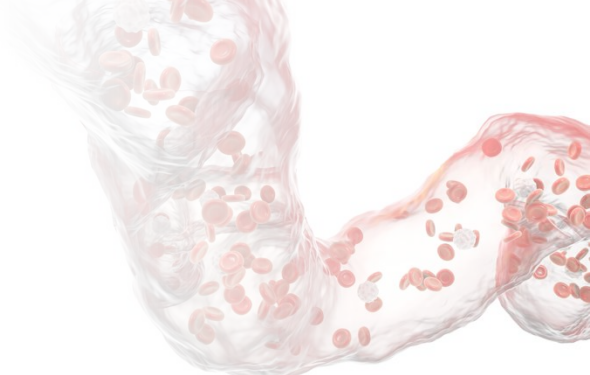
# Patient disposition



# Baseline characteristics

		Placebo N=40 (%)	Obicetrapib 10mg N=26 (%)	Obicetrapib 10mg/ Ezetimibe 10mg N=31 (%)
	Mean Age (years)	60.6	64.8	63.5
	Female %	35	34.6	38.7
	Mean BMI (kg/m <sup>2</sup> )	30.8	29.9	31.8
Race %	White	75	88.5	93.5
	Black/African American	22.5	11.5	6.5
Statin use %	Atorvastatin 40mg/80mg	75	69.2	80.6
	Rosuvastatin 20mg/40mg	25	30.8	19.4
Baseline level (median)	LDL-C (mg/dL)	95	100	87
	HDL-C (mg/dL)	42.5	47	46

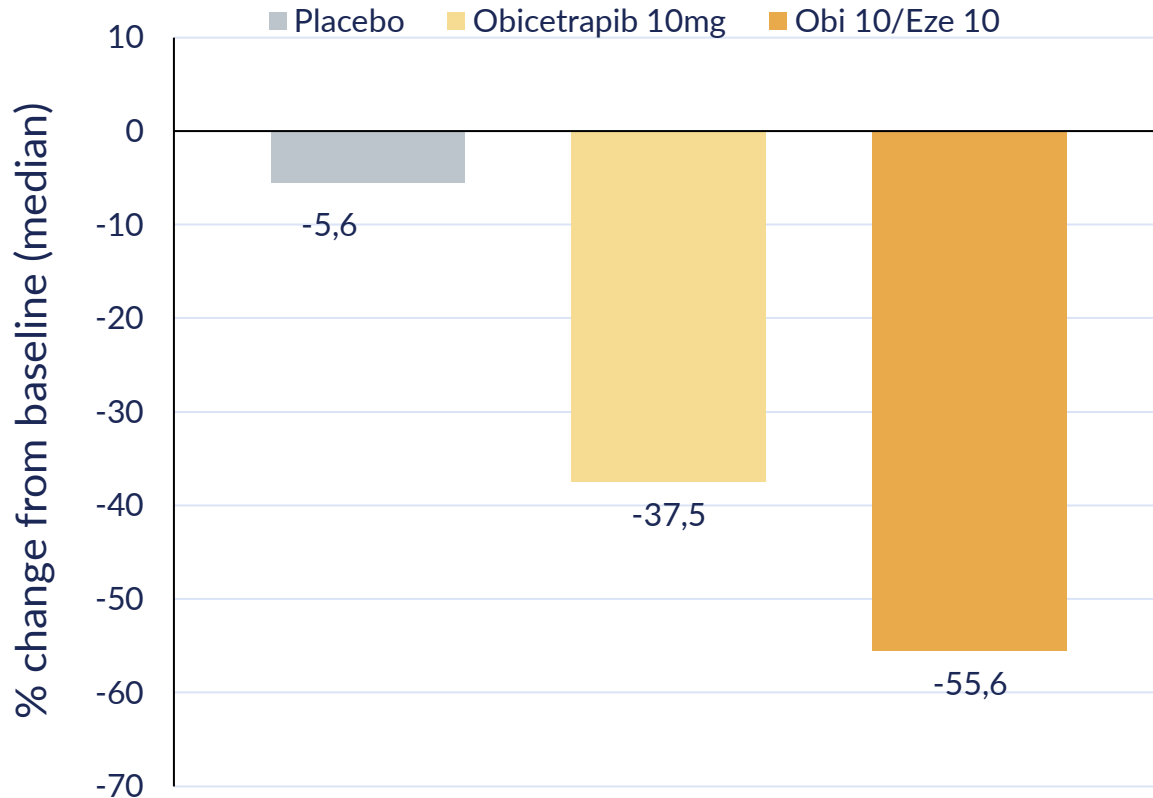
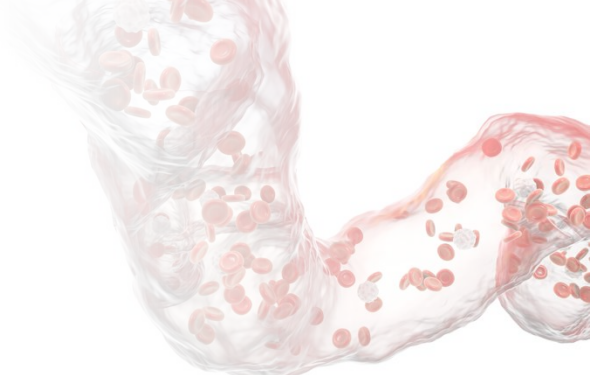
# LDL-C in mg/dL and percent change from baseline



Median (min, max) LDL-C levels (mg/dL) at baseline and EoT

Time	Placebo	Obicetrapib 10mg	Obi 10/Eze 10
<b>Baseline Median</b>	95.5 (60, 211) (N=40)	100.0 (35, 189) (N=26)	87.0 (62, 152) (N=31)
<b>EoT Median</b>	88.0 (55, 188) (N=36)	55.5 (21, 148) (N=26)	39.0 (15, 96) (N=31)
<b>% Change from Baseline (median)</b>	-6.4 (-36.4, 96.7) (N=36)	-43.5 (-78.4, 22.6) (N=26)	-63.4 (-83.7, -29.7) (N=31)
<b>% change from baseline LS mean (95% CI)</b>	-0.85 (-7.75, 6.05)	-39.20 (-47.41, -30.99)	-59.23 (-66.75, -51.71)
<b>P-value</b>	-	<0.0001	<0.0001

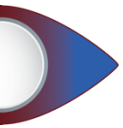
# Non-HDL-C in mg/dL and percent change from baseline



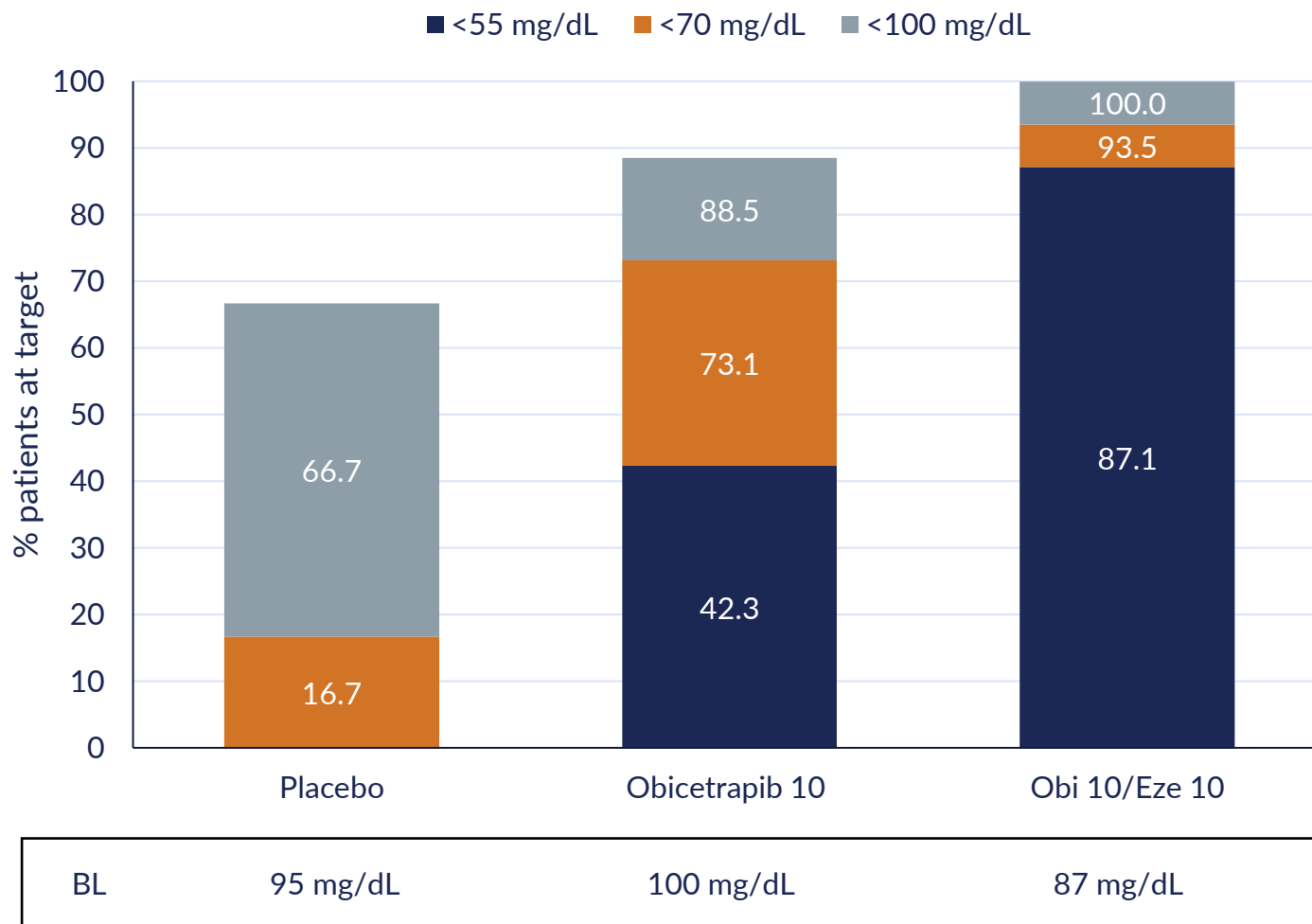
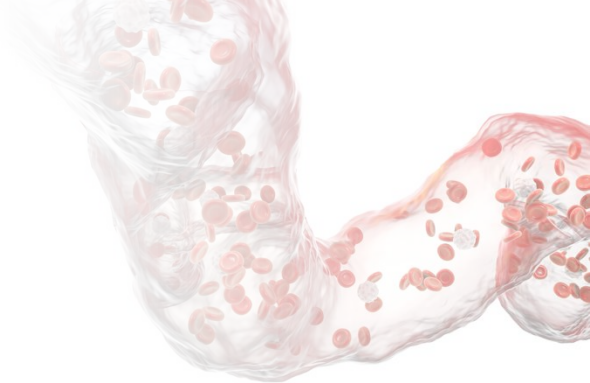
Median (min, max) non-HDL-C levels (mg/dL) at baseline and EoT

Time	Placebo	Obicetrapib 10mg	Obi 10/Eze 10
<b>Baseline Median</b>	125.5 (73, 227) (N=40)	121.5 (57, 209) (N=26)	116.0 (77, 189) (N=31)
<b>EoT Median</b>	113.0 (82, 231) (N=36)	78.5 (48, 164) (N=26)	61.5 (25, 118) (N=31)
<b>% Change from Baseline (median)</b>	<b>-5.6</b> (-34.9, 83.6) (N=36)	<b>-37.5</b> (-59.2, 20.0) (N=26)	<b>-55.6</b> (-76.2, 30.8) (N=31)
<b>% change from baseline LS mean (95% CI)</b>	-0.84 (-6.78, 5.10)	-33.82 (-40.88, -26.77)	-54.02 (-60.49, -47.56)
<b>P-value</b>	-	<0.0001	<0.0001

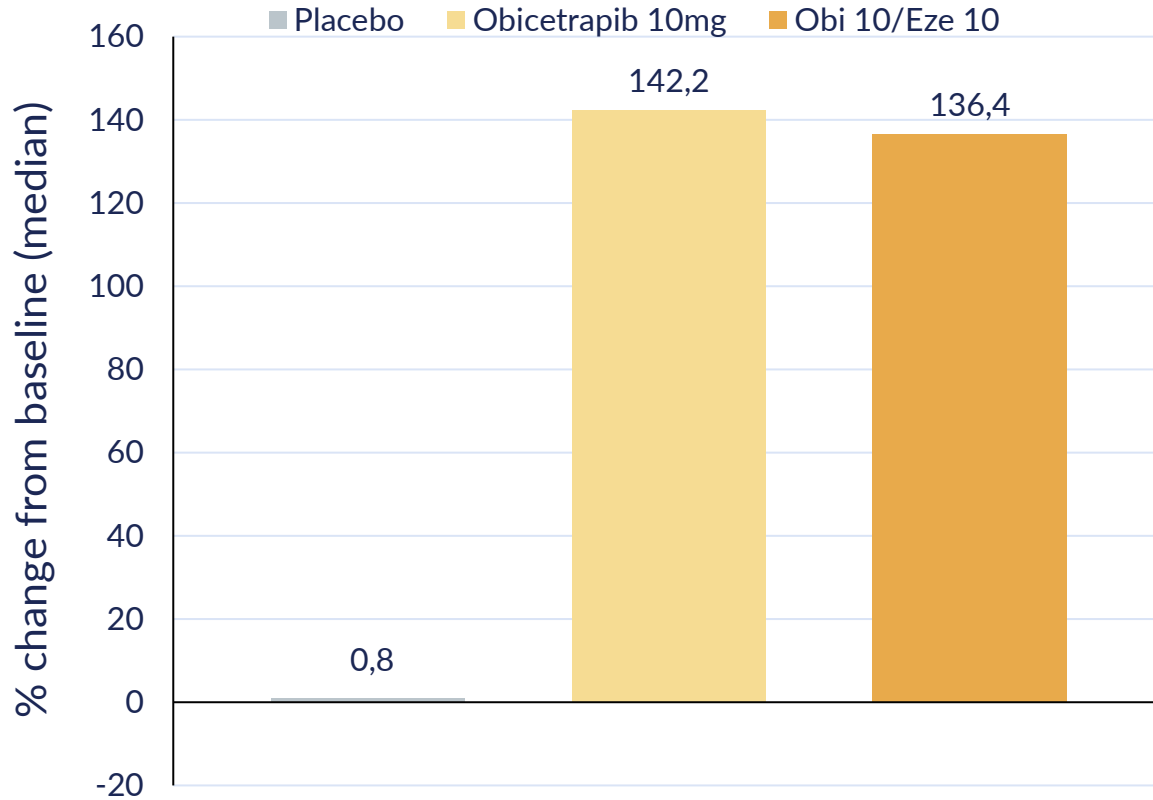
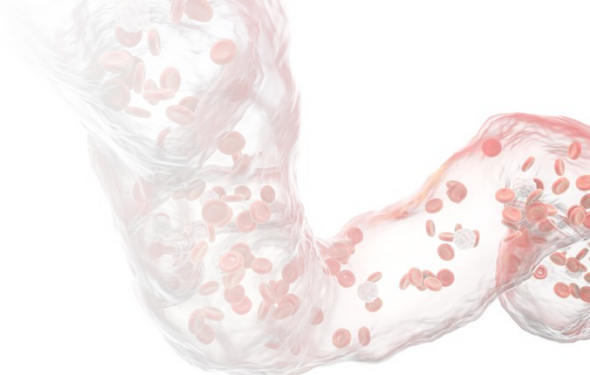




# LDL-C target attainment



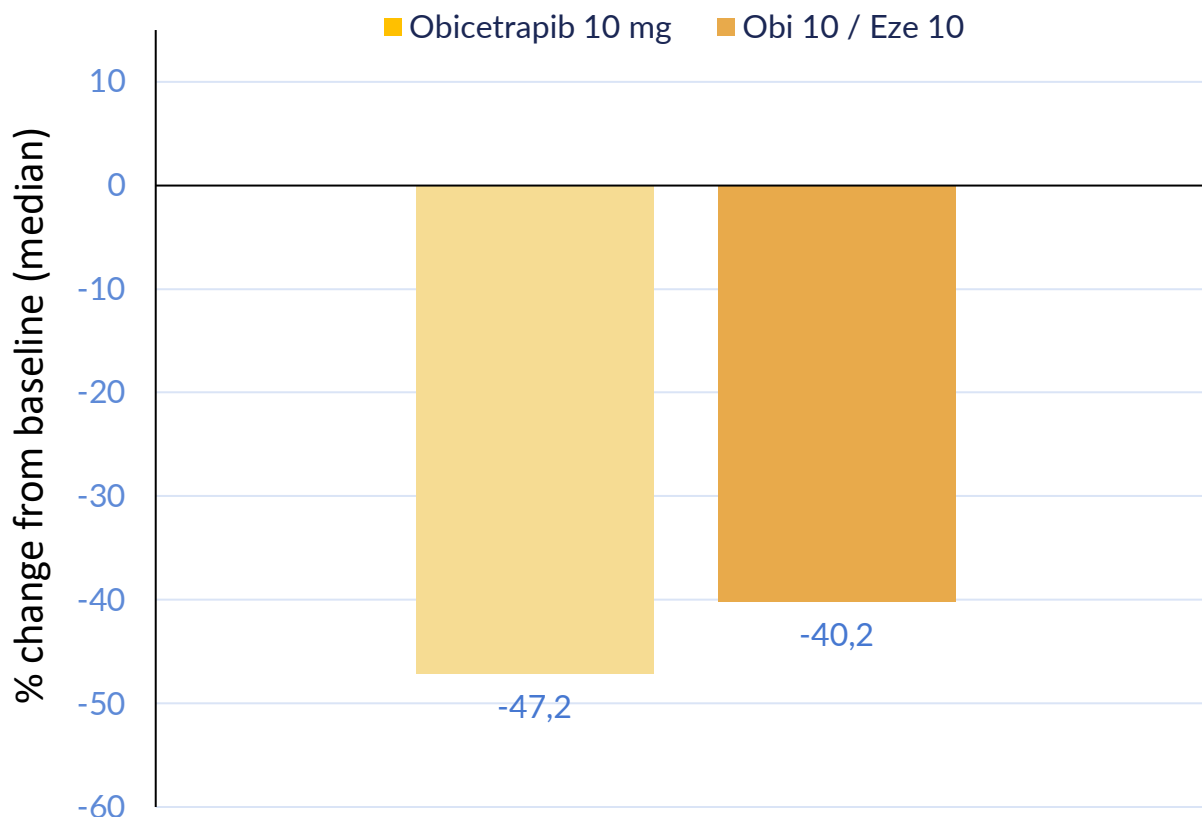
# HDL-C in mg/dL and percent change from baseline



Median (min, max) HDL-C levels (mg/dL) at baseline and EoT

Time	Placebo	Obicetrapib 10mg	Obi 10/Eze 10
<b>Baseline Median</b>	42.5 (31, 68) (N=40)	47.0 (28, 111) (N=26)	46.0 (26, 76) (N=31)
<b>EoT Median</b>	44.5 (28, 83) (N=36)	120.5 (58, 185) (N=26)	112.0 (52, 184) (N=31)
<b>% Change from Baseline (median)</b>	0.8 (-33.3, 45) (N=36)	142.2 (34.9, 310.7) (N=26)	136.4 (46.5, 261.3) (N=31)
<b>% change from baseline LS mean (95% CI)</b>	-0.32 (-13.66, 13.01)	150.80 (134.62, 166.99)	146.60 (129.16, 158.04)
<b>P-value</b>	-	<0.0001	<0.0001

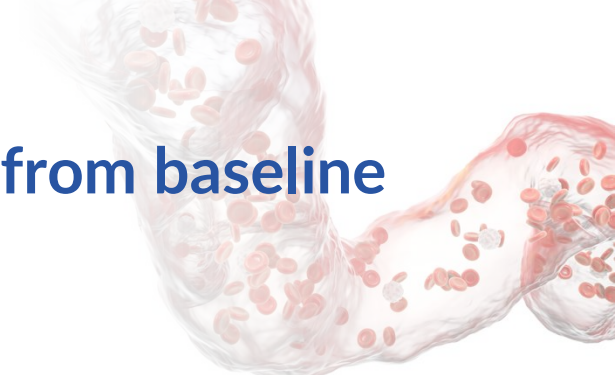
# Lp(a) in nmol/L & percent change from baseline



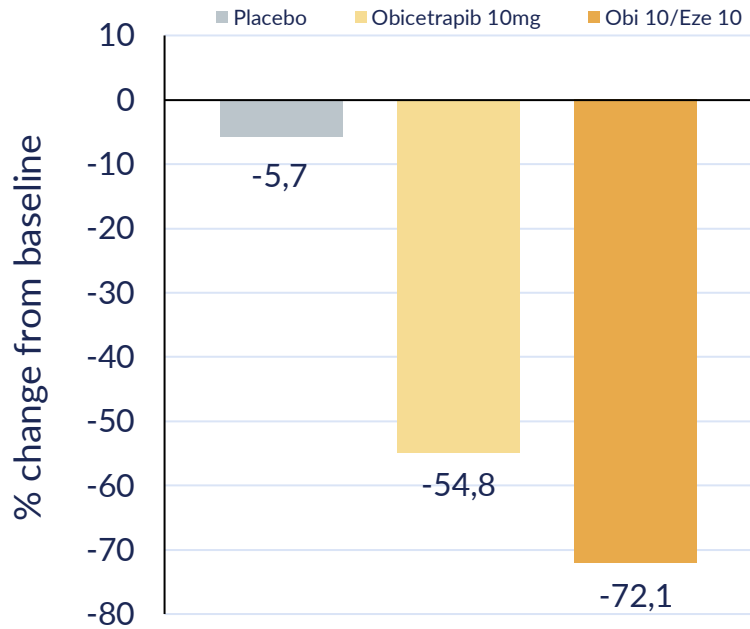
Median (min, max) Lp(a) levels (nmol/L) at baseline and EoT

Time	Obicetrapib 10 mg	Obi 10 / Eze 10
<b>Baseline Median</b>	44.0 (0.8, 372.4) (N=24)	27.6 (0.2, 479.9) (N=31)
<b>EoT Median</b>	13.8 (0.9, 329.9) (N=24)	8.6 (0.1, 520.8) (N=31)
<b>% Change from Baseline (median)</b>	-47.2 (-97.5, 214.5) (N=24)	-40.2 (-92.4, 702.0) (N=31)

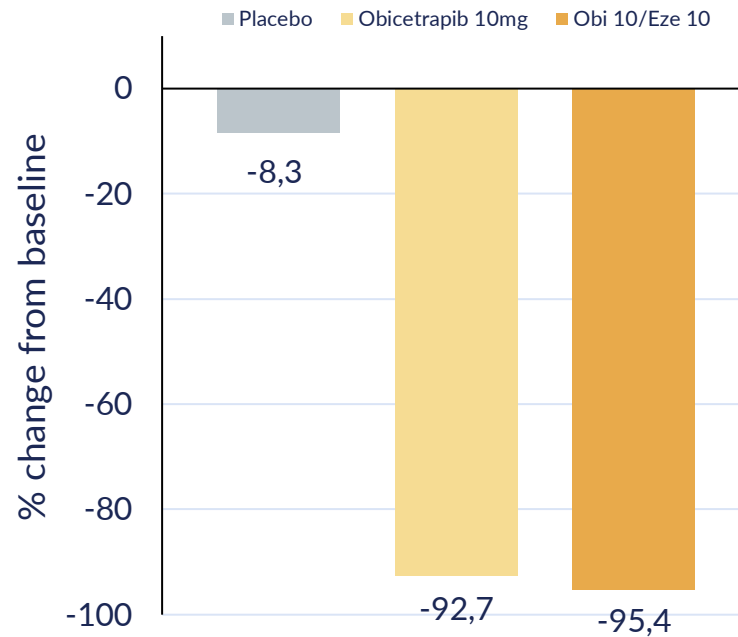
# Total, small LDL particles and LDL-particle size percent change from baseline



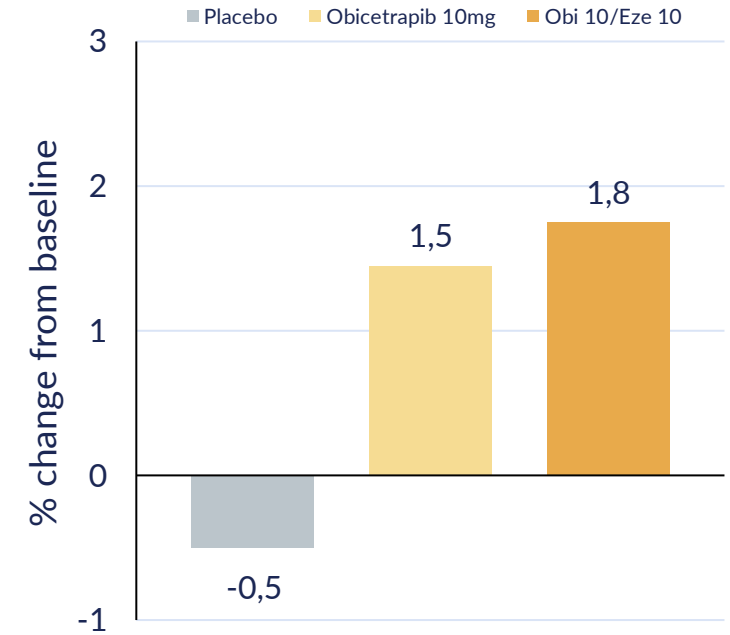
## Total LDL Particles



## Small LDL Particles

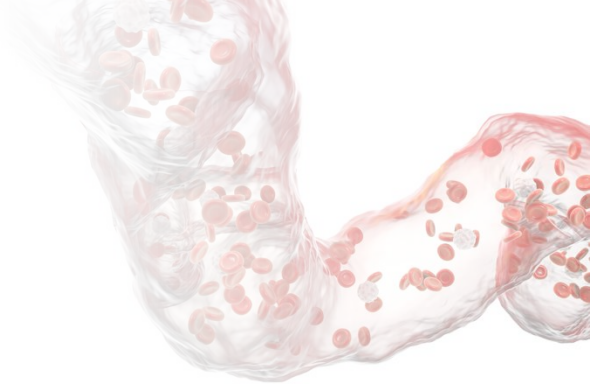


## LDL Particle Size





# Lipoprotein fractionation, NMR



## NMR Relative Risk

Lipoprotein fractionation	Optimal	Moderate	High
LDL-P (nmol/L)	<935	935-1816	>1816
Small LDL (nmol/L)	<467	467-820	>820
LDL Size (nm)	>20.5	N/A	≤20.5

NMR=neuro magnetic resonance.

## ROSE2 Results

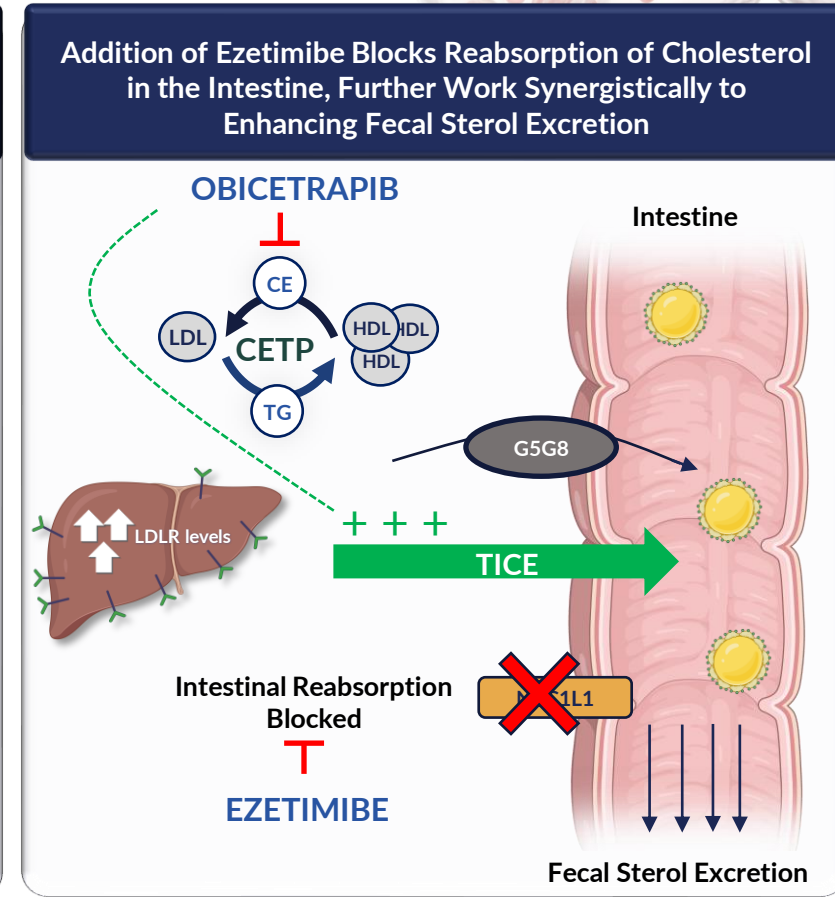
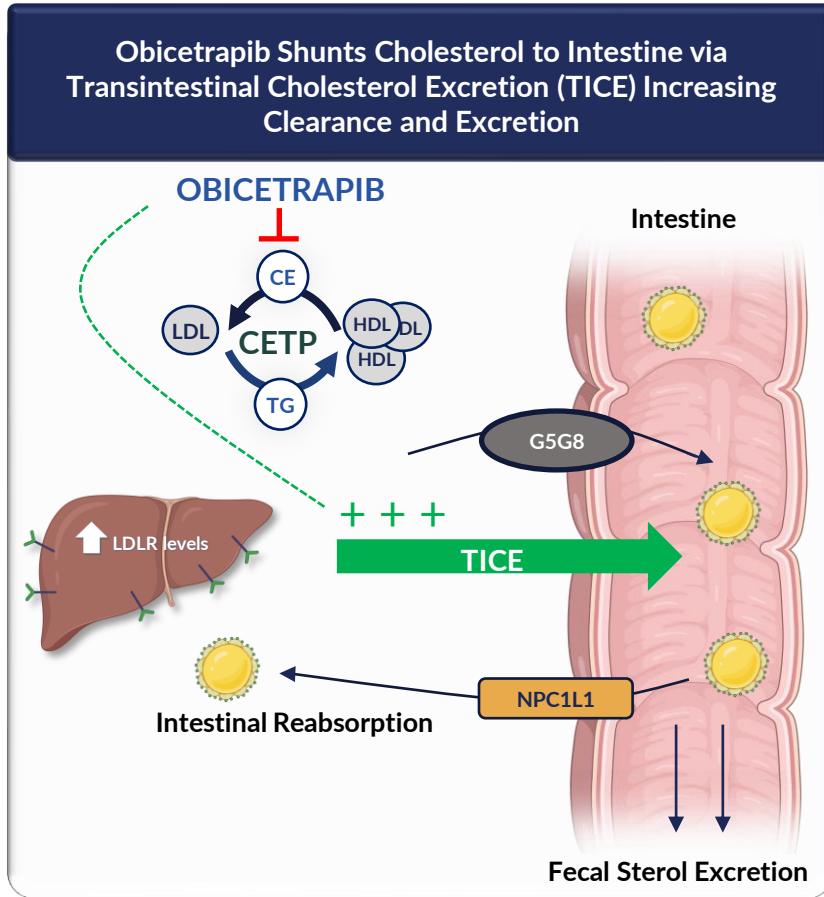
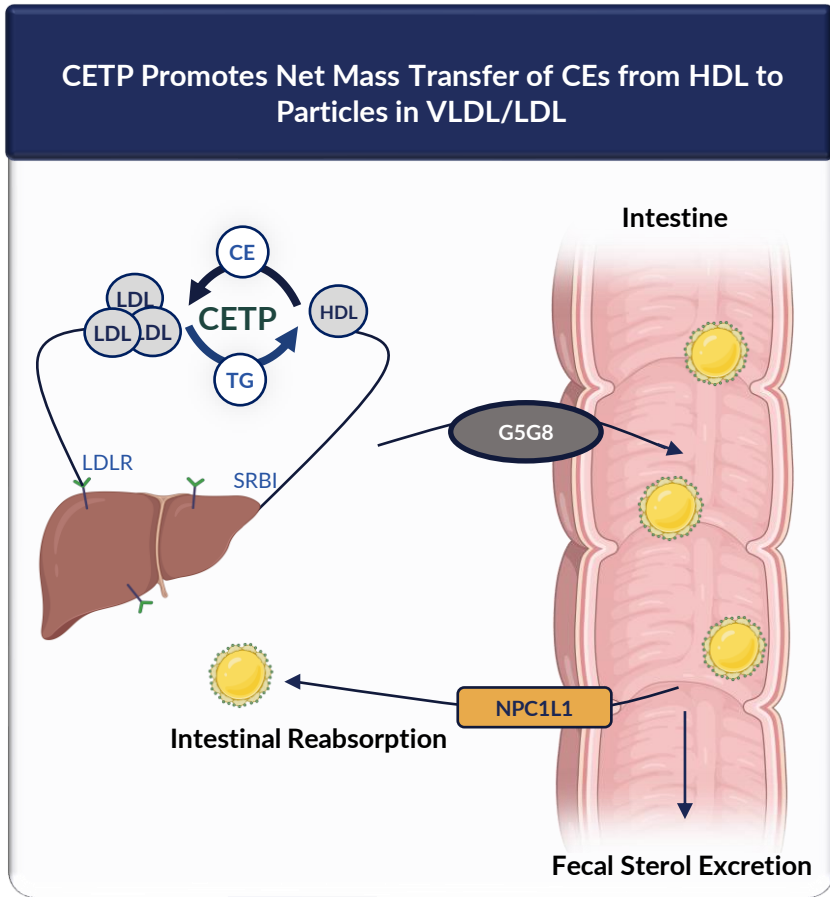
Placebo	Obi 10	Obi 10/Eze 10
947	435	286
662	52	34
20.3	21.0	21.0

## Safety: TEAEs, TESAEs, and withdrawal overview (safety population)

	Placebo N= 40, N (%)	Obicetrapib 10 mg N= 39, N (%)	Obi 10 mg / Eze 10 mg N= 40, N (%)
<b>TEAEs (%)</b>			
TEAEs	16 (40)	8 (20.5)	11 (27.5)
Related TEAEs	2 (5.0)	4 (10.3)	5 (12.5)
Severe TEAEs	2 (5.0)	1 (2.6)	0 (0)
<b>TESAEs</b>			
TESAEs, total	1 (2.5)	1 (2.6)	0 (0)
Deaths	0	0	0
<b>Withdrawal's study / medication</b>			
TEAEs leading to discontinuation of study drug	2 (5.0)	2 (5.1)	1 (2.5)

N=total number of subjects in each treatment group.  
n=number of subjects who experienced an event.  
%=100 x n/N.

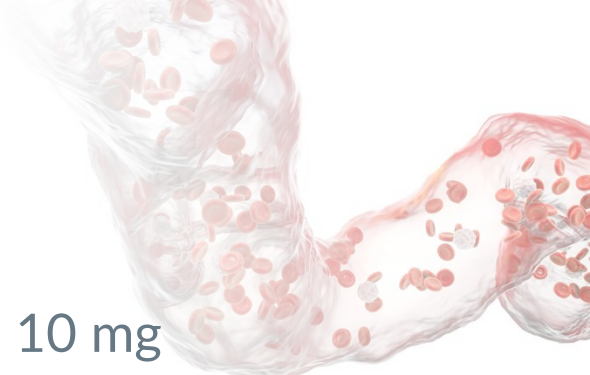
# NPC1L1 inhibition with ezetimibe potentially resulting in increased net sterol clearance



- CE, cholesteryl ester; CETP, cholesteryl ester transfer protein; MOA, mechanism of action; NPC1L1, Niemann-Pick C1-Like 1; LDL, low-density lipoprotein; LDLR, low-density lipoprotein receptor; TG, triglyceride; VLDL, very low-density lipoprotein.
- NewAmsterdam Pharma Data on File.



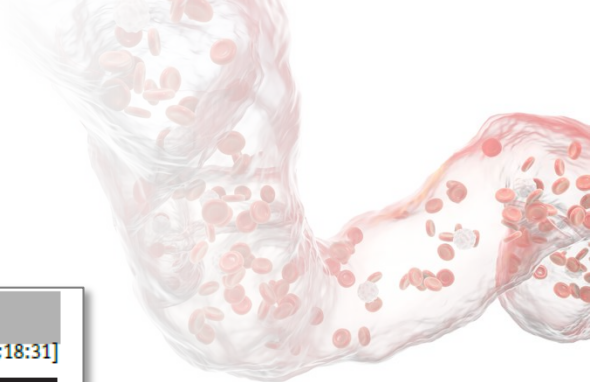
## Conclusions

- Obicetrapib 10 mg and the combination of obicetrapib 10 mg and ezetimibe 10 mg were observed to reduce median LDL-C levels by -43.5% and -63.4%, respectively, on top of HIS therapy
  - The combination of obicetrapib 10 mg and ezetimibe 10 mg was observed to reduce total LDL particles and small LDL particles by 72.1% and 95.4%, respectively
  - 87.1% of patients taking the combination of obicetrapib 10 mg and ezetimibe 10 mg were observed to achieve an LDL-C level <55mg/dL
  - Obicetrapib 10 mg and the combination of obicetrapib 10 mg and ezetimibe 10 mg on top of HIS therapy were well tolerated
  - These data support the continued development of a fixed dose combination of obicetrapib 10 mg plus ezetimibe 10 mg
- 





# Publication now available in JCL



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**Journal of  
Clinical  
Lipidology**

Original Research

**Obicetrapib plus Ezetimibe as an adjunct to high-intensity statin therapy: A randomized phase 2 trial**

Christie M. Ballantyne, MD, FACP, FACC\*, Marc Ditmarsch, MD, John JP Kastelein, MD, PhD, Adam J. Nelson, MD, PhD, Douglas Kling, BS, MBA, Andrew Hsieh, PharmD, Danielle L. Curcio, BS, MBA, Kevin C. Maki, PhD, Michael H. Davidson, MD, Stephen J. Nicholls, MD, PhD