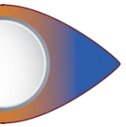

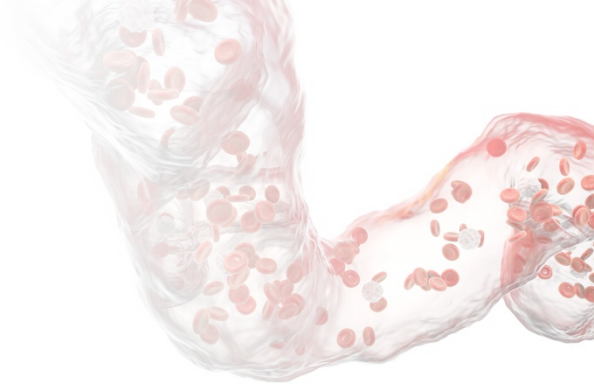

rose

A Placebo-Controlled, Double-Blind, Randomized, Phase 2 Dose-Finding Study to Evaluate the Effect of Obicetrapib 5 and 10 mg as an Adjunct to High-Intensity Statin Therapy

Stephen J Nicholls, Marc Ditmarsch, John J Kastelein, Scott P Rigby, Douglas Kling, Danielle L Curcio, Nicholas J Alp, Michael H Davidson

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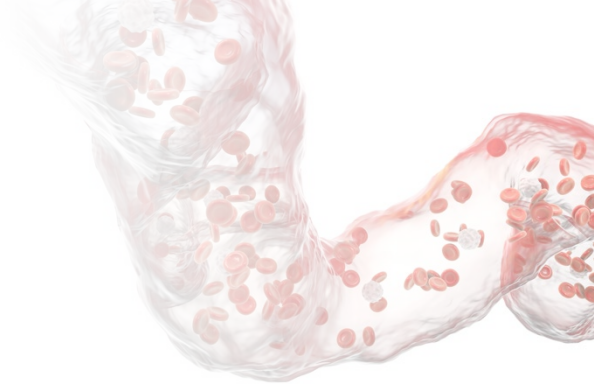
Rationale



- Statins are generally well used to reduce LDL-C levels.
- Despite treatment with high-intensity statin therapy (HIS), two thirds of patients do not reach their target LDL-C level.
- Accordingly, there is a need for new therapies to produce effective reduction in LDL-C levels when used in combination with HIS therapy.
- Early studies with the CETP inhibitor obicetrapib demonstrated reductions of LDL-C levels by 45%.[1]

1. Hovingh GK, et al. *Lancet*. 2015;

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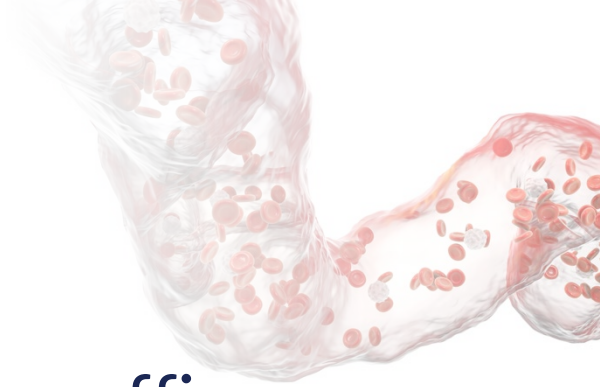
Objective



The primary objective was to evaluate the lipid lowering efficacy, safety and tolerability of obicetrapib 5 and 10 mg in patients treated with high-intensity statin therapy compared to placebo

ROSE study: Obicetrapib and High Intensity Statin therapy (HIS)

Objective **To evaluate the effect of obicetrapib on top of HIS on LDL-C**

Inclusion criteria

- A stable dose of HIS (A 40 / 80; R 20 / 40) 8 weeks prior to screening
- Fasting LDL-C levels >1.8 mmol/L

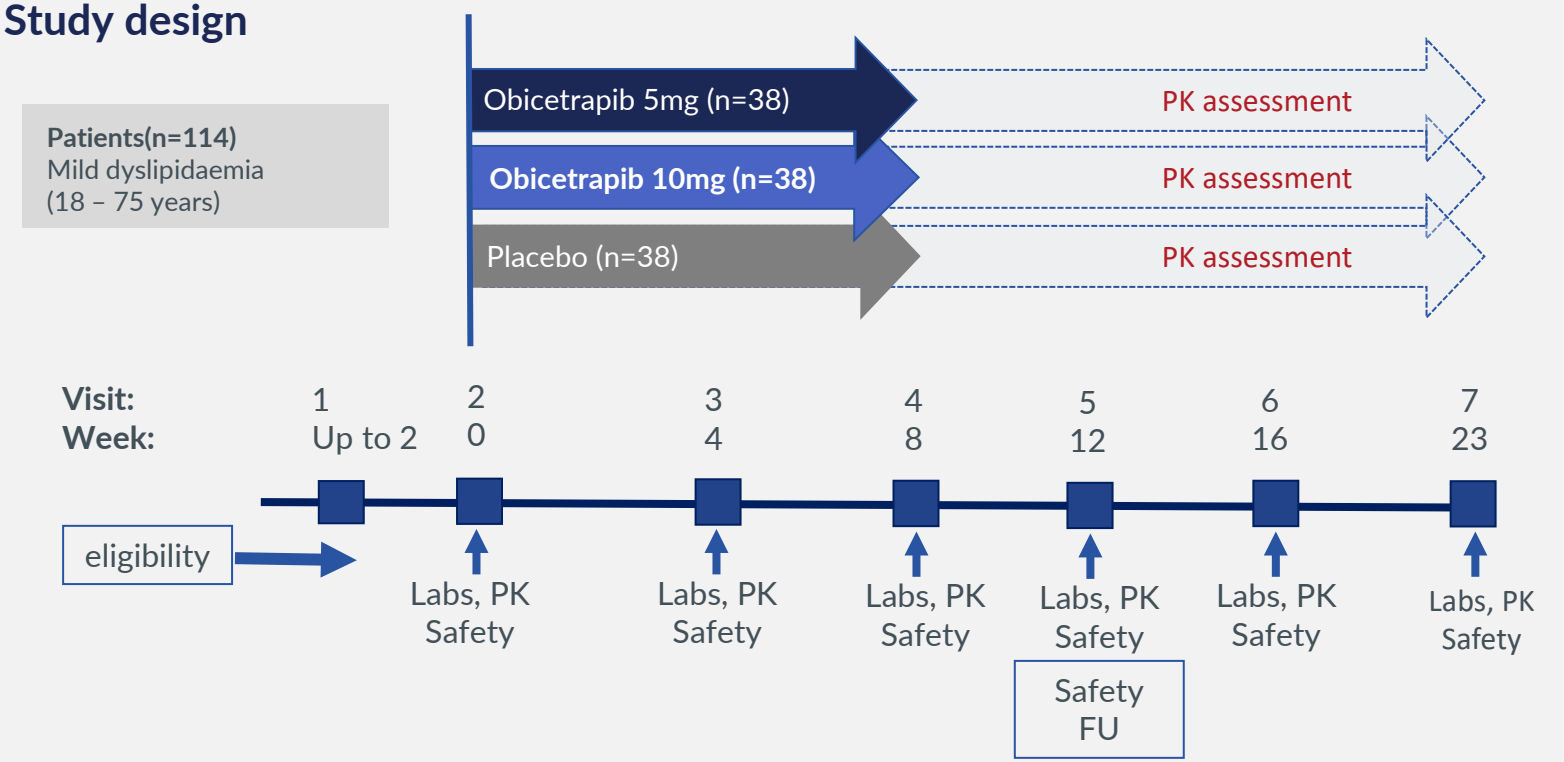
Exclusion criteria

- Current significant CV disease
- Diagnosis of type 1 or type 2 diabetes mellitus;
- Uncontrolled hypertension

Primary efficacy endpoint

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

Study design



Pre-specified assessment of LDL-C levels by preparative ultra-centrifugation and Friedewald

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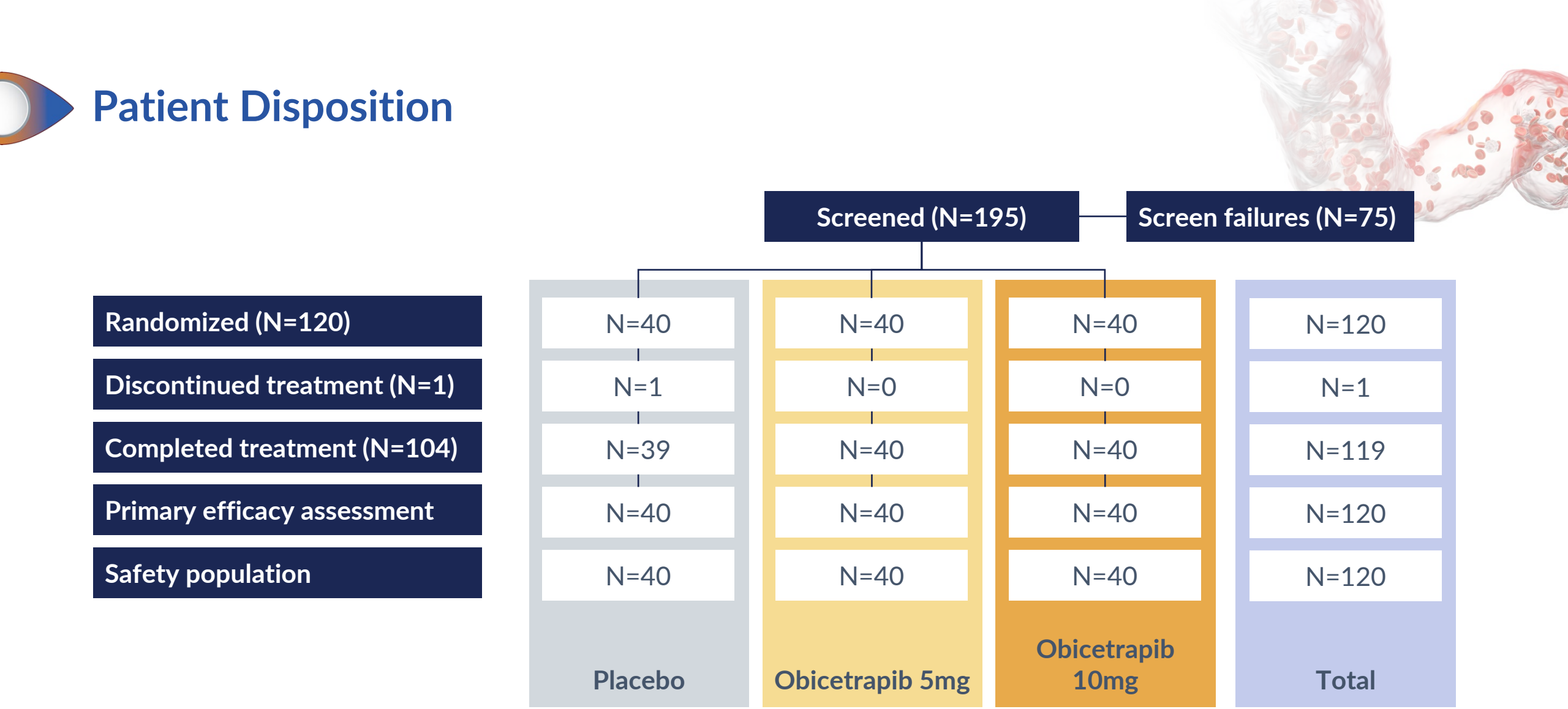
Patient Disposition



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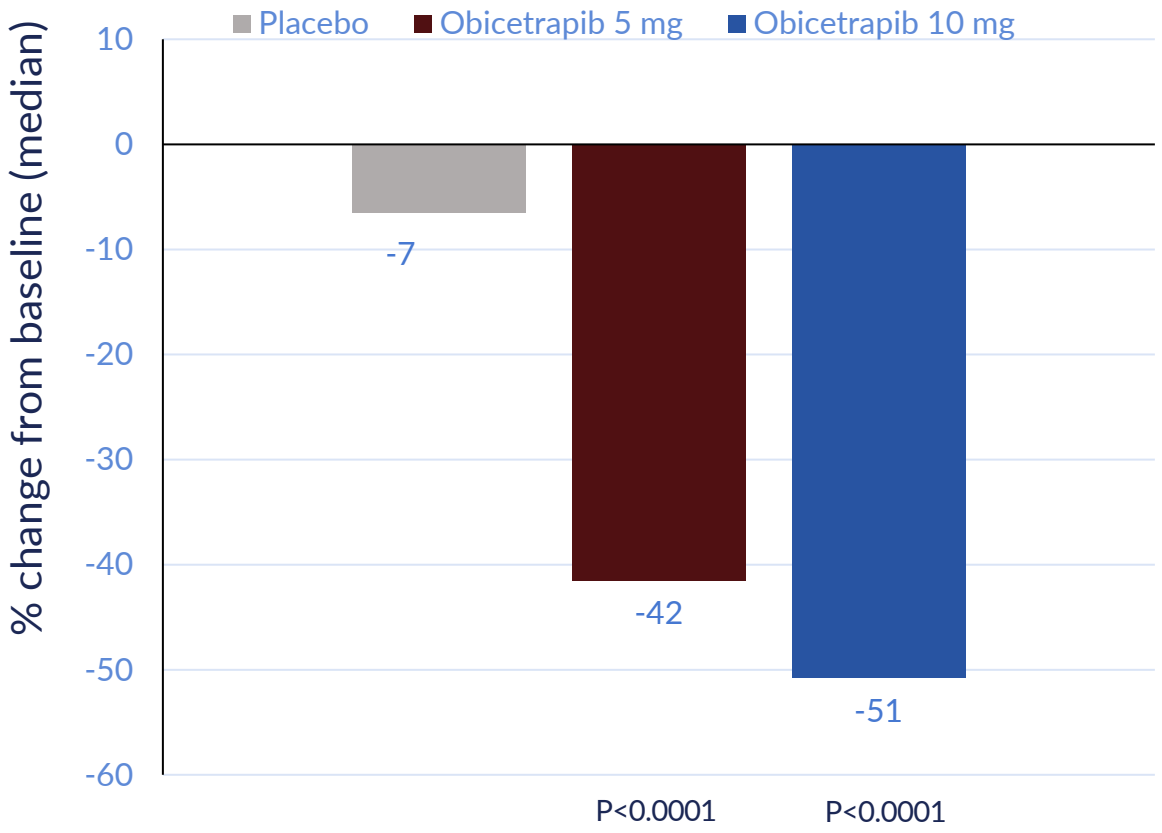
Baseline characteristics

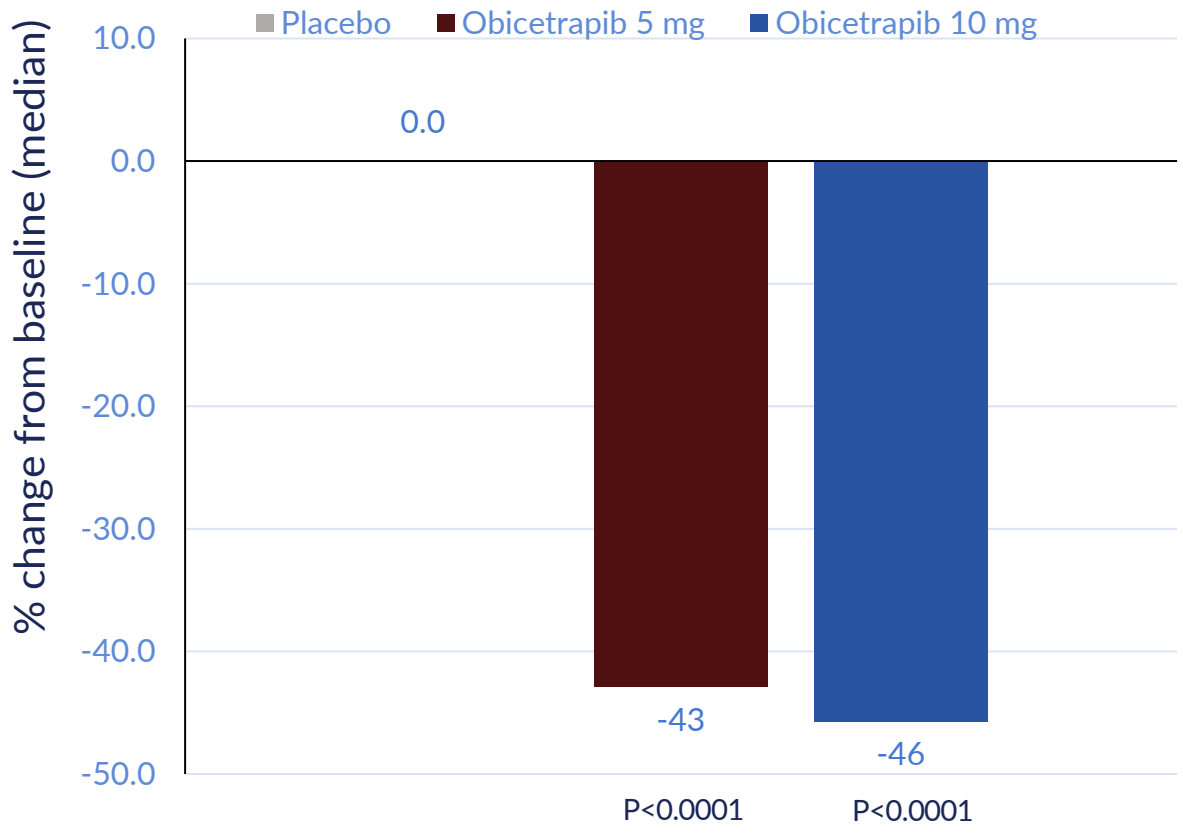
		Placebo (N=40)	Obicetrapib 5 mg (N=40)	Obicetrapib 10 mg (N=40)
	Mean Age (yrs)	61.3	61.1	62.9
	Female %	52.5	42.5	37.5
	Mean BMI (kg/m^2)	30.2	32.2	30.8
Race %	White	80.0	75.0	75.0
	Black / African American	17.5	25.0	12.5
Statin use (%)	Atorvastatin 40mg	50.0	50.0	62.5
	Atorvastatin 80mg	20.0	25.0	27.5
	Rosuvastatin 20mg	5.0	12.5	7.5
	Rosuvastatin 40mg	25.0	12.5	2.5
Baseline level	LDL-C (mg/dL by PUC)	90.0	95.0	88.0
	HDL-C (mg/dL)	44.5	46.5	44.0
	Lp(a) (nmol/L)	45.3	89.4	29.9

LDL-C Percent change from baseline by different measurement approaches

Preparative Ultra-centrifugation



Friedewald



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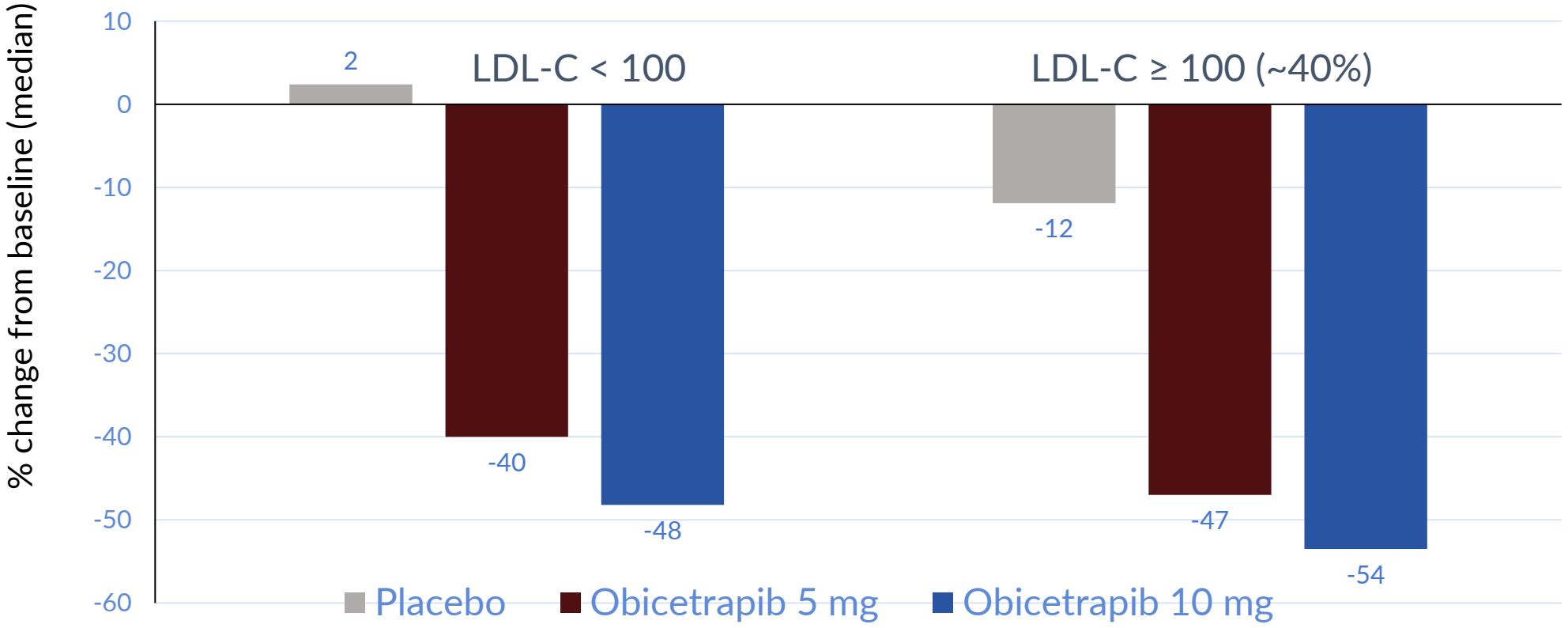
LDL-C Percent change from baseline for patients ≥100 and < 100 mg/dL

Friedewald



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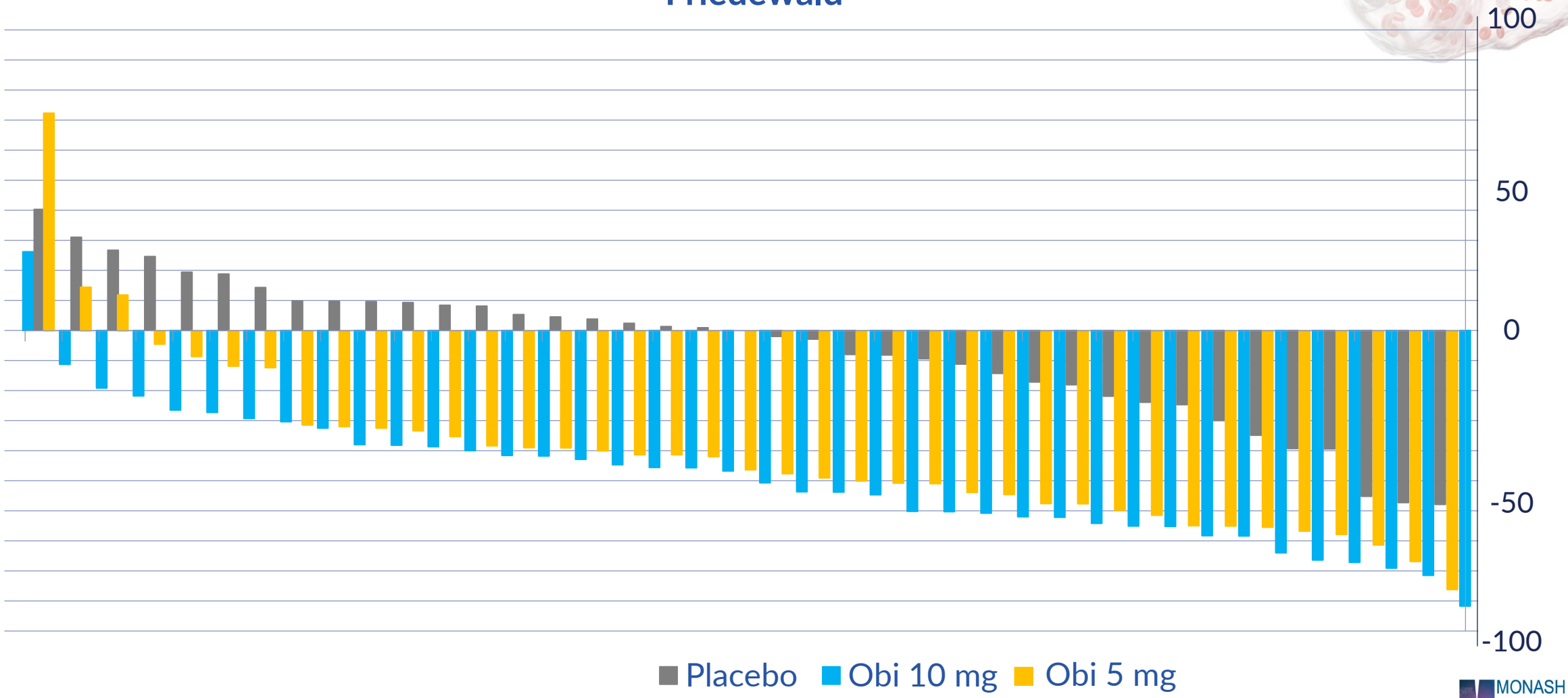
Waterfall plot LDL-C % change from baseline placebo, obi 5 & 10 mg



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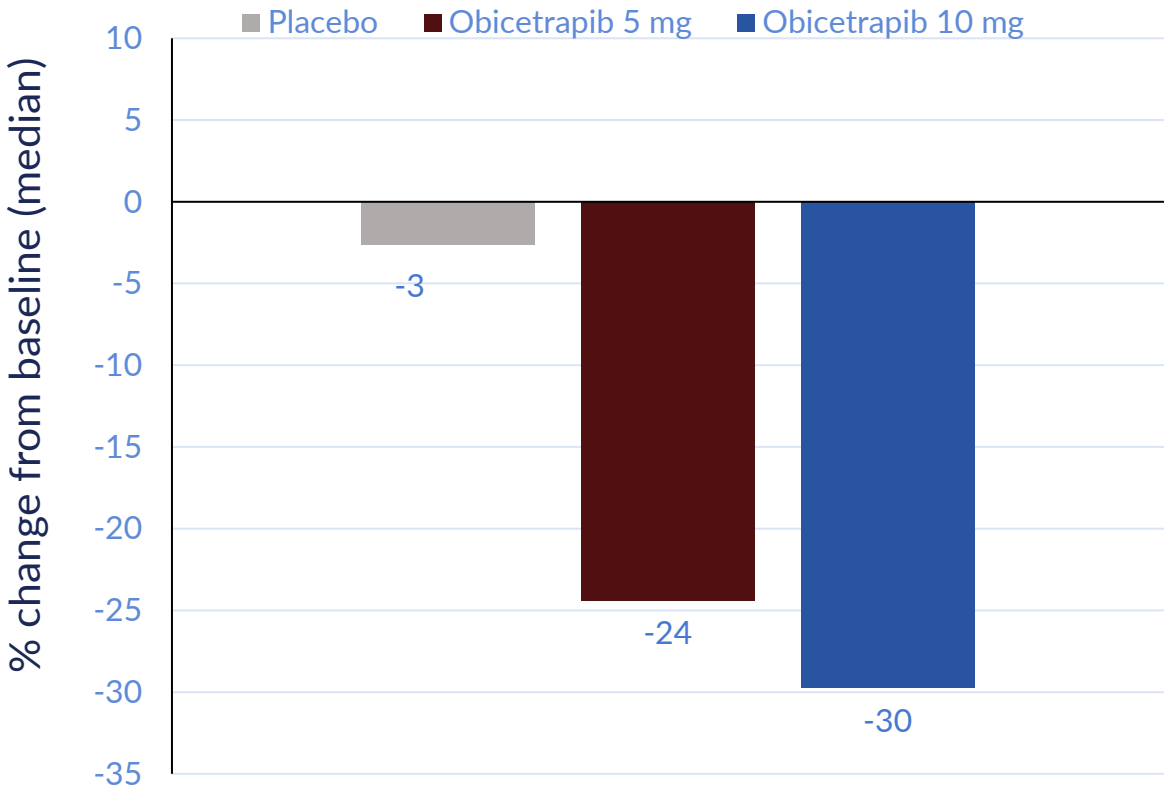
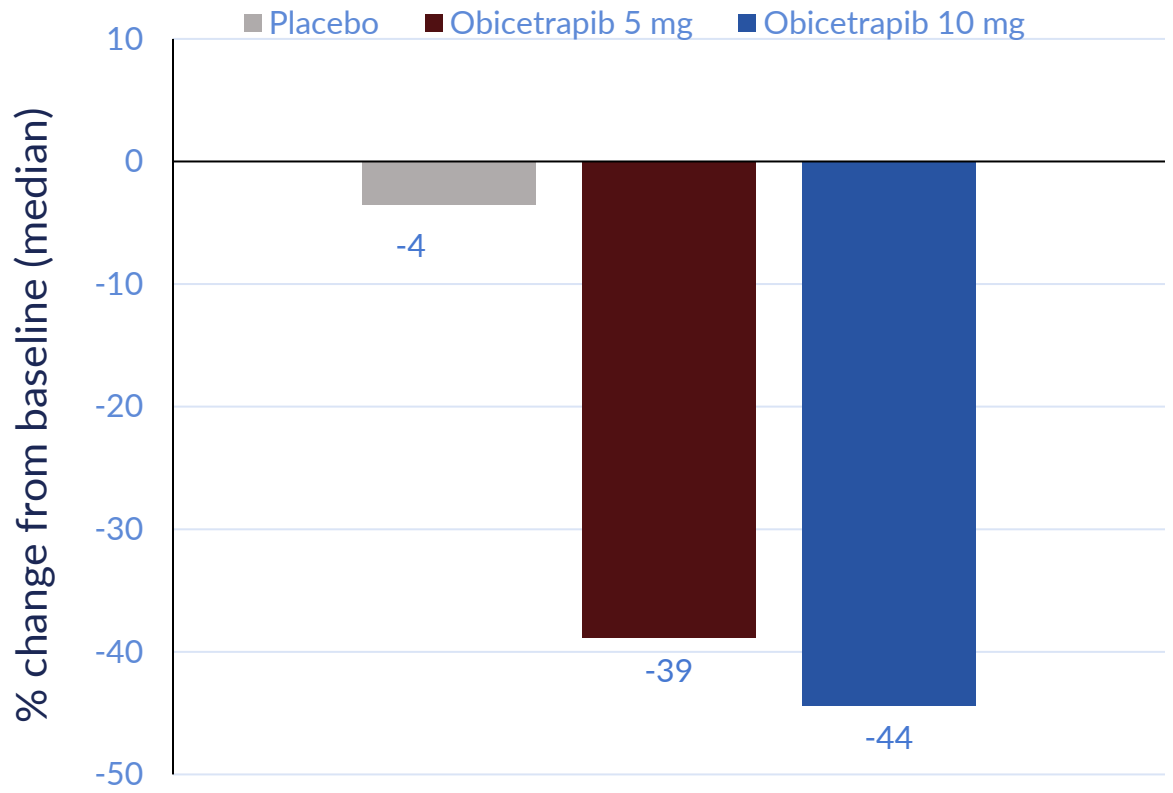
ApoB & non-HDL-C Percent change from baseline

ApoB



Non-HDL-C



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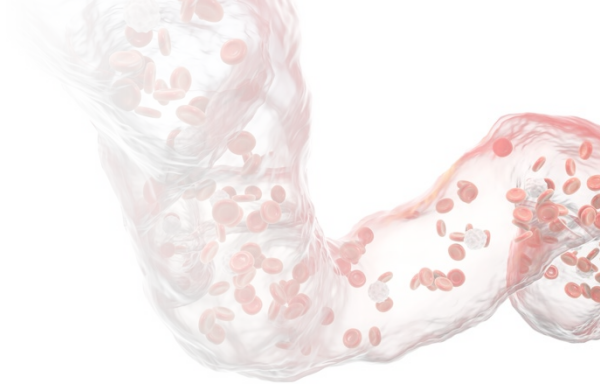
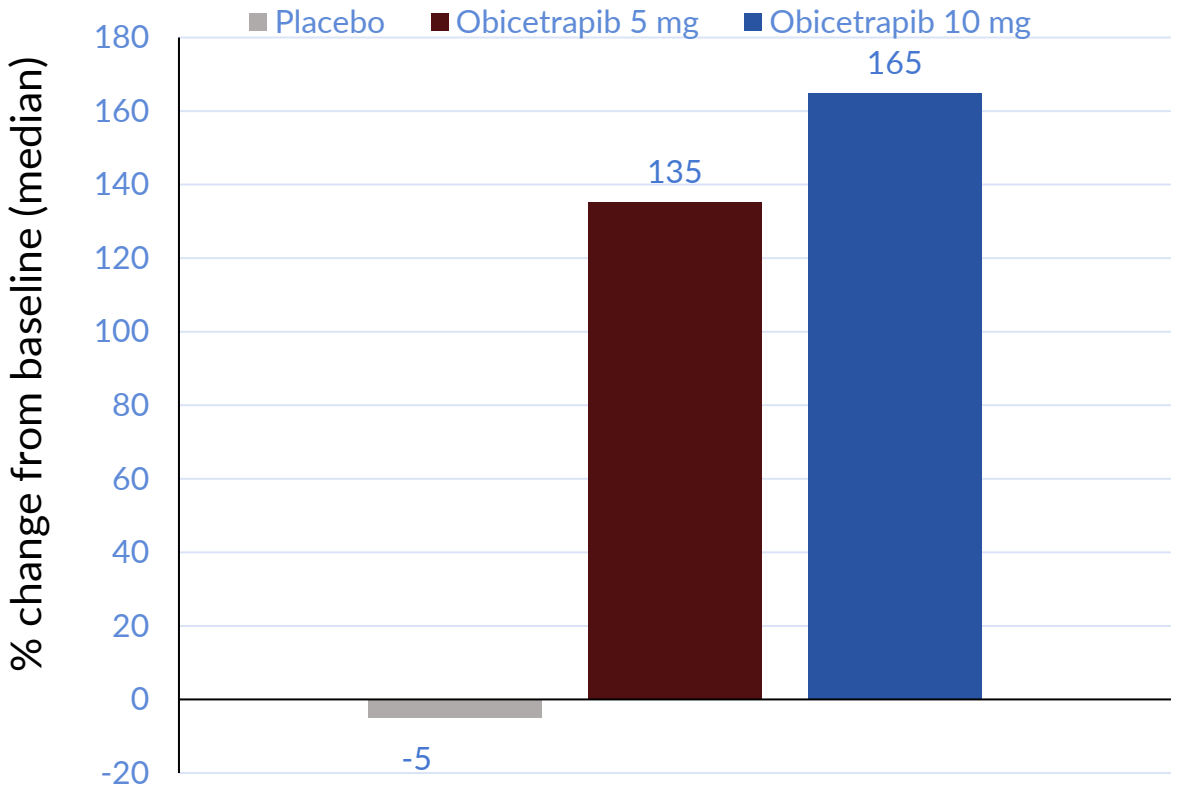
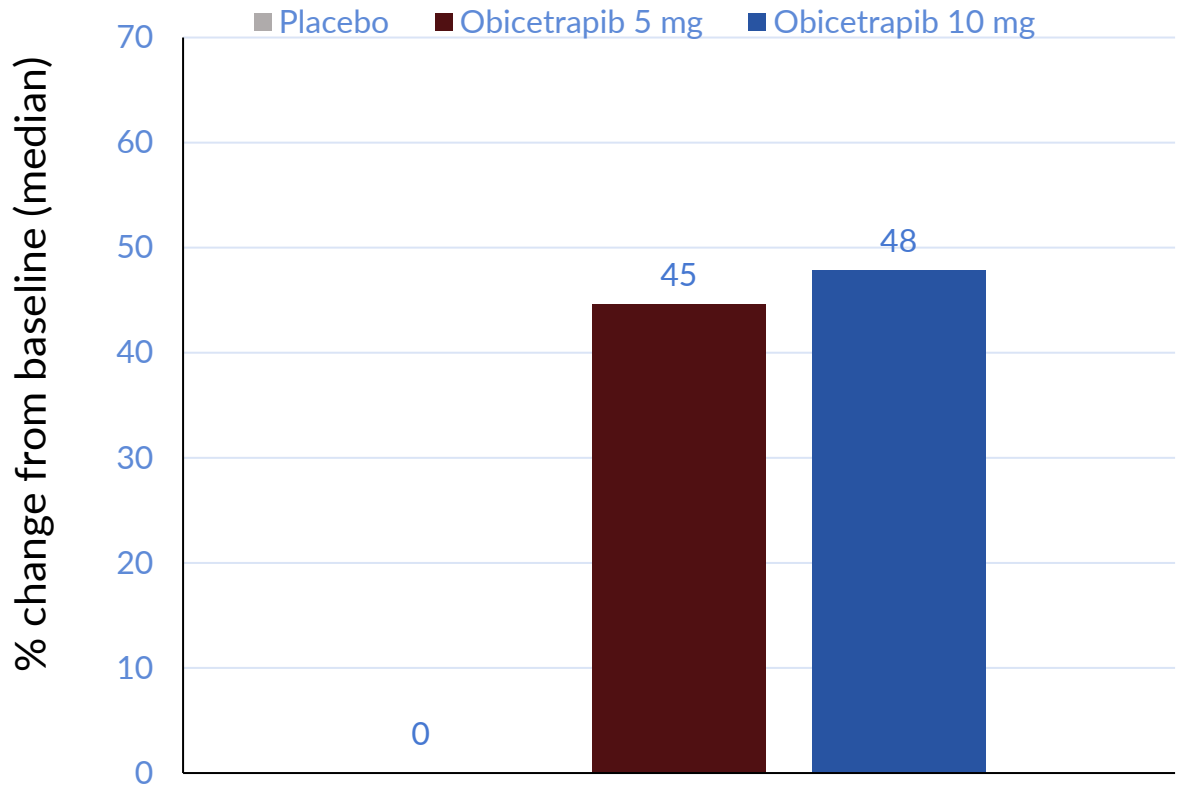
HDL-C & ApoA1 Percent change from baseline



HDL-C



ApoA1



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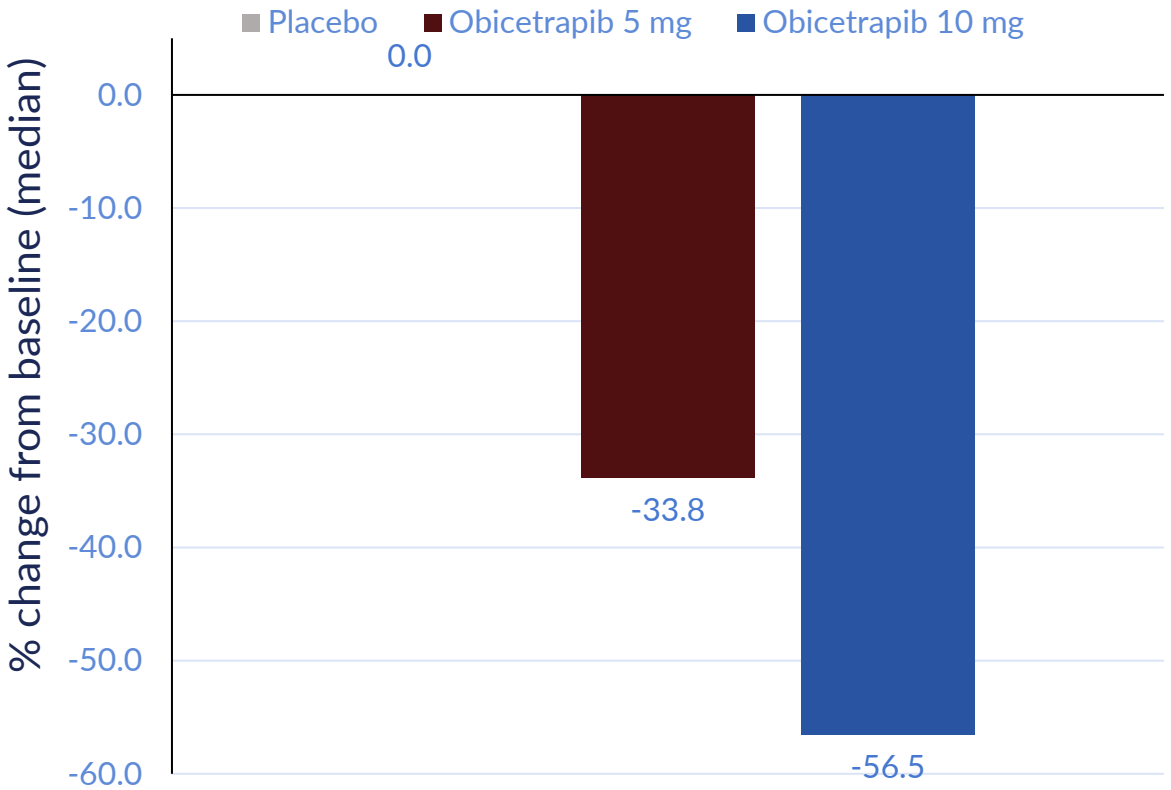
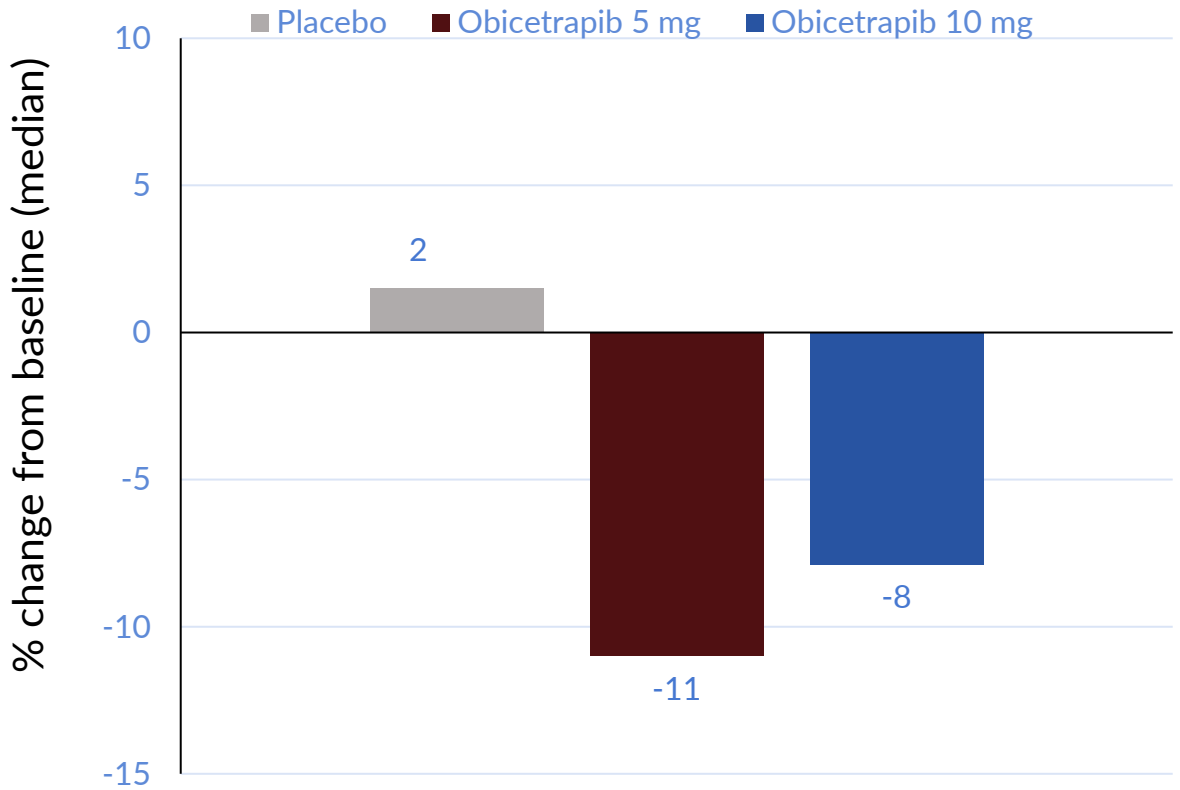
Lp(a) and Triglycerides Percent change from baseline

Lp(a)



Triglycerides



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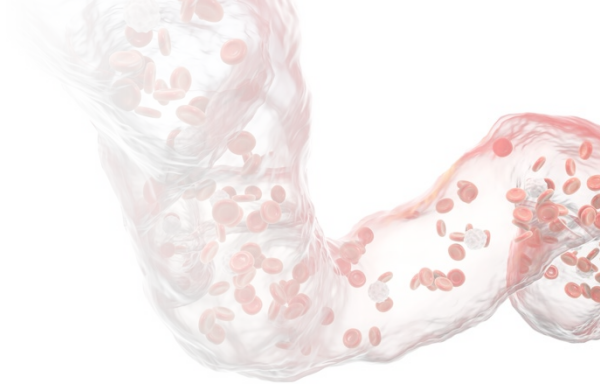
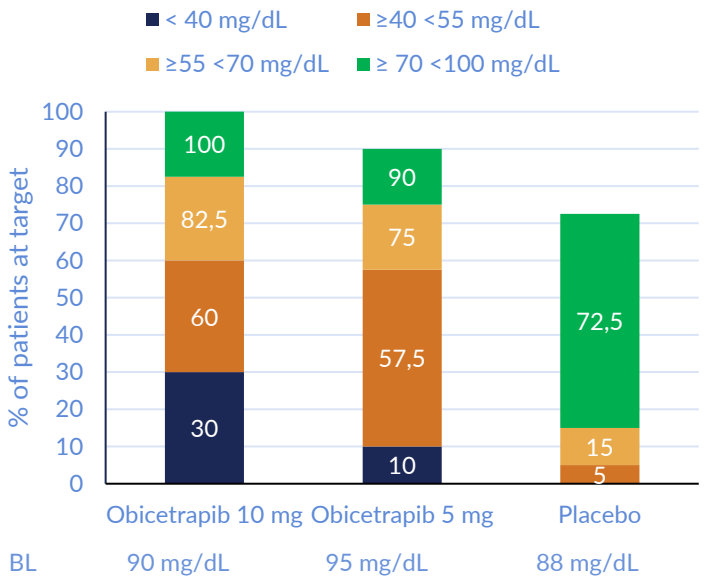
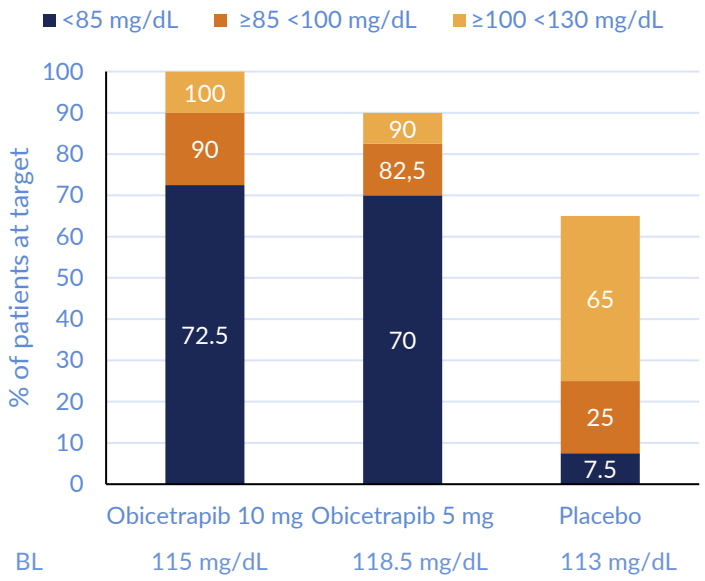
LDL-C, non-HDL-C, ApoB target attainment



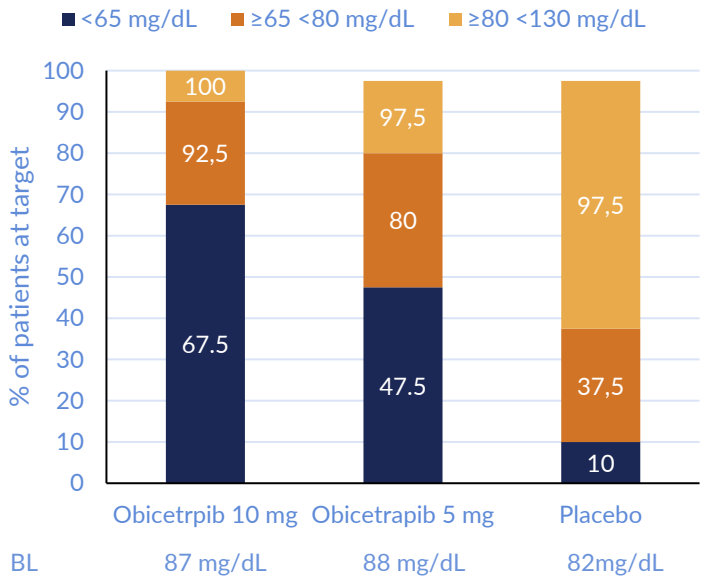
LDL-C target attainment



Non-HDL-C target attainment



ApoB target attainment



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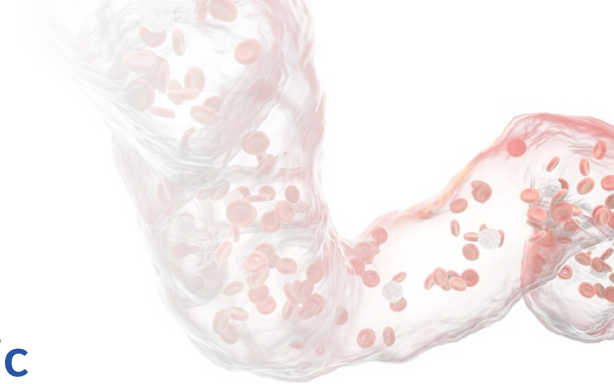
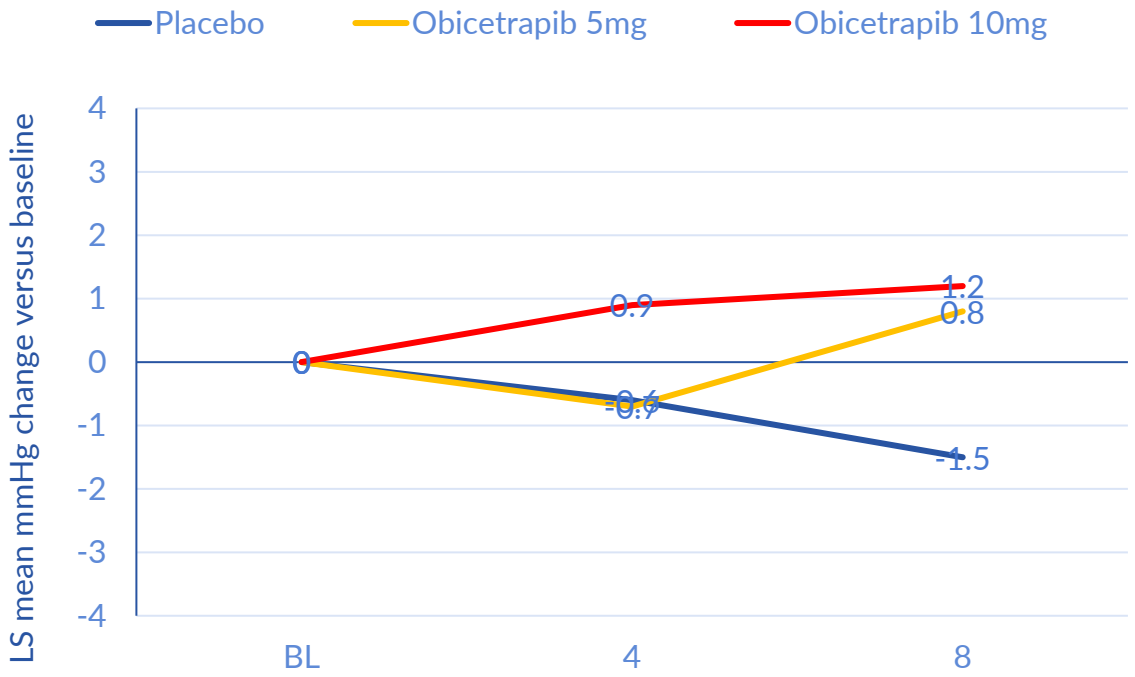
Safety - AEs, SAEs and withdrawal overview

	Placebo (N=40)	Obicetrapib 5 mg (N=40)	Obicetrapib 10 mg (N=40)
AEs (%)			
AEs	19 (47.5)	13 (32.5)	8 (20.0)
related AEs	4 (10.0)	2 (5.0)	1 (2.5)
severe AEs	1 (2.5)	0	0
SAEs			
SAEs, total	2 (5.0)	0	0
Deaths	0	0	0
Withdrawal's study / medication			
AEs leading to discontinuation of study drug	1 (2.5)	0	0

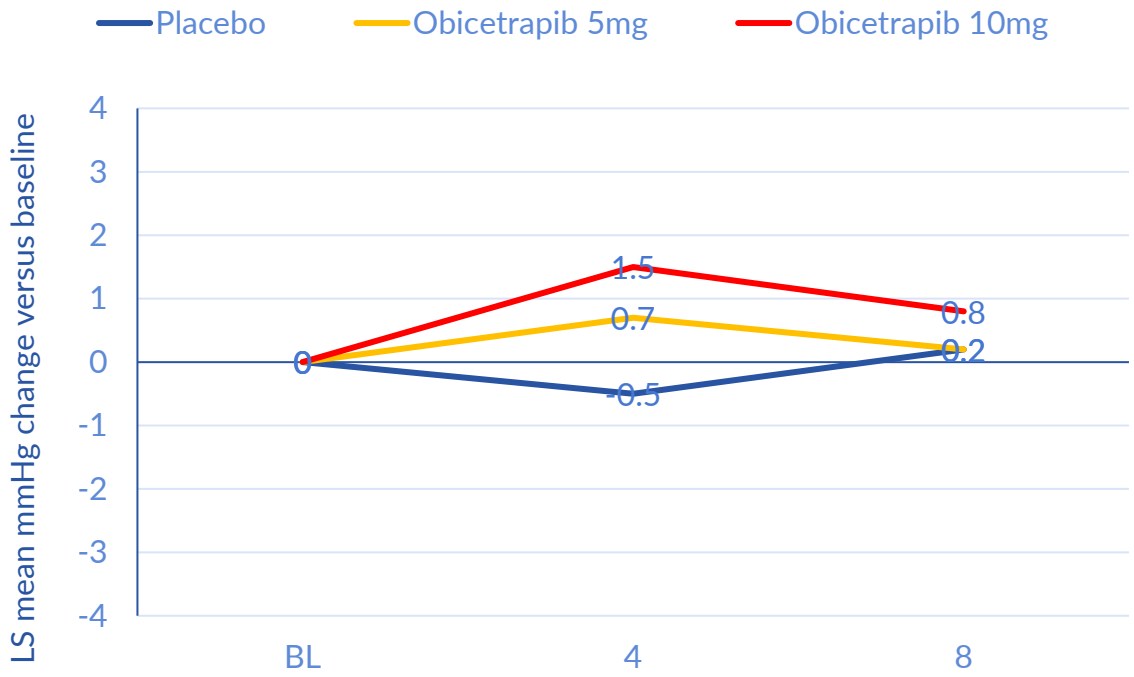
Diastolic & Systolic blood pressure over time



Diastolic



Systolic



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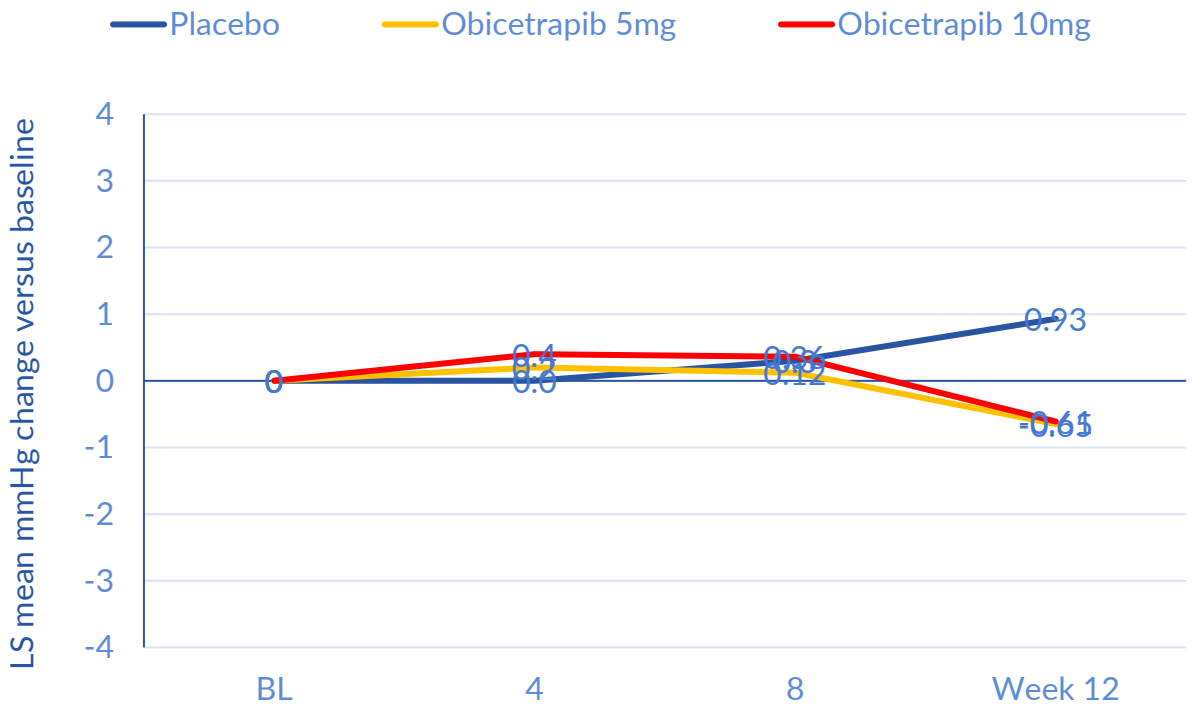
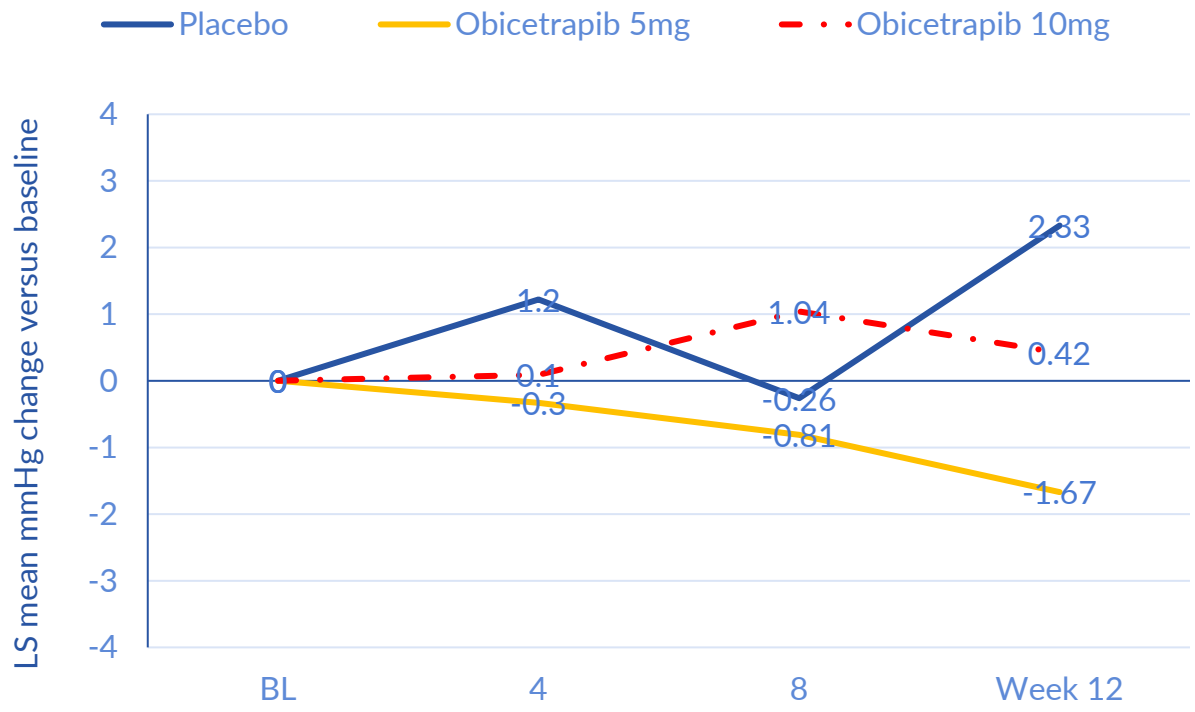
Pooled (ROSE, TULIP, OCEAN) BP data – Diastolic & Systolic BP

Diastolic



Placebo (N)	189	184	180	121
Obi 5 mg (N)	135	134	130	63
Obi 10 mg (N)	161	159	155	112

Systolic



Placebo (N)	189	184	180	121
Obi 5 mg (N)	135	134	130	63
Obi 10 mg (N)	161	159	155	112

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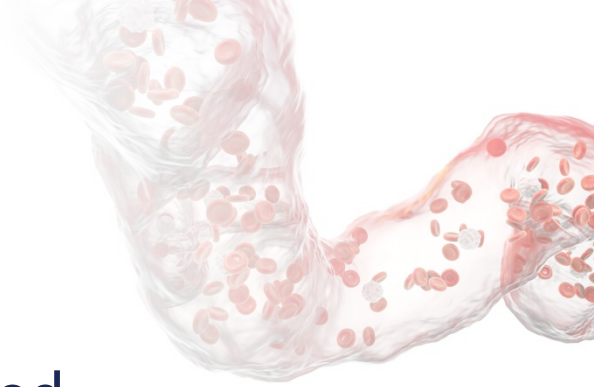
Conclusions



- Obicetrapib 5 and 10 mg on top of HIS therapy was well tolerated
- Obicetrapib 5 and 10 mg on top of HIS therapy reduced median LDL-C levels by -42% and -51% from baseline, respectively
- Obicetrapib LDL-C lowering comparable at all baseline LDL-C levels
- Obicetrapib LDL-C lowering is not mitigated in combination with HIS
- Obicetrapib LDL-C lowering is similar with both LDL-C quantitation methods
- Obicetrapib can be a valuable addition for high risk ASCVD patients who do not achieve their target LDL-C guideline goals despite the use of HIS therapy.