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Randomized, open-label, study comparing efficacy and safety of lerodalcibep to inclisiran in patients with, or at very high risk for CVD, requiring additional LDL-C reduction: (LIBerate-VI)

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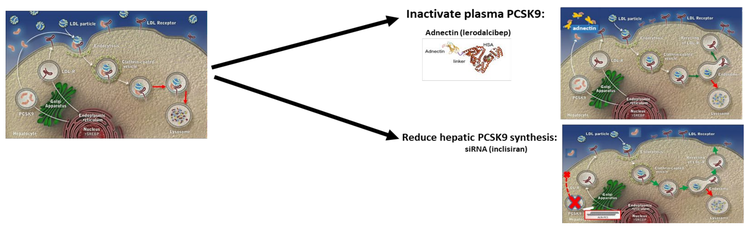
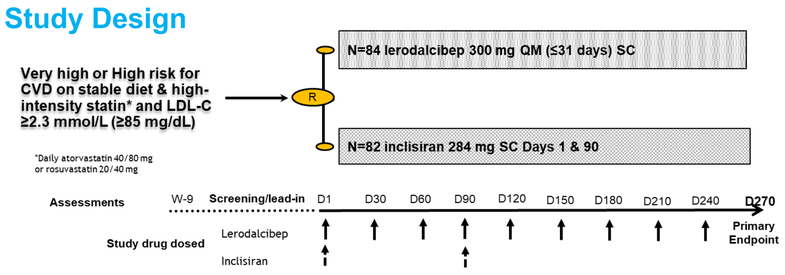
BACKGROUND & METHODS

Lerodalcibep: 11kDa anti-PCSK9 domain (Adnectin), derived from human fibronectin, fused with HSA with plasma half-life 12 to 15 days. Binds to serum PCSK9, blocks PCSK9 binding to LDLR. Small size (77kDa), high solubility, 300 mg in 1.2 mL QM



Study Design



Intervention: Randomized 1:1 to SC monthly 1.2 mL lerodalcibep 300mg or 1.5 mL inclisiran 284 mg on D1 and D90

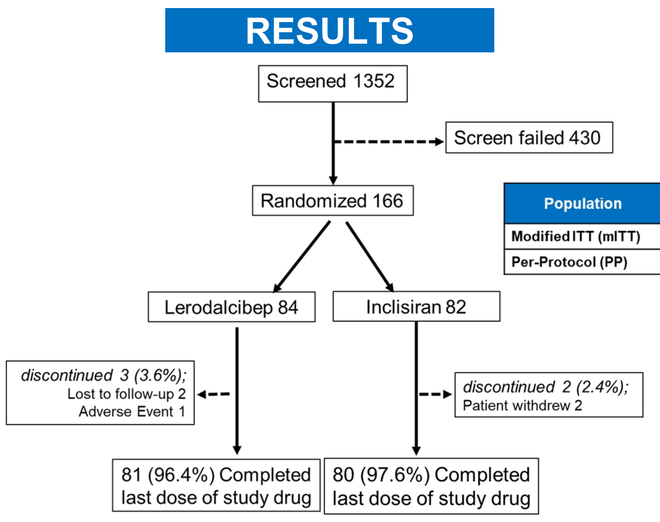
Setting: 21 clinical centers in 5 countries in Europe

Primary efficacy endpoints: LDL-C % change from baseline at Day 270.

Secondary outcomes: achievement of EAS/ESC LDL-C targets, other lipid and apolipoproteins changes.

Safety analysis: all patients randomized + dosed with study drug.

RESULTS



Population	Lerodalcibep N (%)	Inclisiran N (%)
Modified ITT (mITT)	81 (96.4%)	79 (96.3%)
Per-Protocol (PP)	71 (84.5%)	79 (96.3%)

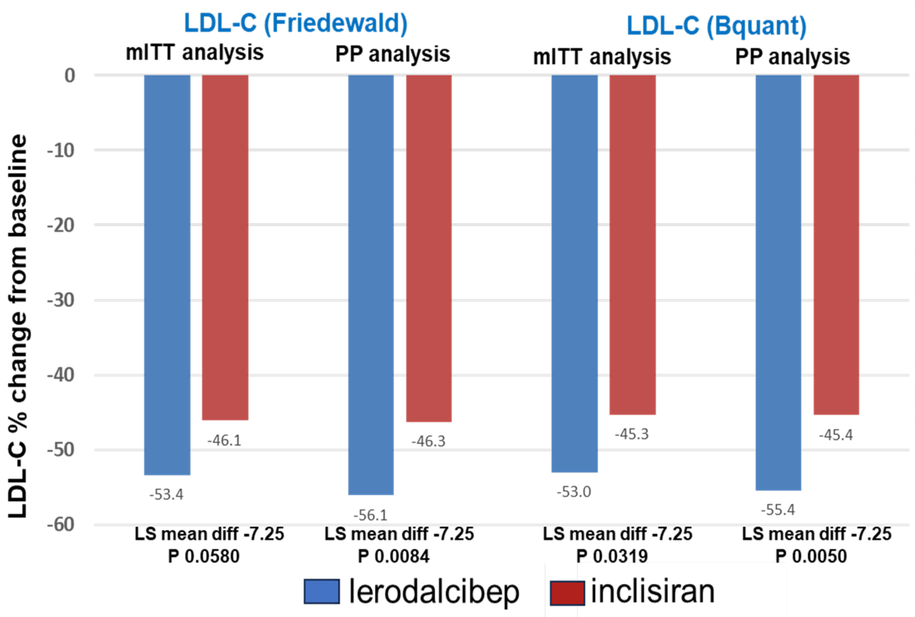
Baseline Demographics and Clinical Characteristics

Characteristic	Lerodalcibep (N=84)	Inclisiran (N=82)
Age – yr (range)	60.3 (18-82)	61.2 (33-82)
Sex – male/female (%)	65/35	70/30
Race: White (%)	98	100
Body mass Index – kg/m² mean(SD)	28.4 (4.6)	28.6(4.2)
CVD Risk: Secondary Prevention - Documented CVD no. (%)	42 (50%)	42 (51%)
Primary prevention: Very-High risk for CVD no. (%)	21 (25%)	12 (16%)
High-risk for CVD no. (%)	21 (25%)	27 (33%)
Diabetes Mellitus no. (%)	12 (14.3%)	11 (13.4%)
Heterozygous Familial Hypercholesterolemia no. (%)	40 (47%)	34 (41.5%)
Lipid modifying therapy		
Statin; any dose	100%	100%
High intensity statin	100%	99%
Ezetimibe	53.5%	40.2%
Lipid measures at baseline –mmol/L; mean(SD)		
LDL-cholesterol (Friedewald calculated)	2.77 (0.62)	3.01 (1.31)
LDL-cholesterol (UltraCentrifugation)	2.81 (0.57)	3.03 (1.29)
Non HDL-cholesterol	3.43 (0.70)	3.70 (1.38)
HDL-Cholesterol	1.43 (0.44)	1.38 (0.43)
Triglycerides	1.46 (0.69)	1.52 (0.89)
Apolipoprotein B (g/L)	1.01 (0.18)	1.05 (0.31)
Lipoprotein (a) mean/median nmol/L	156.7/59	149.1/61.5
PCSK9 ng/mL mean (SD)	355 (115)	340 (100)

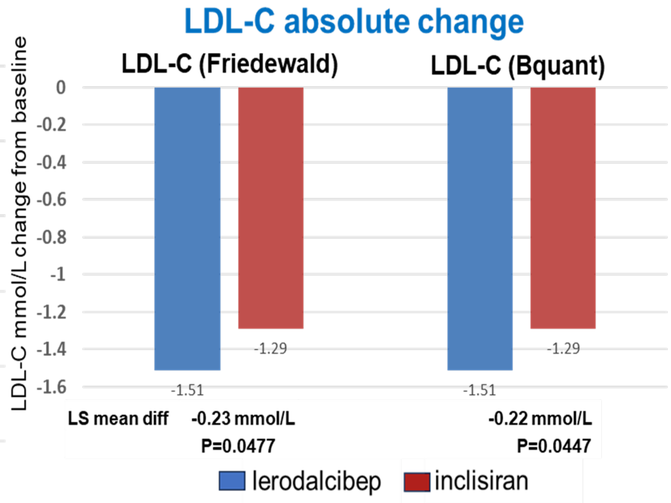
DISCLOSURE INFORMATION

Clinical trial was funded by LIB Therapeutics
Trial Registrations: EudraCT: 2021-002871-20
Clinicaltrials.gov NCT05004675

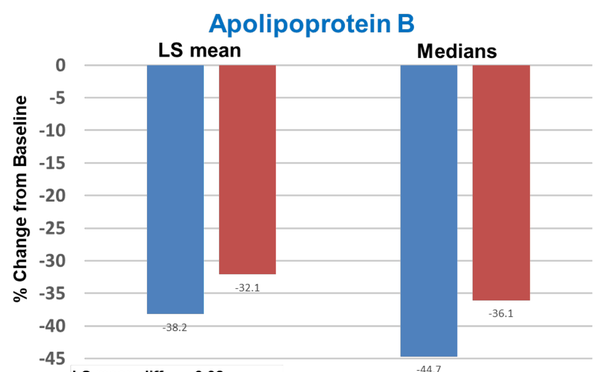
Primary endpoint: LDL-C Mean % change from baseline at Day 270



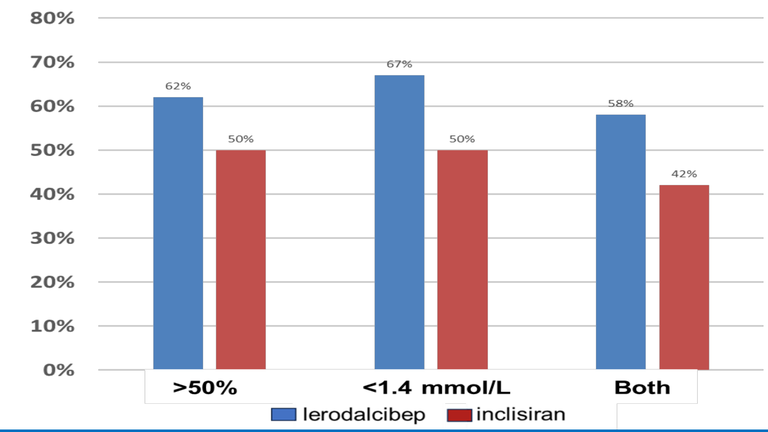
LDL-C absolute change



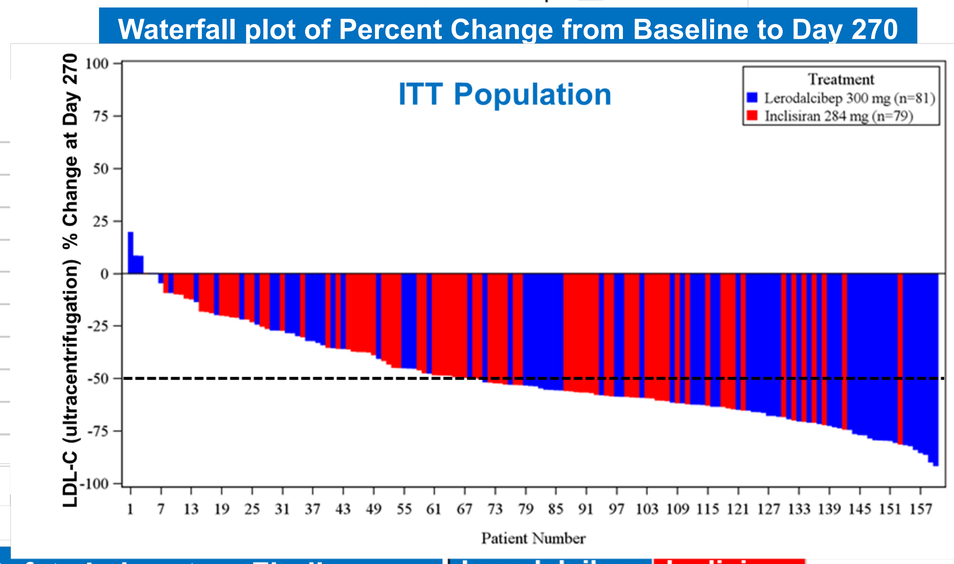
Non-HDL-C, Apo B and Lp(a): Change at Day 270



Percent achieving EAS/ESC Targets : Day 270



Waterfall plot of Percent Change from Baseline to Day 270



Adverse Events and Key Safety Laboratory Findings

	Lerodalcibep (N=84)	Inclisiran (N=82)
Adverse events- n (%); Patients with at least one adverse event	72 (85.7)	77 (93.9)
Patients with at least one event leading to withdrawal of study drug	2 (2.4)	1 (1.2)
Serious adverse events: Patients with at least one serious AE	9 (10.7)	9 (11.0)
Deaths	0	0
Other cardiovascular adverse events (adjudicated)		
Prespecified exploratory cardiovascular events	0	2
Fatal and non-fatal myocardial infarction	0	1
Fatal and non-fatal stroke	0	0
Frequent adverse events		
Nasopharyngitis	10 (11.9)	10 (12.2)
COVID-19	9 (10.7)	8 (9.8)
Back pain	9 (10.7)	4 (4.9)
Arthralgia	6 (7.1)	5 (6.1)
Injection site reaction (ISR); N (%) of subjects	11 (13.1)	1 (1.2)
Total ISR events (% of doses)	3.3%	1.2%
Discontinuations due to ISR (%)	0	0
Liver & Muscle Function ALT or AST >3x < 5 x ULN (N)	1	0
CK, AST or ALT > 5x ULN	0	0
Haematology Platelet count < 75x10⁹ /L	0	0

SUMMARY & CONCLUSION

- **Lerodalcibep and Inclisiran provided excellent efficacy and were well tolerated**
- **At the primary endpoint on Day 270 CVD patients on Lerodalcibep**
  - ✓***Achieved greater mean % and absolute reductions in LDL-C than Inclisiran by both Friedewald and ultracentrifugation measurements***
  - ✓***Achieved the EAS/ESC targets in more patients than with Inclisiran.***
  - ✓***Achieved greater reductions in non-HDL-C, Apo B and Lp(a)***

- **Lerodalcibep provides a novel, 3rd generation effective alternative to existing PCSK9 inhibitors:**
  - ✓Substantial LDL-C reductions on top of high intensity statins and ezetimibe
  - ✓Ability for the majority of patients to achieve the EAS/ESC guideline targets
  - ✓Robust reductions in all atherogenic lipids and lipoproteins
  - ✓Very large and persistent reductions in free PCSK9 at 4-week trough
  - ✓Provides monthly, small (1.2 mL), SC dose for patient home use