# DISCLOSURES

Dr. Bittner discloses the following:

1. Current research grants and contracts to her institution:
   - Amgen, Novartis, Wake Forest Atrium (Subcontract of NIA grant)

2. Service on DSMB: Verve Therapeutics, Eli Lilly

3. Past consultant: New Amsterdam Pharma; Pfizer

4. Past research contracts to her institution
   - Esperion, DalCor, Astra-Zeneca – National Coordinator
   - Sanofi – ODYSSEY OUTCOMES Steering Committee

ODYSSEY OUTCOMES was funded by Sanofi and Regeneron

BACKGROUND
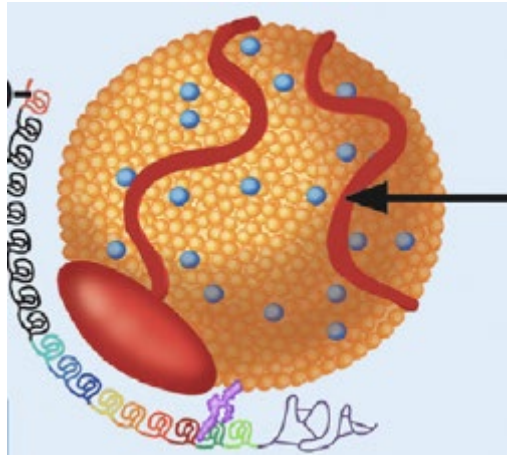
Lp(a): 1 apoB
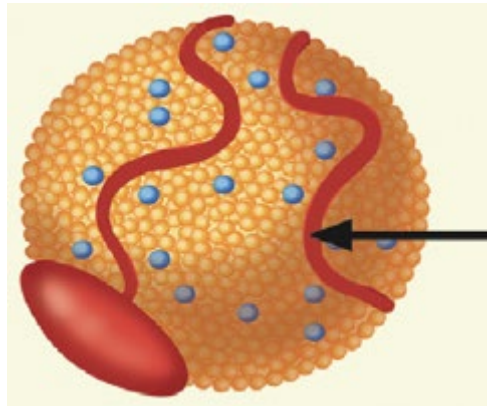
LDL: 1 apoB

- Recent studies* suggest that **on a per particle basis**, Lp(a) is more strongly associated with major adverse cardiovascular events (MACE) than LDL, although both contain 1 molecule of apoB.

- The ODYSSEY OUTCOMES trial (N=18,924) compared the effect of alirocumab with placebo on MACE in patients after recent acute coronary syndrome receiving intensive or maximally tolerated statin therapy.

*Björnson E, et al. JACC 2024;83(3):385–395; Marston N et al. JACC 2024; 84:470-472; Kovar J, Havel RJ. JLR 2002;43:1026-34

HYPOTHESIS

In statin-treated patients with recent acute coronary syndrome, Lp(a) and its change on treatment with alirocumab are more strongly associated with MACE than other apo B-containing lipoproteins when evaluated **on a per particle basis**.

METHODS

- Apo(a) and apoB were measured by mass spectrometry at baseline and month 4 (M4) in 11,957 of 18,924 (63%) ODYSSEY OUTCOMES participants with available samples.

- **The number of Lp(a) particles** was determined from the molar concentration of apo(a).

- **The total number of apoB-containing particles** was determined from the molar concentration of apoB.

- **The number of non-Lp(a) apoB particles** was calculated as [total apoB] – Lp(a) particles.

- MACE (1° study endpoint): death from coronary heart disease, nonfatal myocardial infarction, fatal and non-fatal ischemic stroke, or unstable angina hospitalization

MODELING MACE

Within Placebo Group

- Predictors:
  - Baseline Lp(a)
  - Baseline non-Lp(a) apoB

- Proportional hazards models
  - Unadjusted
  - Adjusted for age, sex, race, history of diabetes, hsCRP

Within Alirocumab Group

- Stratified by baseline Lp(a)
  - <125 nmol/L
  - ≥125 nmol/L

- Predictors
  - Absolute change in Lp(a)
  - Absolute change in non-Lp(a) apoB

- Proportional hazards models
  - Adjusted for baseline Lp(a) and non-Lp(a) apoB
  - Adjusted for baseline concentrations and age, sex, race, history of diabetes, hsCRP

MODELING: PLACEBO GROUP

	Baseline Level (nmol/L)	MACE HR (95% CI) For 50 nmol/L *Increment* in Baseline Level	
		Unadjusted	Adjusted†
Lp(a)	43 (14, 146)	1.079 (1.047, 1.112)*	1.088 (1.053, 1.124)*
ApoB not on Lp(a)	1466 (1242, 1763)	1.022 (1.015, 1.029)*	1.019 (1.011, 1.026)*

* P<0.001

† Adjusted for age, sex, race, DM, hs-CRP. There was no interaction with hs-CRP.

MODELING: ALIROCUMAB GROUP

	Baseline Level (nmol/L) Median (Q1, Q3)	Absolute Change (nmol/L) Median (Q1, Q3)	MACE* HR (95% CI) for 50 nmol/L Decrement With Treatment	P-Value
Lp(a) <125nmol/L				
Lp(a)	22 (10, 50)	-7.1 (-16.0, -2.0)	1.096 (0.728, 1.653)	0.66
ApoB not on Lp(a)	1508 (1291, 1797)	-777.5 (-1023.5, -534.5)	0.986 (0.974, 0.999)	0.0288
Lp(a) ≥125nmol/L				
Lp(a)	201 (157, 270)	-40.9 (-67.5, -16.4)	0.800 (0.684, 0.936)	0.0055
ApoB not on Lp(a)	1349 (1130, 1640)	-737.6 (-960.1, -507.1)	1.002 (0.978, 1.026)	0.88

* Adj. for baseline concentrations, age, sex, race, DM, hs-CRP. There was no interaction with hs-CRP.

CONCLUSIONS

- Placebo Group:
  - **On a per-particle basis**, both baseline Lp(a) and non-Lp(a) apoB predicted MACE, but with stronger prediction by Lp(a).

- Alirocumab Group:
  - **Baseline Lp(a) <125 nmol/L: on a per particle basis,** reduction in MACE with alirocumab was predominantly related to reduction in non-Lp(a) apoB.
  - **Baseline Lp(a) ≥125 nmol/L: on a per particle basis**, reduction in MACE with alirocumab was predominantly related to reduction of Lp(a).

- In patients with recent ACS, Lp(a) may be an important target of treatment with Alirocumab, particularly in patients with elevated Lp(a) levels.