FAQ: Beyond LDL: Lipoprotein(a), Apolipoprotein B, and the Next Wave of Cardiovascular Risk Reduction

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Purpose

This document addresses frequently asked questions about the clinical relevance of lipoprotein(a) and apolipoprotein B in cardiovascular risk assessment, and reviews how current and emerging pharmacologic therapies influence these biomarkers.

FAQs

1. **What are lipoprotein(a) [Lp(a)] and apolipoprotein B (ApoB)?**

Lp(a) and ApoB are considered cardiovascular risk-enhancing biomarkers that can help justify more aggressive lipid lowering therapy when the treatment decision remains uncertain. ApoB is a structural protein present on all atherogenic lipoproteins. ApoB reflects the number of atherogenic particles present, rather than the cholesterol content, and more accurately reflects an individual's atherosclerotic cardiovascular disease (ASCVD) risk compared to measuring LDL cholesterol. LDL cholesterol measures cholesterol content not the particle burden, which is what drives plaque formation.

Lp(a) is a genetically inherited LDL-like particle with additional atherogenic, proinflammatory, and prothrombotic effects.

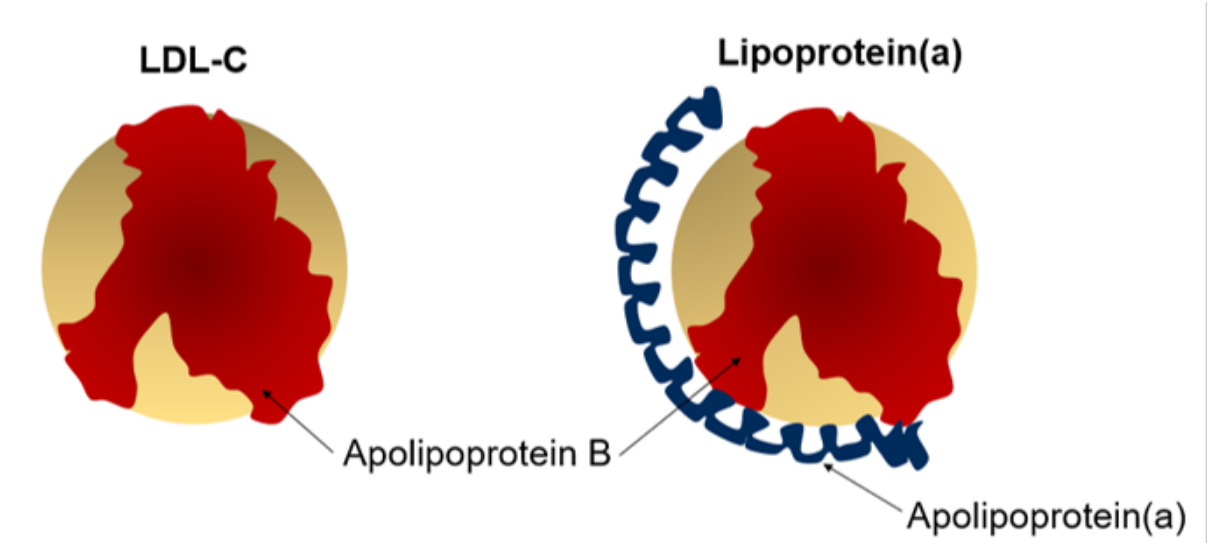

Figure 1- Lipoprotein (a) and Apolipoprotein B[2]

2. What can we learn from measuring Lp(a) and ApoB?

Both ApoB and Lp(a) can help identify residual ASCVD risk that LDL-C alone may miss[1,4]. Elevated apoB or Lp(a) can help providers decide to start a statin, use high-intensity statin therapy, or consider adding additional LDL-lowering therapies.

Lp(a) Risk Stratification[6]:

Classification	Range (mg/dL)	Range (nmol/L)
Low Risk	<30	<75
Intermediate Risk	30-50	75-125
High Risk	≥50	≥125

ApoB Treatment Thresholds[7]:

ASCVD Risk Category	LDL-C (mg/dL)	Non-HDL-C (mg/dL)	ApoB (mg/dL)
Very High Risk	55	85	55
High Risk	70	100	70
Borderline to intermediate risk	100	130	90

Key ApoB Pearl: If LDL-C is at goal, but ApoB is elevated, there is residual risk that remains

3. Who should we screen for these markers?

ApoB[7]

-Initial Evaluation
-4-12 weeks after changes in LLT
-Clinical or metabolic changes
-Cascade screening

Lp(a)[1,5]

-Universal screening for all adults once in their lifetime
-Selective screening for pediatric patients with other risk factors
-Cascade screening

4. How do current therapies impact Lp(a) and ApoB[2]?

Medication	Change of Lp(a)	Change of ApoB	Overall recommendation
statins	+ 0-15%	- 20-50% (dependent on statin)	Treat high ASCVD risk or elevated LDL. Not recommended to treat elevated Lp(a)
ezetimibe	- 0-7%	- 10-20% with statin	May help lower apoB with statin Not recommended to treat elevated Lp(a)
niacin	- 20-40%	- 15-25%	Not recommended to reduce ASCVD risk
bempedoic acid	neutral	- 15-25%	May help lower apoB in statin-intolerant patients. Not recommended to treat elevated Lp(a)
evolocumab, alirocumab (PCSK9 mAb)	- 23-47%	- 45-60%	Recommended for most benefit on CVRR* in patients with higher baseline Lp(a) Very effective for high baseline apoB or familial hypercholesterolemia

*CVRR- cardiovascular risk reduction

5. What emerging therapies influence Lp(a) and ApoB?

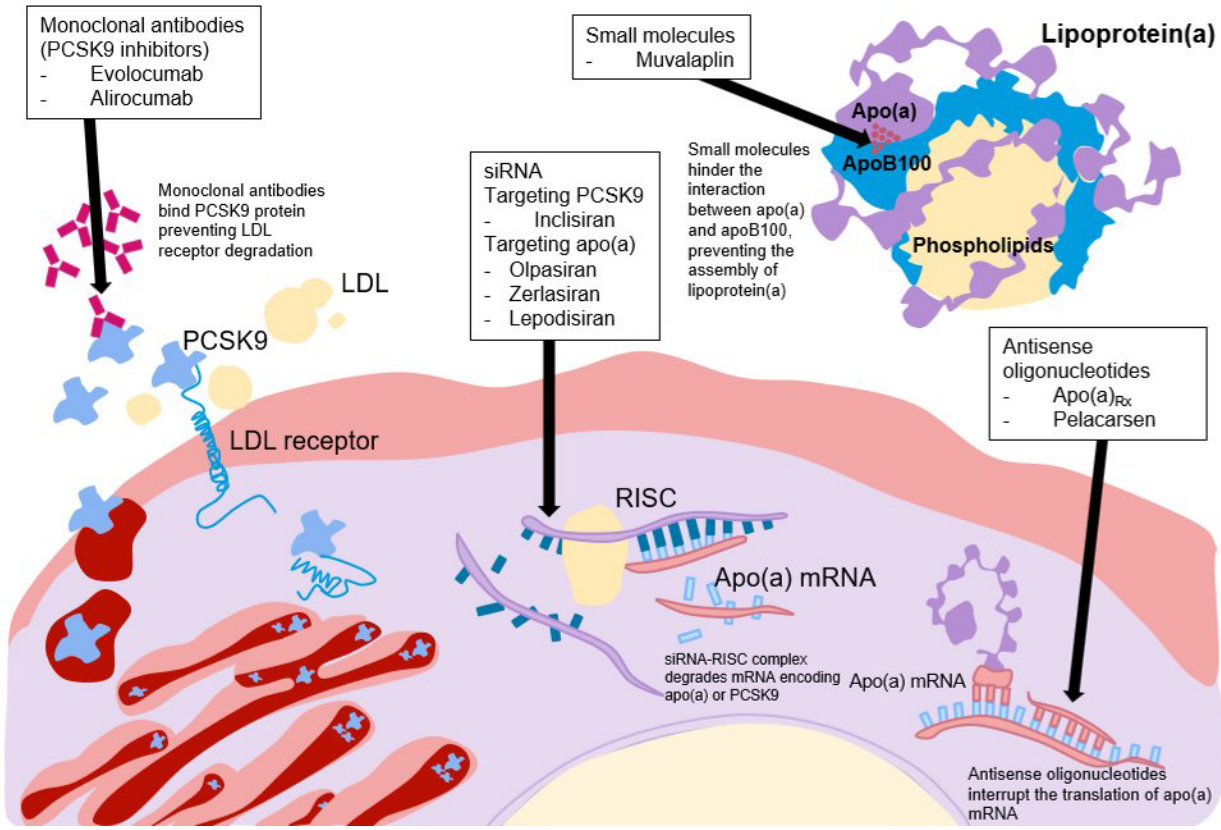

Figure 2- ***Mechanisms of action and target sites of approved and in-development pharmacologic agents for lipoprotein(a) reduction***[3]

Therapeutic Landscape for Lipoprotein (a)[2]

Medication	MOA	Trials	LDL	Lp(a)	ApoB
pelacarsen	ASO	Phase 2: Phase 3: Lp(a)HORIZON (Feb 26) Lp(a) FRONTIERS CAVS (Mar 30)	- 23-27%	Not available	- 15-18%
olpasiran	siRNA	Phase 2: OCEAN(a)- Dose Phase 3: OCEAN(a)-Outcomes Trial (Dec 26)	- 18.5%	Not available	- 11.5%
lepodisiran	siRNA	Phase 2: ALPACA Phase 3: ACCLAIM-Lp(a) (Mar 29)	Not available	Not available	Not available
zerlasiran	siRNA	Phase 2: ALPACAR- 360	- 26-32%		- 15-24%

muvalaplin	Small molecule	Phase 2: KRAKEN Phase 3: MOVE- Lp(a) (Mar 31)	Not available	Decrease all doses	- 16%

6. What are the key takeaways for pharmacists?

Pharmacists can identify patients for testing and optimize therapy based on these biomarkers. They can advocate for patients through referrals to specialists and provide education to patients and family members around screening, lifestyle, and device training. Pharmacists should stay aware of funding resources for new and emerging medications.

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