

## ASSESSING RISK

# Lp(a) Screening for Individuals at High ASCVD Risk



### WHAT IS Lp(a)?

A LDL variant, in which apo(a) is covalently bonded to Apo B, Lp(a) has been established as a pathogenic entity and proven to be an independent risk factor for atherosclerotic cardiovascular disease (ASCVD).

*Elevated levels of Lp(a) are estimated to be prevalent in 20% of the population.*

**INCREASE IN MORTALITY**

**INCREASE IN CV EVENTS**

**INCREASE IN Lp(a)**

### CAUSAL EFFECT

Epidemiological, Mendelian randomization and GWAS studies confirm high Lp(a) is a causal factor:

- Myocardial Infarction
- Coronary Heart Disease
- Ischemic Stroke
- Calcific Valvular Aortic Stenosis
- Coronary, Femoral and Carotid Stenosis CVD Mortality

**THESE CAUSAL RELATIONSHIPS ARE INDEPENDENT OF CONCENTRATIONS OF OTHER LIPIDS AND LIPOPROTEINS, INCLUDING LDL CHOLESTEROL.**

### WHAT LEVEL IS HIGH RISK?

**Lp(a) >50 mg/dL or >100 nmol/L:**

- Corresponds to the 80th population percentile in populations which are predominately Caucasian
- African Americans have higher Lp(a) levels than Caucasians (74 nmol/L vs 20 nmol/L) but it is unclear if a different risk threshold should apply
- Some labs report elevated Lp(a) as > 30 mg/dL or > 75 nmol/L, which is roughly equivalent to the 75th percentile in Caucasian populations

**Lp(a)  
CUTOPOINT**

**> 50 mg/dL or > 100 nmol/L for both men and women**

### WHO SHOULD GET SCREENED?

#### Primary Prevention

##### • Adults and Youth with:

- A personal history of premature ASCVD and/or ischemic stroke
- Familial Hypercholesterolemia
- Primary severe hypercholesterolemia (LDL-C  $\geq$  190 mg/dL)
- First-degree relatives with premature ASCVD (<55 years of age in men or <65 years of age in women)
- Children or parents with elevated Lp(a)

#### Secondary Prevention

##### • Adults with:

- Premature ASCVD (<55 years of age in men or <65 years of age in women)
- Recurrent or progressive ASCVD, despite optimal lipid-lowering
- Calcific valvular aortic stenosis (VAS)
- Less-than-expected LDL-C lowering on statin therapy

### WHEN ORDERING AN Lp(a) TEST

- Testing doesn't require fasting
- Results may be affected by inflammation
- Results may be reported in mg/dl or nmol/L with measurement in nmol/L preferred due to greater accuracy
- The test is widely available and generally inexpensive
- May not be covered by insurance
- Levels generally don't change over a person's lifetime

### WHAT NOW? TREATMENT

- **Lifestyle therapy**, including a heart-healthy dietary pattern and regular physical activity, is recommended although not effective in lowering Lp(a)
- **Manage LDL Related Risk** by maximizing LDL-C lowering therapies shown to reduce ASCVD
  - **High intensity statin therapy or maximally tolerated statin therapy** remains the cornerstone of treatment despite minimal effects on Lp(a) levels
  - **Non-statin therapy (Ezetimibe, PCSK9 Inhibitor)**- It is reasonable to consider combination therapy with Ezetimibe or a PCSK9 inhibitor in "high" and "very high risk" patients on maximally tolerated statin therapy who remain above their LDL-C (and Non-HDL-C goals).
- **Manage Lp(a) Related Risk**
  - Consider therapies (i.e. PCSK9 Inhibitors) that lower both LDL-C and Lp(a) and reduce ASCVD risk
  - In very select patient populations (i.e. recurrent ASCVD events on optimal lipid lowering treatment), consider lipoprotein apheresis
- Avoid lipid-lowering agents that lower Lp(a) but have not been shown to have benefit in clinical outcome trials (niacin, hormone replacement therapy)