

# Discussant: Safety and efficacy of AKCEA-APO(a)-L<sub>rx</sub> to lower lipoprotein(a) levels in patients with established cardiovascular disease

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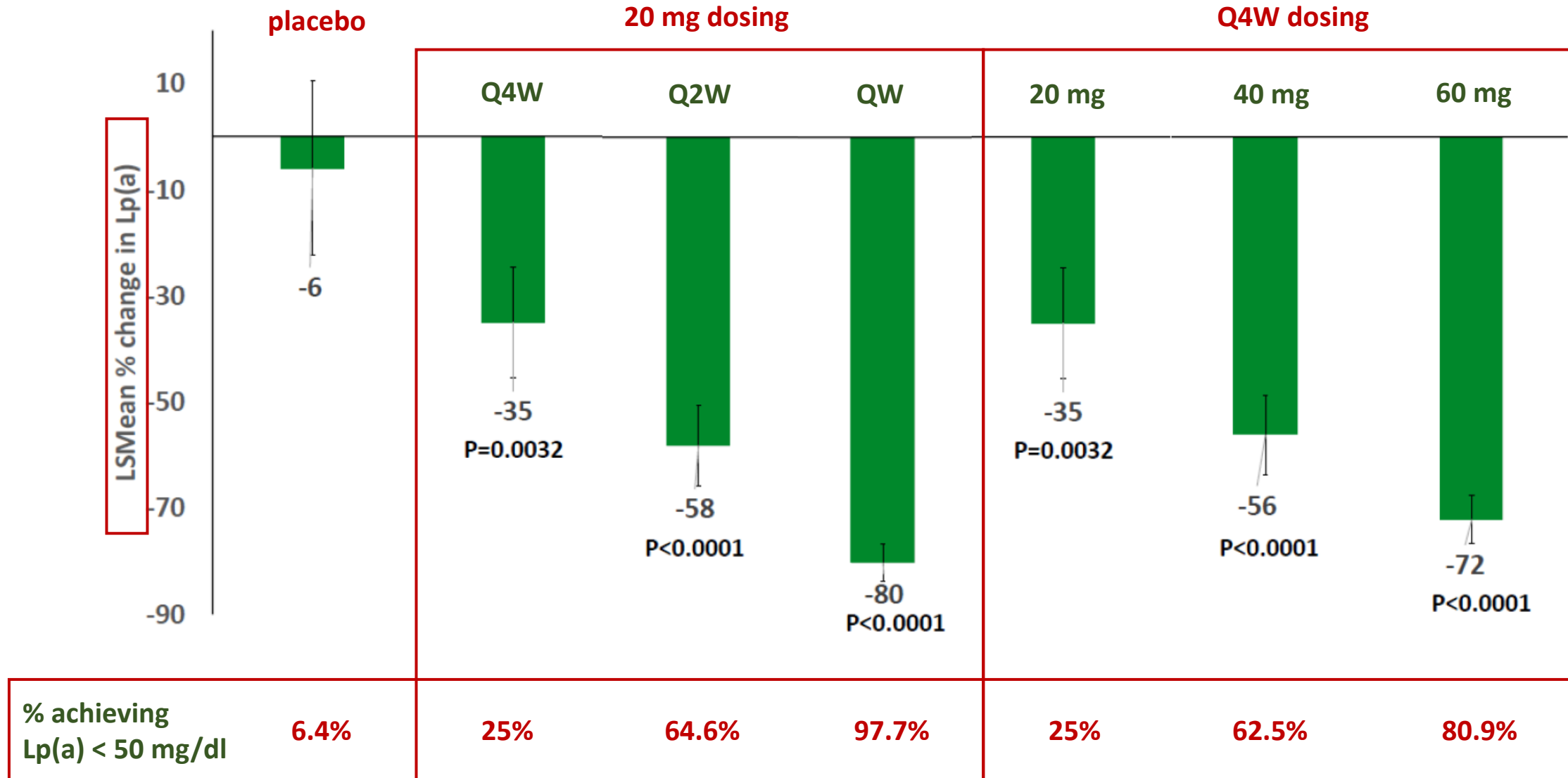
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**SCIENTIFIC** 20  
**SESSIONS** 18

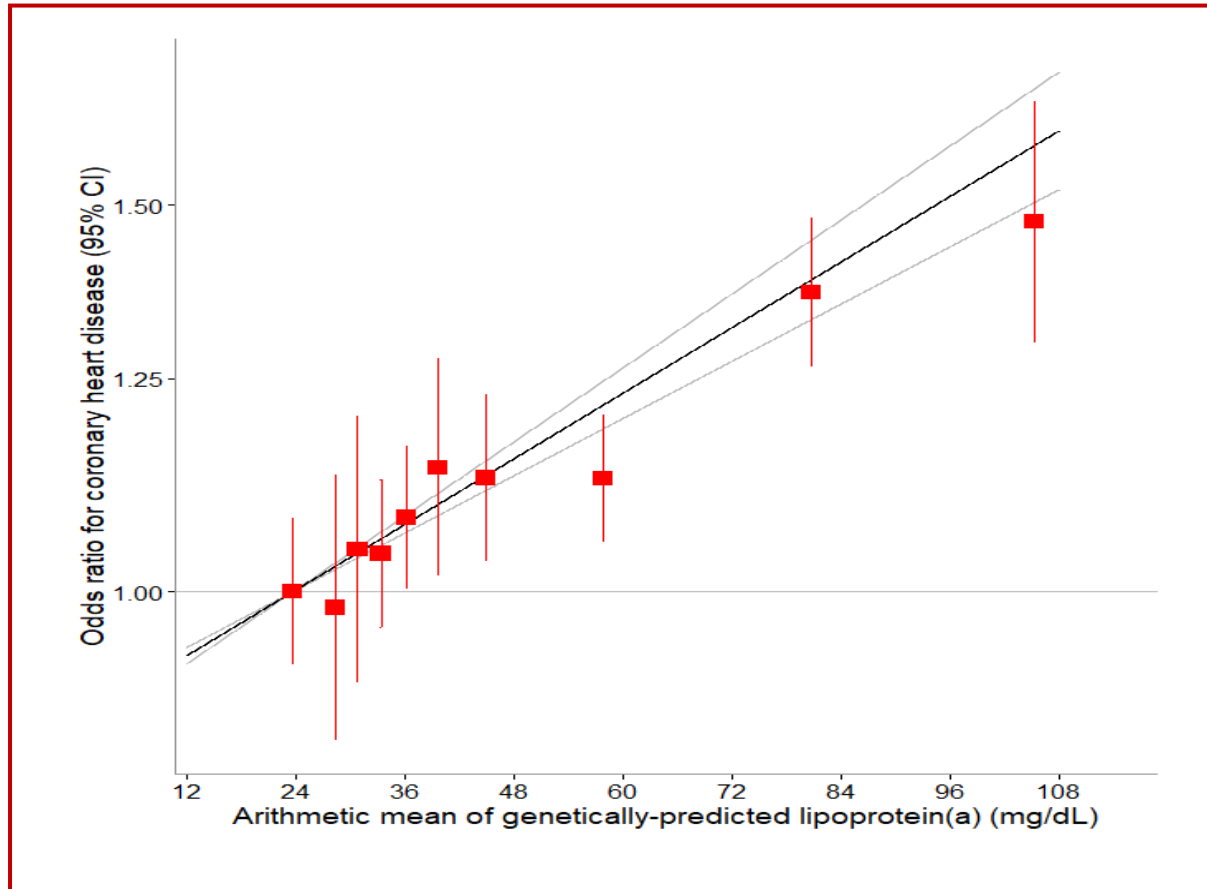


# AKCEA-APO(a)-L<sub>rx</sub> primary and key secondary outcomes

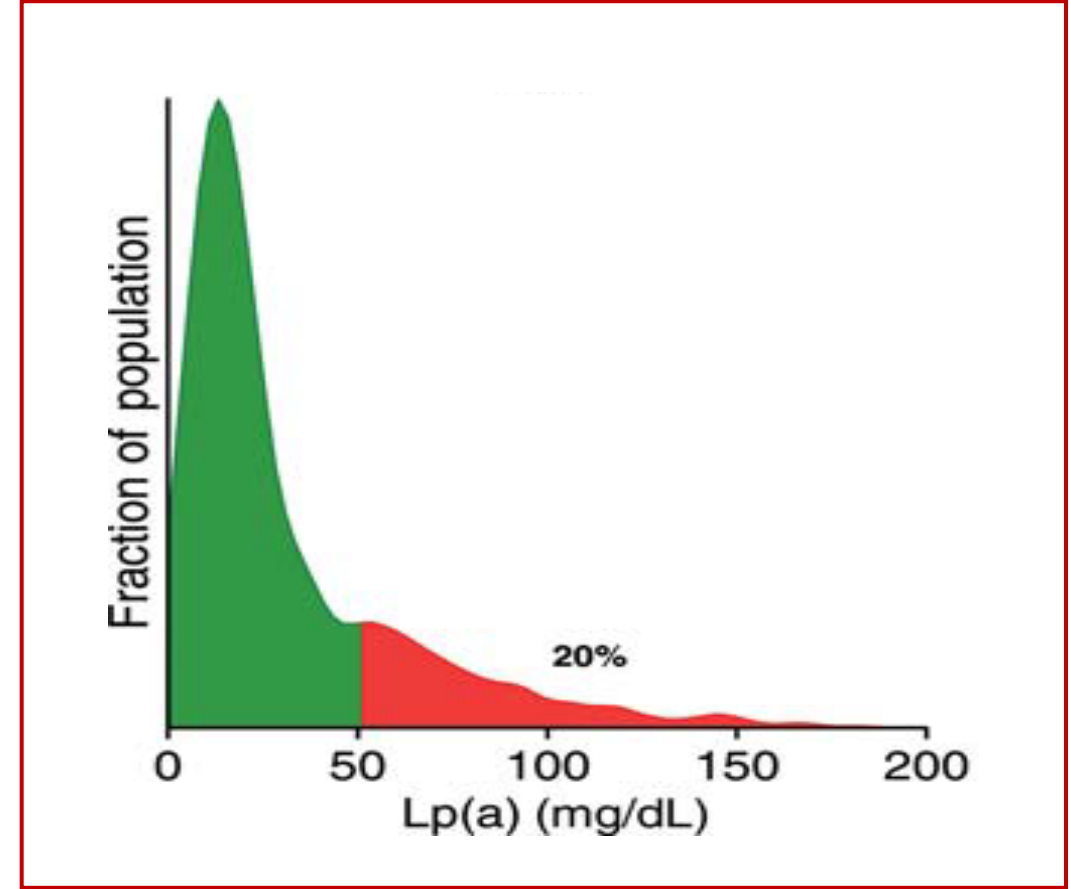


# Causal effect of ABSOLUTE change in Lp(a) on CHD

Log-linear association between absolute changes Lp(a) and CHD



Highly skewed distribution of plasma Lp(a)



# Absolute changes in Lp(a) and LDL-C

	Placebo	20 mg dosing			Q4W dosing		
Dose		Q4W	Q2W	QW	20 mg	40 mg	60 mg
% change in Lp(a)	6%	35%	58%	80%	35%	56%	72%
Placebo corrected % change in Lp(a)	ref	29%	52%	76%	28%	50%	66%
Absolute Δ Lp(a) Mean, SD (nmol/L)	-15.2 (34.6)	-95.9 (94.4)	-130.3 (66.1)	-187.8 (80.3)	-95.9 (94.4)	-116.9 (71.7)	-149.5 (67.5)
Absolute Δ Lp(a) Mean, SD (mg/dl)	-6.1 (13.8)	-38.4 (37.7)	-52.1 (26.4)	-75.1 (32.1)	-38.4 (37.7)	-46.8 (28.7)	-59.8 (27.0)
Placebo corrected Absolute Δ Lp(a) Mean, SD (mg/dl)	ref	-32.3	-46.0	-69.0	-32.3	-41.7	-53.7
Absolute Δ LDL-C Mean, SD (mg/dl)	0.9528	-4.6	-8.2	-15.6	-4.6	-15.8	-4.6
Ratio of Δ Lp(a) : LDL-C		1/8	1/7	1/5	1/8	1/4	1/14

# Conclusions

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- AKCEA-APO(a)-L<sub>rx</sub> safely and effectively lowered Lp(a)
- **Results directly inform design of pivotal phase 3 CVOT:**
  - *Study population:* participants with baseline Lp(a) > 60-70 mg/dl
    - **target study population median Lp(a) ≥ 100 mg/dl**
  - AKCEA-APO(a)-L<sub>rx</sub> dose: 20 mg QW
  - *Expected mean proportional reduction in Lp(a):* ≈ 65-75%
  - *Expected mean **absolute decrease Lp(a):*** ≈ 70 mg/dl
  - *Expected CV proportional risk reduction:* ≈ 15% RRR
    - *After 4 or more years of treatment*

