Intraindividual Variability in Serial Lipoprotein(a) Concentrations among Placebo-Treated Patients in the OCEAN(a)-DOSE Trial

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BACKGROUND

- As lipoprotein(a) [Lp(a)] concentration is primarily genetically determined (70->90%), levels are presumed to be largely stable over time and need to be measured only once.
- However, data assessing intraindividual variability in Lp(a) concentrations over time are limited.

OBJECTIVE

To examine the intraindividual variability in Lp(a) concentrations for individuals with stable ASCVD and elevated baseline Lp(a) values in the placebo arm of OCEAN(a)-DOSE.

METHODS

- OCEAN(a)-DOSE, a phase 2, randomized trial of the Lp(a)-lowering siRNA therapy olpasiran, enrolled 281 patients with stable ASCVD and Lp(a) >150 nmol/L.
- Analyses were conducted in patients randomized to placebo (N=53) with serial Lp(a) values every 4 to 12 weeks through 72 weeks (820 total serum samples).
- Intra-individual biological variation (CV_i) was calculated as standard deviation of Lp(a) values over time in an individual divided by the mean of those Lp(a) values.
- All Lp(a) values were measured using a central laboratory and the validated Roche Tina-quant Gen.2 assay reporting in molarity (assay CV 0.7% at 105 nmol/L).

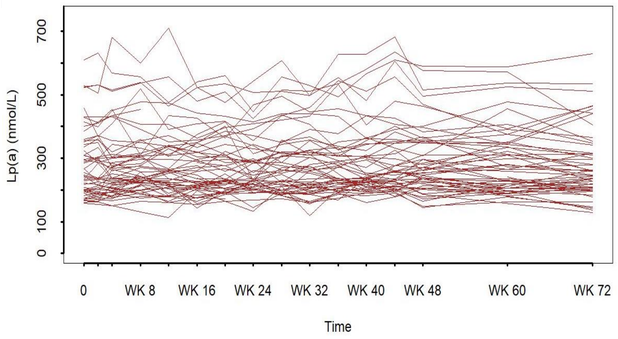
RESULTS

- A total of 53 patients were randomized to placebo and had at least one post-randomization Lp(a) measurement available.

RESULTS

- Median number of Lp(a) measurements per subject was 16, and median follow-up was 1.7 years (IQR 1.4-1.7 years). Overall, this allowed for 820 assessments of Lp(a).
- Median Lp(a) concentration at baseline among patients treated with placebo was 246 [IQR 200, 343] nmol/L and was relatively stable over time.
- Each individual's Lp(a) levels across all study visits are shown in **Figure 1**. There existed notable variability between serial values for many placebo-treated patients in the study population.

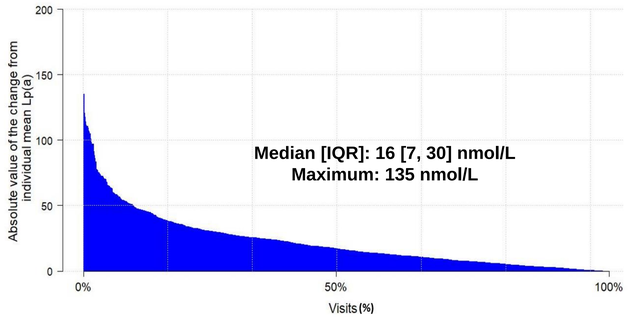
Figure 1. Intraindividual Lp(a) values over time



- The median absolute fluctuation in Lp(a) concentration across all their study visits when compared with an individual's mean Lp(a) value was 16 [IQR 7, 30] nmol/L, with a maximum absolute difference of 135 nmol/L from an individual patient's mean Lp(a) (**Figure 2**).

RESULTS

Figure 2. Median absolute value of the change in Lp(a) levels from individual mean



- The median of the absolute values of the percent changes in Lp(a) concentrations across all visits when compared with an individual's mean Lp(a) was 6% [IQR 3%, 11%].
- 25% of patients experienced an upward or downward ≥25% change from their individual mean on at least 1 visit (**Figure 3**), and 53% experienced an upward or downward ≥50 nmol/L change on at least 1 visit.

Figure 3. Maximum absolute value of % change in Lp(a) from individual mean

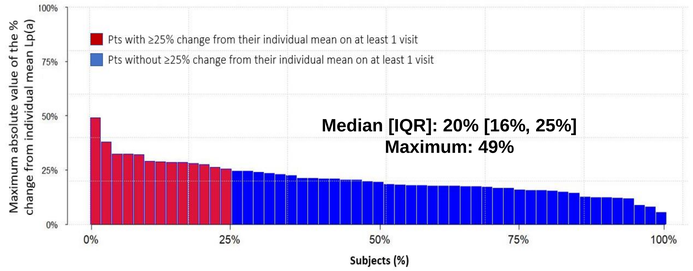
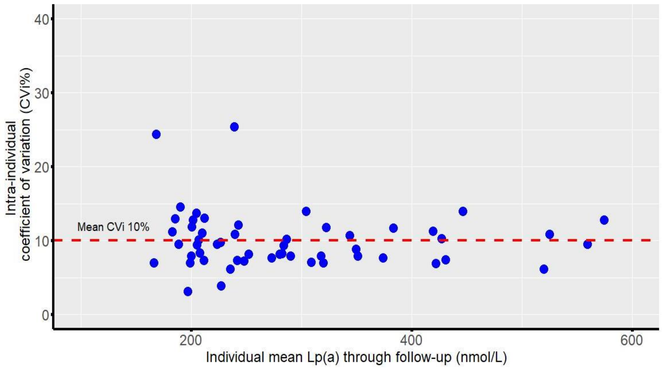


Figure 4. Intraindividual variation (CV_i) of Lp(a) levels



- Whereas the overall Lp(a) concentration remained similar across visits (standard deviation 2.6% of the mean), the intra-individual variation over time (CV_i) was 10% [SD 3.9%] of an individual's mean. This variation remained similar across a range of mean Lp(a) values for each participant.
- By comparison, CV_i for LDL-C across study visits was 15.6% [SD 7.4%] and for triglycerides was 22.0% [SD 7.8%].

LIMITATIONS

- Modest sample size, baseline elevated Lp(a) in all pts

CONCLUSIONS

- Among patients with elevated baseline Lp(a) concentration, there was notable intra-individual variability in Lp(a) concentration over 72 weeks of follow-up.
- These findings suggest that Lp(a) levels may need to be measured more than once in a lifetime.

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