RESULTS (I)

A. Deconvolution Flags LP-X Samples

B. LP-X by NMR vs Agarose Gel

C. LP-X & LP-Z by NMR Deconvolution

REFERENCES

1. The effects of MEDI6012 on lipoproteins in familial LCAT deficiency patients and a new NMR method for quantifying lipoprotein-X

Lita A. Freeman, Maureen L. Sampson, Robert D. Shamburek, Boris L. Vaisman, James Otvos, Sotirios K. Karathanasis, Alan Remaley.

ABSTRACT

BACKGROUND

Familial LCAT Deficiency (FLD) is characterized by lipoprotein abnormalities, including increased levels of triglyceride-rich lipoproteins and LDL, decreased HDL and LCAT activity, and severe cardiovascular disease. The drug MEDI6012 is under clinical evaluation for the treatment of FLD.

METHODS

LP-X analysis was performed on plasma from FLD patients treated with MEDI6012 and on plasma from patients with familial hyperlipidemia (FH), and from patients with severe hypertriglyceridemia (sH TG). Samples were also analyzed for lipids (Cholesterol-C and Free Cholesterol-E) and LCAT activity. The lipoprotein phenotype was determined by agarose gel electrophoresis (Sec III).

RESULTS

1. A new MR signature for LP-X was identified by NMR Lipoprofile analysis testing the Vantera NMR clinical analyzer of synthetic purified LP-X and plasma from patients with severe biliary cholestasis and Familial LCAT Deficiency (FLD).

CONCLUSION

NMR may be a useful methodology to quantitate LP-X in diseases of LCAT insufficiency, like FLD, and as a pharmacological biomarker to assess treatment effectiveness with MEDI6012 treatment.

RESULTS (II)

A. Lipids of FLD patient plasma treated with MEDI6012 ex vivo

B. Agarose gel profile of FLD patient plasma treated with MEDI6012 ex vivo

C. NMR Assays for LP-X

D. Correlation Between Gel vs NMR Assays for LP-X

SUMMARY

1. An NMR signature for LP-X was identified by NMR Lipoprofile testing the Vantera NMR clinical analyzer of synthetic purified LP-X and plasma from patients with severe biliary cholestasis and Familial LCAT Deficiency (FLD).

2. LP-X is readily detected in these samples by agarose gel electrophoresis followed by filipin staining.

3. Incubation with varying concentrations of MEDI6012 reduced LP-X in a dose-dependent manner by both agarose gel electrophoresis and NMR. The coefficient of determination (R²) between the two methods was greater than 0.95.