Abstract Number: 515

Coronary Atheroma Regression from Serial Infusions of Autologous Selectively Delipidated Preβ-HDL-enriched Plasma on Coronary Atheroma in Patients With Homozygous Familial Hypercholesterolemia in the HALO-FH Trial

Brian Ghoshhajra, Borek Foldyna, Massachusetts General Hosp, Harvard Medical Sch, Boston, MA; Daniel Gaudet, Etienne Khoury, Univ de Montréal and ECOGENE-21 Clinical and Translational Res Ctr, Chicoutimi, QC, Canada; Steven R Sloan, Boston Children's Hosp, Harvard Medical Sch, Boston, MA; Prediman K Shah, Cedars–Sinai Smidt Heart Inst, Los Angeles, CA; Steven R Jones, Johns Hopkins Univ, Baltimore, MD; Ron Waksman, Rebecca Torguson, Medstar Washington Hosp Ctr, Washington, DC; Ernst Schaefer, Tufts Univ, Boston, MA; H. Bryan Brewer, HDL Therapeutics, Inc., Vero Beach, FL

BACKGROUND

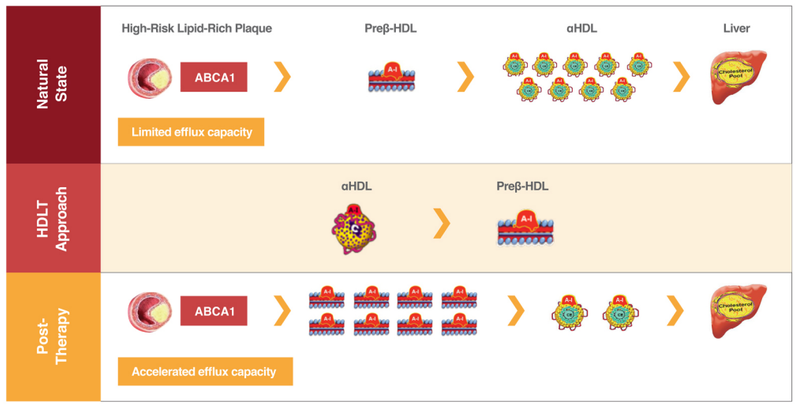
Lipid-rich plaques are prone to rupture causing major adverse cardiac events (MACE). Selective delipidation of plasma via HDL Therapeutics' PDS-2™ System converts αHDL to preβ-HDL, the most effective form of HDL for cholesterol removal from arterial plaques.

Progression of the Normal Artery to an Artery Containing a High-Risk Lipid-Rich Plaque

PREβ-HDL IS THE KEY DRIVER TO REDUCING LIPID-RICH PLAQUES*

The low level of preβ-HDL limits the ability of HDL cholesterol efflux capacity to remove lipids from high-risk plaques

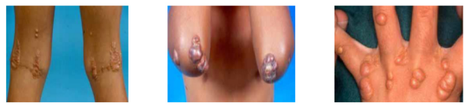
- PDS-2 therapy significantly increases preβ-HDL levels and accelerates the cholesterol efflux capacity to reduce high-risk lipid-rich plaques and turn it into a low-risk lipid-depleted state
- ABCA1 is the key receptor in the cholesterol efflux process to remove lipids from high-risk lipid-rich plaques
- Only preβ-HDL (~5% of circulating plasma) is able to bind to the ABCA1 receptor to accelerate the cholesterol efflux capacity and remove lipids from high-risk plaques; αHDL (~95% of circulating plasma) does not bind to the ABCA1 receptor



*Brewer HB. The Evolving Role of HDL in the Treatment of High-Risk Patients with Cardiovascular Disease, *J Clin Endocrinol Metab* 2011;96(5):1246-1257. https://doi.org/10.1210/jc.2010-0163.

OBJECTIVE

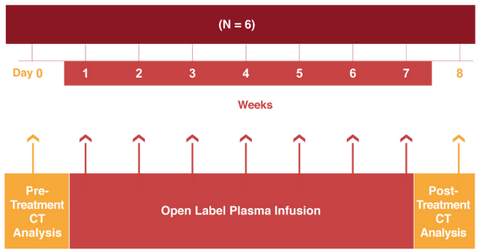
To determine the effect of 7 weekly serial infusions of autologous selectively delipidated preβ-HDL-enriched plasma on coronary atheroma, assessed by quantitative coronary computed tomography angiography (CCTA), in patients with homozygous familial hypercholesterolemia (HoFH).



METHOD

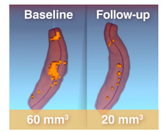
Open-label study of 6 subjects with HoFH at 3 centers. Inclusion criteria were subclinical atherosclerosis (≥20% luminal stenosis) on baseline CCTA, stable lipid-lowering therapy for ≥ 4 weeks prior, and meeting criteria for serial apheresis. All subjects received 7 weekly infusions of autologous selectively delipidated preβ-HDL-enriched plasma and baseline and final CCTA. The primary endpoint was the quantitative atheroma cross- sectional area for each plaque, and plaque composition. Plasma prior to and after each infusion was subjected to gel electrophoresis for preβ-HDL particle levels.

HALO-FH: HDL Acute Lipid Optimization in Homozygous Familiar Hyperlipidemia



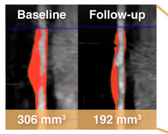
PLAQUES WERE DETECTED, CHARACTERIZED, AND QUANTIFIED USING CCTA

HALO-FH subject with coronary artery disease, prior MI

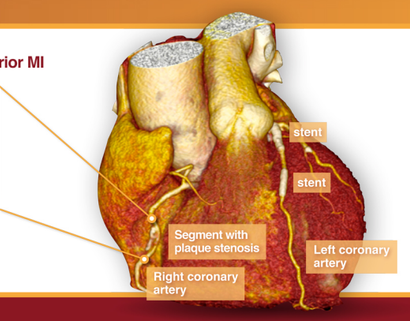


Necrotic core volume

Markedly decreased necrotic core (highest risk atheroma)



Total atheroma volume

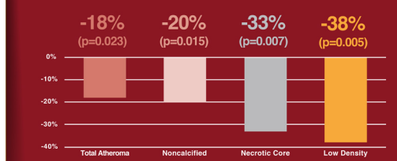


RESULTS

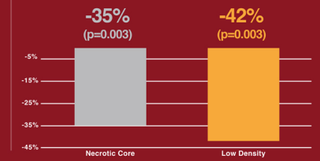
Efficacy: 16 coronary plaques were identified. The primary endpoint was met with a statistically significant 18% reduction in total atheroma cross-sectional area between baseline and follow-up (9.9±3.5 vs. 8.2±2.4 mm²; p=0.023). This included a 20% reduction of noncalcified plaque (p=0.015), and reductions in the low-density (-38%; p=0.005) and necrotic core (-33%; p=0.007) components. The percentage of preβ-HDL particle levels increased significantly (p<0.001) by 65.92%.

Safety: Treatment with delipidated plasma via HDL Therapeutics' PDS-2 System was well tolerated.

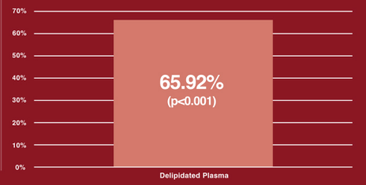
Coronary Atheroma Area Regression



Coronary Atheroma Volume Regression



PDS-2™ Therapy Results in a Marked Increase in Preβ-HDL in Delipidated Plasma



Notes: In HALO-FH Trial 16 lesions in 6 patients were analyzed.

CONCLUSION

We observed coronary atheroma regression after 7 weekly serial infusions of autologous selectively delipidated preβ-HDL-enriched plasma in patients with HoFH. This was accompanied by an increase in preβ-HDL particle levels and a reduction in the low-density and necrotic core plaque portions (i.e., those associated with high-risk plaques prone to rupture and higher rates of MACE).

Clinical Implications: Autologous selectively delipidated preβ-HDL-enriched plasma is a first of its kind treatment to rapidly reverse coronary atherosclerosis in patients with HoFH who are at increased risk for MACE.

DISCLOSURES

B. Ghoshhajra: Other Research Support; Modest; Siemens Healthcare (institutional), National Institutes of Health. B. Foldyna: None. D. Gaudet: Research Grant; Modest; Aegerion (Novelion Therapeutics), Amgen, Regeneron, Sanofi. Consultant/Advisory Board; Modest; Akcea, Amgen, Aegerion, Esperion, HDL Therapeutics, Regeneron, Sanofi. E. Khoury: None. S.R. Sloan: None. P.K. Shah: None. S.R. Jones: Research Grant; Modest; David and June Trone Family Foundation. R. Waksman: Consultant/Advisory Board; Modest; Abbott Vascular, Amgen, AstraZeneca, Biosensors, Biotronik, Boston Scientific, Cardioset, Cardiovascular Systems, Chiesi, MedAlliance, Medtronic, Philips Volcano, Pi-Cardia LTD. R. Torguson: None. E. Schaefer: Employment; Modest; Boston Heart Diagnostic Company. H. Brewer: Ownership Interest; Significant; Chief Scientific Offer, HDL Therapeutics, Inc.