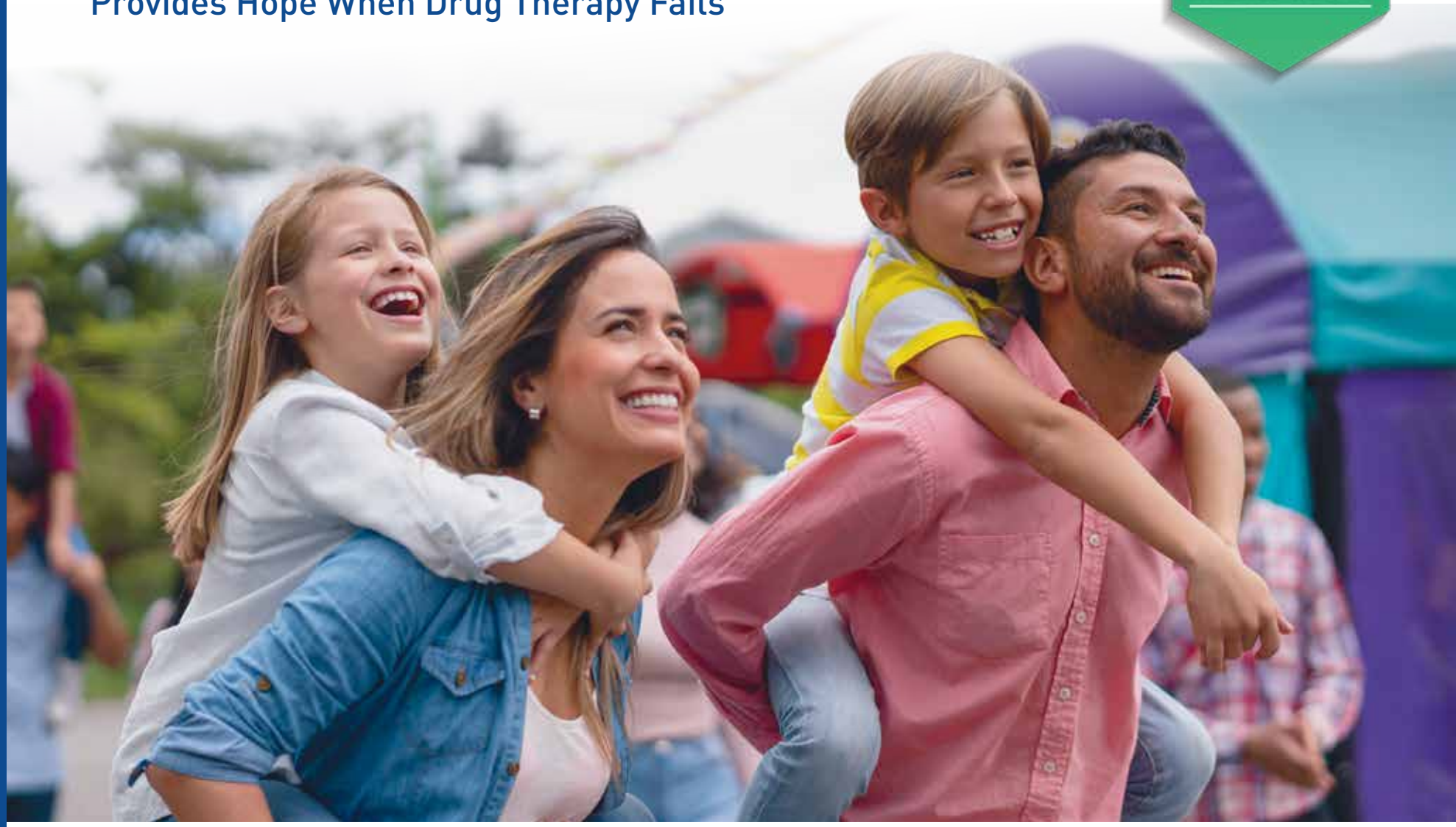
LIPOSORBER®

Provides Hope When Drug Therapy Fails™

NEW
EXPANDED
INDICATION



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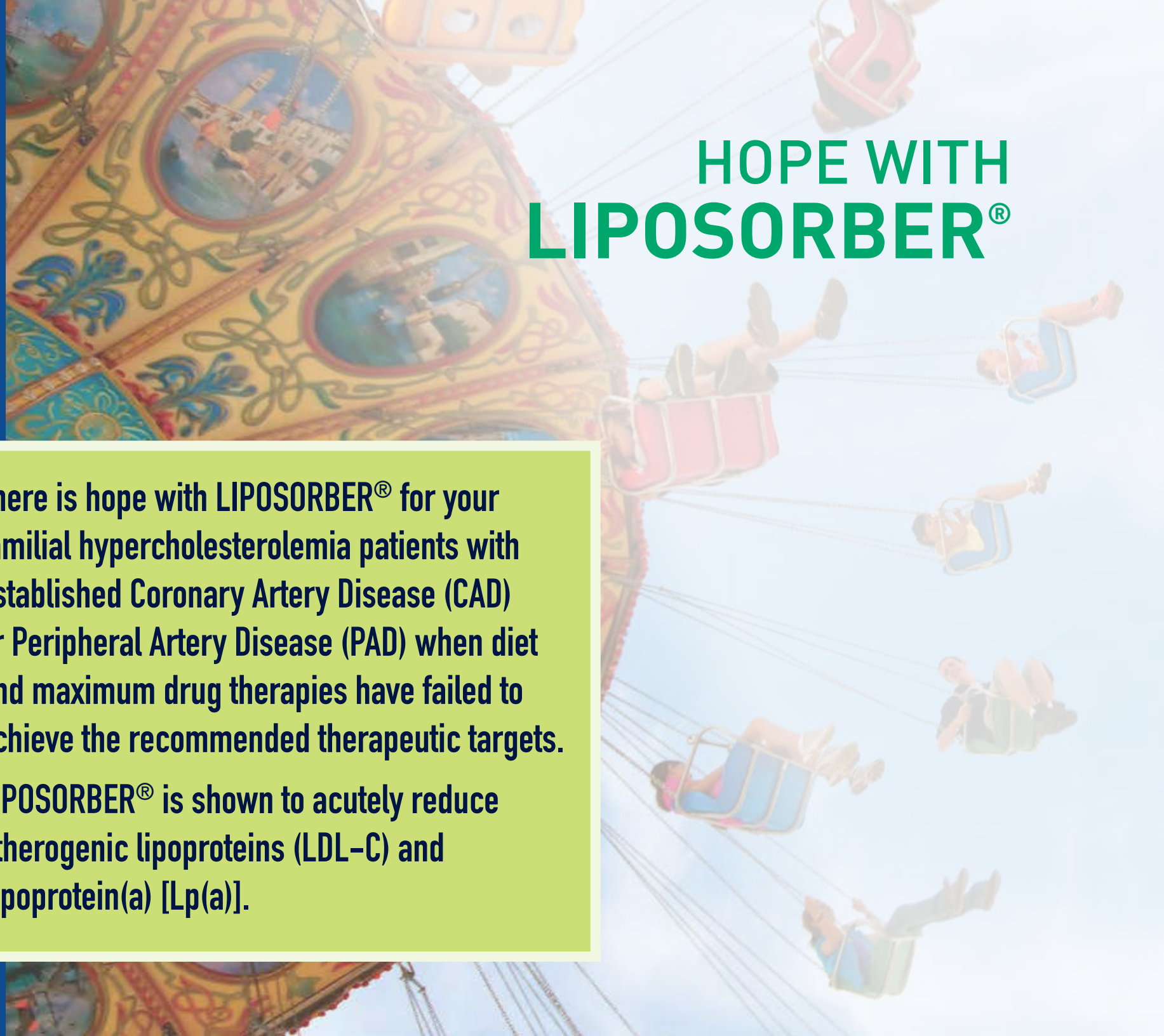
GETTING YOUR FH PATIENTS TO
RECOMMENDED THERAPEUTIC TARGETS
IS POSSIBLE WITH LIPOSORBER®



HOPE WITH LIPOSORBER®

There is hope with LIPOSORBER® for your familial hypercholesterolemia patients with established Coronary Artery Disease (CAD) or Peripheral Artery Disease (PAD) when diet and maximum drug therapies have failed to achieve the recommended therapeutic targets.

LIPOSORBER® is shown to acutely reduce Atherogenic lipoproteins (LDL-C) and Lipoprotein(a) [Lp(a)].

EXPANDED INDICATION

LIPOSORBER® is indicated for use in clinically diagnosed Familial Hypercholesterolemic patients with either documented Coronary Artery Disease (CAD)* or Peripheral Artery Disease (PAD)†, if:

- **LDL-C ≥70 mg/dL**

OR

- **Lp(a) ≥60 mg/dl (or 130 nmol/L)**

And diet and maximum tolerable combination lipid-lowering drug therapies have failed to achieve the established therapeutic targets per professional guidelines.[1]

***Documented CAD**: Diagnosed by: - Invasive OR CT Coronary Angiography; Electron Beam CT (EBCT); History of: Myocardial Infarction, Percutaneous Coronary Intervention, Coronary Artery Bypass Grafting

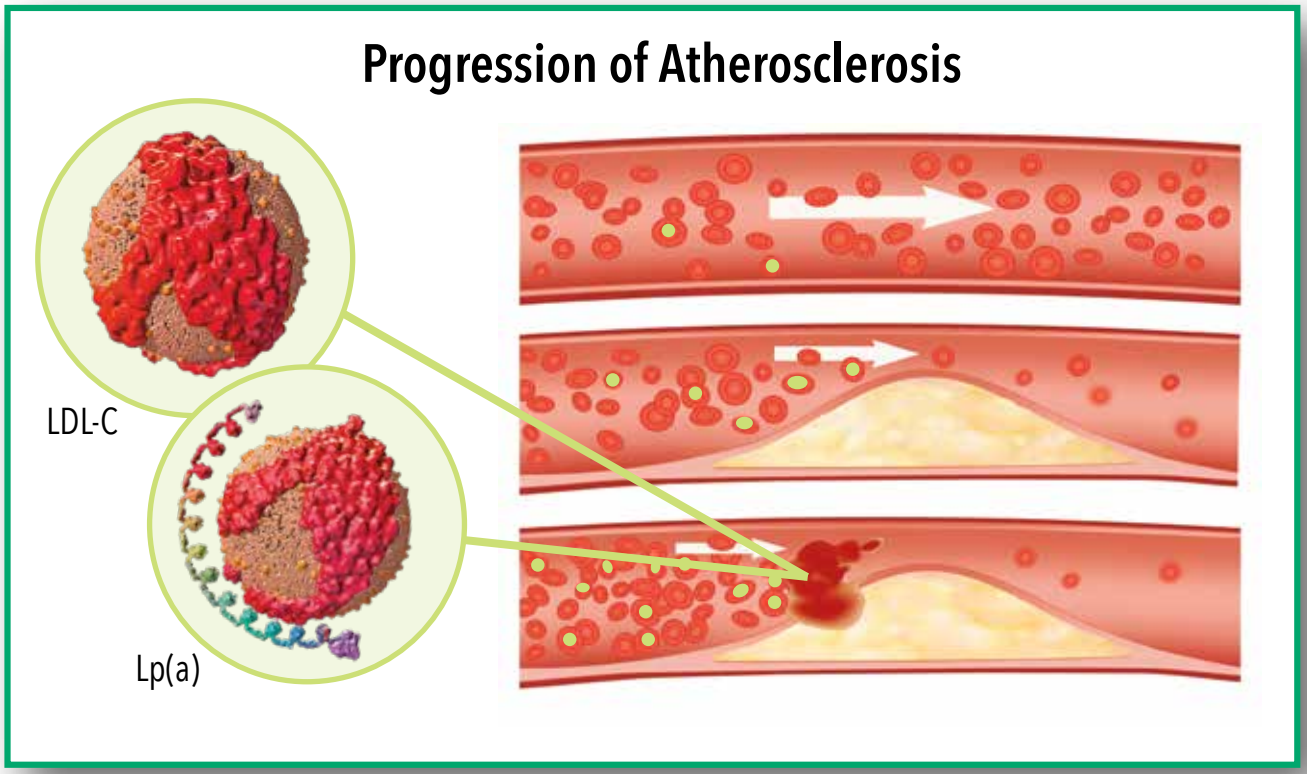
† Documented PAD: Diagnosed by: - Symptoms and/or Physician exam; Ankle-Brachial Index (ABI); Ultrasound Exam; Pulse Volume Recording (PVR); Peripheral Vascular Angiography; History of: Peripheral Vascular Intervention/Peripheral Vascular bypass surgery/minor or major amputation. (Reference: FDA Approval/IFU 4.21.2020)

THE DISEASE BURDEN

Facts and Statistics

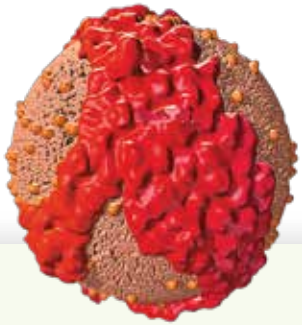
Atherosclerosis and Artery Stenosis are driven by high LDL-C and/or Lp(a). They are major underlying causes of Coronary Artery Disease (CAD).

Coronary artery disease is characterized by chronic progressive changes in the blood vessel walls. These changes are influenced by various independent risk factors for atherosclerosis development, including increased Lp(a) and LDL-C.[2]

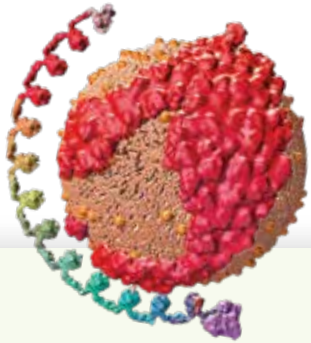


LDL-C and Lipoprotein(a)

A Dual Threat[2]



LDL-C



Lp(a)

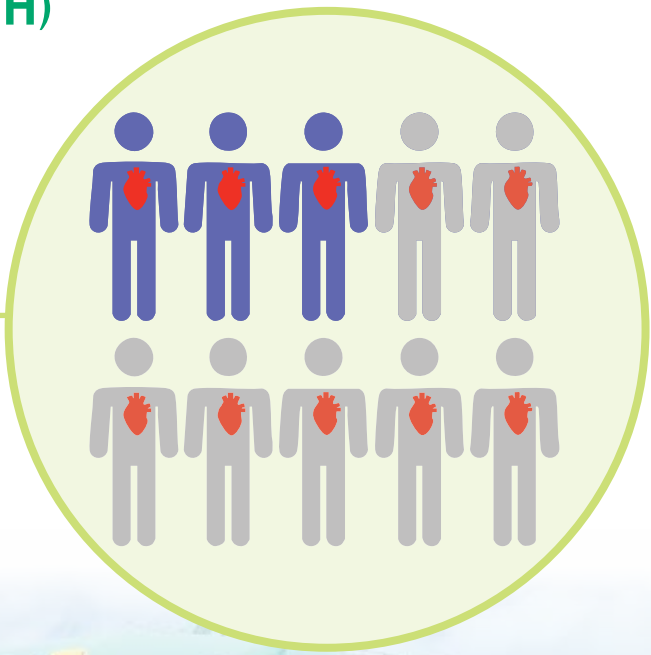
	LDL-C		Lp(a)	
EFFECT	Atherosclerosis		Atherothrombotic	
COMPONENT	LDL-Particle		LDL-like Particle + Apolipoprotein(a)	
MECHANISM	Intimal Cholesterol Deposition, Inflammation & OxPL		Intimal Cholesterol Deposition, Inflammation & OxPL + Indirectly through Fibrinolysis Inhibition	
SITE	Macrovascular	Microvascular	At Plaque Rupture	At Turbulent Blood Flow
CRITICAL EVENT	Myocardial Infarction Peripheral Arterial Disease Atherosclerosis Stenosis	Neuropathy Retinopathy	Myocardial Infarction Ischemic Stroke	Atherosclerotic Stenosis Aortic Valve Stenosis

FAMILIAL HYPERCHOLESTEROLEMIA (FH)

Challenges and Unmet Needs

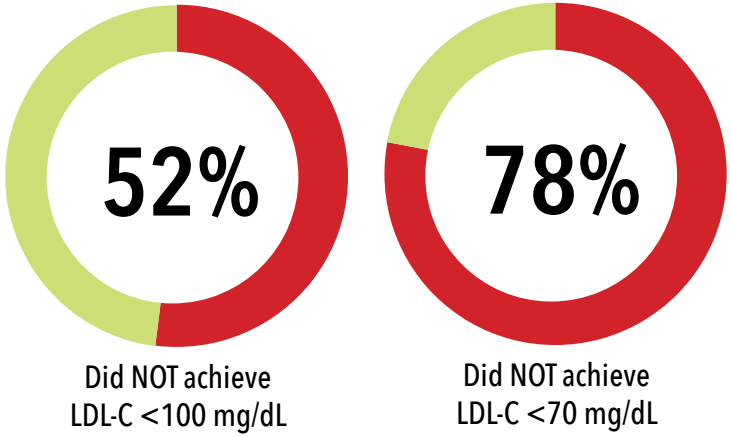
An estimated **1 in 250** Americans have FH; however,

70% have not been accurately diagnosed.[3]



FH PATIENTS need to be on a THERAPEUTIC TRACK.

Untreated FH patients have **20 times** the risk of developing coronary artery disease, compared with the general population.[4]

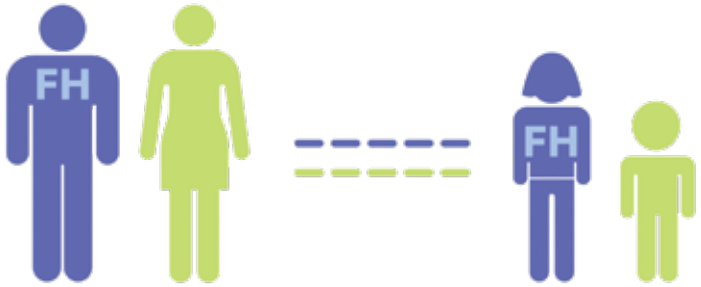


Unfortunately, the **majority of FH individuals may not be achieving the LDL-C therapeutic targets.**

In a study of 1,900 FH adult individuals, **52%** of patients did not achieve LDL-C<100mg/dL. **78%** of patients did not achieve LDL-C<70mg/dL despite 2/3 of patients taking two or three lipid-lowering therapies.*[5]

*Study follow-up was 20 ± 11 months

Each child of a person with FH has a **50% chance of inheriting** the disorder.[6]



Therefore, it becomes essential to screen parents, siblings and children of a person diagnosed with FH.

ABOUT LIPOSORBER®[1]

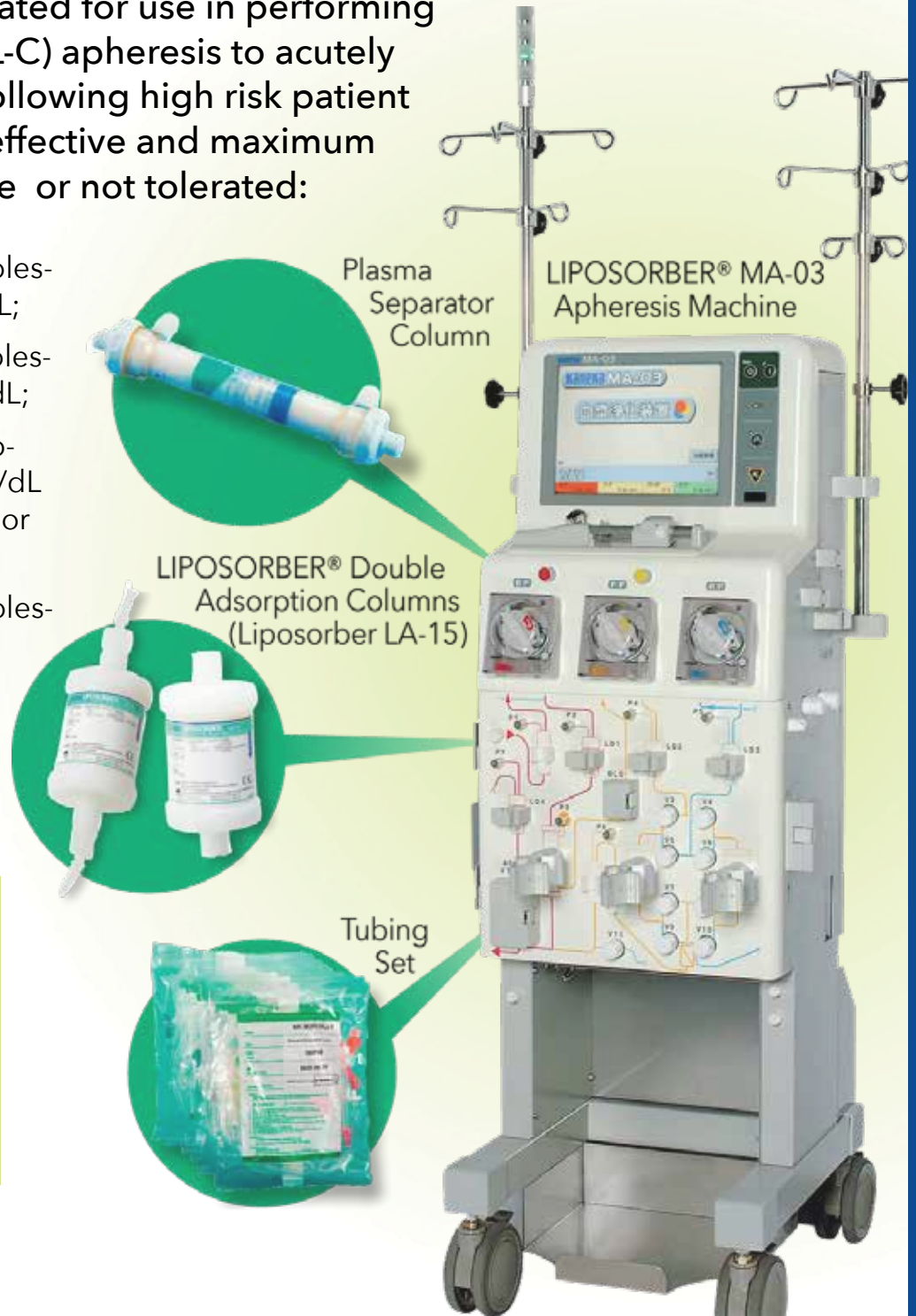
The LIPOSORBER LA-15 System is indicated for use in performing low density lipoprotein cholesterol (LDL-C) apheresis to acutely remove LDL-C from the plasma of the following high risk patient populations for whom diet has been ineffective and maximum drug therapy has been either ineffective or not tolerated:

Group A. Clinically diagnosed Familial Hypercholesterolemic Homozygotes with LDL-C > 500 mg/dL;

Group B. Clinically diagnosed Familial Hypercholesterolemic Heterozygotes with LDL-C ≥ 300 mg/dL;

Group C. Clinically diagnosed Familial Hypercholesterolemic Heterozygotes with LDL-C ≥ 70 mg/dL and either documented coronary artery disease or documented peripheral artery disease; and

Group D. Clinically diagnosed Familial Hypercholesterolemic Heterozygotes with lipoprotein(a) [Lp(a)] ≥60 mg/dL (or 130 nmol/L) and either documented coronary artery disease or documented peripheral artery disease.

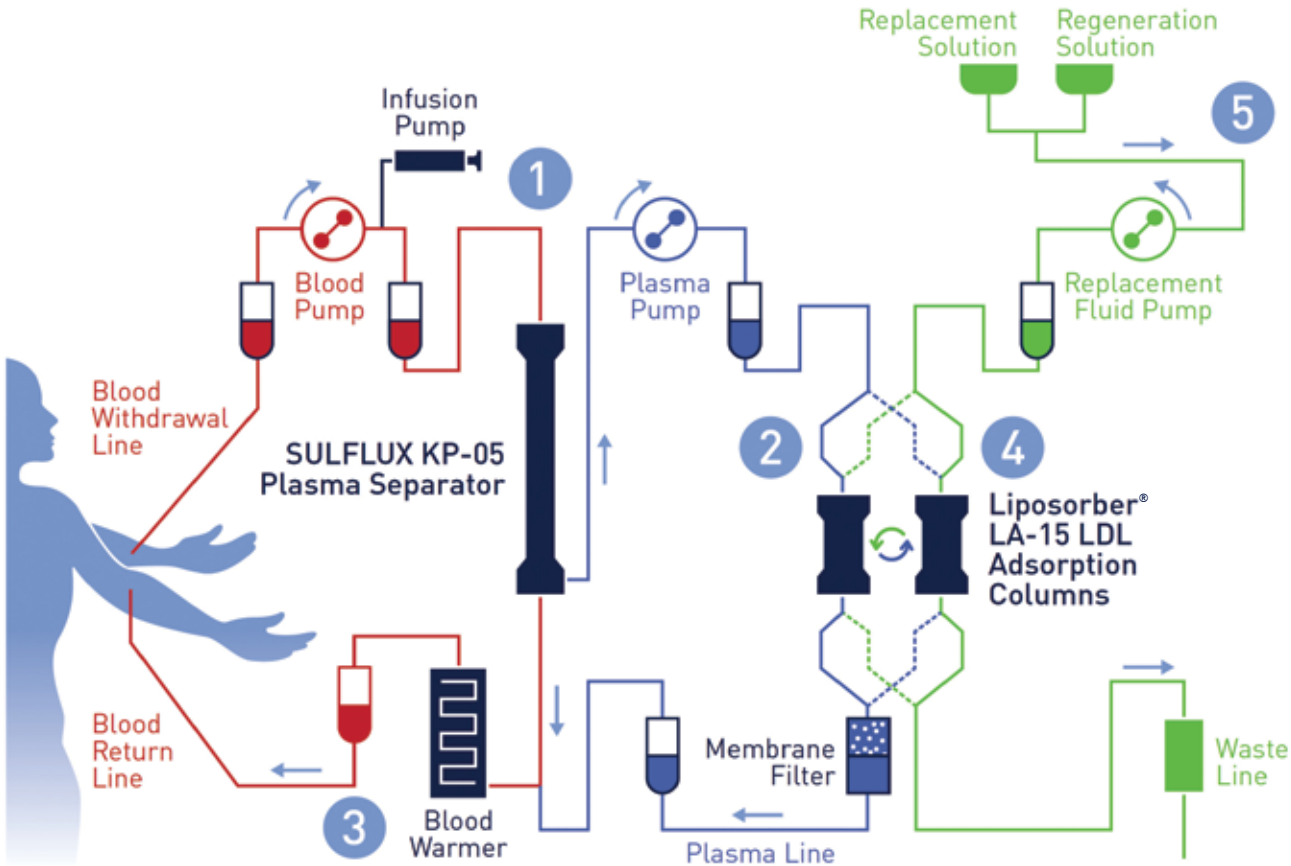


TREATMENT FREQUENCY

Patient Levels	Regimen
LDL-C ≥300mg/dL	1 Session Every Week
LDL-C 70-200 mg/dL	1 Session Every 2 Weeks
Lp(a) ≥60mg/dL (130 nmol/L)	1 Session Every 2 Weeks

HOW LIPOSORBER® WORKS[1]

Each treatment lasts 2-4 hours on average.



Blood Line:
Takes blood out, puts blood back in

Plasma Line:
Moves separated plasma and removes LDL, Lp(a) and VLDL using Liposorber LDL Adsorption Columns

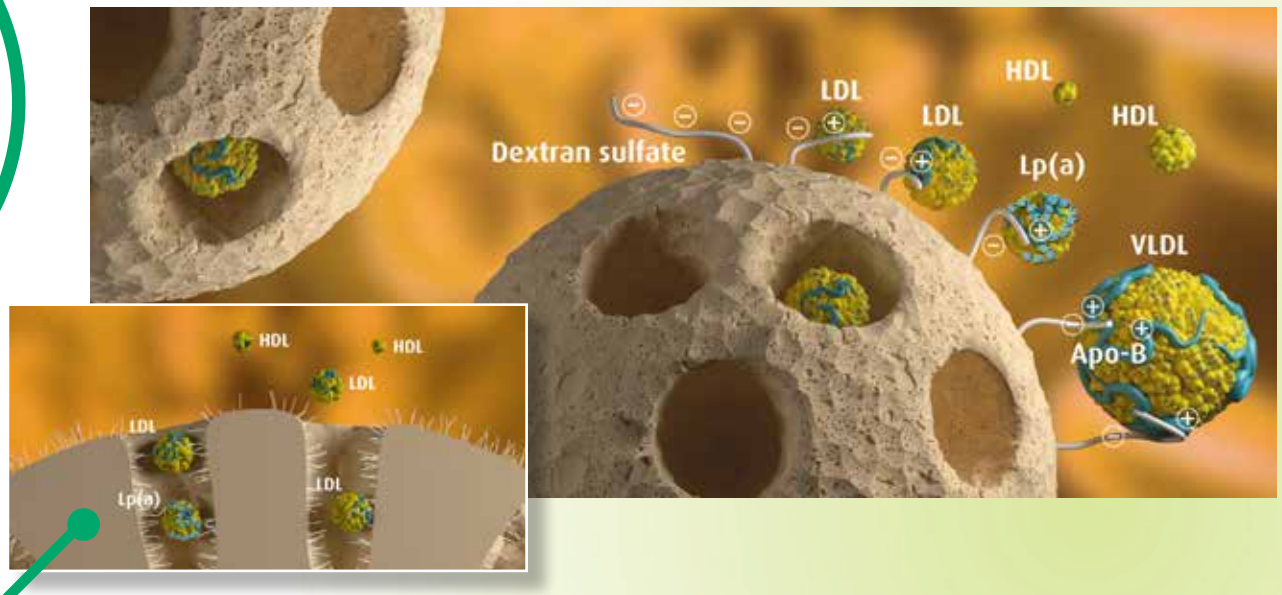
Regeneration Line:
Prepares primary and secondary adsorption columns for the next cycle and eliminates waste to allow for continuous treatment

1. Blood is withdrawn and goes through the plasma separator.
2. Plasma passes through the LIPOSORBER Adsorption Column, selectively removing LDL, Lp(a) and VLDL.
3. Plasma is recombined with blood cells and returns to the blood warmer, then is returned to the patient.
4. After the first cycle is complete, the computer-regulated machine automatically switches the plasma flow from the primary LIPOSORBER Adsorption Column to the secondary column after 600 ml of blood has been processed.
5. The primary column is regenerated, eluting waste and re-primed to be ready for the next adsorption cycle.

SELECTIVITY FEATURE[1]

LIPOSORBER® selectively removes LDL-C, Lp(a), and VLDL

The Principle of the LIPOSORBER® LA-15



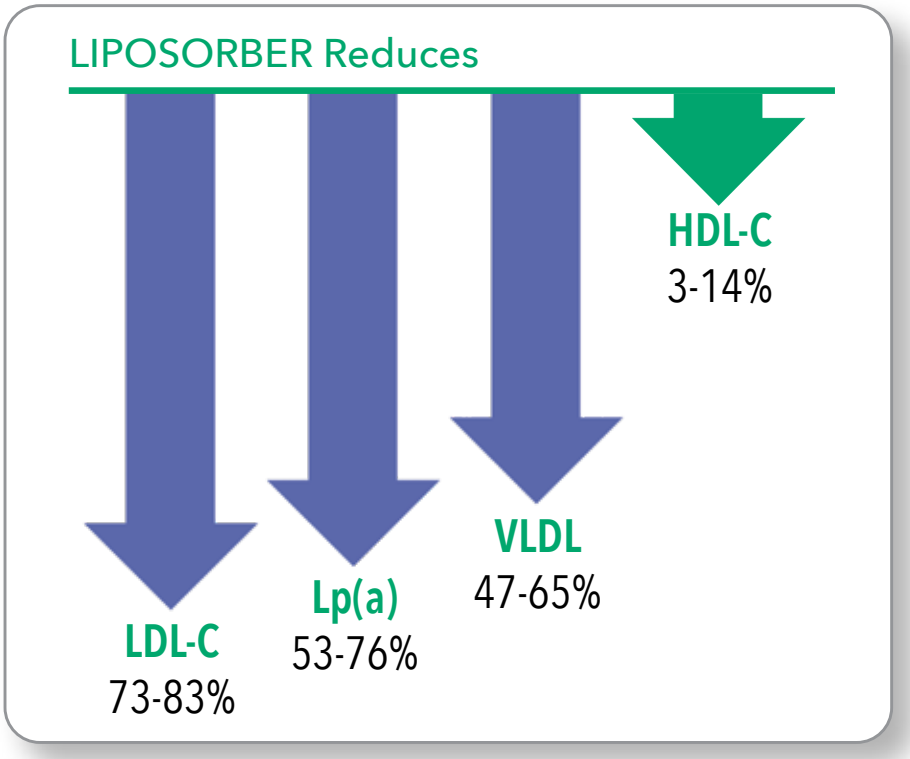
The adsorbent columns are made of dextran sulfate cellulose beads, which provides specific binding to Apo-B containing lipoproteins such as **LDL-C, Lp(a), and VLDL.**

These three are **selectively removed** by the electro-static interaction between the negatively charged dextran sulfate and the positively charged moiety of Apo-B. Unlike therapeutic plasma exchange (TPE), LIPOSORBER minimally affects other blood components.

LIPOSORBER® EFFICACY PROFILE

LIPOSORBER Acutely Reduces Atherogenic Lipoproteins

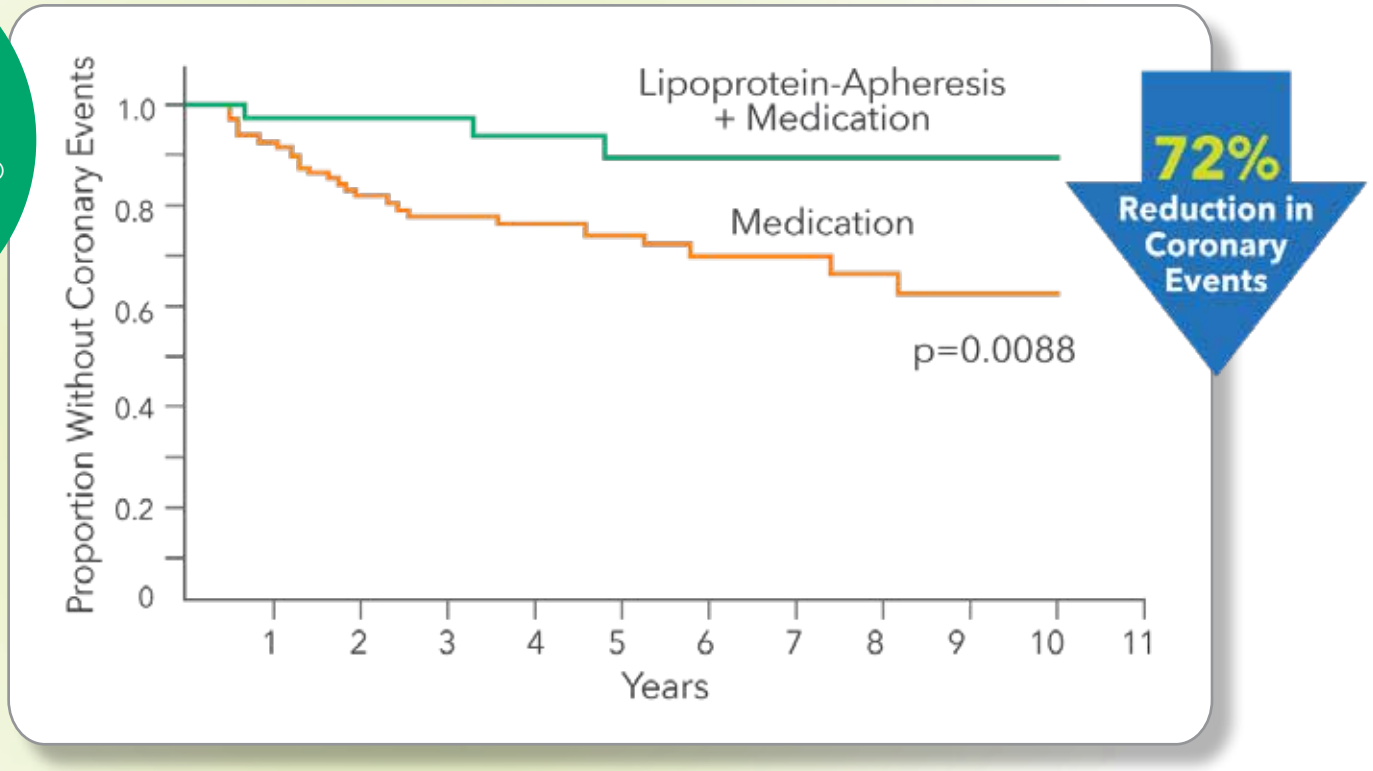
The system effectively removes harmful atherogenic lipoproteins such as Apo-B containing lipoprotein (Lp(a), LDL-C, and VLDL) associated with serious cardiovascular disease and vascular complications in familial hyper-cholesterolemia patients.[5]



LIPOSORBER® CLINICAL OUTCOMES

Long-term effectiveness of low-density lipoprotein-apheresis (LA) on coronary heart disease in familial hypercholesterolemia (FH) was studied. Investigators examined long-term efficacy and safety of LA in heterozygotes familial hypercholesterolemia (HeFH) patients with history of CHD. LA was shown to be an effective & well tolerated treatment for HeFH: 58% acute reduction in LDL-C levels and 72% reduction in total coronary events.[7]

Long Term Efficacy of **LIPOSORBER®**



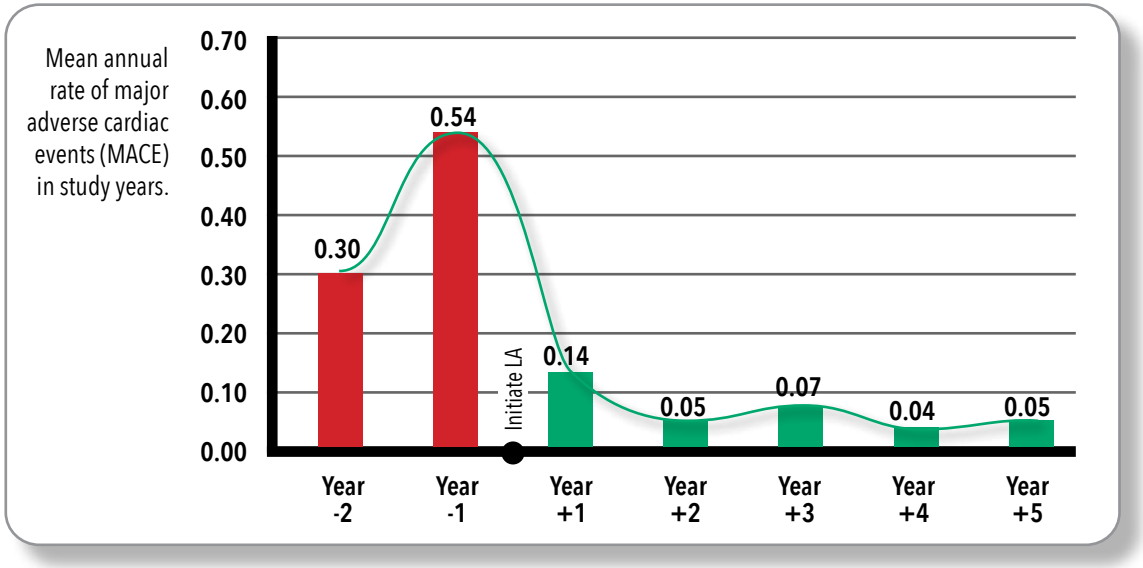
Pro(a)–LIFE STUDY[8,9]

LIPOPROTEIN-APHERESIS & Lp(a) Patients

The aim of Pro(a)-Life was to assess the effectiveness of lipid-apheresis in high-risk patients with elevated Lp(a) >60 mg/dL and progressive cardiovascular disease. The study evaluated the event rates for major adverse coronary events (MACE) and adverse cardiac or vascular events (ACVE) **in 170 patients** with prospective 5 years of follow-up, and demonstrated:

- **After 2 years, Lp(a) was significantly reduced by 68.8± 9.5% and LDL-C by 67.2±10.2% (p<0.0001).**
- **MACE was reduced annually by 78% (p<0.0001) NNT=3 after 1 year and reduced 85% annually after 5 years from initiating LA.**

Clinical Course of Patients with Lipoprotein(a)-Hyperlipoproteinemia and Progressive Cardiovascular Disease[8]



LA is an effective & well tolerated therapeutic tool that significantly reduces cardiovascular events in FH patients who have progressive cardiovascular diseases with elevated Lp(a) ≥60mg/dL.

LIPOSORBER® is indicated in FH patients with cardiovascular disease and Lp(a) ≥60 mg/dL.

LIPOSORBER®:
VASCULAR BENEFITS ASSOCIATED WITH LIPID LOWERING

LACMART Study:[10]

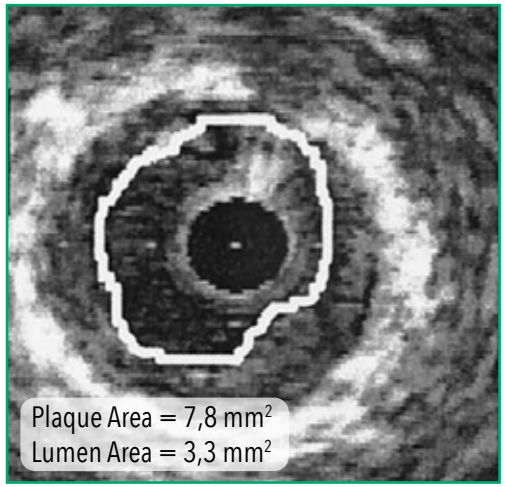
The Low Density **L**ipoprotein-**A**pheresis **C**oronary **M**orphology **A**nd **R**eserve **T**rial

Aggressive lipid lowering therapy by using LIPOSORBER® with maximum tolerable drug therapies **stops progression of coronary atherosclerosis in FH patients.**

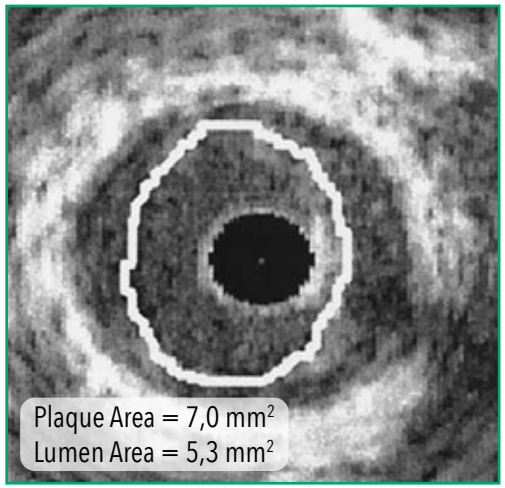
Achieve the recommended **THERAPEUTIC TARGET**

IVUS Imaging

Baseline LAD #8



Follow-Up LAD #8



Matzusaki et al. (LACMART) and Tatami et al demonstrated that an aggressive lipid-lowering therapy by applying lipoprotein-apheresis in combination with lipid-lowering drugs induced (coronary) atherosclerotic plaque regression in FH patients.*

Change in Parameters from Coronary Angiogram and IVUS

	LDL-A Group			Medication Group			
	Baseline	Follow-Up	Net Change	Baseline	Follow-Up	Net Change	p Value*
MLD (mm)	1.99 ± 0.73	2.11 ± 0.81	0.12	2.24 ± 0.89	2.16 ± 0.84	−0.08	0.008
Plaque area (mm^2)	8.45 ± 4.22	7.76 ± 4.34	−0.69	7.19 ± 2.88	8.08 ± 3.14	0.88	0.017
Lumen area (mm^2)	9.84 ± 5.43	9.87 ± 5.55	0.03	9.13 ± 4.33	8.63 ± 3.18	−0.51	0.52
Vessel area (mm^2)	18.29 ± 8.84	17.63 ± 9.05	−0.66	16.4 ± 5.63	19.0 ± 4.36	0.3	0.26

Data presented are mean value SD. *Data obtained from two-way repeated-measures analysis of variance. IVUS intravascular ultrasound; LDL-A low density lipoprotein-apheresis; MLD minimal lumen diameter.

SAFETY PROFILE[1]

LIPOSORBER® LA-15 received FDA approval in 1996. It has been in worldwide use since 1986 with more than 600,000 LIPOSORBER® treatments performed on over 6,000 patients. Typically, the adverse events associated with LIPOSORBER® treatment are those observed in any procedure involving the circulation of blood outside the body.

FDA Approved since 1996.

Performed on over 6,000 patients.

ADVERSE EVENTS

The most common adverse events are hypotension (0.8%), nausea/vomiting (0.5%), and flushing/blotching (0.4%). Other adverse reactions include angina/chest pain, shortness of breath fainting, light-headedness and anemia.

CONTRAINDICATION

Angiotensin converting enzyme [ACEI(s)] inhibitors are contraindicated with LIPOSORBER due to possible bradykinin reaction. ACE Is should be replaced with angiotensin II receptor blockers (ARBs) or any other antihypertensive agent – as determined by the prescribing physician.

For complete safety information, including adverse events and contraindications, please refer to the Instructions For Use Manual: **bit.ly/liposorbersafety**

HOW LIPOSORBER® CAN BENEFIT YOUR PRACTICE

Use LIPOSORBER to attain the recommended therapeutic target for your familial hypercholesterolemia patients with elevated Lp(a).

Offer a comprehensive lipid-lowering treatment line to your practice.

Practice benefits include:

- Comprehensive lipid lowering service
- Insurance coverage by Medicare and most commercial insurers
- User-friendly automated continuous-flow system
- Therapy can be performed in hospital outpatient or physician office-based setting

Comprehensive support for starting a program includes:

- Clinical staff training*
- Nurse hot-line support
- Technical support
- Educational awareness initiatives, seminars, and grand rounds

LIPOSORBER Provides Hope When Drug Therapy Fails™

Consider LIPOSORBER for your FH patients with elevated Lp(a) levels when drug therapies (statins, PCSK9is) fail to achieve the recommended therapeutic targets per established clinical guidelines.

*Personnel must be qualified to perform extracorporeal procedures and complete required training program.

If you're interested in **starting a lipoprotein-apheresis program** in your area or need help referring a patient for treatment, please contact us at **800-526-3522** or info@liposorber.com

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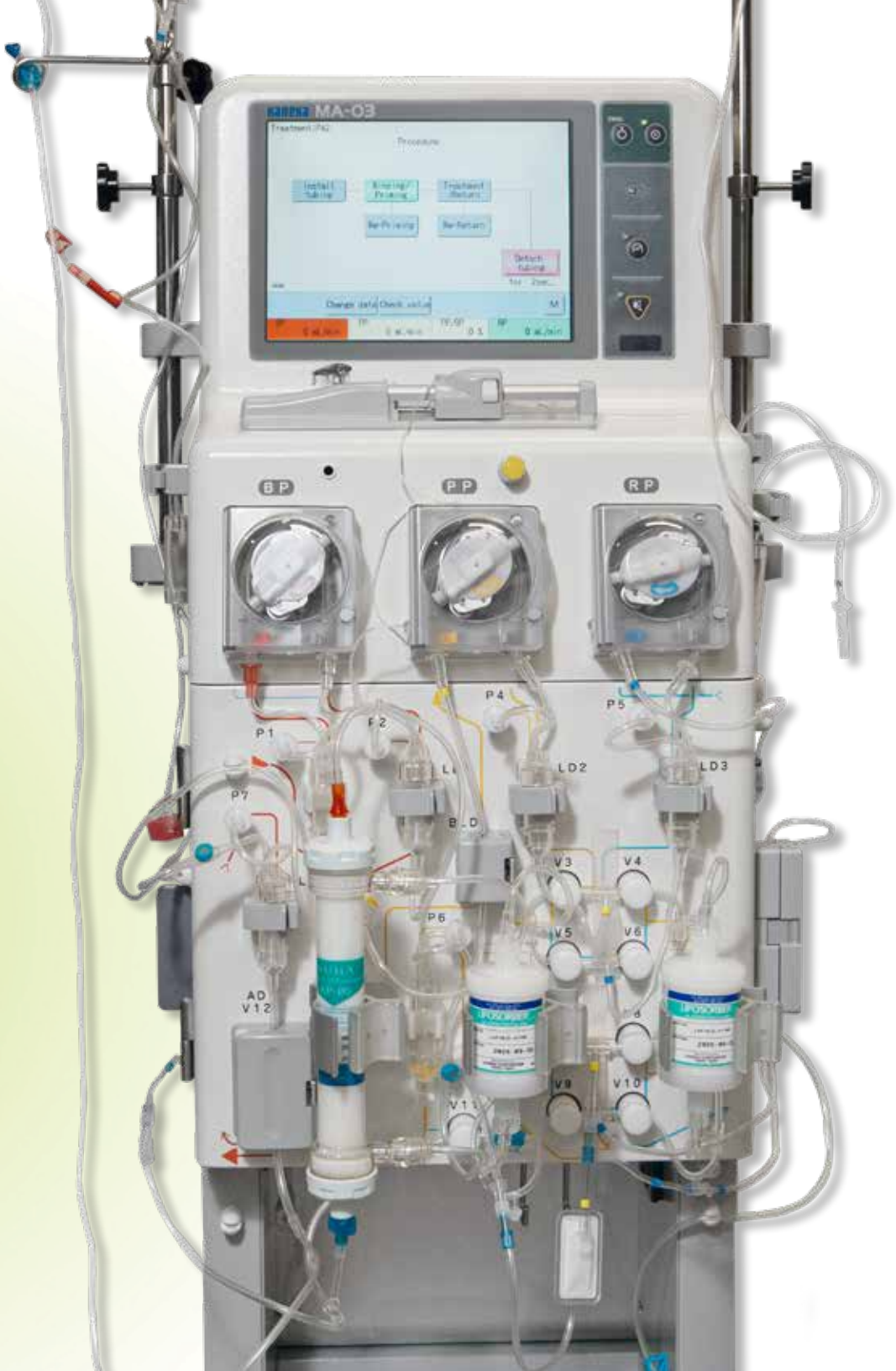
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