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LIPOSORBER®

Provides Hope When Drug Therapy Fails™

For Your Pediatric and Adult Primary FSGS Patients

kaneka



LIPOSORBER[®]

An innovative therapeutic approach for pediatric and adult primary FSGS patients when:

- standard therapies have failed or are not well-tolerated and patient's $GFR \geq 60 \text{ ml/min/1.73m}^2$
- FSGS recurs after renal transplantation

Enabled nearly **50%** of steroid-resistant primary FSGS patients to attain complete or partial remission*

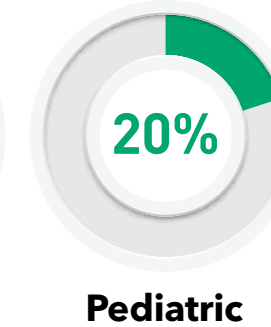
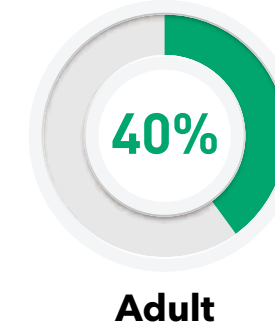


WHAT IS FSGS?

- **Focal Segmental Glomerulosclerosis (FSGS) is a progressive kidney disease characterized by a histopathologic pattern of injury** caused by various mechanisms with **podocyte injury** as the essential common pathology.¹
- Podocytes are highly susceptible to damage when there is lipid overload.²
- Lipids and lipid-related enzymes have a major role in modulating podocyte function in glomerular disorders.²

PREVALENCE OF FSGS

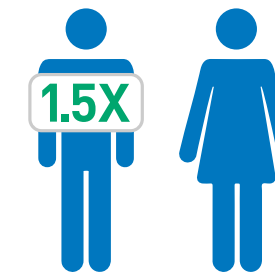
FSGS is currently the most common primary glomerular disease causing kidney failure in the United States and the leading cause of kidney disease worldwide.¹



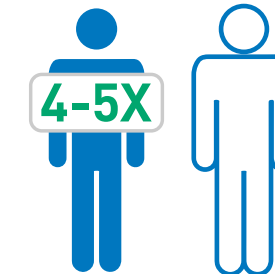
FSGS is estimated to be responsible for 40% of adult nephrotic syndromes and 20% of pediatric nephrotic syndromes.²



More than 5,400 FSGS patients are diagnosed in the U.S. annually.⁹



In adults, FSGS is more common in males, with an approximate 1.5-fold increased incidence compared to females.³



The incidence of FSGS is around 4 times higher in black patients compared to white patients.²²

*The duration of the study was 2 years.

PREVALENCE OF RECURRENT FSGS IN KIDNEY TRANSPLANT

- Today, approximately 20,000 people in the US live with end stage kidney disease (ESKD) due to FSGS.⁹
- About 1,000 FSGS patients a year receive kidney transplants.⁹
- Within hours to weeks after kidney transplantation, FSGS recurs in approximately 30-40% of adults and up to 50% in children.⁹

Adults¹⁷



FSGS recurrence occurs in one-third of kidney transplant patients within an average of 1.5 months.

5X

Risk of kidney transplant failure increases almost five-fold after recurrent FSGS.



The median time from recurrence to graft loss is within 7 months.¹⁸

Pediatric¹⁸



Recurrence of non-genetic FSGS has a reported incidence of up to 50% in post-kidney transplant.



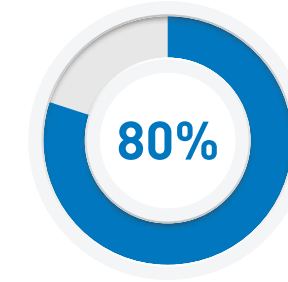
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Almost one-half of patients lose their transplanted kidney within a period of 5 years after FSGS recurrence.

Recurrence of FSGS is associated with a reduction in graft survival.

This is especially true for patients who have not responded to treatment.¹⁷

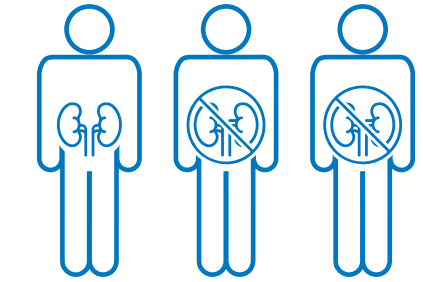
GAPS IN THERAPY



About 80% of primary FSGS patients are resistant to steroids.⁵



A large proportion of patients with steroid-resistant FSGS progress to ESKD.⁶



Calcineurin inhibitors achieved complete remission in only one-third of patients.⁷



Consider LIPOSORBER® for your primary FSGS patients who have failed to achieve complete or partial remission with standard treatment.

ABOUT LIPOSORBER®

LIPOSORBER Provides Hope When Drug Therapy Fails™

Indications For Use:

The LIPOSORBER LA-15 System is indicated for use in the treatment of adult and pediatric patients with nephrotic syndrome associated with primary focal segmental glomerulosclerosis when:

- standard treatment options, including corticosteroids and/or calcineurin inhibitor treatments, are unsuccessful or not well tolerated and the patient's glomerular filtration rate (GFR) ≥ 60 ml/min/1.73 m² -or-
- the patient is post renal transplantation.⁸

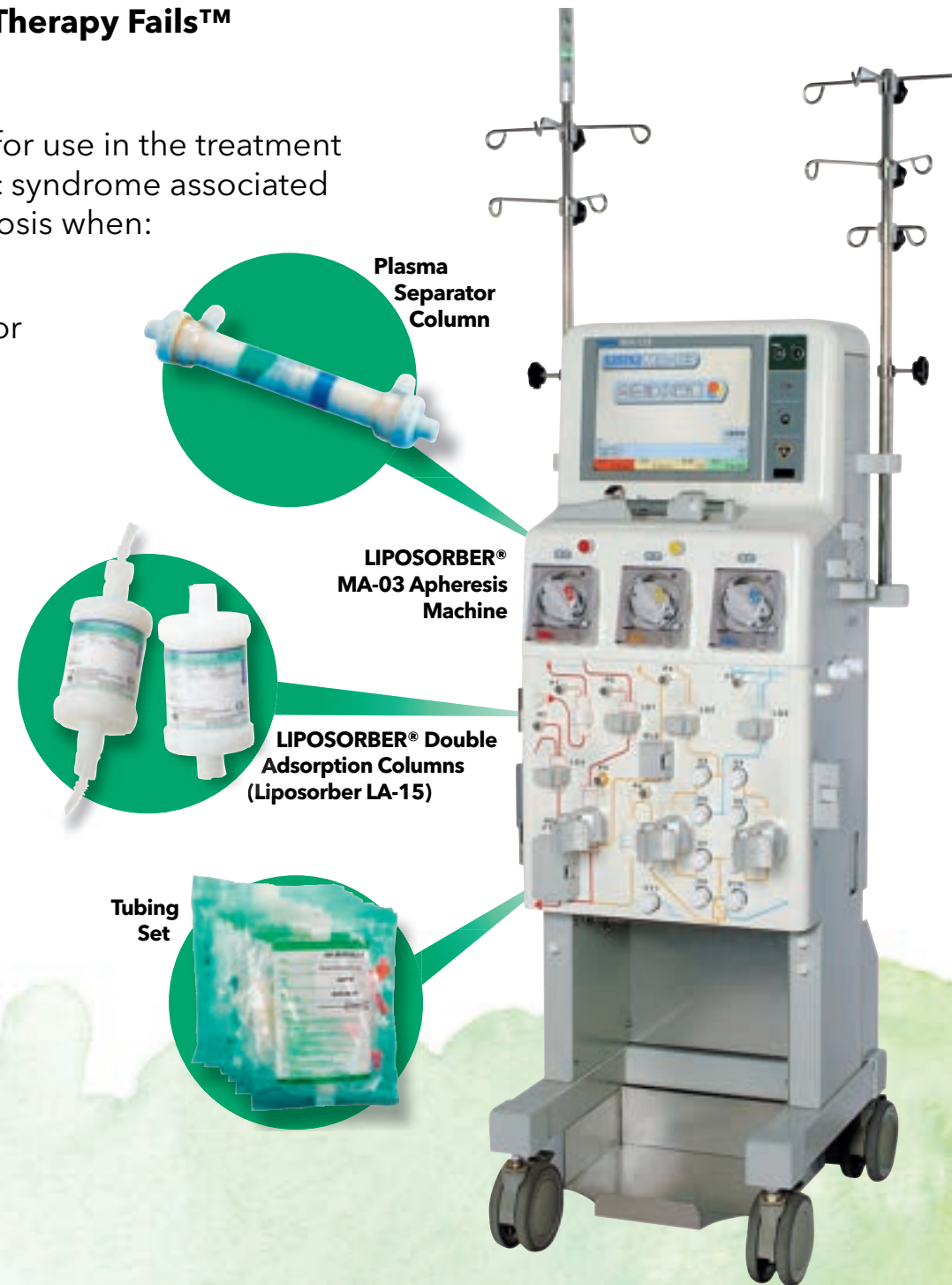
The only FDA authorized Humanitarian Use Device (HUD) for the treatment of patients with nephrotic syndrome associated with primary FSGS.⁸

Rx Only

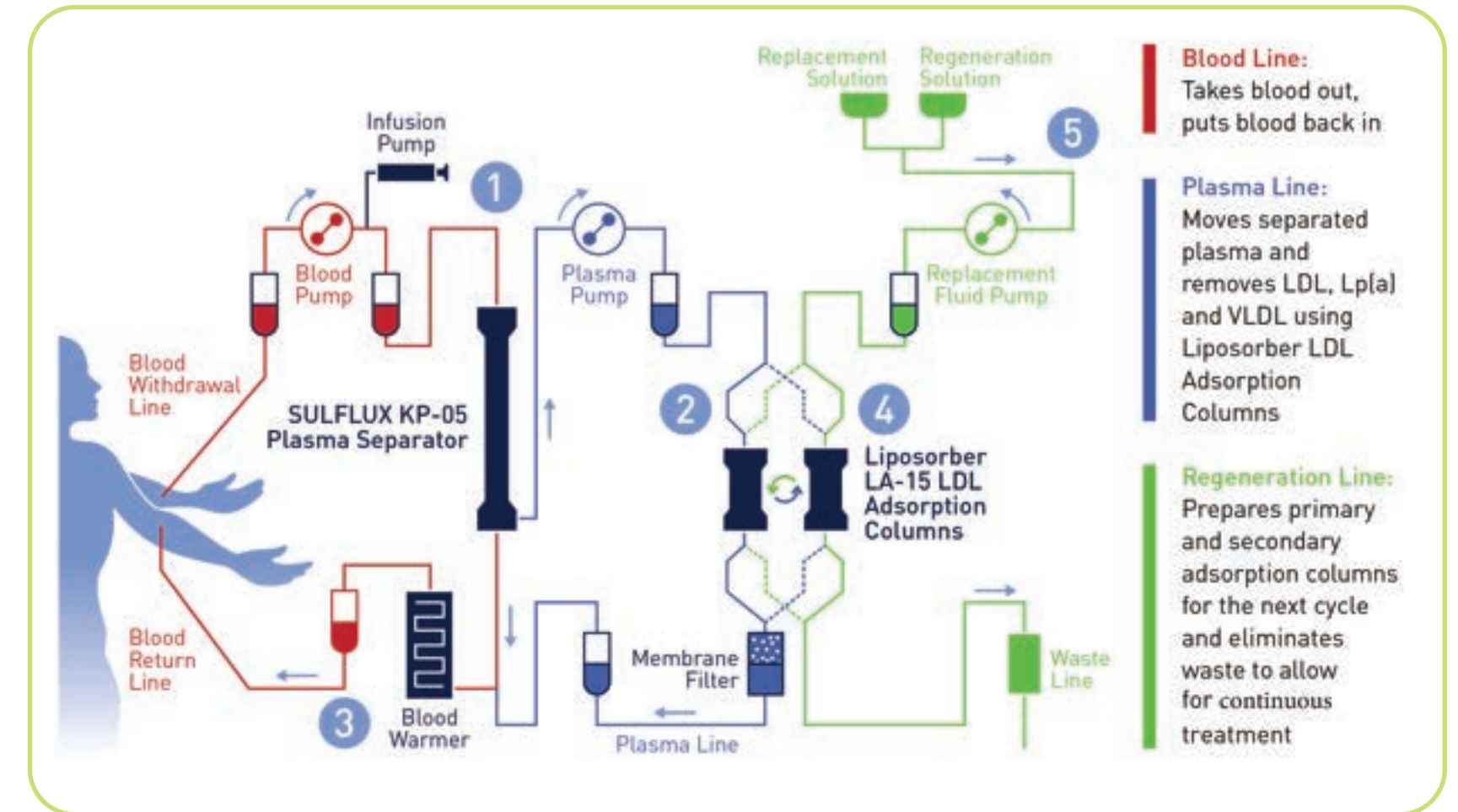
Treatment Frequency:⁸

2x a week for **3** weeks followed by **1x** a week for **6** weeks

Each treatment lasts **2-4 hours** on average.



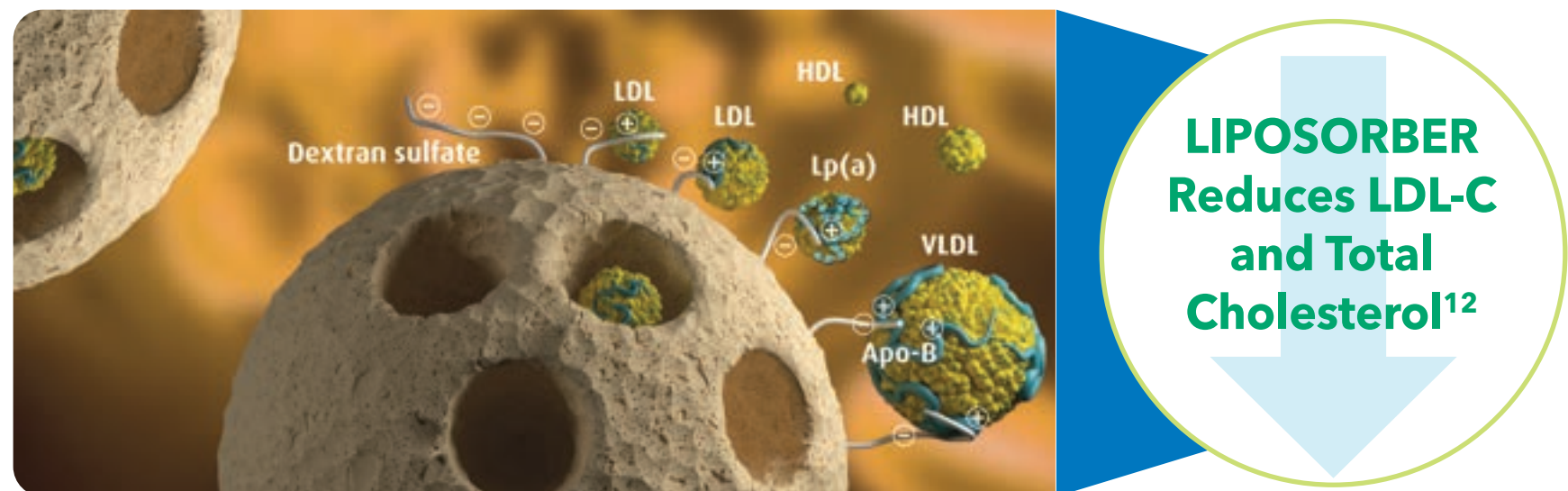
HOW LIPOSORBER® LA-15 WORKS



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 passes through the blood warmer, then is returned to the patient.
4. Once the primary LIPOSORBER Adsorption Column processes 600 ml of blood, the computer-regulated machine automatically switches the plasma flow to the secondary column.
5. The primary column is regenerated, eluting waste and re-primed to be ready for the next cycle of adsorption.

LIPOSORBER® SELECTIVITY FEATURE

The adsorbent columns are made up of **dextran sulfate cellulose beads**, which provide specific binding to certain lipids such as LDL-C, Lp(a), and VLDL.

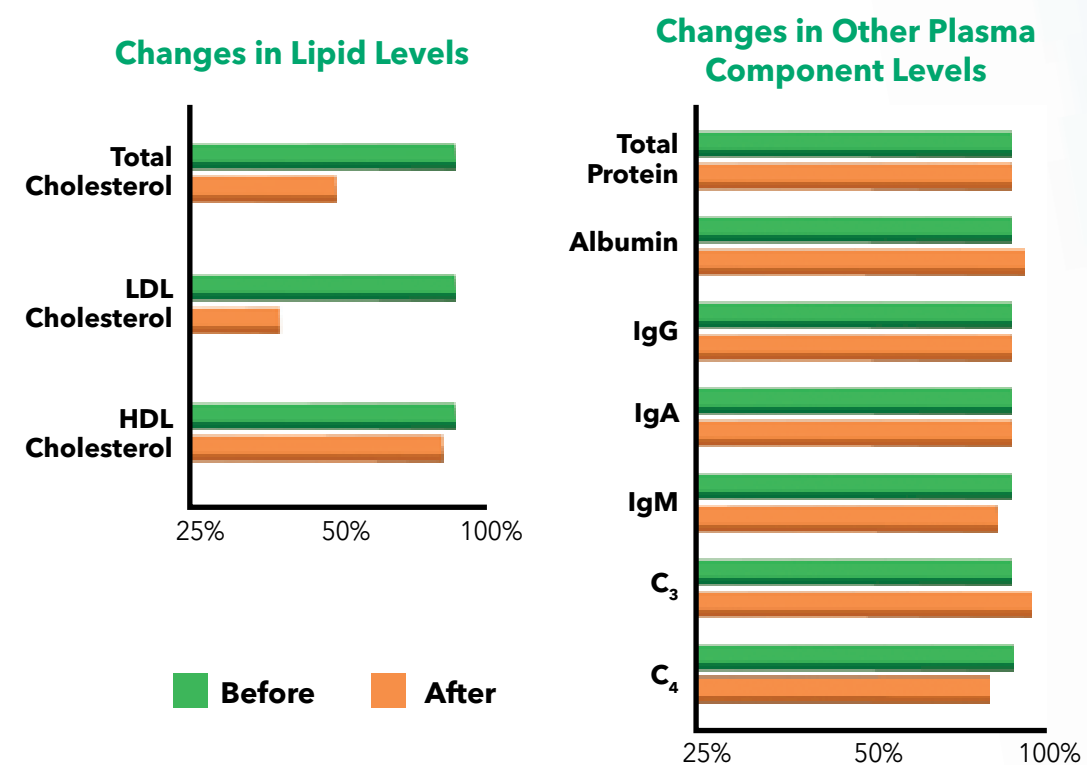


By effectively decreasing total cholesterol and LDL-C, **LIPOSORBER promotes:**

- ➔ **Direct podocytes effects:**
 - Decreases lipotoxicity to the glomeruli¹⁹
- ➔ **Immunologic effects:**
 - Improves response to corticosteroid and cyclosporine¹¹
- ➔ **Anti-inflammatory effects (e.g., IFN- γ and IL-12):**
 - Removal of pro-inflammatory factors, such as cytokines and chemokines¹⁰

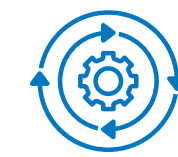
SELECTIVITY AND EFFICACY OF LIPOSORBER®

Unlike therapeutic plasma exchange (TPE), **LIPOSORBER minimally affects other blood components.**¹⁰



Remission of proteinuria

LIPOSORBER LA-15 therapy has induced complete or partial remission of proteinuria in up to 50% of patients with both drug-resistant and recurrent FSGS.¹²



Improved responsiveness

Lipoprotein-apheresis (LA) therapy improves corticosteroid and cyclosporine action and responsiveness in patients with drug resistance, which is likely due to the restoration of cellular uptake and the inhibition of drug efflux.¹¹

LIPOSORBER®: EFFICACY WITH PRIMARY FSGS PATIENTS

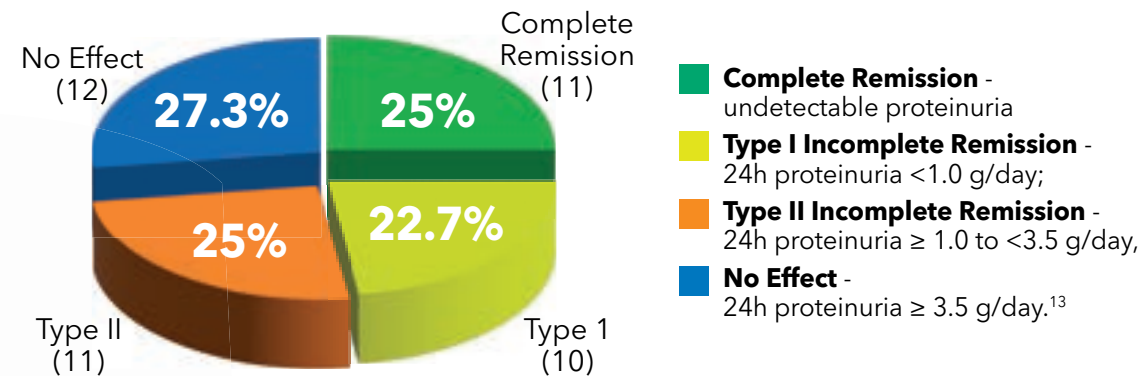
Treatment-resistant FSGS and prior therapeutic failure

In the **POLARIS study**, regardless of the type of primary disease, lipoprotein-apheresis (LA) rapidly improved proteinuria in nearly half of the patients with nephrotic syndrome (NS) who failed to respond to standard therapies.¹²

Short-Term Outcomes:

- Increase in response to the corticosteroids.¹¹
- Significant decrease in proteinuria as soon as 1 month after the last apheresis.¹²
- Improvement in renal function in drug resistant FSGS.¹⁴
- No significant adverse reactions/events during or after LA therapy were reported.¹³

Long-Term Outcome of Steroid-Resistant FSGS Patients¹²



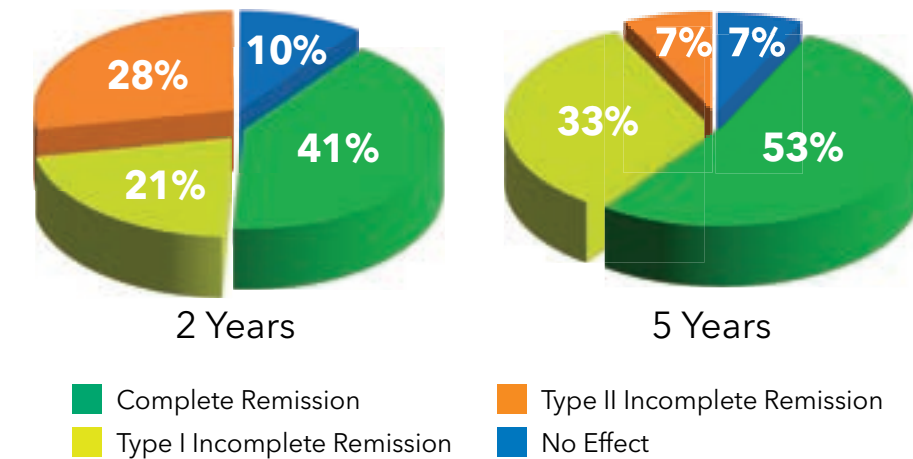
Enabled nearly 50% of steroid-resistant FSGS patients to attain complete or partial remission.*¹²

*The duration of the study was 2 years.

LIPOSORBER®: EFFICACY WITH RECURRENT FSGS, INCLUDING POST-KIDNEY TRANSPLANT PATIENTS

Retrospective study of 41 patients with refractory FSGS including 7 patients who developed recurrent FSGS after renal transplantation and had not responded to plasma exchange therapy.¹⁵

Prognosis at 2 and 5 Years After Treating with Lipoprotein-Apheresis (LA)¹⁵



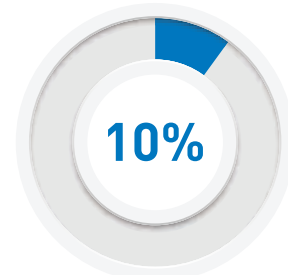
Study Outcomes:¹⁵

- At one month, all patients experienced reductions in urinary protein to creatinine ratios.
- 62% of patients achieved complete or partial remission within 2 years.
- 86% of patients achieved complete or partial remission within 5 years.

LIPOSORBER®: EFFICACY WITH RECURRENT FSGS IN POST-KIDNEY TRANSPLANT PEDIATRIC PATIENTS¹⁶

Lipoprotein-Apheresis (LA) induced remission of focal segmental glomerulosclerosis (FSGS) recurrence in pediatric renal transplant recipients, in combination with pulse corticosteroid.

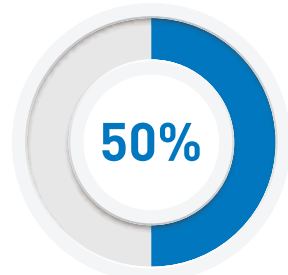
FSGS in pediatric patients is typically difficult to treat:



10%

ESKD

Will progress to end stage renal disease (ESKD).



50%

FSGS Recurrence

FSGS can occur in up to 50% of renal allografts following kidney transplantation.



100%

Future Transplants

With FSGS recurrence, nearly all pediatric patients will experience recurrence in subsequent kidney transplants.



Four pediatric centers in the US and UK employed a protocol using LA and pulse solumedrol in **seven patients** to treat recurrent FSGS after kidney transplantation.

All patients included in the series demonstrated immediate, or early, recurrence of FSGS, which clinically presented as nephrotic-range proteinuria within hours to days after implantation of the kidney.

LIPOSORBER®: EFFICACY WITH RECURRENT FSGS IN POST-KIDNEY TRANSPLANT PEDIATRIC PATIENTS (continued)

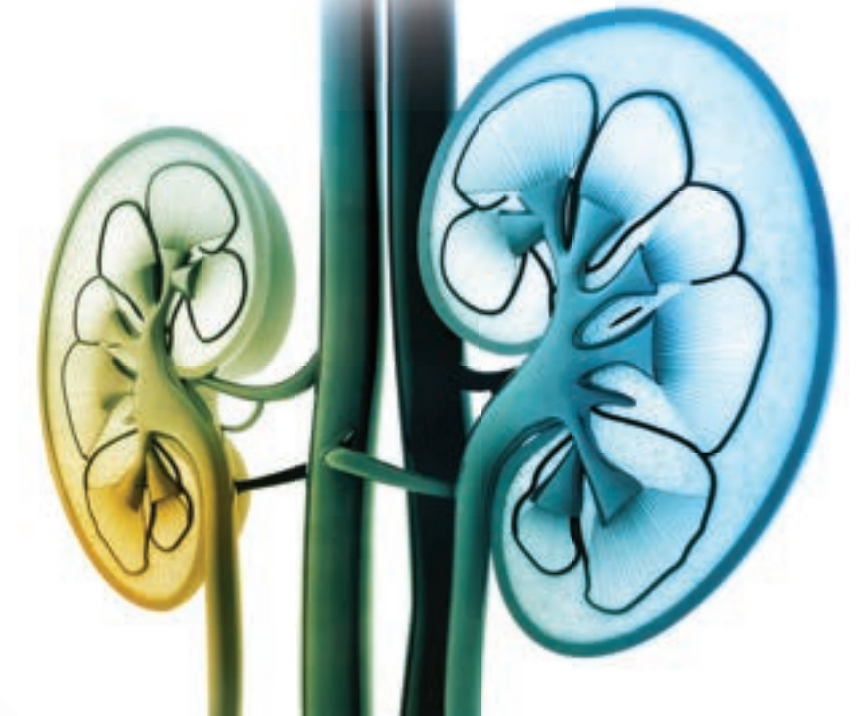


100%

After being treated with LIPOSORBER*:

100% of patients experienced reductions in urinary protein to creatinine ratios. All patients also demonstrated improvements in their estimated GFRs at their most recent follow-up since LA discontinuation. **All seven patients experienced complete or partial remission.**¹⁶

LIPOSORBER therapy has the potential to preserve the graft and prevent restarting of dialysis.¹⁶



*treatment duration range 9-22 weeks

SAFETY PROFILE



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, lightheadedness and anemia.¹

*Please see liposorber.com for a full list of adverse events.



CONTRAINDICATION

Angiotensin converting enzyme [ACEI(s)] inhibitors are contraindicated with LIPOSORBER® due to possible bradykinin reaction. ACEI(s) should be replaced with angiotensin II receptor blockers (ARBs) or any other antihypertensive agent as determined by the prescribing physician.⁸

Additional Notes:

The safety of Lipoprotein-apheresis using the LIPOSORBER LA-15 System in FSGS has not been established for patients less than 21 kg in body weight or patients less than 5 years of age.

For additional contraindications and complete safety information, visit: bit.ly/liposorberifu



HOW LIPOSORBER® CAN BENEFIT YOUR PRACTICE

Offer a comprehensive treatment line for your primary FSGS patients.

Practice benefits include:

- Reimbursement consultation
- 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 primary FSGS patients who have failed to achieve complete or partial remission with standard therapies.

If you are 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

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