Torgow Family
Recurrent Focal Segmental Glomerulosclerosis Conference

Hyatt Regency Washington on Capitol Hill
400 New Jersey Avenue, NW
Washington, DC 20001
And Via Zoom Virtual Platform

December 9, 2024

EXECUTIVE SUMMARY

Background

The Recurrent Focal Segmental Glomerulosclerosis (rFSGS) Conference was held on December 9, 2024, and organized by Simone Sanna-Cherchi, M.D., Columbia University Irving Medical Center and Gary Torgow and Elie Torgow from the Sterling Group. Approximately 175 participants attended the event.

Focal segmental glomerulosclerosis (FSGS) is a rare kidney disease that results in kidney failure and, in most cases, requires dialysis or transplantation. rFSGS represents an even rarer subset of disease and is characterized by the recurrence of FSGS within the first few weeks post-transplant. rFSGS currently has no cure. Obtaining adequate funding support for research or drug development for rFSGS through public and private funding structures is very difficult. This rare orphan disease significantly affects the lives of patients and their families, presenting an unmet need for allocating funding to help understand the causes of rFSGS and find a cure. This conference brings together a team of dedicated doctors and scientists and patients' family members who are motivated to contribute time and effort to finding a cure—but financial assistance is needed to make effective treatment a reality.

The objectives of the conference were to—

- Convene a diverse group comprising rFSGS patients and their families, doctors, researchers, political leaders, and funders.
- Gather and share patient stories and experiences.
- Meet and hear from doctors and researchers about rFSGS and new opportunities for collaboration and investigation.
- Identify and encourage political support, research grants, and other funding mechanisms and contributions toward the science and cure of rFSGS.
- Identify people in the medical and scientific fields who can further assist in the research advancements toward a cure for rFSGS.
- Engage the U.S Food and Drug Administration, National Institutes of Health, and any other agencies that could help foster and support research and development for rFSGS.

Overview and Highlights

The conference opened with remarks from Dr. Sanna-Cherchi. He shared information about the Genetic Studies of Constitutional Disorders research study and encouraged patients to sign up. The morning session consisted of patient stories, including an introductory video with interviews of patients across the country with rFSGS, and two sessions of stories shared by patients and family members of patients. The

afternoon session included encouraging statements from politicians and updates on scientific advancements from researchers and physicians. The conference included the exchange of preclinical and clinical information, patient perspectives, political and community engagement, and a keynote presentation.

rFSGS: The Challenge, the Solution

Clinicians addressed the significant challenges posed by rFSGS, emphasizing the urgent need for innovative solutions and noting the difficult journey patients endure with multiple kidney transplants and repeated cycles of plasmapheresis. FSGS recurrence occurs in approximately 17 percent of adult and 40 percent of pediatric kidney transplant recipients with FSGS.

Research Gaps and Opportunities

- Increasing research efforts and fostering collaboration are important for developing sustainable solutions for rFSGS; policymakers were encouraged to focus on rare diseases.
- Patient-centric clinical trials tailored to the unique needs of rFSGS patients are lacking.

A Multifaceted Approach to Build an Innovative Therapeutic Landscape for rFSGS

The importance of fostering a strong community within the rFSGS population was discussed throughout the conference. Given that the risk of recurrence is significantly higher after a second kidney transplant, collaboration among patients, caregivers, scientists, and policymakers is essential to driving progress in rFSGS research. FSGS is a complex disease and understanding both the timing and patterns of FSGS recurrence post-transplantation are key to advancing treatment. Drawing on NIH's legacy of biomedical research, continued investment in studies is vital to uncovering the mechanisms behind recurrence.

Research Gaps and Opportunities

- The mechanisms driving rFSGS after transplantation are not well known.
- Patient-centered research and improved biomarkers for early detection are crucial for advancing research on rFSGS therapies.
- Collaborative networks are essential to improving outcomes for both pediatric and adult patients living with rFSGS.
- Funding mechanisms could be expanded for small investigator-led and feasibility clinical trials, leveraging the National Institute of Diabetes and Digestive and Kidney Diseases multicenter research resources and focusing on ancillary studies and data repositories to support next-generation scientists.
- An interesting area of research could be to identify disease-specific changes in native versus transplanted kidneys.

Patients' Perspectives

The conference emphasized the critical role of patient perspectives, with two dedicated sessions inviting patients and families to share their experiences and engage with the community. Several patients shared their stories, which was followed by a discussion.

- One patient, diagnosed with FSGS at age 3, received a kidney transplant at age 12 and experienced recurrence of FSGS 24 hours after the transplant was performed; however, subsequent treatment with abatacept led to 8 years of remission. Now in an M.D./Ph.D. program at the University of Miami, this patient draws on his experience to inspire patient involvement in research and encourage others to pursue fulfilling lives beyond their diagnoses.

- A spouse of a patient with rFSGS shared that her husband led an active life before his diagnosis but has adapted to his new lifestyle. Their family is grateful for the small moments, such as when her husband feels well enough to cook a meal for their family.

- A parent of one patient shared how her family felt blindsided when her daughter was diagnosed with nephrotic syndrome during her freshman year of high school, going into kidney failure less than 2 years later. Despite experiencing recurrence after her kidney transplant, her daughter has been doing her best to live life to the fullest.

- The National Kidney Registry (NKR) Voucher Program allows a living kidney donor to choose the most convenient time frame for their kidney donation surgery and provide one or more vouchers to loved ones, who can then be prioritized to receive a living donor kidney through the NKR if or when they need a transplant.

- A parent of another patient described her son's 8-year journey with FSGS, cycles of dialysis, and transplantation. The emotional challenges can be overwhelming, although witnessing adults managing FSGS gives hope to families with children living with FSGS.

- Another patient shared her experience with failed treatments, including steroids, immunosuppressants, dialysis, plasmapheresis, and transplants. Despite failed therapies, she has learned to manage her disease and is focused on living her life to the fullest.

- One patient shared that he has been living with rFSGS since age 2. He relied on dialysis for 28 years before scientific advancements enabled a successful kidney transplant, which was performed more than 8 years ago. This patient was diagnosed with and treated for T-cell lymphoma during this time post-transplant. His experience led to a surprising discovery: Treatment for T-cell lymphoma can resolve proteinuria in FSGS. These findings underscore the importance of precision medicine for tailored therapies.

Research Gaps, Outcomes, and Opportunities

- Patients emphasized the emotional toll of rFSGS, describing feelings of devastation and guilt post-transplant, particularly concerns about "disappointing the live donor."

- An overwhelming sense of hope and encouragement emerged from the conference, with patients' shared experiences regarding family connections leading to a sense of community among attendees.

- Patients highlighted the importance of maintaining hope, even amid the mental and emotional strain of treatment failures and fears of transplant rejection.

- The disparities in care due to socioeconomic, racial, and educational factors introduce challenges for patients, particularly for African American patients, who experience a higher risk of kidney disease. Addressing disparities through inclusivity in research and treatment is critical.

- Patients value honesty and transparency from clinicians. Attendees expressed appreciation for clinicians who expand collaborations and share resources to help patients. Such clinicians include those serving as the patient's support network throughout the treatment process.

Political and Community Engagement

The conference included government representatives from both U.S. parties.

- The attending policymakers will push for increased NIH budgets and innovative research programs dedicated to FSGS.

- Gaps remain in aligning pharmaceutical, medical, and political efforts to accelerate therapy development for rFSGS.

- Policymakers highlighted the pivotal role of patients in advocating for research funding, sharing their stories, and engaging with Congress.

- Policymakers emphasized the need to increase political collaboration and strengthen bipartisan partnerships to sustain long-term funding commitments for rFSGS research.

- Several policymakers highlighted the important role of pharmaceutical companies in drug discovery and innovation.

- Policymakers noted that the United States' leading global innovations in medicine, health treatments, and biotechnology is integral for national security and defense because it places us at the forefront of world leadership.

Words of Encouragement from Mr. Gary Torgow

Mr. Gary Torgow opened the afternoon session with a message of hope and encouragement for the rFSGS community to persist in their efforts. He expressed gratitude to Dr. Sanna-Cherchi for uniting the community with a shared goal of finding a cure for rFSGS, and to Ms. Danielle Johnikin, Conference and Exhibit Manager, The Scientific Consulting Group, Inc., for organizing event logistics. Mr. Torgow shared his personal inspiration from his grandson, who is an rFSGS patient. He highlighted the importance of kindness and mutual support, sharing anecdotes that motivate him to continue his charitable efforts, including helping a widowed 90-year-old man by paying off his mortgage. He concluded with a powerful reminder that everyone deserves to be treated with dignity and compassion. He expressed his hope that this conference will serve as a catalyst for advancing efforts to find a cure for rFSGS.

Keynote Lecture: Novel Mechanisms and Therapies for rFSGS

Dr. Saleem, M.D., Ph.D., University of Bristol (UK), a leading expert in renal therapeutics, spoke on the complex mechanisms underlying rFSGS are poorly understood. Circulating factors play a key role in disease recurrence post-transplant, and identifying these factors is critical to intervention. Molecular differences among nephrotic syndrome subgroups, including steroid-resistant disease and monogenic factors, have been identified, and potential biomarkers for disease recurrence and progression provide promising pathways for novel treatments. Additionally, advancements in molecular subgrouping improve understanding of steroid-resistant and monogenic nephrotic syndromes. Precise patient sampling and systematic data collection are crucial to accounting for disease heterogeneity. This can be achieved through interdisciplinary collaboration among clinicians, researchers, and patient communities to accelerate discoveries.

Research Gaps and Opportunities

- Circulating factors causing FSGS recurrence after transplant are not well understood. Several participants agreed that further studies to pinpoint and validate circulating factors driving recurrence is a priority research area.

- Systematic sampling protocols, particularly differentiating nephrotic and remission phases, can ensure robust and reliable data across studies.

- More research funding designated for biomarker discovery is needed to predict recurrence and guide treatments. Precision medicine is crucial to understanding and treating the diverse nature of rFSGS. Every patient serves an important role in elucidating the complexity of rFSGS.

Clinical and Genetic Predictors of rFSGS

Predictors of FSGS recurrence include race (higher risk in White patients), low serum albumin (<3 g/dL), young age at diagnosis (<30 years age), severity of native kidney disease, history of prior failed transplants, and rapid progression to end-stage renal disease. Only 15–25% of rFSGS cases have predictive tools, so an understanding of recurrence in the remaining population is needed. A clinician stressed that the condition should be diagnosed with the first drop of urine after anastomosis (during the transplantation procedure) that demonstrates the presence of proteinuria.

Research Gaps and Opportunities

- Misleading terminology around FSGS complicates the diagnosis and treatment differentiation between primary and recurrent cases.

- Clinicians and researchers agreed that establishing protocols for consistent patient sampling—including post-transplant biopsies—at appropriate stages are important for understanding recurrence.

- Policymakers and researchers are urged to recognize rFSGS as a severe and underfunded condition. Expanding international collaboration and data sharing is essential to advancing research.

- Participants discussed expanding research into diagnostics for underserved FSGS patients to ensure broader research applicability.

Clinical Trials for rFSGS: What We Have and What We Need

Clinicians emphasized the critical need for more robust patient data and an increase in clinical trials for rFSGS. Recurrence in rFSGS is linked to circulating factors rather than issues with the transplanted kidney itself. Therapies like plasmapheresis, lipopheresis, and immunoadsorption are available; however, randomized controlled trials (RCTs) to confirm their efficacy in treating rFSGS are needed.

Research Gaps and Opportunities

- Several clinicians emphasized the need for a centralized, coordinated effort to drive scientific and clinical progress in rFSGS through collaboration and education.
- Barriers to clinical trials include inconsistent global practices; challenges with recruitment due to cultural, logistical, and system issues; and difficulty in engaging clinicians and families because of inadequate resources and training.
- Increasing RCTs to evaluate rFSGS therapies, fostering global partnerships to align research priorities and resources, and centralizing funding and infrastructure to streamline clinical trial recruitment are essential to discovering therapies for FSGS.

Utilization of Patient-Derived Pluripotent Stem Cells and Organoids to Study rFSGS

Kidney organoids—stem cell–derived tiny tissue cultures that can mimic the structure, organization, and some functions of kidneys—have the potential to advance the understanding and treatment of rFSGS. Much remains unknown about the genetic, molecular, and circulating factors predisposing patients to rFSGS.

Research Gaps and Opportunities

- Organoids allow researchers to replicate rFSGS progression and test therapeutic responses in a patient-specific manner.
- Organoids provide a framework for precision medicine by tailoring treatments to the genetic and molecular profiles of each patient.
- Organoids reduce the need for trial and error in prescribing therapies to improve patient outcomes.
- Collaborative efforts to harness these tools and explore epigenetic and immune-cell interactions influencing organoid function and rFSGS recapitulation are vital to advancing rFSGS research.

Building a Collaborative Resource to Resolve the Causes and Find New Therapies for rFSGS

The return on investment from funding research and resources for rare diseases, specifically rFSGS, can be substantial. An unmet need exists for precision medicine and genetic studies to better understand and treat rFSGS. rFSGS research is underfunded, with few studies conducted on genetic mutations or biomarkers. Genetic biomarkers can increase the development of new drugs by two- to threefold, underscoring their importance for advancing therapies.

Research Gaps and Opportunities

- Expanding genetic studies and biomarker discovery in collaboration with the pharmaceutical industry can drive drug development and improve diagnosis.
- Research outcomes can be improved by developing an infrastructure for collaborating, sharing data, and providing resources globally among the rFSGS community.
- Patients and families play a vital role in driving research progress through active participation and advocacy.

Current State and Future Avenues for rFSGS

Industry collaboration is vital for accelerating drug discovery and bringing solutions to rFSGS patients. Despite a projected 28% compound growth rate in kidney disease drug discovery, challenges persist in rFSGS research because of the misleading nomenclature of FSGS that describes the pathology but not the disease itself, as well as limited investment in rare diseases and heterogeneity in clinical presentations, undefined clinical trial endpoints, lack of understanding of molecular mechanisms, and high FSGS recurrence post-transplant.

Research Gaps and Opportunities

- Increasing awareness of rFSGS alongside industry collaborators and redesigning clinical trials to evaluate genotype–phenotype correlations may improve research outcomes.
- Prioritizing -omics profiling can help clinicians and researchers understand recurrence mechanisms.

Conclusion

The rFSGS Conference concluded with Mr. Elie Torgow expressing his gratitude for uniting the community in its mission to combat rFSGS. He commended the collective effort of patients, families, clinicians, researchers, funders, and policymakers working together to find a cure. Mr. Torgow shared the story of his son, who was diagnosed with FSGS at age 7. After receiving a kidney transplant from Mr. Torgow's brother at age 10, the disease recurred within 48 hours. Despite these challenges, Mr. Torgow and his family remain optimistic, expressing profound gratitude for the physicians who supported their journey.

The goal of this conference was to strengthen the rFSGS community in striving toward the shared goal of finding a cure for rFSGS. The hope and plan are to continue fostering collaboration, learning from each other's experiences, securing new research funding, and paving the way for new treatments.

Conference Organizing Committee

- Simone Sanna-Cherchi, M.D., Columbia University
- Gary Torgow, Sterling Group
- Elie Torgow, Sterling Group

Program Directors

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- Simone Sanna-Cherchi, M.D., Columbia University

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- Kimberly J. Reidy, M.D., The Children's Hospital at Montefiore
- Eloise Salmon, M.D., University of Michigan
- Matthew Sampson, M.D., M.S., Boston Children's Hospital
- Patricia L. Weng, M.D., David Geffen School of Medicine at the University of California, Los Angeles

Speakers and Moderators

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- Rasheed Gbadegesin, M.D., M.B.B.S., Duke University School of Medicine
- Debbie Gipson, M.D., M.S., National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health
- Paul C. Grimm, M.D., Stanford University School of Medicine and Stanford Medicine Children's Health
- Namrata Gargee Jain, M.D., Hackensack Meridian Health
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- Priya Verghese, M.D., M.P.H., Northwestern University Feinberg School of Medicine
- Astrid Weins, M.D., Ph.D., Harvard Medical School

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Panelists

- Antonio Fontanella, Miami, FL
- Alexis Kane, Bennington, VT
- Vincent Moolenaar, Amsterdam, the Netherlands
- Shannon Mulroy, New York, NY
- Sachet Walker/Aiden Walker, Detroit, MI
- Mariann Wang, New York, NY

Policymakers

- Honorable Senator Roger Marshall, Kansas
- Honorable Congressman John Moolenaar, 2nd District of Michigan
- Honorable Senator Debbie Stabenow, Michigan
- Honorable Congresswoman Haley Stevens, 11th District of Michigan
- Honorable Congressman Shri Thanedar, 13th District of Michigan