Patient Recruitment into a Multicenter Randomized Clinical Trial for Kidney Disease: Report of the Focal Segmental Glomerulosclerosis Clinical Trial (FSGS CT)

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Abstract

We describe the experience of the focal segmental glomerulosclerosis clinical trial (FSGS CT) in the identification and recruitment of participants into the study. This National Institutes of Health funded study, a multicenter, open-label, randomized comparison of cyclosporine versus oral dexamethasone pulses plus mycophenolate mofetil, experienced difficulty and delays meeting enrollment goals. These problems occurred despite the support of patient advocacy groups and aggressive recruitment strategies. Multiple barriers were identified including: (1) inaccurate estimates of the number of potential incident FSGS patients at participating centers; (2) delays in securing one of the test agents; (3) prolonged time between IRB approval and execution of a subcontract (mean 7.5 ± 0.8 months); (4) prolonged time between IRB approval and enrollment of the first patient at participating sites (mean 19.6 ± 1.4 months); and (5) reorganization of clinical coordinating core infrastructure to align resources with enrollment. A Web-based anonymous survey of site investigators revealed site-related barriers to patient recruitment. The value of a variety of recruitment tools was of marginal utility in facilitating patient enrollment. We conclude that improvements in the logistics of study approval and regulatory start-up and testing of promising novel agents are important factors in promoting enrollment into randomized clinical trials in nephrology. Clin Trans Sci 2013; Volume 6: 13–20

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Introduction

Nephrology as a general discipline, compared to 12 other major medical subspecialties, ranks at the bottom in the performance and completion of randomized clinical trials (RCT).[1] There are a number of potential explanations for this suboptimal implementation of clinical research trial opportunities. First, the diseases of interest are generally uncommon necessitating multicenter studies. Second, patients with early chronic kidney disease (CKD) are often asymptomatic and may not appreciate the presence or severity of the underlying disease or the long-term threat that it represents to their health, features that may adversely impact patient motivation to enroll in research projects. Third, because of the considerable gap in our understanding of the pathogenesis of most kidney diseases there is a paucity of discrete targets and novel options for the safe and effective treatment of most disorders. Fourth, many nephrology services do not have adequate personnel and resources allocated to the performance of clinical research. Fifth, although RCTs are considered the "gold standard," they are expensive and time-consuming.[2] Finally, there is no organized infrastructure in nephrology comparable to the oncology study groups, neonatal network, or acute respiratory disease collaborative that can facilitate the performance of RCTs for the full spectrum of rare kidney diseases.

In the face of these challenges, there remains a pressing need to conduct RCTs to guide the optimal utilization of available therapies and to test novel treatments for pediatric and adult patients with kidney diseases. This is especially critical for those conditions whose natural history include the progression to end-stage kidney disease (ESKD), or recurrence of the disease after kidney transplantation. ESKD represents one of the most costly medical conditions due to intense patient disease burden, impact on quality of life and the high-financial cost to society (http://www.usrds.org/2011/view/v2_11.asp).

Successful performance of RCTs provides optimal evidence about the efficacy of commonly used but untested interventions and helps clarify meaningful outcomes when testing newer therapeutic options. Unfortunately, many RCTs do not meet projected recruitment targets and, therefore, they are underpowered to achieve their primary and main secondary end points.[3] Although novel trial designs and alternative methods of statistical analysis such as Bayesian approaches may decrease the required sample size requirements,[4] it is important to identify impediments to successful pediatric and adult patient accrual and completion of RCTs.

The focal segmental glomerulosclerosis clinical trial (FSGS CT), funded by the National Institutes of Diabetes and Digestive and Kidney Diseases of the US National Institutes of Health UO1 grant mechanism, included 138 patients with primary steroid-resistant FSGS over a 5-year period. Participants were randomized to one of two treatment arms—cyclosporine versus mycophenolate mofetil and dexamethasone. However, it fell far short of its anticipated goal of 500 participants. Even though the study is the largest RCT that has ever been conducted in patients with this condition in North America, the validity and interpretation of the findings have been hampered by the limited enrollment.[5,6,7] This report prepared by the Recruitment and Retention Committee (RRC) of the FSGS CT is intended to achieve the following

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four objectives: (1) describe the methodology used during the planning phase of the RCT to estimate the anticipated patient enrollment and optimal trial design; (2) analyze the recruitment activity at all participating sites in the clinical trial; (3) summarize the time course of site activation and patient recruitment; and (4) conduct a *post hoc* survey of site investigators regarding factors that affected patient enrollment.

Methods

Before the trial was implemented, several strategies were employed to maximize enrollment including: (1) collaboration with a patient advocacy group—the NephCure Foundation; (2) deploying a survey of participating sites about the number of potential study participants who would be candidates for the RCT and the feasibility and acceptability of trial interventions options across pediatric (PED) and internal medicine (IM) nephrologists. The second component was assessed to increase engagement and consensus among potential investigators in nephrology practices.

A prestudy survey of investigators was conducted to estimate the number of potential study participants and determine the acceptability of potential treatment options and drug regimens by managing physicians in rank order. Although the FSGS CT initially consisted of five core sites, the findings are presented for the three consolidated core centers that ultimately supervised enrollment of patients into the trial.

To identify facilitators and barriers to enrollment into the FSGS CT, a third-party anonymous Web-based survey of physician investigators was deployed after the completion of the trial and publication of the primary outcome. Investigators were asked about the impact of a number of factors on recruitment at their site (See Appendix). These included achieving a consensus within their division to be part of the study, IRB approval, executing the contract, support from the clinical cores, availability of the core coordinators, adequacy of start up funds, adequacy of reimbursement, and availability of supplemental funds at the sites. The responses were recorded on a 5-point Likert scale (1, major impediment; 3, neutral; and 5, major help). The survey was deployed three times using Qualtrics and respondents had the option to participate in a drawing for 100 US dollars.

Results are expressed as frequencies and mean ± standard error of the mean (SEM). The survey responses from those who enrolled at least 1 patient were compared with those who failed to enter a single study participant, using chi-square analysis.

Results

Planning phase

The NephCure Foundation advocated for a trial for the treatment of FSGS before the allocation of funding and request for trial proposals issued by the NIH as a part of the U01 mechanism. Following NIH peer review and selection of the trial leadership, collaboration with the patient advocacy group continued with dissemination of information about the trial on their Website, newsletters and other publications, community educational events, and partnership to fund ancillary research efforts focused on genetics and FSGS.

During the planning phase for the FSGS CT, the Steering Committee participated in several in-person, day-long meetings to draft an acceptable protocol. The NIH guidelines for the trial mandated an active control treatment for comparison with any proposed experimental intervention rather than a placebo arm. This led to an extensive review of the literature to define the standard of care for patients with FSGS and to delineate reasonable options for the active control and test therapy that would be acceptable to the largest majority of participating investigators. Based on this survey of the existing literature and participating site survey results, treatment arms were selected and the full trial design protocol and manual of operations were completed. Responses were received from 91 sites (50% response rate)—67 PED and 24 IM practices, providing information about the number of incident patients with primary FSGS who had been treated between 2001 and 2002. The total number of incident primary FSGS cases at all surveyed sites was 479 in 2001 and 481 in 2002. The mean number of cases per site was 5.8 ± 9.2 in 2001 and 5.9 ± 9.2 in 2002 (*Figure 1*). Nearly 67% of the sites had 1–5 patients in each year and nine (10%) sites had 10–60 patients in both years of the survey period. Based on these projections, the Steering Committee anticipated that 500 patients with incident primary FSGS could be successfully enrolled into the FSGS CT over a 26-month period, assuming a 50% enrollment rate. This sample size would enable the study to achieve an 80% power to detect a 12% difference in the response rate between the control cyclosporine treatment arm and the experimental arm consisting of the combination of oral dexamethasone pulses and mycophenolate mofetil.

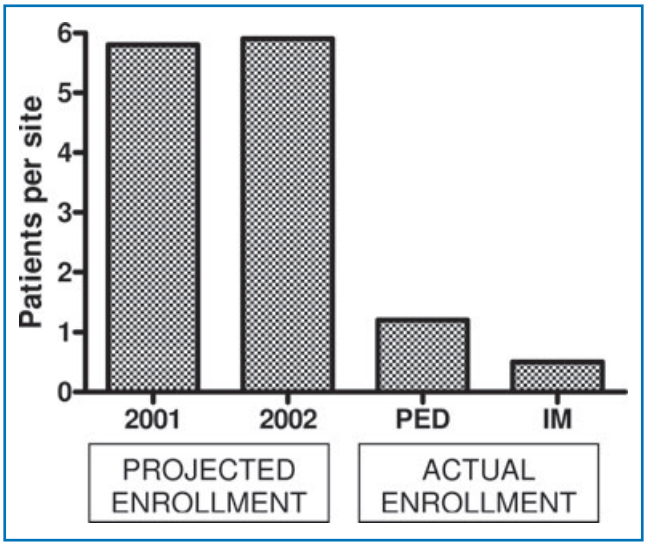

Figure 1. Number of patients reported to have been seen in years 2001–2002 (projected enrollment) and the number of at PED and IM sites entered into the study (actual enrollment).

The NIH charge to the FSGS CT Steering Committee was to include children and young adults in the trial. Therefore, patients between the ages of 2–40 years were targeted at sites with PED and/or IM practices. To include adolescents and young adults who were under the care of IM nephrologists, a list of these practitioners was grouped separately from sites that treated only PED or IM patients. The major source of IM practices was the Glomerular Disease Collaborative Network (a research collaborative based at UNC-Chapel Hill); however, other IM practices that treated older pediatric and young adult patients from around the United States were represented.

Donation of one of the study drugs to be tested in the trial had been pledged by the pharmaceutical company during the

Figure 2. Geographical distribution of the patients who were enrolled in the FSGS based on the zip code of the participating site where they were treated.

planning phase of the FSGS-CT. After the trial had been funded and after more than 12 months of negotiations with the company, this donation was rescinded. As a result, the NIDDK was forced to purchase the specific study medication.

Analysis of site recruitment

Of the 116 potential sites that initially offered to participate in the trial, 104 sites (90%) obtained IRB approval and met the logistic requirements to enroll patients. There were 52 PED sites, 26 MED sites, and 26 sites that treated both groups of patients. All of these centers had an executed contract in place for payment of the clinical effort required by the study. At least one patient was successfully enrolled into the study at 53 (51%) participating centers. The majority (n = 37) enrolled 1–3 patients and 16 sites enrolled 4 or more participants. The mean number of PED patients enrolled at each site was 1.2 ± 0.2 and the mean number of IM patients enrolled per site was 0.5 ± 0.1. Overall, the mean enrollment per site was only 29% of the projected number of participants, for example, 1.7/5.9 (*Figure 1*). The three centers that recruited the most patients into the trial were located in the Bronx, NY, New Hyde Park, NY, and Chapel Hill, NC, and they also served as the three Clinical Coordinating Centers for the study. The geographic distribution of the patients who were enrolled in the FSGS CT, based on the zip code of the participating site is illustrated in *Figure 2*.

During the course of the FSGS CT, 192 patients were enrolled and 54 were subsequently excluded from the study. The two most common reasons for this course of events were a level of proteinuria that was below the inclusion criterion (n = 20) and failure to confirm the diagnosis of primary FSGS after central review of the kidney biopsy by a study pathologist (n = 22).[7] During the course of the trial, the level of proteinuria needed to qualify for enrollment was lowered from 2 to 1 (protein [g]/creatinine [g]) to promote recruitment. There was no systematic attempt to monitor encounters with all patients who qualified but declined to participate in the study.

Study activation

The FSGS CT officially opened to patient enrollment on November 18, 2004. The mean time to obtain IRB approval among the participating sites was 1.9 ± 5.1 months. An important barrier to the timely opening of the study was a delay of over 12 months due to administrative difficulties in securing one of the test agents. The mean interval that elapsed between obtaining IRB approval and executing a subcontract to support the clinical research activity was 7.5 ± 0.8 months. In total, the median time from distribution of the final protocol to completion of all necessary regulatory requirements and enrollment of the first patient at a participating site was 19.6 ± 1.4 months (*Figure 3*).

Efforts to increase recruitment

Enrollment into the FSGS CT was slow from the onset of the study and, therefore the enrollment period was extended from 26 to 40 months in an attempt to foster recruitment. Over the course of the FSGS CT and in response to low enrollment, aggressive marketing efforts were increased by (1) updating the study Website, (2) creating a low-literacy and culturally appropriate short video (10 minutes) in English and Spanish that featured clinicians and patients who participated in the RCT; (3) quarterly newsletters; (4) investigators lectures within the medical community; (5) inviting site investigators to participate in trial leadership committees; (6) expanding the eligibility criteria (higher age and BMI cutoffs, lower eGFR cutoff, altered definition of steroid resistance and lower qualifying level of proteinuria); and (7) engagement of nephropathologists to assist with identification of potential patients from biopsy diagnosis. No significant improvement in enrollment was observed with these approaches

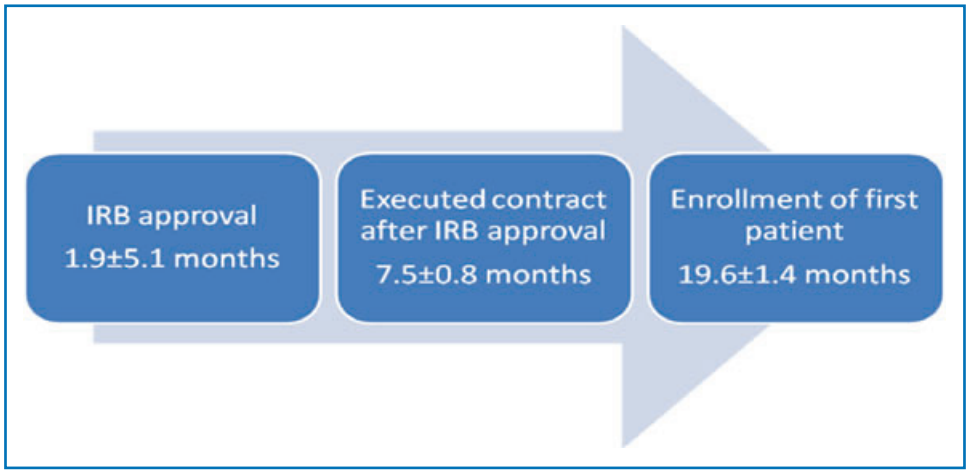

Figure 3. Timeline of FSGS CT study outlining key events in the set up and performance of the study.

Post hoc recruitment survey of site investigators

Responses were received from 47 (45%) of the 104 sites that obtained IRB approval for the study and were logistically ready to enroll patients. Of the respondents, 39 completed all of questions, but only 40% chose to enter their name in the incentive lottery. Most respondents worked in academic centers (87%) and the rest (13%) were in private practice. The majority of respondents enrolled exclusively PED patients (61%) or a combination of children and adults (18%). Only 21% of the respondents were from IM nephrology sites, mostly from the Eastern United States. Although the vast majority of sites used their local or core IRB (86%), most of the IM participants obtained approval from a central IRB.

The scores on achieving practice group consensus, IRB approval/contract-related issues, clinical core support, and adequacy of start-up/patient reimbursement expenses ranged from 2.4 to 3.3 out of 5 (most helpful) in the Likert scale. The item with the lowest score was availability of supplemental funds at the participating site (2.4 ± 1.0) and none of the items were considered either a minor or major help.

When asked about the value of the recruitment tools on a 1–4 scale (1, not at all; 4, absolutely helpful), the two most helpful interventions to promote enrollment were the video that introduced the trial (3.7 ± 1.6) and participation in trial leadership committees (3.7 ± 1.5) whereas the least helpful were newsletters (2.8 ± 1.3) and brochures (2.9 ± 1.3). The investigators were queried about whether they thought any of the eligibility criteria had an adverse effect on enrollment. On a scale of 1–4 (1, not at all; 4, absolutely), none of the features had a mean score above 2.7. The item with the highest score (2.7 ± 1.1) was prior treatment with one of the study medications. A summary of some of the key recurrent free text answers is provided in the *Table 1*.

The survey responses from the 19 sites (16, 84% in academic settings) that enrolled at least 1 patient (mean of 4.3 ± 4.3 patients) were compared with 20 responses from sites that failed to enter a single study participant (18, 90% in academic settings). Nonenrolling sites scored support from the core center lower than enrolling sites, OR = 5.9, 95% [CI 1.3–27.3] ($p < 0.05$). Their identified facilitators/barriers and open-ended responses are summarized in the *Table 1*.

Discussion

The FSGS CT was the largest multicenter RCT ever performed in North America to address the management of this challenging medical condition. The overall design with two active treatment arms reflected the input of patients and families with FSGS who lobbied the federal government to support an RCT for this glomerular disease. It featured close collaboration between pediatric and IM nephrologists. The implementation of the RCT was consolidated into three central cores and was organized in a manner to facilitate communication and data transfer from the participating sites to the data coordinating center with the assistance of the clinical coordinating centers.[6,7]

Overall, recruitment achieved only 138 of 500 projected patients, 28% of the target sample size. In large measure, this reflected the overly optimistic projections of potential participants at each site. In fact, actual enrollment was approximately 30% of the number of patients who had been seen at participating sites in the 2 years before initiation of the study. There is no apparent explanation for this acute drop off in incidence of primary FSGS at the broad list of potential sites. However, it is conceivable that the pretrial estimates of potential patients at each site included both primary and secondary causes of FSGS and did not account for the study eligibility criteria adopted by the trial. Alternatively, the original estimates may have been overly optimistic and the incidence of FSGS did not decline during the study period. This barrier could be resolved by having longitudinal patient databases/registries that can be queried when clinical trials are proposed.

Despite the inclusion of patient and patient-advocacy groups' input as well as aggressive marketing and communications strategies, a number of barriers that were beyond the control of the

General
• Low prevalence of disease at site
• Presentation with advanced renal disease
• Patient unwillingness to maintain randomized treatment if there is no immediate evidence of efficacy
Medications
• Prior exposure to study drugs
• Concern about exposure to steroids, especially in adults
• Choice of specific study drugs, e.g. cyclosporine versus tacrolimus
• Specific doses of study drugs
Study design
• Requirement for confirmation of FSGS on stored biopsy material
• Exclusion of patients with steroid resistance but histological evidence of minimal change nephrotic syndrome
• Specific eligibility criteria—age, BMI, eGFR
• Rigid standards for blood pressure control

Table 1. Recurring themes in responses of FSGS CT investigators to *post hoc* survey.

study investigator team hindered enrollment. These included test agent availability, financial considerations, and contract execution timelines. The inability to obtain one of the study drugs that had been pledged to the trial resulted in a significant delay in initiation of the trial. No explanation was provided by the pharmaceutical company for the delay in providing and ultimately deciding to withdraw material support for the trial. It is uncertain if more formal arrangements between investigators and those providing study agents can prevent this problem. However, there is precedent for delineation of the responsibilities of the drug sponsor in a memorandum of understanding drafted before commencing a clinical trial.[8] The experience from the FSGS CT would suggest that making this a required step in the preparation for a study may help avoid unanticipated legal difficulties and delays in the performance of an RCT. Investigators identified limited payment to patients based on prevailing local IRB standards;[3] limited per patient reimbursement to physicians because of sponsor-related funding constraints as specific financial challenges to the FSGS CT. Finally, contract execution by academic institutions required an average of 7 months from the time of protocol dissemination. This contract timeline may have had a major adverse impact on the trial if all test agents were available.

Despite the importance of adequate recruitment of patients into pediatric clinical trials, there is not a great deal of published data focusing on this topic.[9] Most of the literature about the performance of RCT has been written by social scientists and is based on work performed at centers outside the United States. Thus, it may not be available to clinical nephrologists or directly applicable to their practice. In addition, there are almost no contributions that specifically address kidney diseases in general or focus on glomerulopathies. For example, in HIV vaccine trials, barriers to participation have been broken down into locus of the barrier (personal vs. social) and the nature of the barrier (risk vs. cost).[10] Reaching out directly to patients using disease specific Website or registries that target individuals with rare disorders can begin the process of surmounting patient related barriers to participation in clinical trials.[11,12] However, FSGS is more prevalent among minorities who may not have easy access to technology or Web-based marketing. Our data suggest that novel methods of communication using videos to introduce the study at the clinical sites are the highest rated recruitment tool compared to standard written material such as brochures, newsletters, and regional press releases. Research is needed to assess the efficacy of various recruitment tools in a variety of study environments. The role of Web-based marketing and the use of social networks require prospective evaluation particularly among populations who do not have easy access to this media.

We did not directly survey patients to determine whether there were features about the FSGS CT that may have discouraged them from consenting to the study. In addition, there is no information about patients who were approached about the trial but who declined to participate. This would have enabled a comparison between those who enrolled and those who refused. Issues of confidentiality have hindered data collection from patients who opt out of a trial. Novel approaches for obtaining consent and collecting data about all potentially eligible research subjects in a given trial may assist in the design of strategies to foster enrollment during an ongoing study and for future trial development.

Physicians and other health care providers play a key role in recruitment into trials. Failure to invite every eligible patient to participate in a study may be due to simple inaction or investigators' perception of the feasibility and soundness of the trial.[13] In our anonymous *post hoc* survey of investigators, these concerns were indeed a barrier to participation as reported by 17/39 (44%) of the respondents. It was assumed that there was adequate physician buy-in to the FSGS CT because the nephrologists were comprehensively surveyed about the availability of patients and their acceptance of the proposed treatment arms. Physician reluctance to enroll patients in the FSGS CT could have been underestimated if they were not forthcoming about their true opinions regarding the experimental treatments. The lack of consensus regarding the treatment arms, enhanced in part by the lack of a novel treatment modality, also played a role in dampening the enthusiasm of patients and physicians to participate in the study as noted in the *post hoc* survey free text responses. Offering innovative treatments could potentially overcome physician inertia in enrolling patients. However, this favorable effect might be counterbalanced by a hesitancy of physicians to move forward with a new therapy that has a worrisome or unknown side effect profile. The availability of innovative treatments options may also enhance patient willingness to participate in a RCT. This is consistent with previous findings in surveys indicating that the degree of perceived clinical benefit is the most important factor fostering a greater likelihood of patient participation in an RCT.[14]

One of the unique features of the FSGS CT was the wide age range for eligibility. The goal was to perform a study that would address the treatment of a broad sample of patients. However, this may have been an unacknowledged impediment to enrollment because site investigators may have assessed the potential toxicity of the test therapies differently dependent on whether they treated pediatric or adult patients. For example, extended treatment with dexamethasone may have been considered more hazardous in older patients with primary FSGS. This highlights the importance of full physician buy-in to a trial at its inception, during the planning phase, and through to successful enrollment and treatment. Based on the suboptimal enrollment into the FSGS CT, we can only encourage greater transparency by site investigators about the number of potential patients, acceptance of the study regimen, and accurate articulation of what they need to successfully identify and recruit study participants. Clarity on all of these points is essential to the Steering Committee of a trial and ensures optimal utilization of funding resources available for a study.

The long-time lag between initiating the IRB approval process and enrolling the first patient at a site may also have undermined recruitment into the FSGS CT. Despite the use of multiple recruitment strategies, a delay of more than 12 months between distribution of a study protocol and initiation of enrollment into a trial may be an insurmountable obstacle to achievement of a recruitment target. Having a dedicated study coordinator, scientific leadership within the study team of investigators, and lectures by site investigators may also enhance commitment of physicians to a large RCT like the FSGS CT.

Optimal study design may diminish the problem of recruitment[15] and as reported by Luzi et al.,[16] organized communication about an HIV vaccine study between the sponsor and physicians and patients involved in the project, enhanced physician buy-in and support for clinical trials. Improving procedures during screening and the informed consent process and the use of semi-automated systems to identify potential study participants have been utilized successfully to promote recruitment.[17,18] Finally, the role of payments to patients and families and balancing reimbursement for time spent on the study

versus coercion is an ethical issue that is often discussed as a patient barrier to enrollment.[19–21] Lack of sufficient reimbursement to offset transportation, childcare and work loss costs are barriers to enrollment and retention. In our survey of various institutional factors (IRB approval, execution of study contracts, support from the study infrastructure, and availability of personnel and financial resources at the site), no single factor was clearly identified as a hindrance or facilitator of patient recruitment. It is uncertain if this reflects vague responses to the survey or a more fundamental failure to identify the root cause of poor enrollment into RCT. We acknowledge the limited response rate to the survey and recognize that it would be premature to generalize the findings to RCT done in other subspecialties or in different circumstances.

There are several strengths of this report. First, in addition to describing recruitment before and after a large multicenter RCT, it incorporates a survey of site investigators after completion of the trial. Second, it depicts how recruitment into the study was addressed by ongoing issues that arose over the course of the trial. A major weakness is the low response (44%) to the survey which may have introduced a bias. There is a lack of information about patients who refused to enroll in the study. Finally, there was no systematic collection of information about the sites, the demographics and qualifications of the personnel who supervised the study, and the actual financial and research resources available to support the trial.

The FSGS CT addressed a disease that remains somewhat obscure to the general population. Patient advocacy groups like the NephCure Foundation and a registry for patients with the nephrotic syndrome that has been established by the NIH-funded NEPTUNE cohort study are important tools to promote awareness of kidney disease. However, much work is still needed to publicize the importance and human cost of glomerular diseases such as FSGS and the need for clinical research. This may be a difficult factor to control because of the individualized nature of medical care in the United States and the fiduciary responsibility to the individual patient, which may run counter to the ethic of participation in RCT.

Conclusion

Like many other trials, recruitment into the FSGS CT fell far short of the projected sample size, resulting in a study with limited power and diminished ability to achieve its objectives. In part, this reflects the rarity of this glomerular disease, the lack of accurate patient census and informative registries at the potential recruitment sites, the paucity of suitable novel targets for phase III RCT, and a reluctance of nephrologists to relinquish their determination of individual patient treatment. There were logistical issues such as the time required to obtain IRB approval and the lengthy process of executing a contract for the clinical research work that hinder recruitment. Most recruitment tools that are currently in use have not been studied systematically in a prospective manner and those in common use appear to have minimal impact on patient enrollment. Potential strategies to enhance recruitment into RCTs such as the FSGS CT include: Improved patient education about the severity of kidney disease, development of novel agents for testing in RCT, streamlining the start-up and regulatory approval process, increasing reimbursement to participating centers and study participants to cover the high institutional and participant costs incurred by clinical trials, and devising new strategies to communicate with patients and physicians before and during an RCT.

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Appendix: FSGS CT Investigators *post hoc* Survey

Dear FSGS Trial Investigator,

The FSGS trial was the first national study to helps us learn about effective treatments for patients with this challenging medical condition that carries such a poor prognosis, yet patient recruitment was difficult. In an effort to learn about the potential barriers to enrollment, we would appreciate your candid responses. Be assured that this 7-question survey is ANONYMOUS and will take you 5 or fewer minutes to complete. Your responses will guide future research efforts. Before you begin, please have handy the answer to the first question below.

1. Please tell us, how many patients were consented in the FSGS Clinical Trial at your site?

2a. What is your practice setting (academic, private)
○ Academic ○ Private

2b. Who is your core Principal Investigator?
○ D. Gipson ○ R. Kaskel ○ R. Fine/H. Trachtman

2c. What age range of patients did you approach for the study?
○ Children and adolescents only ○ Adults only ○ Children, adolescents and adults

2d. What type of IRB did your study use for the trial?
○ Institutional or local IRB ○ Your core institution's IRB ○ A central IRB

2e. What is your time zone?
○ Pacific Time ○ Central Time ○ Mountain Time ○ Eastern Standard Time

3. How much did the eligibility criteria affect enrollment?

	1 = Not at all	2 = Somewhat	3 = Quite a bit	4 = Absolutely	Do not know
Patient age criterion					
Trial medication regime					
Prior treatment with drugs chosen for the FSGS trial					
Patient weight criterion					

4a. Please specify the impact of other inclusion/exclusion criterion (open-ended question)

4b. What could we have done differently to improve enrollment (open-ended question)

5. Please tell us the impact of the following factors on recruitment at your site …

	1 = Major impediment	2 = Minor impediment	3 = Neutral	4 = Minor help	5 = Major help
Achieving consensus support for the trial in your group					
Getting IRB approval					
Executing a contract for the study					
Support from the clinical cores					
Availability of clinical coordinator for the trial					
Adequacy of start up funds					
Adequacy of the clinical per patient reimbursement provided by the study					
Availability of supplemental funds at your site					

6. Please tell us how helpful these tools were …

	1 = Not at all	2 = Somewhat	3 = Quite a bit	4 = Absolutely	Do not know/did not use
Video introducing the trial					
Newsletters					
Brochures					
Regional press releases					
Lectures by co-investigators					
Investigator meetings					
Participation in leadership committees for the FSGS Trial					

7. Were there any solutions at your site that we need to be aware of? (open-ended question)