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THE VOICE OF THE PATIENT

Externally Led Patient–Focused Drug Development Meeting on IgA Nephropathy

August 19, 2019, Hyattsville, MD
Report Date: December 8, 2020

Submitted as patient experience data for consideration pursuant to section 569C of the Federal Food, Drug and Cosmetic Act to: Center for Drug Evaluation and Research (CDER),
U.S. Food and Drug Administration (FDA)

This report reflects the National Kidney Foundation's and Alport Syndrome Foundation's accounts of the perspectives of patients and care-partners who participated in an Externally Led Patient-Focused Drug Development Meeting, an effort to support the FDA's Patient-Focused Drug Development Initiative

VOICE OF THE PATIENT

Report on the Externally Led Patient-Focused
Drug Development Meeting on IgA Nephropathy

Contributors to the design and execution of the meeting, the collection of the information, and development of this document were:

David L. Feldman, PhD, National Kidney Foundation (Author)

Elizabeth M. White, PhD, White Biotech Solutions, LLC (Medical writer; author)

Bruce Julian, MD, Professor Emeritus of Medicine, Division of Nephrology, University Alabama (Birmingham) (Co-chair)

Pietro Canetta, MD, Assistant Professor of Medicine, Columbia University Medical Center (Co-chair)

Bonnie Schneider, Director and Founder, IGA Nephropathy Foundation of America, Inc.

James McCann, Editorial Director, National Kidney Foundation

James Valentine, MHS, JD, Hyman, Phelps, & McNamara (Moderator)

Sarah Kim, National Kidney Foundation (Logistics coordinator)

DISCLOSURES

Dr. Julian declares the following relationships: He is a co-founder of Reliant Glycosciences, LLC and holds equity in the company.

Dr. Canetta declares the following relationships: Investigator (at CUMC) in industry-funded therapeutic studies in IgAN (Mallinkrodt, Calliditas, EMD-Serono).

Mr. Valentine is employed by Hyman, Phelps & McNamara, P.C., a law firm that that represents sponsors developing drugs and patient advocacy organizations.

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VERSION DATE

This Voice of the Patient report has not been revised or modified since December 8, 2020.

STATEMENT OF USE

The National Kidney Foundation and IGAN Foundation of America have permission to submit this Voice of the Patient Report to the FDA External Resources webpage; linking to the FDA website will not violate the proprietary rights of others.

POINTS OF CONTACT

David L. Feldman, PhD | Medical Project Director, National Kidney Foundation | david.feldman@kidney.org

Bonnie Schneider | Director and Founder, IGA Nephropathy Foundation of America, Inc. | bonnie@igan.org

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INTRODUCTION

On August 19, 2019, the National Kidney Foundation (NKF) and IGA Foundation of America (IGANF) held an Externally Led Patient-Focused Drug Development (EL-PFDD) Meeting on IgA nephropathy (IgAN) in Hyattsville, Maryland. The broad goals of the meeting were to inform the Food and Drug Administration (FDA) and other stakeholders (e.g., drug developers) on:

- IgAN patients' experiences and perspectives regarding the symptoms and burdens of IgAN and its impact on their daily lives
- Factors that influence patients' decisions on entering clinical trials for IgAN
- The currently available therapies for IgAN, patients' experiences with these treatments, and their aspirations for new treatments

This EL-PFDD meeting was a parallel effort with FDA's PFDD initiative, which gathers patient input, especially on diseases for which treatments are inadequate or nonexistent. Recently, the agency passed the PFDD leadership to patient advocacy groups to organize and conduct EL-PFDD meetings.

This report is submitted to the FDA to serve as patient experience data or related information for the agency's consideration in the review of applications for new drugs to treat or prevent IgAN that are submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) or section 351(a) of the Public Health Service Act, pursuant to section 569C of the FD&C Act. In particular, such information may inform the FDA regarding the benefit-risk balance of treatment options, the severity of the disease, and the urgency of unmet medical needs.

Background and guidance on EL-PFDD meetings can be found at the following link: *https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drug-development-meetings*

Through this meeting, patients, families, and care-partners shared with the FDA their unique insights into the impact of IgAN on their daily lives. Perspectives on currently available treatment options and strategies for disease management, as well as expectations for the future treatments, were also shared.

This EL-PFDD meeting also included a distinctive in-depth focus on understanding patient perspectives on the design of clinical trials for IgAN and their willingness to participate under a variety of study designs. In particular, insights were collected regarding clinical trials that may be conducted under the

Accelerated Approval Program. Norman Stockbridge, MD, Director of Division of Cardiovascular and Renal Products, Office of New Drugs, Center for Drug Evaluation and Research (CDER), FDA characterized this unique approach in his opening remarks:

> "It's still fairly clear usually, when we approve something, we are fairly confident that it's, on the whole, safe and effective...But there is a compromise that is associated with product development for rare diseases, and this afternoon we're going to be talking about a possible further compromise, in which the evidence base, upon approval, is not everything you'd really have liked for it to be…But in addition to the risk associated with having a product on the market that's not entirely certified, there is an obligation on the part of the patients who participate in the post-marketing study that the study completes. Even though there is some evidence of benefit, there is an obligation on people's part to participate in a trial that actually resolves the question."

MEETING OVERVIEW

Overall design of meeting

This EL-PFDD meeting on IgAN focused on key broad topics addressed in three sessions: 1) the patient experience of living with IgAN, including disease symptoms and the daily impact of the disease, 2) patients' perspectives and preferences regarding clinical trials for IgAN, and 3) the patient perspective on the current challenges of treating IgAN.

The goals of this meeting were to provide FDA with an overall understanding of:

- Patients' perspectives on living with IgAN, with a focus on their daily disease burdens
- Factors that influence patients' willingness to enter clinical trials for IgAN, including patients' and care partners' perspectives on enrolling in trials requiring kidney biopsies, clinical trial endpoints that are meaningful to patients, and trials conducted under the Accelerated Approval Program
- Patients' views on the pitfalls of current therapies and the desirable characteristics of potential new therapies, and their insights into trade-offs they are willing to make for such therapies.

Discussion during the meeting provided the FDA and other stakeholders with the opportunity to hear directly from patients and their care-partners about the above topics. The voices of IgAN patients were heard through patient testimonies, live polling of the in-person and webcast audiences, and open discussions with the meeting attendees. An overview of the meeting can be seen in the Meeting Agenda (Appendix 2).

Patient panels

To provide initial patient input and to prepare the audience for discussions on patients' experiences of living with IgAN and their perspectives on treating IgAN, panels on these two topics were assembled before the meeting. Each panel consisted of five patients, selected by NKF and IGANF representatives from their memberships. Criteria for selecting panelists were set to maximize representativeness by achieving clinical and demographic diversity on each panel. Each panelist delivered a five-minute testimony on their experience related to their session's topic. A patient panel was not employed for the discussion on clinical trials for IgAN.

Polling questions

The demographic composition of the patient and care-partner attendees (in-person and webcast) was revealed by polling questions. Following each panel, topic-specific polling questions were posed to the participants toward capturing their perspectives on the different discussion topics. Patients' preferences concerning enrolling in clinical trials for IgAN treatments were also solicited through polling questions; Polling questions were based on a pre-meeting survey of prospective attendees, input from the meeting co-chairs, and literature.

The polling questions below were posed to patient and care-partner participants. Care-partners responding to polling questions were asked to respond on behalf of the patients for whom they provide care. Responses to polling questions are described in the text and depicted graphically.

Polling was conducted via an online platform through which in-person and remote webcast attendees could respond. Only patients and care-partners were asked to participate in polling. Responses were projected instantly for audience viewing and described simultaneously by the moderator.

Moderated audience discussion

Polling was followed by a moderated audience discussion, during which the in-person audience was invited to share their experiences with IgAN and were asked follow-up and clarifying questions by the moderator.

Post-meeting comments

To expand on the perspectives gathered at the meeting, patients and care-partners were encouraged to submit comments to NKF and IGANF after the meeting. Comments were accepted until September 19, 2019.

Enduring documentation of meeting

The archived webcast recording, this meeting report, and the meeting transcript are available on the following websites:

NKF: *https://www.kidney.org/events/local-event/nkf-and-igan-pfdd-iga-nephropathy*

IGANF: *https://igan.org/resources/*

KEY THEMES FROM PATIENTS' VOICES

Throughout the day's activities, the voices of IgAN patients conveyed clearly the following key messages:

- Patients with IgAN continuously deal with very difficult issues in their daily lives. The symptoms that most negatively affect daily life include:
    - Being tired, exhausted or fatigued
    - Experiencing "brain fog"
    - Anxiety and/or depression
    - High blood pressure
    - Gastrointestinal problems
    - Swelling (e.g., ankles, face, etc.)
- Emotional and social difficulties commonly accompany IgAN, and are attributed to these key factors:
    - Others don't know what it's like to live with IgAN
    - General daily function is limited
    - Social isolation
    - Family stress
    - Difficulty with relationships outside of family
    - Uncertainty and unpredictability of the disease
- Disease symptoms and side effects from medications prevent patients with IgAN from engaging in the activities that are important to them and that they enjoy, including:
    - Participation in sports or other physical activities
    - Attendance at work or school
    - Going outdoors (aversion because of heat or cold intolerance)
    - Participating in social activities
- The clinical measures that patients consider most relevant to their condition include:

    - Kidney function [glomerular filtration rate (GFR)]
    - Protein leakage (proteinuria/albuminuria)
    - Delay the need for dialysis or transplant

- Many patients are willing to participate in clinical trials, particularly if the side effects are limited, but a high percentage have been unaware or are not eligible for trials:
    - Patients feel that eligibility for clinical trials needs to be expanded to include pediatric patients.
    - Patients feel that eligibility for clinical trials needs to be expanded to include patients who have had a kidney transplant.
    - The requirement for more than one kidney biopsy in a year significantly reduces the willingness of patients to participate in a clinical trial.

- Patients expressed a willingness to participate in clinical trials conducted under an Accelerated Approval Program and to remain in such trials for the long-term, even after the drug is continuing to be studied is approved and marketed:
    - Majority of patients voiced a high tolerance for risk, and a commitment to remaining in clinical trials for one, two, and even three years after a drug is on the market, even if they had to remain in a placebo arm.
- There are currently no FDA-approved therapies that target the disease-specific mechanism of IgAN, or that significantly reduce progression towards end-stage kidney disease:
    - Treatments focus on managing high blood pressure and reducing inflammation
    - Angiotensin converting enzyme inhibitors and receptor blockers are the cornerstones for medical treatment for IgAN; they are not curative
    - Thirteen percent of patients polled believe their current treatments do not work at all, and only 14% responded that their treatments work “very well”
    - Patients reported managing their IgAN in part by lifestyle changes focused on diet (e.g., limitations on salt and protein) and exercise (e.g., yoga)

- The side effects of corticosteroid treatments, such as prednisone, are long-lasting and have a strong impact on IgAN patients, the most serious and life-altering effects include:
    - Weight gain and swelling (edema)
    - Muscle, bone, and joint damage
    - Irritability, moodiness, and aggressiveness

- Patients would be very confident in their decision to take a new medicine that has been approved based on evidence from clinical measures including:
    - Reduced proteinuria

    - Slowing the rate of loss of kidney function
    - Improvements in how they would feel, function and/or survive
- Overwhelmingly, IgAN patients desire a new treatment option that will halt the progression of disease or delay the need for dialysis:
    - Enthusiasm for such a treatment is significantly reduced if the side effect profile is more severe than current medications.

The insights collected and reported in this Voice of the Patient Report reflect perspectives of people living with IgAN and may help direct the FDA, in partnership with pharmaceutical companies, to develop the critical medicines that are needed by this community. These insights may now be used to help develop a benefit-risk framework that the FDA can utilize in their regulatory decision making. Preliminary recommendations for this benefit-risk framework can be found in this report.

REPORT OVERVIEW

This Voice of the Patient Report summarizes the perspectives shared by patients and care-partners at the EL-PFDD meeting through panelists' testimonies (Appendix 3), graphical depiction of responses to polling questions posed during the meeting (Appendices 4.1 – 4.4, 5), and moderated audience discussions (guided by discussion questions: Appendix 6). In addition, comments submitted to the NKF and IGANF after the meeting are included (Appendix 7).

This report intends to support the understanding by the FDA, medical product developers, academic researchers, and other stakeholders of: 1) the burden on patients and their families living with IgAN and its symptoms; 2) patients' preferences regarding clinical trials for IgAN therapies, and 3) patient perspectives on the treatments currently used to manage their condition and their aspirations for ideal future treatments. By describing the patient experience with IgAN, this document highlights the serious nature of IgAN and the significant unmet needs of IgAN patients and will enable the FDA to incorporate the patient voice when advising manufacturers on their drug development programs, evaluating products for marketing approval, and assessing benefit-risk for products under review.

Patient input in this report may also be of value to the drug development process more broadly. For example, the patient perspectives may guide pharmaceutical companies in their discovery and development processes by exposing previously unappreciated patient burdens of IgAN. That is, by describing unmet needs regarding symptoms of IgAN, information in this report may direct research decisions toward targeting disease mechanisms that underly symptoms important to patients.

Information in this report can also inform endpoints in clinical trials, support the development of patient-reported outcomes measures, and help to design clinical trials to test hypotheses that are inherently meaningful to patients.

In this report, patients and care-partners are collectively referred to as "participants," "attendees," or "respondents." When responses to polling questions are reported, the responses are those from patients and care-partners in the meeting room and from the webcast audience. "Care-partner" refers to a family member, partner, or friend who provides direct care for the patient.

Percentages from polling questions reported in the text and as numerals in the Appendix figures are rounded-off from the original data. Consequently, the sum of percentages for a given graph may not total 100% and the bar heights may not always reflect precisely the percentages within.

We note that, while the in-person and webcast attendees at this meeting represented a clinically and demographically diverse group, the extent to which this group reflected the IgAN patient population at large is unknown, in part due to the lack of quality epidemiology and natural history information on IgAN.

The terms and language used in this report to describe IgAN symptoms and impacts, views on participating in clinical trials, and treatment experiences reflect those used by in-person attendees. There may be symptoms, impacts, treatments, or other aspects of the disease that are not included in the report.

OVERVIEW OF ATTENDEES

Attendance

Approximately 125 people attended the EL-PFDD meeting in person while 206 people attended through the live webcast. Nine representatives from the FDA were present.

Demographics of meeting participants

Responses to the demographic polling questions revealed the diverse nature of the in-person and webcast participants.

DEMOGRAPHIC POLLING QUESTIONS

Connection to IgAN, residence, age, gender, diagnosis, clinical status

Polling Questions 1–7; Appendix 4.1

Connection to IgAN

Sixty one percent of participants were people with IgAN, and 39% were care-partners. (Figure 1; Appendix 5)

Residence

The polling revealed that 96% of attendees were U.S.-based, most being from the U.S. East Coast (54%) and Midwest (29%). Five percent were from the West (Mountain time zone) and 8% were from the West Coast. Five per cent of participants were from outside North America. (Figure 2; Appendix 5)

Age

Most (85%) of respondents were between 18 and 59 years old, while 5% of participants were younger than 18. (Figure 3; Appendix 5)

Gender

Sixty-two percent of respondents identified as female and 38% identified as male. (Figure 4; Appendix 5)

Diagnosis

Most patients received their diagnosis more than 10 years ago (32%) followed by between 5 to 10 years ago (27%). (Figure 5; Appendix 5)

Ninety-six percent of respondents had received a diagnosis of IgAN, 4% were diagnosed with IgAN and IgA vasculitis (IgAV, formerly Henoch Schönlein Purpura, HSP, and none reported a diagnosis of IgAV alone. (Figure 6; Appendix 5)

Dialysis or kidney transplant status

The large majority of participants (76%) were not on dialysis and had never received a kidney transplant. Twelve percent were kidney transplant recipients in remission; 7% were kidney transplant recipients with recurrent IgAN; 6% were on dialysis and had never received a kidney transplant; and none were kidney transplant recipients who were on dialysis (e.g., due to a failed transplant). (Figure 7; Appendix 5)

BACKGROUND ON IgA NEPHROPATHY

IgA nephropathy (formerly Berger's disease) is a rare disease, but it is the most common glomerulonephritis in the world.[1,2] IgAN affects the kidney's glomeruli, the microscopic blood vessels that filter the blood.

PATHOGENESIS OF IgA NEPHROPATHY

The causes of IgAN are becoming increasingly understood and have been reviewed recently.[1,2] For unknown reasons, patients with IgAN create an aberrant (poorly glycosylated) form of the antibody IgA (IgA1) that circulates in the blood in high quantities. The body's immune system recognizes this IgA1 as foreign and produces antibodies against it (anti-IgA1 antibodies). IgA1 and anti-IgA1 antibodies form immune complexes with each other and complement proteins in the blood. These circulating immune complexes deposit in the glomeruli, causing inflammation and damage. Because of this immune complex mechanism, IgAN is classified as an autoimmune disease. Further damage allows red blood cells and proteins to pass through the damaged filter into the urine.

There is evidence to suggest that genetic factors play a role in IgAN. It has been suggested that IgAN is a complex polygenic disease, meaning that there are many genes and possibly environmental factors that contribute to an individual's risk of developing the condition.

A large body of clinical evidence favors interpretations that IgAN and IgA vasculitis (IgAV) are related diseases,[3,4,5] different manifestations of the same disease,[6,7,8] or are on the same disease spectrum.[1,9] IgA vasculitis is an immune complex vasculitis that affects small vessels, primarily in the skin, gastrointestinal tract, and joints. In IgAV , IgA-dominant immune complexes deposit in these vessels, leading to inflammation and vascular damage. Symptoms include palpable purpura, gastrointestinal problems, including abdominal pain and bloody diarrhea, joint pain, and kidney involvement. Indeed, IgAV has been proposed to be a systemic form of IgAN.[10] Therefore, patients on the IgAN/IgAV spectrum are frequently burdened with multiple, burdensome, extrarenal symptoms.

EPIDEMIOLOGY OF IgA NEPHROPATHY

IgA nephropathy is the most common glomerulonephritis worldwide,[1] and while its clinical course is indolent in most cases,[11] IgAN is an important cause of end stage kidney disease (ESKD; formerly end stage renal disease, ESRD). The true prevalence of IgAN is unknown since diagnosis requires a kidney biopsy. The estimated incidence of biopsy-confirmed IgAN in the US is about 1 case/100,000

persons/year.[1] In a study of glomerulonephritis patients who were biopsied, IgAN was suggested to be the most common cause of ESKD in white, young adult Americans.[12] A community study in Kentucky suggested that males are 2-3 times more likely to be affected by IgAN than females.[13] Because the onset of IgAN is often in the second or third decades of life,[14] teens and young adults comprise a sizable portion of the disease population. Certain ethnic groups are at disproportionately high genetic risk, including East Asians and Native Americans.[15]

DIAGNOSIS OF IgA NEPHROPATHY

IgA nephropathy might be suspected when a patient has bloody (e.g., tea- or cola-colored) urine following a respiratory tract illness such as a sore throat or a cold. Laboratory tests will determine if there are abnormal levels of protein (proteinuria) or blood (hematuria) in the urine and will measure the levels of protein, cholesterol, and wastes in the blood. The glomerular filtration rate (GFR), which determines how well the kidneys are filtering wastes from the blood, may be low in advanced stages of the disease. Although a doctor may suspect that their patient has IgAN based on family or clinical history, physical exam, and urine and blood tests, a kidney biopsy is required for a definitive diagnosis of IgAN.

CLINICAL COURSE AND SYMPTOMS OF IgA NEPHROPATHY

The most common clinical presentation of IgAN is macroscopic hematuria, frequently concurrent with or following an upper respiratory infection. Some patients with established IgAN may also experience hematuria and other symptoms as flares when they have infections or even after exercise.

While the natural history of IgAN is highly variable and the disease typically follows a slowly progressive course, a recent study of 251 IgAN patients in the US reported that 53% progressed to ESKD over about 20 years. Life expectancy in this cohort was reduced by 10 years,[16] possibly related to chronic dialysis (R. Wyatt, personal communication).

In its early stages, IgAN is often asymptomatic. However, as the disease progresses, the most well-known life-affecting symptoms of IgAN are edema and fatigue. The latter is unpredictable, can last for several days, and does not correlate with the overall condition of the patient. Such fatigue can make daily functioning impossible. The severity of the edema is correlated to the amount of proteinuria, and often worsens as the disease progresses.

Other symptoms reported by patients[17] but that are not well recorded in the literature include low-grade fever or flu-like symptoms, flank pain ranging from a dull ache to debilitating spasms, and myalgias. Many patients also describe needing unusually long time periods to recover from colds, the need for plentiful sleep (12 hours or more per day), and mood swings. Patients sometimes experience strong or foul breath during periods of illness and fatigue. The effects of IgAN appear to be seasonal, being exacerbated in winter/spring. Children may lose sensitivity to temperature and may underdress for cold weather. Others experience extreme abdominal pain, which can be mistaken for appendicitis or renal colic.

CURRENT TREATMENT AND MANAGEMENT OF IgA NEPHROPATHY

There are currently no disease-targeted therapeutics approved for the treatment of IgAN. The cornerstone of current treatment approaches is to suppress the renin-angiotensin-aldosterone system with angiotensin receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACEi), or both to control blood pressure and proteinuria. Glucocorticoids (e.g., prednisone) are commonly used, and in some cases, immunosuppressive agents are prescribed. Some patients may also be prescribed a cholesterol-lowering drug (statin) to lower the risk of developing cardiovascular disease. Diet modifications such as salt reduction or the addition of omega-3 fish oil are also commonly indicated. Thus, care for IgAN is largely non-specific and supportive, often with resultant side effects, especially from glucocorticoids.

CURRENT RESEARCH BEING CONDUCTED TO DEVELOP NEW THERAPIES FOR IgA NEPHROPATHY

In the last decade, understanding of the etiology and pathogenesis of IgAN has increased to the extent that therapeutic interventions targeting pathogenetic mechanisms specific to IgAN are in development at several pharmaceutical companies. As of this writing, there are 25 planned, ongoing, or completed Phase 2 and 3 clinical trials in the U.S.[18] that cover a variety of potential mechanisms of action, including complement pathway inhibition, B-cell inhibition, improved corticosteroids, and combinations of renin-angiotensin system blockers and other agents.

TOPIC 1: LIVING WITH IgA NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS

In this session of the meeting, the emphasis was on perspectives from patients and care-partners related to the burdens of living with IgAN and the symptoms of this disease. The session began with personal testimonies from patients and care-partners living with IgAN. This was followed by perspectives from participants through polling of the in-person and remote audiences and then a moderated group discussion with the in-person audience. The patient input from this session is summarized below.

PATIENT TESTIMONIES

The full testimonies from each patient can be found in Appendix 3. Some of the most relevant and impactful comments made by each patient are presented below.

Maureen (Adult IgAN Patient):

> "I had trouble waking up in the morning. I became consistently late to work or calling in sick. I was always tired, puffy, cranky, and having to pee a lot without the feeling of emptying my bladder. **I never felt well.** This caused me to lose a full-time position in [the] hospital. **As my fatigue worsened, it became difficult to maintain my household and tend to my daughter**.
>
> "The symptoms that affect me the most now are fatigue, edema, insomnia, hypertension, vitamin D deficiency, and brain fog. Chronic fatigue is especially hard. You may look well on the outside. **Inside, you feel as if you are filled with lead. Even getting out of bed to get a drink of water can be difficult on a bad day.** Fatigue also makes monitoring of blood pressure difficult, even though it's necessary to do.
>
> **"…one time while driving, my [six-year old] daughter…saw me nodding off while I began to swerve off the shoulder of the highway. My child screamed, 'Mommy, wake up!'**
>
> "…I developed bone and mineral disorder…**I've spent thousands of dollars on failed root canals resulting in nine tooth extractions**…**My face has changed, and I don't like to smile anymore in pictures."**

Sue (Adult IgAN Patient):

> "There are a few symptoms that come with a disease that affect my life the most. The first is the **constant weariness**. It seems like I can never get enough sleep…If I'm in a meeting, I struggle to keep my eyes open. If I am staring at the computer too long, my eyes start to cross and close. I can accomplish a lot in the morning, but many days, by afternoon I can lose focus quickly. **It not only affects my days at work. It also keeps me from going out and enjoying evenings with friends.**

"When I had my first biopsy, one of the diagnoses was HSP [Henoch-Schönlein purpura]. It was several years before I was affected by it. It started with GI [gastrointestinal] symptoms, mostly cramping and diarrhea. Tests showed there were no problems with my stomach. Then I had itchy legs. Soon, there were small red dots on my legs, which eventually became very dark purple-red splotches. It was very painful, and I started experiencing lightheadedness.

"Something I have dealt with since I was treated with high doses of prednisone right after being diagnosed is heat intolerance. Heat never bothered me before, but **by the time I was done with the prednisone treatment, I could not tolerate anything above 75 degrees.** It has been that way now for 14 years without prednisone. **I truly suffer** and it makes me dread summer when I should be enjoying all the outdoor activities of the season."

John (Adult IgAN Patient):

"You never know waking up how the day is going to be. **While you may feel fine in the morning, the afternoon can change very quickly.**

"This disease is different for everyone. You never know what your next blood work will show. I've said to many people, 'I feel better than I did last month, but I won't know what's happening until the next blood work.' **The stress of waiting for the blood work results to come back, praying for no change or positive change**, is something I have to deal with on a regular basis."

Tim (Adult IgAN Patient):

"On my best days, I hardly notice it, with little fatigue, dehydration, or headache, and I appear to be a normal, healthy middle-aged man, even though I don't always feel that way. **On my worst days, I'm unable to get out of bed in the morning until the muscle cramping, pain, and fatigue subside.** If the onset is in the middle of the day, I need to stop whatever I'm doing, follow my daily treatment plan and hope the symptoms pass quickly…**I'm irritable to people around me** because I'm in constant pain and I have no control over it. **I become depressed** because it's a reminder of my chronic incurable disease that could shorten my lifespan.

"With every acute episode I suffer, I know irreparable kidney damage is occurring. **I'm not mentally sharp** because these anxious thoughts are fighting whatever task I'm supposed to be focusing on amid the mental fog that results from constant lack of quality sleep and energy.

"**The possibility of needing** frequent **dialysis or** [being] placed on **a transplant** waiting list **is frightening.** And in the case of transplant, there's a good chance the disease will reestablish in the transplanted kidney. As such, I'm constantly thinking about what's the healthiest possible option for someone with my condition."

Kimberly (Adult IgAN Patient):

"A major side effect of uncontrollable blood pressure are the headaches. Some days, it's a dull headache at the base of my head. Other days, it's a **debilitating thunderclap headache**…Sometimes the headaches go away. Most of the time they don't. **On the toughest days, I pull all the shades and lay in bed in complete silence with intermittent trips to the bathroom to vomit."**

Ryan (Pediatric IgAN Patient):

"2019 was supposed to be a really good year for my family and me. Instead I got sick with the flu (I thought)…I had the chills, sweats, and I couldn't eat because of the pains in my stomach. I was nauseous and had diarrhea. I was so tired I would sleep day and night. I started peeing a dark brown color. Then it started hurting when I went. That's when I told my mom. She about fainted. The look on her face told me something was wrong.

"I was put on a lot of medicine. Blood pressure medicine, stomach medicines, mood medicine, even a cancer medication. **Prednisone** is another one I'm taking, which has **made me very tired, moody, hungry, and mean. I even yell at everyone. I refuse to do what my parents ask. I am mean to my little brother.** I eat too much, and I know that it's the medication I am on [that] makes me super-hungry.

"I love to play baseball. I've been playing since I was four years old. Now I can't even play. I can't be in the sun a lot. The CellCept and prednisone drugs I have to take require me not to be in the sun for long, or I could get sick and then the medication won't work as well. Plus, it's way too hot. I get tired within 20 – 30 minutes. I'm so overweight I can't run.

School sucks. Kids call me 'kidneys.' And even the kids that I was cool with. I hate going. I don't have a life now."

POLLING AND MODERATED AUDIENCE DISCUSSION

The responses to polling questions for this session are summarized below. A full description of the polling questions and graphical representation of the results are presented in Appendix 4.2; and Appendix 5 respectively.

Commonly experienced symptoms of IgA nephropathy

Polling Questions #1, 2; Appendix 4.2

Participants were presented with a list of symptoms that are commonly associated with IgAN and questioned about which they had experienced (Figure 8; Appendix 5). This poll revealed that patients with IgAN experience a wide range of difficulties including being tired, exhausted, or fatigued (16%), anxiety and/or depression (15%), high blood pressure (13%), heat or cold intolerance or sensitivity

(11%), swelling (ankles, face, etc.; 10%), gastrointestinal problems (9%), high cholesterol (8%), recurrent infections and kidney failure/ESKD (5% each), gout (4%), and other symptoms (4%).

Participants were asked to identify which three of the symptoms listed previously (listed in Figure 8; Appendix 5) most negatively impact their daily life (Figure 9; Appendix 5). The most commonly chosen symptoms included being tired, exhausted or fatigued (30%), anxiety and/or depression (19%), high blood pressure (18%), swelling (ankles, face, etc.; 8%), and gastrointestinal problems (8%).

Psychosocial symptoms and general impacts of IgA nephropathy

Polling Questions #3, 4; Appendix 4.2

Participants were shown a list of psychosocial effects and asked whether they had experienced any of these while coping with their IgAN (Figure 10; Appendix 5). Patients with IgAN frequently experienced social and emotional consequences, including anxiety (23%), hopelessness (18%), depression (18%), social isolation (15%), low self-esteem (13%), and difficulty with relationships outside of family (13%).

Participants were also asked about general negative impacts on daily life related to IgAN (Figure 11; Appendix 5). Respondents most commonly reported that they felt that others did not know what it is like to live with IgAN (31%). Other concerns expressed were that their general daily function is limited (21%), they cannot participate in sports or other physical activities they enjoy (18%), family stress is common in their lives (15%), and they miss work or school more than they are comfortable with (14%).

The audience discussion that followed the polling questions was conducted in the context of the Topic Discussion Questions shown in Appendix 6. Participants confirmed and expanded on the responses to the polling. Patients and care-partners commented on the symptom burdens they bear—the top symptoms that most significantly affect their lives, the activities that are important to them but which they are unable to do because of IgAN, and the range of negative impacts their symptoms have on their daily lives.

The following is a sample of insightful comments that were made by attendees during the moderated audience discussion. Some comments were also taken from the post-meeting 30-day open comment period.

Major symptoms that most significantly affect lives

Discussion Question #1; Appendix 6

When participants were asked to discuss the top burdensome symptoms they experienced they reported being faced with a variety of symptoms, including fatigue, depression, and other difficulties.

> "…mine is fatigue…I'm just trying to sew a dress or something. It's taken me five weeks. It used to take me an afternoon. **I try to balance a checking account. That's a good three, four hours. I'm from banking. It used to take me 10 minutes…It's just getting increasingly worse"**

> "The worst [symptom] has been chronic anemia…As I got closer to end stage, **my anemia got worse I couldn't even climb a set of stairs without taking two to three breaks. I couldn't open a bottle of water."**

> "I think **depression** is for me the most [burdensome symptom] that I'm struggling with. I have **a new baby coming in a couple of weeks** and even as I picture all the activities that I want to have with him, **I don't see how I am going to have the strength to being [sic] with my baby."**

> "One of the things up there is **gastrointestinal. It's so unpredictable**, and so that is a fear. It's constant. The **vomiting constantly**, daily. That's our [patient and care-partner] biggest."

> "I get sick at the drop of a hat…"

> "I'm a caretaker, **[my husband] had awful bouts of gout**…he has depression to begin with…and he also had cellulitis along with the gout. The regular medicine doesn't help him…**it causes him to have to sleep in another room, sometimes feet elevated, icing his feet every day. And the depression that it causes him is unbearable.** And the people that live with them [sic], you're heartbroken. I don't know what else to say about that. It's just, I feel like three [bouts] in two months is an awful lot."

> "I can't stress enough the toll this disease takes on my life. **EVERYTHING changed."**

Sleep-related issues were commonly discussed

> "I can say that **in the last, probably, 13 years since I was diagnosed that I've had two days where I have actually felt good and that was because I actually had two good night[s] sleep** within that period of time."

> "I fall asleep at the drop of a hat. I can't tell you the last time I ever was able to watch a show on TV. It's just that everything is impossible and I'm getting tired. I'm sorry. I'm getting tired of it. **I'd like to live again. Even my grandchildren won't come over anymore because Grammy keeps falling asleep** and I'm not as fun as what I used to be."

> **"**I think for the first time I've heard several people talk about insomnia with this disease and I have suffered with that for about 20 years, and of anything, not getting sleep is so critical to how you function every single day. I feel tired all the time and it really limits what I choose to do because I know that I only have so much energy and so that means I don't get things done that I'd like to do.**"**

> **"...**when I was really sick, **I could sleep 12, 14 hours a day and still feel like I'd been hit by a ton of bricks."**

Flare-ups were discussed at length. Participants were asked to identify factors that provoke flare-ups and to describe how they feel during such episodes. These periods of heightened symptoms were reported as causing, and resulting from, IgAN-associated anxiety.

> "**What I find triggers a flare up is stress-related issues**…anything from not having sleep to stressful things going on with work or home. And…illness, any kind of cold…flu season is the worst time and even when you're not sick, you're fighting something…and that causes a lot of flare up[s], as well."

> "Overall, just a feeling I get kind of pressure and throbbing. I know my kidneys are a little off if I'm not peeing as normally. Also fatigue and possibly cola-colored urine."

> "…I feel worse [during a flare-up], but also the anxiety and stress; it's kind of like a circle…if I eat salty foods or something that I'm not supposed to, that also will...trigger me not to be feeling well with my kidneys."

> "I was having a good couple of months where everything was under control, so I decided to participate in a Tough Mudder [fundraising event]. And that was a really bad decision because...I was out of work for two weeks just because with the muscle spasms and my hypertension was [sic] out of control."

Reduced ability to conduct activities because of their IgA nephropathy

Discussion Question #2; Appendix 6

Participants were questioned about activities that were important to them, but which they could not do at all, or as fully as they would like. Audience members discussed a spectrum of activities that they were unable to perform or could perform only with difficulty.

> "My heat intolerance, and it's really hard on me in the summers because I love being outdoors and I can't [go out]…Currently I'm staying with my [elderly] parents and my mother is always cold…they set [the thermostat] at about 73 and I mean, I can't do anything. I start washing the dishes and I'm just miserable and my hair gets soaking wet…"

"My child cannot go to school any longer. I now have to homeschool her because of missing so many days and failing classes because the teachers don't understand…She was so exhausted. If she went to school all day, then she would come home and sleep. So, then she couldn't do homework, then she couldn't go to dance. She couldn't do all the things that she loved, and so it was a give-and-take."

"…I [went on] dialysis…kind of destroyed every plan you had."

"Stopped working; I'm sick all the time. If it would affect one part of your life, that would be one thing, but it just affects everything."

"Working as an account manager, most of our real business relationships happen after business hours, so **it's hard to explain to your clients that you can barely walk because you have a gout attack in your toe** and at the same time you keep yawning and yawning. And for them, it's just…you are not interested in making this business relationship."

"I always feel tired because of this disease and I don't have enough energy to even play with my 2-year-old daughter…**I have lots of dreams,** like to travel to beautiful places **but this disease is stopping me from planning because it feels like my life is about to end any time.**"

"I've been dancing since I was three and before I went into nephrotic syndrome two years ago, I qualified for point and that was my goal. So, I went with my friend to get fitted. I didn't get the point shoes."

"**While [I was] in end-stage with IgAN,** we were unable to travel…We had family both three hours and six hours away and couldn't even travel that far to see them…that was significant for us, not being able to go see friends or family, but instead of pleading with them to come see us…**I couldn't go to med school during that time.**"

"I try to supplement income with my art and doing craft shows…many of them are in the summer and I can't do them because they're outdoors and I can't tolerate [the heat]…it's just not being able to enjoy things. It's really hard."

Impact of symptoms on patients' daily lives on the best and worst days

Discussion Question #3; Appendix 6

Participants recounted the impact of their symptoms on their best and worst days, revealing a variety of difficulties.

> "I started…to be scared of my next appointment with the doctor and the laboratories [laboratory results], **I got to a point that I called to cancel my appointment because I was afraid to get the results and tell my family that I was doing really bad.** It's been affecting me in a very horrible way."

> "I feel like I might be the only 23-year-old on the planet that doesn't drink, especially living in, like, Southern California. It's interesting socially because I get anxious—like, telling someone I have a disease, because I don't want to be looked at, like, 'Oh, you have a disease. I feel bad for you.'"

> "The other thing is with the job; he's [son] trying to climb the corporate ladder and he doesn't want anybody to know about [his IgAN], so he really hides his disease. He's not really proactive because he's afraid and it's tough…"

> "…the difficulty with relationships outside of the family is a big piece of it, because I think our disease…like a lot of chronic conditions, it's invisible. So, it's, 'You don't look sick.' That's the most common thing you hear. You don't have any symptoms. And so, it's challenging to open up and be vulnerable with people about this disease and to bring people into your circle."

> "All-in-all his quality of life, as well as that of his family has truly suffered. **He hasn't had a job in at least 10 years. He and my sister seem to constantly fight.** He can never take part in the kid's trips or vacations because he is too tired or has to be back for dialysis. Even just something as simple as mowing the lawn is impossible."

How patients' condition and its symptoms have changed over time

Discussion Question 4; Appendix 6

Discussants revealed how their disease has changed since they have received their diagnoses. Descriptions included changes in symptoms and emotions.

> "I went into the doctor [and] said, 'Will give me something? I've had this tiredness.' It had been going on before 2012. **It's just getting increasingly worse.**"

> "So I think one of the things that's hard is that when you have IgAN and you have these bouts of good and bad moments…just because you feel good, you have to remember that self-care…that you're going to trigger something if you push yourself too far…Even though you feel good, internally there are things that are going on."

Participants' most important worries about their IgA nephropathy

Discussion Question 5; Appendix 6

When patients were queried about what worries them most about their IgAN, they discussed a spectrum of concerns, the common thread being uncertainty for the future.

> "Something that's got me worrying right now is I start a new job on September 9th and my big worry is **how are my new employers going to take, if I start having flareups again…If I start having to go to doctors again often**, how are they going to take that?"

> "We all like to believe we can [sic], if we do the right thing, if we eat well and take our medication, everything is going to be fine. We want that assurance. But it feels like with this disease…you can do everything right and you will have a flareup…and so that kind of increases your anxiety because you don't know whether you're going to have a flare up or not."

> "He [son] has been stable, but as you know how unpredictable this disease can be, that can change at any time. Just when I feel everything is going good [sic] I always have that thought in the back of my head that he may get worse. He is only 21 and I worry about his future."

> "And I also worry as **being a single person with no children that my future…if I end up going on dialysis,** if I end up getting worse—**who's going to take care of me?** What's the insurance situation?"

> "So, I guess my worry in the future is how expensive is this going to become? Will I be able to afford a kidney transplant if I have to have one? What will dialysis cost?"

> "I was lucky enough a year ago to get a transplant. And **my biggest worry is whether or not my kidney is going to continue to work—I already had one rejection—and whether or not the IgAN will affect my new kidney.**"

> "So now that I'm going to be working with the public again, am I going to be picking up things again? There's [sic] a lot of fears for me, as far as it goes."

> "I was in remission…up till last year I actually had my first flare up. And what worries me now is that this was caused by stress that I actually internalized and I…never…told people what was stressing me out. And…what freaks me out now is having to go through that again."

TOPIC 2: CLINICAL TRIALS FOR IgA NEPHROPATHY UNDER TRADITIONAL APPROACH

This session sought to explore the IgAN community's willingness to participate in various types of clinical trials, with a focus on the requirements for trials designed using the Accelerated Approval Program.

The session began with an introductory presentation on traditional clinical trials and those designed under the Accelerated Approval Program. Then, a series of polling questions were posed and subsequently explored further in a moderated discussion toward understanding patients' views on enrolling in clinical trials. These discussions were guided largely by the responses to the polling questions and by Discussion Questions #1 (Topic 2) and Questions #2, 3 (Topic 3); Appendix 6.

POLLING AND MODERATED AUDIENCE DISCUSSION

Responses to the polling questions from this session are shown below, followed by comments made during the moderated discussion for each question. The polling questions and graphical representation of the responses are depicted in Appendices 4.3 and 5 respectively (Figures 12–17).

Patients' experience with, and perception of, clinical trials for a new drug for IgA nephropathy

Polling Question 1; Appendix 4.3

When asked about their experiences with clinical trials, participants revealed a range of involvements.

Most of the respondents reported that they had not participated in a trial because they did not know about the opportunity (48%) or they were not eligible (34%). Nine percent of respondents had participated in a trial and would do so again, 4% were participating in a trial at the time of the meeting, 3% were unsure of their answer, and 1% had not participated in a trial, although they were aware of the opportunity and eligible. None of the respondents reported that they had participated in a trial and would not do so again or that they would never enroll in a clinical trial.

> "I had a very good experience with mine…I lived three hours away from Columbus [OH], but I was going back and forth down to Columbus to be able to do this study and it was very positive."

> "My daughter is 15. She is not eligible for a clinical trial. She has tried every drug that is out there, and she is treatment resistant. I would put her in a trial tomorrow just for the hope of slowing this disease down. **We need you to allow younger ages in these trials. We parents are desperate.**"

> "The first time that I applied to do a trial, I was already in end-stage renal [kidney] disease and was waiting for a transplant and I was denied because of that…I have now had my transplant for nearly two years and have applied for another, but had been denied and termed **ineligible because I've had my transplant even though I have recurrent IgAN**..."

> "I was not eligible due to not having a biopsy in the last five years and a bad experience going through the first biopsy with a lot of pain, discomfort for a week or so afterwards…Going through the biopsy the second time was definitely worth it to try and get into a study because there was nothing else that's [sic] out there."

Most important factors for deciding on whether to participate in a clinical trial

Polling Question 2; Appendix 4.3

Participants were presented a list of twelve factors from which they were asked to select five as the most important for deciding on whether to participate in a clinical trial. (Figure 13; Appendix 5)

The most common responses to this polling question were: potential side effects from a new drug (20%), followed by the possibility of receiving placebo/sugar pill (15%), distance to trial site (11%), the need to stop current treatment (9%), if the study drug was effective in an earlier trial for specific benefits most meaningful to patients (9%), whether a kidney biopsy is required (8%), the frequency of exam appointments (8%), and knowing if the patient can make the commitment to participate (8%).

> "**I think if the side effects were similar to prednisone** or, in particular, would not go away when you stop taking the drug…**I actually probably would not do it then.**"

> "**I'd be careful whether it was going to affect…[my] new kidney transplant.**"

> "With the trial that I tried, within two days of taking the new drug, I broke out in a rash, which is par for the course when I ever try new drugs. I told them… 'I'm willing to continue because it's not itching yet. If it starts itching and I start being miserable,' I said, 'Who knows? Maybe it'll go away,' and they said, 'Absolutely not. Discontinue now.'"

Patients' preferences for enrolling in a clinical trial that required kidney biopsies

Polling Question 3; Appendix 4.3

Participants were asked to select the greatest number of biopsies they would endure. (Figure 14; Appendix 5)

Sixty-two percent of respondents indicated that they would enroll in a clinical trial if one kidney biopsy was required within one year. If two or three kidney biopsies were required within one year, 12% each would enroll. Surprisingly, only 13% of respondents reported that they would enroll in a trial if no kidney biopsies were required.

> "…I do want to try to benefit everybody, but there's also the risk with the kidney biopsies, whether we have it one time or…five times. So, putting ourselves and our kidneys with whatever preserved function we have at a greater risk for complications, that's my reasoning for one [biopsy]…If maybe we had really good statistical [information on the] significance of the medication and that it really is impactful…I might push to two…the biggest issue is the…possible damage to the kidneys…"

> "I was going to go into another drug trial, but they required a second biopsy for the trial and unfortunately my biopsy failed in a rather dramatic fashion, we'll call it. So, I'm gun shy of doing another biopsy."

> "I was…nervous about getting the second biopsy because the first with [sic] a lot of pain, days laying [sic] in bed, etc. and I think the technology has gotten better to do it. **I still would not do more than one in a year**, just obviously for the risks…"

TOPIC 3: CLINICAL TRIALS FOR IgA NEPHROPATHY UNDER ACCELERATED APPROVAL PROGRAM

POLLING AND MODERATED AUDIENCE DISCUSSION

To understand patients' willingness to enroll in a clinical trial conducted under an Accelerated Approval Program, the following hypothetical study design was provided. This introduction was followed by polling questions.

You are considering whether to enroll in a randomized, double-blind clinical trial for a potential drug for IgAN:

- The first phase of the trial will evaluate whether the treatment lowers proteinuria.
- If the trial shows a large enough effect on proteinuria, the drug will be approved under the Accelerated Approval Program.
- To verify that the product slows the loss of kidney function, patients who enrolled in the trial must remain in the trial in their assigned treatment arm for one to two more years for the post-marketing extension phase.

After the above introduction, patients were asked a group of polling questions to reveal their willingness to participate in clinical trials designed and executed under the Accelerated Approval Program. The polling questions and ensuing audience discussions concentrated on uncertainties related to this type of clinical trial.

Patients' views on enrolling in a clinical trial under the accelerated approval program and remaining through the post-marketing extension phase

Polling Question #4, 5, 6; Appendix 4.3

Participants were asked how likely they would be to enroll in a clinical trial under the Accelerated Approval Program and remain through the post-marketing extension phase with the understanding that they could be in the placebo arm. (Figure 15; Appendix 5)

In response to this polling question, 44% of respondents answered that they would be very likely to enroll and remain in this trial. Thirty two percent were moderately likely, 18% were somewhat likely, and 6% would not enroll in the trial.

During the discussion around this question, participants revealed the dominant factors determining whether they would enroll and remain in this trial. These focused on the potential for side effects from the test agent and concern over replacing current therapies with a placebo. Patients also expressed fear of compromising their remissions. The lack of current effective treatments and a sense of altruism also factored into their decisions.

> "…my reasoning behind…not wanting to participate is…**when I stop [cyclosporine]**, even though my [proteinuria] levels are so low, **I come out of remission** within about…a month and a half. So, **in the double-blind study, that's such a great risk…coming out of remission and…causing even further damage...If there was a possibility of you staying on your own treatment regimen and the new medication**…to enhance what you already have in treatment, **I would be more apt to do that.** Because I would at least still be on my…current treatment regimen." [Further queries to this patient by the moderator elicited:] "100%, I would [enroll]. If I got the standard of care, what I'm usually doing now plus the [treatment arm]."

> "…medications I'm currently on...[are] providing me with a great deal of benefit, particularly around my blood pressure. So, if I had to go off my current meds, I would not be willing to participate. And I currently don't have very many side effects really from my current medication. So if this new medication, **if I did experience [from the test agent] a lot of side effects that were significant…that would be a factor as to whether I would be willing to stay in the study**…in a long-term basis…as long as already I hadn't experienced a lot of uncomfortable side effects or significant side effects, yes, I would stay in the study."

> "I think the reason why I wouldn't want to be on a placebo is because time is very crucial in this disease. It could progress, you know, at any time. Because you just always fear that your kidneys are going to fail…And you don't know how much time you have. So, I feel like it would be a loss, you know?"

> "Number one [concern is] about existing treatments and how the new drug would interact with the existing treatments. Number two, in my case, my kidney function was pretty steadily declining over time, probably over two years to the point where I needed a transplant. And at that point, I wouldn't know if I'd be able to take the drug or continue to take it or I'd have to be out of the study. And then I would possibly endanger the efficacy of the study by withdrawing and not having enough people to maintain the study afterwards."

> "…my 'yes' is, again, because **my daughter is not responding to any other treatments, so why the heck not?** "

> "I'm currently in a remission and so I would…consider myself not eligible because I don't have active disease right now."

> "I said yes, I'd be willing to…it's kind of that group effort to actually get the drug out to market. So…I would be willing to do it even if I was on the placebo arm."

One discussant indicated that the extra level of uncertainty associated with the extension phase of an Accelerated Approval Program clinical trial would prevent her from participating.

Participants were reminded that if a drug shows large enough effect on proteinuria, it would be approved under the Accelerated Approval Program. But those in the study would be asked to stay in that trial for one or more years during the post-marketing extension phase after the drug is on the market and available to the public**. They were then asked for how long they would stay in their assigned treatment arm of a post-marketing extension phase of a clinical trial.**

Fifty-one percent of respondents responded that they would remain in their assigned treatment arm for one year, 28% would remain for two years, and 10% would remain for three years. Eleven percent responded that they would not remain in their treatment arm for any time during the extension phase. (Figure 16; Appendix 5)

Discussants voiced enthusiasm about remaining in a post-marketing extension phase, even with the possibility of receiving the placebo.

> "…if she [daughter] does end up with the placebo and has to stay on it, I said for a year. Just because nothing's working anyway, so why not try something that could, and could benefit others as well [?]"

> "I would be willing to do it even if I was on the placebo arm…two years, maybe three."

> "Personally, my numbers are pretty good, so I would be, you know, more than happy after meeting a lot of people in this room that struggle a lot worse. You know, it's…a couple of years I could give and try to help others."

Participants were then reminded that drugs approved under the Accelerated Approval Program may be removed from the market if the confirmatory trial fails to verify the previously shown benefit. If a significant number of patients drop out of a trial during the post-marketing phase, the trial results may be difficult to interpret, and the trial may fail to verify the benefits.

With this now in mind, **participants were asked how likely would they be to enroll in this clinical trial and remain throughout the post-marketing extension phase bearing in mind that premature**

discontinuation from the trial could jeopardize the results of the trial and marketing status of the drug? (Figure 17; Appendix 5)

In response to this polling question, 76% of respondents replied that they would be very likely to enroll and remain in this trial. Nine percent were moderately likely, 7% were somewhat likely to enroll, and 8% would not enroll in the trial.

The audience discussion confirmed patients' willingness to enroll and remain in a post-marketing extension phase trial. In particular, their reasoning included a desire to contribute to the IgAN community.

> "…this is one of those where it's kind of that group effort to actually get the drug out to market…**I would be willing to do it even if I was on the placebo arm**…two years, maybe three."

> "So at the rate of progression of this disease, at that rate of spillage for me, I know that if I can play out another two, three years maximizing my therapy, my angiotensin receptor blocker, I absolutely am most likely to stay in the study so we can hit the primary efficacy end points. For sure, absolutely."

> "Are we willing to take the risk? I know I am. I know everybody else in this room is. We have very promising agents right now, very promising. Whether they're phase one, phase two or entering phase three. And there is a huge gap in the treatment of this disease. You listen to everybody in this room talk about prednisone and how it affects our lives. The children, kidney transplant, dialysis, all this."

Patients' views on gathering relevant evidence from clinical trials for IgA nephropathy

Polling Question #7; Appendix 4.3

Participants were presented with a list of possible parameters that could be measured in a clinical trial (traditional or Accelerated Approval Program) and asked which three of these parameters they considered relevant to their IgAN. (Figure 18; Appendix 5)

The most common response to this polling question was kidney function (GFR, 29%), followed by protein leakage (proteinuria/albuminuria, 26%), delaying time to dialysis or transplant (26%), and general quality of life (9%).

TOPIC 4: CURRENT CHALLENGES TO TREATING IgA NEPHROPATHY

The objective of the session was to understand patient's views on the efficacy of current treatments and what attributes for new medicines patients desire. The patient input from this session, which included patient testimonies, polling, and moderated discussions with the in-person audience is summarized below.

PATIENT TESTIMONIES

To understand the perspectives of IgAN patients regarding current and desired future treatments, a panel of patients shared their thoughts and experiences with these points. The full testimonies from all patients can be found in Appendix 3. Samples of the most relevant and impactful comments made by each panelist are below.

Lillie (Pediatric IgAN Patient):

> "The **prednisone made me gain 40 pounds in three months and gave me really bad acne**. As a teenager, that was horrible. **Kids made fun of me all the time**…
>
> "**My kidney disease isn't what makes me feel bad all the time. It's the medication side effects that make me feel awful.** I have to go to physical therapy because my joints and bones are deteriorating from the long-term use of prednisone. My hips are out of alignment and I have to walk with crutches at times.
>
> "I take a multivitamin, calcium and vitamin D twice a day; Protonix for my stomach aches the medicine causes; CellCept twice a day; Zoloft; lisinopril; iron; melatonin to help me sleep; and birth control to control my hormones since they're all messed up from other medications."

Barb (Adult IgAN Patient):

> "I was originally given lisinopril, but I could only take it for a week because the side effects of extreme tiredness and dizziness were totally intolerable. At the same time, my diabetes drug was changed from metformin to glimepiride. In the hospital, I was given blood. Due to the additional blood not working, I was given iron tablets…They made me vomit all day, so I was put on Venofer…
>
> "When my veins collapsed from the Venofer treatments, I had a venous port inserted into my chest. The first port failed due to a blood clot in the tube. The second port became necessary and I was put on to Coumadin, which requires an INR test twice a week to regulate the dosage. Difficulties regulating the Coumadin led to a change [to] Xarelto...While I'm on Xarelto, I have to go in monthly to confirm that the port is giving of [sic] blood and to get heparin injections in the port for maintenance.

"To help slow the progression of my IgAN, it is imperative that I control my blood pressure, diabetes, and cholesterol, and limit my sodium intake…I take calcitriol to control my hyper-parathyroidism and I take omega-3 to control cholesterol and to slow the progression of IgAN."

Chris (Adult IgAN Patient):

"…I focus on regular exercise and maintain a healthy but realistic diet. For extra measure, I've completely cut out alcohol, red meat, protein powders, and dairy products from my diet. I'm not certain that the absence of these items will improve my prognosis, but **I'm willing to try anything that will allow me to live a full and healthy life because this is really the only aspect of having this disease that I feel I have control over**…

"Assuming there is no complete cure for IgAN, I wish for a medication capable of slowing its progression and relieving its physical burdens. Eliminating the hematuria, proteinuria, and fatigue would significantly improve my daily life. However, if I had to choose, **I would prefer a drug that slows the progression of the disease over any other symptom treatment because I'd choose a long life with pain and adversity over a short life.**"

Karen (Adult IgAN Patient):

"**My nephrologist prescribed 80 milligrams of prednisone a day** for six months saying that it would cure the disease and enable me to get pregnant again. A month into the prednisone regimen, **I got prednisone-induced diabetes; I gained 70 pounds; had major joint issues; and could barely walk due to the extreme swelling in my feet and ankles from all the treatments**...

"Being told IgA[N] may lead to dialysis and a transplant at age 65 turned into [me] being diagnosed and then six months later after starting prednisone, I needed a transplant…Things were going well after my transplant. My labs were amazing, and I felt great, but at a one-year biopsy it came back that IgAN had in fact, moved into my new kidney…**I am terrified of reliving being told that I might again need dialysis or a second transplant**...

"I would love to have options to cure this disease or medications that actually slow the progression and reduce symptoms that come with it. I would be interested in a clinical trial for post-transplant patients, but I would not want to do anything to harm my new kidney or to cause any additional side effects than I already have."

Kimberly (Adult IgAN Patient):

"In hopes of stabilizing my kidneys, I was prescribed prednisone. For over six months, I took 60 milligrams daily. Initially, my proteinuria and my hematuria decreased…At about five months into treatment, I had 25 pounds of weight gain, my face ballooned, and of course, I got the notorious fat hump at the back of my neck. What I didn't expect was the furry face, tooth sensitivity, missed periods, and sleepless nights."

> "Over the last nine months, I've taken labetalol, losartan, benazepril and hydrochlorothiazide for high blood pressure…These medications wear off by the afternoon. We've tried splitting the doses between evenings and mornings, but that hasn't seemed to help much."

POLLING QUESTIONS AND MODERATED DISCUSSION

Patients' current treatments and their efficacies

Polling Questions #1, 2, 3; Appendix 4.4

In this portion of the meeting patients were asked about treatments they currently take and how effective these therapies are.

Participants were shown a list of drug classes generally relevant to IgAN and were asked to identify which medications they take.

The most common answer to this question was blood pressure drugs (33% indicated ACE, ARB, beta-blocker, "water pills," others), followed by other drugs not listed as options, including non-prescription remedies (23%), drugs affecting the immune system such as anti-inflammatories etc. (17%), statin or other drugs for cholesterol (13%), and anti-depressants or anti-anxiety drugs (7%). (Figure 19; Appendix 5)

> "What I would say if we went around and asked every single person in this room what was their regimen…to treat the disease. We probably end up at about 90 different responses."

When asked how well patients' current treatments reduce their most significant symptoms, 46% of respondents answered that their treatments reduce their most significant symptoms "somewhat" and 23% responded "moderately well." Only 14% responded that their treatments reduce these symptoms "very well" and 13% believed they have no effect at all. Four percent of respondents did not currently take any treatments. (Figure 20; Appendix 5)

The audience discussion validated the responses to this latter polling question and participants lamented that their treatments did not adequately reduce their most significant symptoms. Indeed, most of the discussion focused on alternative therapies that patients took to find relief from symptoms.

> "Something that I've been off and on seven years since treatment or since diagnosis was a plant-based diet…Every time I do eliminate the extra animal protein it does help."

"But whenever I went back on to a plant-based diet, I saw my proteinuria drop from 1400 down to now 700…and my GFR has gone back above 60."

"…speaking about blood pressure, the only thing that has been working for me, is when I'm on my ideal weight. **I've been taking olmesartan, losartan, benazepril…they never make any difference on my blood pressure.** Everything depends on if I had a long walk in the morning… when I removed the meats, it's when I feel the best."

"And for my joints there is a root that is called turmeric. And that thing just works. I don't know how, but the pain is gone, and I feel really good about it."

"…meditation and yoga has [sic] been a really big thing for me. Especially yoga, with the inflammation…[and meditation for] symptoms with mental health, and anxiety, and the stress."

"I took CQ-10…and also I juiced a lot in addition…I think it did help a lot. I went to a whole foods diet, eliminated all nitrates, nitrites, and anything that had preservatives in it. …I also use ginger, curcumin, nettle tea, take vitamin D with K, minerals…I think, if I'm diligent…it helps a great deal [with inflammation]. Even the herbal remedies and everything. It helps a great deal. …I overall felt more energy. I felt good. I felt less toxicity in my body. And I felt like I was protecting my cells. I felt good about what I was doing psychologically."

"Over the course of my disease I tried numerous treatments. I tried tonsillectomy, prednisone, which just left me with a 40-pound weight gains [sic], stretchmarks, and it didn't help. I tried to Acthar injections. I tried a vegetarian diet, gluten-free diet, and I ended up on the worst treatment…Hemodialysis."

"A lot of people think that you feel better on dialysis, and you don't. I would get blood pressure highs and lows, so that I would be puking on the machine. And I'd have to end my treatments early. I would be so fatigued. I would come home and just go to sleep."

Participants were shown a list of symptoms commonly associated with IgAN and asked which of these symptoms are not addressed by their current treatments.

Respondents ranked the top four symptoms not addressed fully by current treatments as follows: being tired, exhausted, or fatigued (26%), anxiety and/or depression (14%), other symptoms not listed (13%), and heat or cold intolerance or sensitivity (12%). (Figure 21; Appendix 5)

In addition to reporting a lack of efficacy of certain therapies, patients frequently mentioned side effects from their current treatments, most notably prednisone.

"…**nothing helps with the chronic fatigue."**

"So not only am I fighting symptoms from IgAN, **I am also fighting symptoms from the many medications that doctors aren't sure are actually helping**… We need research and funding to find ways to stop the problem from [at] the source."

"**I've had an 80-pound weight gain due to…prednisone**, and now I can't get rid of it. **I have an irregular heartbeat. One day it's tachycardia, next day it's bradycardia. Next day I'm having a-fib**…"

"Treatments that have failed me is [sic] taking prednisolone, as my body was not responsive to it. I've been taking it around 1.6 years, but nothing changed and protein and blood in urine still exist. My side effects that I hate most during current treatment is [sic] I've put on weight, my face is round, I always feel hungry, and gout due to uric acid is increased."

"I have body aches, especially from the **residual side effects of prednisone treatment six years ago**, such as torn muscles, muscle and joint aches. Tearing of the muscle led to missing work, physical therapy, as well as pain I felt from simple things, such as walking. I've always been into sports but never had any injuries such as those that have resulted from prednisone treatment for IgAN."

"…I had prednisone-induced diabetes and also prednisone-induced glaucoma."

"…for me it was more of the side effects of the medication than it was the symptoms of the disease. I mean, prednisone certainly made me moody. I put on 25 pounds and had lots of aches and had to go through several procedures to make sure all my bones and hip is [sic] still in place and there was no degeneration."

"…there was [sic] several ACE inhibitors that I had taken…I had to change because of the horrible side effects. So, it's not only prednisone, but the **blood pressure medicines that are the first line of defense. And some of them are intolerable.**"

"**It's over 50% of patients in this room are getting no help or very little.** Gosh guys, please listen, please. That's all I can say."

"**I remember leaving the hospital after my son was diagnosed and I asked my doctor, 'What is next?' And she simply said, 'just pray.' It shouldn't be the answer.**"

"**Prednisone has altered my life** so much that I didn't want to burden anyone. **I stayed alone and single for eight years.** I isolated myself because of the effects of prednisone and sometimes **I wonder, 'What if I didn't take it?**'"

"I was on prednisone for about five months…it did not help me at all."

"But you can't just stop it [prednisone], because more terrible things could happen to you."

> "The only good thing that happened being on prednisone… I had chronic asthma and in eight years I have not had an episode of asthma after being on that high dosage."

Patients' views on the risk vs. benefit of taking a new drug

Polling Question #4; Appendix 4.4

To uncover how patients think about balancing risk and benefits of new treatments, participants were asked the following question:

If the side effect profile of a new drug was more severe than you currently experience with your treatments, but clinical evidence indicated that the drug would significantly slow the progression of your disease and/or improve your quality of life, how likely would you be to take this drug?

Under this scenario, 40% of patients responded that they would be very likely to take this hypothetical drug, 26% would be moderately likely, 24% would be slightly likely, and 11% would not consider taking it. (Figure 22; Appendix 5)

> "I think that for me the biggest thing would have been disease management without the use of steroids...the use of prednisone with the amount of side effects that come with it is unfortunate."

Confidence in taking a new drug for IgA nephropathy

Polling Questions #5, 6, 7; Appendix 4.4

This set of polling questions probed patients' perspectives on deciding whether to begin a new therapy. Patients were shown the following scenarios and asked about their feelings on taking a new drug for IgAN.

You are deciding whether to take a new (recently FDA-approved) drug for your IgAN. Would you feel confident basing your decision to take the drug if it was approved based on evidence indicating that it reduced proteinuria?

In response to this polling question, 86% of respondents answered that they would be very confident, 13% would be moderately confident, 1% would be somewhat confident in taking the drugs. None of the respondents would have no confidence in this evidence. (Figure 23; Appendix 5)

The discussion then focused on the 86% of respondents who indicated their confidence in taking a drug that was approved based on proteinuria. Asking for a show of hands, the moderator queried whether the latter group would take the drug if it had only a 50% chance of being meaningful to them. Few, if any participants indicated that such uncertainty would negatively affect their decision to take the drug.

You are deciding whether to take a new (recently FDA-approved) drug for your IgAN. Would you feel confident basing your decision to take the drug if it was approved based on evidence indicating that it slowed the rate of loss of kidney function?

In response to this polling question, 92% of respondents reported that they would be very confident, 7% would be moderately confident, and 1% would have no confidence in taking the drug. (Figure 24; Appendix 5)

You are deciding whether to take a new (recently FDA-approved) drug for your IgAN. Would you feel confident basing your decision to take the drug if it was approved based on evidence indicating that it improved how patients feel, function, and/or survive?

In response to this polling question, 76% of respondents indicated that they would be very confident, 21% would be moderately confident, 1% would be somewhat confident and 1% would have no confidence in taking the drug. (Figure 25; Appendix 5)

Preferences for future drugs for IgA nephropathy

Polling Questions #8; Appendix 4.4

Finally, patients were asked, without considering side effects of a drug, which one of the following 1) reversing the decline in kidney function, 2) improving quality of life, or 3) prolong life, would be most important to them in a future therapy?

Eighty-seven percent of respondents responded that evidence that the drug would reverse decline in kidney function (i.e., halt progression of IgAN, delay the need for dialysis) was most important. Nine percent replied that improving quality of life or preventing future reduction in quality of life was most important, and 4% replied that prolonging life was most important. (Figure 26; Appendix 5)

"I think the most important thing to me would be something that would slow the progression of the disease. I was on a heavy regimen of prednisone for three years in order to try to keep my kidneys going as long as I could and then I had to have a transplant."

"**It would be the halting and slowing the progression of the disease process** in turn that will correct the others [symptoms]. It'll prolong your life. It'll give you a better quality…I don't want to go on dialysis."

"…for me the biggest thing would have been disease management without the use of steroids."

"I mean it's a trade-off—do you want to live or do you want to look good at that point?"

"[I] just turned 30 and my son's two and a half, so I want to have a good, strong quality of life."

CONCLUSIONS

In this EL-PFDD Meeting on IgAN, patients recounted their symptom burden, experiences with treatments, and their willingness to participate in clinical trials. Their voices support the following conclusions:

- The symptom burden of IgAN is great; it has a significant impact on daily life of patients.
- The majority of IgAN patients and care-partners do not consider that their current treatments adequately address their symptoms
- Patients expressed willingness to enroll in clinical trials for IgAN in traditional clinical trials and those designed under the Accelerated Approval Program. Moreover, they were willing to enroll in such trials despite the possibility of assignment to a placebo arm and they were willing to remain in trials during post-approval extensions.
- Some of the patients' primary concern regarding enrolling in clinical trials was possible side effects of a test agent. However, there was significant enthusiasm for taking a new treatment that has side effects greater than current treatment but that shows promise to slow IgAN progression and/or improve quality of life.
- Patients expressed hope for, and would have highest confidence in taking, treatments that prevent decline in kidney function (preventing reduction in GFR and prolonging time to the need for dialysis or kidney transplant).
- Overall, this meeting revealed the urgency for developing efficacious and safe treatments for IgAN. The IgAN patient community is willing to participate in clinical trials to test such agents.

PRELIMINARY BENEFIT-RISK FRAMEWORK PROPOSAL FOR IgA NEPHROPATHY

Benefit-risk assessment is the foundation for FDA's regulatory review of human drugs and biologics. These assessments capture the Agency's evidence, uncertainties, and reasoning used to arrive at its final determination for specific regulatory decisions. Additionally, they serve as a tool for communicating this information to those who wish to better understand FDA's thinking. Background and guidance on benefit-risk assessments can be found at the following link: *https://www.fda.gov/industry/prescription-drug-user-fee-amendments/enhancing-benefit-risk-assessment-regulatory-decision-making*

The input provided by people with IgAN and their representatives at the EL-PFDD Meeting was used to prepare the preliminary benefit-risk table on the next page. This is a sample framework that is intended to provide an understanding of the benefit-risk aspects for two of key decision factors, "Analysis of Condition" and "Current Treatment Options," that factor into the benefit-risk assessment. This sample framework is likely to evolve over time and could be incorporated into a benefit-risk assessment framework for a drug under review.

SAMPLE BENEFIT-RISK FRAMEWORK FOR IgA NEPHROPATHY

Dimension	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition	**The symptoms that most negatively affect daily life of IgAN patients include:** • Being tired, exhausted or fatigued; experiencing "brain fog" • Anxiety and/or depression • High blood pressure • Gastrointestinal problems • Swelling (ankles, face, etc.) • Heat or cold intolerance/sensitivity **Emotional and social consequences are common and attributed to these key factors:** • Others do not know what it is like • General daily function is limited • Social isolation • Family stress • Difficulty with relationships outside of family • Uncertainty and unpredictability of disease **Disease symptoms and treatment side effects prevent patients with IgAN from engaging in activities:** • Participation in sports / physical activities • Attendance at work or school • Ability to go outdoors (heat or cold intolerance) • Social activities	**IgAN is a rare autoimmune kidney disease, the causes of which are not fully understood. It is the most common glomerulonephritis worldwide. The natural history is highly variable; the disease typically follows a slowly progressive course. Many patients are willing to participate in clinical trials, particularly if the side effects are limited, but a high percentage have been unaware of trials or are not eligible.** • Eligibility for clinical trials needs to be expanded to include pediatric patients and patients who have had a kidney transplant. • The requirement for more than 1 kidney biopsy per year significantly reduces the willingness of patients to participate in a clinical trial. **Patients are willing to participate in clinical trials conducted under an Accelerated Approval Program and to remain in the trials long-term.** • Majority of patients voiced a high tolerance for risk and a commitment to remaining in clinical trials for 1 or 2 years after a drug is on the market.
Current Treatment Options	**There are currently no FDA-approved therapies that target the disease-specific mechanism of IgAN, or that significantly reduce progress toward ESKD.** • Treatments focus on managing high blood pressure and reducing inflammation: ACE inhibitors ARBs slow disease progression and form the cornerstone of medical treatment for IgAN, but they are not curative. • Patients often implement lifestyle changes focused on diet and exercise. **The side effects of prednisone are serious, long-lasting, and life-altering. Issues include:** • Weight gain and swelling • Muscle, bone, and joint damage • Irritability, moodiness, and aggressiveness	**13% of patients believe their current treatments do not work at all; only 14% believe they work "very well." Patients would be very confident in a decision to take a new medicine approved based on:** • Reduced proteinuria • Slowing the rate of loss of kidney function • Improvements in how they feel, function/survive **The clinical measures patients consider most relevant to their condition include the following:** • Kidney function (GFR) • Protein leakage (proteinuria / albuminuria) • Delay in time to dialysis or transplant **Overwhelmingly, IgAN patients desire a new treatment option that will halt the progression of disease and delay the need for dialysis.** • Enthusiasm is significantly reduced if the side effect profile is more severe than patient's current therapy.

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APPENDIX 2: RESOURCE MATERIALS

MEETING AGENDA

The meeting agenda can be found at the following link:

kidney.org/EL-PFDD-IgANephropathy-agenda

MEETING RECORDING

The full recording of the Externally Led Patient-Focused Drug Development Meeting on IgA Nephropathy can be found at the following link:

kidney.org/EL-PFDD-IgANephropathy-video

SLIDE PRESENTATIONS

The slides presented at the meeting can be found at the following link:

kidney.org/EL-PFDD-IgANephropathy-slides

APPENDIX 3: PATIENT TESTIMONIES

APPENDIX 3.1

Table of panelists who presented testimonies on respective topics

Topic 1: LIVING WITH IgA NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS

Maureen	Adult patient
Sue	Adult patient
John	Adult patient
Tim	Adult patient
Ryan	Teenage patient

Topic 4: CURRENT CHALLENGES TO TREATING IgA NEPHROPATHY

Lillie	Teenage patient
Barb	Adult patient
Chris	Adult patient
Karen	Adult patient
Kimberly	Adult patient

Patient panels were not utilized for Topics 2 and 3.

APPENDIX 3.2
FULL TESTIMONIES PRESENTED BY PATIENTS

TOPIC 1: LIVING WITH IgA NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS

Maureen (Adult IgAN Patient)

Hello, my name is Maureen. I live in Bayville, New York, with my 16-year-old daughter Isabella. I work as a private home care nurse. I've tried to complete my RN degree three times. Each time, my education was interrupted due to health issues related to IgAN and other autoimmune disease[s]. I had chronic strep throat as a child, and around the same time I recall having high protein and red blood cells in my urine. I also had photosensitivity, and other allergic reactions.

My doctors did not think these issues were significant. I now believe this was the onset of kidney disease. At 24, I became pregnant, in 2003. At the time, I was working 80-hour weeks, and I was a full-time college student. Due to stress, I had preeclampsia with high blood pressure, rapid heart rate coupled with edema. A few years after pregnancy, my health began to rapidly decline. I had trouble waking up in the morning. I became consistently late to work or calling in sick. I was always tired, puffy, cranky, and having to pee a lot without the feeling of emptying my bladder. I never felt well. This caused me to lose a full-time position in [the] hospital [where I worked]. I assumed it was stress related and possibly depression. As my fatigue worsened, it became difficult to maintain my household and tend to my daughter.

I recall one time while driving, my daughter—six years old at the time—saw me nodding off while I began to swerve off the shoulder of the highway. My child screamed, "Mommy, wake up!" which was the common phrase I heard in those days. My daughter at this young age would worry about me when I couldn't get out of bed. One morning, she brought me ice pops and cheese quesadillas she had microwaved herself. I felt a tremendous mountain of hopelessness, failure, and guilt.

In 2009, I had a flare-up. I had Cola-colored urine, my back and side throbbed with inflammation. One day, my legs tripled in size. My face and extremities filled with fluids, with my blood pressure running 280/180; I was scared. I went to a walk-in clinic, and was prescribed blood pressure medicine, and told to follow up with cardiologists. The cardiologist put me on metoprolol for tachycardia.

Within a month, I was having uncontrollable loss of fluids from both ends, with projectile vomit for hours. I was going into kidney failure.

At the ER, I learned that my GFR was 23. Shortly after that, I had a biopsy which confirmed I had IgAN. I was told I had 10 years to live without treatment. Needless to say, I chose the recommended high-dose prednisone treatment. Within 18 months, my IgAN was in remission, and my GFR rose from 23 to 59. But after eight years of my kidneys being remission, they slowly began to decline, with GFR hovering 40s and 30s. I became unable to work again, and at times, bedridden.

The symptoms that affect me the most now are fatigue, edema, insomnia, hypertension, vitamin D deficiency, and brain fog. Chronic fatigue is especially hard. You may look well on the outside. Inside you feel as if you are filled with lead. Even getting out of bed to get a drink of water can be

difficult on a bad day. Fatigue also makes monitoring of blood pressure difficult, even though it's necessary to do.

Over time, I developed bone and mineral disorder. I fractured my tailbone twice from falls after prednisone. My back problems cause me to have chronic pain, and at times, to be bedridden. My L5 and L6 [vertebra] fused on their own to my coccyx. I now take daily pain medicine so I can function properly. But I still have trouble during rest or prolonged activities. I've spent thousands of dollars on failed root canals resulting in nine tooth extractions. Having missing teeth is embarrassing. It's also difficult to chew certain foods—especially difficult, since my diet is already restricted. My face has changed, and I don't like to smile anymore in pictures.

Having kidney disease has lowered my self-esteem. Pain and fatigue also keep me from doing my favorite activities. I used to run five miles a day. Now I have to limit and choose my activities each day. My GFR is currently 29, the lowest it has been since diagnosis, 13 years ago. My biggest challenge is carrying on knowing that someday my kidneys may fail. My biggest fear is not being able to work and provide for my child. Thank you.

Sue (Adult IgAN Patient)

Good morning. My name is Sue. I am 58 years old, and live in Erie, Pennsylvania. I will be starting work at a credit union next month, and have my own art business on the side where I draw portraits, teach art to senior citizens, and those with dementia, and have my own photo greeting card line. 15 years ago, I began experiencing gross hematuria and, after many tests and a kidney biopsy, I was diagnosed with IgAN and HSP, Henoch-Schönlein purpura.

I am one of the lucky ones who have been able to stay stable and have not progressed to dialysis thus far. There are a few symptoms that come with a disease that affect my life the most. The first is the constant weariness. It seems like I can never get enough sleep. I do my best to get at least seven to eight hours of sleep each night, but some days I have a hard time getting through the day without wanting a nap.

If I'm in a meeting, I struggle to keep my eyes open. If I am staring at the computer too long, my eyes start to cross and close. I can accomplish a lot in the morning, but many days, by afternoon I can lose focus quickly. It not only affects my days at work . It also keeps me from going out and enjoying evenings with friends. It isn't a problem to go out for a quick dinner with friends, but I don't like to stay out late, as I'm just too tired after a long day of work.

When I had my first biopsy, one of the diagnoses was HSP [Henoch-Schönlein purpura]. It was several years before I was affected by it. It started with GI symptoms, mostly cramping and diarrhea. Tests showed there were no problems with my stomach. Then I had itchy legs. Soon, there were small red dots on my legs, which eventually became very dark purple-red splotches. It was very painful, and I started experiencing lightheadedness. At that point, my doctor insisted I call 911. I was taken by ambulance from work to the ER and admitted.

The doctors couldn't figure out what I had, putting me in isolation. They had every type of physician come to see me, including [specialists in] infectious diseases. My nephrologist came in and excitedly remarked, "You have Henoch-Schönlein purpura." And then he went into the history of it. Mystery solved. The vasculitis was on both legs and throughout my GI system. To clear it up, I was put on a regimen of prednisone. These days, even if my legs just start to itch, I

immediately think of the HSP and watch for the red spots.

Along with IgAN being an immune disorder, if someone coughs or sneezes near me, I tend to catch whatever they have, or at least it feels like it. I have become so phobic of large groups of people in confined rooms that I don't even go to church anymore, and I missed that fellowship. But the hugging, touching, and close quarters, especially during flu season make me nervous. At least twice I've been thrown out of remission due to picking up a bug leading to bronchitis, then to pneumonia, and one of those times resulting in my second kidney biopsy because my protein spill went up to three grams. That was after a client had come into my office hacking and coughing and towing their sick child who had just been removed from school. I wish I could have been allowed to hand out masks on my door.

I used to love to travel, fly anywhere, but now I dread having to share the air and the tight quarters of a plane. But now I dread having to share the air and the tight quarters of a plane. I even bought a personal air purifier that gives me a little comfort, but I nearly always end up sick two to three days after I have traveled, causing me to miss work or cancel plans. I have learned not to make plans for a few days after I travel, just in case. I flew here to the meeting; fortunately, they were short flights in smaller planes.

The fear of getting sick, leading to a flareup truly impacts my life. Just this past Christmas, I got sick. The flareup caused me to pee pure blood. By the time I got to the urgent care, the blood was only detected through the urine test because it was no longer visible. They thought I was nuts when I gave them the sample, after telling them that I had been peeing visible blood only two hours before. This led to a cystoscopy to rule out anything urinary and then it was chalked up as a flare-up. I have had two additional flareups just in the past six weeks.

Something I have dealt with since I was treated with high doses of prednisone right after being diagnosed is heat intolerance. Heat never bothered me before, but by the time I was done with the prednisone treatment, I could not tolerate anything above 75 degrees. It has been that way now for 14 years without prednisone. I truly suffer and it makes me dread summer when I should be enjoying all the outdoor activities of the season. I am drenched within minutes of going outside. And if I'm inside and there is no air conditioning, I feel like I will suffocate. I truly love when I start seeing the colors of autumn appear, for I know that relief is near, and I can enjoy the outdoors.

It is hard to have an invisible disease. I'm not lazy, I'm tired. I'm not a wimp; I just cannot tolerate heat and I truly am suffering from not being inside in the air conditioning. I am not a hermit. I just choose to stay healthy.

Thank you for letting me share my story.

John (Adult IgAN Patient):

Hello. My name is John. I am 44 years old and live with my wife Maureen and our two dogs in Westbury, New York, where I run an agent's office for State Farm. I was diagnosed with IgAN in 2005 and confirmed by my first biopsy in 2006. I was stable for a while, but my creatine and protein started to increase to a point where I started a heavy dose of prednisone treatment for six months.

The symptoms that I experience the most would have to be tiredness and body aches. The

tiredness really affects my life and that of my wife, as we have to alter plans around times where I can rest or be in places where I can sit and relax if needed. Simple things like going out to dinner, hanging out at a barbecue, et cetera, have all been altered by this disease.

People say, "Oh, you look fine." The truth is, that if I don't get the proper rest on day one, the next few days I will suffer. In order to stay as healthy as possible, a sleep schedule is very important, and uninterrupted sleep is very important because if woken up, it is very hard to fall back to sleep. I tend to try to go to bed about 9 o'clock every night. On a good night, I can get eight to nine hours of sleep to have a productive next day.

I have body aches, especially from the residual side effects of prednisone treatment six years ago, such as torn muscles, muscle and joint aches. Tearing of the muscle led to missing work, physical therapy, as well as pain I felt from simple things, such as walking.

I've always been into sports but never had any injuries such as those that have resulted from prednisone treatment for IgAN. To this day, my mobility in my knee has never been the same. To give you an example, if I play a round of golf, it usually involves an hour or two of icing afterwards, just to keep the swelling down to my knee and ankles, which have been the worst lately.

Prednisone, while a good drug for inflammation, had so many side effects for me, such as insane hunger, weight gain, muscle weakness, insomnia, to name a few. I've been dealing with these aches and pains on a daily basis ever since. These aches and pains can alter things such as sleep, doing simple chores around the house, or at work [sic]. While on prednisone, I would have trouble sleeping and get up at 4:00am, so I would go out on a bike ride for an hour or so, just not to wake my wife and the dogs. By the end of the workday, I would feel exhausted, but unable to sleep.

I'm an athlete and always been into sports, such as baseball and golf. I had to give up playing competitive softball due to many injuries from the weakness in muscles and joints, plus a fear of further damage to the kidney [sic] while playing. Golf is a sport that I still love to compete [sic], but there are always days where I must try to take a cart instead of walking the course, which I love to do. On a good day, I can play 18 holes and feel fine, but on a bad day I get tired after nine.

You never know waking up how the day is going to be. While you may feel fine in the morning, the afternoon can change very quickly. Back when I was diagnosed in 2005 and confirmed by the first biopsy in 2006, I didn't think much of this disease, as it was caught on a routine physical. Looking back on it now, the only sign I really missed was being tired, but always thought it was due to working two jobs, trying to stay active in sports, as well as [to] have[-ing] a social life. Now, most of my friends understand when we have to go out for early dinners and to socialize, but others still see how my life is truly affected, like my wife and I do on a daily basis.

This disease is different for everyone. You never know what your next blood work will show. I've said to many people, "I feel better than I did last month, but I won't know what's happening until the next blood work." The stress of waiting for the blood work results to come back, praying for no change or positive change is something I have to deal with on a regular basis.

The treatment for this disease up until now is lacking, to say the least. All of us here, the thousands in the support groups on Facebook and those on the webinar are praying for better

treatment and a cure for IgAN. Thank you very much for your time and interest in helping us with IgAN.

Tim (Adult IgAN Patient)

Good morning. My name is Tim. I am a lifelong Wisconsinite and currently residing in Madison, where I also attended college, receiving degrees in zoology, environmental studies, and biotechnology. I'm 36 years old and work as a product development specialist at a biotech research company.

When I was 18, I first thought my dark tea colored urine was simply due to dehydration from the baseball double header I played the day prior. However, both the additional symptoms that followed and the longevity with which they persisted told me that this was something different. Over the next two years, I had eight episodes of this, along with constant fatigue, headaches, dehydration, muscle cramps, flank pain, moderate proteinuria, and sleep problems that affected my energy level, mental state, and academic and professional performance. It was difficult to give full effort to my studies or my job when just getting out of bed in the morning and walking around was a struggle due to back pain and cramps.

Maintaining focus on daily tasks was also tough due to poor sleep quality and general fatigue. With my kidney health declining, I embarked on my doctor's recommended treatment plan along with vigilant tracking of my health. Some months later after a successful kidney biopsy, I received an official diagnosis of IgAN. While it was a great relief to finally get answers, the focus on daily management of this disease had just begun.

Fast forward almost 20 years to today, I'm essentially at a standstill with regards to disease progression, based on my nephrologist's assessment. My GFR is stabilized. I haven't had an episode of macroscopic hematuria in almost a decade and my protein output is steady at slightly above the normal average. As a result, my nephrologist visits have dropped in frequency from monthly at the start to now just once every two years.

However, while the major acute symptoms don't arise as frequently or as severely as they did before, they haven't disappeared completely. It will always be a daily battle with this disease in trying to slow its inevitable progression.

On my best days, I hardly notice it, with little fatigue, dehydration, or headache, and I appear to be a normal, healthy middle-aged man, even though I don't always feel that way. On my worst days, I'm unable to get out of bed in the morning until the muscle cramping, pain and fatigue subside. If the onset is in the middle of the day, I need to stop whatever I'm doing, follow my daily treatment plan and hope the symptoms pass quickly. I'm also irritable, depressed, and not mentally sharp during these episodes. I'm irritable to people around me because I'm in constant pain and I have no control over it. I become depressed because it's a reminder of my chronic incurable disease that could shorten my lifespan.

With every acute episode I suffer, I know irreparable kidney damage is occurring. I'm not mentally sharp because these anxious thoughts are fighting whatever task I'm supposed to be focusing on amid the mental fog that results from constant lack of quality sleep and energy. However, I do count myself lucky since I know others afflicted with the disease have suffered more than I have.

The disease hasn't negated me from physically participating in athletic events, [or] enjoying outdoor activities. or [hasn't] required [sic] significant changes in my diet, so I'm blessed there. But while the physical impacts haven't increased as I've aged, the impact on my immediate and long-term mental health is real. Living with this disease, where existing treatment options only slow the rate of damage, coupled with a 40% chance of progressing to end-stage kidney disease within 25 years does take a toll on my mental state.

The possibility of needing frequent dialysis or [being] placed on [the] transplant waiting list is frightening. And in the case of transplant, there's a good chance the disease will reestablish in the transplanted kidney. As such, I'm constantly thinking about what's the healthiest possible option for someone with my condition. Adding an overarching layer to the daily decisions needed in my personal and professional life is not a welcome thought, but I've always tried to maintain a positive and gracious attitude throughout my journey with this disease.

However, I'm not alone in this journey. Those around me have been impacted in the past and will continue to be in the present and future. Probably the toughest part of my early experience with the disease was not the decline in my physical health, but rather witnessing the stress and strain on my parents, especially my mother, when viewing their son during hospital stays, subject to all manner of tests while dealing with an unknown cause. And again, during my times post-diagnosis where the symptoms were especially cumbersome and painful, the helplessness and frustration they experienced was evident along with the guilt I carried being the cause of that burden.

And with scientific evidence showing potential genetic links to the disease, it's possible to be passed on a future offspring. While I have no family history of this disease, it does factor into decisions about having biological children of my own.

Increased efforts to find a cure or at least more effective treatments for IgAN and are essential. Physical impact could be lessened, the anxiety minimized, and the energy devoted to managing the disease could be better allocated elsewhere in my life. But I continue to hold and promote hope for this and future generations and that's the purpose [of] my testimony today. Thank you.

Ryan (Pediatric IgAN Patient)

Hello, my name is Ryan and I live in Wright City, Missouri. It's a small town, about one hour away from St. Louis, Missouri. I turned 13 years old in September of 2018. I'm my mom's first born. I'll be going into eighth grade this coming fall.

2019 was supposed to be a really good at year for my family and I [me, sic]. Instead, I got sick with the flu – I thought. Right before bringing in the new year, I had the chills, sweats and I couldn't eat because of the pains in my stomach. I was nauseous and had diarrhea. I was so tired I would sleep day and night. I started peeing a dark brown color. Then it started hurting when I went. That's when I told my mom. She about fainted. The look on her face told me something was wrong. My mom took me to see the doctor the very next day.

My doctor thought it was a urinary tract infection. He put me on an antibiotic and wanted blood work done. At the lab, the nurse couldn't draw my blood. She tried at least twice in each arm. She told my mom to bring me back the next morning. My mom was not happy with that answer, so my mom decided that we were going to Cardinal Glennon Hospital in St. Louis, Missouri.

St. Louis is about 45 miles east, or so, away from where I live now. The hospital is another 10 to

15 miles further east.

When we went to the hospital, the nurses took me back right away, like they knew something was wrong. It took them 18 tries to get my blood drawn. They brought in every type of nurse they had, even the first response team. It was so scary. I knew something was really wrong with me then. The next morning my kidney doctor came in and talked with my family and me.

He told us that I needed to have a biopsy of my kidneys. When the results came back, he explained that they were able to get 80 filters from the biopsy, in which it showed 20% of my kidneys were already dead. Twenty-two of the 80 filters they took showed they were already in bad shape, which meant my kidney function was not good at all. I ended up staying in the hospital for a week. I didn't understand why or how or what happened. All I knew is that I couldn't eat anything good. Nothing with salt, no meats, no soda, and that I was dying (and that I thought I was dying).

I was put on a lot of medicine, blood pressure medicine, stomach medicines, mood medicine, even a cancer medication. Prednisone is another one I'm taking, which has made me very tired, moody, hungry and mean. I even yell at everyone. I refuse to do what my parents ask, and I am mean to my little brother. I eat too much, and I know that it's the medicine I am on [that] makes me super hungry. I used to be so tired all the time. I didn't go to school a lot. I was so tired I couldn't function.

Since January, some things in my life have gotten easier to deal with, like with what I can and can't eat. My parents have worked really hard on finding me things that have taste…that taste good.

Other things have gotten worse, like my attitude, and my weight – it's still not good. I hope when I get off the prednisone, my weight will get better.

I love to play baseball. I've been playing since I was four years old. Now I can't even play. I can't be in the sun a lot, the CellCept and prednisone I have to take requires me not to be in the sun for long or I could get sick and then the medicine won't work as well.

Plus, it's way too hot. I get tired within 20 or 30 minutes, I'm so overweight I can't run.

School sucks. Kids call me "kidneys". And even the kids that I was cool with. I hate going. I don't have a life now.

CellCept] is another medicine I'm on, is a medication for people with cancer. It has made my hair fall out a little. I have to have my blood pressure taken three times a day.

The doctors have told me that I will need a kidney transplant and or dialysis, maybe even both. I have to go see my kidney doctor about one to two times a month or so now. My mom has to call in my blood pressure every week. If my doctor likes what my blood pressure numbers are, then I may not even have to go see him that month.

My mom sometimes will get me Chick-fil-A after my appointment, but I can only get a small grilled and a small no – salt fry with water to drink but I'm good with that.

So, yes, I hate this disease. I wish there was a magic pill to take it away. I wish no matter how

many salads I have, I wouldn't get any fatter. I wish this would all go away.

Thank you.

TOPIC 4: CURRENT CHALLENGES TO TREATING IgA NEPHROPATHY

Lillie (Pediatric IgAN Patient)

Hi. My name is Lillie and I live in New Hill, NC, with my parents and my dog, a Pomeranian named Razz. I am 15 years old and am getting ready to start my sophomore year of high school.

I was diagnosed with IgA nephropathy when I was eight years old and was mostly stable until I was 13 years old, and that is when my kidneys started to decline. I had to go to the hospital a lot that year. I was put on prednisone via IV pulses and oral. The doctor hospitalized me to give me three days of IV steroids. The IV was scary. They had to give me Ativan to calm me down. The Ativan had the opposite effect and that was pretty awful. I started hallucinating and couldn't sit still. I thought the church that was outside my hospital window was a monster coming to get me. That time I was in the hospital for four days. Now I'm great at IVs.

The prednisone made me gain 40 pounds in three months and gave me really bad acne. As a teenager that was horrible. Kids made fun of me all the time. I am also on Lisinopril, CellCept and I've done Rituximab infusions.

My kidney disease isn't what makes me feel bad all the time; it's the medication side effects that make me feel awful. I have to have physical therapy because my joints and bones are deteriorating from the long-term use of prednisone. My hips are out of alignment and I have to walk with crutches sometimes. I had to get an elevator pass at school because my school was four stories tall and I couldn't make it from the first floor to the fourth floor in time for class. I've danced at the same dance studio since I was three years old.

When I started to take the prednisone, my body hurt so bad, I had to stop dancing that year. Luckily, this year I am back to dancing, but sometimes it is really hard since my flexibility isn't what it used to be , and I have to take Tylenol after class because I hurt so bad. But I am so happy to be dancing again!!!!

I had to fight through the pain to do what I love. I just danced in June at the Magic Kingdom in Walt Disney World at the afternoon parade.

I also developed some fluid behind my heart from the prednisone and it makes it hard to breathe sometimes. I have had 14 ingrown toenails removed because the doctor told me the medicine is making my toenails and skin grow at different rates causing the in-growns [nails]. They are constantly infected, which makes me then have to take antibiotics. The podiatrist told me that if I get any more, he is going to put me under anesthesia and shave off the top layer of my bone on my big toes so that my toenails won't grow anymore.

My anxiety is pretty bad. I see a psychiatrist and a therapist to help and [I] take Zoloft.

Since I always feel so sick and am really tired a lot, it caused me to miss a lot of school. That made it hard to keep up in high school. I wasn't doing so good in school, so my mom had to pull me out and homeschool me. That was hard because I was always a straight-A student.

I take a lot of different vitamins, too. My nephrologist told me that some of my minerals and vitamins are low. I am a little different from other IgA nephropathy patients because my doctor told me I have to eat red meat once a week. It helps keep my minerals up, so I have less muscle spasms in my legs. I take a multivitamin, calcium, and vitamin D twice a day; Protonix for my stomach aches the medicine causes; CellCept twice a day; Zoloft; lisinopril; iron; melatonin to help me sleep; and birth control to control my hormones, since they are all messed up from the other medications.

I finally weaned off the prednisone at the end of March after being on it for one year and 5 months. I am finally starting to feel better. I have more energy and am not in pain as often anymore. I think a lot of it's mindset. I have just decided I'm not going to let this defeat me anymore.

I am really excited about some of the medications that are in phase 3 trials right now. I have heard really good things about them. I wish I could enroll in a clinical trial because none of the medications I take are slowing down my disease, but I can't because the trials are not available to kids. I would love a medication that is specifically for this disease instead of just treating my symptoms which makes me take more pills.

I like to talk to people about my disease and the problems I've had with my medications because the more people that hear about it, maybe more people will try to help. A lot of kids are treatment resistant—that's what my doctor calls me—and the medications out there now aren't helping. I think it would help a lot if we could be included in clinical trials, so maybe the medication can start working sooner and we can be helped before we need dialysis and a transplant.

I am not telling you all of this so you feel sorry for me. I am telling you so you can make changes, make things better, and learn from my story and others. This disease is not fun; it is scary and sad. But you can make a difference.

Barb (Adult IgAN Patient)

Hello, my name is Barb and I live in Brunswick, Ohio, with my husband and best supporter, Bill. I am a retired Pediatric Certified Medical Assistant.

In 1999, I was diagnosed with diabetes, and started on metformin. In 2008, I had low white blood cells and iron-deficient anemia. In 2013, my blood work showed abnormal values for everything, and I was still anemic. They hospitalized me, gave me a kidney biopsy, gave me the wonderful news; I have IgAN.

I was originally given lisinopril, but I could only take it for a week because the side effects of extreme tiredness and dizziness were intolerable. At the same time, my diabetes drug was changed from metformin to glimepiride. In the hospital I was given blood. Due to the additional blood not working, I was given iron tablets. They made me vomit all day, so I was put on Venofer infusions 5 days a week.

During the next four plus years, the Venofer infusions progressively declined one treatment per quarter.

When my veins collapsed from the Venofer treatments, I had a venous port inserted into my

chest. The first port failed due to a blood clot in the tube. The second port became necessary and I was put on Coumadin, which requires an INR test twice a week to regulate the dosage. Difficulties regulating the Coumadin, lead to a change to Xarelto. I don't care for Xarelto because there's no way of checking whether it is working or not like with the INR test and Coumadin. While I'm on Xarelto I have to go in monthly to confirm that the port is giving of [sic] blood and to get heparin injections to maintain the port.

I suffer from insomnia, because I am constantly thinking about my IgAN.

I believed I could cure the disease simply by drinking excessive amounts of herbal teas which would detoxify my kidneys and flush away allthe dead mutated IgA proteins. I feel it is working since I am in remission; I don't have hematuria, don't spill proteins, and my GFR is maintaining at 28.8 or thereabouts.

To help slow the progression of my IgAN it is imperative that I control my blood pressure, diabetes, and cholesterol, and limit my sodium intake between 1500 and 2000 milligrams per day. I take calcitriol to control my hyperparathyroidism and I take omega 3 to control my cholesterol and to slow the progression of IgAN.

The downside of having IgAN is having the numerous other conditions, diseases that accompany this disease. I know fluid retention is not a disease, but when you're trying to lose weight and you gain 10 pounds overnight, it doesn't work. My nephrologist then prefers me to take 40 to 60 milligrams of Lasix to prevent the fluid retention. I despise the Lasix because I'm always in the bathroom.

I kept my A1c at 5.8 for 14 years. It suddenly jumped to 8.4, even with glimepiride. At the same time, my blood pressure suddenly went from 110/75 to 170/100 and is irregular. Currently, I take metoprolol for blood pressure and rosuvastatin for cholesterol.

My [bed]room looks and feels like a hospital room. The head of my bed is elevated to a 60-degree angle when I sleep. The supplies and bottle of distilled water for my Bi-Pap [bilevel positive airway pressure device] for sleep apnea are kept by my bed. My BP cuff, B-12 bottles, and supplies for the injections, my glucometer, and supplies are on my dresser. My loop recorder for monitoring my heart is at the head of my bed.

When I get upset and say, "I don't care what happens; I am done with this," I will travel. Consequently, I feel guilty because I'm not going to bring my supplies, I'm not taking the best care of my body, but worst of all, I'm going to have answer to my nephrologist. I can't even imagine what it's going to be like if he ever decided to put me on dialysis. I'm totally overwhelmed now what's going to happen then.

When I'm depressed, I will go to the hospital, and rock the babies that are too sick to go home. Children have always made me feel better. God can make miracles happen and He does. I have become closer to God and I talk to Him constantly. listen to classical music, which transports me into my own world of peace. The thought of no cure for the disease is totally petrifying.

For my ideal treatment, I would desire my kidneys not to be scarred due to the scarring being reversed [sic]. I would also prefer IgAN to be prevented from reoccurring.

Even if I would get a kidney transplant, I still run that risk, but most importantly, I would prefer to be low risk to my health.

Thank you for listening. We all appreciate it.

Chris (Adult IgAN Patient)

Hello, my name is Chris. I am 23 years old, and work out of Irvine, California, as a data analyst for Coca-Cola. Nearly four years ago, I was diagnosed with IgAN while attending the United States Merchant Marine Academy. It began with gross hematuria and proteinuria one morning before class. Over the course of the next month, the doctors at the academy ordered countless blood and urine samples followed by an ultrasound to see what was causing the blood and protein in my urine. Nothing provided answers. It wasn't until I underwent a kidney biopsy that they finally discovered I had IgAN, and due to the rareness of the disease, I had more questions than anybody could answer; the uncertainty of the situation was crippling. Shortly thereafter, I was medically discharged due to the lack of a practical treatment for the disease and its "potentially disabling prognosis."

After returning home, I saw a nephrologist and received an explanation as to what IgAN is, how seriously it affects me, and what steps I can take to slow its progression. The advice my doctor told me [was] to maintain a low protein and sodium diet, and to keep an eye on my blood pressure.

I went home and began researching literally anything that could potentially harm my kidneys. My diet became so strict that it was unsustainable. I lost nearly 40 pounds that year. I was consuming almost no protein and [avoiding] nearly all foods with sodium, which made maintaining a healthy weight nearly impossible. I was afraid that I'd accidentally accelerate the progression of my disease by eating the wrong food.

After that first year, I adopted a more practical diet and slowly returned to a healthy weight. The solution for me was increasing my calorie intake by eating more vegetables and whole grains. Now, I focus on regular exercise and maintain a healthy, but realistic diet. For extra measure, I've completely cut out alcohol, red meat, protein powders, and dairy products from my diet [sic].

I'm not certain that the absence of these items will improve my prognosis, but I'm willing to try anything that will allow me to live a full and healthy life because this is really the only aspect of having this disease that I feel I have control over—so I take full advantage it.

Since being diagnosed, my lab results have remained promising; my blood pressure remains low and my proteinuria has been minimal. My hematuria, however, remains. During my annual check-ups, my doctor tells me that I should live a healthy life given that nothing changes and I pray every single day that this holds true; it is the only thing giving me hope.

Considering the countless unknown variables that may be contributing to my favorable lab results, it is impossible for me to say that the efforts I am making make a difference. I do know, however, that no amount of clean eating or exercise I do negate certain symptoms of this disease.

First, the hematuria and proteinuria remain present regardless of my activity level or diet. I've noticed that remaining less active and drinking more water leads to clearer urine, however,

physical activity is my main source of happiness in life. After a long day of surfing, hiking, or working out, the blood and protein become increasingly evident, reminding me of the permanence of this disease. This often triggers my depression, despite my efforts to keep a positive outlook on the situation. I can't help but wonder how much longer I'll be able to continue my current lifestyle with IgAN, but I'd rather pursue my passions than live a life wishing I could.

Lastly, the severe fatigue has been a considerable challenge for me since my diagnosis. It seems that no amount of sleep can compensate for my worst days of fatigue. I feel drained both physically and mentally, making it difficult to stay active, remain sharp at the office, and carry myself with the energy and positivity I strive so hard to maintain.

Assuming there is no complete cure for IgAN, I wish for a medication capable of slowing its progression and relieving its physical burdens. Eliminating the hematuria, proteinuria, and fatigue would significantly improve my daily life. However, if I had to choose, I would prefer a drug that slows the progression of this disease over any other symptom treatment, because I'd prefer a long life with pain and adversity over a short life.

Karen (Adult IgAN Patient)

Hi, my name is Karen. I'm 40 years old and live in Pennsylvania with my husband, my son, and our dog, Hercules. I'm a benefits consultant for a national broker. This is my story of being diagnosed with IgA[N], having a transplant, and then within the first year being diagnosed with IgAN again with my newly donated kidney.

For a few years before my son was born in 2012, I struggled with proteinuria without a clear diagnosis. It was low enough that I was only treated for hypertension, considering it was a constant urinary tract infection that came out of nowhere after a trip to Hawaii. While I was pregnant, I was treated with labetalol to control my blood pressure. Around five months into my pregnancy, my proteinuria went from 50 to 15,000. A few months after my son's first birthday, my biopsy did, in fact, confirm that I had IgA nephropathy.

My nephrologist prescribed 80 milligrams of prednisone a day for six months saying that that would cure the disease and enable me to get pregnant again. A month into the prednisone regimen, I got prednisone-induced diabetes; I gained 70 pounds; had major joint issues; and could barely walk due to the extreme swelling in my feet and ankles from all the treatments.

During this time, I took labetalol, amlodipine, lisinopril and hydrochlorothiazide, which did not control the prednisone-induced high blood pressure. I also took insulin injections and Januvia for the prednisone-induced diabetes. A few months into the treatment, I asked to taper down the prednisone because I could not take the side effects anymore. My nephrologist did finally agree. Meanwhile, though, during that time of taking all the medications, my labs were getting worse and worse. I did taper the prednisone down slightly and started taking CellCept.

I went to [The Hospital of the] University of Pennsylvania in the fall of 2012 for a second opinion about my treatment and that nephrologist told me to prepare myself for dialysis and getting a transplant. Being told IgA[N] may lead to dialysis and a transplant at age 65 turned into [me] being diagnosed and then six months later after starting prednisone, I needed a transplant. Needless to say, I was terrified at that news.

In the fall of 2013, I started nighttime peritoneal dialysis at home. Dialysis kept me alive while waiting for a transplant. The hardest part of dialysis was being connected to a machine every night by 8:00pm, so that I could get my treatment and then also get to work on time the next day. The hard part was that I missed laying with my son at night for our bedtime routine every night because I had to be hooked up to that machine. This broke my heart.

After a year and a half of dialysis, I received my new kidney on February 11th, 2015. Immediately after surgery, I felt better than I could even explain. I had a lot more energy and was able to do so much more with my son, which made my heart and my life so much happier.

After my transplant, I stayed on labetalol, amlodipine, lisinopril for blood pressure, and Renvela for high phosphorus. I also started taking tacrolimus and CellCept, as [well as] my antirejection meds and pantoprazole for GI symptoms due to the medications. After a few months, my blood pressure plummeted, and I was taken off all blood pressure medications.

Things were going well after my transplant. My labs were amazing, and I felt great, but at a one-year biopsy, it came back that IgAN had in fact, moved into my new kidney. While on dialysis I was told that this could happen, but that it was rare.

I was devastated.

The transplant team added 2.5 milligrams of prednisone to all my other antirejection meds and we hoped for the best. Considering my prior history with prednisone, I was not happy to say the least. I feel that prednisone does nothing good for me, especially since my proteinuria over the years post-transplant has fluctuated and steadily increases instead of decreases.

I have gained a lot of weight from the prednisone. I now have sleep apnea, and high blood pressure is back again. I also have severe fatigue that leaves me feeling very tired, even after a full night's sleep, and foot and ankle swelling, and I have not been able to get pregnant again. I worry every month how my labs will look and if the IgAN will continue to do damage to my kidney.

Currently, I take the prednisone and fish oil, along with the tacrolimus, azathioprine, pantoprazole, nifedipine, labetalol, which all are supposed to help calm the IgAN. I protect my transplant and keep my blood pressure normal, but still I have increasing proteinuria. This makes me believe that no treatment I'm on currently is really helping to calm the IgAN or do anything really for me. Because of this, my transplant team wants to do another biopsy.

I am terrified of reliving being told that I might again, need dialysis or a second transplant. I am frightened and depressed; [I] know that there is no cure for this condition, there are no real medicines that can help, and no trials that are approved for transplant recipients. All I can do is hope more research is done on IgAN and that there could be more trials for someone in my situation in the future. I feel helpless because my doctors say there is nothing I can do to affect what this disease is doing to me.

I would love to have options to cure this disease or medications that actually slow the progression and reduce symptoms that come with it. I would be interested in a clinical trial for post-transplant patients, but I would not want to do anything to harm my new kidney or to cause any additional side effects than I already have. It feels like once you get a transplant, you are

seen as “good to go” and no longer in danger, that you're in a sense cured, but when you live it every day, you feel the danger of possibly needing another transplant every time you wait to hear your monthly blood test results. Thank you for your time today.

Kimberly (Adult IgAN Patient)

Good afternoon. My name is Kimberly and I'd like to thank you for allowing me to come and speak with you today. I was diagnosed with IgA nephropathy only nine months ago. At 42 years old, you think you've heard it all. I clearly was mistaken. I'd never heard of this disease and no clue the impact it would have on my already strenuous and demanding life. I am a single mother of two. I was born and raised in California, but being a previous military wife, I had followed my spouse around the country supporting his career for over 12 years. We eventually ended up here in Maryland in 2008. I'd started a new career in the IT field as a database analyst supporting a weapons program for the Navy. Over the last 13 years, I worked hard and went from the bottom of the totem pole all the way to winning my own $44 million contract. Today, I manage nine software projects and have built an incredibly talented team of over 41 people.

Working in a fast-paced environment to meet the ever-changing needs of a military customer makes for long and stressful, but very, very rewarding days. Military spouses can only depend on themselves, constantly moving around, no family to help with kids; you learn to be a fixer of everything. It's very hard for me to accept that I cannot fix this disease. I now have to rely on doctors and hope they find the right treatment.

Over the last nine months, I've taken a labetalol, losartan, benazepril, and hydrochlorothiazide for high blood pressure. The biggest challenge to controlling my blood pressure is the extreme amount of stress from my job. These medications wear off by the afternoon. We've tried splitting the doses between evenings and mornings, but that hasn't seemed to help much.

A major side effect of uncontrollable blood pressure are [sic] the headaches. Some days, it's a dull headache at the base of my head. Other days, it's a debilitating thunderclap headache. I try Extra Strength Tylenol first, but that's no cure or no match for these headaches. In fact, I have one right here. Right now.

I've been prescribed tramadol, Fioricet and amitriptyline. Sometimes the headaches go away. Most of the time they don't. On the toughest days, I pull all the shades and lay in bed and [in] complete silence with intermittent trips to the bathroom to vomit.

In hopes of stabilizing my kidneys, I was prescribed prednisone. For over six months, I took 60 milligrams daily. Initially, my proteinuria and my hematuria decreased. However, not low enough for my doctor's liking. At about five months into treatment, I had 25 pounds of weight gain, my face ballooned, and, of course, I got the notorious fat hump at the back of my neck. What I didn't expect was the furry face, tooth sensitivity, missed periods, and sleepless nights. Insomnia's probably the worst side effect. After two weeks of not being able to sleep, my doctor finally gave in and prescribed Ambien. My family and coworkers are grateful that sleepless monster has been laid to rest.

Other medications included in my treatment are fish oil and aspirin. I'm not even sure if these are helping, but I continue to take them daily. I am on my third nephrologist, whom I'm grateful for taking me as a patient. My first visit with him was about a month ago. I explained my tooth

sensitivity, my missed periods, and that my hips and my shoulders are experiencing more pain. He quickly attributed the symptoms to the high doses of prednisone for such a long time. Taking my treatment under control, he instantly began a reduction of prednisone and started me on CellCept. Although I'm still struggling with the side effects of prednisone, the only additional side effects since starting my new treatment is occasional diarrhea. I'm encouraged that my latest test results indicate an increase in kidney function. However, I've just been prescribed vitamin D2 for deficiency, as well as pravastatin for high cholesterol.

I'm very concerned about joint pain and I'm not even sure if it will go away. It affects nearly everything I do in my life. I have difficulty using stairs, sitting, carrying groceries, cleaning, gardening, and my new favorite hobby, kayaking.

I have played the piano for over 30 years. Just recently because of my shoulder pain, I'm not able to play as often as I'd like. I pray that my joint pain doesn't migrate to my fingers.

The biggest adjustment for me has been the lifestyle change, going sodium free. Most people don't realize how difficult it is for us to go to the grocery store. Previously, it was a 30-minute trip. Now, it takes nearly two hours because I have to read every label.

I thank my mother for teaching me her incredible cooking skills. I can make sodium-free food that would even knock the socks off of Bobby Flay. A few of my family favorites are French onion dip, bacon and spaghetti with meatballs.

I wish I'd known I had kidney disease before nine months ago. I wonder what I could have done to taken [sic] steps sooner to save them.

For this determined mother of two, I feel blessed each day I'm able to get out of bed, so I can be their role model, their provider, and their cheerleader. The absolute sacrifice will be one day they may give me a kidney in return.

Thank you.

APPENDIX 4: POLLING QUESTIONS

APPENDIX 4.1
DEMOGRAPHIC POLLING QUESTIONS

Figures 1 – 7; Appendix 5

1. I am:
    a. An individual with IgAN
    b. A care-partner of someone with IgAN

2. Where do you live?
    a. East Coast (Eastern time zone)
    b. Midwest (Central time zone)
    c. West (Mountain time zone)
    d. West Coast (Pacific time zone)
    e. Canada
    f. Mexico, Caribbean Islands
    g. Outside of North America (Europe, South America, etc.)

3. What is your age?
    a. Younger than 18
    b. 18-29
    c. 30-39
    d. 40-49
    e. 50-59
    f. 60-69
    g. 70 or greater

4. Do you identify as:
    a. Male
    b. Female

5. What is the length of time since your diagnosis of IgAN?
    a. Less than 1 year ago
    b. 1 to 2 years ago
    c. 2 to 5 years ago
    d. 5 to 10 years ago
    e. More than 10 years ago
    f. I'm not sure.

6. Did you receive a diagnosis of:
    a. IgAN
    b. HSP (Henoch-Schönlein purpura = IgA vasculitis)
    c. Both IgAN and HSP

7. I am:
    a. Not currently on dialysis and have never received a kidney transplant
    b. Currently on dialysis and have never received a kidney transplant
    c. A kidney transplant recipient in remission
    d. A kidney transplant recipient with recurrent IgAN
    e. A kidney transplant recipient and currently on dialysis (e.g., failed transplant)

APPENDIX 4.2
TOPIC 1: LIVING WITH IgA NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS

Figures 8 – 11; Appendix 5

1. Have you experienced any of the following difficulties? (Select all that apply.)
    a. High blood pressure
    b. High cholesterol
    c. Anxiety and/or depression
    d. Being tired, exhausted, or fatigued
    e. Gout
    f. Gastrointestinal problems
    g. Recurrent infections
    h. Swelling (ankles, face, etc.)
    i. Heat or cold intolerance or sensitivity
    j. Kidney failure (ESKD)
    k. Other
    l. I do not have symptoms

2. Which THREE of the following symptoms most negatively impact your daily life?
    a. High blood pressure
    b. High cholesterol
    c. Anxiety and/or depression
    d. Being tired, exhausted, or fatigued
    e. Gout
    f. Gastrointestinal problems
    g. Recurrent infections
    h. Swelling (ankles, face, etc.)
    i. Heat or cold intolerance or sensitivity
    j. Other
    k. I do not have symptoms

3. Which have you experienced while coping with your IgAN? (Select all that apply.)
    a. Depression
    b. Anxiety
    c. Low self-esteem
    d. Social isolation
    e. Difficulty with relationships outside of family

f. Hopelessness
g. None of the above

4. Which of the following statements is true for you, as related to living with IgAN? (Select all that apply)
   a. I miss work or school more than I'm comfortable with.
   b. Family stress is common in my life.
   c. Others don't know what it's like to live with IgAN.
   d. I cannot participate in sports or other physical activities I enjoy.
   e. My general daily function is limited by IgAN.
   f. None of the above

APPENDIX 4.3
TOPIC 2: CLINICAL TRIALS UNDER TRADTIONAL APPROACH

Figures 12 – 14; Appendix 5

1. What is your experience with, and perception of, clinical trials for a new drug for IgAN?
   a. I am currently participating in a trial.
   b. I have participated in a trial, and I would do so again.
   c. I have participated in a trial, and I would not do so again.
   d. I have not participated in a trial, because I didn't know about the opportunity.
   e. I have not participated in a trial, because I was not eligible.
   f. I have not participated in a trial, although I was aware of the opportunity and eligible.
   g. I would never enroll in a clinical trial.
   h. Not sure

2. Of the following factors related to a test drug in a clinical trial, select UP TO FIVE that you rank as most important to your decision about participating in a clinical trial:
   a. Whether I might get Placebo ("sugar pill")
   b. Whether I need to stop my current treatment
   c. Potential side effects from a new drug
   d. How the drug is taken (by mouth, IV, injection in muscle)
   e. In earlier trials, was study drug effective for specific benefits most meaningful to me?
   f. Knowing if I can make the commitment to participate in a clinical trial
   g. Frequency of exam appointments
   h. Distance to trial site
   i. Length of trial
   j. Whether a kidney biopsy is required
   k. Negative things I have heard about clinical trials
   l. Other

3. Would you enroll in a clinical trial if it required (Select the greatest number of biopsies you would accept):
   a. No kidney biopsy
   b. 1 kidney biopsy within 1 year
   c. 2 kidney biopsies within 1 year
   d. 3 kidney biopsies within 1 year

APPENDIX 4.4
TOPIC 3: CLINICAL TRIALS UNDER THE ACCELERATED APPROVAL PROGRAM

Figures 15 – 17; Appendix 5

You are considering whether to enroll in a randomized, double-blind clinical trial for a potential drug for IgAN.

- The first phase of the trial will evaluate whether the treatment lowers proteinuria.
- If the trial shows a large enough effect on proteinuria, the drug will be approved under the Accelerated Approval Program.
- To verify that the product slows the loss of kidney function, patients who enrolled in the trial must remain in the trial in their assigned treatment arm for 1 to 2 more years for the post-marketing extension phase.

4. How likely would you be to enroll and remain in the trial throughout the post-marketing extension phase, with the understanding that you could be in the placebo arm?
    e. Very likely
    f. Moderately likely
    g. Somewhat likely
    h. I would not enroll in the trial

5. For the trial described above, for how long would you be willing to stay in your assigned treatment arm during the post-marketing extension phase?
    i. 1 year
    j. 2 years
    k. 3 years
    l. Not willing to stay in my treatment arm for any time during the extension phase

Drugs approved under the accelerated pathway may be removed from the market if the confirmatory trial fails to verify the previously shown benefit. If a significant number of patients drop out of a trial during the post-marketing phase, the trial results may be difficult to interpret, and the trial may fail to verify the benefit.

6. How likely would you be to enroll in the trial and remain throughout the post-marketing extension phase bearing in mind that premature discontinuation from the trial could jeopardize the results of the trial and marketing status of the drug?
    m. Very likely
    n. Moderately likely
    o. Somewhat likely
    p. I would not enroll in the trial.

7. What TOP THREE measurements (in a traditional or accelerated clinical trial) do you consider relevant to your IgAN?
    q. Protein leakage (proteinuria, albuminuria)
    r. Kidney function (GFR)
    s. Blood in urine (hematuria)
    t. Swelling (edema)
    u. Fatigue

v. Depression and/or anxiety
w. General quality of life
x. Delaying time to dialysis or transplant
y. Other

APPENDIX 4.5
TOPIC 4: CURRENT CHALLENGES TO TREATING IgA NEPHROPATHY

Figures 18 – 26; Appendix 5

Patients' current treatments and their efficacies

1. Select the medications you use for IgAN (Select ALL that apply):
   a. ACE, ARB, beta-blocker, "water pill" (or other drug for blood pressure)
   b. Allopurinol (for gout or high uric acid)
   c. Statin (or other drug for cholesterol)
   d. Veltassa (or other drug for high potassium)
   e. Sevelamer (or other drug for high phosphate)
   f. Anti-depressant or anti-anxiety drug
   g. Drugs affecting immune system (anti-inflammatories, etc.)
   h. Other (including non-prescription remedies)
   i. I do not take medication.

2. How well does your current treatment reduce the most significant symptoms of your disease?
   a. Very well
   b. Moderately well
   c. Somewhat
   d. Not at all
   e. I do not currently take any treatments.

3. Which symptoms do you have that are NOT addressed fully by your current treatments? (Select ALL that apply.)
   a. High blood pressure
   b. High cholesterol
   c. Anxiety and/or depression
   d. Being tired, exhausted, or fatigued
   e. Gout
   f. Gastrointestinal problems
   g. Recurrent infections
   h. Swelling (ankles, face, etc.)
   i. Heat or cold intolerance or sensitivity
   j. Other
   k. I do not have symptoms.

Risk-benefit

4. If the side effect profile of a new drug was more severe than you currently experience with your treatments, but clinical evidence indicated that the drug would significantly slow the progression of your disease and/or improve your quality of life, how likely would you be to take this drug?
    a. Very likely
    b. Moderate likelihood
    c. Slight likelihood
    d. I would not consider taking it.

Preferences for future drugs for IgA nephropathy

You are deciding whether to take a new (recently FDA-approved) drug for your IgAN. Would you feel confident basing your decision to take the drug if it was approved based on evidence indicating that it:

5. Reduced proteinuria?
    a. Very confident
    b. Moderately confident
    c. Somewhat confident
    d. No confidence

6. Slowed the rate of loss of kidney function?
    a. Very confident
    b. Moderately confident
    c. Somewhat confident
    d. No confidence

7. Improved how patients feel, function, and/or survive?
    a. Very confident
    b. Moderately confident
    c. Somewhat confident
    d. No confidence

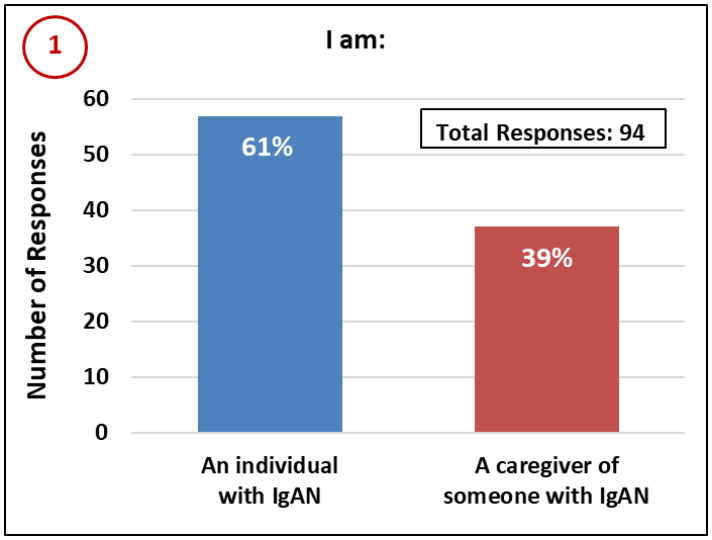
8. Without considering side effects of a drug, which ONE of the following would be most important to you in a future therapy?

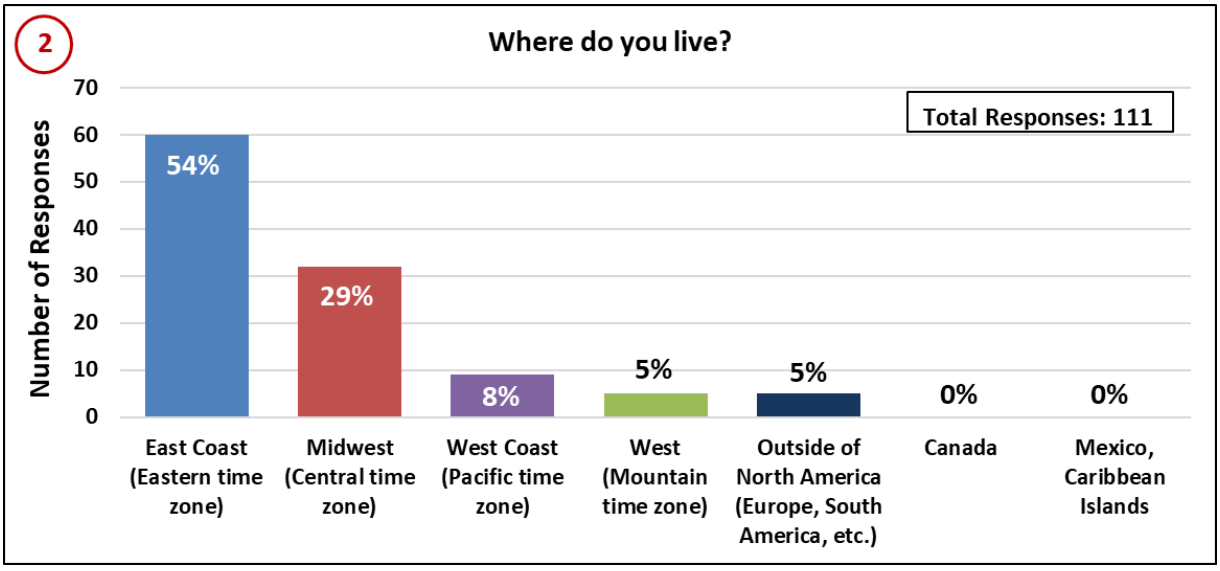
    Evidence that the drug will:
    a. Reverse decline in kidney function (i.e., halt progression of IgAN, delay need for dialysis)
    b. Improve your quality of life or prevent future reduction in quality of life
    c. Prolong your life

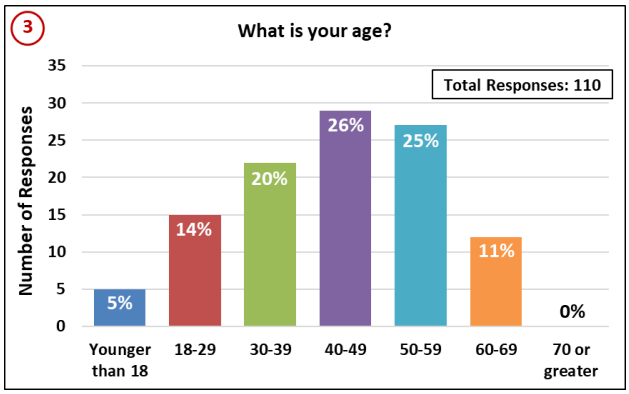
APPENDIX 5: GRAPHICAL RESULTS FROM POLLING QUESTIONS

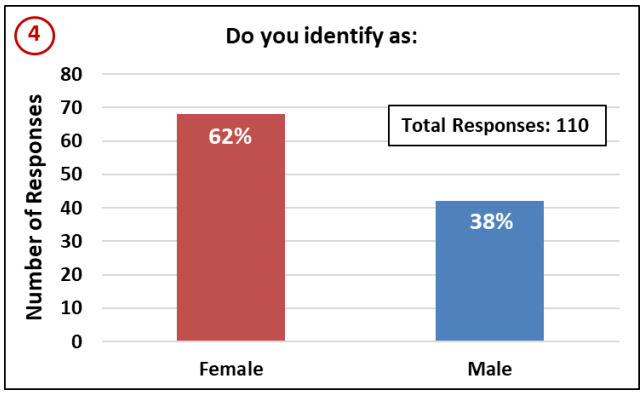
DEMOGRAPHICS OF ATTENDEES

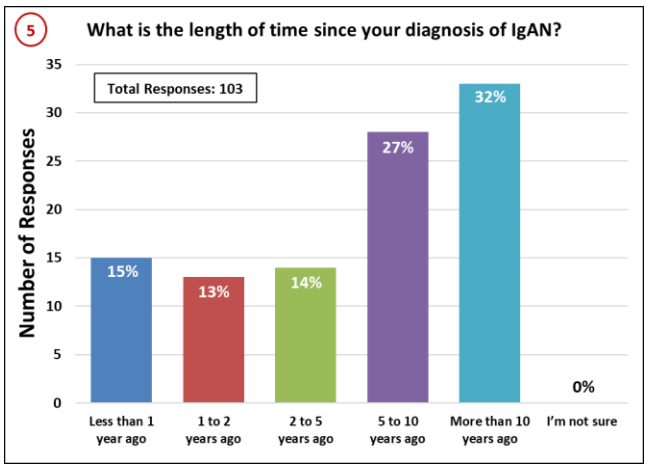
See Appendix 4.1 for Polling Questions

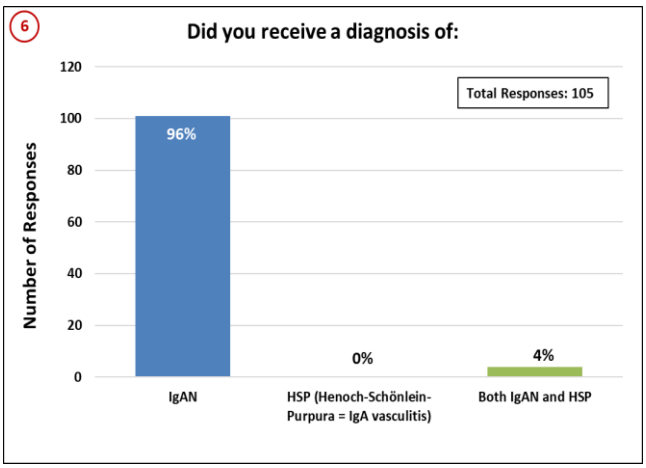


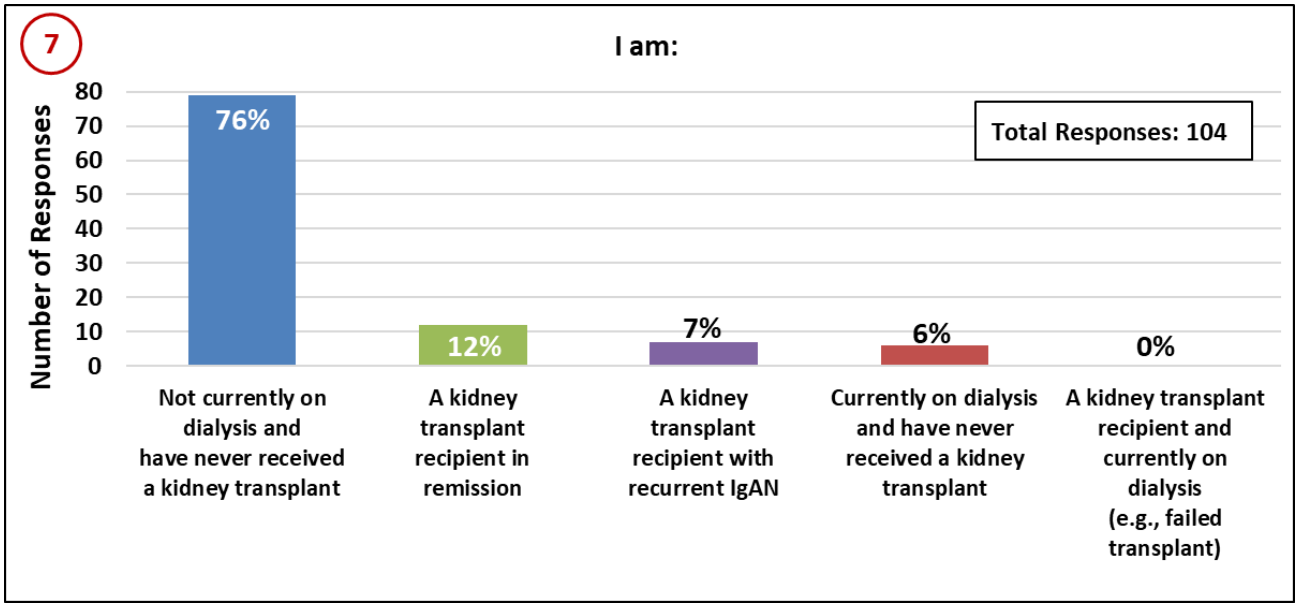



3
What is your age?
Total Responses: 110
Number of Responses
35
30
25
20
15
10
5
0
5%
14%
20%
26%
25%
11%
0%
Younger than 18
18-29
30-39
40-49
50-59
60-69
70 or greater


4
Do you identify as:
Total Responses: 110
Number of Responses
80
70
60
50
40
30
20
10
0
62%
38%
Female
Male

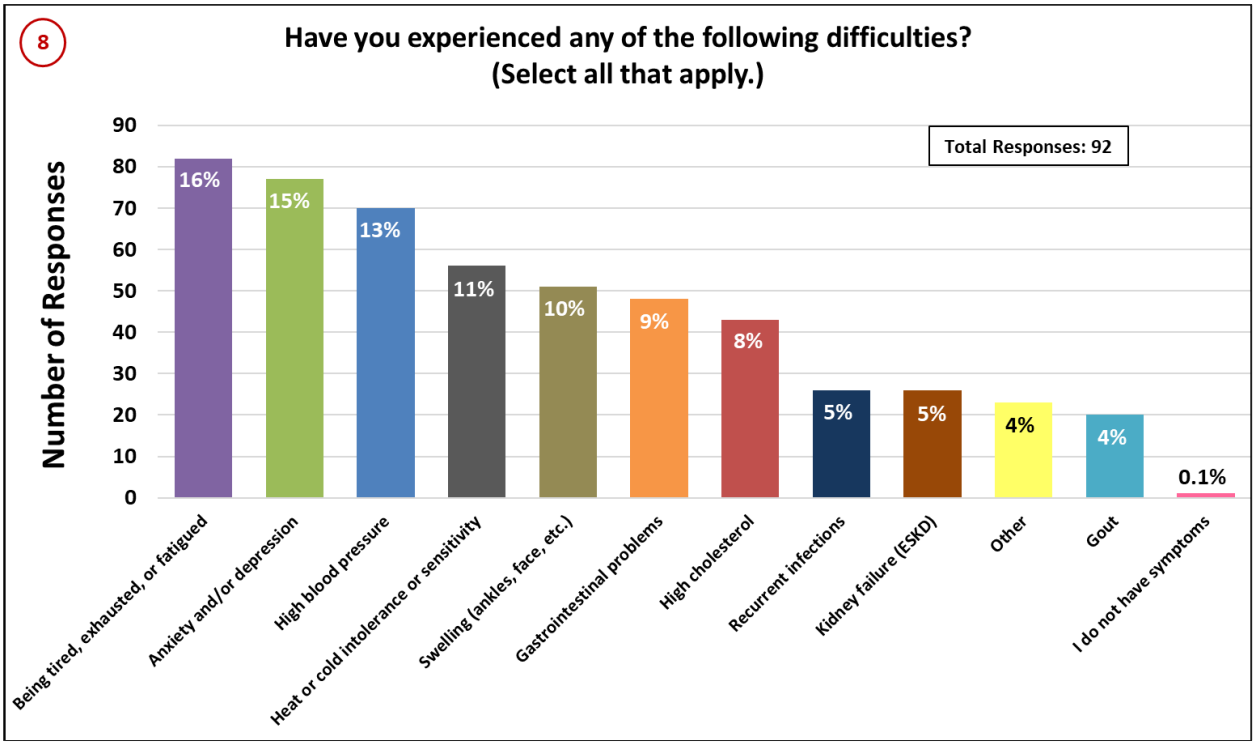

5
What is the length of time since your diagnosis of IgAN?
Total Responses: 103
Number of Responses
35
30
25
20
15
10
5
0
15%
13%
14%
27%
32%
0%
Less than 1 year ago
1 to 2 years ago
2 to 5 years ago
5 to 10 years ago
More than 10 years ago
I'm not sure

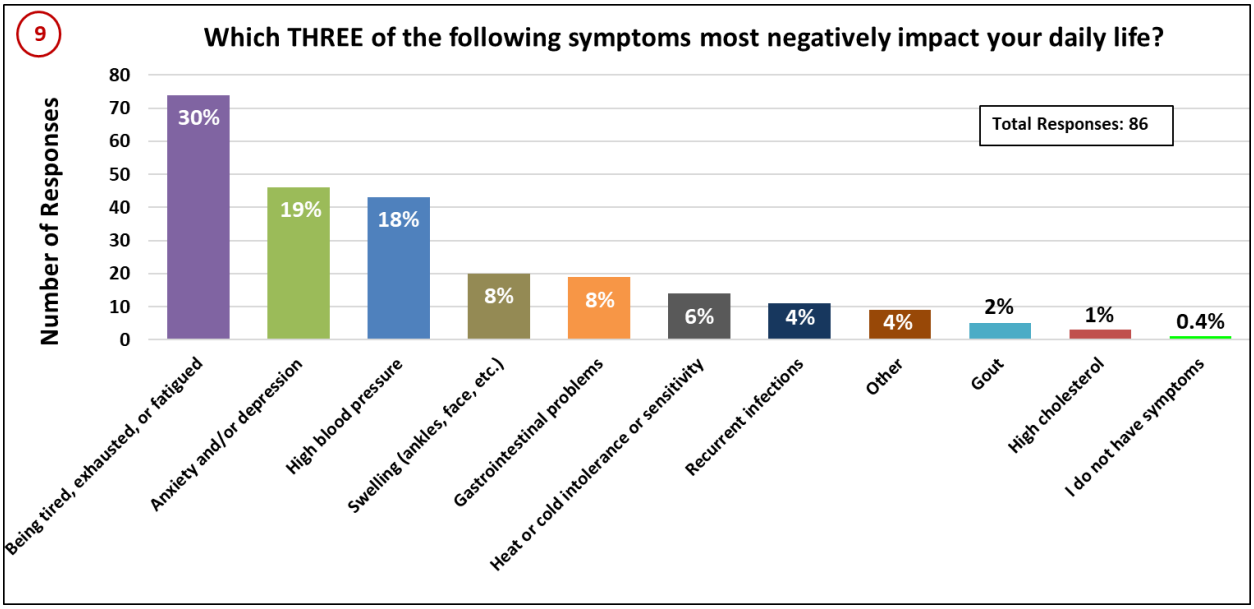

6
Did you receive a diagnosis of:
Total Responses: 105
Number of Responses
120
100
80
60
40
20
0
96%
0%
4%
IgAN
HSP (Henoch-Schönlein-Purpura = IgA vasculitis)
Both IgAN and HSP

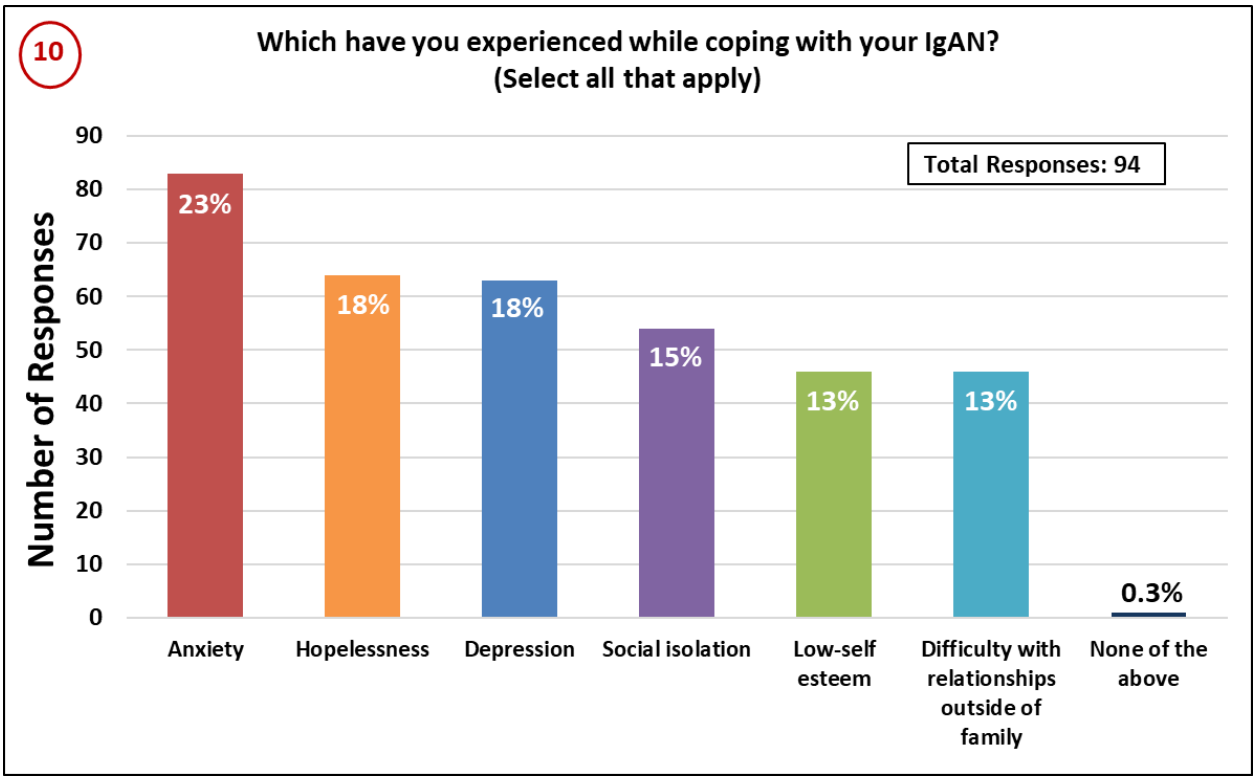

7
I am:
Total Responses: 104
Number of Responses
80
70
60
50
40
30
20
10
0
76%
12%
7%
6%
0%
Not currently on dialysis and have never received a kidney transplant
A kidney transplant recipient in remission
A kidney transplant recipient with recurrent IgAN
Currently on dialysis and have never received a kidney transplant
A kidney transplant recipient and currently on dialysis (e.g., failed transplant)

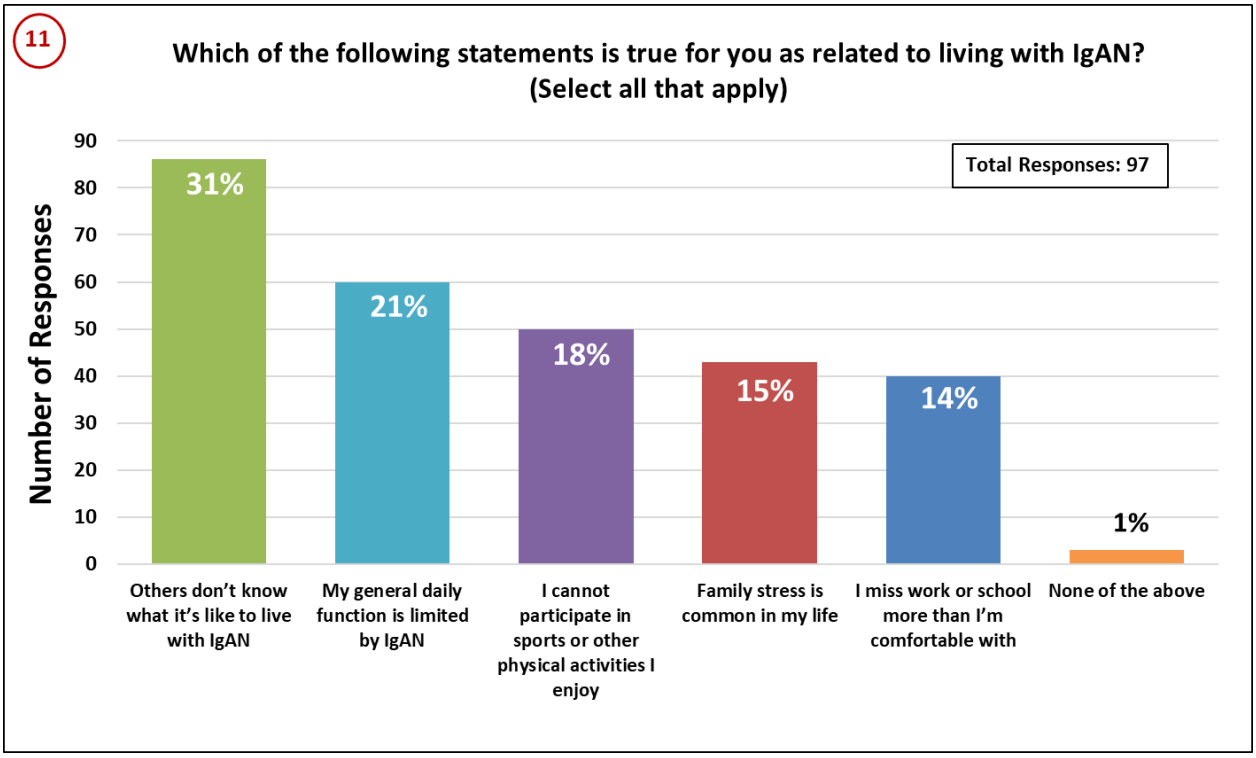
TOPIC 1: LIVING WITH IgA NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS

See Appendix 4.2 for Polling Questions



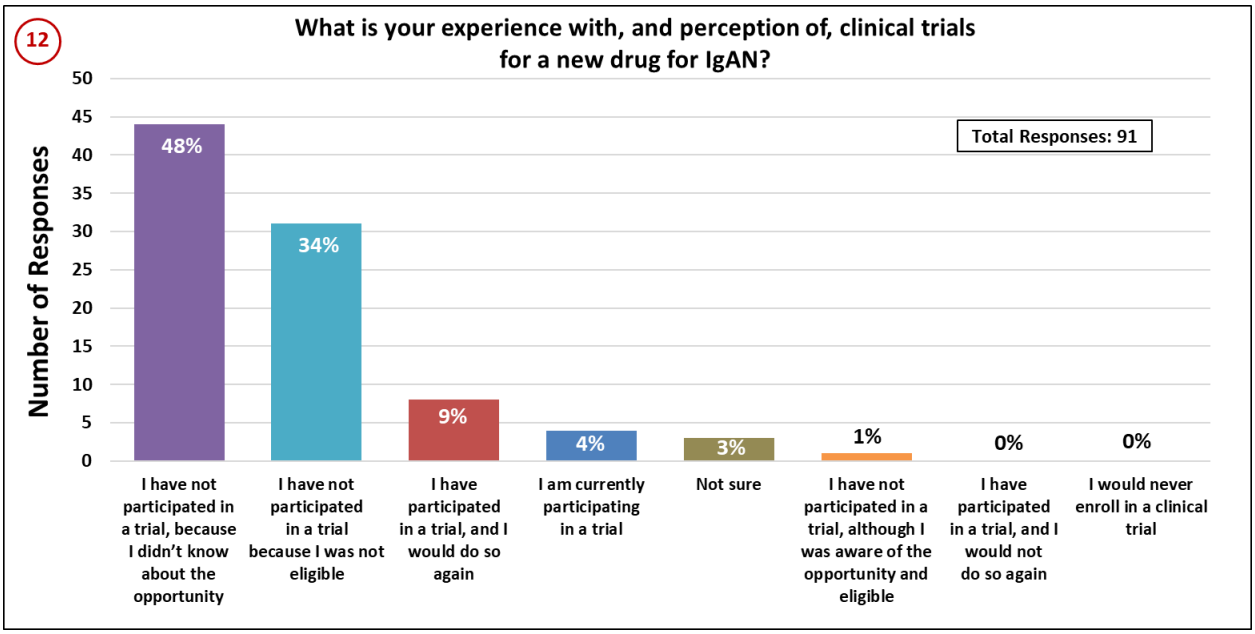


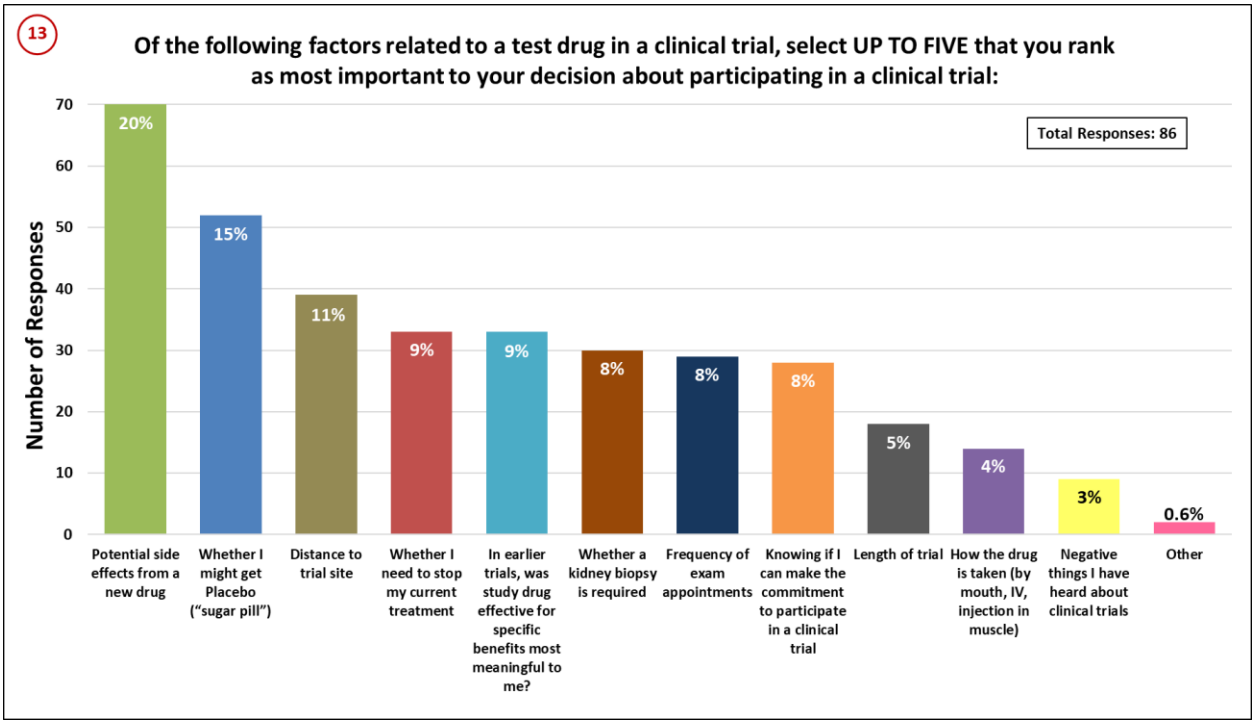

10
Which have you experienced while coping with your IgAN?
(Select all that apply)
Number of Responses
90
80
70
60
50
40
30
20
10
0
Total Responses: 94
23%
18%
18%
15%
13%
13%
0.3%
Anxiety
Hopelessness
Depression
Social isolation
Low-self esteem
Difficulty with relationships outside of family
None of the above

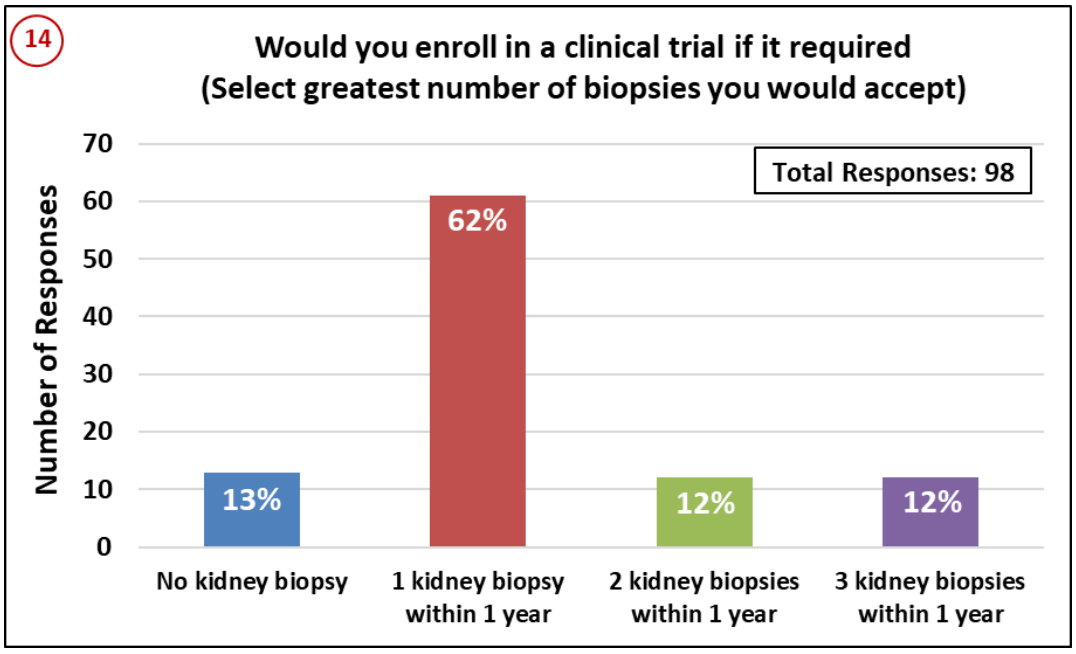

11
Which of the following statements is true for you as related to living with IgAN?
(Select all that apply)
Number of Responses
90
80
70
60
50
40
30
20
10
0
Total Responses: 97
31%
21%
18%
15%
14%
1%
Others don't know what it's like to live with IgAN
My general daily function is limited by IgAN
I cannot participate in sports or other physical activities I enjoy
Family stress is common in my life
I miss work or school more than I'm comfortable with
None of the above

TOPIC 2: CLINICAL TRIALS UNDER TRADITIONAL APPROACH

See Appendix 4.3 for Polling Questions

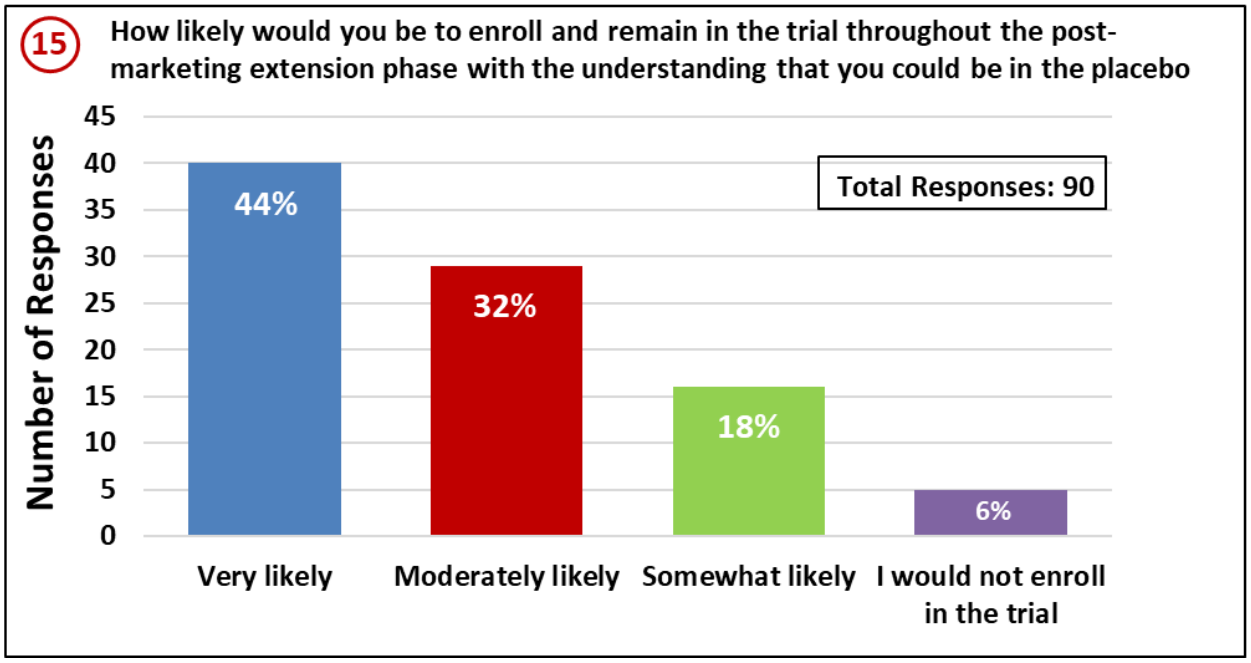


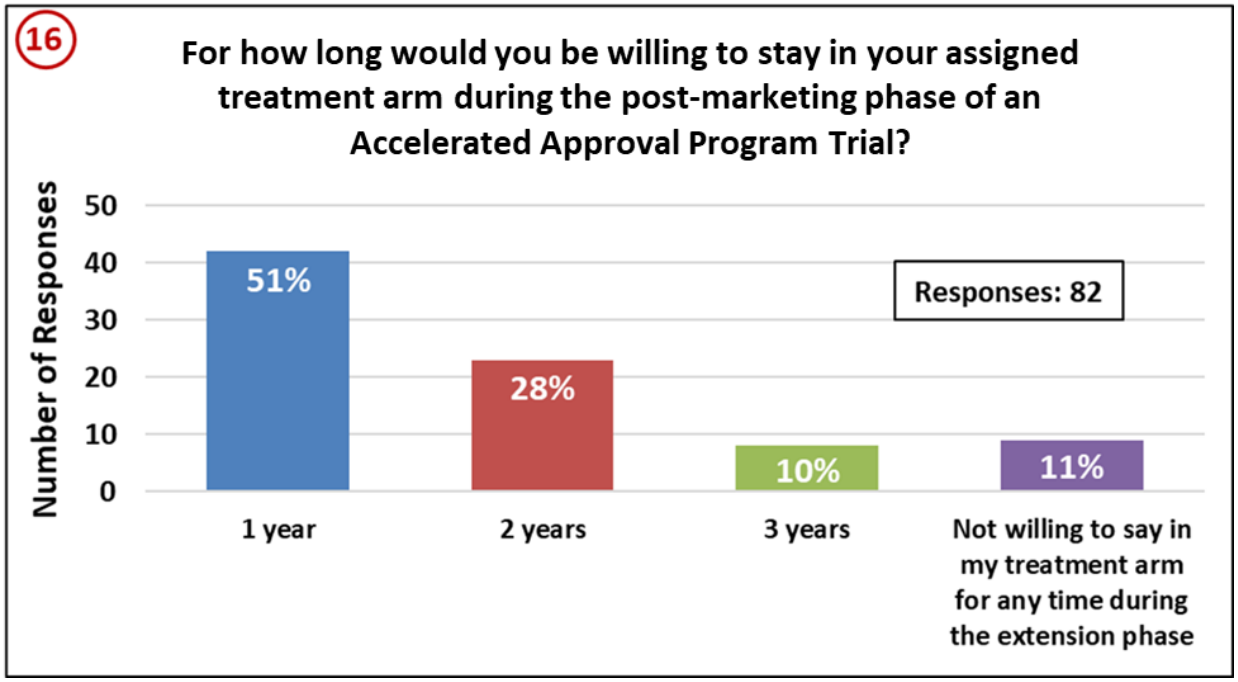


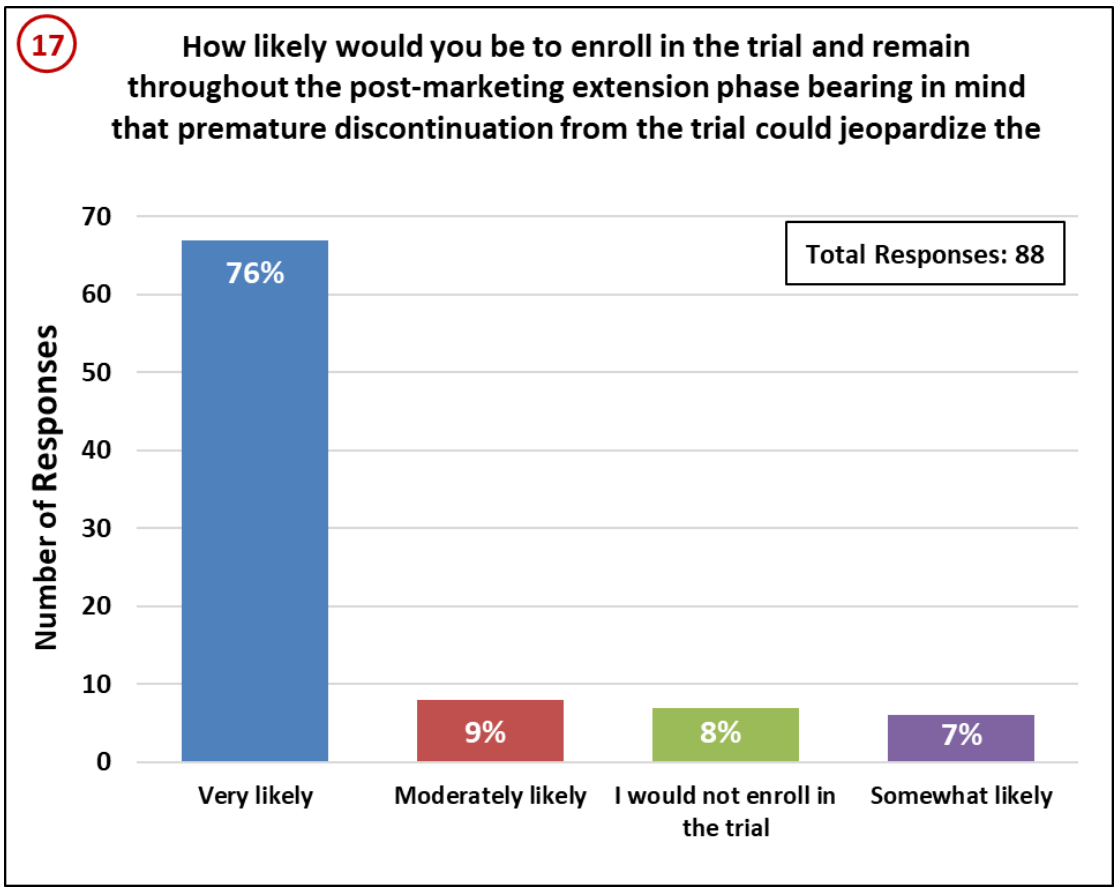

14
Would you enroll in a clinical trial if it required
(Select greatest number of biopsies you would accept)
Number of Responses
70
60
50
40
30
20
10
0
Total Responses: 98
13%
62%
12%
12%
No kidney biopsy
1 kidney biopsy within 1 year
2 kidney biopsies within 1 year
3 kidney biopsies within 1 year

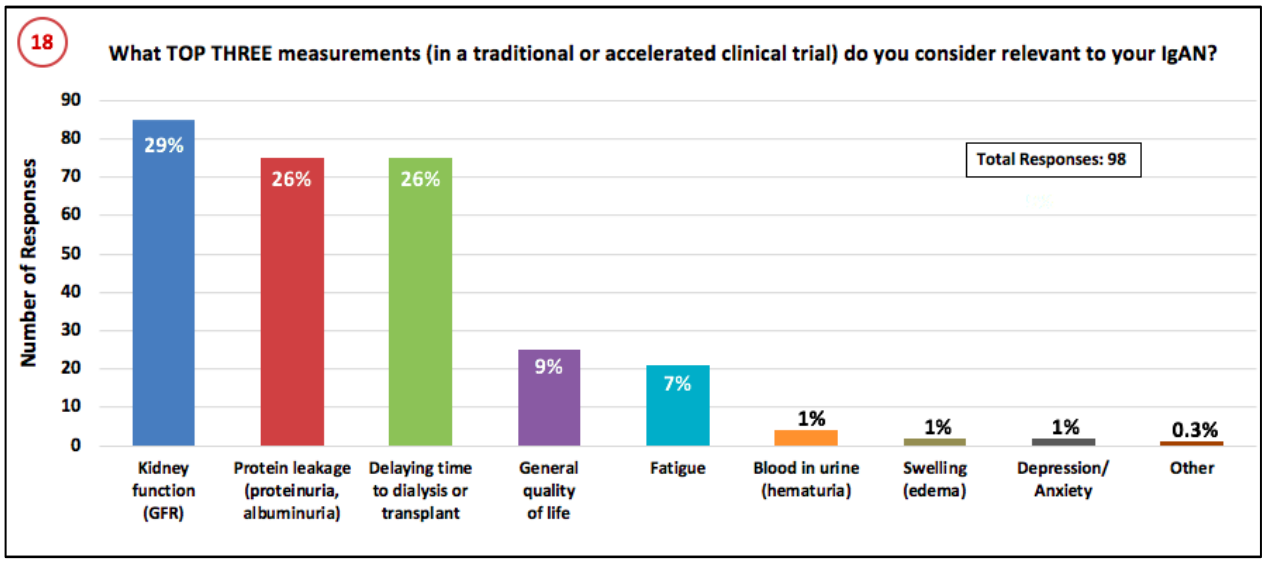
TOPIC 3: CLINICAL TRIALS UNDER ACCELERATED APPROVAL PROGRAM

See Appendix 4.4 for Polling Questions



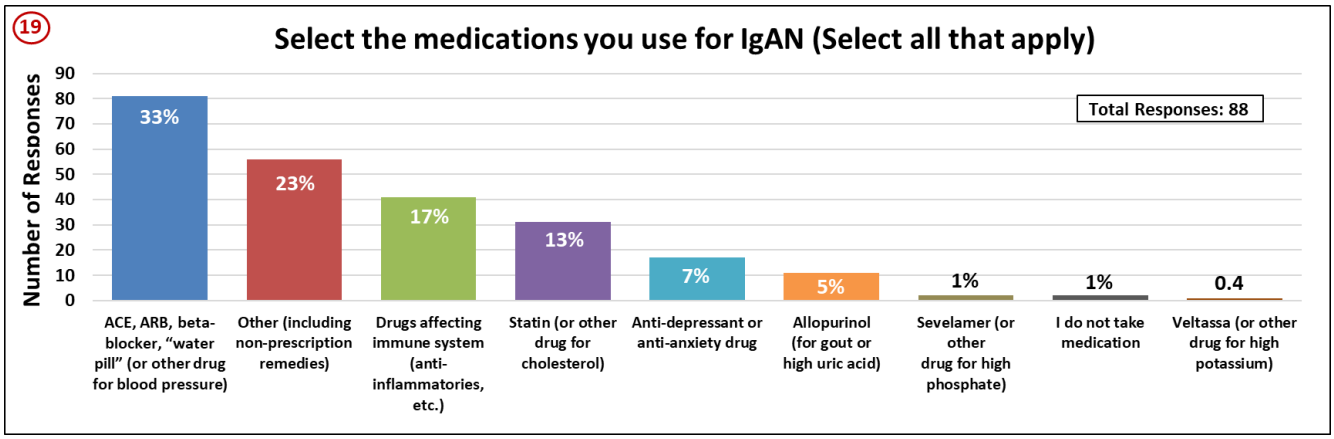


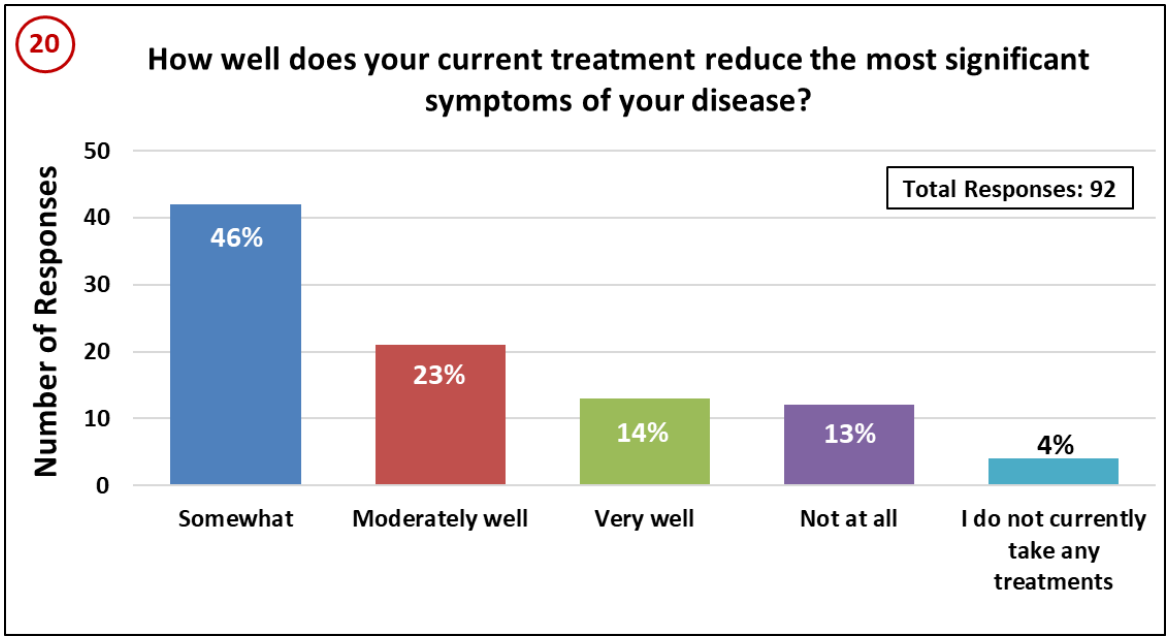

17
How likely would you be to enroll in the trial and remain throughout the post-marketing extension phase bearing in mind that premature discontinuation from the trial could jeopardize the
Number of Responses
70
60
50
40
30
20
10
0
Total Responses: 88
76%
9%
8%
7%
Very likely
Moderately likely
I would not enroll in the trial
Somewhat likely

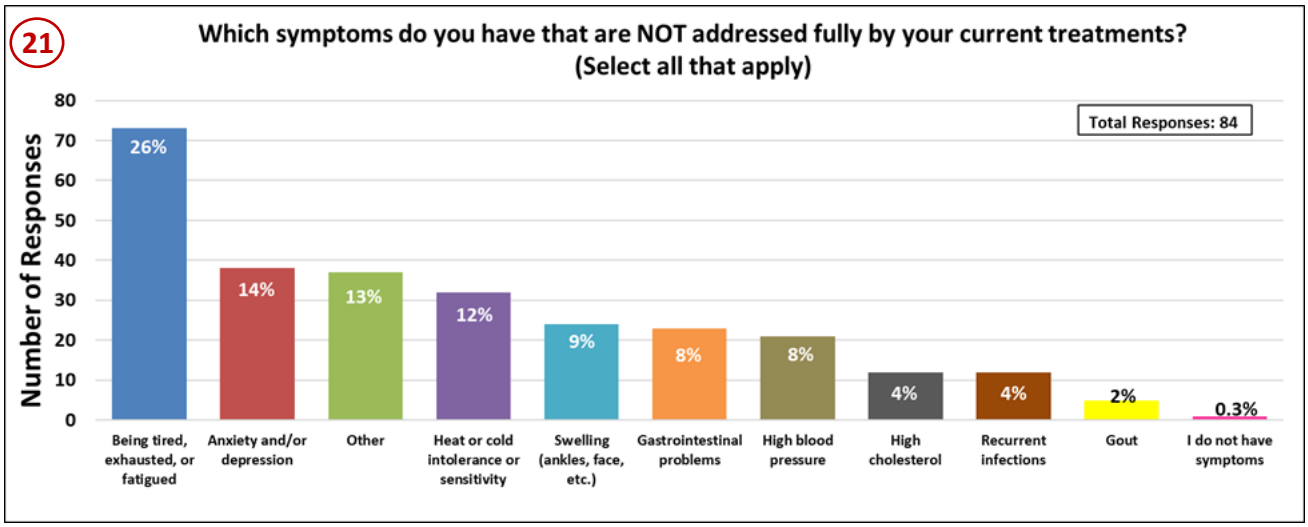

18
What TOP THREE measurements (in a traditional or accelerated clinical trial) do you consider relevant to your IgAN?
Number of Responses
90
80
70
60
50
40
30
20
10
0
Total Responses: 98
29%
26%
26%
9%
7%
1%
1%
1%
0.3%
Kidney function (GFR)
Protein leakage (proteinuria, albuminuria)
Delaying time to dialysis or transplant
General quality of life
Fatigue
Blood in urine (hematuria)
Swelling (edema)
Depression/ Anxiety
Other

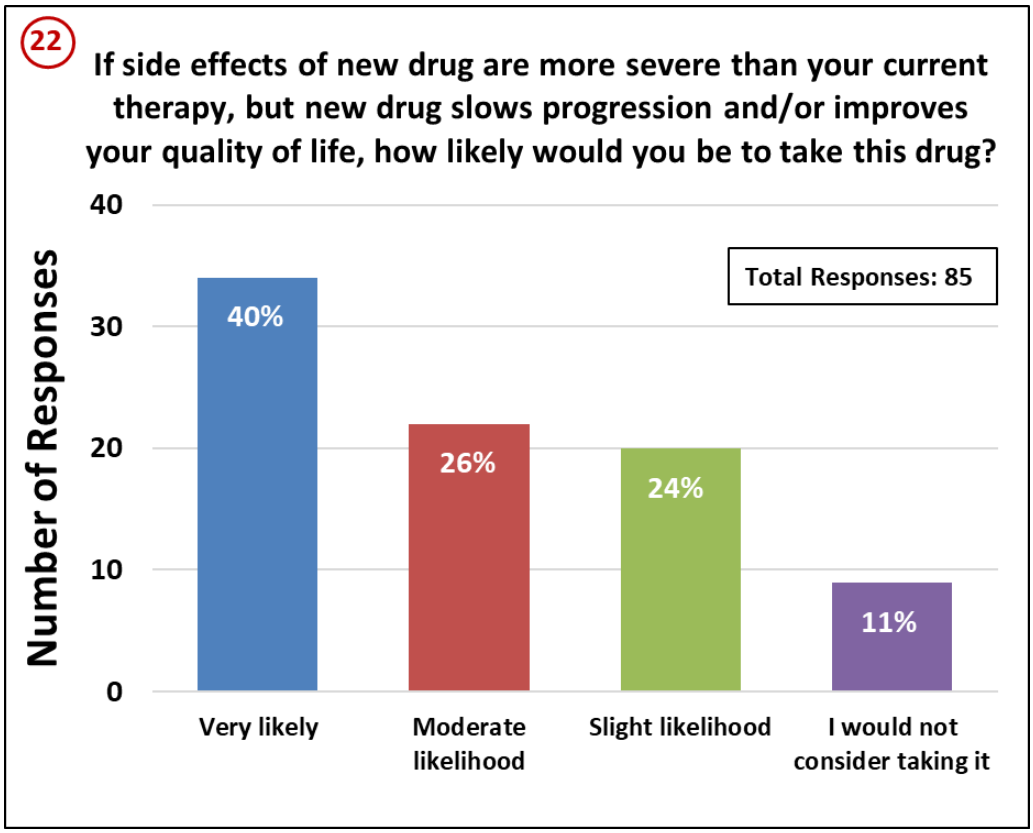
TOPIC 4: CURRENT CHALLENGES TO TREATING IgA NEPHROPATHY

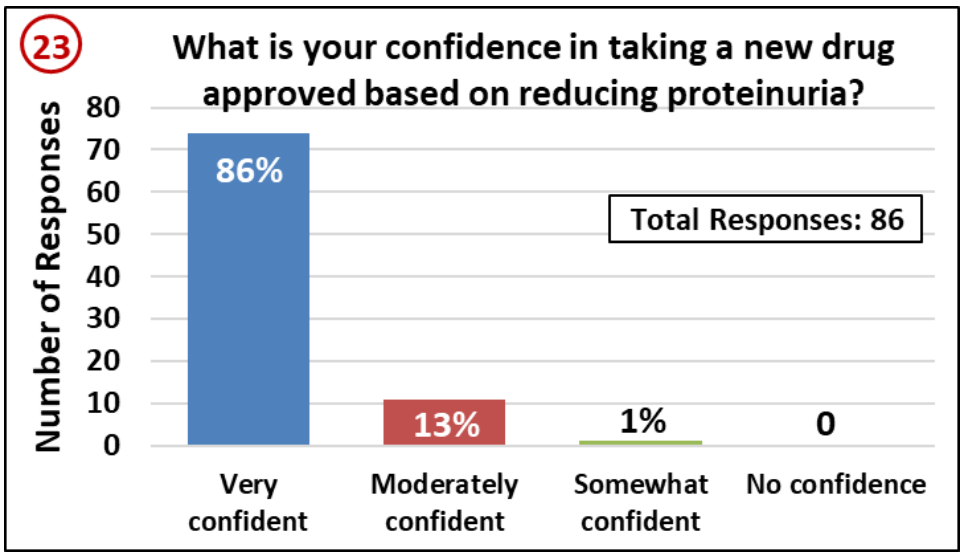
See Appendix 4.5 for Polling Questions

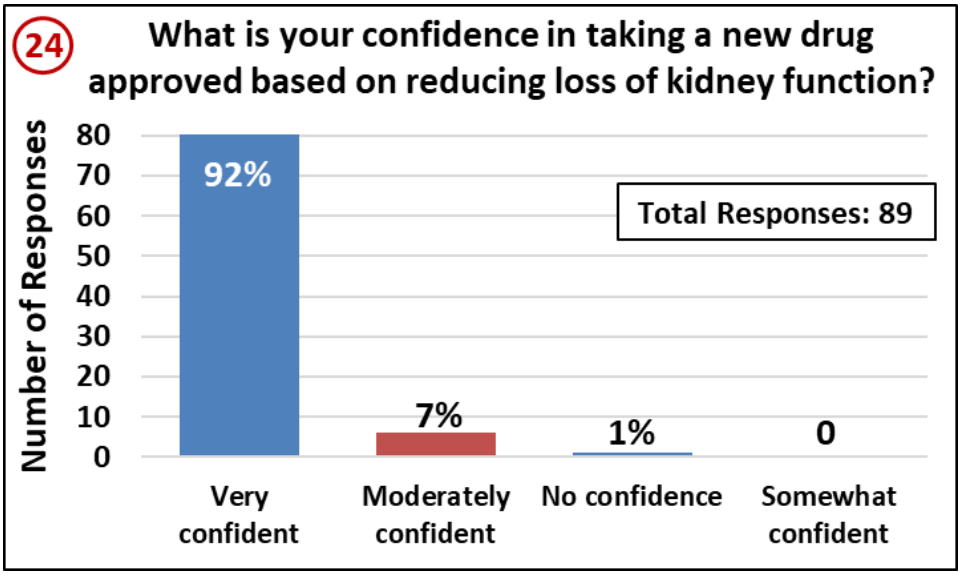


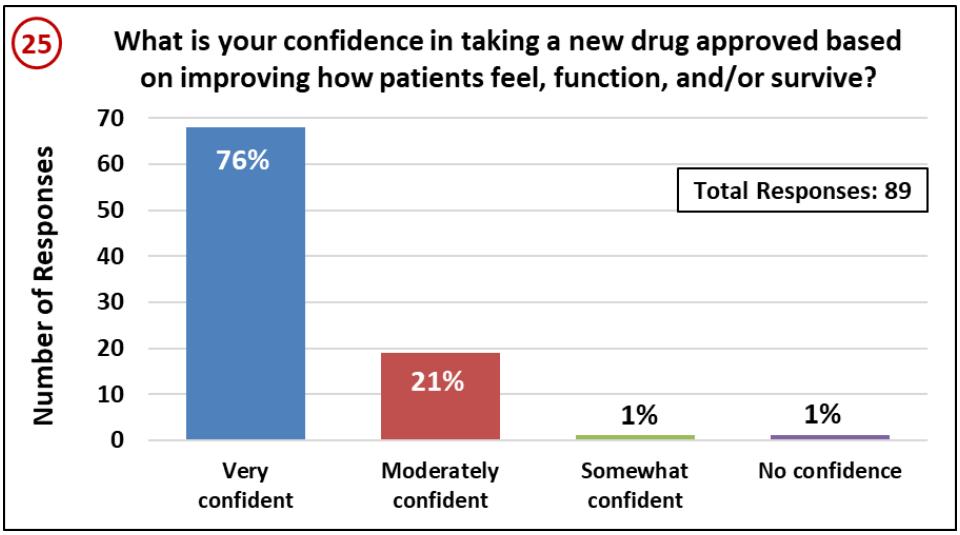


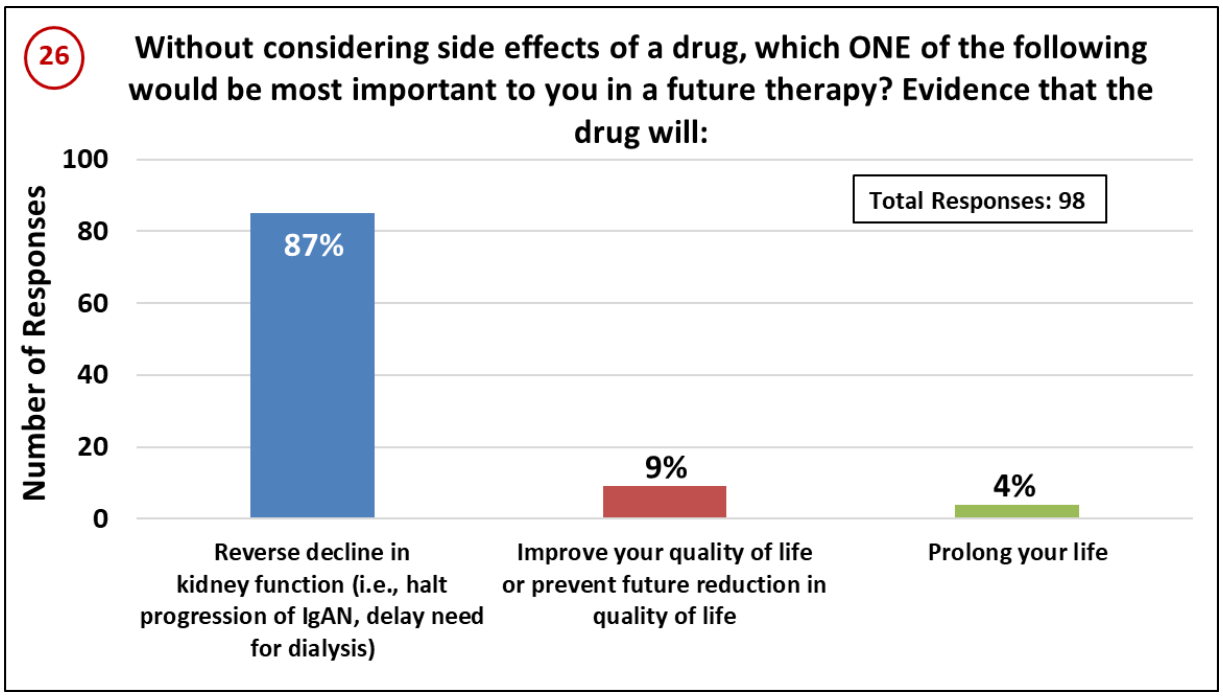

21
Which symptoms do you have that are NOT addressed fully by your current treatments?
(Select all that apply)
Total Responses: 84
Number of Responses
80
70
60
50
40
30
20
10
0
26%
14%
13%
12%
9%
8%
8%
4%
4%
2%
0.3%
Being tired, exhausted, or fatigued
Anxiety and/or depression
Other
Heat or cold intolerance or sensitivity
Swelling (ankles, face, etc.)
Gastrointestinal problems
High blood pressure
High cholesterol
Recurrent infections
Gout
I do not have symptoms


22
If side effects of new drug are more severe than your current therapy, but new drug slows progression and/or improves your quality of life, how likely would you be to take this drug?
Total Responses: 85
Number of Responses
40
30
20
10
0
40%
26%
24%
11%
Very likely
Moderate likelihood
Slight likelihood
I would not consider taking it


23
What is your confidence in taking a new drug approved based on reducing proteinuria?
Number of Responses
80
70
60
50
40
30
20
10
0
86%
13%
1%
0
Total Responses: 86
Very confident
Moderately confident
Somewhat confident
No confidence


24
What is your confidence in taking a new drug approved based on reducing loss of kidney function?
Number of Responses
80
70
60
50
40
30
20
10
0
92%
7%
1%
0
Total Responses: 89
Very confident
Moderately confident
No confidence
Somewhat confident


25
What is your confidence in taking a new drug approved based on improving how patients feel, function, and/or survive?
Number of Responses
70
60
50
40
30
20
10
0
76%
21%
1%
1%
Total Responses: 89
Very confident
Moderately confident
Somewhat confident
No confidence


26
Without considering side effects of a drug, which ONE of the following would be most important to you in a future therapy? Evidence that the drug will:
Number of Responses
100
80
60
40
20
0
Total Responses: 98
87%
9%
4%
Reverse decline in kidney function (i.e., halt progression of IgAN, delay need for dialysis)
Improve your quality of life or prevent future reduction in quality of life
Prolong your life

APPENDIX 6: DISCUSSION QUESTIONS

TOPIC 1: LIVING WITH IgA NEPHROPATHY: DISEASE SYMPTOMS AND THEIR DAILY IMPACTS

1. Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life?
2. Are there specific activities that are important to you but that you cannot do at all, or as fully as you would like, because of your condition?
3. How do your symptoms and their negative impacts affect your daily life on the best days? On the worst days?
4. How have your condition and its symptoms changed over time?
5. What worries you most about your condition?

TOPIC 2: CLINICAL TRIALS IN IgA NEPHROPATHY USING TRADITIONAL APPROACH

1. If you knew a clinical trial was planned for IgAN, what information would you want to know to inform your decision on enrolling in the trial?

TOPIC 3: CLINICAL TRIALS IN IgA NEPHROPATHY USING ACCELERATED APPROVAL PROGRAM

You are considering whether to enroll in a randomized, double-blind clinical trial for a potential drug for IgAN.

- The first phase of the trial will evaluate whether the treatment lowers proteinuria.
- If the trial shows a large enough effect on proteinuria, the drug will be approved under the Accelerated Approval Program.
- To verify that the product slows the loss of kidney function, patients who enrolled in the trial must remain in the trial in their assigned treatment arm for 1 to 2 more years for the post-marketing extension phase.

1. What factors would you consider when deciding whether to participate in this study?
2. If a drug is approved based on proteinuria alone, while this is considered to be reasonably likely to translate into ultimate clinical benefit for patients, there is some uncertainty if the drug will actually have a benefit on disease progression or how patients feel.
    a. If a benefit on proteinuria only had a 50% chance of being meaningful for patients, how would that impact your decision to use that drug?

TOPIC 4: CURRENT CHALLENGES TO TREATING IgAN

1. What are you currently doing to help treat your condition or its symptoms?
2. How well does your current treatment regimen treat the most significant symptoms of your disease?
    a. How well do your treatments address specific symptoms?
    b. Which symptoms are not addressed as well?
3. What are the most significant downsides to your current treatments and how do they affect your daily life?
4. Assuming there is no complete cure for your condition, what specific things would you look for in an ideal treatment for your condition?

APPENDIX 7: POST-MEETING COMMENTS FROM WEBCAST AUDIENCE

During the 30-day open comment period following the meeting, NKF and IGANF received seven comments from patients. These de-identified comments are below, edited only for spelling and clarity.

Comment

I am a mother of a son with a clinical diagnosis of IgA nephropathy. I would like to express to you how this has impacted my life. He was found to have microhematuria and proteinuria at a routine physical. I felt like my life did a 360. Normal one minute and then fear of the unknown. This was about 8 years ago. He sees his nephrologist yearly and takes losartan. He has been stable, but as you know how unpredictable this disease can be, that can change at any time. Just when I feel everything is going good, I always have that thought in the back of my head that he may get worse. He is only 21 and I worry about his future. You always want the best for your child and never want them to have to go through medical issues. I am praying that a cure will be found or at least better treatments that can halt this disease. The watch and wait plan is so cruel to the patient and family. I want to thank you for all that you do.

Comment

Thank you so much for all of your hard work on the meeting yesterday. It was really uplifting to know that there is work being done on our disease.

Will there be any studies on diet? I have been working with a holistic doctor and have at this time stabilized with minimal-to-no protein spill (knock on wood). Like many of the patients, I spent years with brain fog, extreme fatigue, easily sick, etc. In 2013, I had a GFR of 51 and gross hematuria. I was sent to a urologist for two years and had all kinds of tests done. They found nothing wrong. In 2015, I was sent to a nephrologist who suspected IgAN, as I had lots of food intolerances and had a poor immune system. Once my protein spill reached 1,529 [mg] I had a biopsy done and they found some scarring of one kidney and confirmed IgAN. By that time, I had already been experimenting with gluten free [diet] and removing food intolerances which definitely helped with the brain fog and the intense anxiety where I could fall asleep while driving—I still get tired easily—but nothing like before. I was unclear about not eating protein and experimented with the paleo and API diets thinking it [they (sic)] would help my immune system and food intolerances. I now see that my GFR took a dive during those periods, but they were short-lived and my GFR had risen into the 70's by the time I got my biopsy and dipped slightly to 67 just after. I kept good records of all my labs and what I was doing at the time. It was a bit confusing because my GFR had risen, but my protein spills had gotten worse. I still didn't have high blood pressure.

Once I was diagnosed, I met with a holistic kidney doctor. After putting me on a regime [regimen (sic)] of diet and supplements, my GFR went to 81 in 3 months and my protein was gone. However, during that time, my blood pressure rose and I came down with shingles. I had several cases of the flu, and a lot of stress in my life. My GFR dropped to 69 and my protein spilled to 779. I was put on lisinopril, which immediately started helping with my blood pressure and protein. However, it made me dizzy. I ended up decreasing my intake to 1.25mg, down from 10

mg and it started working really well. That was in July of 2017. I'm still on 1.25mg and my last tests showed GFR of 70 and no protein. It was really hard to keep up with all of the supplements and dietary restrictions that my holistic doctor had me on. I'm thinking of going back on it again though to see if I can help my kidneys anymore, but I am happy that I am currently stable. I'm just concerned that next time I get sick It might drop another 10 points and stay there.

Although my blood pressure is well within normal range, my body is in a lot of pain. My joints hurt often and I get very tired. Luckily, I own my own business and can take naps. I don't know if the tiredness is from my food and environmental intolerances, from getting older (I'm 52), or from IgAN. I also don't know if my joint and shoulder pains are from too many hours on the computer or perhaps something else (I also have a non-cancerous brain tumor). I also have a bit of swelling and aching in my lower calves around my ankle and I have slight foot burning which my neurologist said was not peripheral neuropathy nor do I have diabetes. I work out 4–5 days a week. [I] Eat a lot of fruits and veggies, watch my protein and salt and am slender at 5' 3" 110pds [pounds (sic)].

I truly wish more research was being done about how food and supplements affect IgAN patients rather than just drugs. Most of us have had to learn from each other. Although I consider my neurologist one of the best in our city, she has no real advice on diet or nutrition, except avoid salt, since my potassium and phosphorus levels are ok. So many people are eating poorly out there and need help from their doctors and medical professionals to tell them what to do as they won't pursue it on their own. I feel being diligent with my diet has really helped me and I also feel that if there were more information backing it, I would be more diligent and less apt to verge off the path, wondering if it was really helping since there is [are (sic)]no studies to back it.

Anyway, just another story for you to add to the collection for the FDA.

Thanks for taking the time to read this and for your dedication to our cause.

Comment

Hi! I was born and raised in the Philippines and [am] now living here in Canada. I was diagnosed with IgA nephropathy Class IV in 2014 and since then life has never been the same.

I had to have check-up[s] from [sic] every now and then, plus medication that needed to [be] take[n] but as I can tell it really is not helping me at all. I'm still sick. I always feel tired because of this disease and I don't have enough energy to even play with my 2-year-old daughter.

I have lots of dreams, like to travel to beautiful places, but this disease is stopping me from planning because it feels like my life is about to end anytime.

I fear that if this disease continues to progress, I might not be able to see my child grow up.

I had tried prednisone, CellCept, tacrolimus and a lot more but it didn't really help. My function just keeps on declining.

I wish and hope that if there is a medicine already found for this disease, it will be out now in the market so that everyone who has this disease will have their life back.

Comment

I listened to the entire seminar.

My 21-year-old granddaughter was recently DX [diagnosed] with IgA[N] and I have to say after the completion I found myself very sad and frightened for her. She is also epileptic. At present she is on fish oil and HCTZ [hydrochlorothiazide].

She was on lisinopril, but she complained of dizziness and her BP [was] low.

She also complains of fatigue often and headaches. [Her] urine is foamy and [she had] elevated protein. She is beautiful and newly married to a Marine. I have encouraged her to watch her NA [sodium] intake. Also her legs are very edematous.

She drinks a lot of water, ever since she was young.

Thank you for taking the time to read this note and if you have any suggestions, please let me know.

Comment

I wanted to thank you for hosting the meeting, and for the interesting information that was shared.

I could not make it to the event—but wanted to express a short impact statement as well.

My brother-in-law was diagnosed with IgAN shortly after his daughter was born.

He had many complications over the last 14 years—including and infection with MRSA, multiple fissulas [fistulas (sic)] that were infected, a blood fungal infection—to name just a few

He has been on dialysis for about two years now. All in all, his quality of life, as well as that of his family has truly suffered. He hasn't had a job in at least 10 years. He and my sister seem to constantly fight. He can never take part in the kid's trips or vacations because he is too tired or has to be back for dialysis. Even just something as simple as mowing the lawn is impossible.

He was such a vibrant and vivacious guy. Funny. Goofy.

Now he is depressed, absent, lost.

I have watched how my niece and nephew tiptoe around the subject. They know way too much for a 14- and 10-year-old about kidney disease...hypertension...prednisone.

I work in biotech and know the difficulty of bringing a new drug to market. The development, bringing the product to commercial production scale. Then the clinical trials. I have been in this business 18 years and have seen many failures—and very few success stories. But I do hope that with some recent innovations, FDA and sponsor support—that we will see some improvement in this disease area.

I don't believe that my brother in law will be able to walk his daughter down the aisle…[or] possibly not even teach his son how to drive. How long can one survive on dialysis without a transplant—and even then, the prognosis is dire. I wish you all the best.

Comment

I was diagnosed with IgA nephropathy just six months ago. I went to my doctor for a yearly check-up and my blood pressure was through the roof. I work out four days a week and eat a very healthy diet, so my doctor chocked [chalked (sic)] it up to genetics, wrote me a prescription, drew labs, and sent me on my way. A few days later I received a phone call stating that my kidneys were functioning at 20%, and that I should stop taking the medication she prescribed and take a different one. I was never referred to a nephrologist. Luckily, I have a mother in law that [who (sic)] works as a dialysis nurse and she was able to have me seen by a nephrologist quite quickly. The next few days were horrible. Test after test. Finally, after a kidney biopsy, IgA nephropathy was confirmed. I can't stress enough the toll this disease takes on my life. EVERYTHING changed. The foods that were considered healthy before, now contained too much protein, potassium, phosphorus, and salt. I lost 20 pounds in one month. Terrified to eat something at the risk my kidneys would shut down and I would be forced to begin dialysis. I now take a plethora of medication that actually doesn't do anything for the actual problem; it just treats the symptoms of IgAN. So, not only am [I] fighting symptoms from IgAN, I am also fighting symptoms from the many medications that doctors aren't sure are actually helping. Kidney disease is the secondary problem caused by IgAN. We need research and funding to find ways to stop the problem from the source. I have two small children and the thought of them growing up without a mother, shreds my heart into pieces. It is such a hopeless feeling to know that you are basically just waiting until your kidneys give out to hopefully receive a transplant only to have a risk of reoccurrence. Currently, I am doing everything I can to keep my "numbers" good. We in the IgAN community humbly ask that the FDA do everything in their power to find a solution for this awful disease. Thank you for your consideration.

[signed] 31-year-old female

Comment

Good day to you

I'm writing this email for feedback on current [status of] IgAN disease that I've been suffering since I am [was (sic)] 27 yrs old and now I am 35 yrs old (8 years).

FYI, I'm mother for 2 children (son is 6 yrs old and daughter is 2 yrs old) and having high blood pressure and IgAN.

Currently I'm taking medicine as below:

a) Diltiazem hydrochloride–90mg (1 time per day)

b) Candesartan cilexetil–16mg (1 time per day)

c) Allopurinol–100mg (1 time per day)

d) Prednisolone–5mg (1 time per day)

e) Lipitor (atorvastatin) –20mg (1 time per day)

1) IgAN was not much give [ing (sic)] me an impact, as I didn't feel anything from this disease. I feel like I'm still healthy and can do whatever I want.

But I do less on exercise and do more on housekeeping at my house…every day before… going to work and also during [the] weekend.

2) The symptoms [sic] that I've struggle most [with are] is I feel easily tired, but I will fight for [against (sic)] it and ignore [the need] to rest. Sometimes, I will rest for a while then will continue back my work as usual.

3) My biggest worries and fears about IgAN is [are about (sic)] DIALYSIS. I wish that I will keep healthy due to my current eGFR is increase[ing] to 40 (August 2019) compared to 29 (June 2019). As I'm still young and need to work to support my family, I am scared if I need DIALYSIS because it will give many impact[s] to me, especially in financial, working, and daily life.

4) [Among the] Treatments that have failed to [sic] me is taking prednisolone, as my body was [would (sic)] not respond to it. I've been taking it around 1.6 years, but nothing was change and my protein and blood in urine still exist. My side effects that I hate most during current treatment is [are (sic)] I've put on weight, my face is round, always feel hungry and gout, due to urine acid is increase.

That is my current feedback on this matter [and] is for your further action.

I hope [you] will have other solution for better treatment to this IgAN disease besides only DIALYSIS.

Thank you and have a nice day ahead.

APPENDIX 8: ACKNOWLEDGEMENTS

We are grateful to the following sponsors for their generous support of this meeting:

- Calliditas Therapeutics
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