PO1641

An International Delphi Survey on IgA Nephropathy – Results from DEFINE: Physicians Study

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Background

- IgA nephropathy (IgAN) is a common cause of glomerulonephritis that can lead to end-stage kidney disease[1]
- No United States Food and Drug Administration or European Medicines Agency-approved treatments specific to IgAN are available[1]

Rationale

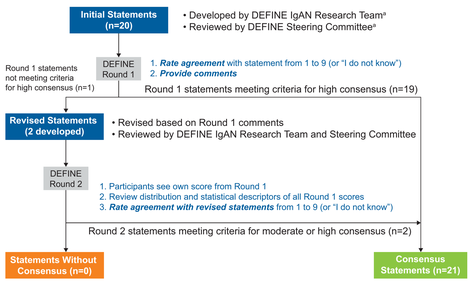
- It is unknown how uniformly nephrologists in different countries manage IgAN
- The ***De****lphi* ***F****ocal Segmental Glomerulosclerosis (FSGS) &* ***I****gA* ***N****ephropathy (IgAN)* ***E****xperts: Physicians (DEFINE: Physicians)* study sought to capture physicians' consensus opinions on pathophysiology, diagnosis, and optimal management of adult and pediatric patients with IgAN or FSGS
- Consensus opinions on the diagnosis and optimal management of FSGS are presented in the companion poster (PO1643, abstract #3604861)

Methods

- *DEFINE: Physicians* was an online 2-round Delphi survey that recruited nephrologists from Canada, France, Germany, Italy, Spain, the United Kingdom, and the United States
- Nephrologists scored 20 statements on IgAN using a 1-9 Likert scale (1=strongly disagree; 9=strongly agree) with an additional option of "I do not know"
  - Free-text responses were collected from participants who rated their agreement as ≤6
- Consensus was defined as a median and mean agreement score of ≥7 and ≥75% of participants scoring agreement (ie, score of 7-9)
  - Statements with ≥90% agreement were considered to have high consensus among the participants
  - Statements with 75% to 89% agreement were considered to have moderate consensus among the participants
- Statements not achieving high consensus in Round 1 were revised based on the free-text response and retested in Round 2 (**Figure 1**)

Results

Figure 1. Overview of *DEFINE: Physicians'* methodology and study results



[a]The DEFINE Steering Committee and IgAN Research Team are groups of experts on the treatment of IgAN and are the authors of this poster.

Survey participants

- The initial survey was open from November 17, 2020, to January 14, 2021, with 207 nephrologists participating in Round 1 (**Table 1**)
- Round 2 was administered from March 29, 2021, to April 13, 2021, with 126 of 157 (80%) adult nephrologists and 32 of 50 (64%) pediatric nephrologists participating again

Table 1. Key characteristics of participants

Characteristic	Nephrologists	
	Adult n=157	Pediatric n=50
Experience as a practicing nephrologist in years, median (range)	18 (5-49)	17 (5-40)
No. of patients with IgAN in the last 2 years,[a] median (IQR)	25 (11-50)	20 (10-70)
Practice setting, n (%)		
Academic center or academic hospital	70 (45)	34 (68)
Nonacademic	87 (55)	16 (32)
Country of practice, n (%)		
United States	69 (44)	26 (52)
Italy	19 (12)	4 (8)
Germany	14 (9)	7 (14)
United Kingdom	15 (10)	5 (10)
France	17 (11)	2 (4)
Spain	13 (8)	5 (10)
Canada	10 (6)	1 (2)
Participants referencing ≥1 clinical guideline when treating patients,[b] n (%)	144 (92)	47 (94)
KDIGO	138 (88)	33 (66)
IPNA	7 (4)	27 (54)

IgAN, IgA nephropathy; IPNA, International Pediatric Nephrology Association; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes.

[a]Refers to patients diagnosed or treated.

[b]Participants were able to select multiple guidelines.

Statements with high consensus in Round 1

- Most IgAN diagnosis and management statements met criteria for high consensus (**Table 2**)

Table 2. Statements with high consensus in Round 1

		Statements rated by all participants	Agreement in Round 1
Pathophysiology	1	Persistently elevated proteinuria is a major adverse prognostic marker in FSGS and IgAN.	97%
Pathophysiology	2	Damage to podocytes and other glomerular cells are amplified by activation of angiotensin and/or endothelin pathways, contributing to high levels of proteinuria and greater risk for progressive kidney injury.	92%
Pathophysiology	3	Persistent proteinuria causes tubulointerstitial injury by inducing and amplifying inflammation, fibrosis, and kidney scarring, thereby driving further disease progression.	98%
Pathophysiology	4	A close correlation exists between the level of proteinuria and the risk of kidney failure; the higher the proteinuria the higher the risk of kidney failure.	96%
Diagnosis	23	IgAN without an associated condition is considered primary or idiopathic. IgAN associated with another condition (eg, IgA vasculitis, chronic liver disease) is defined as secondary.	94%
		Statements rated by adult nephrologists only	
Monitoring/follow-up	19	In both FSGS and IgAN, the goal of therapy is to reduce proteinuria as much as safely possible in order to preserve kidney function as evidenced by stable or improved GFR.	98%
Diagnosis	24	Proteinuria determines prognosis. Patients with proteinuria >1 g/day despite optimized supportive care are at high risk for progressive kidney dysfunction or kidney failure and should be considered for more aggressive treatment.	94%
Diagnosis	25	The International IgAN Prediction Tool should be used at time of kidney biopsy to identify adult patients with a poor prognosis or high risk for kidney failure within 5 years.	90%
Treatment	27	ACE-I/ARBs are used as first-line maintenance treatment in patients with persistent proteinuria, except in circumstances of very advanced disease (eg, GFR <20 mL/min/1.73 m^2) or acute presentation of rapidly progressive glomerulonephritis.	96%
Treatment	29	In rapidly progressive glomerulonephritis (≥50% decline in eGFR over 3 months or less), corticosteroids and cyclophosphamide are treatment options in specific settings where the risk-benefit profile is acceptable.	97%
Monitoring/follow-up	33	Monitoring proteinuria every 6-12 months is recommended for patients with proteinuria <0.5 g/day and normal GFR (glomerular filtration rate).	95%
Monitoring/follow-up	34	Those with proteinuria >0.5 g/day should be monitored more frequently than 6-12 months and monitoring should be individualized on a case-by-case basis.	96%
		Statements rated by pediatric nephrologists only	
Diagnosis	26	Proteinuria determines prognosis. Patients with proteinuria >0.5 g/day/1.73 m^2 or urine PCR >500 mg/g despite optimized supportive care are at high risk for progressive kidney dysfunction or kidney failure and should be considered for more aggressive treatment.	98%
Treatment	30	ACE-I or ARBs are used as first-line maintenance treatment in children with persistent proteinuria.	98%
Treatment	31	If proteinuria levels cannot be reduced to <0.5 g/day/1.73 m^2 or to urinary PCR <500 mg/g with a course of supportive therapy using ACE-Is or ARBs, corticosteroids may be considered in specific settings where the risk-benefit profile is acceptable.	98%
Treatment	32	Children with severe disease on biopsy (severe mesangial and endocapillary hypercellularity or with crescent formations involving >30% of the glomeruli) can be treated with steroid pulses and cyclophosphamide shortly after kidney biopsy.	94%
Monitoring/follow-up	35	The goal of therapy is to prevent kidney damage by reducing proteinuria as much as possible in order to attain long-term complete remission, which is defined as the disappearance of hematuria, accompanied by proteinuria <200 mg/day/1.73 m^2 or PCR <200 mg/g and eGFR within normal range for age.	92%
Monitoring/follow-up	36	Stable disease in remission is defined as proteinuria <200 mg/day/1.73 m^2 or PCR <200 mg/g and with eGFR persistently in the normal range for the patient's age.	98%
Monitoring/follow-up	37	Those with stable disease in remission are monitored at least once every 3-6 months, whereas those with progressive disease should be monitored more frequently and monitoring should be individualized based on disease severity and treatment.	100%

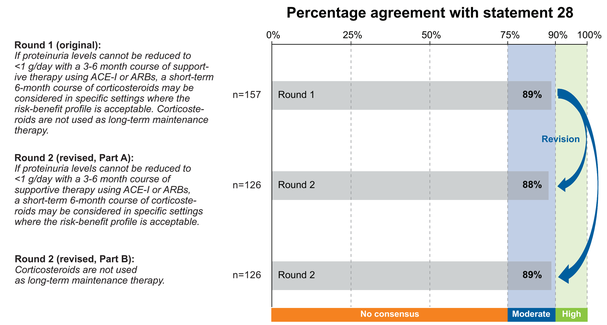
Pathophysiology · Diagnosis · Treatment · Monitoring/follow-up · High consensus (≥90% agreement)

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; IgA, immunoglobulin A; IgAN, IgA nephropathy; PCR, protein-to-creatinine ratio.

Statement not meeting high consensus criteria in Round 1

- Statement 28 had the lowest level of agreement (**Figure 2**)

Figure 2. Statements with moderate consensus in Round 1 and retested in Round 2



ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

Discussion

- There was overall very high consensus for all statements after Round 1
- Statement 28 had the lowest level of agreement (although still moderate)
  - Results from studies such as the STOP-IGAN and TESTING trials[2-5] call into question the risk-benefit profile of corticosteroids
- Nephrologists see proteinuria as an important prognostic marker informing clinical management decisions and that reducing proteinuria as much as possible is important in preserving kidney function (Statements 1-4; **Table 2**)
  - Most agreed that proteinuria itself is a driver of disease by causing kidney damage
- Limitations of this study include:
  - The study was conducted in English and did not include nephrologists from Asia or South America
  - A limited number of women and pediatric nephrologists participated in this survey
  - A limited number of topics were investigated
  - Statements on new or experimental therapies might result in less consensus

Conclusions

- Some nephrologists do not agree on the utilization of corticosteroids in patients who are on optimized supportive therapy but still have elevated proteinuria
  - Most nephrologists do not support the long-term use of corticosteroids and agree that short-term corticosteroids should be used in specific settings where benefits outweigh the associated risks
  - These results suggest that there are concerns about the risk-benefit profile of corticosteroids and new therapies are needed for the treatment of IgAN
- *DEFINE: Physicians* found high levels of consensus of opinion among nephrologists from North America and several European countries who treat patients with IgAN
  - These results suggest that nephrologists from these regions largely agree with one another on how to manage IgAN

References

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Acknowledgments

Logistical support of the Delphi process was provided by ApotheCom (San Francisco, CA) and Psyma (Berwyn, PA) with funding from Travere Therapeutics, Inc. (San Diego, CA). Statistical analyses were performed by Monia Ezzalfani, PhD, of Creativ-Ceutical (Luxembourg), and Christopher Pham, PharmD, of ApotheCom (San Francisco, CA). Authors did not receive compensation for their work on this poster. Writing and editorial support for this poster was provided by Christopher Pham, PharmD, of ApotheCom (San Francisco, CA) and funded by Travere Therapeutics, Inc. (San Diego, CA).

Disclosures

The steering committee and research team (except Marcello Tonelli) received compensation as part of a research agreement with Travere Therapeutics, Inc. (San Diego, CA) for the guidance of the Delphi process including the study design, conception of the study, statement development/revision, and interpretation of research findings.

Contact Information

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Presented at the American Society of Nephrology (ASN) Kidney Week; November 4-7, 2021; San Diego, CA