

Persistence of Signs and Symptoms in Treated Patients with IgAN: Evidence from Real-World Data

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Introduction

- Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide, with an estimated annual incidence of 25 per million¹.
- IgAN presents with numerous clinical manifestations, commonly including hematuria, proteinuria, and hypertension².
- Measurements of proteinuria are considered good indicators of risk of progression to kidney failure, with higher values in IgAN patient associated with a poorer prognosis³.
- This analysis aimed to describe IgAN signs and symptoms in treated patients.

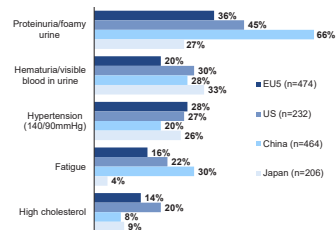
Methods

- Data were drawn from the IgAN Disease Specific Programme™ (DSP), a point-in-time survey of nephrologists, and their IgAN patients, conducted in the EU5 (France, Germany, Italy, Spain, and the United Kingdom), United States (US), China, and Japan between June and October 2021.
- The DSP methodology has been published previously in detail⁴.
- Ethics exemption was obtained from the Pearl Institutional Review Board and Hospital Clinic de Barcelona.
- Nephrologists completed structured online patient record forms for each successive consulting IgAN patient providing information on patient's demographics, IgAN treatment history, and IgAN signs and symptoms.
- Nephrologists could select multiple signs and symptoms experienced by the patient at the point of survey from a preset list of 29 items, developed from background research, physician interviews, and patient interviews.
- Linear regression analysis was used to examine the relationship of time since treatment initiation with current patient estimated glomerular filtration rate (eGFR), proteinuria, and their total number of symptoms.
- Patients were subject to an inclusion criteria. The sample considers patients who had been receiving IgAN treatment for at least seven days since the initiation of line one and they must also have been receiving IgAN treatment at the time of survey.

Results

- In total, 295 nephrologists completed record forms for 1376 patients with IgAN treated for a minimum of one week at time of survey. Mean (SD) patient age was 44.3 (14.1) in the EU5, 43.4 (13.4) in the US, 38.5 (13.1) in China, and 46.9 (16.1) in Japan (Table 1).
- Proteinuria, hematuria, hypertension, and fatigue were the most commonly reported signs and symptoms experienced by patients across the total sample at time of survey (Figure 1).

Figure 1. Physician-reported signs and symptoms experienced by patients at the time of survey



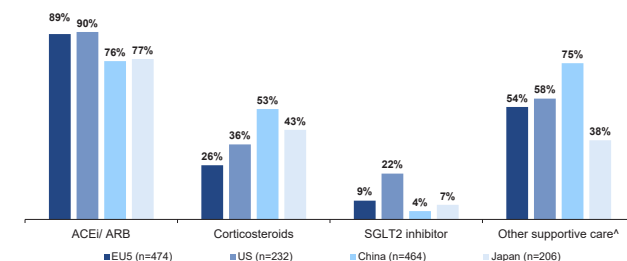
- Despite supportive care treatment (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and sodium-glucose cotransporter-2 (SGLT2) inhibitors), most patients presented with signs and symptoms at time of survey (Figure 2).
- SGLT2 inhibitor treatment was highest in the US at the time of survey (Figure 2).
- Signs and symptoms persisted amongst patients, with many patients considered to be symptomatic despite a longer treatment duration (Figure 3).

Conclusions

- Despite treatment, IgAN signs and symptoms persist in the majority of patients.
- Proteinuria persists in many patients increasing risk of progression to kidney failure.
- eGFR is predicted to significantly decrease despite treatment.
- This shows a need for better treatment options to control signs and symptoms of IgAN and subsequently enhance disease management for patients.

Results

Figure 2. Physician-reported treatment class at the time of survey



*Other supportive care = any treatment that is not an ACEI, ARB, corticosteroid, or SGLT2 inhibitor
ACEI: Angiotensin-Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blockers; SGLT2 Inhibitors: Sodium-Glucose Cotransporter-2 Inhibitors

- Median time since treatment initiation was 121 (45-274) weeks in the EU5, 61 (26-129) in the US, 130 (27-153) in China, and 62 (37-321) in Japan (Table 1).

Table 1. Patient demographics by geographical regions

	EU5 (n=474)	US (n=232)	China (n=464)	Japan (n=206)
Mean age in years (SD)	44.3 (14.1)	43.4 (13.4)	38.5 (13.1)	46.9 (16.1)
Patient gender Male, n (%)	317 (66.9)	131 (56.4)	261 (56.2)	103 (50.0)
Mean patient BMI in kg/m ² , (SD)	25.6 (4.4)	26.0 (4.8)	22.9 (2.5)	23.0 (3.9)
Median time from symptom onset to first consultation (weeks)	4	4	5	7
IQR: 1-9	IQR: 1-10	IQR: 1-16	IQR: 2-19	
Median time from symptom onset to point of survey (weeks)	168	87	108	172
IQR: 70-301	IQR: 40-191	IQR: 39-190	IQR: 71-378	
Median time from treatment initiation to point of survey (weeks)	121	61	62	130
IQR: 45-274	IQR: 26-129	IQR: 27-153	IQR: 38-321	

BMI: Body Mass Index; EU5: France, Germany, Italy, Spain, and the United Kingdom; IQR: Interquartile Range; SD: Standard deviation; US: United States

- Most patients had an eGFR measurement of ≥ 45 mL/min/1.73 m² at time of survey, regardless of how long they had been receiving treatment (Table 2).
- Of those patients treated for more than two years, EU5 31%, US 26%, China 28%, Japan 17% had >1g proteinuria/day where reported (Table 2).

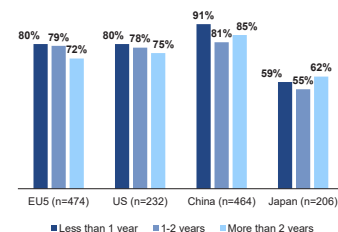
Table 2. Proteinuria and eGFR at time of survey

	EU5			US			China			Japan		
n number	139	82	253	105	50	77	194	96	174	64	29	113
Time since treatment initiation (Years)	<1			<1			<1			<1		
	1-2			1-2			1-2			1-2		
	>2			>2			>2			>2		
Current eGFR (mL/min/1.73 m²)												
n number	139	82	253	105	50	77	194	96	174	64	29	113
eGFR ≥ 45	73%	80%	74%	68%	76%	71%	92%	94%	72%	78%	83%	73%
eGFR <45	27%	20%	26%	32%	24%	29%	8%	6%	28%	22%	17%	27%
Current Proteinuria (where reported)												
n number	121	71	228	90	45	74	183	93	173	55	27	96
>1g/day	47%	41%	31%	48%	36%	26%	34%	19%	28%	11%	4%	17%
≤ 1 g/day	53%	59%	69%	52%	64%	74%	66%	81%	72%	89%	96%	83%

eGFR: Estimated Glomerular Filtration Rate

Results

Figure 3. Percentage of patients considered to be symptomatic at the time of survey grouped by time since first treatment initiation



- Linear regression analysis shows that for every year of treatment, the patient's current eGFR value is predicted to significantly decrease by 1.560 (Table 3).
- Current proteinuria values and total number of symptoms are expected to marginally decrease for every year of treatment, however these result are not significant (Table 3).

Table 3. Linear regression results for the impact of time since treatment initiation (in years) across the total sample

	Number of patients, n	Coefficient	p-value
Current eGFR level (mL/min/1.73 m ²)	1376	-1.560	0.000
Current proteinuria (g/day)	1256	-0.020	0.134
Total number of current symptoms	1376	-0.024	0.193

eGFR: Estimated Glomerular Filtration Rate

eGFR: For every year since treatment initiation a decrease of 0.020 in a patient's current eGFR level is predicted. The coefficient is statistically significant.

Proteinuria: For every year since treatment initiation a decrease of 0.020 in a patient's current proteinuria level is predicted. The coefficient is not statistically significant.

Total symptoms: For every year since treatment initiation a decrease of 0.024 in a patient's total number of symptoms currently is predicted. The coefficient is not statistically significant.

Discussion

- Linear regression results suggest that patients' eGFR values are expected to worsen despite treatment, suggesting that current treatment may fail to prevent eGFR decline in patients with IgAN.
- Similarly, although proteinuria and total number of symptoms are associated with a decline as time since treatment initiation increases, the result is insignificant suggesting that treatment is having a very minor effect.
- Overall, the results demonstrate that currently available and prescribed treatments do not eliminate signs and symptoms of IgAN.
- Future therapies should aim to resolve the present gap for treating signs and symptoms of IgAN.

Limitations

- Data were collected between June and October 2021, which would likely have been too soon to see an impact of the Food and Drug Administration approval of dapagliflozin to treat chronic kidney disease⁵. Therefore, the percentage of US patients receiving SGLT2 inhibitor treatment in this study is higher than expected.
- This unexpected finding, that a high percentage of patients were receiving SGLT2 inhibitors, may be explained by the limitation that the total sample of patients is not probabilistic because the methodology states that the next "n" consulting patients will be included. Additionally, it could be influenced by the fact that many nephrologists (87%) had, at some point, spent time teaching in an academic setting and may therefore have experience with newer treatment options.

Abbreviations

ACEI: Angiotensin-Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blockers; BMI: Body Mass Index; DSP: Disease Specific Programme; eGFR: Estimated Glomerular Filtration Rate; EU5: France, Germany, Italy, Spain, and the United Kingdom; IgAN: Immunoglobulin A Nephropathy; IQR: Interquartile Range; SD: Standard Deviation; SGLT2: Sodium-Glucose Cotransporter-2; US: United States

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Disclosures

- Data collection for the DSP was undertaken by Adelphi Real World as part of an independent survey and data is owned by Adelphi. Novartis is one of multiple subscribers to the DSP and supported this analysis.
- Richard Lafayette has received research funding from NIH, UMichigan, Omers, Vera, Travers, Pfizer, Roche, Chinook, Alexion, Otsuka, Callitidas and NephroNet. He has provided consultancy for Alexion, Omers, Vera, Travers, Pfizer, Roche, Callitidas, Chinook, Aurinia, GSK, Otsuka, Novartis.
- Michel Kroes is a shareholder of Novartis.
- Li Yao has received financial support for research programs from Novartis.
- Dario Roccatello has received financial support for research programs from Novartis, Alexion, GSK, Sandoz, Pfizer and Roche.

Acknowledgments

Editorial assistance under the guidance of the authors was provided by Jade Garratt-Wheeldon of Adelphi Real World in accordance with Good Publication Practice (GPP3) guidelines. The authors acknowledge V.S. Hari Prasad (Novartis, Hyderabad) for designing the poster layout. The final responsibility for the content lies with the authors. This abstract was first submitted to American Society of Nephrology (ASN) Kidney Week 2022 congress. Authors received permission from ASN congress to submit it as an e-poster in WCN congress by providing proper attribution. Citation: Lafayette RA, Kroes M, Aldworth CA, Rodriguez LP, George AT, de Courcy JJ, Golden KJ, Chatterton E, Yao L, Roccatello D. SA-PO657: Persistence of Signs and Symptoms in Treated Patients With IgA Nephropathy: Evidence From Real-World Data [Abstract]. *J Am Soc Nephrol* 33, 2022: Page 784.



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