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Treatment Patterns In Patients With Immunoglobulin A Nephropathy - Evidence From Real-World Data

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CONCLUSION

- The majority of IgAN patients were treated with non-immunosuppressants followed by systemic steroids across all countries and lines of therapy.
- Physicians switched IgAN patients across different treatments for improvement in their disease condition.
- The overall and long-term efficacy, ability to reduce proteinuria and a rapid onset of action were the top reasons for nephrologists to choose the current treatment.
- Unmet need exists for the patients with respect to treatments which can provide sustained overall efficacy and control symptoms of the disease such as proteinuria and hematuria. Novel targeted treatment options for IgAN patients with a safe and effective profile may lead to improvement of patient outcomes.

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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 cases per million.[1]
- The Kidney Disease Improving Global Outcomes (KDIGO) 2021 guidelines recommend that, i) for all IgAN patients' blood pressure be managed ii) patients with proteinuria >0.5 g/day be treated with either an angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs) irrespective of hypertension status, and iii) IgAN patients at high risk of progression to chronic kidney disease despite supportive care, be considered for glucocorticoids treatment.[2]
- Limited evidence is available on treatment patterns in IgAN patients in the large real-world setting.

OBJECTIVE

- This study aimed to assess real-world treatment patterns in patients with IgAN.

METHODS

- Data were drawn from the Adelphi IgAN Disease Specific Programme (DSP™), a cross-sectional survey with retrospective data collection of IgAN-treating nephrologists and their consecutively consulting patients, across the United States (US), Europe (France, Germany, Italy, Spain, and the United Kingdom), China, and Japan, conducted between June – October 2021.
- The DSP methodology has been previously described,[3,4] validated,[5] and demonstrated to be representative and consistent over time.[6]
- Ethics exemption was obtained where required, from the Pearl Institutional Review Board and Hospital Clínic de Barcelona.
- Nephrologists completed structured online records for next 10 patients presenting with IgAN in their practice, including patient demographics, management, and treatment history.
- All analyses were descriptive.

RESULTS

Patient demographics and symptoms

- A total of 293 nephrologists completed records for 1,733 patients (who were receiving treatment at survey). The mean (standard deviation; SD) patient age was 43.4 (14.8) years and 59% were male.
- The median (interquartile range; IQR) duration from symptom onset to IgAN diagnosis for all regions (n = 1,435) was 86.0 (31.0 – 187.0) days. Time from symptom onset to IgAN diagnosis ranged from 70.5 days in China to 124.0 days in Japan (US: n = 228; 76.5 [31.0 – 160.0] days, Europe: n = 468; 88.0 [39.0 – 162.3] days, China: n=558; 70.5 [30.0 – 184.3] days, and Japan: n = 181; 124.0 [61.0 – 395.5] days).
- The median (IQR) time between diagnosis to first line of treatment was 4.0 (0.0 – 23.0) days.
- Patients presented with proteinuria (39% [n = 11] – 78% [n = 120]) and hematuria (28% [n = 7] – 63% [n = 96]) as most prevalent symptoms at the start of current treatment across all classes (i.e. non-immunosuppressants [non-ISTs], corticosteroids, non-steroidal immunosuppressants (ISTs), biologic ISTs, alternative medicines [Chinese traditional], other).

Treatment patterns

- First-line: non-ISTs were prescribed for 81% of patients (**Table 1**). Non-ISTs included many classes of drugs (**Table 1**), these were grouped in best way possible to support organization of treatment lists and minimize physician burden.
- Second-line: overall, 34% of patients switched to second-line therapy (US: 21%, Europe: 33%, China: 41%, and Japan: 33%). After non-ISTs, corticosteroids were most widely prescribed.
- Third-line: a total of 30% of patients switched to third-line therapy (US: 14%, Europe: 24%, China: 42%, and Japan: 21%).

Table 1. Treatment patterns of IgAN patients in the US, Europe, China, and Japan

Treatments	First-line Treatment, n (%)					Second-line Treatment, n (%)					Third-line Treatment, n (%)				
	All Regions	US	Europe	China	Japan	All Regions	US	Europe	China	Japan	All Regions	US	Europe	China	Japan
Patients (N)	**1,591**	**268**	**538**	**541**	**244**	**538**	**57**	**177**	**223**	**81**	**161**	**8**	**42**	**94**	**17**
Non-ISTs*	1292 (81)	239 (89)	470 (87)	423 (78)	160 (66)	458 (85)	54 (95)	164 (93)	175 (78)	65 (80)	139 (86)	7 (88)	38 (90)	79 (84)	15 (88)
Corticosteroids†	716 (45)	117 (44)	192 (36)	254 (47)	153 (63)	236 (44)	25 (44)	77 (44)	107 (48)	27 (33)	95 (59)	‖	26 (62)	56 (60)	9 (53)
Non-Steroidal ISTs‡	294 (18)	66 (25)	61 (11)	159 (29)	8 (3)	141 (26)	19 (33)	35 (20)	81(36)	6 (7)	55 (34)	‖	20 (48)	29 (31)	‖
Biologic ISTs§	51 (3)	22 (8)	21 (4)	6 (1)	‖	15 (3)	‖	5 (3)	6 (3)	‖	7 (4)	‖	‖	6 (6)	‖
Alternative Medicines (Chinese traditional)	195 (12)	‖	‖	195 (36)	‖	86 (16)	‖	‖	86 (39)	‖	34 (21)	‖	‖	34 (36)	‖
Other	160 (10)	11 (4)	25 (5)	116 (21)	8 (3)	71 (13)	‖	5 (3)	57 (26)	6 (7)	32 (20)	‖	‖	31 (33)	‖
Non-ISTs (ACEi/ ARB and SGLT2i)	1,236 (78)	232 (87)	454 (84)	403 (74)	147 (60)	447 (83)	53 (93)	163 (92)	171 (77)	60 (74)	134 (83)	6 (75)	38 (90)	78 (83)	12 (71)

Note: patients could be receiving >1 treatment at a time. Europe: France, Germany, Italy, Spain, and the United Kingdom. ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ISTs, Immunosuppressants; non-ISTs, Non-immunosuppressants; SGLT2i, sodium-glucose cotransporter-2 inhibitors; US, United States. *Non-ISTs includes ARB, ACEi, statins, diuretics, antiplatelets, SGLT2i and others. †For those patients currently on first-line treatment, 99% received oral steroids with less than 1% on subcutaneous or intravenous. ‡Non-Steroidal ISTs includes cyclophosphamide, hydroxychloroquine, mycophenolate mofetil, tacrolimus, azathioprine, leflunomide and cyclosporin, §Biologic ISTs includes Rituximab (MabThera/ rituxan/ rixathon/ ruxience etc.), ‖represents patient numbers <5.

- ARBs and ACEis were the most recently commonly prescribed treatments across most countries at time of survey (US: 44% and 43%; Europe: 43% and 49%; China: 63% and 19%, respectively).

Treatment considerations

- Treatment choice: nephrologists considered the ability to reduce proteinuria and overall efficacy the top reasons for prescribing a treatment (**Table 2**).
- Unmet need: the key areas of improvement identified by nephrologists in the current treatments varied according to the drug class (**Table 3**).
  - Nearly half of the nephrologists (45%) across all countries are concerned by steroid safety. (**Table 3**).

Table 2. Top three factors guiding the current treatment choice of nephrologists, by drug class

Factors	All regions n (%)	US n (%)	Europe n (%)	China n (%)	Japan n (%)
Non-immunosuppressants	**n = 856**	**n = 140**	**n = 357**	**n = 238**	**n = 121**
Overall efficacy	644 (75)	125 (89)	291 (82)	141 (59)	87 (72)
Ability to reduce proteinuria	577 (67)	104 (74)	252 (71)	143 (60)	78 (64)
Long-term efficacy	491 (57)	83 (59)	209 (59)	136 (57)	63 (52)
Steroidal immunosuppressants	**n = 661**	**n = 100**	**n = 171**	**n = 268**	**n = 122**
Overall efficacy	440 (67)	85 (85)	123 (72)	123 (46)	109 (89)
Ability to reduce proteinuria	408 (62)	62 (62)	101 (59)	169 (63)	76 (62)
Rapid onset of action	349 (53)	55 (55)	85 (50)	156 (58)	53 (43)
Non-steroidal immunosuppressants	**n = 95**	**n = 18**	**n = 36**	**n = 36**	‖
Ability to reduce proteinuria	56 (59)	15 (83)	18 (50)	20 (56)	‖
Overall efficacy	50 (53)	10 (56)	18 (50)	19 (53)	‖
Long-term efficacy	45 (47)	8 (44)	19 (53)	17 (47)	‖
Biologic immunosuppressants	**n = 69**	**n = 22**	**n = 27**	**n = 18**	‖
Overall efficacy	43 (62)	18 (82)	11 (41)	13 (72)	‖
Ability to reduce proteinuria	35 (51)	14 (64)	10 (37)	11 (61)	‖
Rapid onset of action	33 (48)	15 (68)	‖	12 (67)	‖

Europe: France, Germany, Italy, Spain, and the United Kingdom; US, United States. ‖represents patient numbers <5.

Table 3. Physician-reported top three areas for improvement regarding current treatment choice delineated by drug class

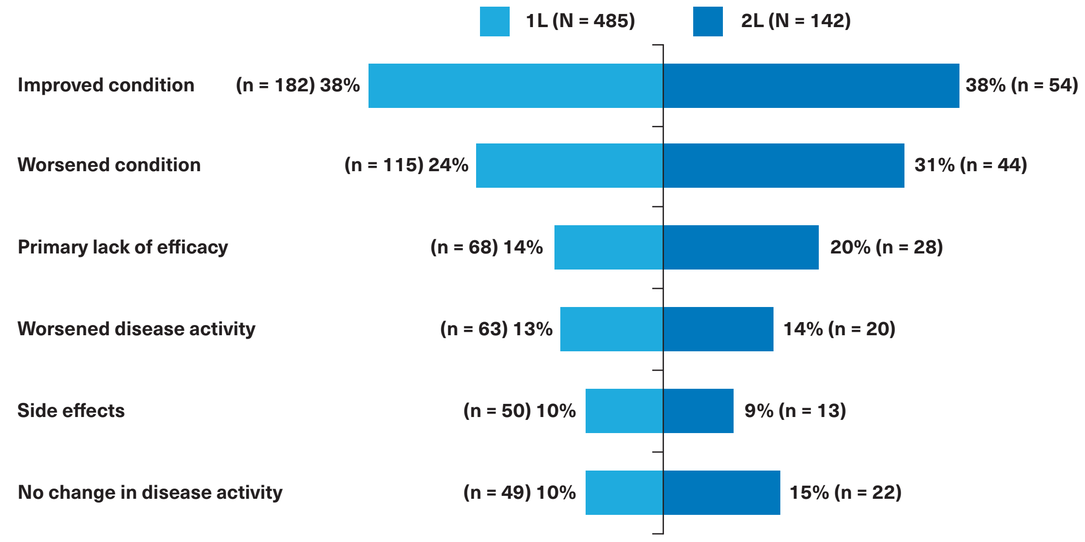
Factors	All regions n (%)	US n (%)	Europe n (%)	China n (%)	Japan n (%)
Non-immunosuppressants	**n = 855**	**n = 140**	**n = 356**	**n = 238**	**n = 121**
Ability to reduce hematuria	183 (21)	46 (33)	72 (20)	45 (19)	20 (17)
Overall efficacy	181 (21)	37 (26)	82 (23)	31 (13)	31 (26)
Treat fatigue or tiredness	172 (20)	34 (24)	91 (26)	43 (18)	‖
Steroidal immunosuppressants	**n = 661**	**n = 100**	**n = 171**	**n = 268**	**n = 122**
Long-term safety	296 (45)	42 (42)	65 (38)	129 (48)	60 (49)
Tolerability	178 (27)	25 (25)	42 (25)	97 (36)	14 (11)
Overall safety	171 (26)	33 (33)	48 (28)	67 (25)	23 (19)
Non-steroidal immunosuppressants	**n = 95**	**n = 18**	**n = 36**	**n = 36**	**n = 5**
Long-term safety	26 (27)	8 (44)	5 (14)	12 (33)	‖
Long-term efficacy	25 (26)	‖	5 (14)	15 (42)	‖
Ability to reduce proteinuria	19 (20)	‖	7 (19)	10 (28)	‖
Biologic immunosuppressants	**n = 69**	**n = 22**	**n = 27**	**n = 18**	‖
Affordable for patient	25 (36)	12 (55)	‖	12 (67)	‖
Treat fatigue or tiredness	19 (28)	10 (45)	5 (19)	‖	‖
Reasonable cost-benefit ratio	19 (28)	8 (36)	‖	7 (39)	‖

Europe: France, Germany, Italy, Spain, and the United Kingdom; US, United States. ‖represents patient numbers <5.

Reasons for switching treatments

- The main physician-reported reasons for switching treatment (multiple reasons could be selected) at first and second lines were: improved condition, worsened condition, primary lack of efficacy, worsened disease activity, side effects and no change in disease activity (**Figure 1**).
- The proportion of patients who were switched to subsequent lines of therapy (first to second line and second to third line, respectively) due to improved condition were both 38% (**Figure 1**).
- Inadequate disease control was noted as reason for switching treatments (worsened condition, primary lack of efficacy and worsened disease activity; 1L: 50%, 2L: 65%).

Figure 1. The main physician-reported reasons for switching treatment at first and second lines



Treatment switch: cessation of one treatment or addition of new treatment, where patients could be using >1 treatment at a time. 1L, first-line; 2L, second-line.

LIMITATIONS

- Participating patients may not reflect the general IgAN population since the DSP only includes patients who are consulting with their physician. This means that patients who consult more frequently have a higher likelihood of being included.
- Recall bias (not able to recollect accurate and complete information), a common limitatiaon of surveys, might also have affected physicians' responses. However, physicians did have the ability to refer to the patients' records while completing the patient record forms thus minimizing the possibility of recall bias.

References

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