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Enclosure:

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What Treatment Factors Matter Most to Patients with IgA Nephropathy? Insights from a Multi-Country Discrete Choice Experiment

Ella Xiaoyan Du, MESc[1]; Yan Meng, PhD[2]; Sasikiran Nunna, PhD[3]; Benjamin Lewing, PhD[3]; Nicholas Vendetti, MS[3]; Christine Hotaru Naya, PhD[1]; Fengyi Jiang, MSc[4]; Keith A. Betts, PhD[1]; Liqun Bai, MD[5]

[1]Analysis Group, Inc., Los Angeles, LA, United States; [2]Analysis Group, Inc., Boston, MA, United States; [3]Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, United States; [4]Analysis Group, Inc., Toronto, ON, Canada; [5]Arizona Kidney Disease and Hypertension Centers in Phoenix, Tucson, AZ, United States

Contact Information: Benjamin.lewing@otsuka-us.com

Otsuka Pharmaceutical Development & Commercialization, Inc.

Introduction

- The treatment landscape for IgA nephropathy has evolved rapidly with multiple treatments with novel mechanisms of action recently receiving US Food and Drug Administration (FDA) approval or currently under investigation.[1]
- These emerging therapies differ in efficacy, risk of adverse events [AEs], and treatment convenience (e.g., formulation type and frequency of administration), requiring patients and healthcare providers to balance multiple considerations when making treatment decisions.
- Understanding how patients prioritize and trade off these attributes can inform treatment choices, improve patient engagement in treatment decision-making, and enhance patient satisfaction.[2-4]
- However, evidence on patient preferences and the factors influencing treatment decision-making in IgA nephropathy remains limited.[5,6]

Study Objectives

To assess and quantify the extent to which different treatment attributes (i.e., efficacy, safety, and convenience) influence patients' preferences for IgA nephropathy treatments across the US, United Kingdom (UK), Canada, and France using a discrete choice experiment (DCE).

Methods

Data source and study population

- A DCE survey was conducted (Jun-Aug 2025) among adults (≥ 18 years) with biopsy-confirmed primary IgAN in the US, UK, France, and Canada, recruited by Medefield via physician referrals, patient databases, and patient advocacy organizations.
- Patient eligibility criteria
  - Inclusion criteria: Patients aged ≥ 18 years, had a biopsy-confirmed diagnosis of IgA nephropathy, resided in the US, UK, France, or Canada, and were willing and able to consent.
  - Exclusion criteria: Patients with secondary IgA nephropathy related to infection-associated IgA nephropathy, hepatic cirrhosis, Henoch–Schönlein purpura (IgA vasculitis), membranous glomerulonephritis, or lupus nephritis; those with end-stage kidney disease; or those who received kidney transplantation or dialysis.

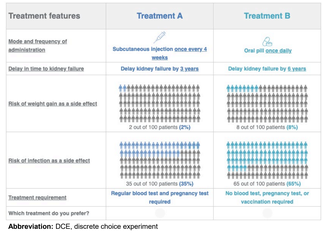
Survey design

- The survey comprised an eligibility screener, questions on patient characteristics and prior treatment history, and a DCE component to assess patients' preferences of different treatment options for IgA nephropathy.
- A DCE is a quantitative survey method used to assess how individuals value different treatment attributes by asking them to choose between hypothetical treatment options that vary in their characteristics.
- Five treatment attributes were identified through a targeted literature review and clinical expert input and were used to construct the DCE choice tasks (**Table 1.** These attributes included efficacy (i.e., delay in time to kidney failure), safety (i.e., risk of infection, risk of weight gain), and convenience (i.e., mode and frequency of administration, treatment requirements).
  - The descriptions of each attribute were presented to patients in plain language to ensure a shared understanding of the terms. Kidney failure was defined as "the point when your kidneys stop working well enough for you to survive without dialysis or a kidney transplant".
  - To ensure clinical relevance, the levels for "delay in time to kidney failure" were informed by reductions in proteinuria from baseline at 9 months reported in relevant trials. These reductions were converted into estimated delays in kidney failure based on findings from a study evaluating proteinuria as a surrogate endpoint for disease progression in IgA nephropathy.[7]
- Each patient was assigned to 12 choice tasks. One additional choice task was included as a dominance check, where the attribute levels associated with one treatment are better than the other, to test the quality of the responses.
- Each choice task contained two hypothetical IgA nephropathy treatment profiles with combinations of attributes at various levels (**Figure 1**), and patients were asked to choose their preferred treatment option.

Table 1. List of attributes and levels

Treatment attributes	Levels
Efficacy	
Delay in time to kidney failure	3 years 6 years 9 years
Safety	
Risk of weight gain as a side effect	2 out of 100 patients (2%) 5 out of 100 patients (5%) 8 out of 100 patients (8%)
Risk of infection as a side effect	35 out of 100 patients (35%) 50 out of 100 patients (50%) 65 out of 100 patients (65%)
Convenience	
Mode and frequency of administration	Oral pill **once daily** Oral pill **twice daily** Subcutaneous injection **once a week** Subcutaneous injection **once every 2 weeks** Subcutaneous injection **once every 4 weeks**
Treatment requirement	No blood test, pregnancy test, or vaccination required Regular blood test and pregnancy test required Vaccination required before treatment

Figure 1. Example of a DCE choice card



Abbreviation: DCE, discrete choice experiment

Statistical analyses

- Descriptive statistics were used to summarize patient demographic and clinical characteristics. Continuous variables were summarized using the mean and standard deviation, while categorical variables were summarized using counts and percentages.
- Preference data were analyzed among patients who passed the dominance test using a conditional logistic regression model, in which the dependent variable was the patient's choice between two hypothetical options in each choice task, and the independent variables were the attribute levels associated with each treatment option.
- Coefficients were used to calculate the relative importance of each attribute, as well as patients' willingness to trade off specified treatment attributes.

Key takeaways

1. While delay in kidney failure was the primary driver of treatment preference, mode and frequency of administration accounted for nearly one-fifth of decision weight.
2. Patients preferred once-per-four-weeks subcutaneous administration over more frequent injections or twice-daily oral dosing.
3. Patients were willing to trade meaningful years of kidney function to reduce treatment burden and improve convenience.
4. Findings highlight the importance of incorporating patient preference, including around dosing and frequency, into shared decision-making.

Results

Study population and patient characteristics

- A total of 176 eligible adult patients with IgA nephropathy were recruited from the US (n=100), UK (n=50), France (n=20), and Canada (n=6) (**Table 2**). 174 of them passed the dominance test.
- Participants had a mean age of 45.5 years; 54% were White (among US participants), 48.9% were female, and 87.5% resided in suburban or urban areas.
- The majority of patients were employed (61.4%), including 39.8% full-time, 7.4% part-time, and 14.2% self-employed (**Table 2**).
- Overall, 30.2% of patients were diagnosed with IgA nephropathy in the past 2 years, 31.3% in the past 2-5 years, 20.5% in the past 5-10 years, and 18.2% more than 10 years ago (**Table 2**).
- The majority had kidney disease at stage 3 or below, with 33.0% at stage 1, 35.8% at stage 2, and 26.7% at stage 3 (**Table 2**).

Table 2. Patient demographic and clinical characteristics

	All patients N = 176
Age (years), Mean ± SD	**45.5 ± 12.0**
Current gender identity, n (%)	
Male	89 (50.6)
Female	86 (48.9)
Prefer not to answer	1 (0.6)
Country of residence, n (%)	
United States	100 (56.8)
United Kingdom	50 (28.4)
France	20 (11.4)
Canada	6 (3.4)
US census region[1], n (%)	**N = 100**
West	75 (75.0)
South	16 (16.0)
Northeast	9 (9.0)
Midwest	0 (0.0)
Race/Ethnicity[1,2], n (%)	**N = 100**
White	54 (54.0)
Black or African American	20 (20.0)
Native Hawaiian or Other Pacific Islander	7 (7.0)
Asian	6 (6.0)
American Indian or Alaska Native	3 (3.0)
Other	3 (3.0)
Prefer not to answer	12 (12.0)
Residential area, n (%)	
Suburban	80 (45.5)
Urban	74 (42.0)
Rural	22 (12.5)
Employment status, n (%)	
Employed full-time	70 (39.8)
Employed part-time	13 (7.4)
Self-employed	25 (14.2)
Homemaker	27 (15.3)
Not employed	23 (13.1)
Retired	13 (7.4)
Other	5 (2.8)
Time since diagnosis, n (%)	
Less than 1 year ago	20 (11.4)
1 to < 2 years ago	33 (18.8)
2 to < 5 years ago	55 (31.3)
5 to < 10 years ago	36 (20.5)
10 to < 20 years ago	19 (10.8)
More than 20 years ago	13 (7.4)
Current stage of kidney disease, n (%)	
Stage 1 (eGFR: ≥ 90)	58 (33.0)
Stage 2 (eGFR: 60 - 89)	63 (35.8)
Stage 3 (eGFR: 30 - 59)	47 (26.7)
Stage 4 (eGFR: 15 - 29)	8 (4.5)

Abbreviations: eGFR, estimated glomerular filtration rate; SD, standard deviation; US: United States.
Notes: [1] The question was only asked among the respondents in the United States. [2] Categories were not mutually exclusive.

Patient preferences results

Regression coefficients

- Among patients who passed the dominance test (n=174), delay in time to kidney failure, risks of infection and weight gain, and mode and frequency of administration had statistically significant impacts on treatment preference, whereas the impact of treatment requirement (i.e., blood test, pregnancy tests or vaccination) on patient preference was not statistically significant (**Table 3**).
  - Patients preferred treatments associated with a longer delay in time to kidney failure, and a lower risk of weight gain and infection ($P<0.05$).
  - Patients preferred treatments that were administered via subcutaneous injections every 4 weeks over those administered via subcutaneous injection weekly or biweekly, or via twice-daily oral dosing ($P<0.05$).
  - There was no statistically significant difference when comparing subcutaneous injections every 4 weeks vs once-daily oral dosing ($P=0.367$).

Relative importance

- The top three treatment attributes to which patients placed the highest relative importance were delay in time to kidney failure (50.3%), risk of infection (25.1%), and mode and frequency of administration (19.0%) (**Figure 2).**

Willingness to tradeoff

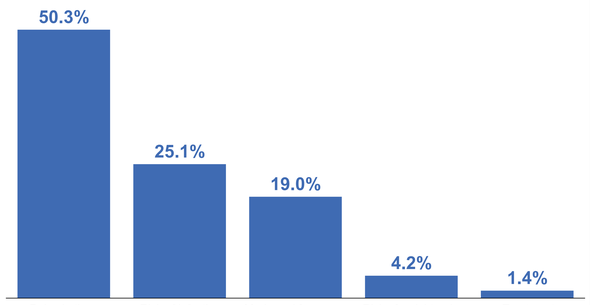
- Patients were willing to accept an average reduction of 2.06 years in delay to kidney failure to avoid weekly injections, 0.84 years to avoid injection every 2 weeks, and 0.54 years to avoid twice-daily oral dosing (**Figure 3**).
- Patients were willing to accept an average reduction of 0.25 and 1.50 years in delay to kidney failure to receive a 3- and 15-percentage-point reduction in the risks of weight gain and infection, respectively (**Figure 3**).

Table 3. Patient preference weights

	All patients[1,2] N = 174		
	Coefficient[2]	**(95% CI)**	***P value***
Efficacy			
Delay in time to kidney failure	0.541	(0.484, 0.597)	< 0.001*
Safety			
Risk of weight gain as a side effect	-0.045	(-0.074, -0.017)	0.002*
Risk of infection as a side effect	-0.054	(-0.061, -0.047)	< 0.001*
Convenience			
Mode and frequency of administration			
Subcutaneous injection once every 4 weeks (Reference)	-	-	-
Subcutaneous injection once every 2 weeks	-0.453	(-0.700, -0.205)	< 0.001*
Subcutaneous injection once a week	-1.114	(-1.358, -0.869)	< 0.001*
Oral pill twice daily	-0.291	(-0.566, -0.015)	0.038*
Oral pill once daily	0.111	(-0.130, 0.351)	0.367
Treatment requirement			
No blood test, pregnancy test, or vaccination required (Reference)	-	-	-
Regular blood test and pregnancy test required	-0.042	(-0.210, 0.126)	0.627
Vaccination required before treatment	0.046	(-0.141, 0.233)	0.628

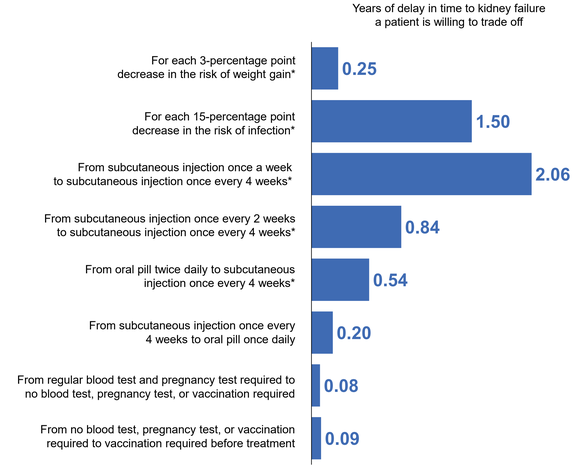
Abbreviation: CI, confidence interval.
*P value < 0.05
Notes: [1] The analysis was performed among all patients who passed the dominance test. Two out of 176 patients failed the dominance test. [2] Regression coefficients were generated from a conditional logistic model that regressed patients' preferences on the attribute's levels of the treatment selected from each choice card.

Figure 2. Relative attribute importance for patients with IgA nephropathy



Note: The relative importance reflects the contribution of each attribute to patients' treatment decision-making. For example, the relative importance of mode and frequency of administration is 19.0%, indicating that patients placed 19% weight on this attribute when choosing a treatment.

Figure 3. Willingness to tradeoff plot for patients with IgA nephropathy



Abbreviation: IgA, immunoglobulin A.
*Attribute levels that have a statistically significant impact on treatment preference (P value <0.05) are indicated by asterisk (*).
Note: The number indicates how many years of delay in time to kidney failure an average patient is willing to trade off in order to avoid a particular attribute level. For example, patients were willing to accept a reduction of 1.5-year delay in time to kidney failure to avoid 15 percentage points of risk of infection.

CONCLUSIONS

Patients with IgA nephropathy considered efficacy, safety, and the convenience of administration when selecting treatment.

Delay in time to kidney failure was identified as the most important attribute, though patients were willing to accept less delay in progression to kidney failure in exchange for lower risks of infection and weight gain, as well as improved treatment convenience.

Among administration options, patients preferred once-per-four-weeks subcutaneous injections over more frequent injections or twice-daily oral dosing. Less burdensome dosing schedules (e.g., once-per-four-weeks administration) may support adherence and long-term treatment persistence.

Taken together, these findings emphasize the importance of safety and convenience to patients' decision-making.

Findings from this study help better understand patients' treatment preferences, with the potential to inform shared decision-making, and support patient-centered treatment discussions.

Limitations

- The sample may not be representative of the broad patient population, as selection bias may exist despite efforts to recruit a diverse group through physician referrals, patient databases, and patient advocacy organizations.
  - Participant distribution was uneven across countries, potentially limiting generalizability across different healthcare systems
  - The predominance of patients with stage 3 or lower kidney disease may limit generalizability to advanced or pre-end stage kidney disease populations. Willingness to tradeoff estimates may shift with perceived prognosis.
- To be considerate of the response burden, only a limited number of key attributes were included in the DCE questions. While the DCE literature suggests 5-7 attributes, additional attributes may have been important to understand patients' preferences.

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Disclosures

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