HSD5

Real-world survey on treatment pathways and patterns for patients with primary Immune Complex Membranoproliferative Glomerulonephritis

Mingyi Huang[1], Lucía Quintana-Gallardo[2], Dima Decker[1], James Jackson[3], Sarah Clayton[3], Emily Green[3], Mollie Lowe[3], Katie Gordon[1], Carly Rich[2]
[1]Apellis, Pharmaceuticals, Waltham, Massachusetts, United States; [2]Swedish Orphan Biovitrum AB, Stockholm, Sweden; [3]Adelphi Real World, Bollington, United Kingdom

INTRODUCTION

- Immune complex membranoproliferative glomerulonephritis (IC-MPGN) is a rare and fast-progressing nephropathy[1]. When a clear aetiology cannot be identified, IC-MPGN is classified as primary[2].
- Treatment guidelines for IC-MPGN are largely undefined due to the lack of targeted therapies. What guidelines do exist suggest supportive glomerulonephritis treatment, though the benefits of immunosuppression remain unclear[3].
- When a patient reaches end stage renal disease, treatment and management options include dialysis or kidney transplantation. However, there is a high risk of disease recurrence in the allograft[4].
- With limited guidance and treatment options, it is important that we understand treatment pathways and how treatments are deployed in clinical practice.

OBJECTIVE

- To describe clinical characteristics, care pathways, and treatment pathways at time of data collection for patients with primary IC-MPGN in the United States of America (US), France, Germany, Italy and Spain (EU4).

CONCLUSIONS

- Nephrologists hold primary responsibility for diagnosing and treating patients with IC-MPGN, following initial consultation with a general practitioner.
- The time delay between initial HCP consultation and diagnosis of primary IC-MPGN was just under a month in the US and just over a month in EU4. Following diagnosis, treatment initiation was delayed by almost two weeks in the US, and almost five weeks in EU4. Together these delays have the potential to contribute to a worsened disease state and elevated proteinuria at treatment initiation.
- The most commonly reported area for treatment improvement by HCPs in US was long term efficacy. In EU4, this was an ability to reduce patient fatigue/tiredness.
- Despite treatment with conventional therapy, almost two fifths of patients were perceived to have a moderate or severe disease severity, a fifth were predicted to progress to end stage kidney disease within the next 3 years, and proteinuria remained elevated above the clinical threshold guideline of 1 g/ 24 hours[3] suggesting the need for more effective treatment options for this patient population.

METHODS

- Data were collected in the US and EU4 between February and June 2024, as part of the Adelphi IC-MPGN Disease Specific Programme (DSP™), a cross-sectional survey with elements of retrospective data collection.
- In the abstract an interim dataset was analysed for EU4. Full data collection was subsequently completed and analysed within this poster.
- The DSP methodology has been previously described[5,6], validated[7], and shown to be representative and consistent over time[8].
- Nephrologists, paediatric nephrologists, and internal medicine specialists (IMs) completed an online patient record form including data on demographics, clinical characteristics, care pathways, and treatment pathways, for a minimum of the next three patients with primary IC-MPGN whom they consulted with in clinical practice.
- Patients were eligible for inclusion if they were aged one year or older and had a confirmed diagnosis of primary IC-MPGN, including biopsy results. Patients with secondary IC-MPGN were not included.
- Analyses were descriptive and described for the total population (US + EU4), unless otherwise stated.

RESULTS

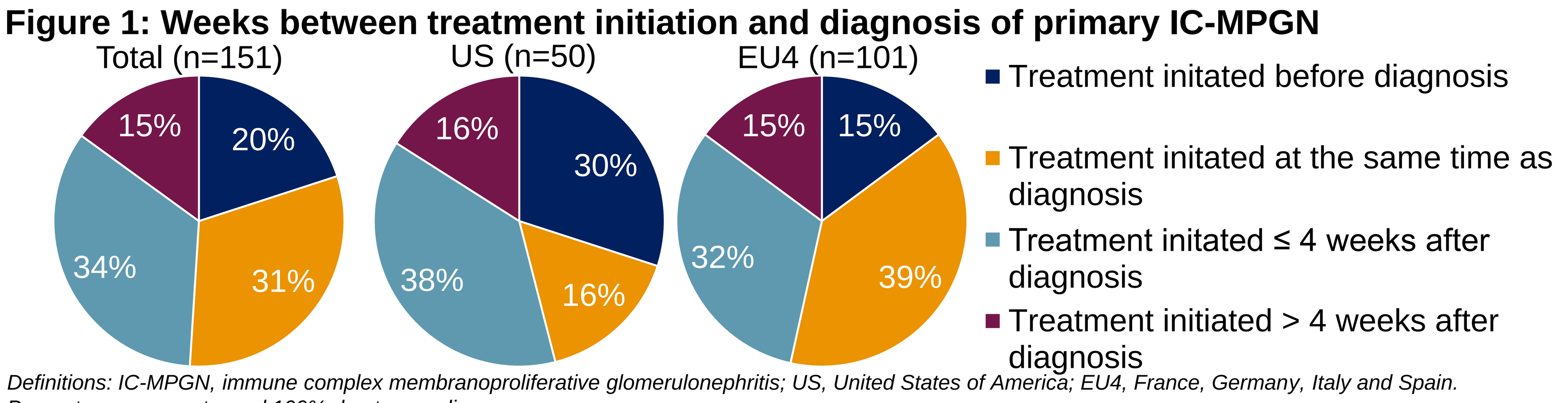
- In total, 47 nephrologists (US: 19, EU4: 28), 7 paedatric nephrologists (US: 1, EU4: 6) and 7 internal medicine specialists (US: 0, EU4: 7) provided data relating to **215 patients** with primary IC-MPGN (US: 83, EU4: 132).
- At the time of data collection, the mean [standard deviation; SD] **patient age was 42.2 [18.0] years** (US: 43.6 [16.4], EU4: 41.3 [18.9]), **11%** patients were paediatrics (US: 4%, EU4: 15%), with a mean age of 13.4 [3.4] years (US: 15.0 [1.0], EU4: 13.2 [3.6]), and **89%** were adults (US: 96%, EU4: 85%) with a mean age of 45.7 [15.8] years (US: 44.7 [15.8], EU4: 46.3 [15.8]).
- In total, **57% of patients were male** (US: 55%, EU4: 58%), 4% of patients had undergone a kidney transplant (US: 2%, EU4: 5%), the **mean time since diagnosis was 2.7 [5.3] years** (US: 1.5 [2.1], EU4: 3.4 [6.4]) and the median, interquartile range (IQR) time was 1.0, 2.0 years (US: 0.8, 1.2, EU4: 1.1, 3.2).
- At the time of data collection, **80% of patients were receiving treatment** for their primary IC-MPGN (US: 72%, EU4: 85%); 13% of patients had received a treatment in the past but were not receiving treatment at time of data collection (US: 18%, EU4: 11%), and 7% of patients had never received treatment (US: 10%, EU4: 4%). Clinical characteristics for patients receiving treatment are presented in Table 1.

Table 1. Clinical characteristics for patients receiving treatment at the time of data collection	Total	US	EU4
24-hour UPE (g/ 24 hours),	(n=145)	(n=57)	(n=88)
At time of data collection, mean [SD]	1.7 [1.5]	1.5 [1.4]	1.8 [1.5]
Immediately prior to current treatment, mean [SD]	3.5 [2.4]	2.7 [2.0]	4.0 [2.5]
At diagnosis, mean [SD]	3.6 [2.4]	3.1 [2.8]	4.0 [2.1]
eGFR (mL/min/1.73 m²)	(n=149)	(n=56)	(n=93)
At time of data collection, mean [SD]	51.1 [24.0]	51.2 [20.7]	51.0 [25.9]
Immediately prior to current treatment, mean [SD]	44.8 [22.4]	45.4 [21.2]	44.4 [23.2]
At diagnosis, mean [SD]	46.0 [21.9]	46.6 [20.9]	45.5 [22.5]
Patients that will progress to ESKD	(n=145)	(n=56)	(n=89)
Within next 3 years, n (%)	37 (26%)	12 (21%)	25 (28%)
In more than 3 years, n(%)	74 (51%)	32 (57%)	42 (47%)
Not at all, n (%)	34 (23%)	12 (21%)	22 (25%)
Physician-perceived disease severity at time of data collection	(n=172)	(n=60)	(n=112)
Mild, n (%)	106 (62%)	38 (63%)	68 (61%)
Moderate, n (%)	58 (34%)	21 (35%)	37 (33%)
Severe, n (%)	8 (5%)	1 (2%)	7 (6%)

Definitions: UPE, urinary protein excretion; eGFR, estimated glomerular filtration rate; ESKD, end stage kidney disease. "Don't knows" excluded for ESKD progression.

- For patients receiving treatment at time of data collection, mean [SD] time between **initial health care practitioner (HCP) consultation and diagnosis of primary IC-MPGN** was 7.7 [11.1] weeks (US: 5.0 [5.1], EU4: 9.1 [13.0]) and the median, IQR time **was 4.0, 6.8 weeks** (US: 3.3, 7.0, EU4: 4.4, 7.0). From initial consultation, **50% of patients waited less than or equal to four weeks for a diagnosis** (US: 56%, EU4: 47%) and 50% waited longer than four weeks (US: 44%, EU4: 53%).
- Overall, the mean time between **diagnosis and the initiation of first treatment was 3.7 [20.9] weeks** (US: 1.7 [7.1], EU4: 4.6 [25.0]) and the **median, IQR time was 0.0, 1.4 weeks** (US: 0.3, 1.9, EU4: 0.0, 1.4) (Figure 1).

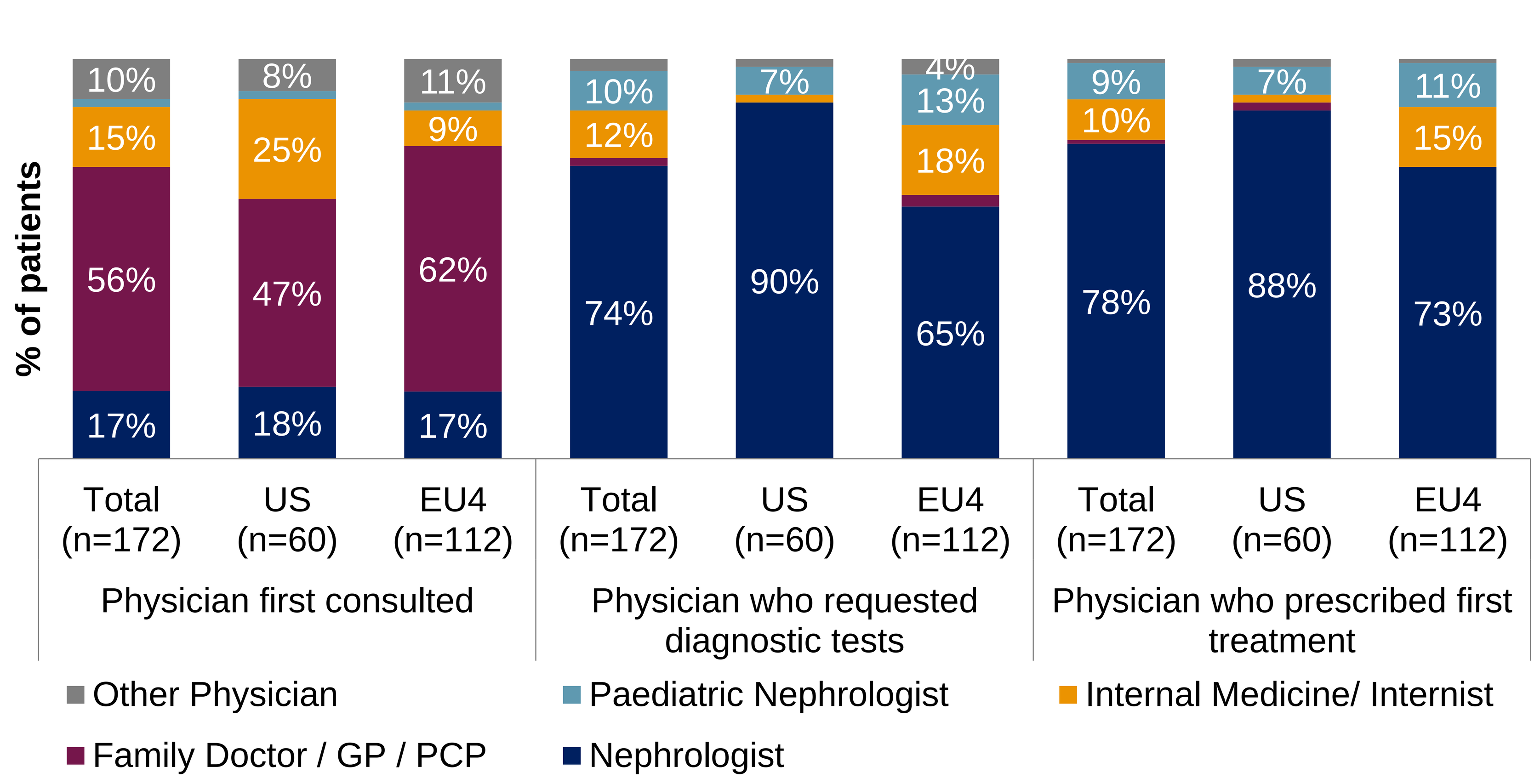
Figure 1: Weeks between treatment initiation and diagnosis of primary IC-MPGN



Definitions: IC-MPGN, immune complex membranoproliferative glomerulonephritis; US, United States of America; EU4, France, Germany, Italy and Spain. Percentages may not equal 100% due to rounding.

- For those patients experiencing a delay >3 months between diagnosis and initial treatment, the **most commonly reported reasons for this delay were waiting for test results** (Total: **100%**, US: 100%, EU4: 100%), another condition took precedence (Total: 50%, US: 0%, EU4: 60%), and symptoms were not prominent enough for treatment initiation (Total: 50%, US: 0%, EU4: 60%).
- **Initial patient consultations were most frequently with primary care practitioners**. For most patients, nephrologists requested diagnostic tests to confirm primary IC-MPGN and provided initial treatment prescriptions (Figure 2).

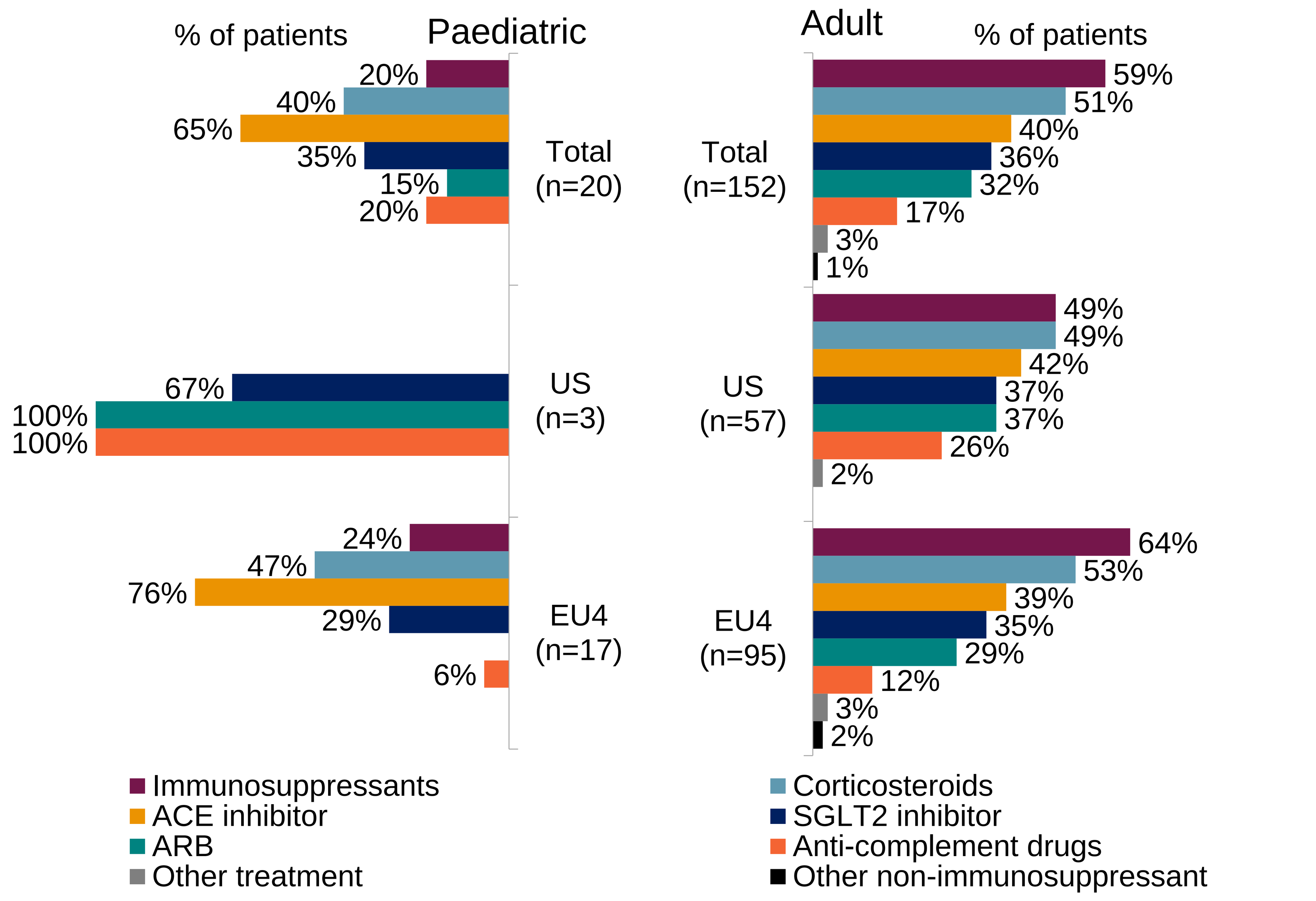
Figure 2: HCP involvement in care pathway for patients with primary IC-MPGN



Note: Data labels ≤3% not shown; data shown for all patients receiving treatment at the time of data collection, with a known response for all of the following: physician first consulted, physicians who requested diagnostic tests, and physician who first prescribed treatment. Other physician includes: urologist, other physician, other specialist, pharmacist, nurse, and physician unknown.
Definitions: IC-MPGN, Immune Complex Membranoproliferative Glomerulonephritis; US, United States of America; EU4, France, Germany, Italy and Spain; GP, general practitioner; PCP, primary healthcare professional.

- Of those patients receiving treatment at the time of data collection, **patients were receiving a mean of 2.4 [1.1] treatments** (US: 2.4 [0.8], EU4: 2.4 [1.2]). **Patients had been receiving their current treatment for a mean of 1.4 [2.3] years** (US: 1.4 [1.9], EU4: 1.3 [2.5]) and a median, IQR of 0.7, 1.0 years (US: 0.7, 1.4, EU4: 0.8, 0.9). Treatments prescribed for primary IC-MPGN at time of data collection are presented in Figure 3.

Figure 3: Treatment prescribed for primary IC-MPGN at the time of data collection



Definitions: IC-MPGN, Immune Complex Membranoproliferative Glomerulonephritis; ACE inhibitor, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin II receptor blockers; SGLT2 inhibitor, Sodium-glucose co-transporter-2 inhibitor; US, United States of America; EU4, France, Germany, Italy and Spain.

- The **most commonly reported reasons for treatment choice were overall efficacy (Total: 71%**, US: 78%, EU4: 67%); ability to reduce proteinuria (Total: 52%, US: 52%, EU4: 52%); ability to stabilise kidney function (Total: 47%, US: 35%, EU4: 54%); and long-term efficacy (Total: 43%, US: 38%, EU4: 46%).
- The **most commonly reported areas for improvement in treatments were long-term safety (Total: 22%,** US: 27%, EU4: 20%); ability to reduce fatigue/tiredness (Total: 22%, US: 13%, EU4: 26%); long-term efficacy (Total: 22%, US: 25%, EU4: 20%), and overall safety (Total: 20%, US: 32%, EU4: 14%).

LIMITATIONS

- The patient sample may not reflect the general population of patients with primary IC-MPGN, as patients who consult more frequently were more likely to be included.
- The cross-sectional design of the DSP prevented any conclusions about causal relationships.

ACKNOWLEDGMENTS
Corresponding author: Carly Rich, carly.rich@sobi.com. The Adelphi primary IC-MPGN Disease Specific Programme™ is an independent survey conducted by Adelphi Real World and subscribed to by Apellis and Sobi AB. Apellis and Sobi AB did not influence the original survey. This analysis was funded by Apellis and Sobi AB.

DISCLOSURES
CR is an employee of and holds shares for Swedish Orphan Biovitrum AB. LQ is an employee of Swedish Orphan Biovitrum AB. MH, DD and KG are employees of Apellis Pharmaceuticals. JJ, SC, ML, and EG are employees of Adelphi Real World.

REFERENCES
1. Noris, M., et al. Nephrol Dial Transplantation 2023; 38(2):283-290. 2. Vivarelli, M., et al., Kidney Int Rep, 2024; 9(1):64-72. 3. KIDGO, Kidney Int. 2021; 100(4S):S1-S276. 4. Alasfar et al., BMC Nephrol, 2016; 11:17:7. 5. Anderson, P., et al. Current Medical Research and Opinion 2008; 24(11):3063-72. 6. Anderson, P., et al. Current Medical Research and Opinion 2023; 39(12):1707-1715. 7. Babineaux SM., et al. BMJ Open 2016;6(8):e010352. 8. Higgins V, Piercy J, Roughley A, et al. Diabetes Metab Syndr Obes 2016;9:371-380.