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C3 Glomerulopathy Current Therapy and Real-World Management - Interim Results from a Multi-Country Study

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INTRODUCTION

- Complement 3 glomerulopathy (C3G) is a rare form of glomerulonephritis, with an estimated incidence of 1-2 per million per year[1].
- C3G is associated with a high risk of disease progression with approximately 50% of patients reaching kidney failure within 10 years of diagnosis[2].
- Currently, no treatments have been proven effective through randomized controlled trials[3].
- KDIGO 2021 glomerular disease guidelines recommend treating with renin-angiotensin-aldosterone system inhibitors (RAASi) to reduce blood pressure and proteinuria, and, in select patients, utilization of immunosuppressants such as mycophenolate mofetil and corticosteroids[3].
- Newer agents, such as eculizumab, are also sometimes used off-label[3].

AIM

- The aim of this analysis was to better understand the current management of C3G in the United States (US), Europe, and Asia.

METHOD

- An analysis was conducted using interim data from the Adelphi C3G Disease Specific Programme (DSP), a cross-sectional survey of C3G-treating nephrologists in US, EU5 (France, Germany, Italy, Spain, United Kingdom), China, and Japan (study ongoing since August 2022; interim analysis based on data until November 2022).
- Nephrologists completed structured forms administered via online links for consecutive patients presenting with C3G.
- Forms included information on current and most recent therapy.

RESULTS

- In this interim analysis, 88 nephrologists had completed records for 277 patients, including 95 in US, 120 in EU5, 39 in China and 23 in Japan.
- At the time of survey:
  - Median patient age was 44 years and 60% of patients were men.
  - 80% of patients had C3 glomerulonephritis (C3GN) and 19% had dense deposit disease (DDD).
  - 82% (n=228) of 277 patients were receiving treatment (**Figure 1**).
    - Of these 228 patients, 69% were receiving RAASi, 76% were on immunosuppressants, and 31% were receiving biologics (**Figure 2**).
  - Mean proteinuria was 2.1 g/day, with 60% of patients having proteinuria ≥1 g/day (**Table 1**).

Figure 1. Treatment status in C3G patients at the time of survey

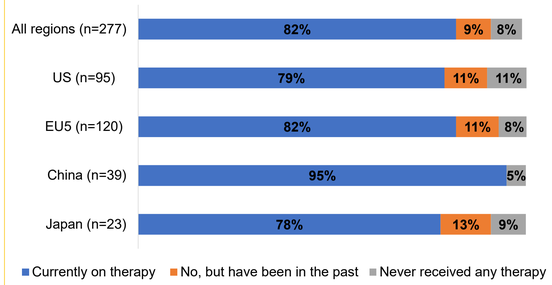
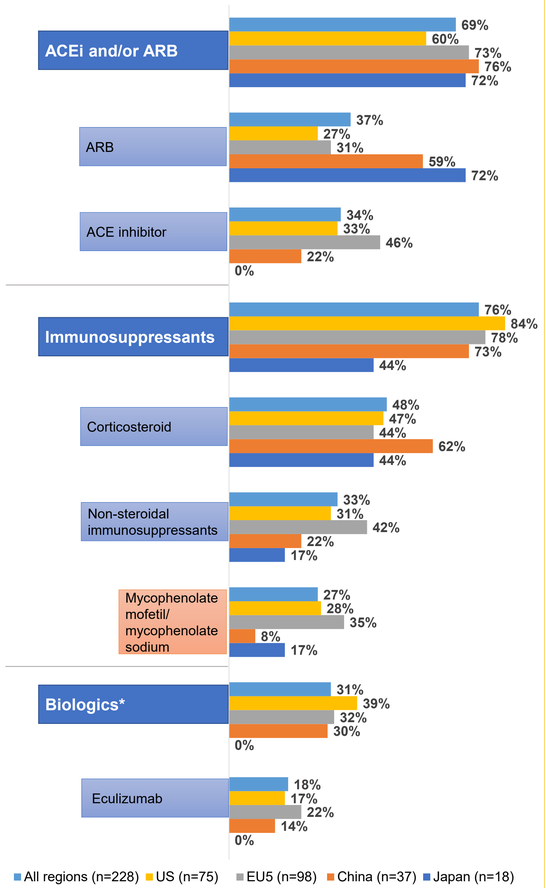


Table 1. Proteinuria at the time of survey

	All regions (n=235)	US (n=66)	EU5 (n=110)	China (n=36)	Japan (n=23)
≥ 1 g/day	141 (60%)	43 (65%)	65 (59%)	25 (69%)	8 (35%)
Mean (SD)	2.1 (2.8)	1.9 (2.3)	2.1 (2.8)	3.1 (4.0)	0.7 (0.9)

Abbreviations: C3G: Complement 3 Glomerulopathy; EU5: France, Germany, Italy, Spain and United Kingdom; SD: Standard Deviation; US: United States

Figure 2. Current therapy of C3G patients at the time of survey



*In addition to eculizumab, other biologics mentioned were rituximab, ravulizumab, other anti-complement drugs and other biologic immunosuppressants

Abbreviations: ACEi: Angiotensin-Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blockers; C3G: Complement 3 Glomerulopathy; EU5: France, Germany, Italy, Spain, United Kingdom; US: United States

CONCLUSIONS

- C3G is a rapidly progressing glomerulonephritis for which there is no approved therapy.
- Most patients in this real-world study were receiving treatment, with both conventional immunosuppressants and biologics frequently added to RAASi.
- Despite receiving treatment with these medications, proteinuria remained high, with 60% of patients having proteinuria ≥1 g/day.
- This study highlights the need for a targeted therapy in C3G which addresses the underlying pathophysiology of the disease.

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