

Persistence of Signs and Symptoms in Treated Patients with C3G: Evidence from

Real-World Data Clare Proudfoot¹, Katharina Pannagl², Briana Ndife³, Serge Smeets¹, Kathleen Murphy³, Jonathan de Courcy⁴, Susanna Libby⁴, Richard Lafayette⁵

Affiliations: ¹Novartis Pharma AG, Basel, Switzerland; ²Novartis Pharmaceuticals UK Ltd, London, UK; ³Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States; ⁴Adelphi Real World, Bollington, UK ⁵Stanford University Medical Center, United States

Conclusions

- Despite treatment, C3G signs and symptoms (S&S) persist in most patients- with 70% of the treated sample experiencing proteinuria – Table 2.
- Proteinuria values remained high in all treated patients, independent of how long they had been receiving their current treatment- increasing the risk of progression to kidney failure **Figure 1.**
- These findings highlight that there remains an unmet need in C3G therapy; with the need for targeted treatment highlighted.

Introduction

- Complement 3 Glomerulopathy (C3G) is a rare kidney disease, with an estimated incidence of 1-2 cases per million in a year¹.
- It is characterized by the dysregulation of the alternative pathway of the complements system, resulting in C3 deposition in the glomeruli².
- The disease is fast progressing, with approximately 50% of C3G patients reaching kidney failure within 10 years of diagnosis³.
- Lack of effective therapies which have the ability to reduce proteinuria and improve CKD stages may result in worse outcomes for patients.

The aim of this real-world analysis is to describe C3G signs and symptoms (S&S) in treated patients.

Methods

- Data were drawn from the 2022 Adelphi C3G Disease Specific Programme™, a cross-sectional survey of C3G-treating nephrologists and their consulting patients in the US, France, Germany, Italy, Spain, UK (EU5), China and Japan between August 2022 and April 2023.
- The DSP methodology has been previously published and was conducted according to the relevant regulations⁴.
- Physicians reported data on patient demographics, C3G treatment history and clinical information including S&S.

Results

Patient Demographics

In total 111 nephrologists completed records for 385 C3G patients (EU5 189; US 100; CN 60; JP 36)- Table 1. 288 of this sample were receiving treatment at the time of survey, and had a start date of their treatment provided, with 60% being prescribed their treatment for less than 1 year.

Table 1: Patient demographics by geographical region.

	EU5	US	China	Japan
Number of patients, n	189	100	60	36
Age at time of survey; median years (SD)	40.0 (18.9)	41.0 (15.7)	39.0 (11.3)	51.5 (12.4)
Age at diagnosis; median years (SD)	37.7 (17.7)	38.4 (15.8)	36.0 (11.0)	48.5 (13.3)
Sex , male; n (%)	113 (60)	56 (56)	34 (57)	24 (67)
BMI ; median Kg/m^2 , (SD)	23.7 (4.1)	25.5 (3.6)	22.9 (2.5)	20.4 (2.8)
Working full or part time; n (%)	90 (49)	60 (62)	36 (62)	27 (77)
Currently receiving treatment; n (%)	161 (85)	79 (79)	53 (88)	28 (78)

SD, Standard Deviation. BMI, Body Max index EU5 – France, Germany, Italy, Spain, and the United Kingdom

Table 2: Treated C3G patient current signs and symptoms by number of years on treatment

Time since treatment initiation (Years)	All with treatment	<1 year	1-2 years	>2 years
Number of patients, n	288	173	61	54
Number of signs & symptoms Mean (SD)	2.4 (1.8)	2.6 (1.8)	2.4 (1.7)	2.0 (1.5)
Proteinuria (g/24hr) ≥1g/24hr (n=263*)	183 (70%)	116 (72%)	40 (75%)	27 (54%)
CKD Stage CKD Stages 3b-5 (GFR <45 mL/min/1.73 m2) (n=274*)	96 (35%)	59 (36%)	19 (33%)	18 (34%)

Figure 1: Top 5 reported S&S by physicians at time of survey

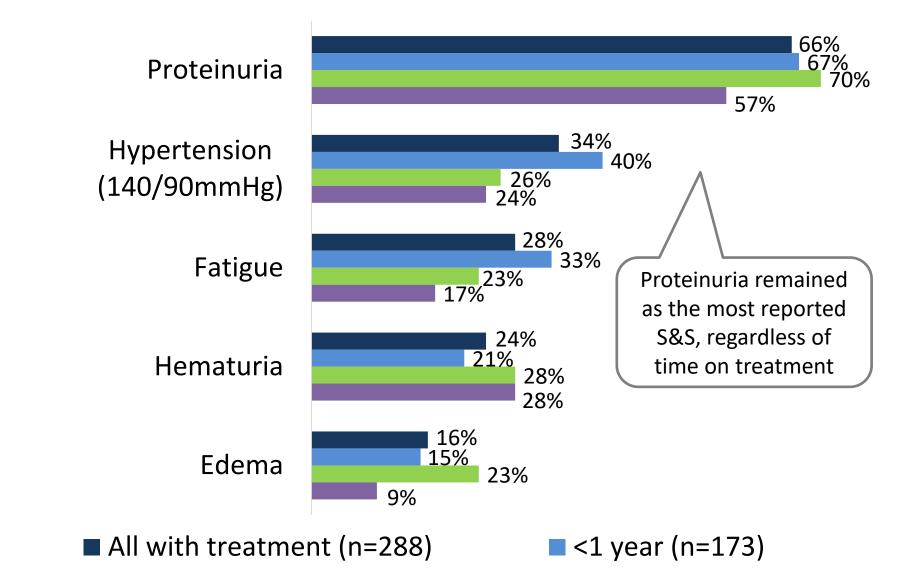
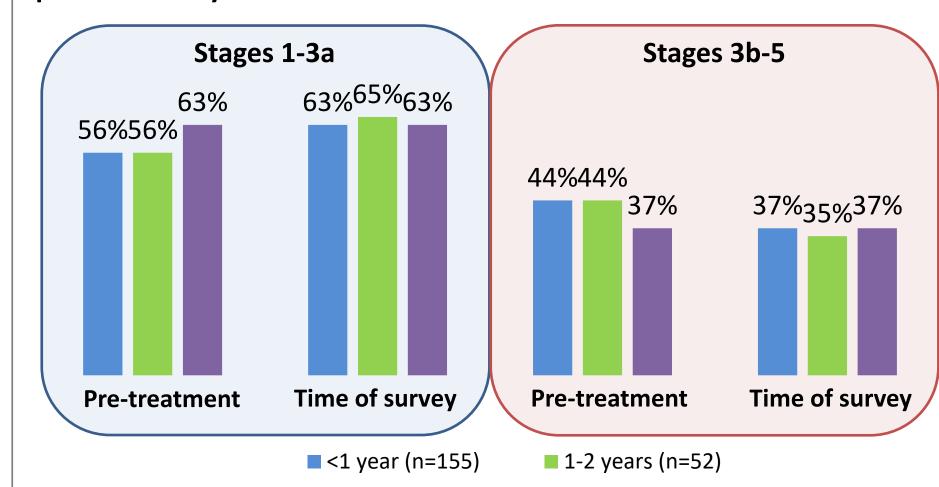


Figure 2: CKD stages of C3G patients prior to current treatment and at point of survey

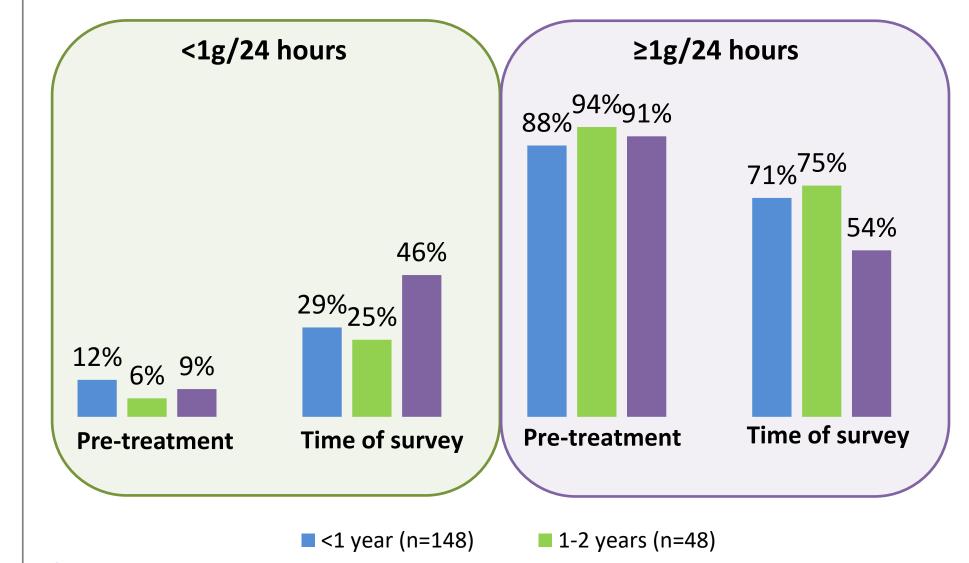


Symptoms reported and CKD stages

- Around 2/3 of the treated sample were reported to have proteinuria at the time of survey – Figure 1, with a similar proportion (70%) experiencing this proteinuria at ≥1g/24 hours – Table 2.
- Time on treatment did not significantly reduce the symptoms reported, with the difference being small between those on treatment for <1 year and those >2 years.
- 253 patients had data available for eGFR reported at pre-treatment initiation and at time of survey; and provided time on current treatment.
- CKD staging remained consistent across all groups, with a slight improvement in CKD stages shown for all. Patients who had been on treatment for longer reported the same CKD stage groupings for time of survey and pre-treatment initiation (63% stages 1-3a and 37% stages 3b-5 respectively) **Figure 2.**

Figure 3: Proteinuria prior to current treatment and at point of survey

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Changes in proteinuria

- 242 patients had data available for proteinuria reported at pre-treatment initiation and at time of survey; and provided time on current treatment.
- Clinical proteinuria values decreased for all groups from initiation of treatment to point in survey, especially for those who have been treated for over 2 years, with the percentage of those experiencing ≥1g/24 hours dropping from 91% to 54% – Figure 3.
- Although proteinuria values did drop, physicians still reported proteinuria as the most common symptom of C3G **Figure 1**.
- Just under 3/4 of the treated population still experienced significant proteinuria, despite the reductions from the current treatment regimen Table 2.

Limitations

Patients included in the DSP sample are the next eligible patients who consult the physician; therefore, it may not truly represent the overall population of patients, as it is more likely to collect data on patients who consult more frequently.

References

1. Medjeral-Thomas NR et al. C3 glomerulopathy: clinicopathologic features and predictors of outcome. *Clinical Journal of the American Society of Nephrology. 2014 Jan 7;9(1):46-53.* **2.** Smith RJH, Appel GB, Blom AM, et al. C3 glomerulopathy - understanding a rare complement-driven renal disease. *Nat Rev Nephrol.* 2019;15(3):129-143. doi:10.1038/s41581-018-0107-2. **3.** Smith RJ et al. C3 glomerulopathy-understanding a rare complement-driven renal disease. *Nature reviews nephrology. 2019 Mar;15(3):129-43.* **4.** Anderson P, Benford M, Harris N, Karavali M, Piercy J. Real-world physician and patient behaviour across countries: Disease-Specific Programmes – a means to understand. Current Medical Research and Opinion. 2008; 24(11):3063-3072..

Disclosures

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