Evidence for meaningful patient benefit of pegcetacoplan in C3G and primary IC-MPGN from the VALIANT Trial

PCR198

Richard Lafayette, Prof., MD[1], Mingyi Huang, PhD[2], Carly Rich, BSc, MSc, PhD[3], Tom Booth, PhD[4], Meg Fluharty, PhD[4], Caleb Dixon, MSc[4],
Sarah Acaster, MSc[4], Sayna Norouzi, MD[5], Fernando Caravaca-Fotán MD PhD[6], Daniel Gale, PhD[7]

[1]Stanford University, Stanford, CA, USA; [2]Apellis Pharmaceuticals, Waltham, MA, USA; [3]Sobi, Stockholm, Sweden; [4]Acaster Lloyd, London, United Kingdom; 5Department of Nephrology, Loma Linda University Medical Centre, Loma Linda, CA, USA; [6]Department of Nephrology, Instituto de Investigación Hospital Universitario 12 de Octubre, Madrid, Spain;[7]University College London, London, United Kingdom.

CONCLUSIONS

Patients with reduced proteinuria report lower fatigue, reduced symptom burden, and higher perceived improvement. Overall, findings support the patient relevance of proteinuria reduction as a meaningful treatment benefit of pegcetacoplan for patients with C3G or primary IC-MPGN in the VALIANT trial.

INTRODUCTION

C3G and primary IC-MPGN are rare diseases, characterized by dysregulation of the complement system and subsequent excessive glomerular deposition of C3 and its breakdown products.[1]

Current treatment strategies include supportive antiproteinuric therapy, non-targeted immunosuppression and kidney replacement therapy which can impact HRQoL and limit daily activities. Despite this burden, there is a lack of effective targeted treatments, and among current treatment options unmet needs remain.[2]

A recent trial (VALIANT: NCT05067127) conducted by Apellis and Sobi evaluated the efficacy of twice weekly subcutaneous infusion of pegcetacoplan for the treatment of C3G and primary IC-MPGN.[3] The trial met its key efficacy endpoint, reduction of proteinuria from baseline, however the strength of association between the clinical endpoints and patient functioning remains unclear.

Therefore, the current study analyzed PRO data from VALIANT to examine associations between HRQoL and biomarkers, to further support the patient relevance of biomarkers and evidence of treatment benefit.

OBJECTIVE

To evaluate the relationship between treatment effect (UPCR reduction) and PROs in participants with C3G and primary IC-MPGN enrolled in the VALIANT trial.

METHODS

Study Cohort: VALIANT was a phase III multicenter study with a 26-week randomized, placebo-controlled, double-blinded period. A total of N=124 participants were enrolled in the study and randomized to pegcetacoplan group (N=63) and placebo (N=61) stratified by transplant status (posttransplant recurrence vs non-transplant) and patients with and without baseline renal biopsies.

PROs analysed included total scores and subdomains of the FACIT-Fatigue, KDQoL-36 and WPAI, as well as the EQ-5D-5L and PGI-C. The current study was restricted to participants with PRO data at baseline and week 26 (N=83)(Table 1).

Table 1. Baseline sample characteristics for patients with PRO data in VALIANT

	Category	N	(%)
Sex	Male	43	52%
	Female	40	48%
Age	Adolescents	39	47%
	Adults (≥18)	44	53%
Transplant status	Non-transplant	76	92%
	Posttransplant	7	8%
Dialysis	No	77	93%
	Yes	6	7%
UPCR	<3000 mg/g	61	74%
	≥3000 mg/g	22	27%

Analysis: An exploratory post hoc analysis was conducted in the VALIANT trial to evaluate differences in PRO scores by measures of patient improvement at week 26.

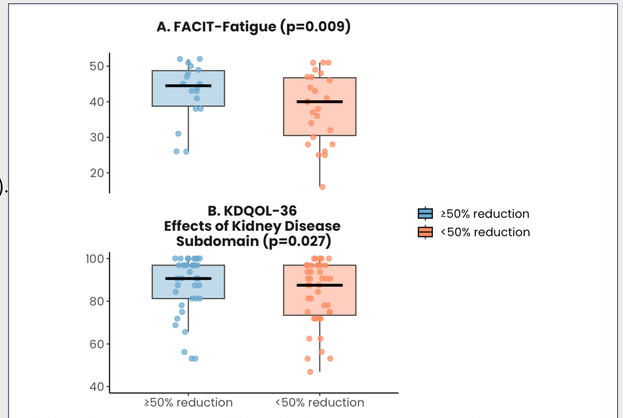
Patient improvement was defined based on PGI-C response at week 26, and by those who reduced UPCR by ≥50% versus <50% from baseline.

Patient reported HRQoL was compared between those who reduced their UPCR by ≥50% versus <50% reduction from baseline, using Kruskal-Wallis or Fisher's Exact Test.

PGI-C response was compared between treatment groups (pegcetacoplan [N=42] versus placebo [N=41]), using Fisher's Exact Test.

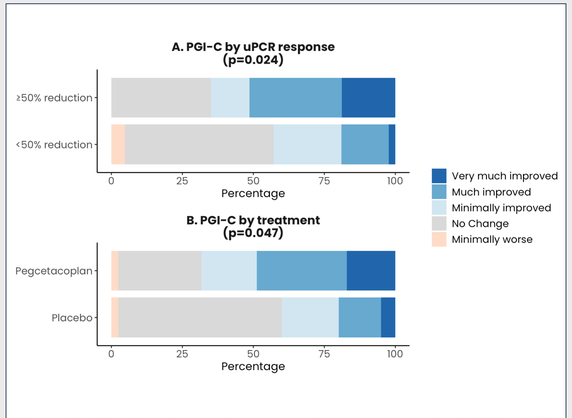
RESULTS

Figure 1: Box-plot displaying the distribution, inter-quartile range and median scores of FACIT-Fatigue and KDQoL-36 Effects of kidney disease subdomain by UPCR response at week 26



Participants who had reduced UPCR by 50% at week 26 were more likely to score higher on FACIT-Fatigue and KDQoL-36 Effects of kidney disease subdomain indicating less fatigue and reduced symptom burden

Figure 2: Distribution of PGI-C by UPCR response and by treatment group at Week 26



More patients treated with pegcetacoplan, and those who reduced their UPCR by 50% reported "much improved" or "very much improved" status on PGI-C at week 26.

Results from the Kruskal-Wallis tests showed that patients with ≥50% reduced UPCR were more likely to report less fatigue, with a median score of 47.5 on the FACIT-Fatigue compared to a median score of 40.0 for those with <50% reduction (H=6.90, p=0.009) (Figure 1A).

Patients with ≥50% reduction in UPCR reported fewer limitations and impairments as assessed by the KDQoL-Effects scale, with median scores of 96.9 and 84.4 for the ≥50% reduced UPCR vs <50% reduced UPCR, respectively (H=4.88, p=0.027) (Figure 1B).

No significant differences were identified for the WPAI:SHP, EQ-5D-5L, or other KDQoL-36 subscales.

PGI-C responses at week 26 differed significantly across both UPCR response (p=0.024, Figure 2A) and treatment arm (p=0.047, Figure 2B).

A higher proportion of patients with ≥50% reduction in UPCR from baseline reported being 'much improved' (N=12, 32.4%) or 'very much improved' (N=7, 18.9%) compared to those with <50% reduction (N=7; 16.7%; N=1, 2.4%) respectively.

Similarly, more participants treated with pegcetacoplan reported being 'much improved' (N=14; 33.3%) or 'very much improved' (N=7, 16.7%) compared to those on placebo (N=6; 14.6%, N=2, 4.9%) respectively.

ISPOR 2026 Philadelphia, PA, USA

Abbreviations: C3G: C3 glomerulopathy; IC-MPGN: Immune-complex membranoproliferative glomerulonephritis; HRQoL: Health-related quality of life; Sobi: Swedish Orphan Biovitrum AB; PRO: Patient-reported outcome; UPCR: Urine protein-creatinine ratio; PGI-C: Patient Global Impression of Change; FACIT: Functional Assessment of Chronic Illness Therapy; KDQoL-36:Kidney Disease Quality of Life-36; WPAI:SHP: Work Productivity and Activity Impairment: Specific Health Problem; EQ-5D-5L:EuroQol 5-Dimension 5-Level questionnaire

References: 1. Kovala, M. et al. (2023). Cells, 12:712. ; 2. Bomback, A.S. et al. (2025). Kidney Int. Rep., 10:17–28.; 3. Nester, C.M. et al. (2024). J. Am. Soc. Nephrol.

Disclosures: This analysis was funded by Apellis and Sobi. Richard Lafayette has received consulting fee from Apellis, Amgen, Biogen, Calliditas, Jade, Biohaven, Alexion, Travere, Novartis, Takeda, Otsuka, Vera and Vertex.; Mingyi Huang is an employee of and hold stocks/shares in Apellis Pharmaceuticals, Inc.; Carly Rich is an employee of and holds stocks/shares in Swedish Orphan Biovitrum AB. Tom Booth is an employee of Acaster Lloyd; Meg Fluharty is an employee of Acaster Lloyd; Caleb Dixon is an employee of Acaster Lloyd; Sarah Acaster is an employee of Acaster Lloyd; Sayna Norouzi has received consulting fee and honorariums from Calliditas, Otsuka, Alexion, Travere, Novartis, Sanofi, HCPLive, was a speaker for Calliditas, Lily, Otsuka, is a member of the board of directors for IgAN Foundation and has received grants from GlomCon, IgAN Foundation, ASN.; Fernando Caravaca-Fotán has previously received sponsorship or honoraria for participation in lectures or advisory boards by Novartis, SOBI, AstraZeneca, Alexion, Bayer, STADA and Otsuka. Daniel Gale has received consulting fee from Alexion, Apellis, Bayer, Boehringer Ingelheim, Calliditas, CSL Vifor, GSK, Novartis, Otsuka, Sanofi, SOBI, STADA, Travere and Vera.; Daniel Gale has received consulting fee from Alexion, Apellis, Bayer, Boehringer Ingelheim, Calliditas, CSL Vifor, GSK, Novartis, Otsuka, Sanofi, SOBI, STADA, Travere and Vera.