first morning spot urine protein/creatinine (Up/c) ratio results for the patients in the placebo arm ($n = 10$) of this randomized, double-blind placebo-controlled study (3:3:2 allocation for 1 mg/kg, 4 mg/kg, and placebo treatment groups). Patients received randomized treatment for 112 days and were followed double-blind to 252 days. First morning Up/c was obtained from first morning spot urine collections for all visits; 24-h timed collections were performed for Day 1 and Day 112 visits. For first morning Up/c, the average of two collections at each study time point was used for analysis.
**RESULTS:** Median age was 42 years, 40% female, 20% black, median eGFR 60 mL/min/1.73 $m^2$, with median Up/c 6.4 g/g (NCT01665391). Correlation coefficient between 24-h timed collection and averaged spot Up/c was $r = 0.63$ (P = .004). For 24-h timed urines, between subject SD = 2.015 g/24 h and within subject SD = 7.328 g/24 h. For averaged first morning spot Up/c, between subject SD = 2.5 g/g and within subject SD = 2.3 g/g.
**CONCLUSION:** In clinical trials subjects with nephrotic syndrome from biopsy-proven FSGS on stable doses of ACEi/ARB medications, 24-h timed collections do not provide additional useful data beyond average of two first morning spot Up/c. These data suggest that labour intensive, cumbersome timed 24-h urine collections should not be performed in clinical trials of nephrotic syndrome patients. Importantly, these data should allow for more precise power and sample size estimates for future interventional clinical trials of nephrotic syndrome.

## MO212 UPDATED INTERIM RESULTS OF A PHASE 1/2 STUDY TO INVESTIGATE THE SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS AND CLINICAL ACTIVITY OF BION-1301 IN PATIENTS WITH IGA NEPHROPATHY

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**BACKGROUND AND AIMS:** Immunoglobulin A nephropathy (IgAN) is the leading cause of primary glomerulonephritis worldwide with limited treatment options, especially for high-risk patients [1]. BION-1301 is a novel humanized monoclonal antibody that blocks a proliferation-inducing ligand (APRIL), a soluble factor that has been shown to be elevated in patients with IgAN and is correlated with poorer outcomes, including increased proteinuria and decreased eGFR [2, 3]. APRIL promotes IgA class switching, the survival of IgA-secreting plasma cells and the excess production of a galactose-deficient variant form of IgA1 (Gd-IgA1), which is an initiating step in IgAN pathogenesis. This leads to the generation of anti-Gd-IgA1 autoantibodies, considered to be the first 'hit' in the multi-hit pathogenesis of IgAN, and the formation of nephritogenic immune complexes that deposit in the kidney, resulting in inflammation and damage [2–4]. Blocking APRIL with BION-1301 is a novel approach to address the underlying pathogenesis of IgAN by reducing circulating levels of Gd-IgA1 and preventing the formation of pathogenic immune complexes. In a Phase 1/2 study of BION-1301 in healthy volunteers (HV), BION-1301 was well-tolerated with no serious adverse events (SAEs), demonstrated a pharmacokinetic (PK) half-life > 30 days and durable dose-dependent reductions in free APRIL (fAPRIL), Gd-IgA1, IgA and IgM, with a lesser effect on IgG [5]. Here we present updated interim results from Part 3 of the study that characterize the safety, PK/PD profile and preliminary efficacy of BION-1301 initially administered intravenously (IV), then subcutaneously (SC), in patients with IgAN.
**METHOD:** Parts 1 and 2 of the Phase 1/2 study (NCT03945318) assessing single and multiple ascending doses of BION-1301 in HV are complete. Part 3 is an ongoing, open-label, multicohort design in patients with IgAN treated with BION-1301 for up to 1 year. Key eligibility criteria for Part 3 include: (i) biopsy-verified diagnosis of IgAN within the past 10 years, (ii) baseline urine protein excretion ≥ 0.5 g/24 h or UPCR ≥ 0.5 g/g and (iii) stable/optimized dose of ACE-I/ARB (or intolerant). Cohort 1 receives 450 mg of BION-1301 administered IV every 2 weeks. After at least 24 weeks of IV dosing, patients' transition to 600 mg of BION-1301 administered SC every 2 weeks. Cohort 2 receives 600 mg of BION-1301 SC every 2 weeks. To evaluate PK/PD effects of BION-1301, serum levels of BION-1301, fAPRIL, anti-drug antibodies (ADA), neutralizing antibodies (NAbs) and Gd-IgA1 were quantitated using ELISA-based immunoassays.
**RESULTS:** Updated data from Cohort 1 will be reported. BION-1301 was well-tolerated in patients with IgAN receiving a 450 mg IV dose every 2 weeks for at least 24 weeks, with no SAEs or early terminations due to AEs. Durable reductions in serum levels of fAPRIL and immunoglobulins were observed in patients with IgAN. Clinically meaningful reductions in proteinuria were seen as early as 12 weeks and were associated with the reduction in Gd-IgA1 levels.
**CONCLUSION:** BION-1301 offers disease-modifying potential by directly targeting the initiating mechanisms underlying the multi-hit immune pathogenesis of IgAN, which is not addressed with currently available treatments. Promising early mechanistic biomarker and clinical activity responses support the therapeutic potential of BION-1301 in IgAN.

## MO213 SARS-COV-2 VACCINATION DID NOT AFFECT THE CLINICAL COURSE OF IGA NEPHROPATHY IN LATVIAN ADULT COHORT

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**BACKGROUND AND AIMS:** The current strategy to fight against the COVID-19 pandemic involves active patient vaccination. Patients with renal and autoimmune diseases are in high risk for severe COVID-19 infection [1]. Therefore they should be prioritized for vaccination. Immunoglobulin A nephropathy (IgAN) is one of the most common primary glomerulonephritis triggered by mucous membrane alteration; however, there is a discussion about vaccination-caused IgA flare [2]. The immunological nature of IgAN and misleading information in public sources leaves patients skeptical about whether to get vaccinated [3]. The study aimed to investigate the impact of SARS-CoV-2 vaccination on the clinical course of IgA nephropathy.
**METHOD:** Adult patients treated in Pauls Stradins Clinical University Hospital with morphologically proven IgAN were included in the study. Patients with secondary IgAN were excluded. Evaluation of clinical and laboratory markers was performed on inclusion visit and on the second visit 6 months later. SARS-CoV-2 vaccination type and status were noted on both visits. Estimated GFR was calculated with CKD-EPI creatinine–cystatin equation. IBM SPSS Statistics version 27 and Microsoft Excel 10 were used for data analysis.
**RESULTS:** The study involved 54 patients, 36 were unvaccinated and 18 were fully vaccinated. A significant difference between the two groups was observed by baseline proteinuria. Other differences were not observed. Fourteen patients were vaccinated with mRNA vaccine, 13 with *Comirnaty* and 1 with *Spikevax,* and four patients were vaccinated with *Vaxzevria* vector vaccine. The differences between the two groups are shown in Table 1. During study period, two patients had COVID-19 infection; a patient in the vaccinated group had COVID-19 prior to vaccination.
**CONCLUSION:** SARS-CoV-2 vaccination did not affect the clinical course of IgA nephropathy. Our study results indicate that SARS-CoV-2 vaccination in IgA nephropathy patients was safe regarding renal function and disease activity markers.

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**Table 1.**

| Characteristics | Vaccinated | Unvaccinated | P-value* |
|---|---|---|---|
| Total, *n* | 18 | 36 | |
| Male/female, *n* (%) | 13/5 (72/28) | 22/14 (61/39) | .425 |
| Age, years | 43.4 (9.8) | 41.6 (11.0) | .451 |
| Baseline eGFR** | 46.1 (30.7) | 49.8 (31.6) | .569 |
| Baseline 24-h proteinuria*** | 0.28 (0.32) | 0.8 (0.97) | .014 |
| Baseline hematuria, *n* (%) | 16 (89) | 28 (78) | .143 |
| Baseline IgA, g/L | 3.5 (1.2) | 3 (0.8) | .147 |
| Baseline C3c, g/L | 1.2 (0.8) | 1 (0.2) | .689 |
| Delta eGFR** | 1.8 (5.4) | −0.5 (8.5) | .612 |
| Delta 24-h proteinuria*** | −0.19 (0.33) | 0.07 (0.65) | .214 |
| Hematuria after 6 months, *n* (%) | 13 (72) | 29 (81) | .44 |
| IgA after 6 months, g/L | 3.6 (1.1) | 3.1 (0.8) | .183 |
| C3c after 6 months, g/L | 1.1 (0.2) | 1.1 (0.2) | .517 |
| Diseased with COVID-19, *n* (%) | 1 (5) | 1 (3) | .614 |

Estimates are given as mean values (standard deviation)
*Results were analyzed using Mann-Whitney *U* test and were expressed as *P*-values.
**Estimated GFR, mL/min/1.73 $m^2$.
***Estimated 24-h proteinuria, g/24 h/1.73 $m^2$.

3. Islam MS, Kamal AM, Kabir A *et al*. COVID-19 vaccine rumors and conspiracy theories: The need for cognitive inoculation against misinformation to improve vaccine adherence. *PLoS One* 2021; 16: e0251605.

## MO214 HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH ANCA VASCULITIS

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**BACKGROUND AND AIMS:** Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) is a debilitating disease that can have a significant impact on a patient's quality of life. The aim of this study was to assess the longitudinal quality of life amongst those diagnosed with AAV using the EQ-5D instrument, which allows for calculation of quality-adjusted life years (QALYs.)
**METHOD:** A total of 343 patients with AAV participated in this study, of which 191 (55.7%) were male, resulting in 2746 episodes. The EQ-5D-5L standardised instrument was used to evaluate health-related quality of life in the domains of mobility, self-care, usual activities, pain/discomfort, anxiety/depression and to generate a summary index score. Overall health was also rated using a visual analogue scale (0–100). EQ-5D questionnaires were completed during routine nephrology clinic attendances and through a vasculitis patient support smartphone app. We used a random effects model to control for multiple entries relating to individual patients.
**RESULTS:** A lower quality of life was seen amongst those with AAV (median index value 0.80, overall population average 0.856). The mean visual analogue scale score was 75.6 ± 17.3 (overall population average 82.8, Fig. 1). Patients' pain and discomfort level (mean 1.95) was most affected while self-care (mean 1.33) was least affected (Fig. 1). An increase in BVAS tightly correlated with a reduction in quality of life. Using the random effects model, the index score was seen to decrease with increasing age with a 2.7% reduction in index score per decade. A 7% reduction in index score was seen during periods of disease activity compared with periods of remission. Patients with end-stage kidney disease requiring dialysis had an 8% reduction in index score. A reduced quality of life was seen following COVID-19 lockdown with a 5% reduction in index score seen. Using a median survival rate of 6.16 years for patients with small vessel vasculitis, we calculated the QALYs for this population as 4.9 years.
**CONCLUSION:** We have defined for the first time the EQ-5D index value over the full disease course in patients with AAV. Notably, we have identified a reduction in quality of life during periods of disease activity. Other studies have demonstrated a reduction in quality of life during active disease using the AAV–PRO questionnaire and the Medical Outcomes Study Short Form-36. A decrease in work productivity has also been noted. Previously reported mean index values of 0.72 and 0.76 were lower than our observed values, although both are significantly reduced compared with population norms. In conclusion, this research highlights the negative impact of AAV on patients' lives.

## MO215 INTRARENAL SINGLE CELL SEQUENCING OF MPO-ANCA ASSOCIATED GLOMERULONEPHRITIS PATIENTS REVEAL NOVEL TARGETABLE TREATMENT OPTIONS

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**BACKGROUND AND AIMS:** The etiopathogenesis underlying myeloperoxidase anti-neutrophil cytoplasmic antibody-associated glomerulonephritis (MPO-ANCA-GN) remains incompletely understood. Furthermore, there are only limited treatment options and treatment resistance of MPO-ANCA-GN is still a common problem.
**METHOD:** To identify new targeted treatment options, intrarenal single-cell RNA sequencing (scRNA-seq) was applied to 11 kidney biopsies from MPO-ANCA-GN patients and 2 health kidney tissues to define the transcriptomic landscape at single-cell resolution. Intrarenal scRNAseq was also applied to a pre-clinical mouse model of MPO-ANCA-GN to show that this model of disease can be used to trial new targeted treatments.
**RESULTS:** We found that kidney endothelial cells in MPO-ANCA-GN patients displayed increased expression of several genes, including *CD9* and *SPARC*, which were closely related to parietal epithelial hyperplasia and crescent formation. NF-$\kappa$B pathway activation was confirmed in a variety of kidney cells in MPO-ANCA-GN patients. Kidney infiltrating immune cells of MPO-ANCA-GN patients were mainly enriched in inflammatory pathways including TNF signalling, IL-17 signalling and NOD-like receptor signalling. These findings were similar in our pre-clinical mouse model of MPO-ANCA-GN. Furthermore, there was an overexpression of inflammasome-related genes (*AIM2, IFI16*) in MPO-ANCA-GN patients. Treatment resistance was associated with increased infiltration of $CD8^+$ T cells and elevated expression of *SPARC*, *LAMA4*, *IL33* and *CFL1* in mesangial cells when compared with patients who achieved remission after induction therapy.
**CONCLUSION:** These results offer new insight into the pathogenesis of MPO-ANCA-GN, treatment resistance and identify new therapeutic targets for MPO-ANCA-GN that can be tested in a pre-clinical model of disease.

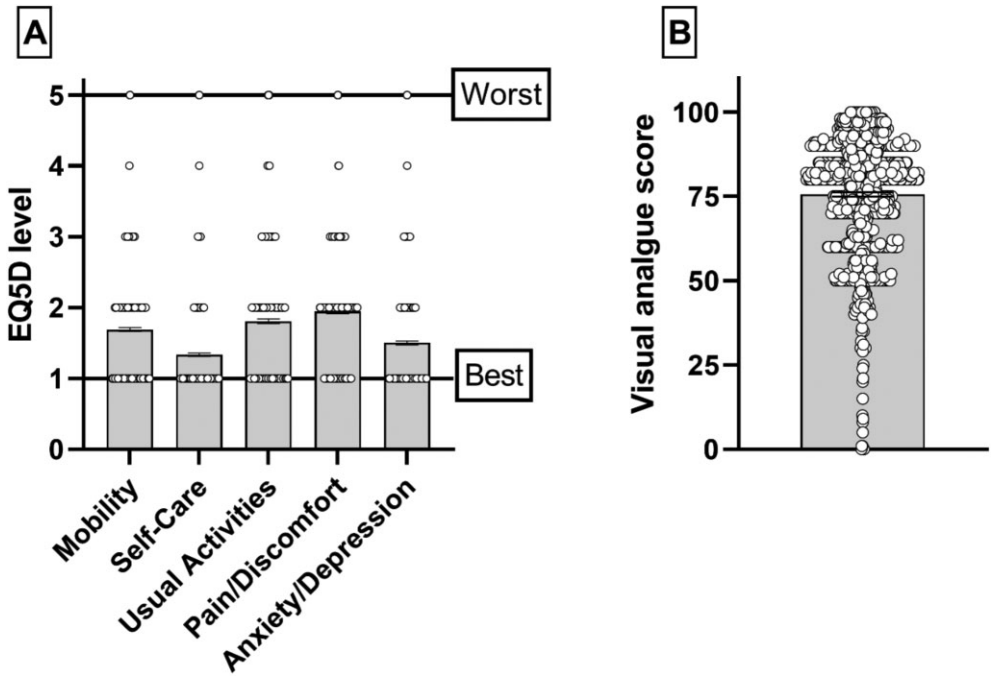


**FIGURE 1:** (A) Domain-specific EQ5D levels and (B) visual analogue score. Both graphs reflect mean and 95% confidence interval.