METHOD: The Phase 1/2 study (NCT03945318) is comprised of three parts. Parts 1 and 2 were blinded, placebo-controlled single and multiple ascending dose designs in HV and have been completed. Part 3 is a multicenter (USA, UK, South Korea), multicohort, open-label study in up to 40 patients with IgAN. Patients in Cohort 1 receive 450 mg of BION-1301 administered IV every 2 weeks for up to 1 year. After completing at least 24 weeks of IV dosing, patients in Cohort 1 transitioned from receiving 450 mg of BION-1301 IV to receiving 600 mg of BION-1301 SC every 2 weeks. Patients in Cohort 2 receive 600 mg of BION-1301 SC every 2 weeks for up to 1 year. Additional cohorts may be added to explore other doses and dosing schedules. Key eligibility criteria for Part 3 include: (1) biopsy-verified diagnosis of IgAN within 10 years, (2) baseline urine protein excretion $\geq$ 0.5 g/24 h or UPCR $\geq$ 0.5 g/g and (3) stable/optimized dose of ACE-I/ARB (or intolerant).
RESULTS: Final HV data from Parts 1 and 2 have been presented at earlier conferences [5]. Part 3 is on-going and updated interim data from patients with IgAN in Cohort 1 who received BION-1301 IV as well as patients who transitioned to SC dosing are planned to be presented at the 59th ERA Congress.
CONCLUSION: The current design of the Phase 1/2 study incorporating SC dosing provides for an improved patient experience and will enable the generation of extended safety, PK, PD, immunogenicity and preliminary efficacy data for the potential use of BION-1301 in patients with IgAN.

MO208 DE NOVO GLOMERULONEPHRITIDES FOLLOWING BNT162B2 COVID-19 VACCINE: A CASE SERIES

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BACKGROUND AND AIMS: The development and massive use of mRNA COVID-19 vaccine BNT162b2 has raised new concerns on triggering *de novo* immune-mediated diseases, in particular rare diseases as glomerulonephritis (GN), even if the security profile is excellent and severe reactions have been rare. In literature few similar cases were recently described [1, 2]. We report six cases of newly diagnosed GN after a two-dose regimen of SARS-CoV-2 vaccine, from a single tertiary care institution in Northern Italy.
METHOD: We described six cases of *de novo* GN occurring after massive use of Pfizer-BioNTech BNT162b2 COVID-19 vaccine from March 2021 to December 2021. All cases were biopsy proven. Baseline characteristics and laboratory findings, treatments and outcomes were based on review of medical records.
RESULTS: From April 2021, we observed two IgA nephropathies (IgA-N), one membranous nephropathy (MN), one membranoproliferative GN (MPGN), one acute interstitial nephritis (aTIN) and one minimal change disease (MCD). Of note, one IgA-N presented with diffuse purpura as in IgA-vasculitis. The median age at vaccination was 52.8 years (min–max 18–67) and three (50%) were female; arterial hypertension was the most common comorbidity (50%). Only one subject contracted COVID-19 before vaccine (16.6%). None of the points showed any sign of renal disease before vaccine; at the time of disease onset, the median creatinine was 1.49 mg/dL (min–max 0.6–10.5 mg/dL) and proteinuria 3.0 g/24 h (min–max 0.9–13.8 g/24 h). All cases presented after the second dose (1 day to 6 months thereafter) and three (50%) were within 3 weeks from the vaccine. Of note, the aTIN developed after the vaccine during a long-time therapy with statins and relapsed after a rechallenge with a statin few months later. All the nephropathies were treated as per center practice, with an overall good response (four partial remissions and one complete remission). Given a target population of about 100 000–200 000 residents in our area, we could estimate an incidence rate of 4–8 cases/100 000 patient-years.
CONCLUSION: This small series has a lot of limitations including the small number of patients and we probably missed some cases in our area. Furthermore, we could not investigate a causal association, even if the timing of disease onset might be suspicious in three cases and the incidence seemed to be almost twice as the expected in Europe (about 2–4/100.000 patient-years). As for SARS-CoV-2 vaccines, it is likely that the mRNA vaccine will result in a more potent inflammatory stimulus than the one observed after inactivated virus-vaccine: maybe some patients had already a subclinical GN and the vaccine constituted a flare leading to the full-blown disease [3].

	Pt1	Pt2	Pt3	Pt4	Pt5	Pt6
Age at vaccine	67	52	53	66	18	40
Sex	M	F	F	F	M	M
Comorbidities	HTN, GERD	Breast K, asthma	HTN, DM, goiter	HTN, prev. TIA	none	HCV (erad), history of iv drug abuse
Time from vaccine to disease onset (days)	22	49	54	160	1	17
Peak creatinine (mg/dL)	1,4	0.6	10.5	0.7	1.6	3.1
Peak U-Prot (g/24)	2.7	3.4	0.9	4.1	1.4	13.8
Histology	IgAN	GNM	aTIN	MCD	IgAN	MPGN (type 1)
Treatment	Oral steroids	RASi	IV and oral steroids	Oral steroids	Oral steroids	Ev cyclophos-phamide + steroids
Outcome	Partial remission	Stable	CR + res CKD	Partial remission	Partial remission	Partial remission
Follow-up (days)	87	41	215	56	35	54

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MO209 BASELINE CHARACTERISTICS OF ADULTS ENROLLED IN THE ONGOING PHASE 3 RANDOMIZED, DOUBLE-BLIND, ACTIVE-CONTROL TRIAL OF SPARSENTAN FOR THE TREATMENT OF IMMUNOGLOBULIN A NEPHROPATHY (PROTECT)

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BACKGROUND AND AIMS: Immunoglobulin A nephropathy (IgAN) is the most common glomerular disease worldwide. Despite optimized standard of care treatment, up to 40% of individuals with IgAN develop kidney failure requiring dialysis or kidney transplantation, consequently seriously affecting their quality of life and mortality. Treatments that reduce proteinuria and risk of kidney disease progression are urgently needed for IgAN. Sparsentan is a novel Dual Endothelin Angiotensin Receptor Antagonist (DEARA) being investigated for IgAN. The Phase 3 PROTECT study is examining the potential long-term antiproteinuric and nephroprotective potential and safety of sparsentan compared with an active control, angiotensin receptor blocker (ARB) irbesartan, in adults with IgAN. Here we report the baseline characteristics for all patients enrolled in the PROTECT trial.
METHOD: PROTECT is an ongoing, global, Phase 3, multicenter, randomized, double-blind, parallel-group, active controlled study designed to evaluate the efficacy and safety of sparsentan versus the active control irbesartan in adults with IgAN with overt proteinuria despite receiving maximized treatment with an angiotensin-converting enzyme inhibitor (ACEi) and/or ARB. The study duration is 270 weeks: a double-blind period of 114 weeks followed by an open-label extension period of up to 156 weeks. The primary efficacy endpoint is the change from baseline in urine protein/creatinine ratio (UP/C) based on a 24-h urine sample at Week 36. Key inclusion and exclusion criteria are shown in Table 1. Patients took their last dose of maximized standard-of-care treatment with ACEi and/or ARB therapy the day before randomization. Patients were randomized 1:1 to sparsentan or irbesartan (target dose