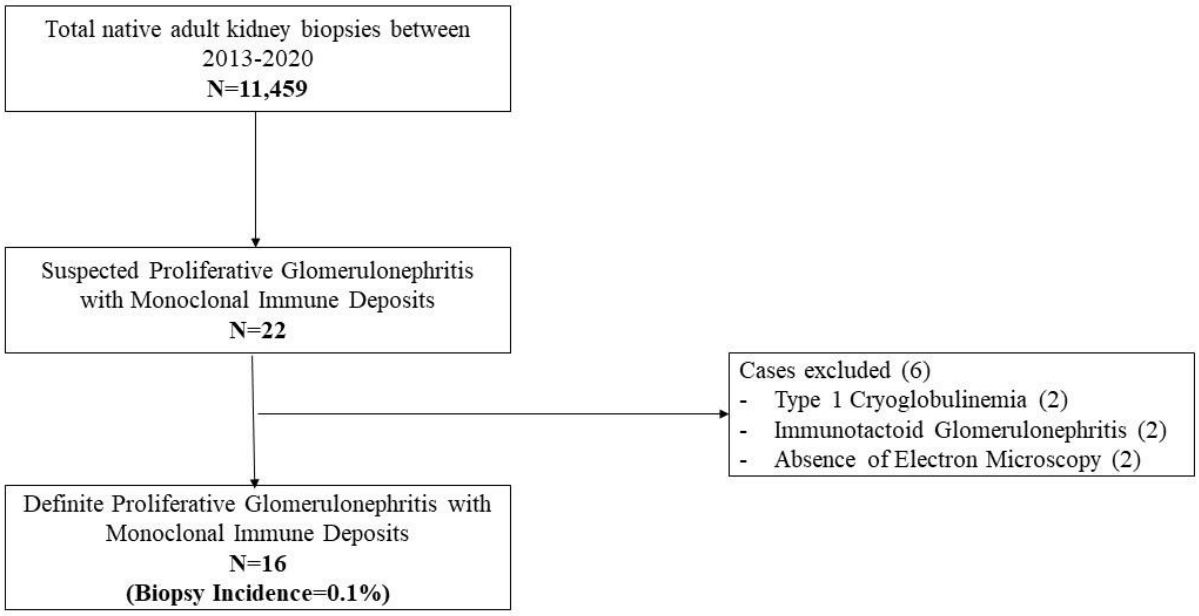
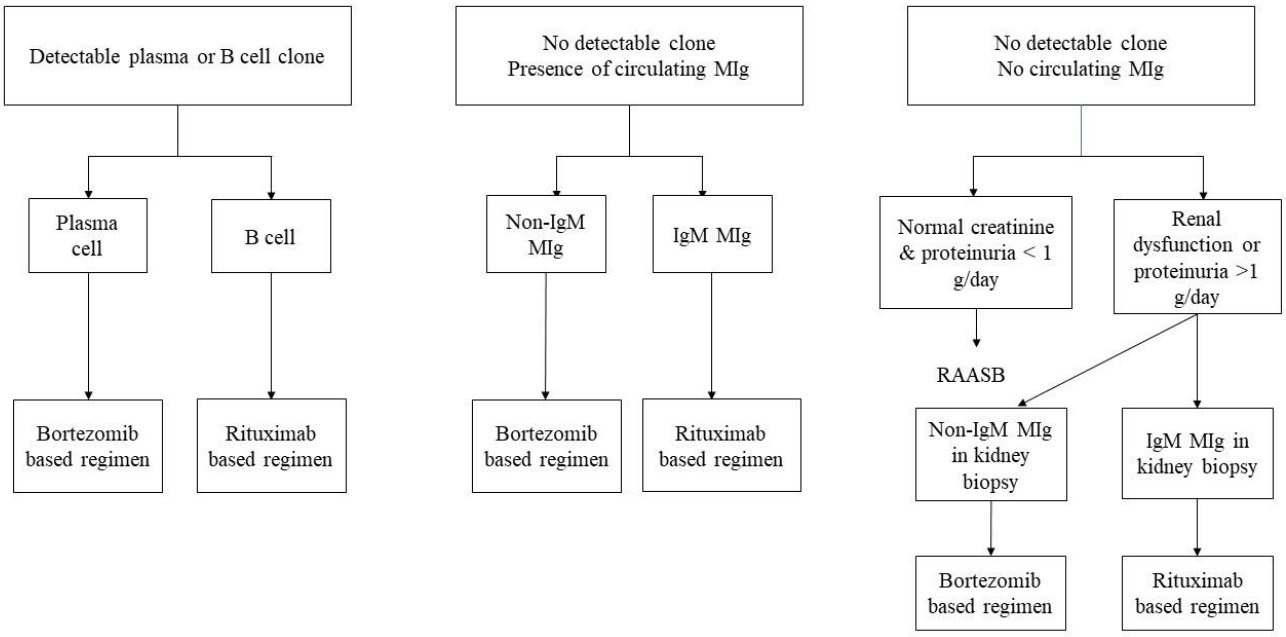
Supplementary Figure 1: Flowchart of GRACE-PGNMID cohort



(GRACE-PGNMID, Glomerular Research and Clinical Experiments- Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposits.)

Supplemental Figure 2: Current treatment recommendations of PGNMID



(MIg, monoclonal immunoglobulin; RAASB, renin angiotensin aldosterone system blockers)

Supplemental table 1: Treatment and outcomes

Parameters	Entire Cohort
Treatment Characteristics (N=16)	
Renin-angiotensin system blockers (n, %)	4 (25)
Treatment agent (n, %)	
Steroid	13 (75)
Alkylating agent	3 (18.7)
Mycophenolate mofetil	3 (18.7)
Calcineurin inhibitor	0
Proteasome inhibitor	2(6.3)
Immunomodulatory drugs	0
Type of therapy (n, %)	
Conservative therapy	3 (18.8)
Immunosuppression	11 (68.8)
Clone directed therapy	2 (12.5)
Outcomes at last follow up (N=11)	
>3 months of follow-up (n, %)	13 (81.2)
Duration of follow-up, months [median (IQR)]	6 (3-27)
Renal outcomes (n, %)	
Complete remission	3 (23.1)

Partial remission	4 (30.8)
Persistent renal dysfunction	1 (7.7)
Kidney failure	5 (38.5)
Hematological outcomes (n, %)	
Multiple myeloma	1 (7.7)
Persistent M spike on serum protein electrophoresis†	3 (75)
Other outcomes (n, %)	
Infections	3 (27.2)
Death	1 (8)

†Evaluable patients (N) for proteinuria outcomes=8 and persistent M spike=4.

Supplemental Table 2: Classification of PGNMID based on the type of monoclonal light chain restriction

Parameter	Kappa-PGNMID (N=9)	Lambda-PGNMID (N=7)	*p* value
Baseline demographic and clinical characteristics (N=16)			
Age, years (mean ± SD)	36.4 ± 13.3	48.4 ± 11.2	0.077
Sex (n, %)			0.315
Males	6 (66.7)	2 (28.6)	
Females	3 (33.3)	5 (71.4)	
Body mass index, kg/m² (mean ± SD)	21.6 ± 3.4	26.9 ± 4.7	0.020
Comorbidities			
Diabetes Mellitus (n, %)	1 (11.1)	1 (14.3)	0.700
Hypertension (n, %)	6 (66.7)	6 (85.7)	0.585
Systolic BP, mmHg (mean ± SD)	134.2 ± 19.4	142.4 ± 11.7	0.342
Diastolic BP, mmHg (mean ± SD)	85.6 ± 13.5	84.3 ± 7.9	0.829
Kidney manifestations (n, %)			
Edema	9 (100)	6 (85.7)	0.438
Oligo-anuria	0	1 (14.3)	0.438
Dyspnea	1 (11.1)	2 (28.6)	0.550
Visible hematuria	0	0	
Systemic manifestations (n, %)			
Fever	0	1 (14.3)	0.438
Bone pain	0	0	
Urine abnormalities (n, %)			
Non-visible hematuria	8 (88.9)	6 (85.7)	0.700
Leucocyturia	4 (44.4)	4 (57.1)	0.500
Casts	3 (33.3)	3 (42.9)	0.549
Serum albumin, g/dL (mean ± SD)	2.6 ± 0.4	2.7 ± 0.8	0.694
24-hour urine protein, g/day [median (IQR)]	5.5 (4-9)	5.8 (4-7.2)	0.791
Kidney function			
Baseline creatinine, mg/dL [median (range)]	1.2 (1-1.5)	1.6 (0.8-2)	0.396
Serum creatinine at biopsy, mg/dL [median (range)]	1.9 (1.1-2.5)	2 (1-3.7)	0.711
eGFR CKD-EPI at biopsy, ml/min/1.73 m² [median (range)]	38.1 (28-93.5)	33 (17.5-74)	0.368
Dialysis dependent at biopsy (n, %)	0	1 (14.3)	0.438
Serology (n, %)			
Low C3	4 (44.2)	2 (28.6)	0.633
Low C4	0	0	

Baseline hematological parameters			
Hemoglobin, g/dL (mean ± SD)	10.6 ± 1.2	9.8 ± 2.2	0.371
Lytic bone lesions (n, %)	0	0	
Hypercalcemia (n, %) †	1 (14.3)	0	0.538
M spike on protein electrophoresis			
Serum protein electrophoresis	4 (44.4)	2 (28.6)	0.633
Urine protein electrophoresis (%)	2 (22.2)	1 (14.3)	0.600
Serum or urine protein electrophoresis (%)	4 (44.4)	3 (42.9)	0.671
Serum immunofixation electrophoresis (n, %) †			
Monoclonal immunoglobulin			0.636
None	5 (71.4)	4 (80)	
IgG	2 (28.6)	1 (20)	
Monoclonal light chain			
None	5 (71.4)	4 (80)	0.636
Kappa	2 (28.6)	1 (20)	
Lambda	0	0	
Serum free light chain assay†			
Monoclonality (n, %)			0.565
No monoclonality	4 (50)	4 (80)	
Monoclonal kappa light chain	4 (50)	1 (20)	
Monoclonal lambda light chain	0	0	
Serum kappa free light chain, mg/dL [median (IQR)]	99 (51.2-128.5)	100 (34.5-407)	0.942
Serum lambda free light chain, mg/dL [median (IQR)]	47 (37-57.5)	65.8 (33.7-173)	0.164
Serum kappa: lambda ratio [median (IQR)]	1.8 (1.2-2.7)	1.1 (1-2.2)	0.240
Bone Marrow (n, %)			
Plasma cells, % [median (IQR)] †	1 (0-4.7)	1 (0.5-8)	0.706
Plasma cells > 10%	0	1 (20)	0.385
Immunohistochemistry †			
No restriction	8 (100)	4 (100)	
Kappa restriction	0	0	
Lambda restriction	0	0	
Baseline histopathological parameters (N=16)			
Light Microscopy (N=16)			
Number of glomeruli (mean ± SD)	13.3 ± 7.7	15.9 ± 4.4	0.457
Globally sclerosed glomeruli [median (IQR)]	26.7 (9-37.5)	10.5 (5-27.8)	0.168
Glomerular lesions (n, %)			
Light microscopy patterns			0.993
Membranoproliferative pattern	4 (44.4)	3 (42.9)	
Mesangial proliferation	3 (33.3)	2 (28.6)	
Diffuse endocapillary proliferation	1 (11.1)	1 (14.3)	
Focal endocapillary proliferation	1 (11.1)	1 (14.3)	
Crescents	3 (33.3)	1 (14.3)	0.585
Tuft necrosis	0	1 (14.3)	0.438
Glomerular neutrophil infiltration	3 (33.3)	3 (42.9)	0.549
Tubular lesions (n, %)			
Acute tubular injury	3 (33.3)	2 (28.6)	0.635
Interstitium (n, %)			
Interstitial inflammation (focal, diffuse) (n, %)	8, 1 (88.9, 11.1)	5, 1 (71.4, 14.3)	0.525
IFTA moderate-severe (n, %)	8 (88.9)	6 (85.7)	0.700
Vascular lesions (n, %)			
Arterio(lar)sclerosis	8 (88.9)	6 (85.7)	0.700
Immunofluorescence staining(N=16)			
Predominant heavy chain deposit (n, %)			0.475
IgG	7 (77.8)	6 (85.7)	
IgM	2 (22.2)	0	
IgA	0	1 (14.3)	
Site of immunofluorescence staining			0.529
Glomerular capillary wall	4 (44.4)	3 (42.9)	

Mesangium	2 (22.2)	0	
Glomerular capillary wall + mesangium	3 (33.3)	4 (57.1)	
Complement (n, %)			
C3	7 (77.8)	6 (85.7)	0.207
C1q	4 (44.4)	2 (28.6)	0.413
C4	2 (22.2)	1 (14.3)	0.475
Mean Staining intensity (Mean ± SD)			
C3	2 ± 1.1	1.1 ± 0.7	0.098
C1q	0.4 ± 0.5	0.4 ± 0.7	0.962
C4	0.2 ± 0.4	0.3 ± 0.7	0.836
Electron microscopy (N=16)			
Site of deposits (n, %)			
Mesangial deposits	6 (66.7)	4 (57.1)	0.549
Subendothelial deposits	7 (77.8)	6 (85.7)	0.600
Subepithelial deposits	4 (44.4)	0	0.088
Foot process effacement (focal, diffuse) (n, %)	3, 5 (33.3, 55.6)	1, 5 (14.3, 71.4)	0.780
Treatment characteristics (N=16)			
Renin-angiotensin system inhibitors (n, %)	3 (33.3)	1 (14.3)	0.585
Type of therapy (n, %)			0.758
Conservative therapy	1 (11.1)	2 (28.6)	
Immunosuppression	7 (77.8)	4 (57.1)	
Clone directed therapy	1 (11.1)	1 (43.3)	
Outcome at last follow-up (N=13)			
>3 months of follow-up (n, %)	8 (88.9)	5 (71.4)	0.550
Duration of follow-up, months [median (IQR)]	6.5 (3-29.2)	4 (3.5-25)	0.766
Renal outcomes (n, %)			0.862
Complete remission	1 (12.5)	1 (20)	
Partial remission	3 (37.5)	2 (40)	
Persistent renal dysfunction	1 (12.5)	0	
Kidney failure	3 (37.5)	2 (40)	
Other outcomes (n, %)			
Infections	2 (33.3)	1 (12.5)	0.667
Death	2 (25)	1 (20)	0.667

BP, Blood pressure; CKD-EPI, Chronic Kidney Disease-Epidemiology Collaboration; eGFR, Estimated glomerular filtration rate; IFTA, Interstitial fibrosis and tubular atrophy; IQR, Inter-quartile range; SD, Standard deviation.
† Evaluable patients (N) for hypercalcemia=13, serum immunofixation electrophoresis=12, Serum free light chain ratio=13, Bone marrow plasma cells=13, Bone marrow immu
nohistochemistry=12, Proteinuria outcomes=12.

Supplemental table 3: Comparison of major cohorts in PGNMID with our study.

Author	Guiard et al.[26]	Vignon et al.[27]	Gumber et al.[4]	Bhutani et al.[3]	Gowda et al.[16]	Maity et al.[7]	Nasr et al.[4]	Nasr et al.[9]	**Current study**
Cohort Duration	1998-2008	1998-2015	2000-2016	2008-2013	2009-2014	2018-2019		1999-2008	2012-2021
Country	France	France	USA	Mayo Clinic (USA)	India	India	Multicentric data, USA	USA	India
Number of patients	26	14	19	60	6	6	17	37	16
Biopsy Incidence (%)	-	-	-	-	3.7	-	-	-	0.1
Age, years [mean ±SD or median (range)]	52 ±16	55 (33-75)	38 (23-58)	56 (47-62)	50 (38-75)	53 ± 10	62 (44-84)	54.5 (20-81)	41.7 ± 13.5
Gender (male: female)	0.6: 1	1.8: 1	1.7: 1	1.1: 1	5: 1	5: 1	3.2: 1	0.6: 1	1: 1
Co-morbidities (%)									
Diabetes Mellitus	-	-	-	-	-	17	-	13	12.5
Hypertension	67	-	-	-	67	17	88	38	75
24-hour urine protein, g/day [median (range)]	5.3 (1.4-10)	4 (0.4-7.8)	3.6 (2.3-8)	3.6 (1.9-8.1)	3.5 (2.1-4.8	4.8 (1.8-11.2)	4.7 (2-12)	5.7 (0.4-17)	5.9 (0.3-15)
Kidney function at biopsy									
Serum creatinine, mg/dL [median (range)]	2.7 (0.6-10.6)	1.56 0.8-3.1)	-	-	3.7 (1.3-5.8)	2.6 (1.4-3.9)	2 (0.9-5.7)	2.8 (0.7-17)	1.9 (0.5-4.7)
eGFR CKD-EPI, ml/min/1.73 m² [median (IQR)]	49 ± 35	52 (22-81)	38 (23-58)	36 (22-52)	-	-	37 (9-93)	-	36 (24-75)
Dialysis dependent (%)	11	-	0	3.5	50	17	-	-	6.3
Baseline hematological parameters (%)									
M spike in serum electrophoresis	23	36	37	15	0	17	-	30	37.5
M spike in urine electrophoresis	8	21	37	2	0	17	73	19	18.8
Detectable monoclonal Ig by serum IFE	-	36	37	20	-	-	-	30	25
Abnormal kappa: lambda ratio	-	7	-	21	0	0	83	25	38.5
Biclonality or mismatch between IFE and kidney IF	0	0	14	7	-	-	12	-	7.7
Bone Marrow plasma cells >10%	9	7	0	0	0	17	56	3	7.1
Monoclonal restriction of bone marrow plasma cells	-	-	-	-	-	-	56	3	0
Detectable nephropathic clone by BM flow cytometry	-	-	32	25	-	-	-	-	-
Light microscopy (%)									
MPGN pattern	46	43	95	65	100	50	76	57	44
Mesangial proliferation	0	50	0	13	0	17	0	3	31
Diffuse endocapillary proliferation	0	-	5	10	0	17	24	27	12
Focal endocapillary proliferation	0	-	0	0	0	0	0	8	12
Membranous nephropathy	54	7	0	12	0	16	0	5	0
Crescents	50	71	-	18	0	17	18	32	25
Immunofluorescence staining									
Monoclonal heavy chain (%)									
IgG	100	-	90	90	100	83	100	100	81
IgM	0	-	10	8	0	0	0	0	13
IgA	0	100	0	2	0	17	0	0	6
Monoclonal light chain (%)									
Kappa	80	50	58	67	100	67	71	73	56
Lambda	20	50	42	33	0	33	29	27	44
Electron microscopy			-		-				
Subendothelial deposits	21	89		-		50	100	100	81
Subepithelial deposits	57	0		-		33	71	57	25
Mesangial deposits	14	89		-		17	100	95	63
Treatment				-		-			
Conservative treatment	0	28	0		17		6	41	19
Immunosuppression	64	57	81		66		27	50	69
Clone directed therapy	36	15	19		17		67	9	12
Outcomes				-					
Follow up duration, months [median (range)]	67.6 (2-216)	30 (12-168)	23 (12-45)		-	9.5 (2-18)	70 (20-154)	30 (1-114)	6 (3-35)
Complete remission (%)	-	-	-		-	-	-	-	23
Kidney failure (%)	24	21	18		67	17	53	22	38
Death (%)	4	7	-		33	-	33	16	9

BM, Bone marrow; Chronic Kidney Disease-Epidemiology Collaboration; eGFR, eGFR, Estimated glomerular filtration rate; IF, Immunofluorescence; IFE, Immunofixation electrophoresis; MPGN, Membranoproliferative glomerulonephritis; PGNMID, Proliferative glomerulonephritis with monoclonal immunoglobulin deposits; SD, Standard deviation.

Supplemental table 4: Recommended work-up and treatment options in PGNMID

Recommended workup in PGNMID	Available treatment options in PGNMID
First line investigations	**Plasma cell clone**
Serum protein electrophoresis	Monoclonal antibody
Serum immunofixation electrophoresis	Daratumumab (Anti CD 38)
Serum free light chain assay	
Bone marrow examination	Cytotoxic agents
Percentage plasma cells	Cyclophosphamide
IHC of plasma cells for kappa and lambda light chains	Melphalan
Flowcytometry for detection of monoclonal plasma and B cells	Proteosome inhibitors
	Bortezomib
	Carfilzomib
	Ixazomib
	Immunomodulatory agents
	Thalidomide
	Lenalidomide
	Pomalidomide
Second line investigations*	**B cell clone**
PET-CT scan of thorax, abdomen and pelvis	Monoclonal antibody
Flow cytometry of peripheral blood to detect small clones of CLL or MBL	Rituximab (Anti CD 20)

* Indicated if all first line investigations are negative
CD, cluster of differentiate; CLL, chronic lymphocytic leukemia; IHC, immunohistochemistry; MBL, monoclonal B cell lymphocytosis; PET-CT, positron emission tomography-computed tomography; PGNMID; proliferative glomerulonephritis with monoclonal imu ne deposits.