Monoclonal Gammopathy of Renal Significance (MGRS) Crib Sheet

More than one disease below can occur in a single patient. Please select the most clinically relevant under Primary Diagnosis and put any others in the Comments box

**AL amyloidosis** (light chain amyloidosis renal biopsy proven) 2521 PRD code ORPHA :85443

**AH amyloidosis** (heavy chain amyloidosis) ORPHA: 442582

**AHL amyloidosis** (light and heavy chain amyloidosis) (2509 renal amyloidosis)

Amyloid confirmed on histology of any tissue with evidence of renal involvement on either; SAP imaging, histology, proteinuria or declining renal function. Immunohistochemistry should have confirmed Kappa or lambda staining. Ideally patient has had confirmation at the NAC but not essential for recruitment to RaDaR.

Distinguishing between AL, AH or AHL is required on histology of any tissue.

**C3 glomerulonephritis with monoclonal gammopathy no code** (C3 Glomerulonephritis ORPHA:329931)

C3 glomerulonephritis or dense deposit disease with evidence of a monoclonal gammopathy. If no evidence of an abnormal clone patients need to be registered under C3 glomerulopathy in the separate RaDaR cohort.

**Crystalglobulinæmia** (PRD 1591 cryoglobinulinaemia secondary to systemic disease – histologically proven)

Extracellular deposits of large monoclonal immunoglobulin crystals within vascular lumens, including arteries and glomerular capillaries.

**Crystal-storing histiocytosis no code**

Histology shows crystal laden histiocytes in the interstitium or glomeruli; monoclonal light chain restriction on immunofluorescence; evidence of a plasma cell clone.

**Fibrillary Glomerulonephritis** PRD code 2606 ORPHA : 97566

Renal biopsy required with electron microscopy essential for diagnosis. EM shows random fibrillary deposits in the mesangium and glomerular capillary walls. (Fibrils are 16-24nm). Congo red stain is negative. Light chain restriction on immunofluorescence and evidence of a monoclonal gammopathy is required to classify as an MGRS lesion.

**Immunotactoid/Glomerulonephritis with Organised Microtubular Monoclonal Immunoglobulin Deposits (GOMMID)** PRD code 2606

Renal biopsy histology diagnosis with microtubules on electron microscopy (fibrils are 30 to 50nm in diameter). EM is therefore required to confirm this as a diagnosis. Light chain restriction on immunofluorescence and evidence of a monoclonal gammopathy is required to classify as an MGRS lesion.

**Intracapillary monoclonal IgM without cryoglobulin**

Seen with Waldenstrom/lymphoplasmacytic Lymphoma. Non- proliferative usually, with large subendothelial and/or intraluminal granular deposits that stain with IgM and with a single light chain. No evidence of a cryoglobulin.

**Intraglomerular/capillary lymphoma/leukaemia**
Light chain cast nephropathy (myeloma cast nephropathy PRD code 2584 biopsy proven)
Myeloma cast nephropathy confirmed on renal biopsy. (Formally called myeloma kidney)

Light chain Proximal Tubulopathy, crystalline  ORPHA:91136 Acquired monoclonal Immunoglobulin light-chain associated Fanconi Syndrome
Rod or rhomboid shaped light chain crystals are localised within proximal tubular epithelial cells.
Classic presentation is with Fanconi syndrome, confirmed through serum and urine testing with evidence of abnormal clone (paraprotein and/or serum free light chains),

Light chain proximal tubulopathy, non-crystalline no code
Evidence of a proximal tubulopathy with light chains in serum and urine testing; monoclonal light chain restriction on immunofluorescence in tubular epithelial granules; cytoplasmic droplets, granules or vacuoles without crystals on renal histology

Non amyloid Monoclonal Immunoglobulin Deposition Disease ORPHA:86861 (MIDD) consisting of either (Light chain deposition disease - LCDD PRD 2597 ORPHA:93558, Heavy chain deposition disease – HCDD ORPHA: 93556, Light and Heavy chain Deposition Disease – LHCDD ORPHA:93557)
Histology shows non organized deposits which are eosinophilic and granular. Immunofluorescence should show monotypic fixation of kappa or lambda along the tubular basement membrane (LCDD and LHCDD) or IgG (HCDD).

EM is required to confirm the diagnosis. Granular, electron dense deposits are seen on the inner aspect of the GBM, in the mesangium and on the outer aspect of the tubular basement membrane.

Proliferative glomerulonephritis with monoclonal immunoglobulin deposits – PGNMID (mesangial proliferative GN PRD 1349)
Mimics immune complex GN. Membranoproliferative, endocapillary proliferative, mesangioproliferative or membranous glomerulonephritis. Immunofluorescence reveals granular positivity for a single light-chain isotype and single heavy chain subtype. EM shows well-defined, non organised deposits.

No evidence of a cryoglobulin (diagnosis of exclusion).

Thrombotic Microangiopathy with monoclonal gammopathy no code (Thrombotic Microangiopathy ORPHA: 93573)
Evidence of a thrombotic microangiopathy on renal biopsy in conjunction with a monoclonal protein.

Type 1 cryoglobulinaemic Glomerulonephritis (PRD 1591 cryoglobulinaemia secondary to systemic disease)
Membran proliferative pattern on renal biopsy; often with intralumen thrombi. Light chain restriction on immunofluorescence; confirmed cryoglobulin in serum

Unclassified MGRS