

Description of two real world cases of MGRS

Case-1: Patient X presented with heavy proteinuria and a concomitant light-chain MG (baseline eGFR 36 ml/min, CKD stage 3b). Renal biopsy revealed a monoclonal immunoglobulin deposition disease of the kappa light chain subtype (LCDD-κ. He achieved a hematological remission (VGPR) and a renal response (eGFR 48 ml/min) post 6 cycles of VCD (bortezomib, cyclophosphamide and dexamethasone) and continues to be dialysis independent and sustained hematological remission at 18-months of follow-up.

Case-2: Patient Y presented with heavy proteinuria and a concomitant MG (IgGκ) [baseline eGFR 24 ml/min, CKD stage 4). Renal biopsy was consistent with LCDD. Patient was started on a combination of cyclophosphamide, thalidomide and dexamethasone (CTD). Following 3 cycles of CTD, he achieved less than partial hematological response and his therapy was changed to VCD. After 2 cycles of VCD, he achieved PR. Renal function however worsened (eGFR 14 ml/min, CKD stage 5) and he became dialysis dependent. He continues on renal replacement therapy at 3-years of follow-up (not a candidate for renal allograft) and is off-chemotherapy due to non-tolerance.

Table S1: Summary of the available literature regarding the renal outcomes and recurrence rates in the renal allograft in MGRS

MGRS entity	Author (year)	Sample size	Treatment regimens used (no. of patients)	Hematological response (no. of patients)	Renal response (no. of patients)	Renal outcome and OS (no. of patients)	Recurrence after renal transplant
MIDD	Sayed et al ⁶⁴ (2015)	53	T (11), V (9), ASCT (4), R (1), Steroids (1), alkylator (6)	CR/VGPR (21) PR/NR (11)	CR/VGPR- GFR increased by 6.1 ml/min/yr PR/NR- 6.5 ml/min/yr loss of GFR	RS- 5.4 yr OS- 14 yr stable/improved function (57%) ESRD (53%)	Recurrence after 1.6 yr and 1.9 yr respectively (2/7=28.5%) No recurrence (4)
	Kourelis et al ⁸⁹ (2016)	88	PI/ASCT (60%)	CR/VGPR (42%) (PI/ASCT- 77%/56%)	Overall-34% CR/VGPR- 57%/17%)	5-Yr RS-57% (CR/VGPR-77%, PR/NR-54%) 5-yr OS-67%	Recurrence (3/9 =33.3%) Hematological progression without renal progression (6)
C3G	Zand et al ²⁴ (2014)	21*	IM before transplant (6), pred (3), Pred+CSA (1) Pred+Cyclo (1), MMF/IVIG (1)	NA	NA	No recurrence (7), recurrence (14) recurrence was earlier in 3 patients with MG	Recurrence (14/21= 66.7%)- amongst them- 50% had graft failure-
	Lloyd et al ⁵⁸ (2016)	12	V-based** (8/4 patients of MM)	HR (1 out of 8)	RRT (5), stable function (3), improvement (1)	ESRD (56%)	Recurrence after 18 months (1/1=100%)
	Chauvet et al ¹¹ (2017)	50	Chemo (29) including V-based (22) IST (8)	Overall-37% (chemo-59%)	Overall-42% Chemo-74%	RS- chemo > no chemo, HR> no HR, CR/VGPR> PR/NR ESRD-50% (Chemo-31%)	Recurrence (4/4 =100%)- all received no chemo before transplant
aHUS	Ravindran et al ¹² (2016)	146 (20 had a MG)	V-2, T-1 TPE/steroids/IST (remaining)	NA	NA	With MG- 50% had ESRD Without MG-33% had ESRD	Recurrence?
PGNMID	Nasr SH et al ⁹¹ (2009)	37	IM (18) Steroid alone (6), Pred+Cyclo/Clb (3) Pred+T (1) Pred +V (1) MMF based (3), Rituximab based (4)	NA	NA	Overall: CR/PR-38%, PRD-38%, ESRD-22% 18 patients with IM: CR/PR (8), PRD (7), ESRD (3)	NA
	Nasr SH et al ²² (2011)	4*	Pred+R (3) Pred+Cyclo (1)	NA	All 4 responded	Reduced proteinuria-4 Reduced creatinine-3 Reduced histologic activity-4	Median 3.8 months after transplant
	Said et al ²⁶ (2018)	26**	IM (16) (after recurrence) R (13), S (12), Cyclo (5), V (3), RCHOP (1), Eculizumab (1), ASCT (1)	NA	Response***- 60% of patients with recurrence	Graft loss-44% Median Graft survival-92 months	89% had recurrence (median- 5.5 months)
	Gumber et al ⁹² (2018)	19	Chemotherapy alone: Clone-directed (4) Non-directed (2) Empirical (10)	NA	CR (6), PR (7), None (3) 1 non-responder initially had PR to second-line therapy	Treatment group (16)- no ESRD No treatment group (3)- all progressed to ESRD 6 relapsed, but 4/5 relapsed cases responded to second-line therapy	No patient underwent kidney transplant.
MN with monoclonal Ig	Guiard et al ¹⁹ (2011)	14	IM (10) Rituximab (2)	NA	Renal response associated with HR	ESRD (3) CR/PR (8) NR (1)	Recurrence (1/2=50%)
ITG	Nasr SH et al (2012) ⁵¹	16	IM (10) Steroid alone (2) Rituximab based (2) ASCT (1)	NA	ITG remission in 3 patients with Lymphoma	Remission-50%, ESRD-17%, PRD-33%	NA
	Mallett et al ⁹³ 2015	11	NA	NA	NA	Overall survival-2.93 yr 75% patient survival and 100% renal allograft survival	Recurrence (1/4 =25%)- median 2.1 yr
FG	Czarnecki PG et al ²⁰ (2009)	7	IM (3) Cyclo-Pred, Dexa, Mel	NA	NA	6 allograft failures- median survival 37 months	Recurrence (5/7 =71%)
	Nasr SH et al ⁵² (2011)	66	IM (29) Steroid alone (8) Steroid +IM (16) IM without steroid (5), Rituximab (3)	NA	NA	CR/PR-13%, PRD-43%, ESRD-44%	36% of 14 at a median F/u of 51 months

MPGN with monoclonal Ig	Lorenz et al ²⁵ (2010)	29 [#]	Rituximab (4) BMT (2), TPE (4)	NA	4 underwent TPE: reduction in proteinuria with TPE (3), dialysis dependent (1), graft loss (1)	MG was higher Amongst rMPGN vs those without rMPGN.	Recurrence (12/29= 44.1%): median of 3.3 months
LCPT	Stokes et al ⁴¹ (2016)	30- crystalline 6- non- crystalline	Crystalline: ASCT+chemo (10), chemo alone (12), Non-crystalline- chemo (5), ASCT (1),	Crystalline: CR (5), VGPR (1), PR (3), SD (21) Non-crystalline: CR (2), SD (2), PR (1)	Improved (7), stable (11), worsening (4), ESRD (0), Death (4) Non-crystalline- improved (1), stable (1), worsened (1)	Crystalline- median renal survival: 135 ± 5.5 months Non-crystalline- median renal survival: 64 ± 17.8 months	NA

* 21 patients with renal transplant were included in this study.

** none of the patients with MG without MM received chemotherapy

+ study included 4 patients with recurrent disease post renal transplant, treatment regimens showed indicate treatment received by the patients' post-recurrence.

++ includes 26 patients of PGNMID allograft

+++response was defined as >50% decrease in proteinuria, <25% increase creatinine

includes 29 patients with recurrent MPGN after renal transplant and treatment indicates the therapy received by the patients after recurrence.

Yr-years, T- thalidomide, V- Velcade, R-Rituximab, ASCT- autologous stem cell transplant, CR- complete response, VGPR- very good partial response, PR- partial response, NR- no response, GFR- glomerular filtration rate, RS- renal survival, OS- overall survival, ESRD- end stage renal disease, PI- proteasome inhibitor, IM-immunomodulatory treatment, Pred- prednisolone, CSA- cyclosporine, cyclo-cyclophosphamide, MMF- mycophenolate, IVIG- IV immunoglobulin, MM- multiple myeloma, HR- hematological response, Chemo- chemotherapy, IST- Immunosuppressive therapy, NA- not available, clb- chlorambucil, PRD- persistent renal dysfunction, R- Rituximab, S- steroids, RCHOP- Rituximab/cyclophosphamide/doxorubicin/vincristine/prednisolone, Dexa- dexamethasone, Mel- Melphalan, rMPGN- recurrent MPGN, SD- Stable disease, TPE- Therapeutic plasma exchange, BMT-Bone marrow transplantation.