SUPPLEMENTAL TABLE 2: PATHOLOGIC FINDINGS

	Diagnosis	IF	P-IF	K/L	EM	ATI	Fibrosis score	% Fibrosis	% inflamm	Casts	Other inclusions	
Case #	**Crystalline LCPT**											
1	SMM	1+	3+	κ	Rods, rhomboid	D	2	40	25			
2	SMM	Neg	3+	κ	Needle	P	1	10	10			
3	MM	neg	2+	κ	Rods, fibrils	D	0	0	0			
4	MM	Neg	2+	κ	Rods	D	0	<5	0			
5	MGRS	neg	2+	κ	Needles; striated	D	1	20	20			
6	MM	1+	3+	κ	Rods, fibrils	D	0	0	0			
7^	MGRS	neg	2+	κ	ND	D	1	10	15			
8	MGRS	1+	2+	κ	Rhomboid	D	1	15	15			
9	SMM	3+	nd	κ	Needle	P	0	5	5			
10	SMM	neg	3+	κ	Rhomboid	D	0	<5	0			
11	SMM	neg	1-2+	κ	Rods, needles	D	1	15	0			
12^	MM	neg	nd	κ	Rhomboid	D	0	0	0			
13	MGRS	neg	2+	κ	Rhomboid	D	0	0	0			
14	MGRS	trace	1+	κ	Needle, rhomboid	D	2	30	25		VEC,	PEC, CSH
15	NHL	neg	1+	κ	Rods, fibrils	P	2	5	5			
16	MGRS	neg	3+	κ	Rhomboid; lattice	D	2	30	15		CSH	
17	MGRS	neg	1+ (IP)	κ	Rods, fibrils	D	2	50	25			
18	MM	neg	3+	κ	ND	D	1	10	0			
19	CLL	1+	3+	κ	Rhomboid, fibrils	D	1	15	0			
20	MGRS afte	nd	3+	κ	Rods	D	0	0	0			
21	MGRS	neg	3+	κ	Rhomboid	D	2	40	40		CSH	
22	MGRS	1+	2+	κ	Rhomboid	D	3	80	10			
23	MGRS	neg	3+	κ	Rhomboid	D	3	60	25			
24	MGRS	neg	2+	κ	Rhomboid	D	2	50	25			
25	SMM	neg	neg	κ*	Rhomboid	D	1	15	10			
26^	MM	neg	3+	κ	Rhomboid	D	1	10	5		VEC,	CSH
27	MGRS	neg	2+	κ	Rhomboid	P	1	10	10			
28	MM	3+	nd	κ	Rhomboid	D	2	30	5	Focal		
29^	MGRS	neg	2+	κ	Rhomboid; fibrils	D	2	40	35			
30	MGRS	Neg	3+	κ	Rhomboid	D	2	40	20			
31	MGRS	1+	3+	κ	Rhomboid	D	2	30	10		VEC	
32	MGRS	neg	3+	κ	Rhomboid	D	0	0	0			
33^	MGRS	neg	1-2+	κ	Rhomboid	D	2	30	10			
34	MGRS	neg	3+	κ	Rhomboid	D	3	65	50	Focal		
35^	MM	3+	nd	κ	Ovoid, rhomboid	P	2	30	30	Focal		
36	MM	nd	3+	κ	Rhomboid	D	1	20	20	Focal		
37	MGRS	neg	2+	κ	Rhomboid	D	1	10	5	Focal		
38^	MGRS	neg	3+	κ	Rhomboid	D	1	15	30	Focal		
39	MM	neg	1+ (IP)	κ	Rhomboid	D	1	10	10	Focal		
40	NHL	3+	nd	κ	Rhomboid	D	1	15	5	Focal		
	Non-crystalline LCPT											
41	MM	nd	2+	κ	Droplets	A	1	15	15			
42	MM	1+	3+	κ	Vacuolar	D	0	10	0	Focal		
43	MM	1+	nd	λ	Vacuolar	D	2	30	5			
44	SMM	2-3+	nd	κ	Droplets	A	2	40	5			
45^	MM	1+	nd	λ	Droplets	A	1	15	5			
46	MM	2+	2+	κ	Droplets	A	0	0	0			

ATI, acute tubular injury: A, absent; D, diffuse; P, patchy. Fibrosis score: 0 = absent, 1 =mild, 2 =moderate, 3 =severe

IF, immunofluorescence on frozen; IF-P, immunofluorescence after pronase digestion; IP, immunoperoxidase; K/L, kappa or lambda light chain

EM, electron microscopy inclusions

VEC, visceral epithelial cell; PEC, parietal epithelial cell; CSH, crystal storing histiocytes

ND, not done

^ second opinion case; *, monoclonal kappa light chain in urine

SUPPLEMENTAL TABLE 1: CLINICAL FEATURES

	Diagnosis	Age (years	HTN	DM	sCr mg/dL	eGFR	Proteinuria g/day	Serum LC	Urine LC	Serum FLC	Fanconi syndrome
Case #	**Crystalline LCPT**										
1	SMM	47	y	n	2	39	3.3	Neg	κ	216	G, P, U, A, AA
2	SMM	57	y	n	2.5	21	2.5	κ	κ		G, U, A
3	MM	47	n	n	1.1	60	1.92	IgG κ	unknown		No
4	MM	59	n	n	1.6	46	1.412	IgG κ + IgG	κ and λ		No
5	MGRS	76	y	n	3.3	17	2	IgG κ	IgG κ		G
6	MM	39	n	n	2.3	34	1	IgG κ	unknown	1700	G
7^	MGRS	43	n	n	1.8	45	7	IgG κ	unknown		G, AA, A
8	MGRS	68	Y	Y	1.9	35	6.7	IgA κ + IgG	unknown		No
9	SMM	51	Y	n	1	65	1.49	Neg	κ		G, Bone, A, P
10	SMM	59	y	n	1.6	46	0.7	IgG κ	κ		No
11	SMM	60	y	n	1.8	40	1.86	Neg	κ		No
12^	MM	42	n	n	0.7	92	2	κ	unknown		No
13	MGRS	58	n	n	1.5	51	3.5	κ + λ	κ + λ		No
14	MGRS	49	n	n	1.4	59	7.25	IgG κ	IgG κ + κ		No
15	NHL	55	n	n	3.7	13	1.5	Neg	κ	0.9	G
16	MGRS	81	Y	n	4.4	12	0.75	IgG κ	IgG κ		No
17	MGRS	75	Y	n	2.5	24	2.9	IgA κ; IgG	unknown	47.6	No
18	MM	75	n	n	2.5	24	3	κ (1.6g)	κ (0.624g)		No
19	CLL	60	Y	n	2	35	2.8	Neg	κ		G, P, U
20	MGRS after 36 r	72	n	n	1.5	35	4	Neg	Neg		No
21	MGRS	85	n	n	6	6	4	Neg	κ		No
22	MGRS	52	n	n	4.4	14	1	Neg	κ		G
23	MGRS	47	n	n	2.2	34	2.6	IgG κ	IgG κ	8.2	G, A, Bone
24	MGRS	65	n	n	2.7	24	2	κ	κ		No
25	SMM	61	Y	n	1.73	48	2.8	Neg	κ		G, P, U
26^	MM	42	n	n	1.1	62	1	IgG κ (1.6g	IgG κ + κ	350	No
27	MGRS	51	Y	n	1.5	53	2.3	Neg	κ		No
28	MM	56	Y	Y	2.86	24	0.123	IgG κ + κ	κ		No
29^	MGRS	44	n	n	3.3	22	2.39	IgG κ	κ		G, A
30	MGRS	81	n	n	2.7	16	5.5	IgG κ	unknown		No
31	MGRS	81	Y	n	2.5	18	2.9	κ	κ	18.5	G
32	MGRS	53	n	n	2	37	0.9	κ	unknown		G
33^	MGRS	71	n	n	1.5	46	3.3	Neg	κ (0.825g)	33.7	G, P, A
34	MGRS	74	Y	n	2.9	15	1.76	IgG κ	unknown		No
35^	MM	82	Y	n	4.9	8	3.5	unknown	unknown		Bone
36	MM	77	Y	n	2.1	29	3.5	IgG κ	κ		U
37	MGRS	58	Y	n	1.3	60	1.28	κ	κ		No
38^	MGRS	87	n	n	4	13	0	Neg	κ		No
39	MM	45	n	n	3.3	21	16	κ	κ	25	No
40	NHL	70	n	n	1.1	51	2.53	IgA κ + κ	IgA κ + κ		No
	Non-crystalline LCPT										
41	MM	87	Y	n	0.6	95	7	IgA κ	κ		No
42	MM	61	Y	n	1.29	45	4.3	IgG κ	unknown		No
43	MM	67	Y	n	9	5	10	IgG λ	Neg		No
44	SMM	87	Y	n	2.3	25	0.15	IgG κ	unknown	24	unknown
45^	MM	70	Y	n	0.7	88	7.4 (1+)	IgG λ + λ	unknown	<0.01	No
46	MM	75	n	n	0.6	97	4.1	κ	κ		No

HTN, hypertension; DM; diabetes mellitus

K, kappa; L, lambda; LC, light chains; FLC, serum free light chain ratio (kappa/lambda); LCPT, light chain proximal tubulopathy

CLL, chronic lymphocytic leukemia; MGRS, monoclonal gammopathy of renal significance;

MM, multiple myeloma; NHL, non-Hodgkin lymphoma; SMM, smoldering myeloma

eGFR, estimated glomerular filtration rate in cc/min/1.73 m2

Fanconi, Fanconi syndrome; Bone, bone pain; G, glycosuria; AA, aminoaciduria; A, metabolic acidosis; P, hypophosphatemia; U, hypouricacidemia

Proteinuria, (dipstick)

^ second opinion case

SUPPLEMENTAL TABLE 3: FOLLOW-UP

	Diagnosis	Treatment		Outcomes										
Case #		SCT	Chemo	Follow-up (months)	Last Cr	Δ SCR	Last eGFR	Last Uvp	Last serum	Last Urine M	Last FLC	Hematologic outcome	Renal outcome	Died (mos)
Crystalline LCPT														
1	SMM	no	D;T;B,D	133	2.14	0.14	33	1.68	Neg	κ	95.7	SD	CKD, FS	
2	SMM	no	None	22	1.7	-0.8	38	1+	κ	κ		SD	CKD	48
3	MM	no	None	141	1.47	0.37	38	1.4	Neg	κ	16.8	SD (MM at 71 mos)	CKD	
4	MM	Yes	L,D;CDEP	132	1.58	-0.02	45	1.4	IgG λ	unk	5.6	SD (MM at 54 mos)	CKD	
6	MM	Yes	B,T,D;P,DR;P,C,ET;B;L,D;Pom	107	1.55	-0.75	50	0.84	IgG κ	κ	316	SD	CKD	
8	MGRS	no	None	70	10	9.1	HD		IgA κ	κ		SD	ESRD	
9	SMM	Yes	D;CDEP;L+D	109	1.35	0.35	41	1.7	Neg	Neg	0.69	CR	CKD, proteinuria, FS	
10	SMM	no	None	98	1.44	-0.16	50	1.87	unk	κ 1.17 g/day	125	SD	CKD, proteinuria	
11	SMM	no	None	95	2.22	0.42	30	1.96	unk	κ 0.9 g/day	118	SD	CKD	
12^	MM	Yes	B,T,L	96	0.5	-0.2	135	neg	κ	unk		PR	NI	
15	NHL	no	CHOP, RTX	76	1	-2.7	58	neg	Neg	Neg		CR	CKD	
16	MGRS	no	None	18	HD	NA	HD		IgG κ	IgG κ		SD	ESRD	18
18	MM	no	L,P	28	2.2	-0.3	28	0.624	Neg	κ		SD	CKD	30
19	CLL	no	D,C,F	7	1.27	-0.63	61	0.7				SD	CKD	31
20	MGRS afte	no	B,D	39	1.6	0.1	32		Neg	Neg	23	CR	CKD	
21	MGRS	no	D	19	2	-4	24	1.5	Neg	κ		SD	CKD, proteinuria	19
22	MGRS	Yes	M	57	2.84	-1.56	24	0.3	Neg	κ 0.91 g/day		SD	CKD	
23	MGRS	no	B,D	39	3.1	0.9	22	2.6	1.1 g	unk	15.8	SD	CKD, proteinuria, FS	
24	MGRS	no	B	36	5	2.3	11					SD	CKD	
25	SMM	no	none	27	1.8	0.07	47	2.6	Neg	κ	20	SD	CKD, FS	
26^	MM	Yes	B,D; L	15	0.9	-0.2	69	0.72	IgG κ	κ 0.72 g/day	21	SD	NI	
27	MGRS	Yes	L,B,D;M	14	1.55	0.05	48	0.8	Neg	κ 0.049 g/day	1.16	VGPR	CKD	
28	MM	Yes	V,C,D;M;L	15	1.59	-1.27	45	0.1	unk	unk		PR	CKD	
31	MGRS	no	T;B	69	3.42	1.92	18	0.9	IgG λ/IgG κ	neg	2.3	SD	CKD	
33^	MGRS	no	C,B,D	5	2.39	0.89	27	1.82	Neg	κ	47.6	SD	CKD, proteinuria	
35^	MM	no	T,D; B,D,M,Pr	9	2.2	0.1	29	3	IgG κ	unk	481	SD	CKD, proteinuria	13
36	MM	Yes	L,D	58	1.3	0	57	0.43	Neg	Neg		CR	CKD, proteinuria	
37	MGRS	no	None	1	unk	unk	unk	unk	Neg	κ		SD	unk	1
38^	MGRS	Yes	T	49	1.09	-2.21	73	0.08	Neg	κ	4.5	PR	NI	
39	MM	no	RTX	26	1.4	0.3	37	0.3	Neg	Neg		CR	CKD	
Non-crystalline LCPT														
41	MM	no	T, Z	14	1.6	1	28	0.03	κ	unk		SD	CKD	14
42	MM	no	"Chemo"	5	1.1	-0.18	54	1.35	IgG κ	κ		SD	CKD, proteinuria	
43	MM	Yes	"Chemo"	24	HD	NA	HD		Neg	Neg		PR	ESRD	24
44	SMM	no	B	17	2.4	0.1	26	0.66	IgG κ	unk	20	SD	CKD	
45^	MM	no	L,B,D	15	0.8	0.1	75	Neg	Neg	Neg	1.02	CR	NI	
46	MM	no	no	10	0.6	0	97	2+	κ	κ		SD	NI, proteinuria	

CR, complete remision; VGFR, very good partial remission; PR, partial remisssion; SD, stable disease

HD, hemodialysis; ESRD, end-stage renal disease; CKD, chronic kidney disease; NI, normal kidney function

B, bortezimib; C, cyclophosphamide; CDEP, cyclophosphamide + dexamethasone + etoposide + cisplatin; "Chemo", unspecified chemotherapy

CHOP: cyclophosphamide + doxorubicin + vincristine + prednisone; D, dexamethasone; DR, doxorubicin; Ev, everolimus; F, fludarabine; L, lenalidomide

M, melphalan; MGRS, monoclonal gammopathy of renal significance; MM, multiple myeloma; NA, not applicable

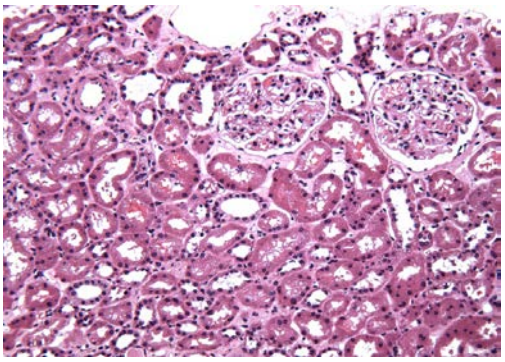
P, cisplatin; Pom, pomalidomide, Pr, prednisone; RTX, rituximab; SMM, smoldering multiple myeloma; T, thalidomide; unk, unknown; Z, zoledronate

^, second opinion case

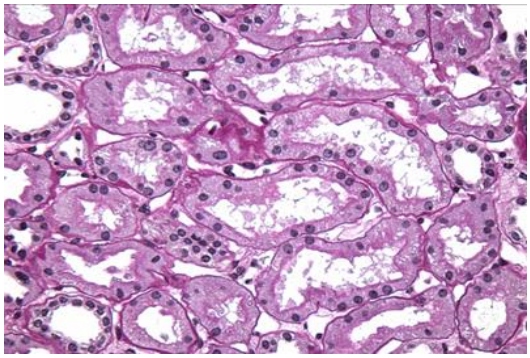
Univariate and Multivariable Correlates of intial and final eGFR												
All LCPT cases												
	Univariate				**Multivariable**							
		r	p-value		r=0.582, P=0.001	Beta	p-value					
initial	age	-0.323	**0.029**		age	-0.119	0.39					
eGFR	serum albumin	0.309	0.056									
vs	IFTA	-0.576	**<0.001**		IFTA	-0.546	**<0.001**					
	% Fibrosis	-0.516	**<0.001**									
	% Inflammation	-0.459	**0.001**									
					r = 0.815							
final	age	-0.473	**0.005**		age	-0.247	0.079					
eGFR	IFTA	-0.485	**0.004**		IFTA	0.066	0.84					
vs	% Fibrosis	-0.527	**0.001**		% Fibrosis	-0.215	0.52					
	% Inflammation	-0.476	**0.004**		% Inflammation	0.029	0.86					
	final Uvprotein	-0.451	**0.016**		final Uvprotein	-0.285	0.11					
	initial eGFR	0.719	**<0.001**		initial eGFR	0.513	**0.006**					
					or							
					without initial eGFR in the model							
					r=0.718, p=0.005							
					age	-0.338	**0.038**					
					IFTA	-0.272	0.46					
					% Fibrosis	-0.148	0.71					
					% Inflammation	-0.02	0.92					
					final Uvprotein	-0.266	0.14					
Crystalline LCPT cases												
	Univariate				**Multivariable**							
		r	p-value		r=0.746, P<0.001	Beta	p-value	or	r=0.691, P	Beta	p-value	
initial	age	-0.577	**<0.001**		age	-0.342	**0.02**		age	-0.408	**0.005**	
eGFR	serum albumin	0.395	**0.021**		serum albumin	0.386	**0.038**					
vs	IFTA	-0.565	**<0.001**		IFTA	-0.115	0.75		IFTA	-0.455	**0.002**	
	% Fibrosis	-0.504	**0.001**		% Fibrosis	-0.511	0.21					
	% Inflammation	-0.516	**0.001**		% Inflammation	0.234	0.27					
					r = 0.842							
final	age	-0.473	**0.005**		age	-0.382	**0.018**					
eGFR	IFTA	-0.485	**0.004**		IFTA	0.036	0.92					
vs	% Fibrosis	-0.527	**0.001**		% Fibrosis	-0.167	0.65					
	% Inflammation	-0.476	**0.004**		% Inflammation	0.079	0.65					
	final Uvprotein	-0.451	**0.016**		final Uvprotein	-0.406	**0.042**					
	initial eGFR	0.719	**<0.001**		initial eGFR	0.33	0.072					

Supplemental Figure 5: Non-crystalline LCPT with possible physiologic light chain trafficking.

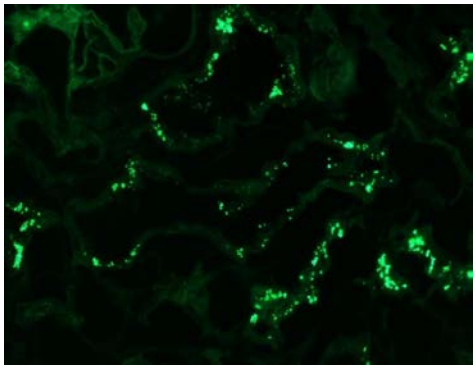
5A



5B



5C



Supplemental Figure 5 legend:

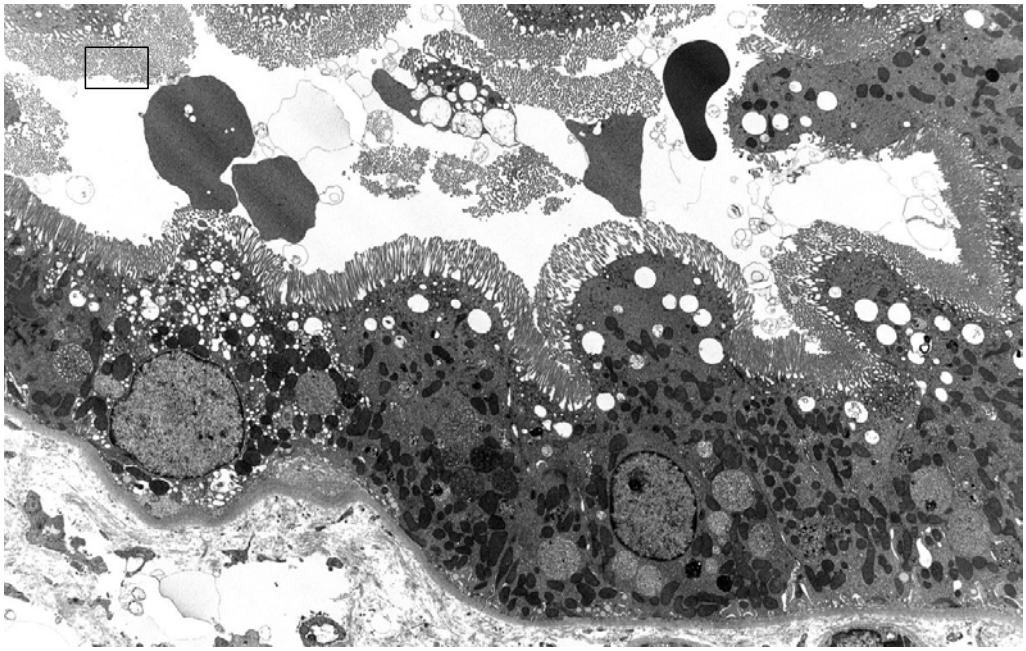
5A. Low power view shows normal appearing proximal tubules with no evidence of acute tubular injury (H&E, x200).

5B. Higher power view reveals intact PAS-positive apical brush border. No intracytoplasmic crystalline inclusions or vacuoles are seen by light microscopy (PAS, x400X).

5C. Immunofluorescence performed on frozen tissue sections reveals droplets that stain intensely for kappa light chain within the cytoplasm of proximal tubular cells (FITC-conjugated antisera to kappa light chain, x400). The staining for lambda light chain was negative (not shown).

Supplemental Figure 5: Non-crystalline LCPT with possible physiologic light chain trafficking.

5D



Supplemental Figure 5 legend (continued):

5D. Electron microscopy of a representative proximal tubule reveals increased number of endosomes (clear membrane bound vesicles) in the apical region. Microvillous brush border is intact. There are scattered rounded phagolysosomes containing non-specific amorphous material in the deeper cytoplasm; however, no crystalline inclusions are identified.