MAYO CLINIC

IKMG

INTERNATIONAL KIDNEY & MONOCLONAL GAMMOPATHY RESEARCH GROUP

FOURTH INTERNATIONAL MEETING

MAY 23/24 – 2019

MONTREAL

Update on Treatment of PGNMID

Nelson Leung, MD

Disclosures

Relevant Financial Relationships

Grant: Omeros Corporation

Advisor: Aduro, BTG, and Takeda

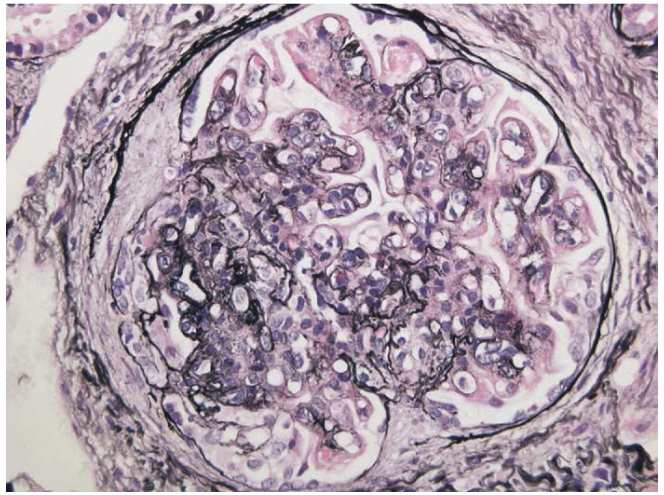
Off-Label/Investigational Uses

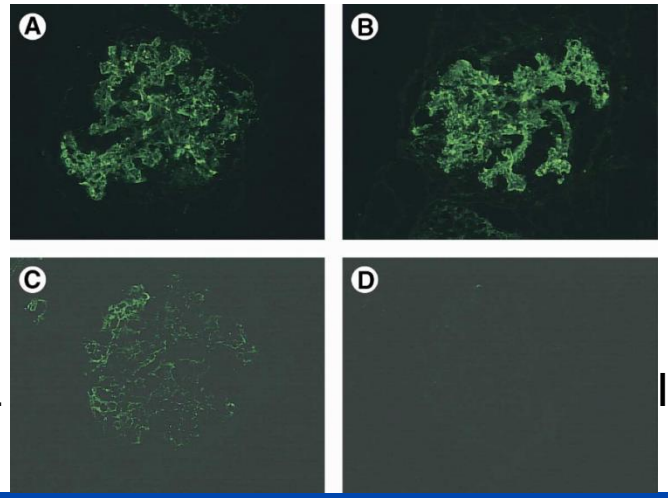
Takeda and Janssen; Bortezomib and daratumumab

Case #1

- 08/2003
  - 35 yo female presents with edema and hypertension
    - Scr was 0.8 mg/dl (70 µmol/L)
    - Proteinuria 10 g/d
- 09/2003
    - Renal biopsy was performed
    - Membranoproliferative glomerulonephritis

Membranoproliferative glomerulonephritis with IgA lambda deposits with paracrystalline substructures



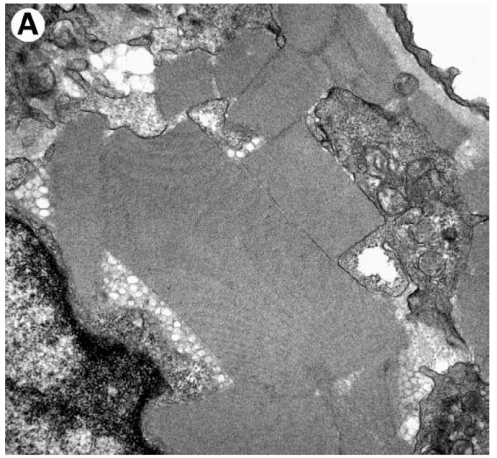


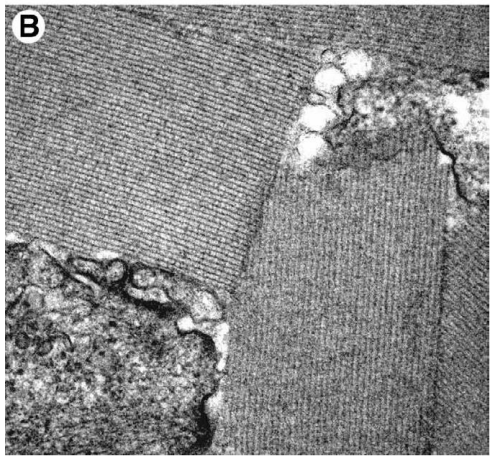
IgA

λ

IgA1

IgA2



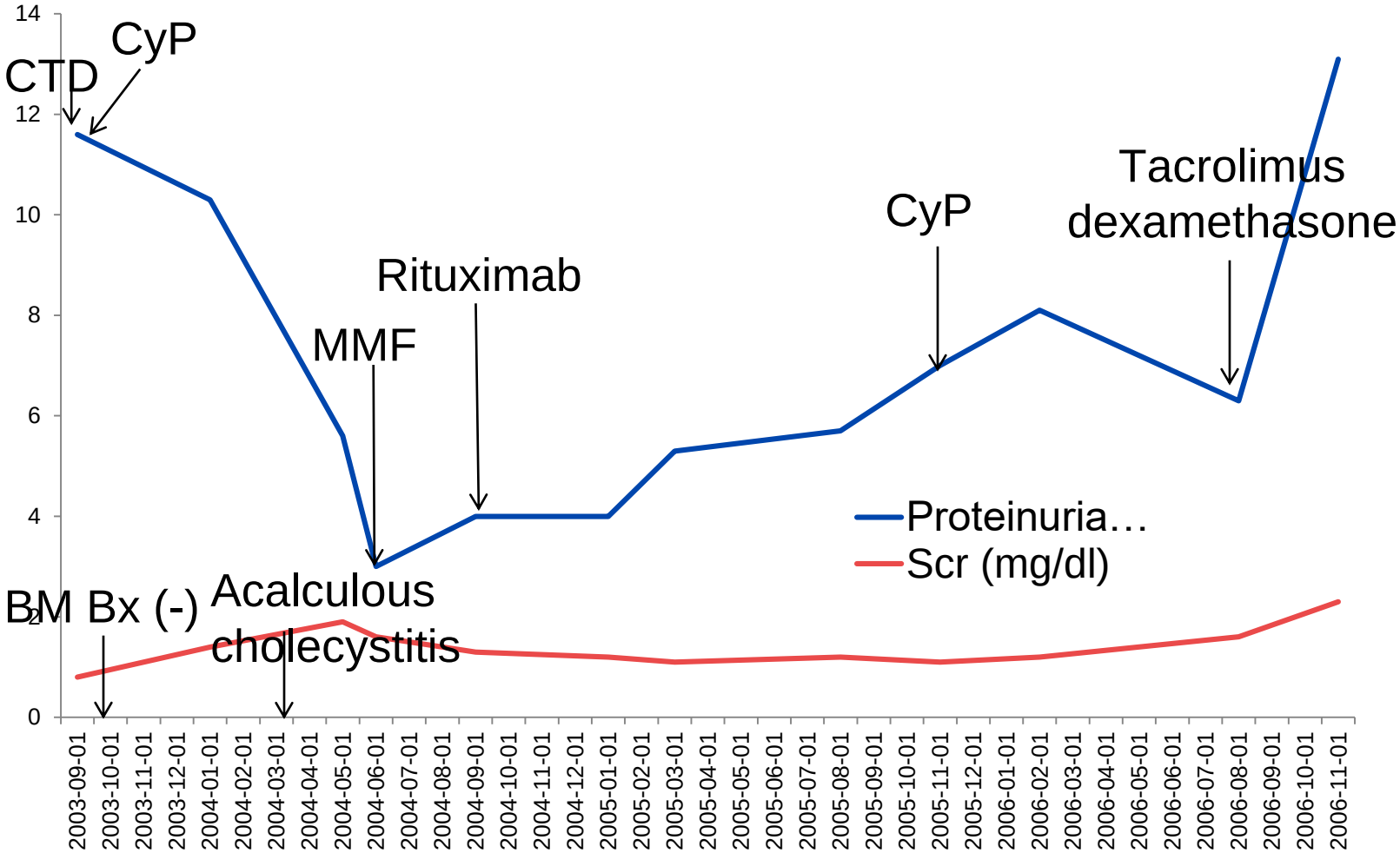


Soares et al. Am J Kidney Dis 2006

Hematologic evaluation

- SPEP – negative
- Serum/urine IFE – negative
- Bone marrow biopsy – no features of clonal proliferation

Disease course of a patient with MPGN with IgAλ



Recurrence of monoclonal IgA lambda glomerulonephritis in kidney allograft associated with multiple myeloma

- 8/2003 nephrotic syndrome
- 6/2008 ESRD
- 6/2011 Living donor kidney Tx Monoclonal IgAλ detected pretransplant
- 12/2011 Scr 1.4 mg/dl (123 µmol/L)
  - Proteinuria 1.7 g/d
  - SPEP and UPEP – IgAλ
  - Serum FLC: κ = 12.3 mg/L, λ= 8.65 mg/L, ratio = 1.43
  - Kidney biopsy – recurrent proliferative GN with IgAλ deposits
  - ***Bone marrow biopsy – 30% λ light chain restricted PC***
- 1/2012 Scr 3.3 mg/dl (290 µmol/L)

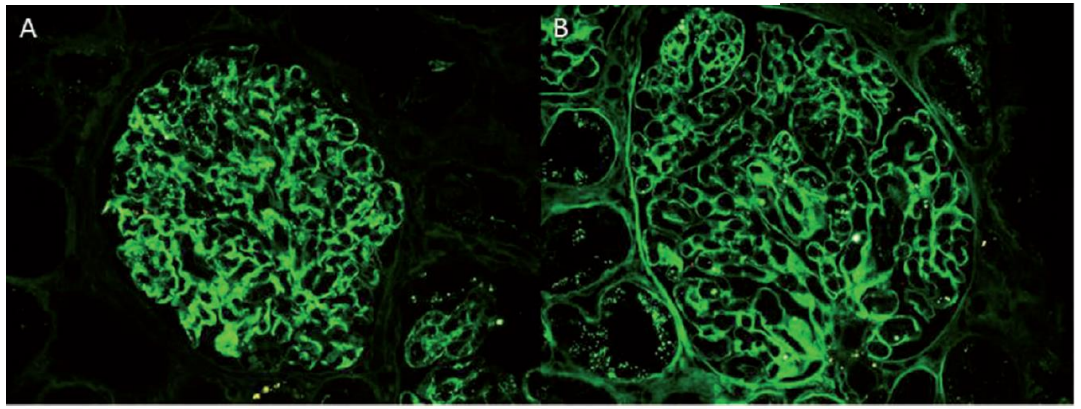
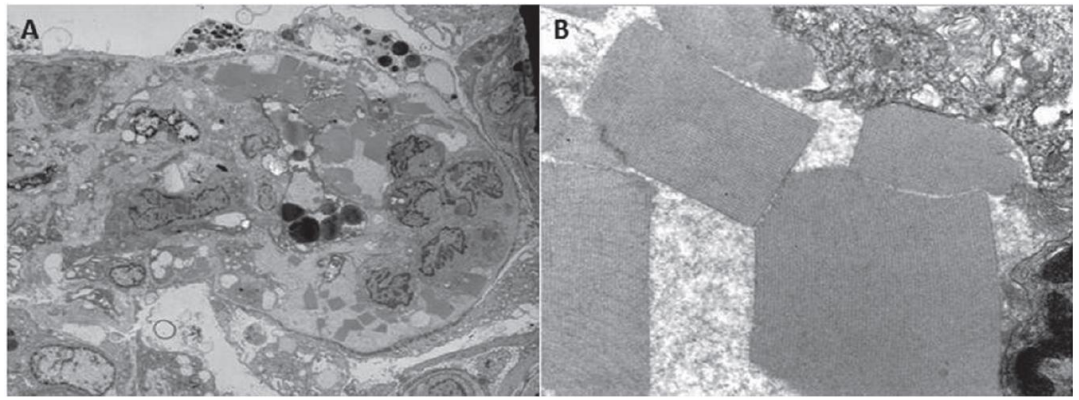


Figure 2. Immunofluorescent histology staining for IgA (A); λ (B).



Herrmann et al. Clin Nephrol 2014

Question

Why was rituximab ineffective in this patient?

A. The dose of rituximab was inadequate

B. Rituximab is ineffective in PGNMID

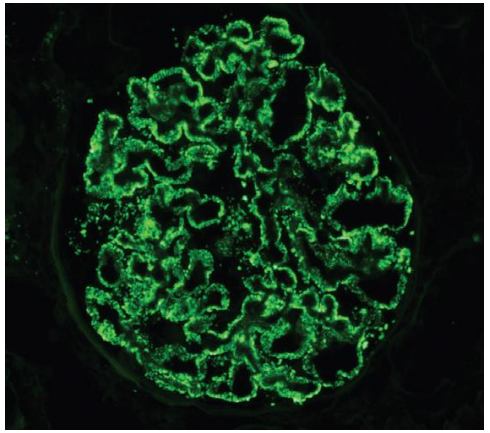
C. Rituximab is less effective after cyclophosphamide

D. All of the above

E. None of the above

Old Paradigm in the Treatment of Kidney Diseases

Histology ⇨ Disease ⇨ Treatment



⇨ Membranous nephropathy ⇨ Rituximab

A RANDOMIZED TRIAL OF METHYLPREDNISOLONE AND CHLORAMBUCIL IN IDIOPATHIC MEMBRANOUS NEPHROPATHY

CLAUDIO PONTICELLI, M.D., PIETRO ZUCCHELLI, M.D., PATRIZIA PASSERINI, M.D., LEONARDO CAGNOLI, M.D., BRUNO CESANA, M.D., CLAUDIO POZZI, M.D., SONIA PASQUALI, M.D., ENRICO IMBASCIATI, M.D., CLAUDIO GRASSI, M.D., BRUNO REDAELLI, M.D., MAURO SASDELLI, M.D., AND FRANCESCO LOCATELLI, M.D.

Membranous Nephropathy Associated With an Unusual Phenotype of Chronic Lymphocytic Leukemia

CHRISTINE A. WHITE, MD, ROBERT O. DILLMAN, MD, AND IVOR ROYSTON MD

The nephrotic syndrome is uncommon in patients with chronic lymphocytic leukemia. When present, the most frequently documented cause is membranous nephropathy, although several other glomerular lesions have also been described. This report describes a patient with chronic lymphocytic leukemia of an unusual surface marker phenotype recently suggested to be associated with an increased incidence of proteinuria. Renal biopsy specimens demonstrated membranous glomerulonephritis. Immunofluorescence staining demonstrated glomerular deposition of IgG and C3, but not the human T-lymphocyte antigen, T65, which had been found on circulating leukemia cells.

Cancer **52:2253–2255, 1983.**

Arthritis Rheum. 2001 Dec;44(12):2836-40.

Response of Wegener's granulomatosis to anti-CD20 chimeric monoclonal antibody therapy.

Specks U[1], Fervenza FC, McDonald TJ, Hogan MC.

Author information

Abstract

We report on the successful, compassionate use of the anti-CD20 chimeric monoclonal antibody rituximab in a patient with chronic, relapsing cytoplasmic antineutrophil cytoplasmic antibody (cANCA)-associated Wegener's granulomatosis (WG). The patient initially responded to treatment with glucocorticoids and cyclophosphamide. However, bone marrow toxicity during cyclophosphamide treatment of a relapse precluded its further use. Azathioprine and mycophenolate mofetil treatment had failed to maintain remission of the WG, and methotrexate was contraindicated. Because the patient's 5-year course was characterized by close correlation of cANCA levels with disease activity, selective elimination of cANCA was deemed a treatment option for his latest relapse. He was given 4 infusions of 375 mg/M2 of rituximab and high-dose glucocorticoids. Complete remission was associated with the disappearance of B lymphocytes and cANCA. Glucocorticoid treatment was then discontinued. After 11 months, the cANCA recurred, and rituximab therapy was repeated, without glucocorticoids. At 8 months after the second course of rituximab (18 months after the first course), the patient's WG has remained in complete remission. Elimination of B cells by rituximab therapy may prove to be an effective and safe new treatment modality for ANCA-associated vasculitis and possibly other autoimmune diseases. This modality warrants closer examination in a carefully conducted clinical trial.

http://www.kidney-international.org

original article

Rituximab treatment of idiopathic membranous nephropathy

FC Fervenza[1], FG Cosio[1], SB Erickson[1], U Specks[2], AM Herzenberg[3], JJ Dillon[1], N Leung[1], IM Cohen[1], DN Wochos[1], E Bergstralh[4], M Hladunewich[5] and DC Cattran[5]

[1]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [2]Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota, USA; [3]Department of Pathology, University of Toronto, Ontario, Canada; [4]Division of Biostatistics, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota, USA and [5]Division of Nephrology, University of Toronto, Ontario, Canada

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 2, 2009 VOL. 361 NO. 1

M-Type Phospholipase A_2 Receptor as Target Antigen in Idiopathic Membranous Nephropathy

Laurence H. Beck, Jr., M.D., Ph.D., Ramon G.B. Bonegio, M.D., Gérard Lambeau, Ph.D., David M. Beck, B.A., David W. Powell, Ph.D., Timothy D. Cummins, M.S., Jon B. Klein, M.D., Ph.D., and David J. Salant, M.D.

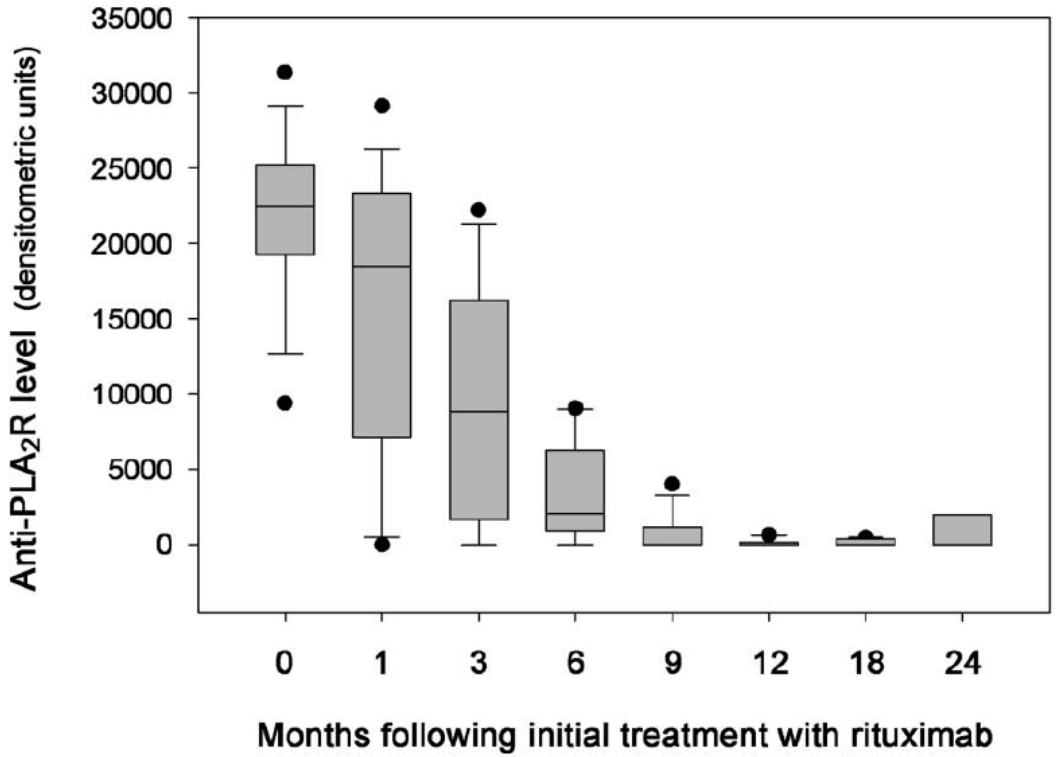
BRIEF REVIEW www.jasn.org

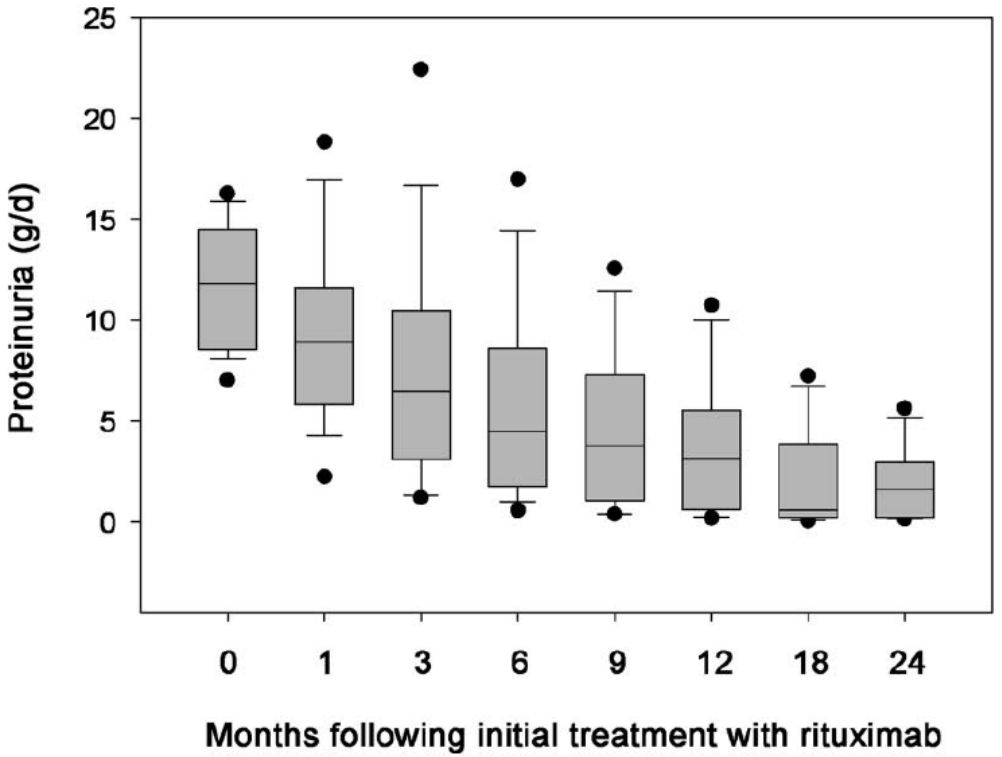
PLA2R and THSD7A: Disparate Paths to the Same Disease?

Laurence H. Beck Jr.

Renal Section, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts

Rituximab-Induced Depletion of Anti-PLA_2R Autoantibodies Predicts Response in Membranous Nephropathy





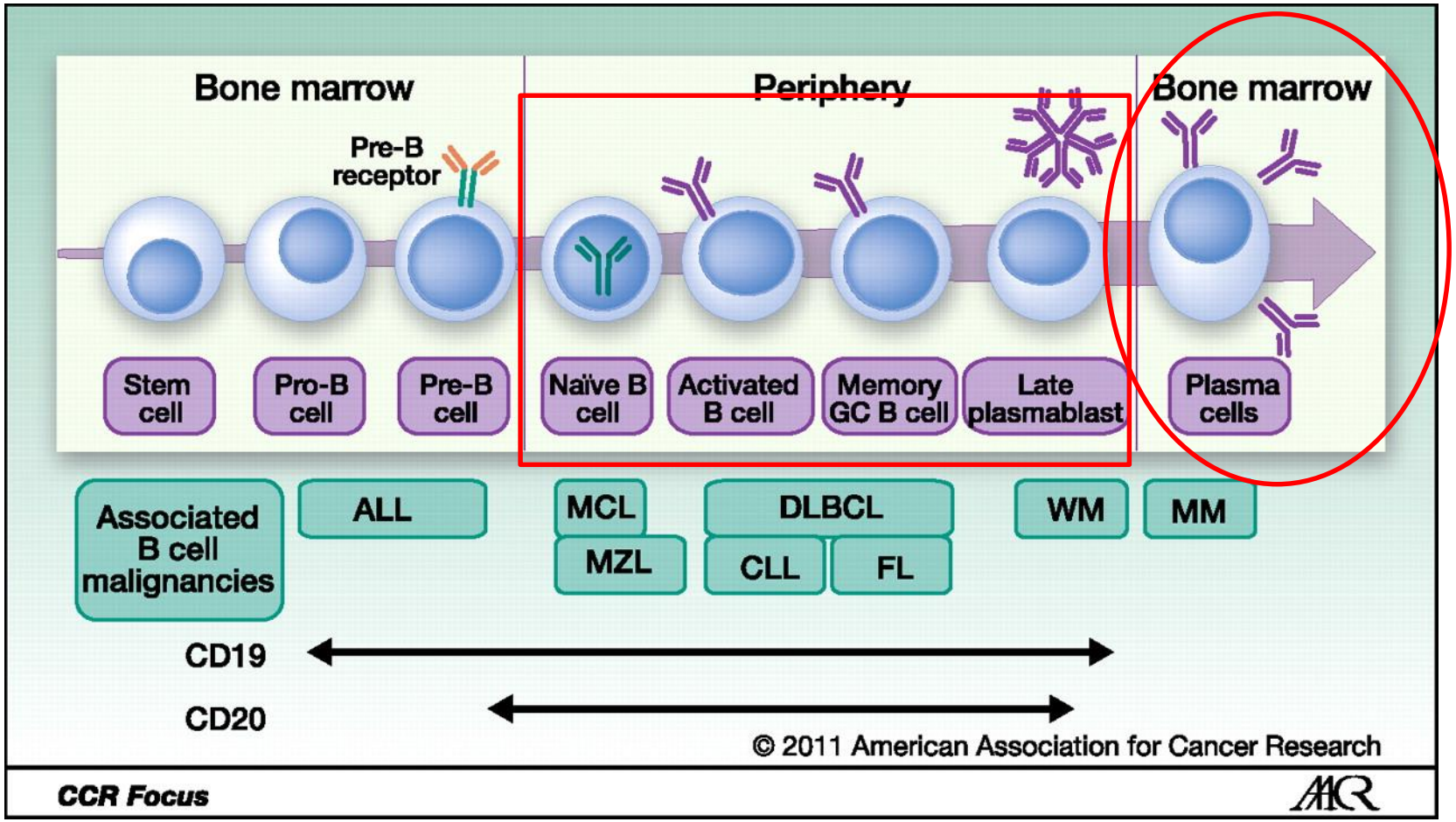
Beck et al. JASN 2011

The Relationship between Hematologic and Renal Response

Hematologic response	Renal response	Proteinuria reduction >75%	Proteinuria reduction >95%
CR	72.4%	73.7%	52.6%
VGPR	55.1%	46.9%	16.3%
PR	25%	25%	0%
NR	25%	0%	0%

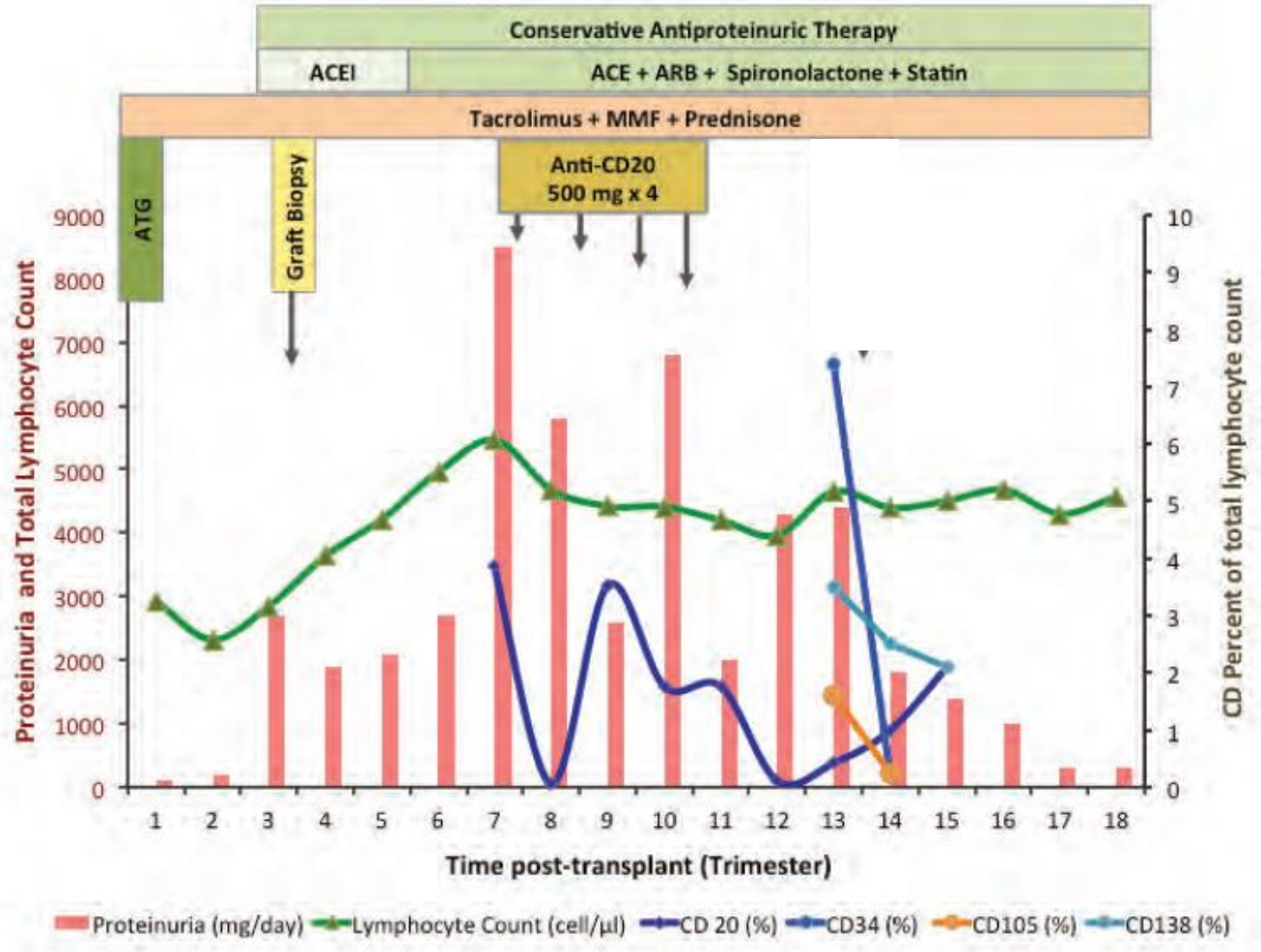
Leung et al. Haematologica 2013

Pattern of expression of CD19 and CD20 antigens during B-cell development and associated malignancies.



Veronique Blanc et al. Clin Cancer Res 2011;17:6448-6458

Bortezomib as a Novel Approach to Early Recurrent Membranous Glomerulonephritis After Kidney Transplant Refractory to Combined Conventional Rituximab Therapy



Barbari et al. Exp and Clin Transplant 2017

Clone directed therapy

A clone-directed approach may improve diagnosis and treatment of proliferative glomerulonephritis with monoclonal immunoglobulin deposits

Ramnika Gumber[1], Jordana B. Cohen[1,2], Matthew B. Palmer[3], Sidney M. Kobrin[1], Dan T. Vogl[4], Alan G. Wasserstein[1], Sunita D. Nasta[4], Melissa B. Bleicher[1], Roy D. Bloom[1], Laura Dember[1,2], Adam Cohen[4], Brendan M. Weiss[4] and Jonathan J. Hogan[1]

Treatment of B-cell disorder improves renal outcome of patients with monoclonal gammopathy–associated C3 glomerulopathy

Sophie Chauvet,[1-3] Véronique Frémeaux-Bacchi,[2,4] Florent Petitprez,[5] Alexandre Karras,[1] Laurent Daniel,[6] Stéphane Burtey,[7] Gabriel Choukroun,[8] Yahsou Delmas,[9] Dominique Guerrot,[10] Arnaud François,[11] Moglie Le Quintrec,[12] Vincent Javaugue,[13,14] David Ribes,[15] Laurence Vrigneaud,[16] Bertrand Arnulf,[17] Jean Michel Goujon,[14,18] Pierre Ronco,[19] Guy Touchard,[13,14] and Frank Bridoux[13,14]

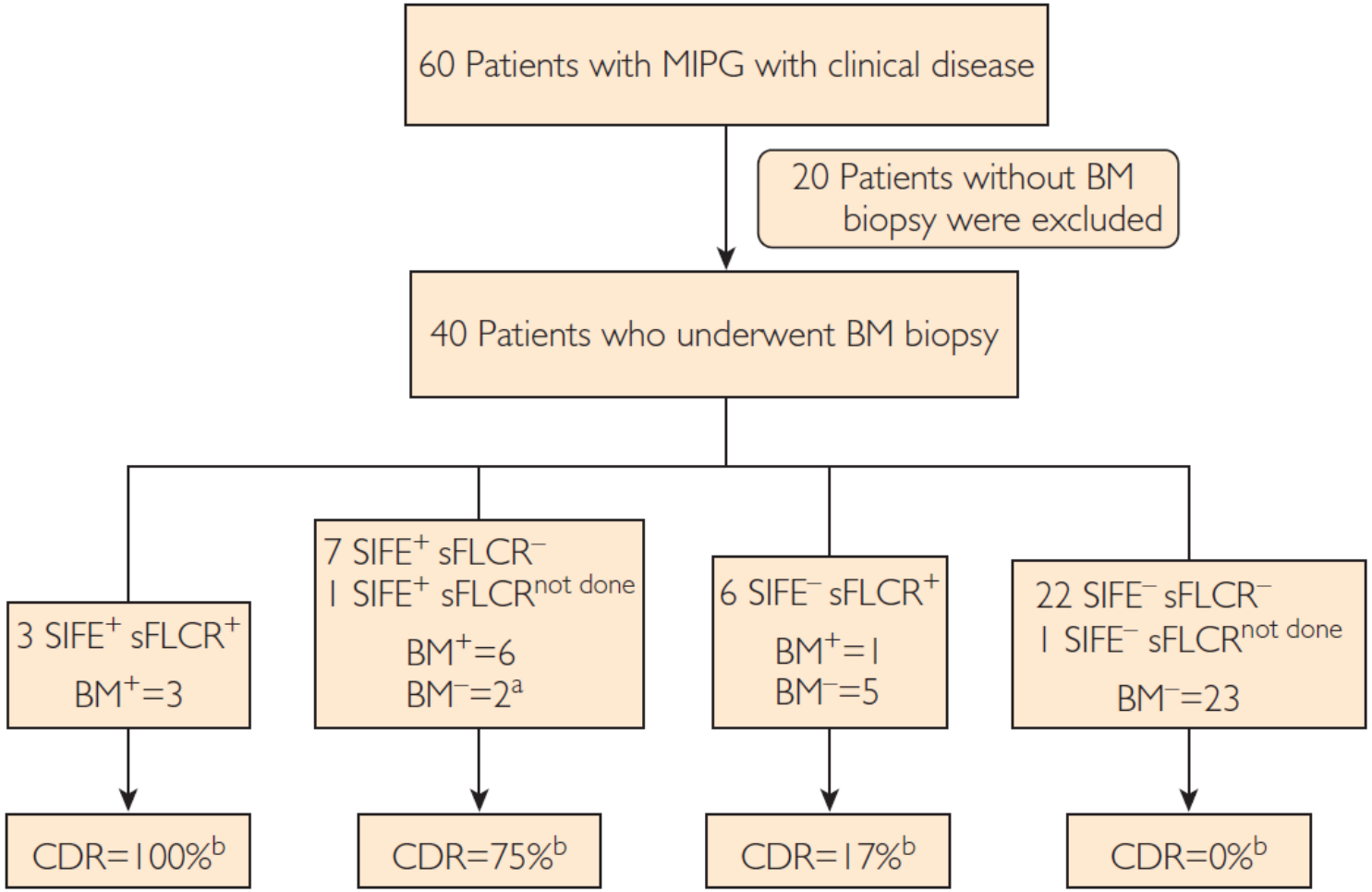
Gumber et al. Kidney Int 2018
Chauvet et al. Blood 2017

A clone-directed approach may improve diagnosis and treatment of proliferative glomerulonephritis with monoclonal immunoglobulin deposits

Ramnika Gumber[1], Jordana B. Cohen[1,2], Matthew B. Palmer[3], Sidney M. Kobrin[1], Dan T. Vogl[4], Alan G. Wasserstein[1], Sunita D. Nasta[4], Melissa B. Bleicher[1], Roy D. Bloom[1], Laura Dember[1,2], Adam Cohen[4], Brendan M. Weiss[4] and Jonathan J. Hogan[1]

	Clone	Therapy	Treatment duration	Response	Time to response (mo)	
					PR	CR
Group 1: clone-detected, clone-directed therapy						
1	Lympho-plasmacytic	RTX/CY/BOR/D	3 mo	CR	14.3	16.3
2	B cell	Chlorambucil	NA	PR	NA	–
3	B cell	RTX/PRED	6 mo	CR	1.2	3.3
4	Plasma cell	CY/BOR/D	6 mo	CR	5.1	33.3
Group 2: clone-detected, nondirected therapy						
5	Plasma cell	MMF/PRED	2.5 mo	None	–	–
6	Plasma cell	PRED	22 mo	PR	15.2	–
Group 3: no clone-detected, empirical therapy						
7	None	RTX/CY/PRED	9 mo	CR	2	8.7
8	None	RTX/CY/PRED	3.5 mo	PR	7.3	–
9	None	RTX	1 cycle of RTX 1000 mg i.v. × 2	CR	3.3	21.1
10	None	CY/PRED	2 mo	PR	5.2	–
11	None	RTX/PRED	6 mo	PR	9.2	–
12	None	RTX/CY/PRED	6 mo	None	–	–
13	None	RTX	6 mo	PR	11	–
14	None	RTX/PRED	6 mo	None	–	–
15	None	RTX/CY/BOR/D	6 mo	CR	1.1	6.5
16	None	BOR/D	6 mo	PR	3	–

Rates of Clonal Detection



Bhutani et al. Mayo Clinic Proc 2015

Clones involved in PGNMID

BM+ patient No.	BM microscopy (aspirate/biopsy)	Flow cytometry	
1	Two small- to medium-sized suspicious nodular lymphocyte aggregates (10% BM)	λ-restricted $CD20^+$ B cells	
2	An atypical lymphoid infiltrate composed of small lymphocytes involving ~30% of the BM cellularity	A monotypic κ B-cell population expressing CD20	
3	Per outside BM report, 8.3% κ-restricted plasma cells that were $CD138^+$, $CD20^+$, and $CD19^+$		
4	Per outside BM report: <5% clonal and atypical plasma cells		
5	Per outside BM report: 5% κ-restricted plasma cells in 50% cellular BM		
6	Slight increased plasma cells in quantity (5%); single interstitial cells and tiny aggregates	Monotypic λ (bright) $CD20^+$ B-cell population forming 0.8% of cells in the sample; rare polytypic plasma cells	Slight increase in $CD20^+$ B cells and $CD138^+$ plasma cells; light chain restriction could not be assessed owing to technical artifact
7	Touch imprint: BM differential within reference limits	Not performed	5%-10% CD138-staining plasma cells showing λ light chain restriction
8	No substantial abnormality	κ light chain–restricted plasma cells identified	Plasma cells number 5%, interstitial distribution ($CD138^+$)
9	Touch imprint: BM differential within reference limits	Small, abnormal plasma cell population (0.2%) with κ light chain restriction noted in a background of polyclonal plasma cells	$CD138^+$ plasma cells (5%); lack definitive light chain restriction
10	Abnormal lymphocytic infiltrates present (80% of cellularity)	λ restricted, $CD20^+$ B cells (82% of total events)	Not performed

Clone detection 17%

- Plasma cell – 50%
- $CD20^+$ - 30%
- $CD20^+CD38^+$ – 20%

Bhutani et al. Mayo Clinic Proc 2015

A clone-directed approach may improve diagnosis and treatment of proliferative glomerulonephritis with monoclonal immunoglobulin deposits

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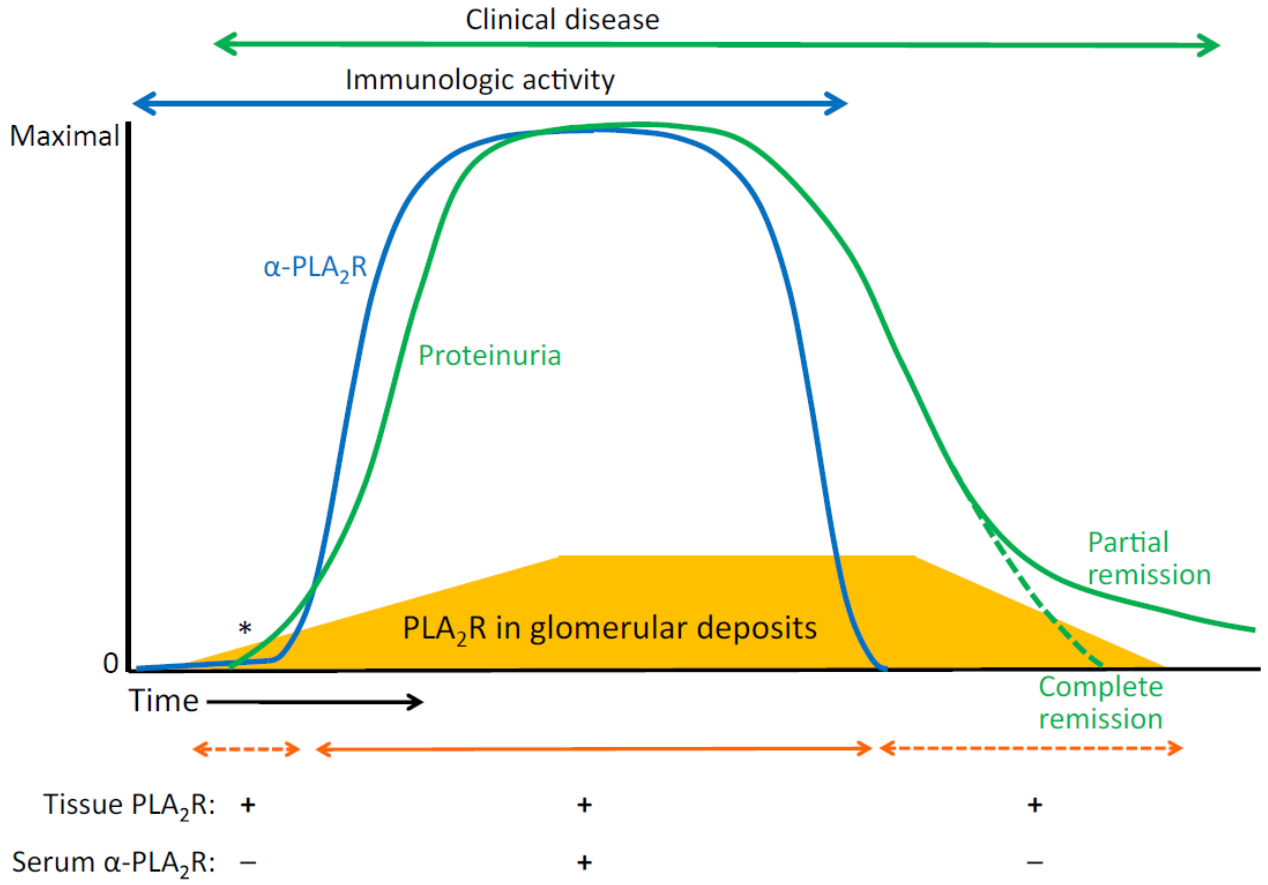
11	None	RTX/PRED	6 mo	PR	9.2	–
12	None	RTX/CY/PRED	6 mo	None	–	–
13	None	RTX	6 mo	PR	11	–
14	None	RTX/PRED	6 mo	None	–	–
15	None	RTX/CY/BOR/D	6 mo	CR	1.1	6.5
16	None	BOR/D	6 mo	PR	3	–

Challenges with treating PGNMID

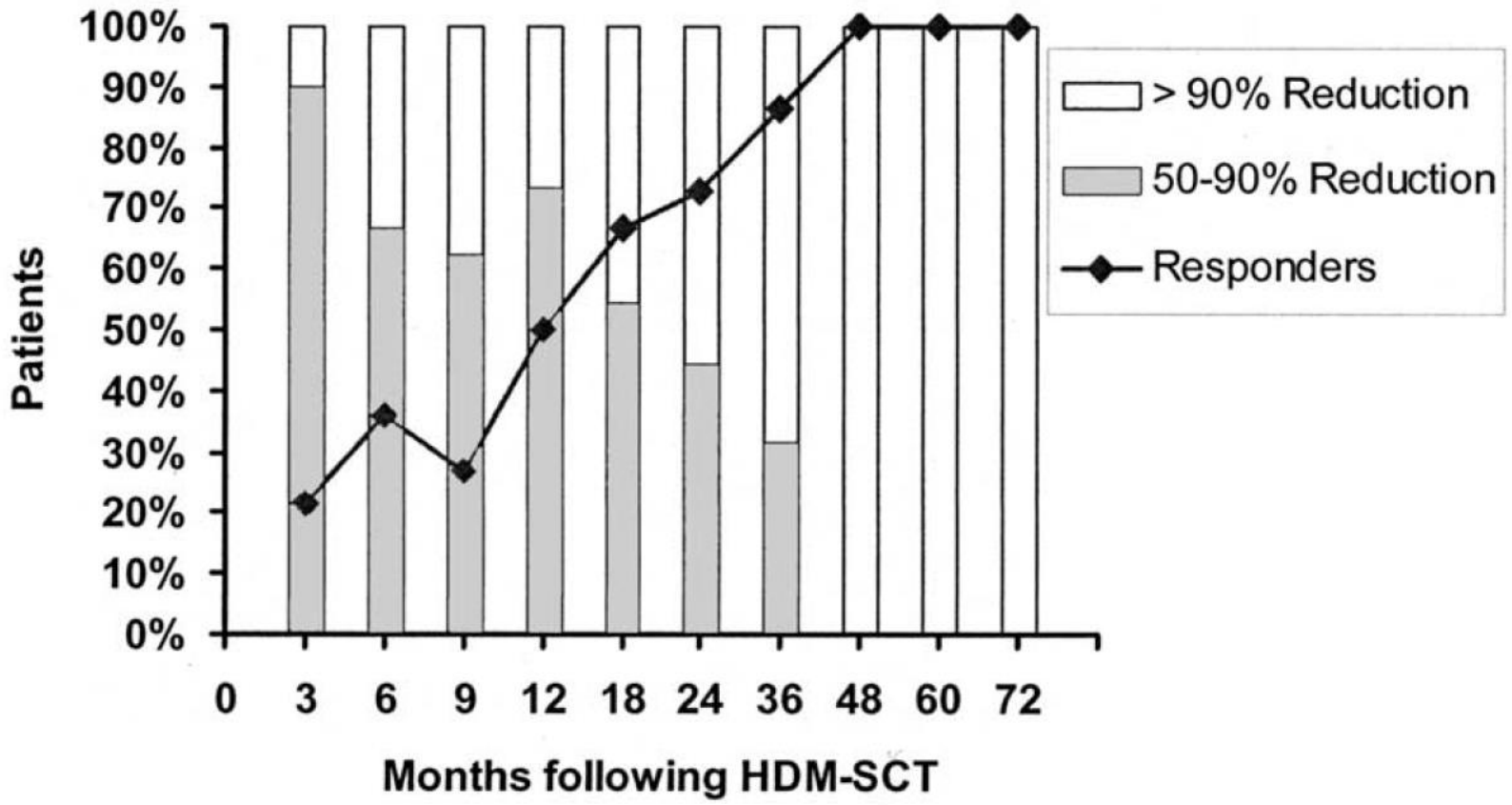
- No monoclonal protein (70-80%)
  - Hematologic response cannot be assessed
  - Need to rely on renal response

Delay Between Anti-PLA2R Titer and Disease Activity



Francis et al. AJKD 2016

Renal Response after ASCT

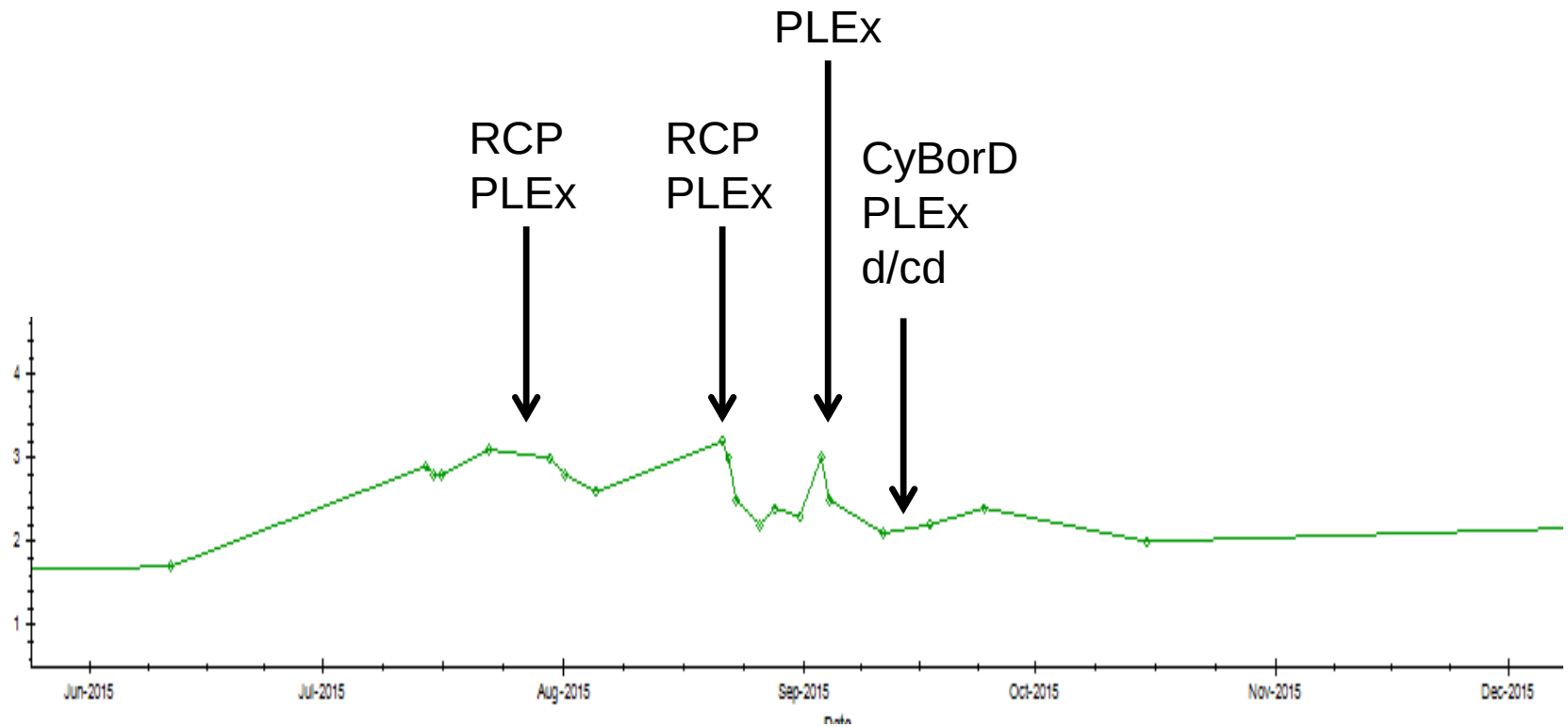


Leung et al. AJKD 2005

Challenges with treating PGNMID

- No monoclonal protein (70-80%)
  - Hematologic response cannot be assessed
  - Need to rely on renal response
- Lack of clone (>80%)
  - **Which clone to target?**
  - Lack of renal response
    - Was the wrong clone targeted?
    - Was the right clone targeted but treatment was not effective?
    - Hematologic response was achieved but there is no renal response?

Treatment course



Challenges with treating PGNMID

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  - Which clone to target?
  - **Lack of renal response**
    - **Was the wrong clone targeted?**
    - Was the right clone targeted but treatment was not effective?
    - Hematologic response was achieved but there is no renal response?

Case #2

- 26 yo female

  PMH

  2003 - AML in complete remission

  2012 - nephrotic syndrome – C3 GN after URI

  - Rx with prednisone/ ACTH/ Rituximab x 3 doses → ESRD

  2016 - February – LRD kidney transplant

  - June – PGNMID in the kidney allograft

  - Rituximab/ cyclophosphamide/ PLEx

  - December – ESRD

  2017 – November – Rituximab x 2

  2018 – March 01 – second LRD kidney transplant

  - April 26 proteinuria detected. Allograft biopsy PGNMID

NEPHROLOGY

Nephrology **23,** Suppl. 2 (2018) 76–80

Brief Communication

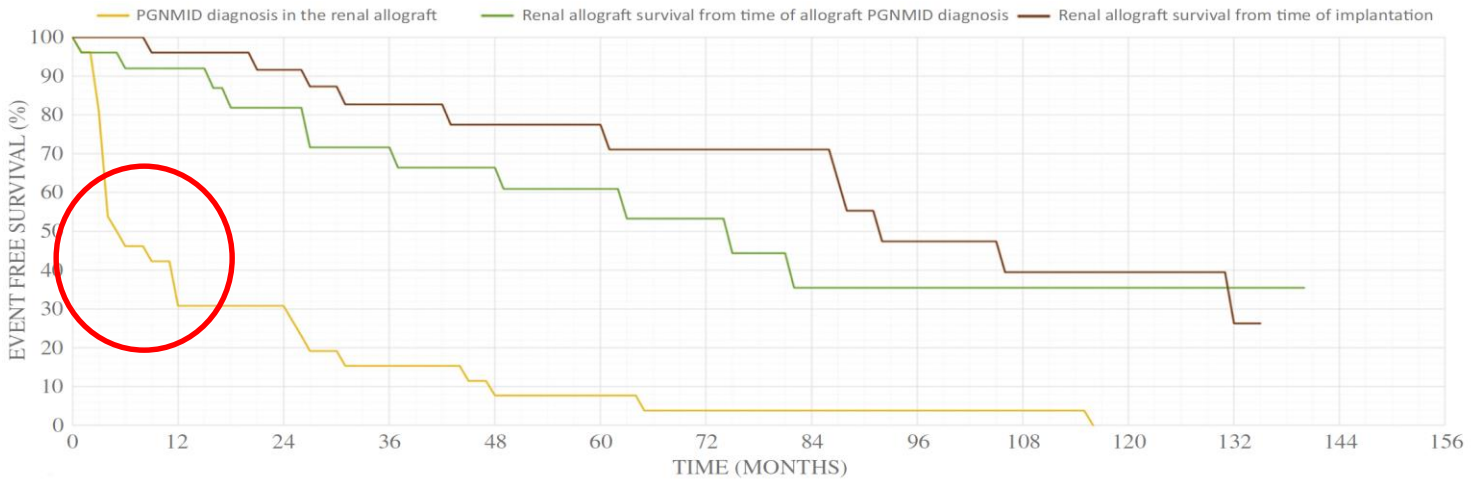
A case of recurrent proliferative glomerulonephritis with monoclonal IgG deposits or *de novo* C3 glomerulonephritis after kidney transplantation

TOMOMI TAMURA,[1]* KOHEI UNAGAMI,[1]* MASAYOSHI OKUMI,[2] YOICHI KAKUTA,[2] SHIGERU HORITA,[3] HIDEKI ISHIDA,[2] JUNKI KOIKE,[4] KAZUHO HONDA,[5] KAZUNARI TANABE[2] and KOSAKU NITTA[1]

[1]Department of Nephrology, [2]Department of Urology, [3]Division of Pathology of Kidney Center, Tokyo Women's Medical University, [5]Department of Anatomy, School of Medicine, Showa University, Tokyo, and [4]Department of Pathology, Kawasaki Municipal Tama Hospital, Kawasaki, Japan

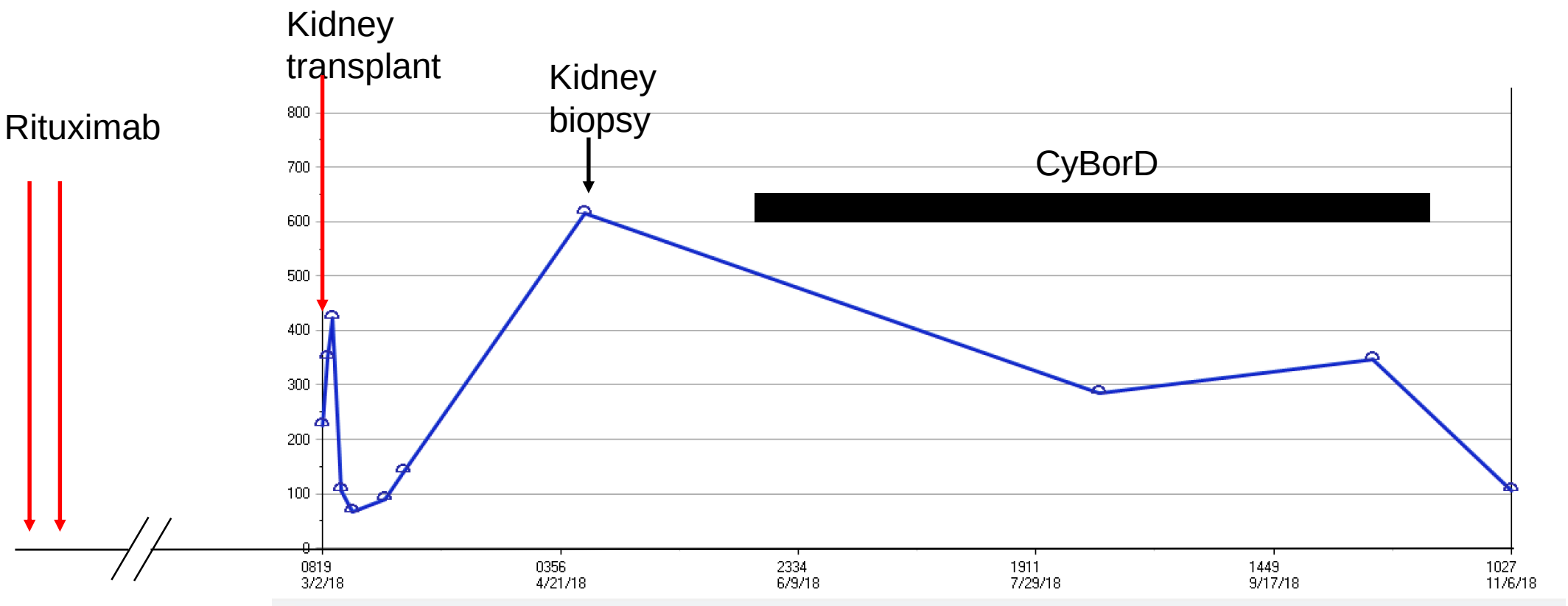
Renal allograft survival of allografts with PGNMID

Recurrence rate = 89%



2 patients who lost their graft had a second kidney transplant and PGNMID recurred within 4 months of the second transplant

Proteinuria



Case #2 cont

2018 – Hematologic evaluation

serum/urine immunofixation negative

bone marrow biopsy/ peripheral blood flow cytometry - negative

– May – CyBorD x 3.5 cycles

- November – abdominal pain and acute kidney injury → allograft pyelonephritis

Challenges with treating PGNMID

- No monoclonal protein (70-80%)
  - Hematologic response cannot be assessed
  - Need to rely on renal response
- Lack of clone (>80%)
  - Which clone to target?
  - Lack of renal response
    - Was the wrong clone targeted?
    - **Was the right clone targeted but treatment was not effective?**
    - Hematologic response was achieved but there is no renal response?

Patient #1

- 62 yo male was found to have progressive kidney disease.
  - Creatinine increased from 1.1 mg/dl to 2.5 in 26 months
  - Proteinuria = 10 g/d
- Renal biopsy (09/07)
  - Type I MPGN
  - Diffuse granular 1+ staining of glomeruli for IgM, and no staining of glomeruli for IgA, kappa light chain, fibrinogen, or albumin
  - Immunofluorescence staining is performed on an outside frozen block for IgG subclasses. The glomeruli show 3+ granular mesangial and capillary loop staining for IgG1 and negative staining for IgG2, IgG3, and IgG4. The staining pattern is compatible with a membranoproliferative glomerulonephritis with monoclonal IgG1 lambda deposition.

Hematologic evaluation

- SPEP – negative
- Serum IFE – IgG lambda
- FLC
  - Kappa – 5.12
  - Lambda – 3.68
  - Ratio – 1.39
- Bone marrow – 10% involvement of chronic lymphocytic leukemia
- Rituximab 1 cycle was given
  - Serum IFE became negative

Treatment course

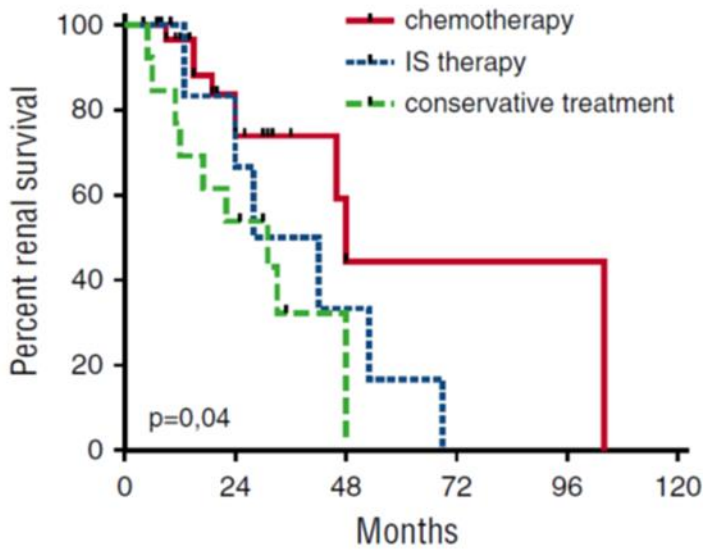
- Minimal response to rituximab
- Progressed to ESRD 4 months after rituximab
- 4/23/13
  - Serum IFE remains negative
  - Underwent DD kidney transplant
  - Time 0 biopsy severe acute tubular injury
- 8/12/13
  - Scr = 1.3 mg/dl
  - Proteinuria 61 mg/d
  - FLC
    - Kappa – 1.27
    - Lambda – 1.09
    - Ratio – 1.17

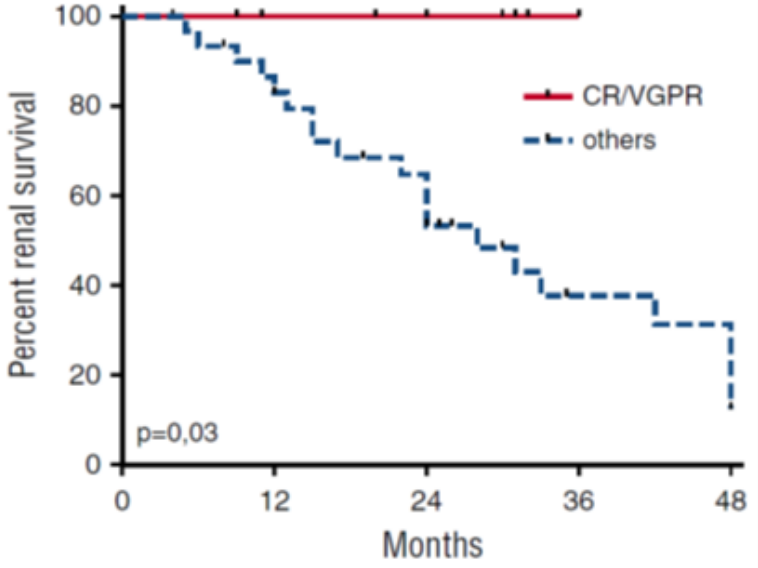
Posttransplant course continues

- Renal allograft biopsy
  - 1) Recurrent proliferative glomerulonephritis with monoclonal IgG deposits
  - 2) Transplant arteriopathy. (Banff: mm0, g0, t0, i0, v0, cg0, ct0, ci0, cv2, cvi1, ahi1, ptc0, C4d0, ti0).
- Flow cytometry
  - A small lambda light chain restricted B-cell clone, consistent with CLL
- Treatment (01/14)
  - Rituximab
  - Cyclophosphamide
  - Prednisone
- 04/16
  - Scr = 1.4 mg/dl
  - Proteinuria = 64 mg/d

Treatment of B-cell disorder improves renal outcome of patients with monoclonal gammopathy–associated C3 glomerulopathy

Sophie Chauvet,[1-3] Véronique Frémeaux-Bacchi,[2,4] Florent Petitprez,[5] Alexandre Karras,[1] Laurent Daniel,[6] Stéphane Burtey,[7] Gabriel Choukroun,[8] Yahsou Delmas,[9] Dominique Guerrot,[10] Arnaud François,[11] Moglie Le Quintrec,[12] Vincent Javaugue,[13,14] David Ribes,[15] Laurence Vrigneaud,[16] Bertrand Arnulf,[17] Jean Michel Goujon,[14,18] Pierre Ronco,[19] Guy Touchard,[13,14] and Frank Bridoux[13,14]

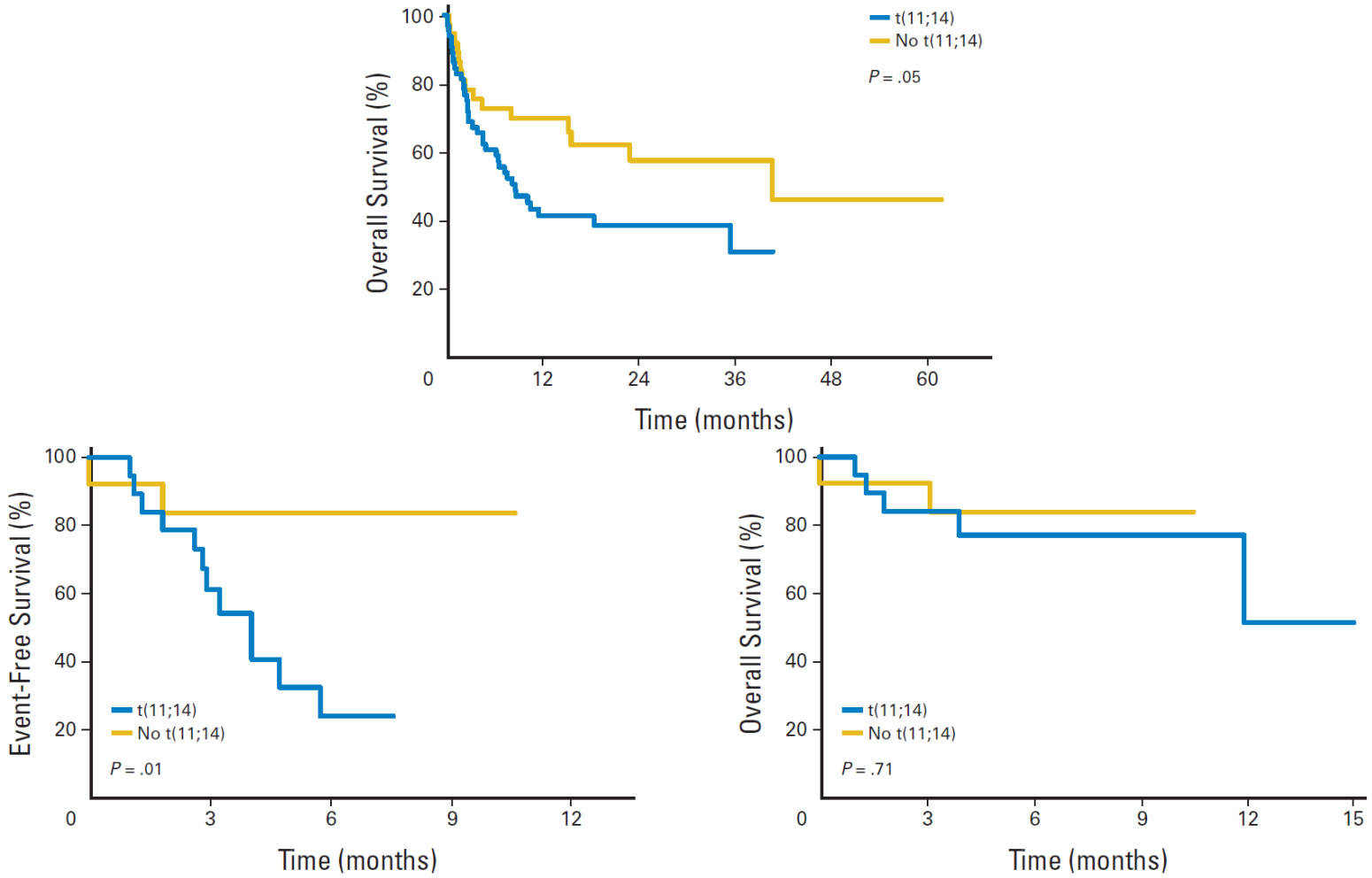




Chauvet et al. Blood 2017

Translocation t(11;14) Is Associated With Adverse Outcome in Patients With Newly Diagnosed AL Amyloidosis When Treated With Bortezomib-Based Regimens

Tilmann Bochtler, Ute Hegenbart, Christina Kunz, Martin Granzow, Axel Benner, Anja Seckinger, Christoph Kimmich, Hartmut Goldschmidt, Anthony D. Ho, Dirk Hose, Anna Jauch, and Stefan O. Schönland

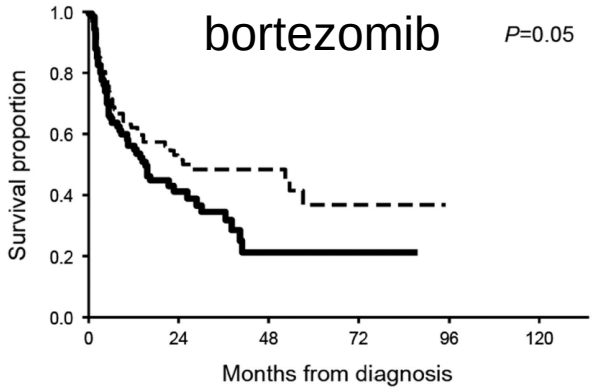


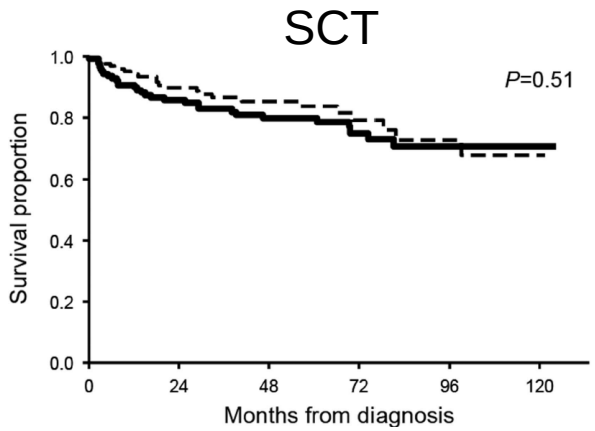
Bochtler et al. J Clin Oncol 2015

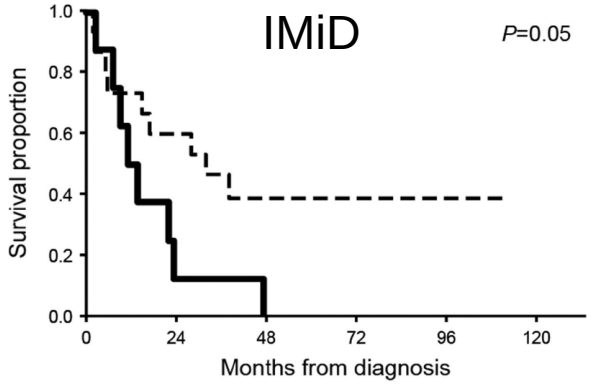
ORIGINAL ARTICLE

Interphase fluorescence *in situ* hybridization in untreated AL amyloidosis has an independent prognostic impact by abnormality type and treatment category

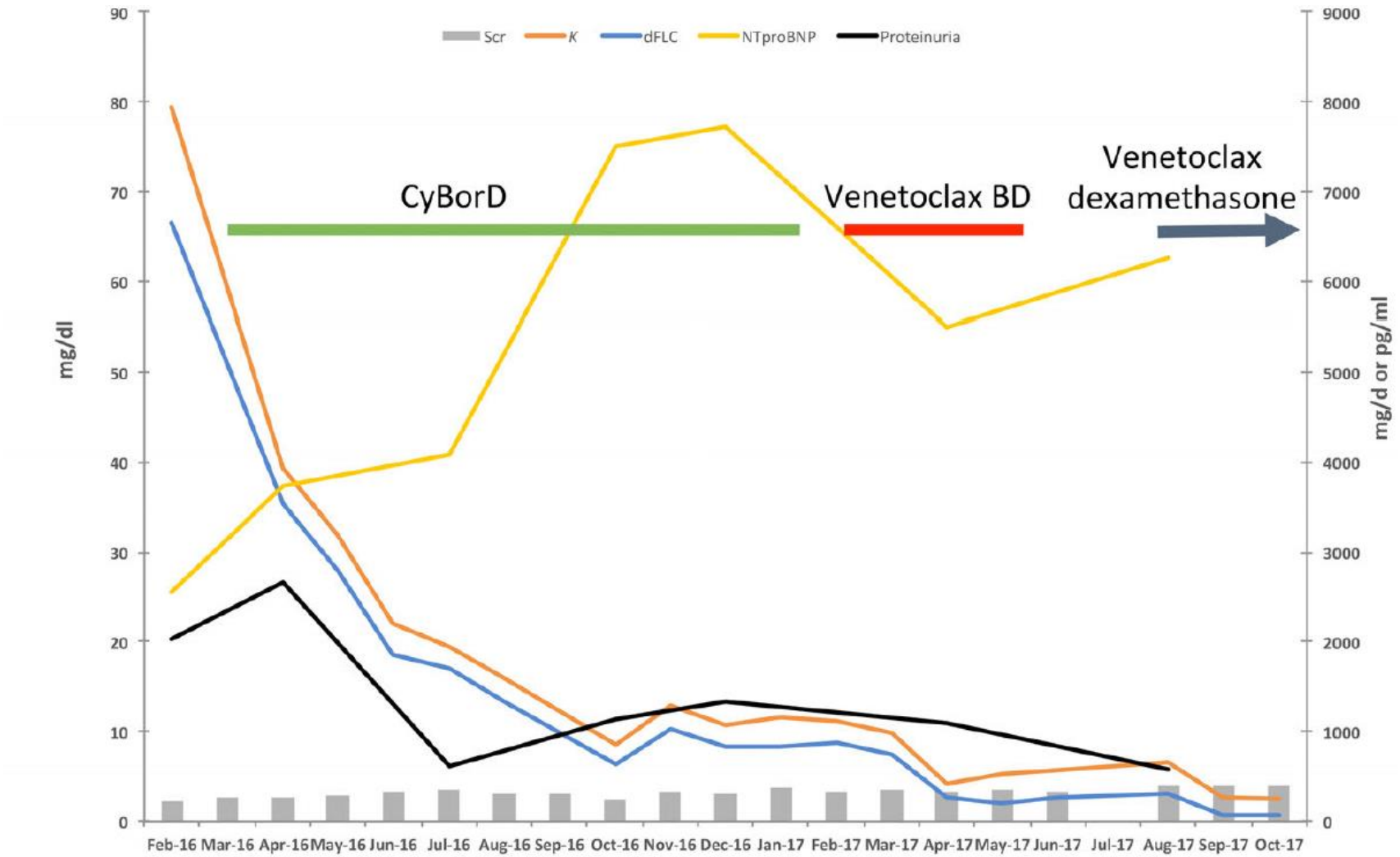
E Muchtar[1], A Dispenzieri[1], SK Kumar[1], RP Ketterling[2], D Dingli[1], MQ Lacy[1], FK Buadi[1], SR Hayman[1], P Kapoor[1], N Leung[1,3], R Chakraborty[1,4], W Gonsalves[1], R Warsame[1], TV Kourelis[1], S Russell[1], JA Lust[1], Y Lin[1], RS Go[1], S Zeldenrust[1], RA Kyle[1], SV Rajkumar[1] and MA Gertz[1]







Muchtar et al. Leukemia 2017



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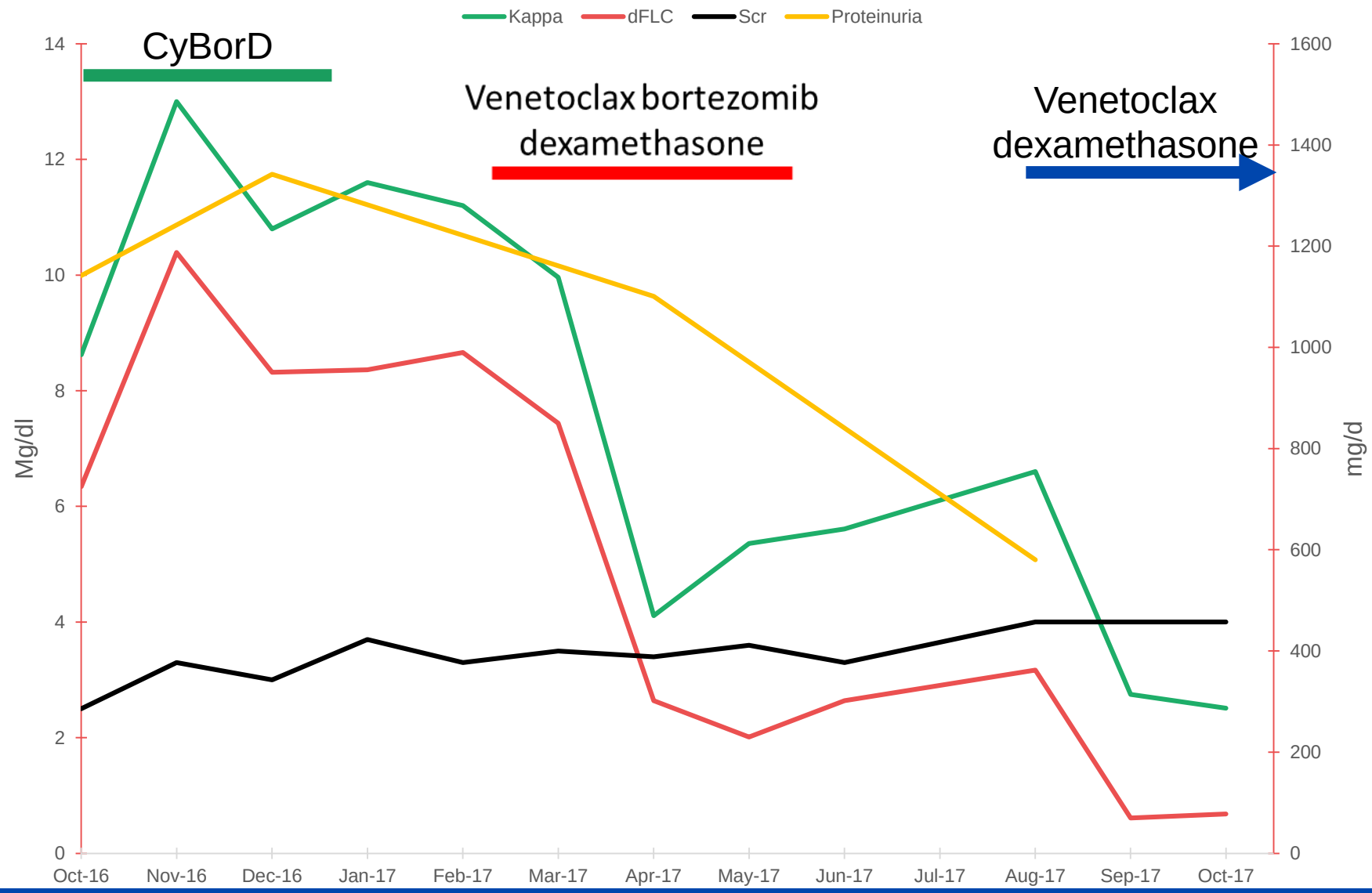
Scr	2,3	2,7	2,7	2,8	3,3	3,6	3,2	3	2,5	3,3	3	3,7	3,3	3,5	3,4	3,6	3,3		4	4	4
k	79,3		39,3	31,9	22	19,5	16		8,62	13	10,8	11,6	11,2	9,96	4,11	5,36	5,61		6,6	2,75	2,51
dFLC	66,6		35,43	27,85	18,51	17,07	13,32		6,34	10,39	8,32	8,36	8,66	7,44	2,64	2,01	2,64		3,17	0,61	0,68
NTproBNP	2556		3741			4083			7506		7724				5491				6264		
Proteinuria	2024		2671			612			1142		1342				1101				580		

MAYO CLINIC

Leung et al. Haematologica 2018



Leung et al. Haematologica 2018

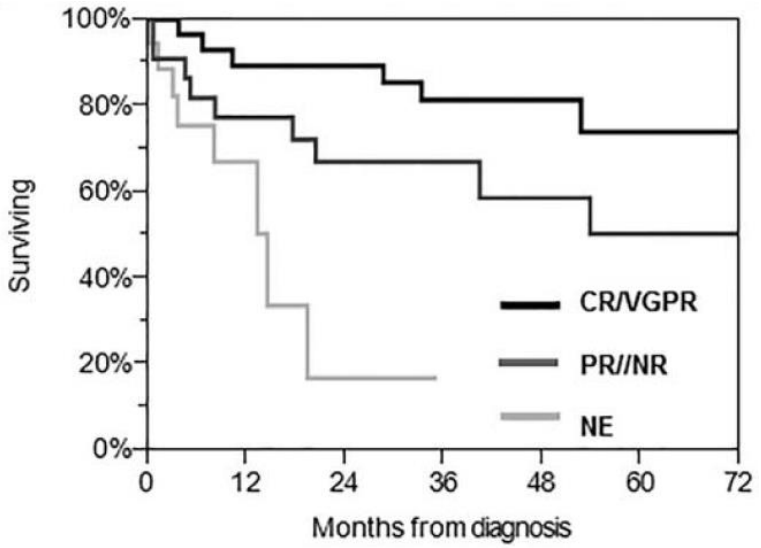
Challenges with treating PGNMID

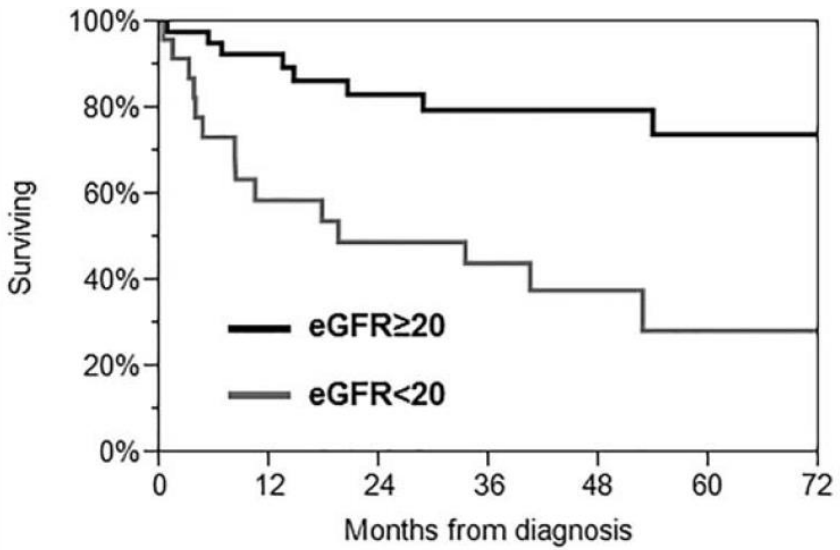
- No monoclonal protein (70-80%)
  - No hematologic markers to follow
  - Need to rely on renal response
- Lack of clone (>80%)
  - Which clone to target?
  - Lack of renal response
    - Was the wrong clone targeted?
    - Was the right clone targeted but treatment was not effective?
    - **Hematologic response was achieved but there is no renal response?**
      - **The point of no return**

AJH

Outcomes of patients with renal monoclonal immunoglobulin deposition disease

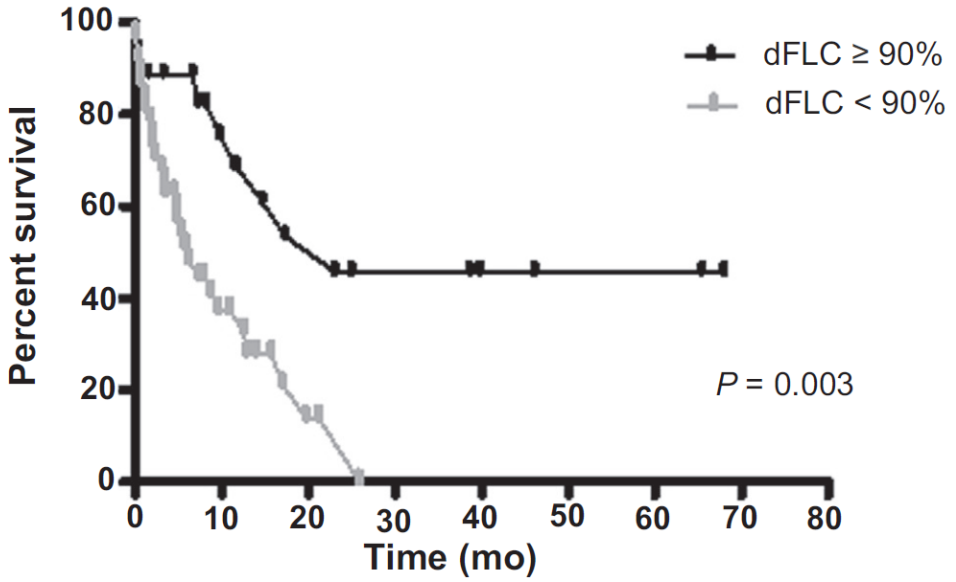
Taxiarchis V. Kourelis,[1] Samih H. Nasr,[2] Angela Dispenzieri,[1] Shaji K. Kumar,[1] Morie A. Gertz,[1] Fernando C. Fervenza,[3] Francis K. Buadi,[1] Martha Q. Lacy,[1] Stephen B. Erickson,[3] Fernando G. Cosio,[3] Prashant Kapoor,[1] John A. Lust,[1] Suzanne R. Hayman,[1] Vincent Rajkumar,[1] Steven R. Zeldenrust,[1] Stephen J. Russell,[1] David Dingli,[1] Yi Lin,[1] Wilson Gonsalves,[1] Elizabeth C. Lorenz,[3] Ladan Zand,[3] Robert A. Kyle,[1] and Nelson Leung[1,3]*

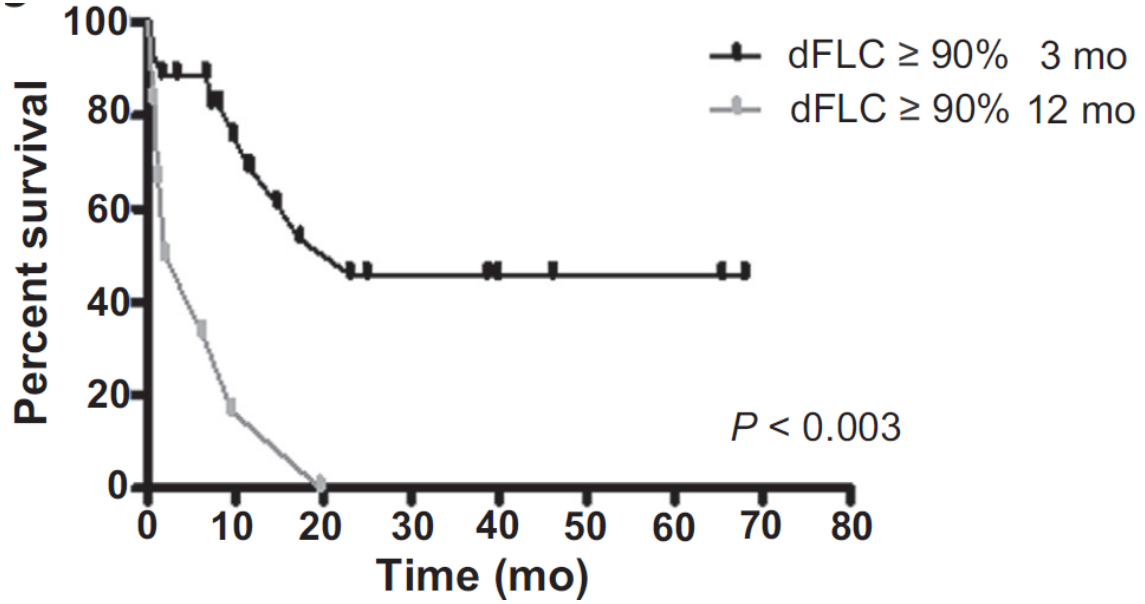




Prolonged renal survival in light chain amyloidosis: speed and magnitude of light chain reduction is the crucial factor

see commentary on page 1321





Rezk et al. Kidney Int 2017

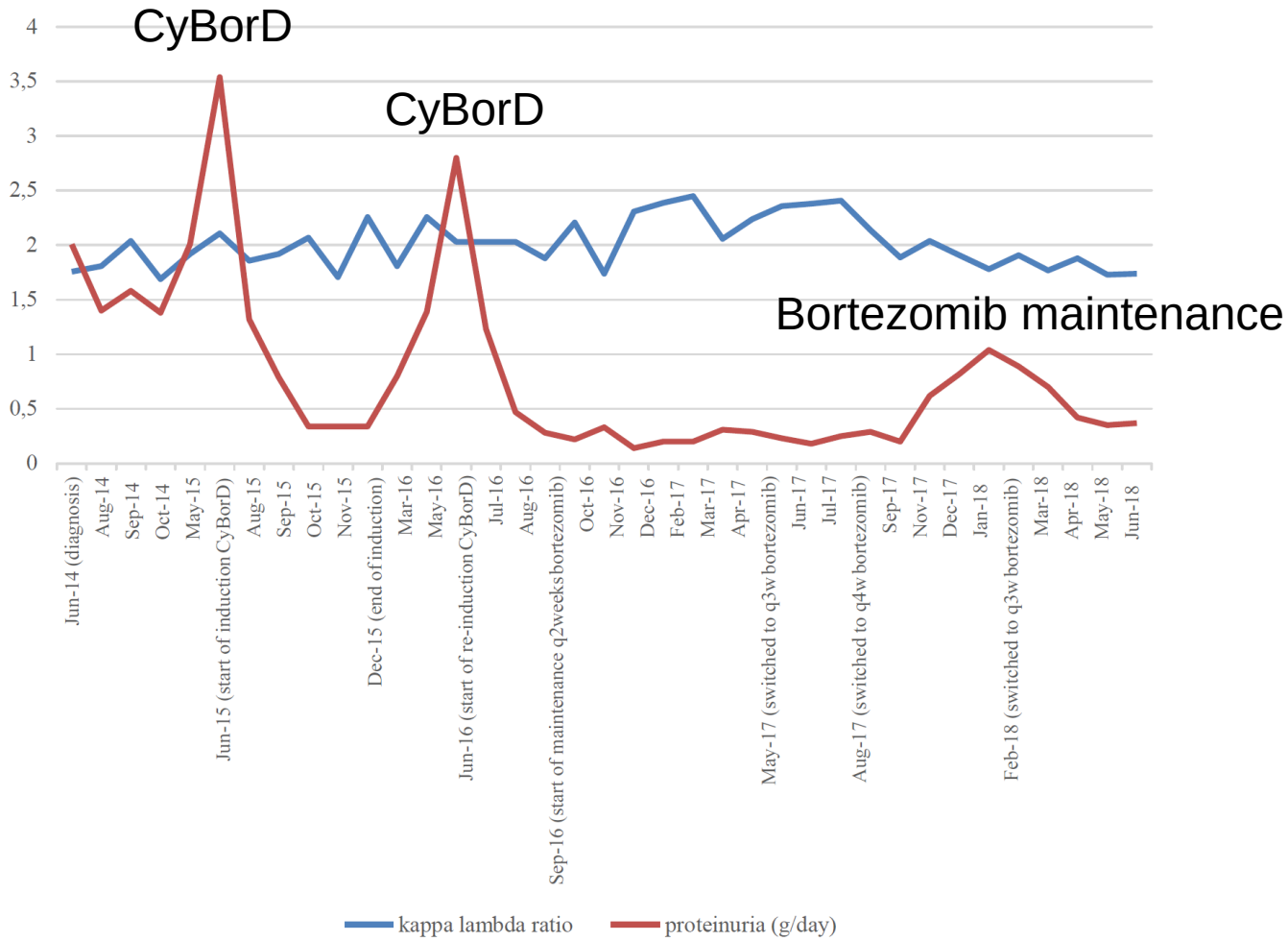
Treatment Duration and Durability of Response

- Treatment duration (cycles)
  - Cohen (bortezomib based) - 4.5 (3 – 6)
  - Ziogas (Vd/VCD) - 5 (4 – 6)
- Duration of response
  - Cohen – after achieving a VGPR with bortezomib based treatment, median time to progression – 8.8 years
  - Kourelis – time to hematologic progression was 55 m in patients with VGPR or better vs 23 months in those with < VGPR.
- Maintenance therapy is usually not required unless the patient has a history of relapse

Cohen et al. Kidney Int 2015
Ziogas et al. Leukemia Lymphoma 2016
Kourelis et al. Am J Hematol 2016

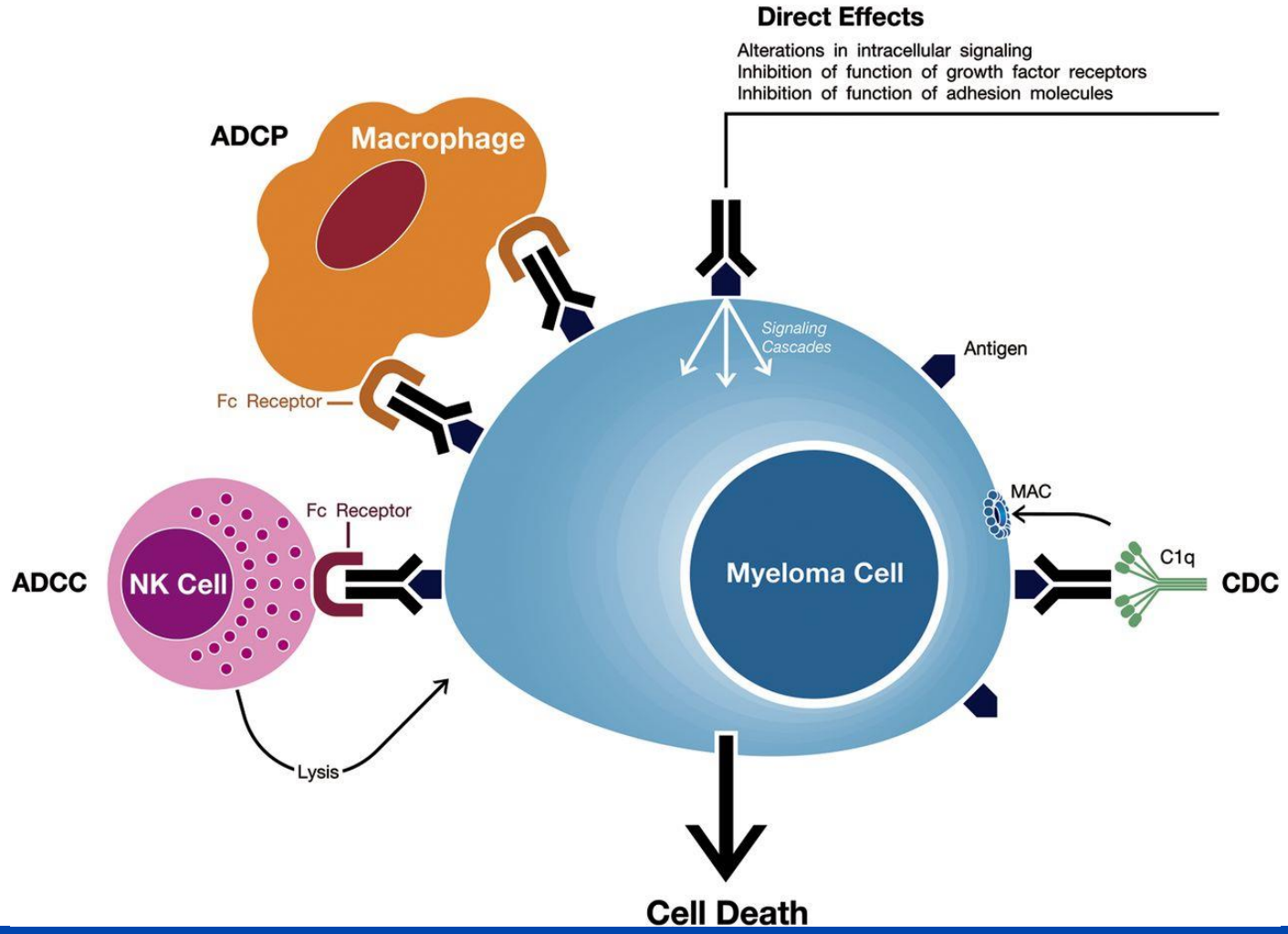
Bortezomib Maintenance for the Treatment of Monoclonal Gammopathy of Renal Significance

Holly Lee[1], Peter Duggan[2], Paola Neri[2], Jason Tay[2] and Victor H Jimenez-Zepeda[2].



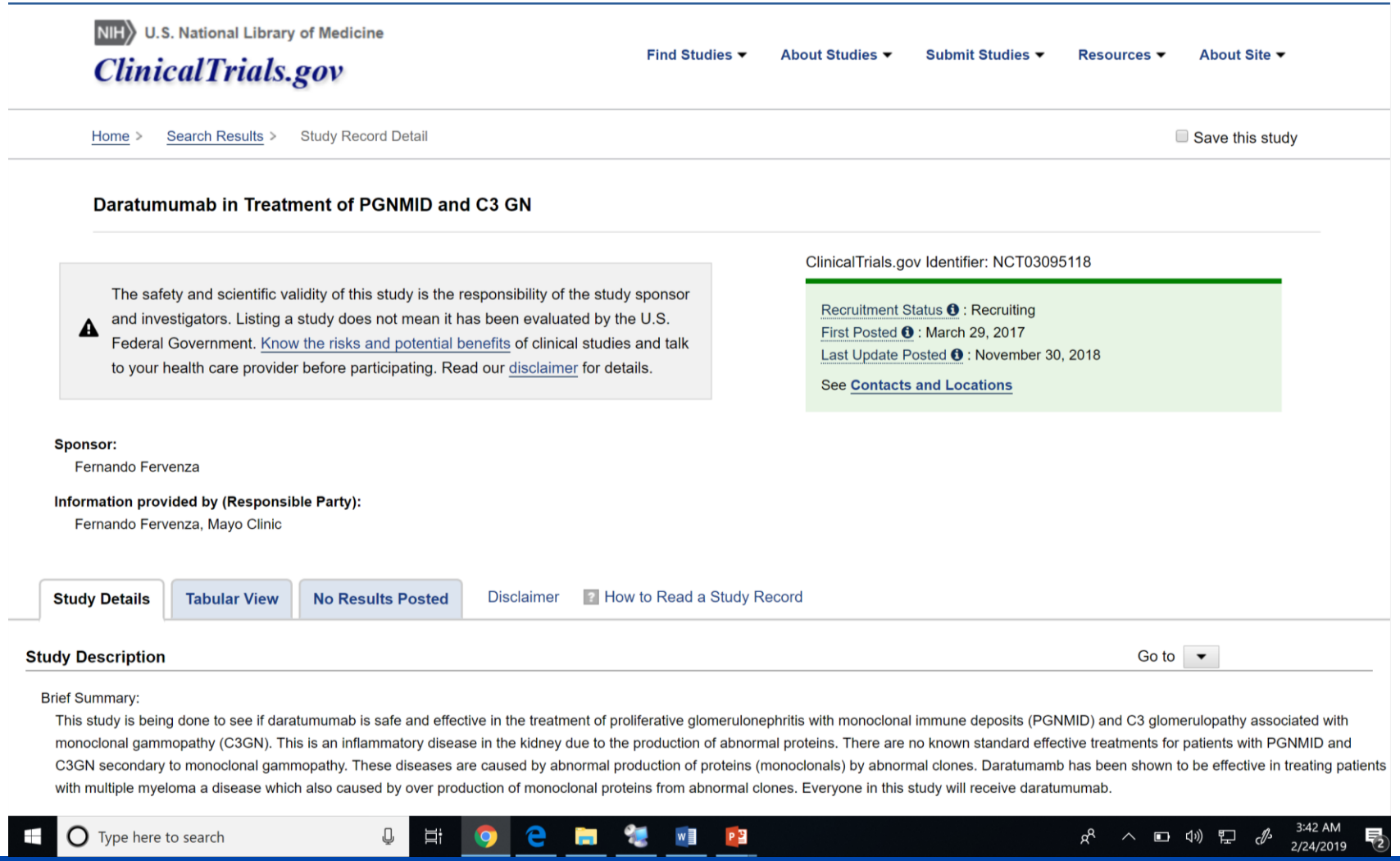
Lee et al. Mediterranean J Hematol and Inf Disease 2019

Antibody mediated cellular toxicity of daratumumab



Niels et al. Blood 2016

Open label Daratumumab



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Daratumumab in Treatment of PGNMID and C3 GN

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03095118

Recruitment Status : Recruiting
First Posted : March 29, 2017
Last Update Posted : November 30, 2018

See Contacts and Locations

Sponsor:
Fernando Fervenza

Information provided by (Responsible Party):
Fernando Fervenza, Mayo Clinic

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

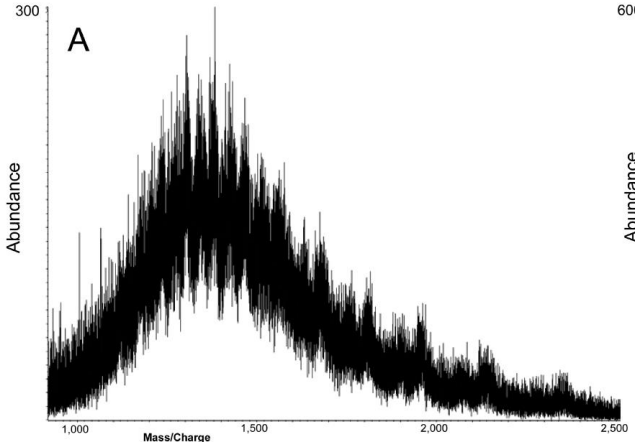
Study Description Go to

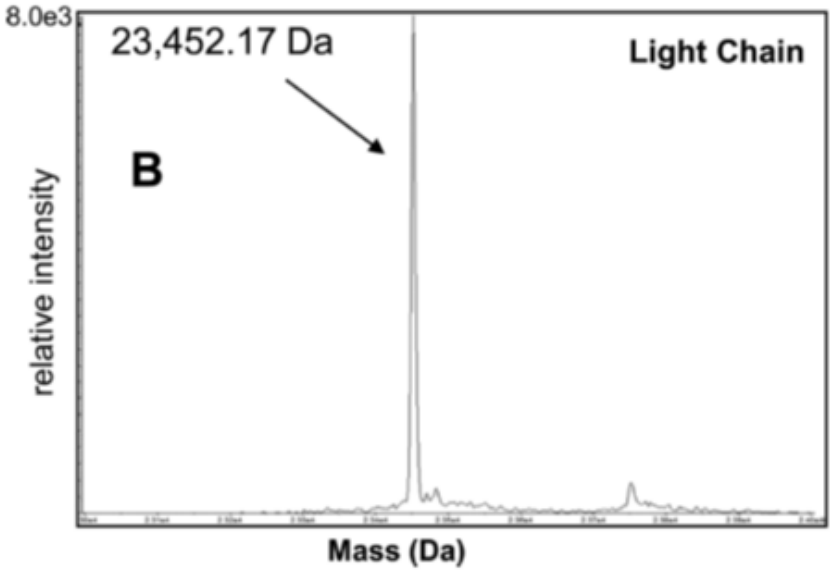
Brief Summary:
This study is being done to see if daratumumab is safe and effective in the treatment of proliferative glomerulonephritis with monoclonal immune deposits (PGNMID) and C3 glomerulopathy associated with monoclonal gammopathy (C3GN). This is an inflammatory disease in the kidney due to the production of abnormal proteins. There are no known standard effective treatments for patients with PGNMID and C3GN secondary to monoclonal gammopathy. These diseases are caused by abnormal production of proteins (monoclonals) by abnormal clones. Daratumamb has been shown to be effective in treating patients with multiple myeloma a disease which also caused by over production of monoclonal proteins from abnormal clones. Everyone in this study will receive daratumumab.

Type here to search 3:42 AM 2/24/2019

Using Mass Spectrometry to Monitor Monoclonal Immunoglobulins in Patients with a Monoclonal Gammopathy

David R. Barnidge,[†] Surendra Dasari,[‡] Chad M. Botz,[†] Danelle H. Murray,[†] Melissa R. Snyder,[†] Jerry A. Katzmann,[†] Angela Dispenzieri,[†] and David L. Murray*[,†]



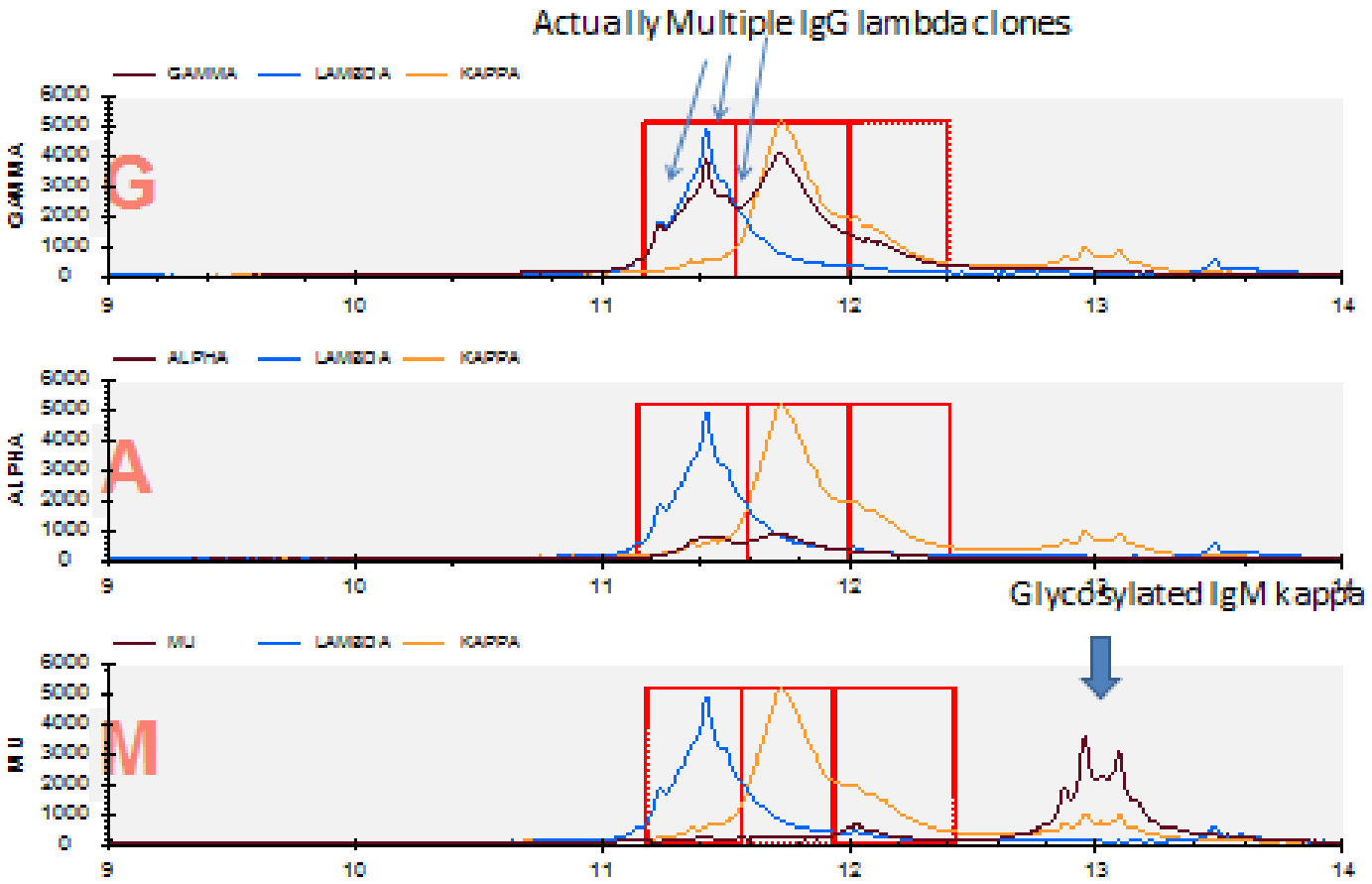


Barnidge et al. J Proteome Res 2014

Single IgG kappa Patient over 7 years

Sample Date	M-spike (g/dL)	IFE	FLC ratio	miRAMM	Mass (Da)	miRAMM Peak Area
2/23/2005	4.8	Pos	Inc.	Pos	23453	3,010,900
3/292006	0.26	Pos	Inc.	Pos	23452	34,839
4/26/2007	0	Neg	Nml	Pos	23452	9,300
10/11/2007	0	Neg	Nml	Pos	23452	11,500
4/23/2008	0.54	Pos	Inc	Pos	23452	152,021
5/7/2009	0.43	Pos	Inc.	Pos	23452	322,400
7/27/2010	3.24	Pos	Inc.	Pos	23452	2,875,100
8/22/2011	0	Neg	Nml	Pos	23452	2100
3/5/2012	0.79	Pos	Inc.	Pos	23452	600,300

Detection of multiple monoclonal IgG lambda clones



Serum immunofixation

Results

Monoclonal Protein Study (Order 2222277946301)

Monoclonal Protein Study

Order: 2222277946301

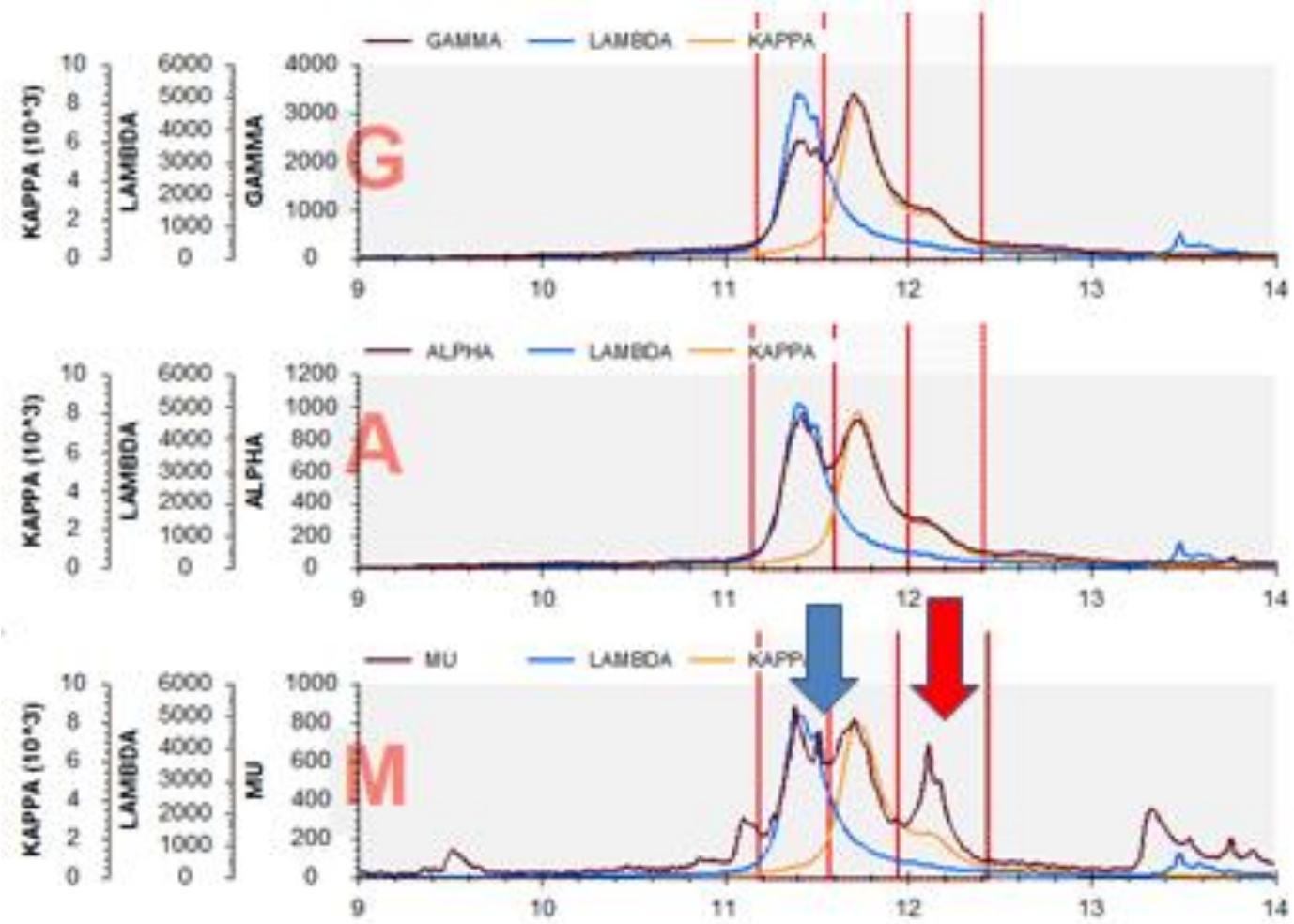
Status: **Final result** Visible to patient: **Yes (Patient Online Services)** Dx: **Glomerulonephritis Membrane Prolifera...**

Newer results are available. Click to view them now.

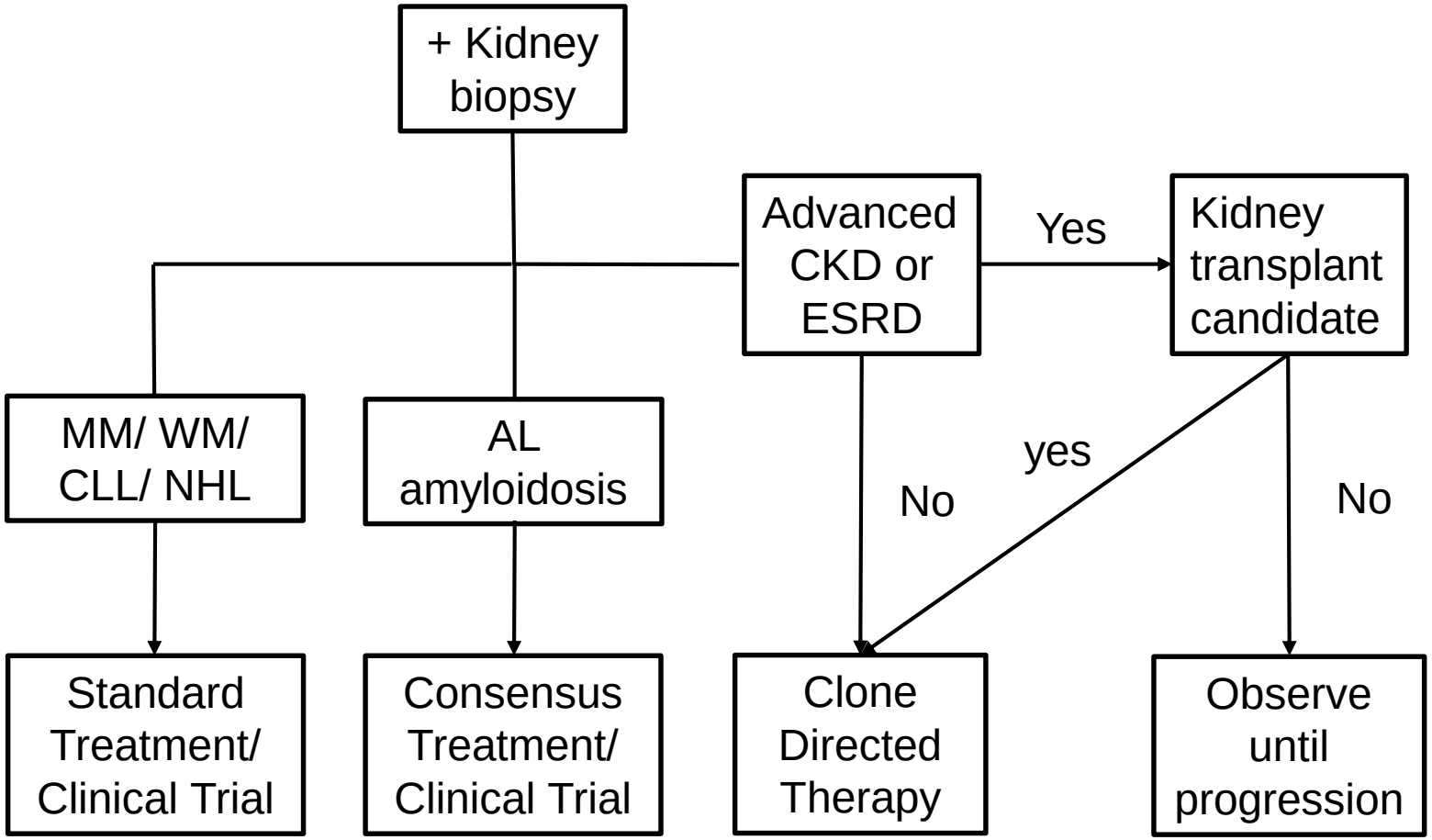
	Ref Range & Units	10mo ago
Total Protein, S	6.3 - 7.9 g/dL	5.0 ↓
Albumin	3.4 - 4.7 g/dL	2.5 ↓
Alpha-1 Globulin	0.1 - 0.3 g/dL	0.2
Alpha-2 Globulin	0.6 - 1.0 g/dL	0.8
Beta-Globulin	0.7 - 1.2 g/dL	0.6 ↓
Gamma-Globulin	0.6 - 1.6 g/dL	0.9
A/G Ratio		1.02
Impression		No apparent monoclonal protein on serum electrophoresis. See Immunofixation.
Immunofixation		No monoclonal protein detected.
Resulting Agency		MCR

Specimen Collected: 07/18/18 13:59 Last Resulted: 07/19/18 15:29

IgM lambda and IgM kappa peaks on Mass-Fix



Treatment Algorithm



Thank you for your attention

Questions

Welcome to mSMART: The Risk Adapted Approach to Management of Multiple Myeloma and Related Disorders

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Witzig, Thomas, M.D.
Zeldenrust, Seven, M.D., Ph.D.

MISSION

Our MISSION is to present the state of the art approach to management of these plasma cells disorders including Myeloma, Amyloidosis, and Waldenstroms Macroglobulinemia. Views expressed here are opinions of a group of experts, based on best available evidence