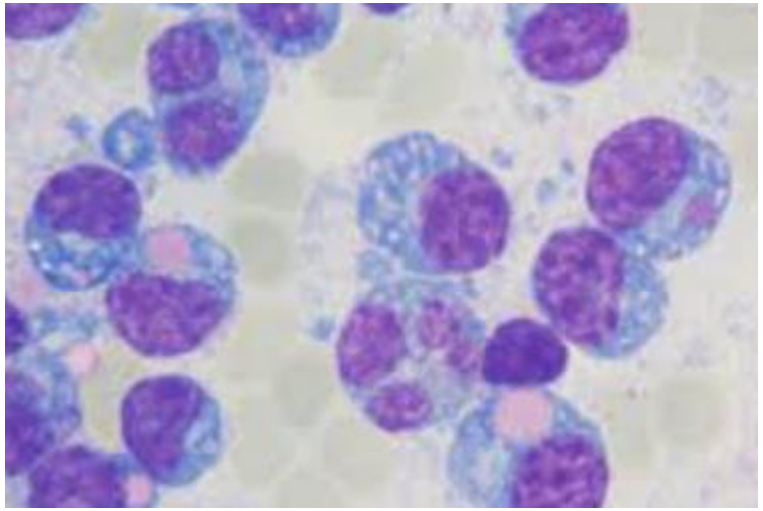
"DISCRASIA DE CÉLULAS PLASMÁTICAS"
Desde la gammapatía monoclonal al mieloma (o no...). Diagnóstico y tratamiento.

Dra. Guillermina Remaggi
FUNDALEU
Buenos Aires, agosto de 2023
CURSO DE MEDICINA INTERNA DE LA A.M.A

ALGUNOS TÉRMINOS

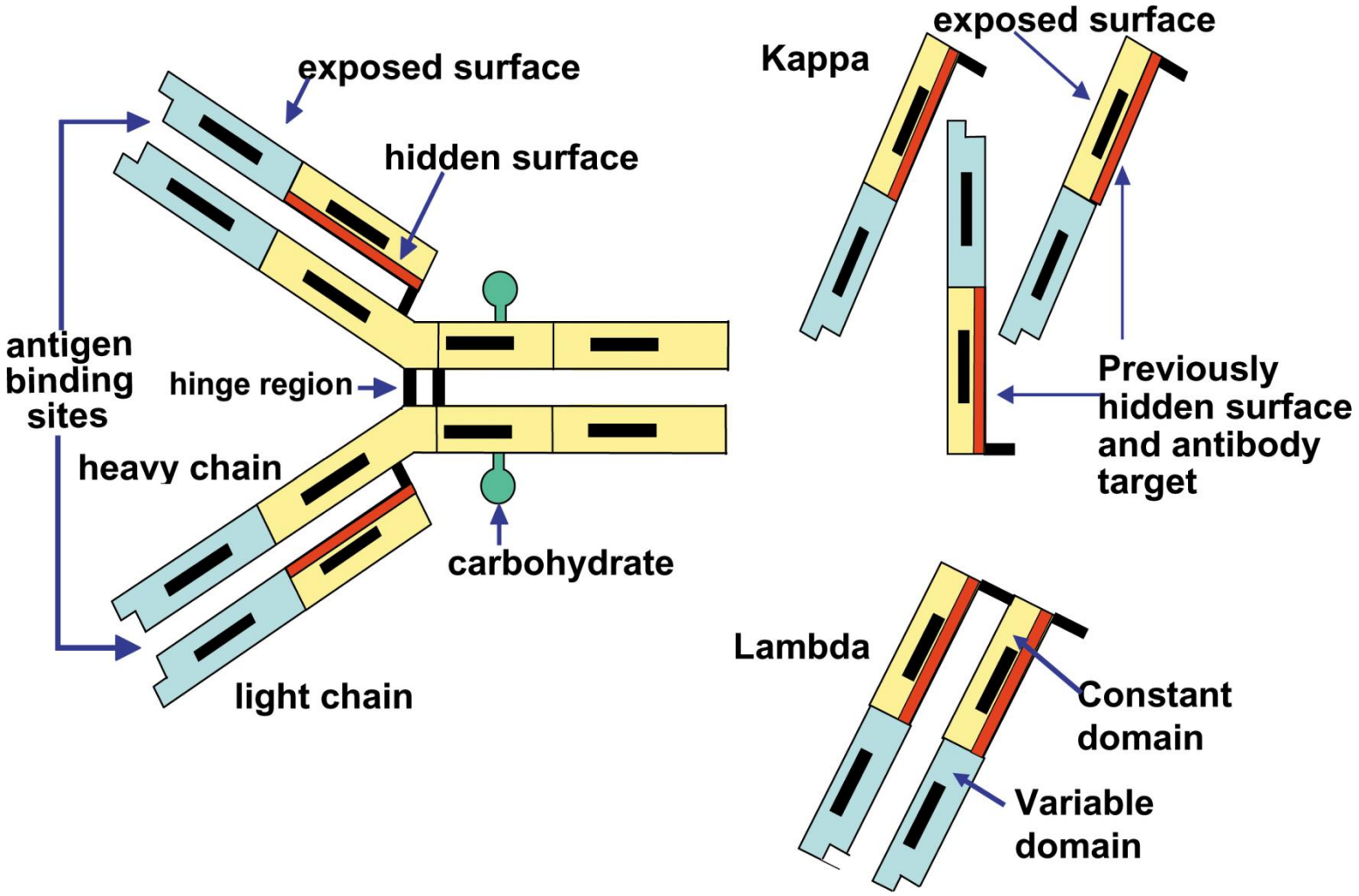
- Célula plasmática
- Inmunoglobulinas
- Banda monoclonal



Estructura de una molécula de anticuerpo

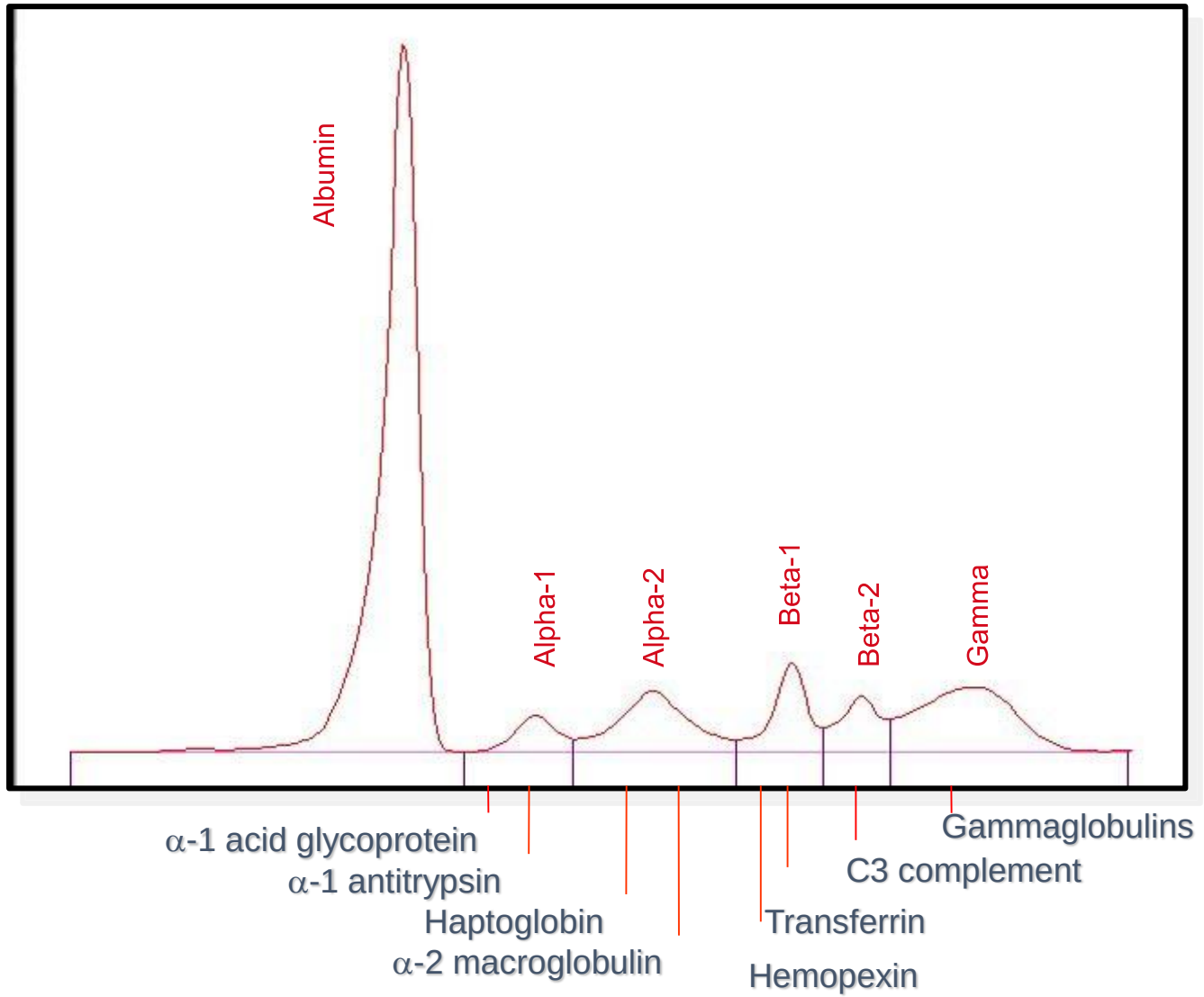
completa: H+ L cadena pesada y liviana

κ y λ libre FLCs.



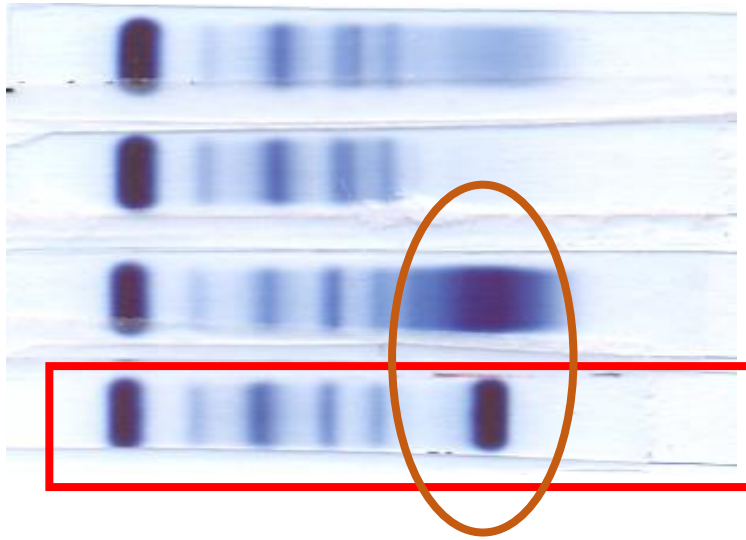
TODO EMPIEZA CON UNA BANDA MONOCLONAL…

PROTEINOGRAMA



LABORATORIO DE PROTEÍNAS

- Componente monoclonal → “M”
- Identificación de la cadena pesada / liviana: IF



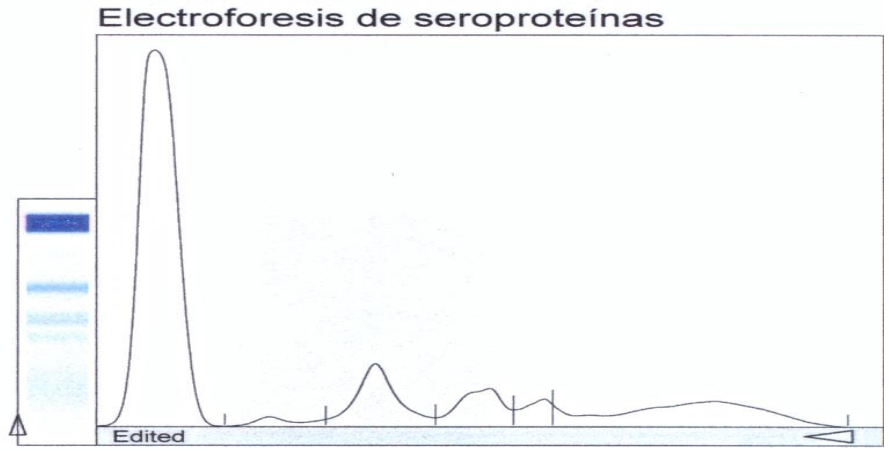
Suero normal

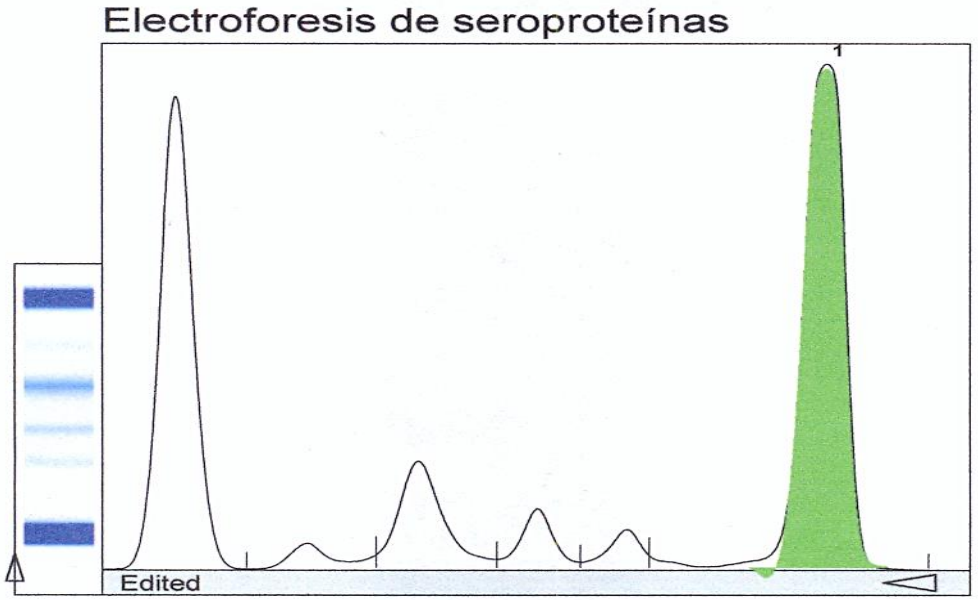
Suero con agammaglobulinemia

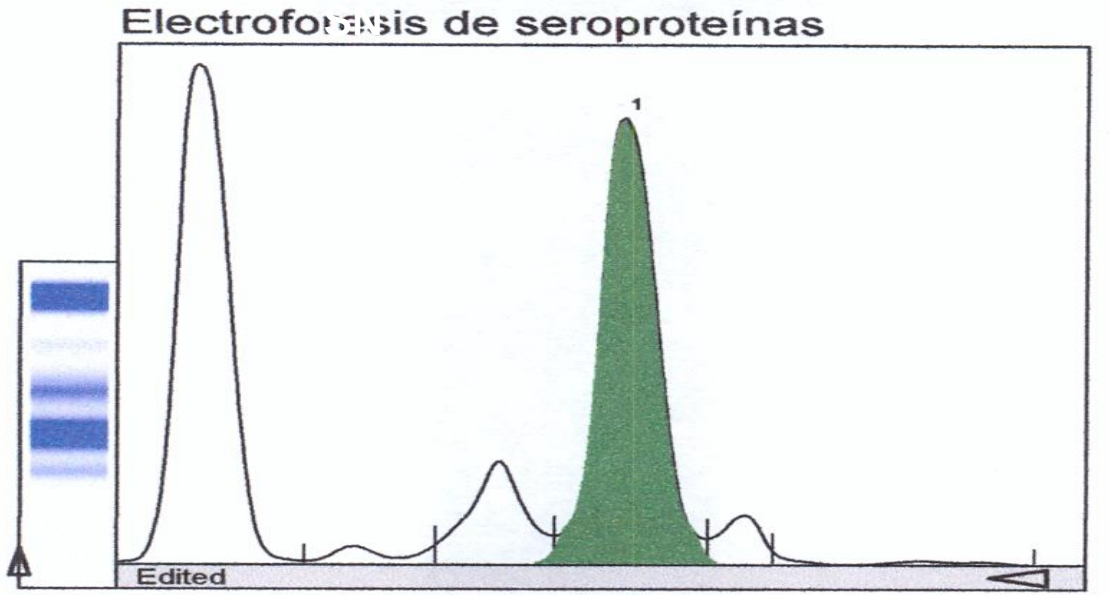
Suero con hipergammaglobulinemia policlonal

Suero con Gammapatía Monoclonal

CUANTIFICAR COMPONENTE MONOCLONAL: SPEP





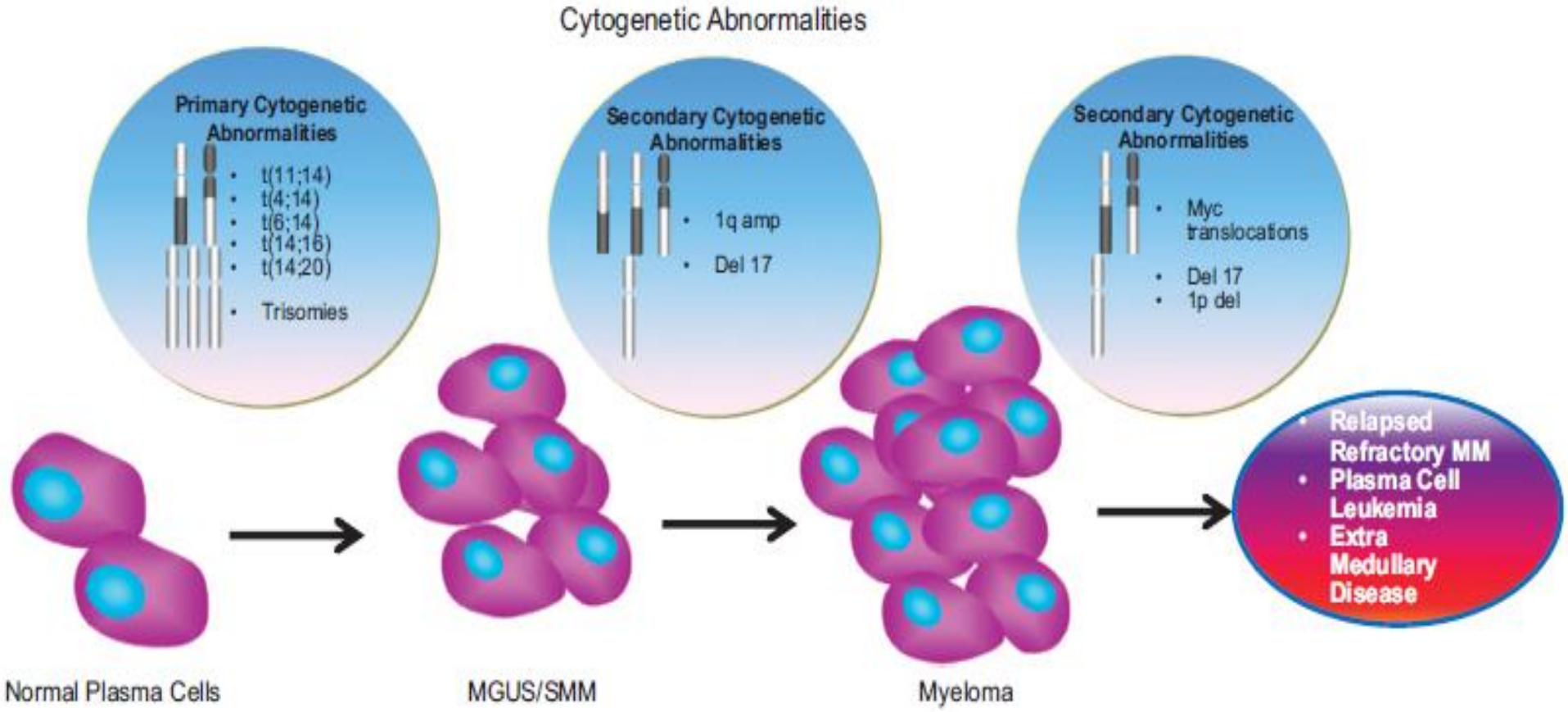


Gentileza Bqca. M. Alejandre

EXAMEN DE ORINA

- ORINA DE 24 HS
- Recomendada su concentración hasta 200 veces para aumentar la sensibilidad
- Sirve para monitorear a los pacientes con M de cadenas livianas:
  - 80% pueden ser monitoreados por orina
  - Los restantes por las cadenas livianas libres
- Proteinograma urinario: albúmina → amiloidosis o enfermedad por depósito de cadenas livianas
- MEDIR PROTEINURIA Y PROTEINOGRAMA - IF

ALTERACIONES CITOGENÉTICAS



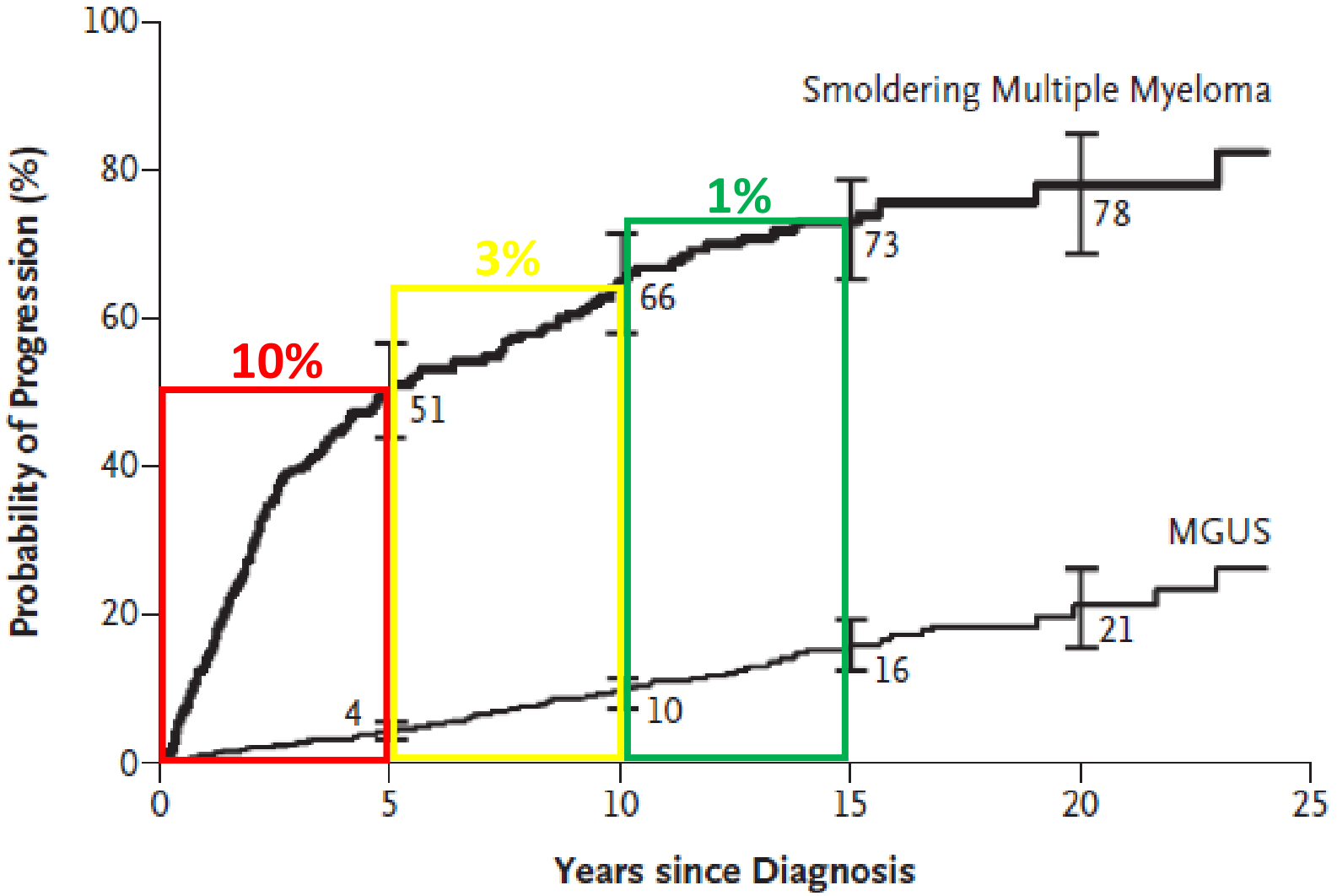
Trisomies, or any one IgH translocation, or combined trisomies and IgH translocations are associated with the establishment of the clone

Secondary Cytogenetic Abnormalities occur with progression; Del 17p, 1qamp, and t(4;14) associated with high risk of progression in SMM

Secondary Cytogenetic Abnormalities occur with progression; Del 17p, t(14;16) and t(14;20) associated with adverse prognosis in MM

Citation: Blood Cancer Journal (2015) **5**, e365; doi:10.1038/bcj.2015.92

AM Rajan[1] and SV Rajkumar[2]



Kyle RA, Rajkumar V. NEJM 2007

MIELOMA MÚLTIPLE SINTOMÁTICO

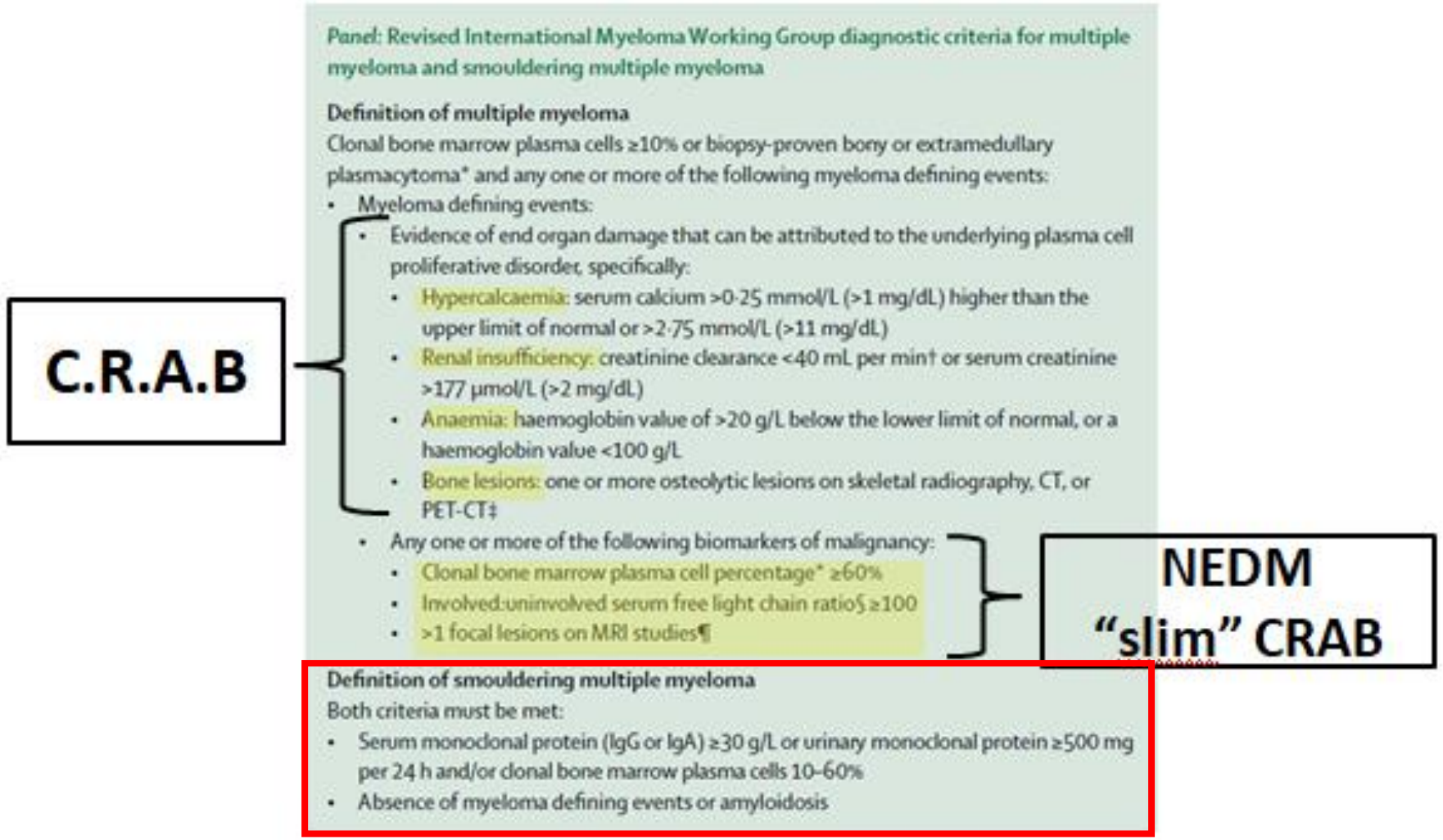
Infiltración de plasmocitos >10% en MO
Inmunoglobulina anormal (IgH o IgL monoclonal) suero y/u orina

Lesión de órgano blanco:

- **C** Calcio >10.5mg/L
- **R** Insuficiencia Renal: creatinina>2mg/dl
- **A** Anemia: Hb<10gr/dL o <2gr el valor normal
- **B** Lesión ósea(Bone) lítica u osteoporosis

síndrome hiperviscosidad,
amiloidosis,
infecciones bacterianas recurrentes (>2 en 12 meses)

NUEVOS CRITERIOS DIAGNÓSTICOS IMWG 2014



Panel: Revised International Myeloma Working Group diagnostic criteria for multiple myeloma and smouldering multiple myeloma

Definition of multiple myeloma

Clonal bone marrow plasma cells ≥10% or biopsy-proven bony or extramedullary plasmacytoma* and any one or more of the following myeloma defining events:

- Myeloma defining events:
  - Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:
    - Hypercalcaemia: serum calcium >0·25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2·75 mmol/L (>11 mg/dL)
    - Renal insufficiency: creatinine clearance <40 mL per min† or serum creatinine >177 μmol/L (>2 mg/dL)
    - Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L
    - Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT‡
  - Any one or more of the following biomarkers of malignancy:
    - Clonal bone marrow plasma cell percentage* ≥60%
    - Involved:uninvolved serum free light chain ratio§ ≥100
    - >1 focal lesions on MRI studies¶

Definition of smouldering multiple myeloma

Both criteria must be met:

- Serum monoclonal protein (IgG or IgA) ≥30 g/L or urinary monoclonal protein ≥500 mg per 24 h and/or clonal bone marrow plasma cells 10–60%
- Absence of myeloma defining events or amyloidosis

Rajkumar et al, Lancet Oncology, Nov 2014

Criterios diagnósticos

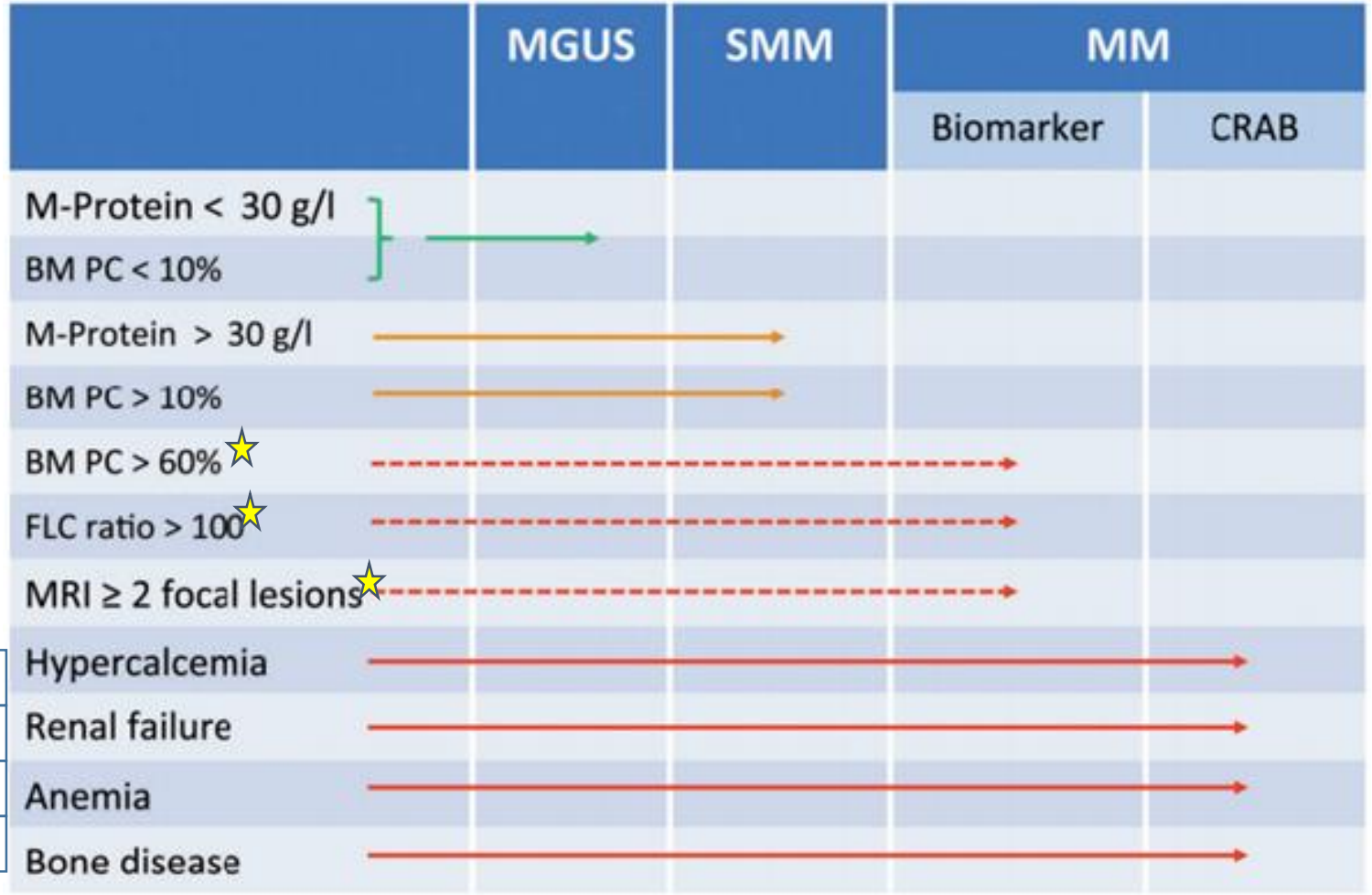
	GMSI	MMI	MMS
Componente M	<30g/L	>30g/l	+ en suero y/u orina
Células Plasmáticas % infiltración	<10	>10	>10
Afectación orgánica	Ausente	Ausente	Presente

- Gamapatía Monoclonal de Significado Incierto - MGUS
- Mieloma Múltiple Asintomático - SMM
- Mieloma Múltiple Sintomático - MM

European Myeloma Network recommendations on tools for the diagnosis and monitoring of multiple myeloma: what to use and when

Jo Caers,[1,2] Laurent Garderet,[3] K. Martin Kortüm,[4] Michael E. O'Dwyer,[5] Niels W.C.J. van de Donk,[6] Mascha Binder,[7] Sandra Maria Dold,[8] Francesca Gay,[9] Jill Corre,[10] Yves Beguin,[1,2] Heinz Ludwig,[11] Alessandra Larocca,[9] Christoph Driessen,[12] Meletios A. Dimopoulos,[13] Mario Boccadoro,[9] Martin Gramatzki,[14] Sonja Zweegman,[6] Hermann Einsele,[4] Michele Cavo,[15] Hartmut Goldschmidt,[16,17] Pieter Sonneveld,[18] Michel Delforge,[19] Holger W. Auner,[20] Evangelos Terpos[13] and Monika Engelhardt[8]

Haematologica 2018
Volume 103(11):1772-1784



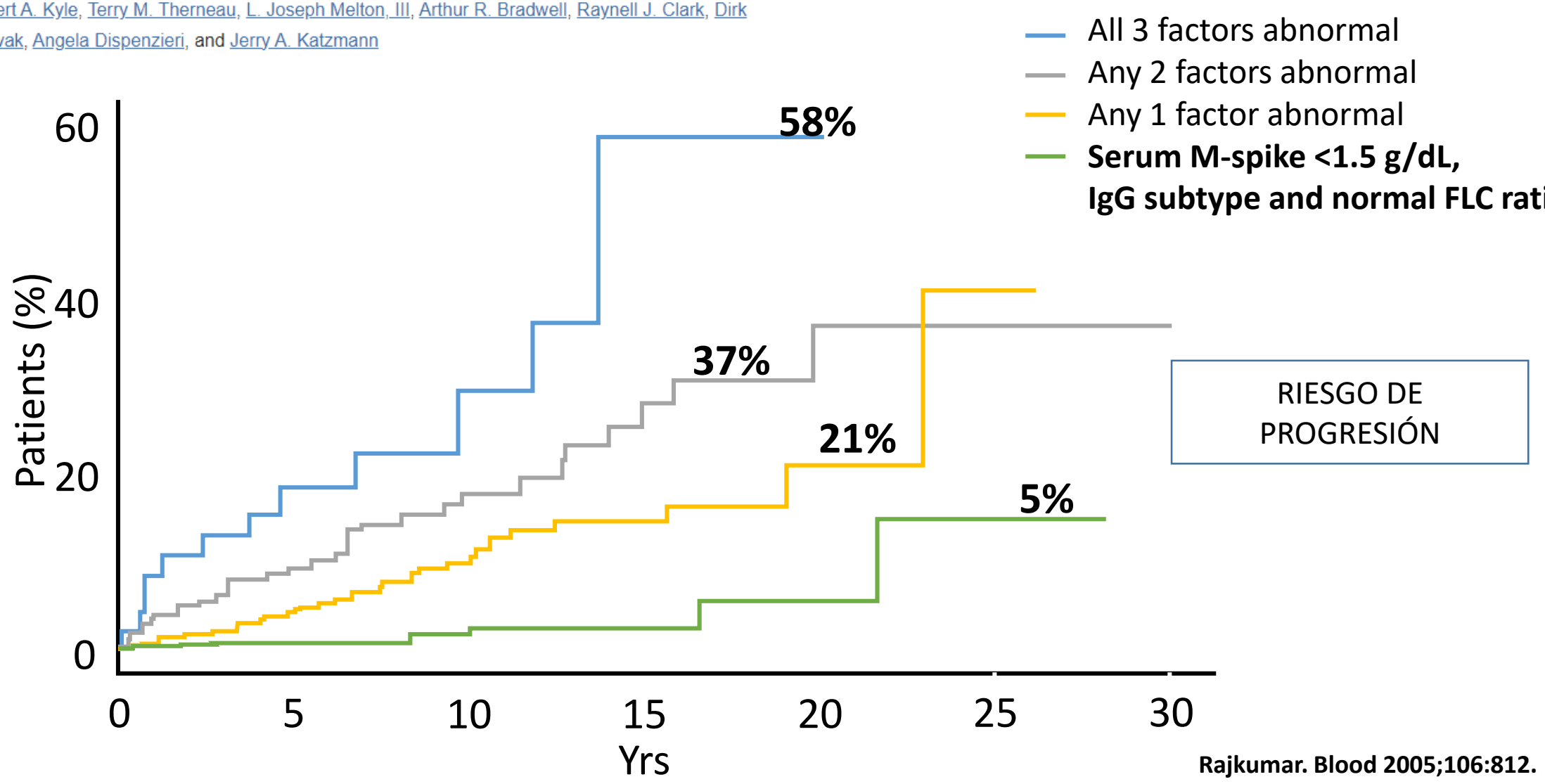
> 11
Crea >2 o clear <40
Hb <10 o ↓2 basal
1 lesión lítica

GAMMAPATÍA MONOCLONAL DE SIGNIFICADO INCIERTO

Blood. 2005 Aug 1; 106(3): 812–817.
Prepublished online 2005 Apr 26. doi: 10.1182/blood-2005-03-1038
PMCID: PMC1895159
PMID: 15855274

Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance

S. Vincent Rajkumar, Robert A. Kyle, Terry M. Therneau, L. Joseph Melton, III, Arthur R. Bradwell, Raynell J. Clark, Dirk R. Larson, Matthew F. Plevak, Angela Dispenzieri, and Jerry A. Katzmann



Rajkumar. Blood 2005;106:812.

blood®
Prepublished online November 28, 2017;
doi:10.1182/blood-2017-09-807560

How I manage monoclonal gammopathy of undetermined significance

Ronald S. Go and S. Vincent Rajkumar

Subtype of MGUS	Diagnostic Criteria	Risk of progression	Pattern of progression
IgM MGUS	All 3 criteria must be met: • Serum IgM monoclonal protein <3 gm/dL • Bone marrow lymphoplasmacytic infiltration <10%* • No evidence of anemia, constitutional symptoms, hyperviscosity, lymphadenopathy, or hepatosplenomegaly that can be attributed to the underlying lymphoproliferative disorder	1% per year	Waldenström macroglobulinemia, AL amyloidosis; rarely IgM multiple myeloma
Non-IgM MGUS	All 3 criteria must be met: • Serum monoclonal protein (non-IgM type) <3 gm/dL • Clonal bone marrow plasma cells <10%* • Absence of end-organ damage such as hypercalcemia, renal insufficiency, anemia, and bone lesions (CRAB) that can be attributed to the plasma cell proliferative disorder	0.5% per year	Multiple myeloma, solitary plasmacytoma, AL amyloidosis
Light Chain MGUS	All criteria must be met: • Abnormal FLC ratio (<0.26 or >1.65) • Increased level of involved light chain (increased kappa FLC in patients with FLC ratio >1.65 and increased lambda FLC in patients with FLC ratio <0.26) • No immunoglobulin heavy chain expression on immunofixation • Absence of end-organ damage that can be attributed to the plasma cell proliferative disorder • Clonal bone marrow plasma cells <10%* • Urinary monoclonal protein <500 mg/24h	0.3% per year	Light chain multiple myeloma and AL amyloidosis

MGUS Risk/ Recommended Tests	UK Myeloma Forum/ Nordic Study Group (2009)[14]	International Expert Consensus (2010)[16]	International Myeloma Working Group (2010)[15]	European Myeloma Network (2014)[17]
Low-Risk MGUS (IgG, <1.5 gm/dL, and normal FLC ratio)	First year, every 3-4 months; then every 6-12 months if stable	First 2 years, every 4-6 months; then every 6-24 months	At 6 months; then every 2-3 years if stable	At 6 months; then every 1-2 years if stable or no follow-up
All other MGUS	At least every 3-4 months	First 2 years, every 4-6 months; then every 6-24 months	At 6 months; then every year if stable	At 6 months; then every year thereafter
Life Expectancy <5 years	Can consider discontinuing follow-up	Not mentioned	Not mentioned	No follow-up
Recommended tests	Quantification of M-protein Serum urea nitrogen CBC Calcium Creatinine Electrolytes Immunoglobulin levels	Quantification of M-protein	Quantification of M-protein CBC	Quantification of M-protein CBC Calcium Creatinine

Las cadenas livianas libres son nefrotóxicas.

- forman fibrillas → amiloidoisis primaria AL
- formar depósitos en la membrana basal renal → enf. de depósito de cadenas ligeras
- Depósitos en el túbulo distal → riñón de mieloma

Al diagnóstico, <u>50% de pacientes con mieloma múltiple (MM) experimentan insuficiencia renal</u>: leves (asintomáticos) hasta insuficiencias graves

12-20% de los pacientes con MM presentan fallo renal agudo: nefropatía de cilindros "riñón de mieloma"

En el riñón de mieloma las cadenas ligeras libres, en asociación con la proteína de Tamm-Horsfall, forman depósitos cerosos que taponan los túbulos distales.

↓

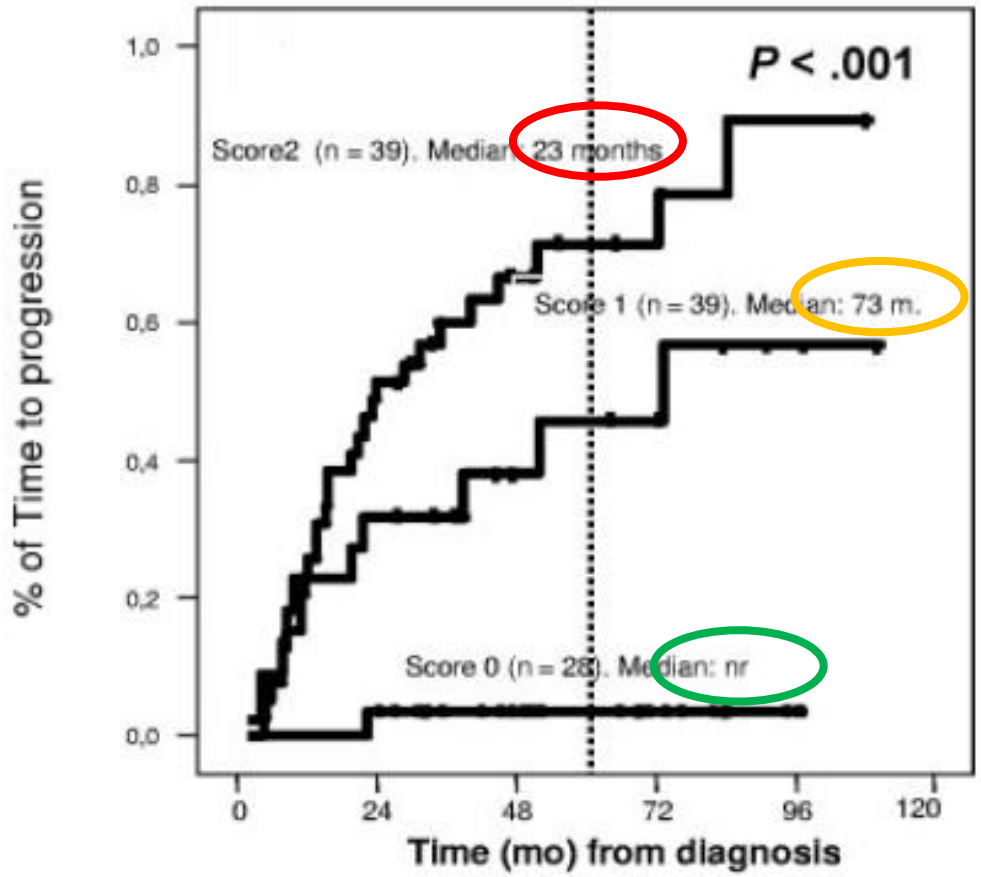
10% de los pacientes : hemodiálisis a largo plazo, mortalidad elevada y opciones de tratamiento limitadas.

MIELOMA “SMOLDERING” (INDOLENTE, ASINTOMÁTICO)

FACTORES DE RIESGO PARA PROGRESAR

- Componente monoclonal >3
- Presencia de proteinuria de BJ (> 1g/d)
- Patrón “evolving” del comp M: aum del comp M >10% en dos evaluaciones sucesivas
- Inmunoparesia: disminución del 25% del valor normal de al menos una de las Ig no implicadas en la Gammapatía Monoclonal.
- Extensión del compromiso de MO
- Porcentaje de CP clonales
- Anomalías CTG de la célula plasmática

EL SCORE ESPAÑOL: PRESENCIA DE >95% CP CLONALES EN MO E INMUNOPARESIS



The score system for SMM was built on the basis of the percentage of immunophenotypically aberrant PC within the BMPC compartment (< 95% aberrant PC, score of 0; ≥ 95%, score of 1) and the presence (score of 1) or absence (score of 0) of immunoparesis. In patients with a score of 1, the median TTP has not been reached; in patients with a score of 2, the median TTP is 73 months; and in patients with a score of 3, the median TTP is 23 months ($P < .001$).

Pérez Persona, Blood 2007.

EL SCORE DE LA CLÍNICA MAYO

Multivariate analysis of prognostic factors for progression of SMM to myeloma and related disorders

Prognostic factor	Hazard ratio (95% CI)	*P*
Bone marrow plasma cells more than 10%	3.1 (1.6-6.3)	< .01
Abnormal FLC ratio less than 0.125 or more than 8	1.9 (1.3-2.7)	< .01
Serum M protein size, more than 30 g/L	1.9 (1.4-2.6)	< .01

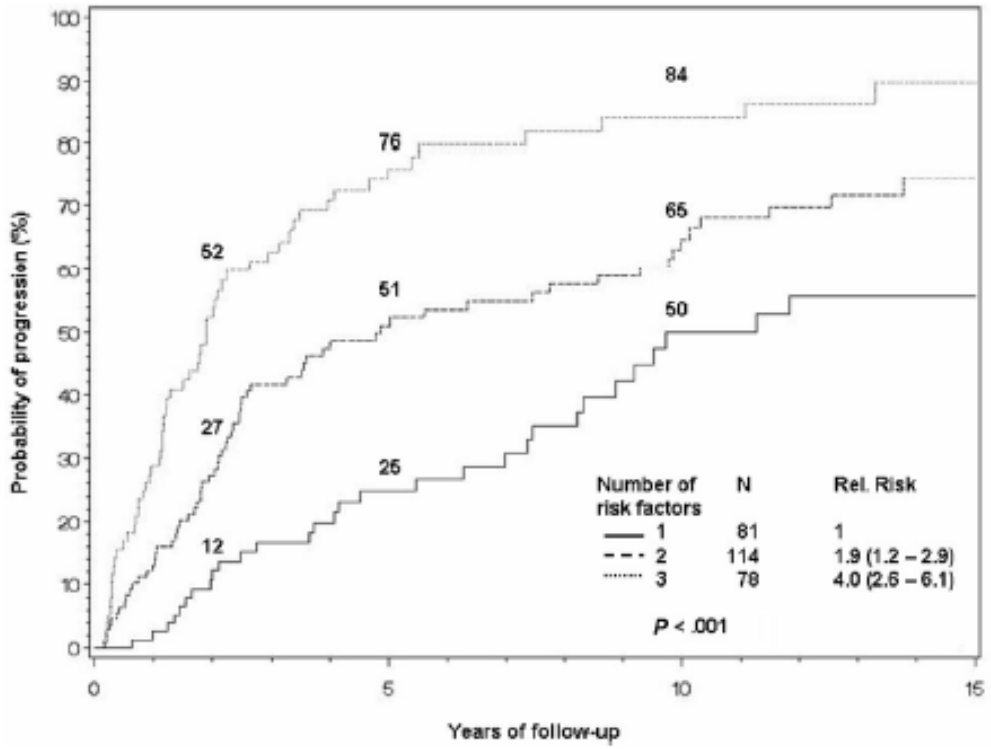


Figure 3. Risk stratification based on bone marrow plasmacytosis, serum M protein, and serum immunoglobulin FLC ratio. Patients are assigned 1 point for meeting each of the following criteria: BMPCs greater than or equal to 10%; serum M protein greater than or equal to 3 g/dL; and serum immunoglobulin FLC ratio either less than 0.125 or more than 8. The median times to progression for 1, 2, or 3 risk factors are 10, 5.1, and 1.9 years respectively.

Dispenzieri, A. Blood 2008

Mateos et al. *Blood Cancer Journal* (2020)10:102
https://doi.org/10.1038/s41408-020-00366-3

Blood Cancer Journal

ARTICLE Open Access

International Myeloma Working Group risk stratification model for smoldering multiple myeloma (SMM)

María-Victoria Mateos[1], Shaji Kumar[2], Meletios A. Dimopoulos[3], Verónica González-Calle[1], Efstathios Kastritis[3], Roman Hajek[4], Carlos Fernández De Larrea[5], Gareth J. Morgan[6], Giampaolo Merlini[7], Hartmut Goldschmidt[8], Catarina Geraldes[9], Alessandro Gozzetti[10], Charalampia Kyriakou[11], Laurent Garderet[12], Markus Hansson[13], Elena Zamagni[14], Dorotea Fantl[15], Xavier Leleu[16], Byung-Su Kim[17], Graça Esteves[18], Heinz Ludwig[19], Saad Usmani[20], Chang-Ki Min[21], Ming Qi[22], Jon Ukropec[22], Brendan M. Weiss[22], S. Vincent Rajkumar[2], Brian G. M. Durie[23] and Jesús San-Miguel[24]

OBJETIVO PRINCIPAL: desarrollar un modelo de estratificación que identifique pacientes con **MS con 50% de riesgo de progresar en 2 años luego del diagnóstico.**

1996 pacientes de 75 centros en 23 países:

La mediana de seguimiento desde el diagnóstico fue de 3 años.

41% progresaron a mieloma al momento de la evaluación

La mediana de TTP fue de 6,4 años.

En conjunto:

- Riesgo de progresión a 2 años: 22%
- Riesgo de progresión a 5 años: 42%
- Riesgo de progresión a 10 años: 64%

Sobrevida global estimada a 5 años: 93.8% .

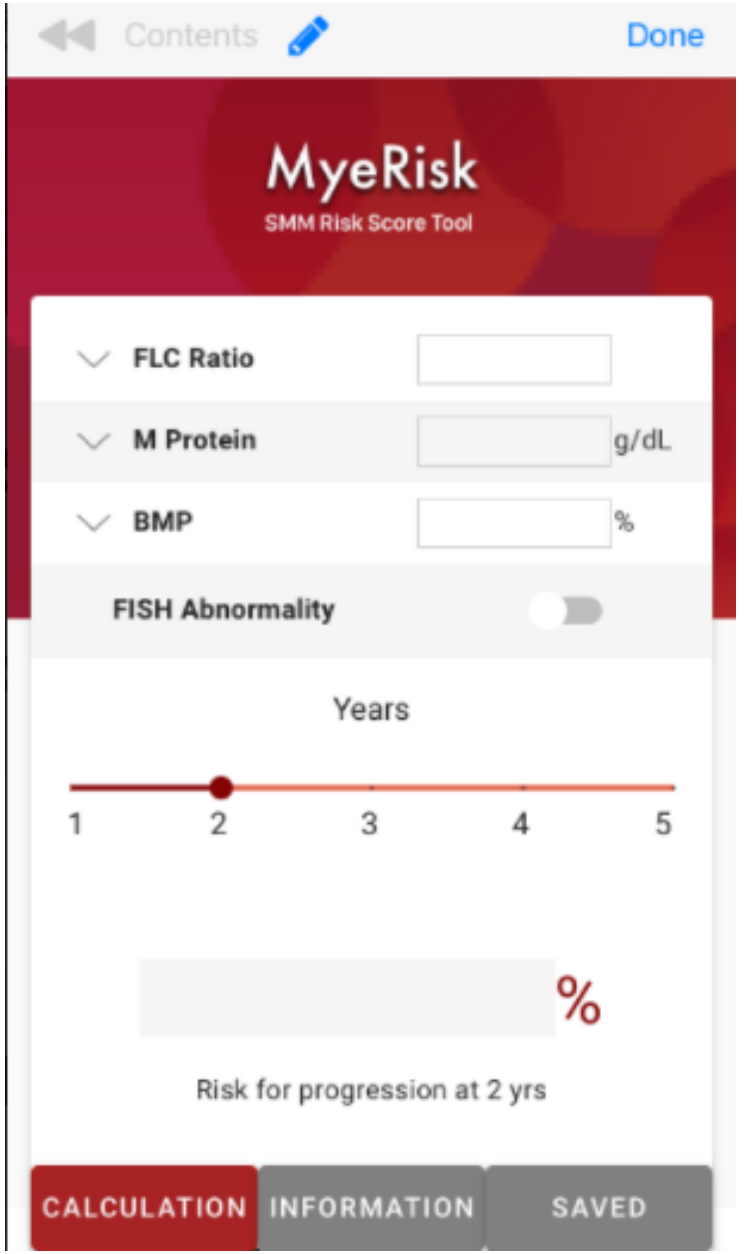
Sobrevida global estimada a 10 años: 88.3%.

Mateos MV, Blood Cancer Journal 2020

FACTORES DE RIESGO

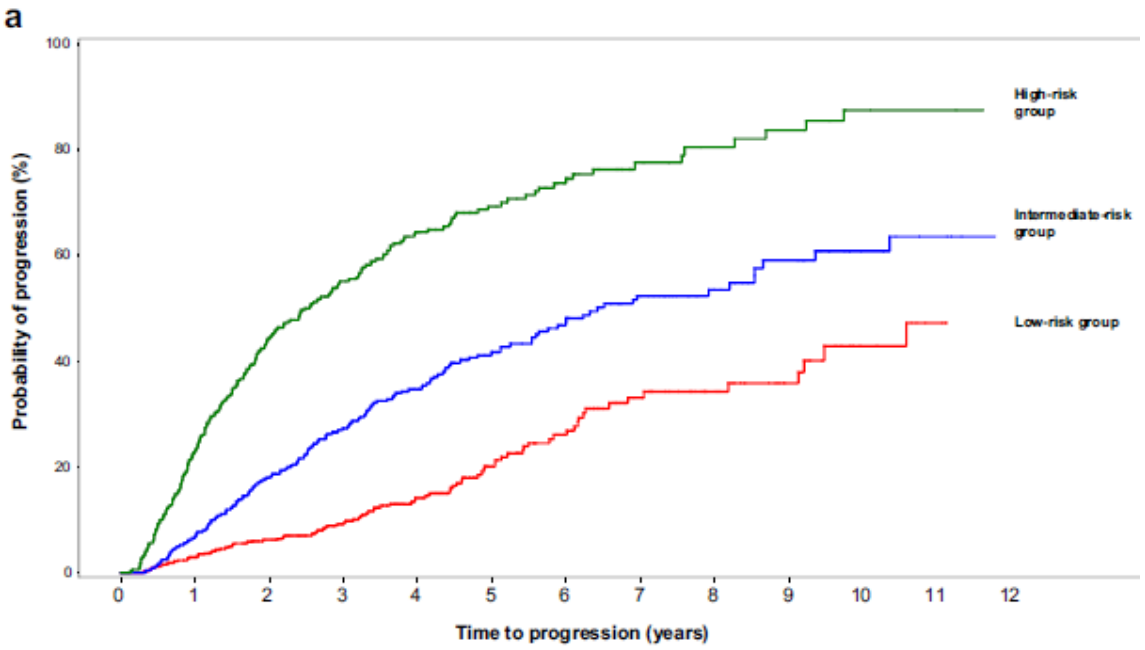
- Infiltración de médula ósea >20%
- Componente monoclonal >2 g/dL
- Radio de cadenas livianas libres (inv/no inv) >20
- FISH

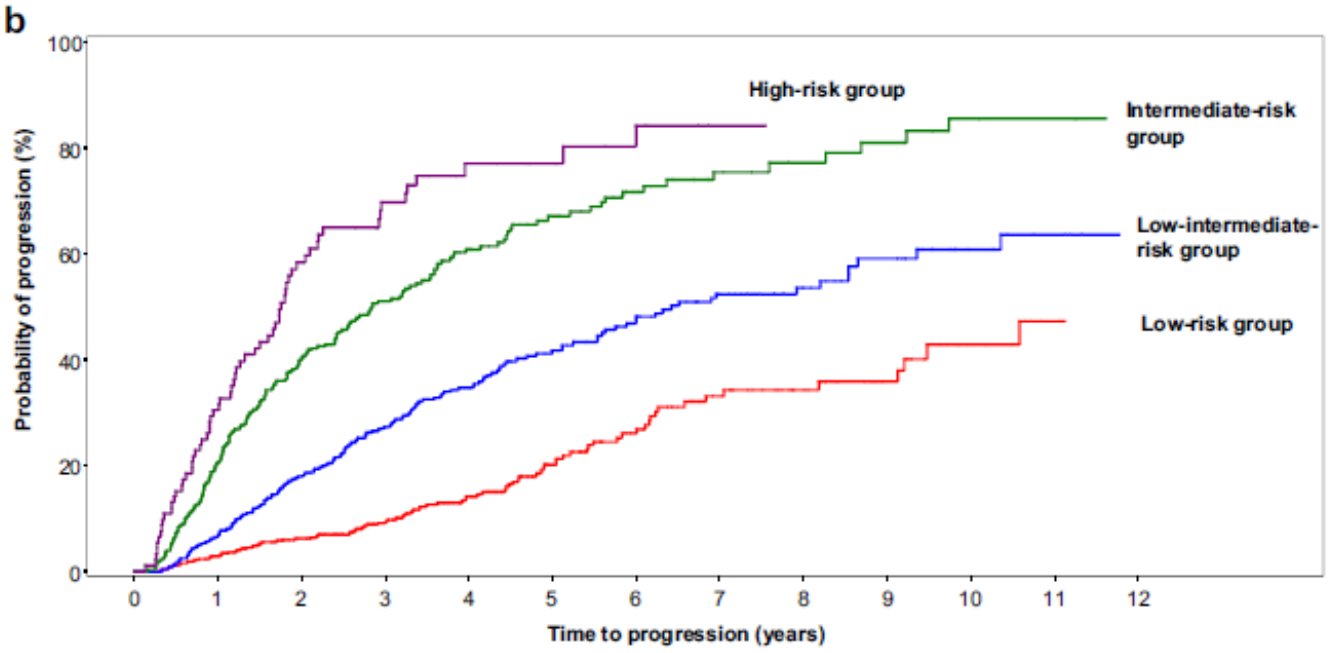
“MyeRISK”


Contents
Done
MyeRisk
SMM Risk Score Tool
FLC Ratio
M Protein
g/dL
BMP
%
FISH Abnormality
Years
1
2
3
4
5
%
Risk for progression at 2 yrs
CALCULATION
INFORMATION
SAVED

Bajo riesgo: ningún factor
Riesgo intermedio: 1 factor
Riesgo alto: 2 – 3 factores

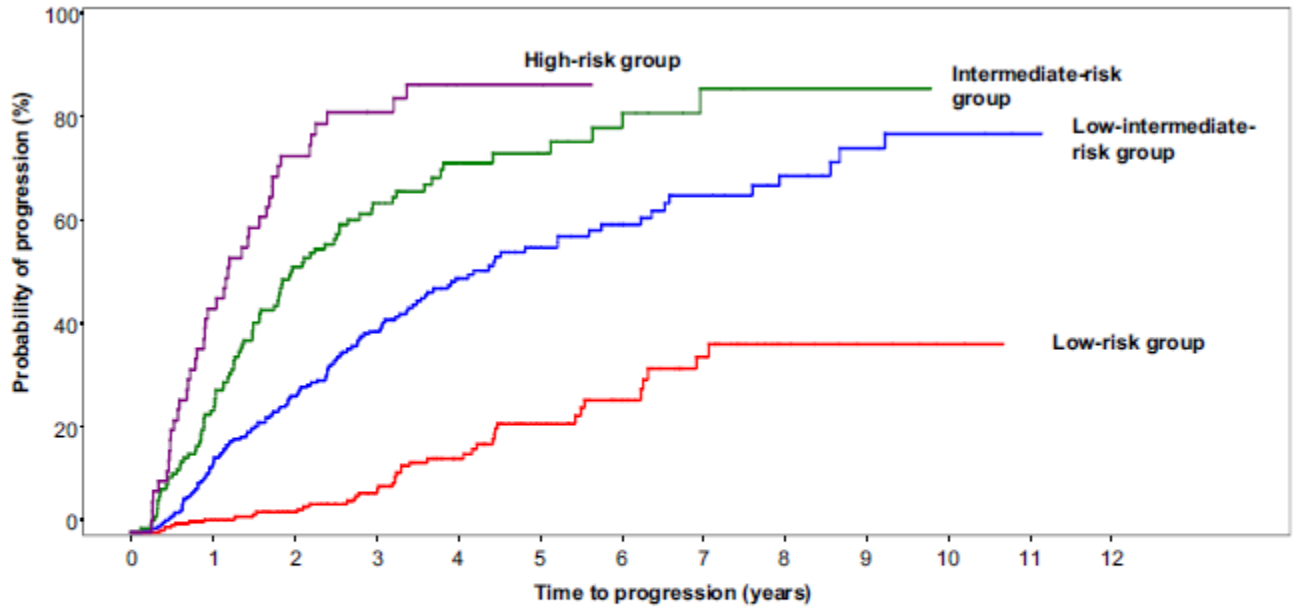
Bajo riesgo: ningún factor
Riesgo intermedio bajo: 1 factor
Riesgo intermedio alto: 2 factores
Riesgo alto: los 3 factores





Mateos MV, Blood Cancer Journal 2020

Usando el rango entero de valores de CP en MO, CCL en suero y pico monoclonal, crearon un score de riesgo: "20-2-20"



Risk Stratification groups	Total risk score	Hazard Ratio (95% CI)	Risk of progression (2 years)	# of patients
Low	0-4	Reference	3.8%	241 (35.0%)
Low-intermediate	5-8	7.56 (3.77 – 15.2)	26.2%	264 (38.3%)
Intermediate	9-12	17.3 (8.63 – 34.8)	51.1%	133 (19.3%)
High	>12	31.9 (15.4 – 66.3)	72.5%	51 (7.4%)

Mateos MV, Blood Cancer Journal 2020

SMM DE ALTO RIESGO: POR QUÉ TRATAR?

- Dos trials apoyan el tratamiento: QUIREDEX y E3A06
- 79 estudios registrados (sep/2021) en *clinicaltrials.gov*

Dos estrategias terapéuticas:

- **Prevenir** el desarrollo de la enfermedad: lenalidomida, Elo-Rd, daratumumab, isatuximab, KRd, Ird.
- **Curar** la enfermedad antes que se presente:
  - Estudio CESAR (grupo español): KRd + trasplante + KRd + lenalidomida x2 años
  - Estudio ASCENT (IMF): dara KRd con o sin trasplante

ENTONCES….

- **2014:** “NUEVOS EVENTOS DEFINIDORES DE MIELOMA” → pacientes considerados previamente MIELOMA SMOLDERING DE ULTRA ALTO RIESGO (> 80% de riesgo de progresión a 2 años) se redefinieron con mieloma con necesidad de tratamiento.

- **2020:** “SCORE 20-2-20” → pacientes con ≥50% DE RIESGO DE PROGRESAR A MIELOMA EN 2 AÑOS son el objetivo terapéutico en evaluación.

- **PRÓXIMO FOCO:**
  - MUTACIONES
  - ALTERACIONES EN EL MICROAMBIENTE TUMORAL, PARÁMETROS INMUNES

CONDUCTA CON PACIENTES DE ALTO RIESGO SEGÚN EL NUEVO SCORE

- Actualmente la conducta clínica frente a un mieloma smoldering sigue siendo la **OBSERVACIÓN CERCANA.**

- Es fundamental la **INCORPORACIÓN EN ENSAYOS CLÍNICOS** de estos pacientes. Objetivos:
  - DETENER LA PROGRESIÓN DE LA ENFERMEDAD?
  - CURAR AL MIELOMA ANTES DE SU DESARROLLO?

- **SEGUIMIENTO MÁS ESTRECHO** de los pacientes de alto riesgo para detectar a tiempo la necesidad de tratamiento.

MIELOMA MULTIPLE

Diagnostic site	Tool	Diagnosis	At response	At follow-up	At relapse
Blood	Advanced techniques: GEP, NGS	Optional	Not required	Not required	Not required
	Blood count and blood smear	Obligatory	Obligatory	Obligatory	Obligatory
	Serum electrophoresis and IF	Obligatory	Obligatory	Obligatory	Obligatory
	Serum free light chain	Recommended ***	Recommended ***	Recommended ***	Recommended ***
	Serum immunoglobulin levels	Obligatory	Obligatory	Obligatory	Obligatory
	Renal and liver function tests	Obligatory	Obligatory	Obligatory	Obligatory
	Calcium	Obligatory	Obligatory	Obligatory	Obligatory
	Lactate dehydrogenase	Obligatory	Obligatory	Obligatory	Obligatory
	Albumin, β2-microglobulin	Obligatory	Recommended	Recommended	Obligatory

- Hemograma completo
- Calcio
- Creatinina
- Hepatograma
- LDH
- β2 microglobulina
- Albúmina
- Proteinograma , inmunofijación
- Dosaje de inmunoglobulinas

Diagnostic site	Tool	Diagnosis	At response	At follow-up	At relapse
Urine	Urine sample to check for proteinuria and Bence-Jones proteins	Obligatory	Obligatory	Obligatory	Obligatory
	24 h urine collection	Recommended†	Recommended†	Recommended†	Recommended†

- Proteinuria (24 hs)
- Proteinograma
- Inmunofijación

Table 2. Recommendations on further examinations at diagnosis, for response assessment, during follow-up and at relapse.

Diagnostic site	Tool	Diagnosis	At response	At follow-up	At relapse
Bone marrow	BM cytology and biopsy to confirm plasmacytosis and monoclonality	Obligatory	Obligatory*	Not required	Obligatory**
	Flow cytometry	Recommended	Optional	Not required	Optional
	Cytogenetics	Obligatory	Not required	Not required	Optional
Blood	Advanced techniques: GEP, NGS	Optional	Not required	Not required	Not required
	Blood count and blood smear	Obligatory	Obligatory	Obligatory	Obligatory
	Serum electrophoresis and IF	Obligatory	Obligatory	Obligatory	Obligatory
	Serum free light chain	Recommended ***	Recommended ***	Recommended ***	Recommended ***
	Serum immunoglobulin levels	Obligatory	Obligatory	Obligatory	Obligatory
	Renal and liver function tests	Obligatory	Obligatory	Obligatory	Obligatory
	Calcium	Obligatory	Obligatory	Obligatory	Obligatory
	Lactate dehydrogenase	Obligatory	Obligatory	Obligatory	Obligatory
	Albumin, β2-microglobulin	Obligatory	Recommended	Recommended	Obligatory
Urine	Urine sample to check for proteinuria and Bence-Jones proteins	Obligatory	Obligatory	Obligatory	Obligatory
	24 h urine collection	Recommended†	Recommended†	Recommended†	Recommended†
Imaging	Low dose whole-body CT	Recommended††	Not required	When symptomatic	Recommended
	PET/CT	Optional	Optional†††	When symptomatic	Optional
	Whole-body MRI	Optional	Not required	When symptomatic	Optional

FISH con sorting de CP

BM: bone marrow; GEP: gene expression profiling; IF: immunofixation; NGS: next generation sequencing; CT: computed tomography; PET: positron emission tomography; MRI: magnetic resonance imaging; *Obligatory for patients in complete response. **Obligatory for patients with light chain escape, oligosecretory disease, *** SFLC monitoring is obligatory for patients with light-chain disease. †Obligatory in the case of proteinuria. ††Obligatory when radiographs do not show osteolytic lesions †††PET/CT is required for confirmation of minimal residual disease negativity.

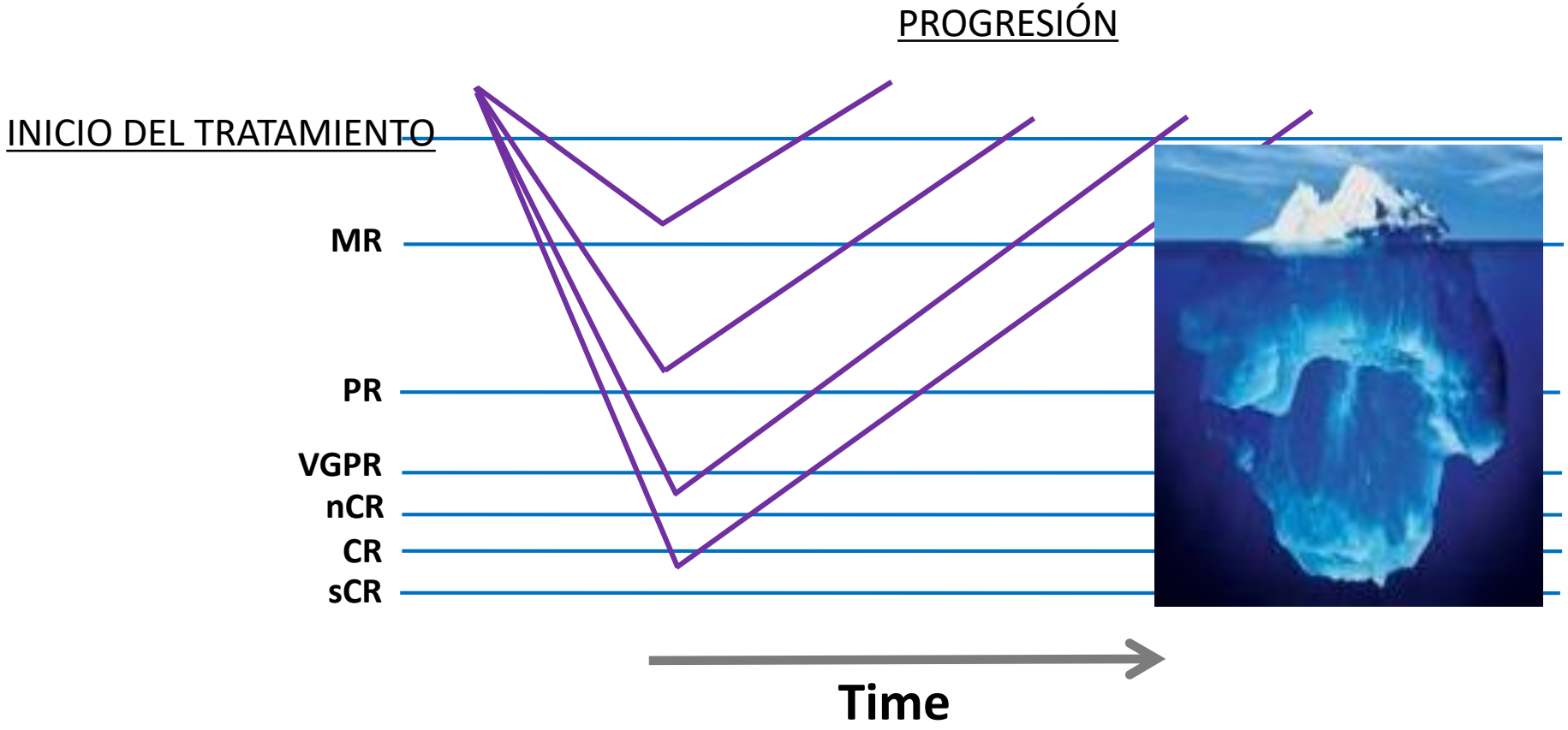
EMN recommendations on tools for the diagnosis and monitoring of MM: what to use and when. Caers, Haematologica 2018

TRATAMIENTO DEL MIELOMA

HISTORIA NATURAL DEL MIELOMA

MGUS=monoclonal gammopathy of undetermined significance.

EFECTOS DE LA PROFUNDIDAD DE LA RESPUESTA

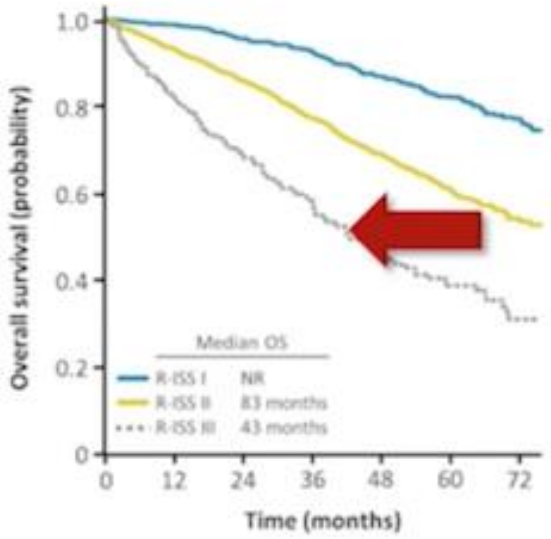


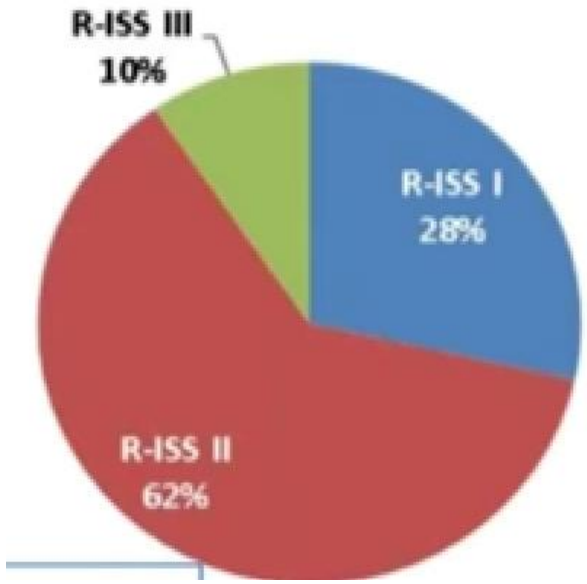
Profundidad de la respuesta en relación al tiempo al nuevo tratamiento

SOBREVIDA Y RIESGO CITOGENÉTICO EN MM: SCORE R-ISS

Prognostic factor	Criteria
ISS stage	
I	Serum β2-microglobulin <3.5 mg/L, serum albumin ≥3.5 g/dL
II	Not ISS stage I or III
III	Serum β2-microglobulin ≥5.5 mg/L
CA by iFISH	
High risk	Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)
Standard risk	No high-risk CA
LDH	
Normal	Serum LDH < ULN
High	Serum LDH > ULN
R-ISS stage	
I	ISS stage I and standard-risk CA by iFISH and normal LDH
II	Not R-ISS stage I or III
III	ISS stage III and either high-risk CA by iFISH or high LDH

OS stratified by R-ISS (n=3,060 evaluable patients*)





* Patients with available serum LDH, ISS stage, and CA by FISH data.
CA, chromosomal abnormalities; iFISH, interphase fluorescent *in situ* hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; R-ISS, revised International Staging System; ULN, upper limit of normal range.

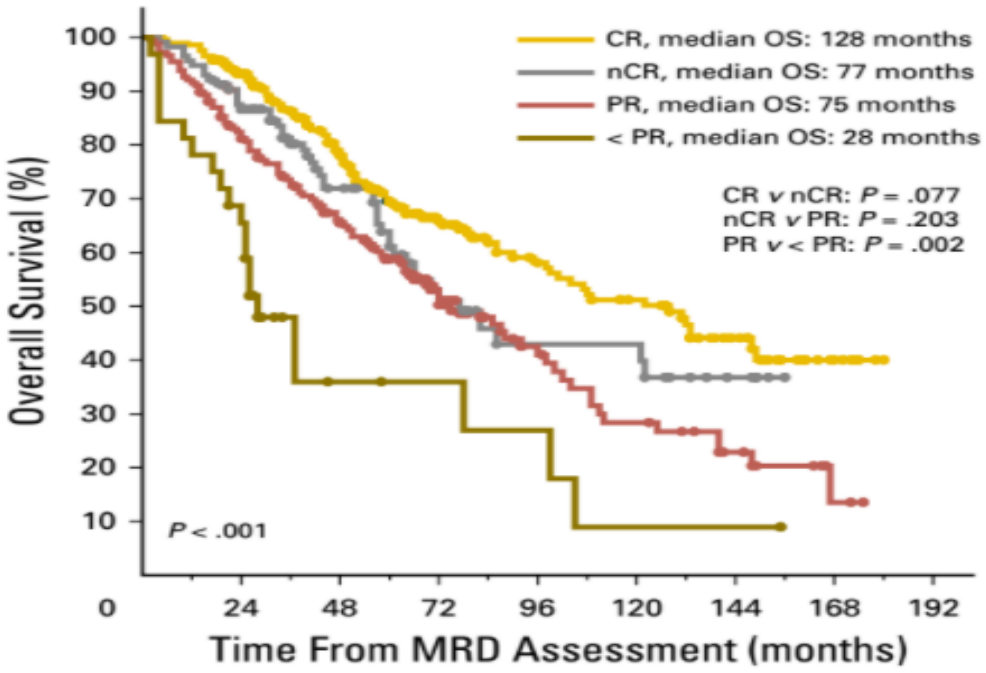
Palumbo A, *et al. J Clin Oncol* 2015; **33**:2863–2869.

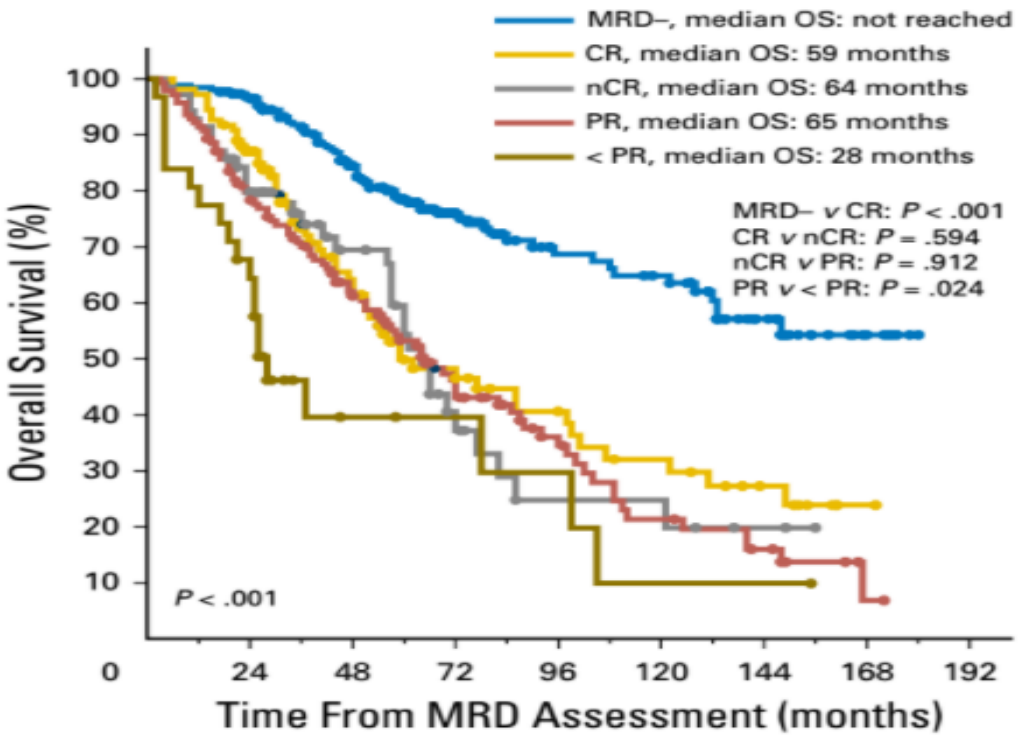
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Depth of Response in Multiple Myeloma: A Pooled Analysis of Three PETHEMA/GEM Clinical Trials

Juan-Jose Lahuerta, Bruno Paiva, Maria-Belen Vidriales, Lourdes Cordón, Maria-Teresa Cedena, Noemi Puig, Joaquin Martinez-Lopez, Laura Rosiñol, Norma C. Gutierrez, María-Luisa Martín-Ramos, Albert Oriol, Ana-Isabel Teruel, María-Asunción Echeveste, Raquel de Paz, Felipe de Arriba, Miguel T. Hernandez, Luis Palomera, Rafael Martinez, Alejandro Martin, Adrian Alegre, Javier De la Rubia, Alberto Orfao, María-Victoria Mateos, Joan Blade, and Jesus F. San-Miguel, on behalf of the GEM (Grupo Español de Mieloma)/PETHEMA (Programa para el Estudio de la Terapéutica en Hemopatías Malignas) Cooperative Study Group

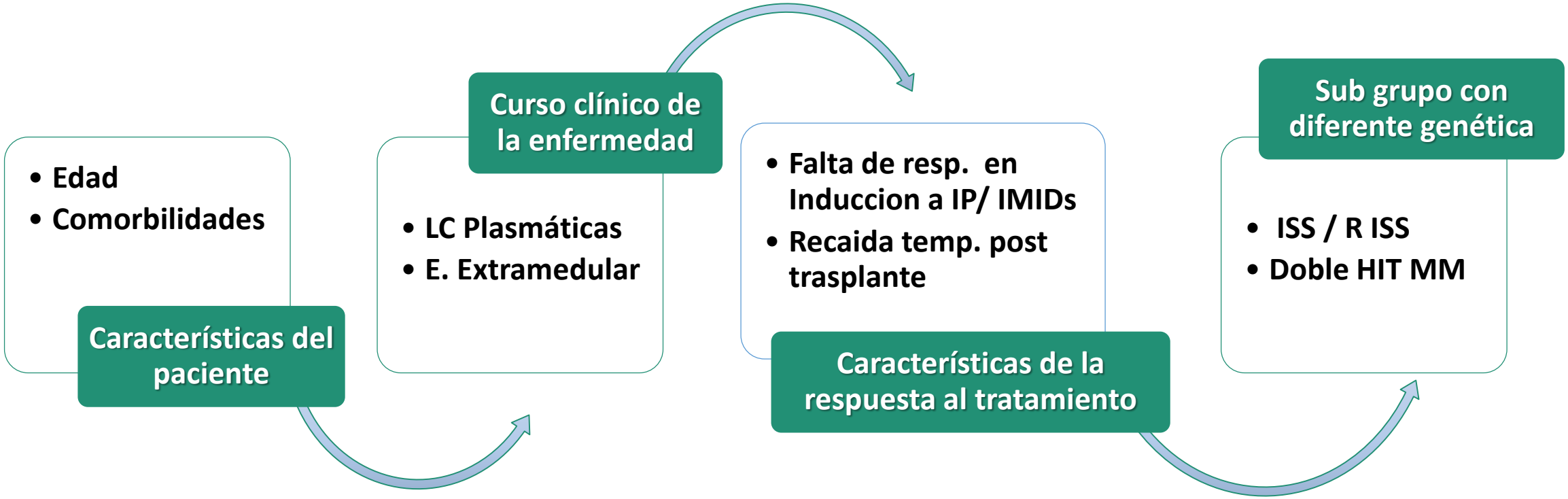
El valor real de la RC descansa en el status de EMR



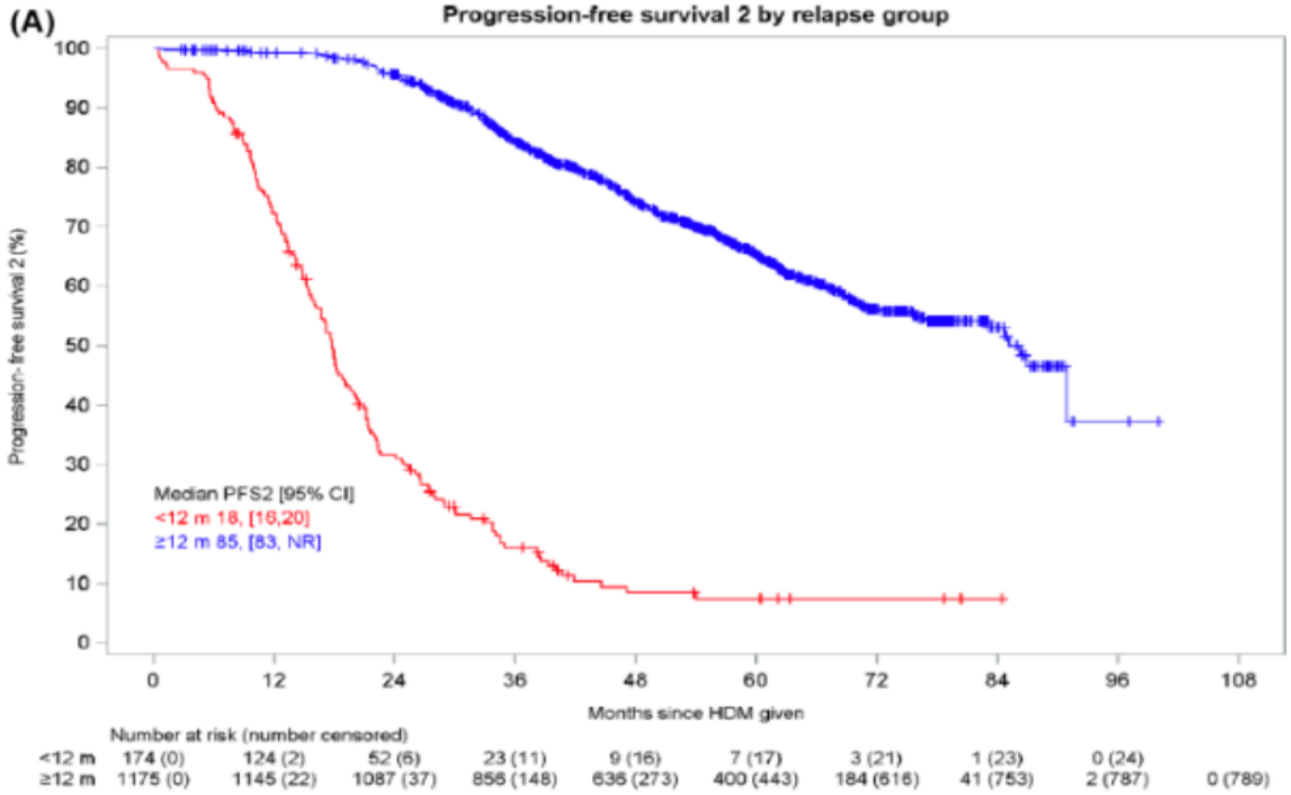


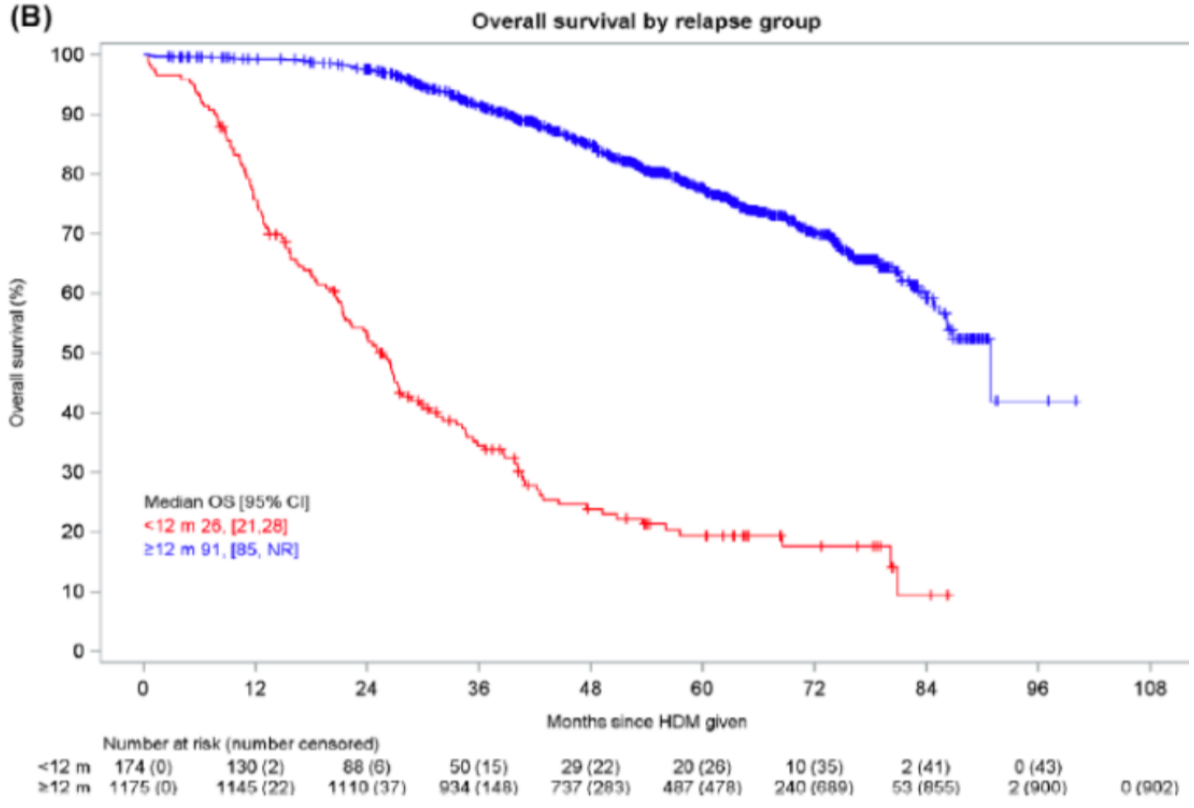
Lahuerta J. et al. J Clin Oncol 2017; 35

FACTORES QUE IDENTIFICAN PACIENTES DE ALTO RIESGO y PEOR EVOLUCION



POR EJEMPLO: RECAIDA TEMPRANA DESPUES DEL TRASPLANTE
Es un predictor de una menor supervivencia en la era de nuevos agentes





Bygrave C, et al. *Br J Haematol.* 2021;193(3):551-555.

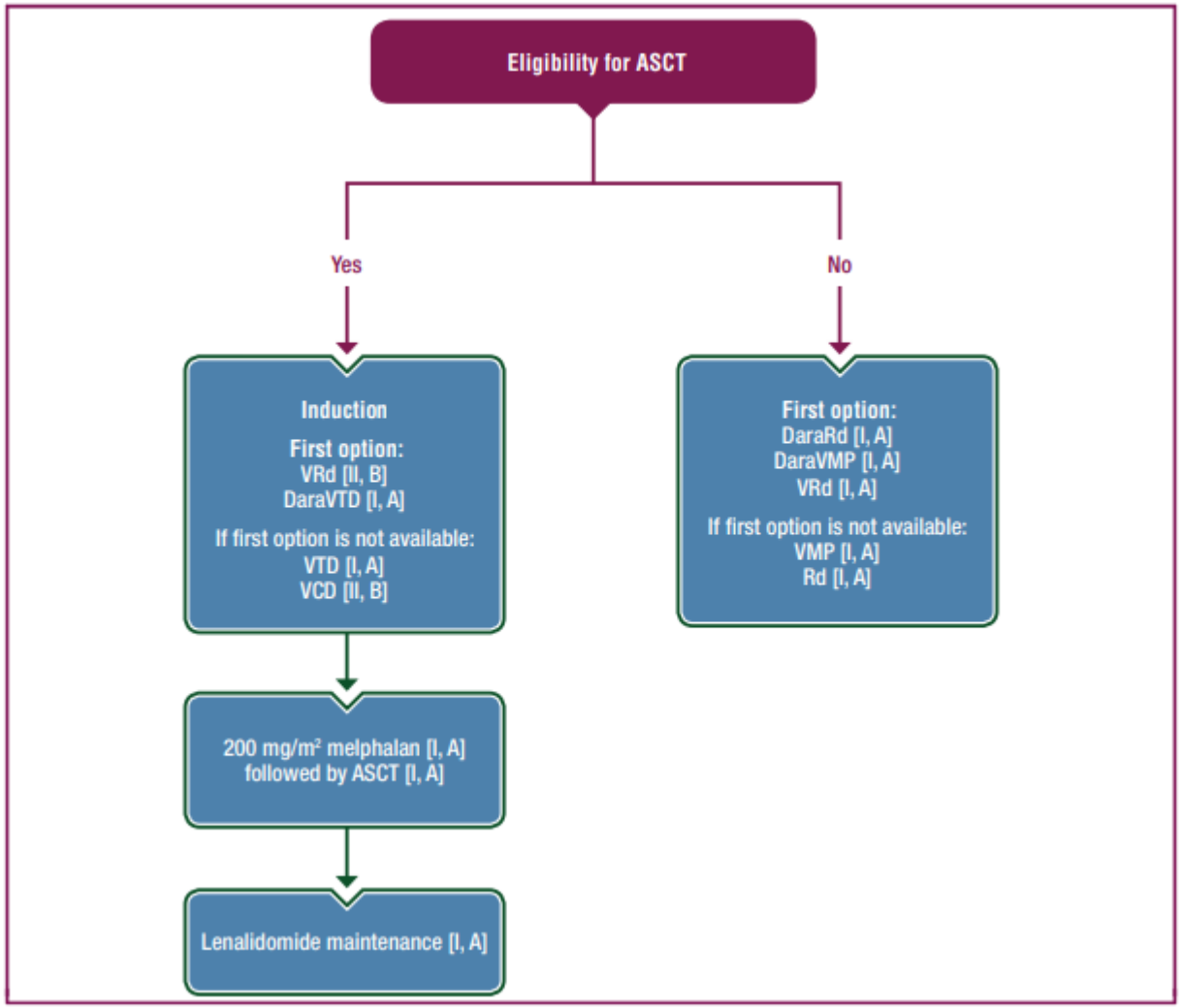
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

M. A. Dimopoulos[1], P. Moreau[2], E. Terpos[1], M. V. Mateos[3], S. Zweegman[4], G. Cook[5], M. Delforge[6], R. Hájek[7], F. Schjesvold[8,9], M. Cavo[10], H. Goldschmidt[11], T. Facon[12], H. Einsele[13], M. Boccadoro[14], J. San-Miguel[15], P. Sonneveld[16] & U. Mey[17], on behalf of the EHA Guidelines Committee* and ESMO Guidelines Committee*

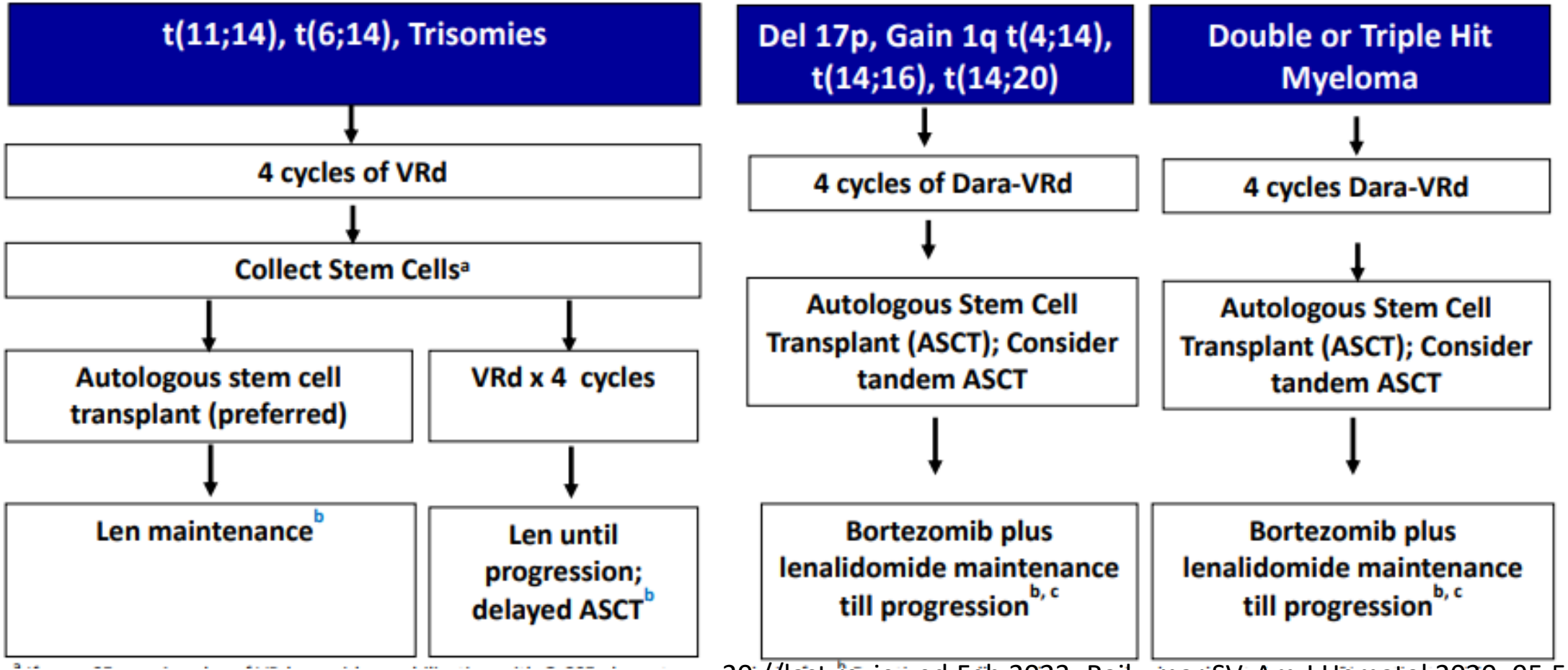


Dimopoulos, Annals of Oncology 2021

MAYO CLINIC

mSMART – Off-Study

Transplant Eligible



v20 //last reviewed Feb 2023; Rajkumar SV. Am J Hematol 2020; 95:548-567

MAYO CLINIC

mSMART – Off-Study

Transplant Ineligible

t(11;14), t(6;14), Trisomies

↓

DRd[a]

Or

VRd or ~9 cycles followed by Len maintenance[a]

t(4;14), t(14;16), t(14;20), Del 17p, Gain 1q

↓

DRd[a]

Or

VRd for ~9 cycles followed by bortezomib plus lenalidomide maintenance[a]

v20 //last reviewed Feb 2023; Rajkumar SV. Am J Hematol 2020; 95:548-567

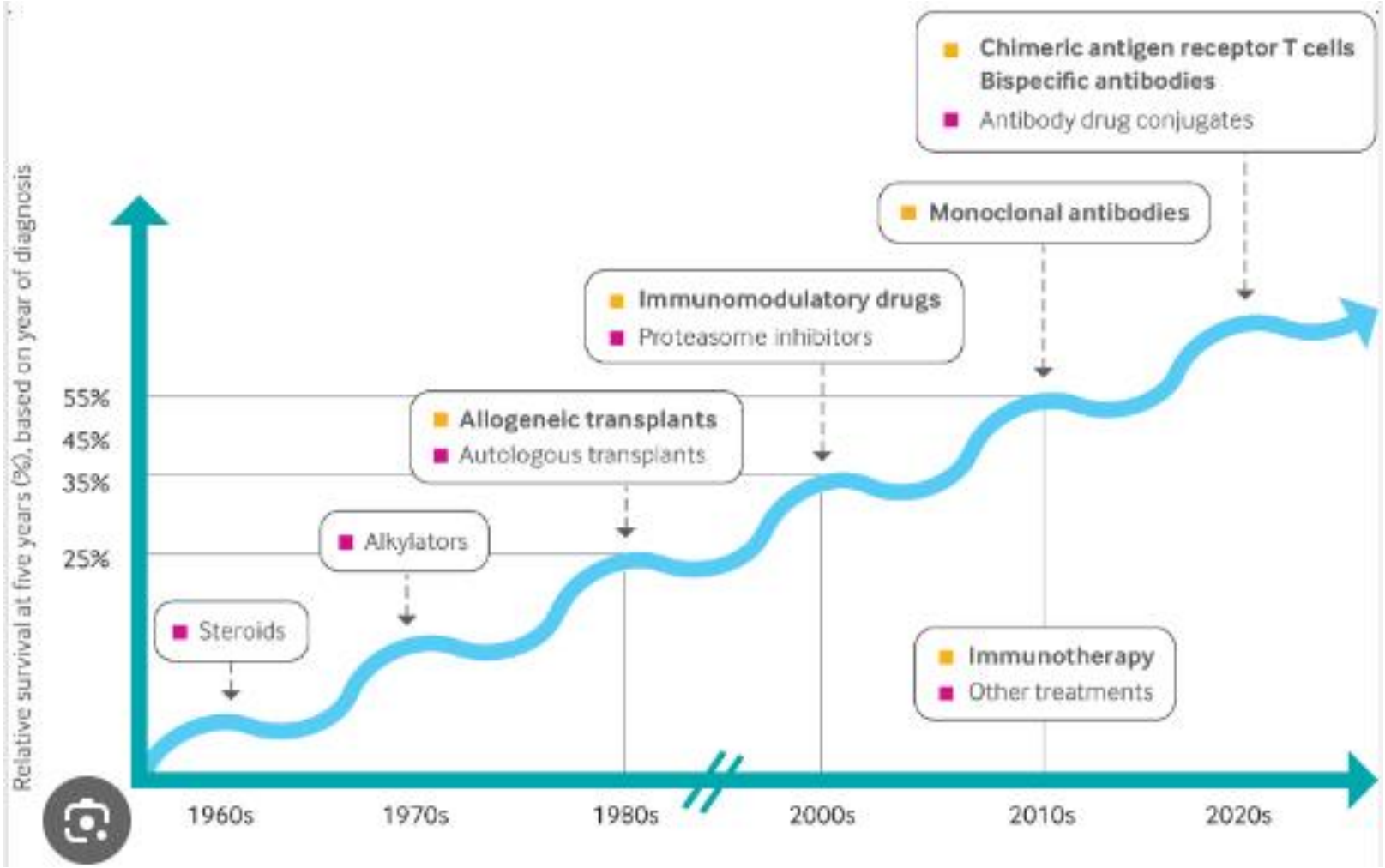
USO DE BIFOSFONATOS ENDOVENOSOS (pamidronato o zoledrónico)

- Mieloma con lesiones osteolíticas: los bisfosfonatos intravenosos deben ser administrados mensualmente.
- Osteopenia/osteoporosis sin lesiones líticas: Si osteopenia u osteoporosis no guarda proporción con la edad, tratar como relacionada al mieloma con bisfosfonatos intravenosos como en pacientes con mieloma con lesiones líticas. De lo contrario tratar con los bifosfonatos orales utilizados para la osteoporosis general.
- Los bifosfonatos EV NO se recomiendan para mieloma indolente.
- La osteoporosis NO es una condición marcadora de mieloma.
- Consulta con odontología previo al inicio de bifosfonatos. Estimular higiene oral (interrumpir al menos 1 mes antes de procedimientos odontológicos)
- Complicaciones: necrosis ósea aséptica de la mandíbula, fracturas subtrocanterianas, albuminuria (controlar proteinuria cada 6 meses)

Clinical Review » State of the Art Review

Emerging immunotherapies in multiple myeloma

BMJ 2020 ; 370 doi: https://doi.org/10.1136/bmj.m3176 (Published 21 September 2020)



Shah, BMJ 2020

QUÉ PASA CON LAS GAMMAPATÍAS MONOCLONALES IgM?

- Evolucionan eventualmente a linfoma linfoplasmocítico (Macroglobulinemia de Wäldesntrom)
- Hacer el análisis mutacional del $MYD88^{L265P}$ en médula ósea en todos los casos de MW (AS-PCR). De estar disponible también el del CXCR4

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 29 (Supplement 4): iv41–iv50, 2018
doi:10.1093/annonc/mdy146
Published online 5 July 2018; updated 08 December 2018

CLINICAL PRACTICE GUIDELINES

Waldenström's macroglobulinaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

E. Kastritis[1], V. Leblond[2], M. A. Dimopoulos[1], E. Kimby[3], P. Staber[4], M. J. Kersten[5,6], A. Tedeschi[7] & C. Buske[8], on behalf of the ESMO Guidelines Committee*

Kastritis, Annals of Oncology 2018

Table 1. Diagnostic work-up

Recommended

- History and physical examination
  - Include familial history for WM and other B cell lymphoproliferative disorders
- Review of systems (B symptoms[a], organomegaly, hyperviscosity symptoms, neuropathy, Raynaud's disease, rash, peripheral oedema, skin abnormalities, dyspnoea)
  - Include fundoscopic examination if IgM is high and hyperviscosity is suspected
- Laboratory studies:
  - Complete blood count
  - Complete metabolic panel
  - Serum Ig levels (IgA, IgG, IgM)
  - Serum and urine electrophoresis with immunofixation
  - Serum B2M level
  - Viral serology (HBV, HCV and HIV)
- BM aspiration and biopsy
  - IHC (required for diagnosis)
  - Flow cytometry (optional; consider if IHC not available)
  - Testing for *MYD88*^{L265P} gene mutation
- CT of the chest, abdomen and pelvis (if clinically indicated and in all patients being considered for therapy)

Optional (if clinically indicated)

- Cryoglobulins
- Cold agglutinin titre
- Serum viscosity
- Screening for acquired von Willebrand disease
- 24-h urine protein quantification
- Serum FLCs
- NTproBNP, cardiac troponins
- EMG, anti-MAG, anti-GM1 (consultation with neurologist)

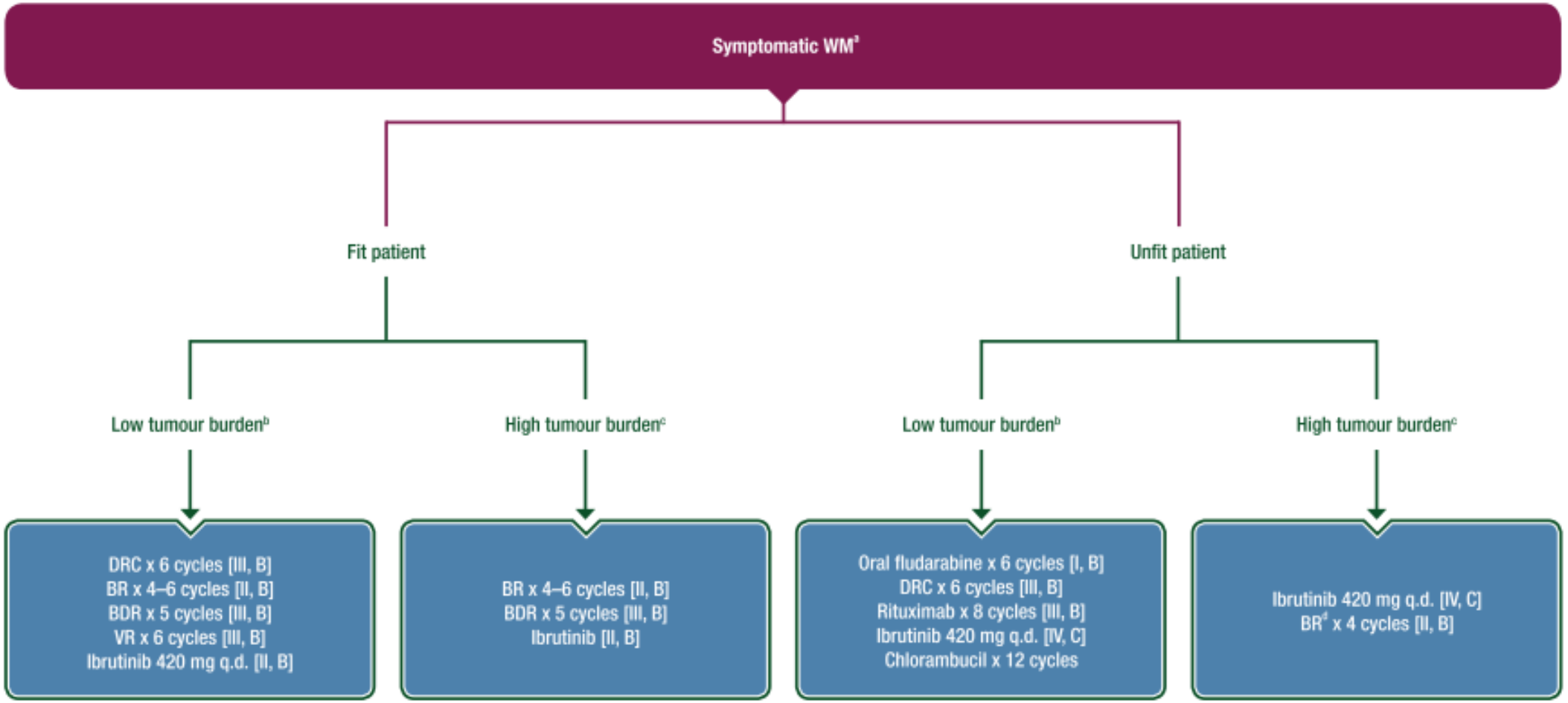


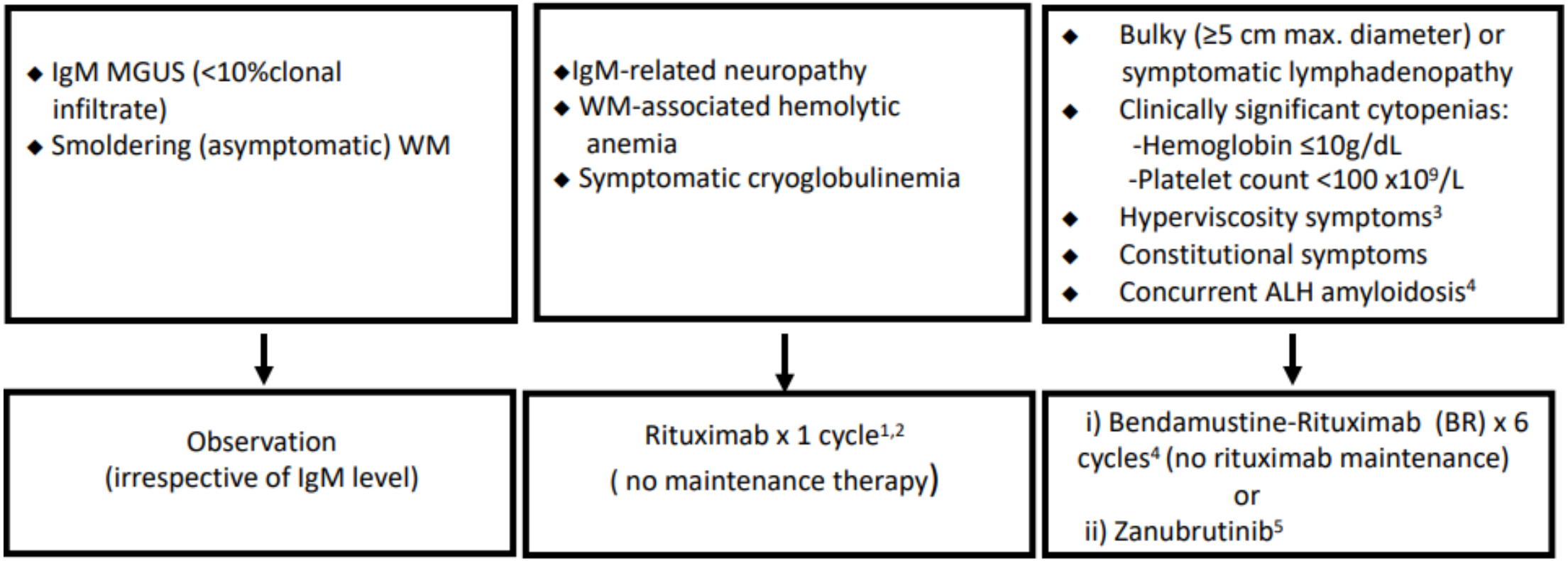
Figure 1. Treatment algorithm for patients with newly diagnosed WM.
[a]In case of hyperviscosity, plasmapheresis should be used concomitantly with systemic therapy [IV, A]. In case of high IgM levels and at risk for IgM-related complications, plasmapheresis may be used pre-emptively [IV, A].
[b]No major cytopaenias, hyperviscosity or organomegaly.
[c]Presence of any of the following: severe cytopaenias, hyperviscosity, organomegaly.
[d]BR for unfit patients may require dose reductions for bendamustine and use of G-CSF and/or antibacterial/antiviral prophylaxis.
BDR, bortezomib/rituximab/dexamethasone; BR, bendamustine/rituximab; DRC, rituximab/cyclophosphamide/dexamethasone; G-CSF, granulocyte colony-stimulating factor; IgM, immunoglobulin M; q.d., once a day; VR, bortezomib/rituximab; WM, Waldenström's macroglobulinaemia.

Volume 29 | Supplement 4 | October 2018
doi:1

Kastritis, Annals of Oncology 2018

MAYO CLINIC

Newly Diagnosed Waldenström Macroglobulinemia



[1]Initiate plasmapheresis if symptomatic hyperviscosity develops in the setting of IgM flare. Avoid rituximab monotherapy if baseline IgM level ≥ 4000 mg/dL and consider preemptive plasmapheresis prior to initiating rituximab to avert IgM flare associated hyperviscosity symptoms.